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DISINFORMATION ACTIVITIES CONNECTED WITH INFECTIOUS DISEASES- THE CASE OF COVID-19

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Abstract

The emergence and rapid spread of the SARS-CoV-2 virus and the COVID-19 disease have led to a global and massive surge in malicious information influence operations. Disinformation is the primary tool that influences operations. The deliberate dissemination of disinformation related to the pandemic is an example of how risks of a hybrid nature can be transferred into hybrid threats against targeted societies and states. The modus operandi at the national and international levels was quite similar. This is proven by the analysis we conducted in the first few weeks after the virus appeared in Croatia. In this paper, we will present several characteristic cases that can be used as a template for identifying upcoming threats. These examples indicate the existence of organized and targeted malicious activity against different target audiences intending to exploit (encourage, deepen) existing vulnerabilities and create new ones, incite emotions that cause social divisions, induce feelings of insecurity, defeatism, powerlessness, hopelessness, suspicion, disruption and collapse of democratic structures and processes, including health/medical infrastructure. These activities were aimed at controlling and weakening the defense capabilities of attacked societies and the states. Social networks, various online forums as well as mobile messaging applications have been identified as the most-used communication channels for disinformation dissemination.

Keywords: **COVID-19, disinformation, hybrid threats, social networks, internet**

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INTRODUCTION

The outbreak of an unknown disease that led to numerous deaths in the Chinese city of Wuhan in December 2019, and its rapid spread at the national and international levels, mobilized numerous experts in various fields of science. Several research activities were initiated to find answers to the key questions: (a) reliable and accurate identification of the agent that caused this disease, (b) finding a way to slow down and stop the spread of the disease, and (c) finding a sustainable, effective, and harmless medicine that is suitable for human use. Very quickly, it became clear that this crisis would be significantly different from many different crises that humanity has faced in the past.

From the very beginning of the COVID-19 outbreak, numerous instances of disinformation were recognized. Attempts were made to shift the responsibility for the outbreak of the disease to the "other side". This "other side" was/is a political (or any other) opponent who was accused of intentionally releasing the virus among the population. China accused the USA and the UK of deliberately creating a virus specifically adapted for the Chinese and Russian people to negatively affect the development and capabilities (political, security, defense, economic, demographic) of China and Russia (1). On the other hand, (dis)information also began to appear in Western media, emphasizing China's manipulation of viruses (2) in the research center in Wuhan (3) as well as the possibility that the virus reached the public

(either accidentally or intentionally) from that center (4). Societies and states affected by the virus (as well as those yet to be affected) found themselves in the situation of searching for new ways and methods of fighting not only the virus, but also various disinformation that were related to the virus's origin, spread, and possible health treatments. The faster spread of the virus and the negative consequences it caused were followed by the rapid dissemination of disinformation. At the same time, as will be discussed later, in at least one case, an attempt was made to use the pandemic situation for strong attacks (case of international terrorism) against the entire society to cause irreparable damage to human health.

About disinformation

Modern crises, and especially future ones, require citizens to actively participate in crisis management and the elimination of unwanted negative consequences. The dissemination of accurate and complete information to the population is a crucial condition for effective and sustainable strategic communication and crisis management. The population must make decisions based on accurate, verified, complete, and facts distributed in an undamaged integral form, and situated in the real-time and space context of events, persons, and processes. This indicates the need to address several challenging issues: (a) communication with the population is one of the key prerequisites for effective future strategic communication and crisis management; (b) determination of institutions responsible for communicating messages from certain domains of human life (not everyone can and must not communicate about everything); (c) clearly defining responsibilities in the communication system; (d) developing responsibility in the leading media as communication channels; (e) ensuring the responsibility of social networks and other providers/intermediaries of information in the digital space, as well as search engines for published/offered information. Of course, it is neither the goal nor the point to introduce any kind of censorship. However, responsibility for what is written, said, and published, especially for disinformation that can cause harm to people and communities if acted upon, needs to be defined, established, and penalized according to the legal framework.

What is disinformation, and what are the consequences for society and the state if such malicious information content remains in the corpus of public knowledge? By definition, disinformation is (5):

Deliberately distorted, incomplete, and partially or completely incorrect information, the client and the real author of which are hidden. Its goal is to induce the target audience, by influencing them on a cognitive level, to make decisions that harm them, i.e., short-term and/or long-term changes to their corpus of public information knowledge.

The European Commission defines disinformation similarly (6):

Disinformation is false, inaccurate, or misleading information designed, presented, and promoted for profit or intending to harm the public.

This definition has a structural error. It does not explicitly address the possibility that information, while true in its content and accurate, can simultaneously qualify as disinformation. Although one could argue that such a nuance is implied in the mention of "misleading" information, it is crucial to state explicitly: that there are numerous situations where information, accurate in its content, is situated in a completely different time and space context, attributed to incorrect or fictional author. This contextual manipulation renders the information incomplete, as it is taken out of its real context, and susceptible to a different interpretation, thereby leading the recipient to make incorrect decisions.

It is essential to emphasize two theorems about disinformation that indicate all the harmful effects of unrecognized disinformation remaining in the corpus of public knowledge (7):

1st Theorem: If the public (user) perceives disinformation as true, then disinformation is true in its consequences.

2nd Theorem: If the public (user) perceives objective information as untrue, then the objective information is untrue (false) in its consequences.

Disinformation and pandemic

As already emphasized, a pandemic is a crisis that affects the entire population, not just those who are directly infected. During the pandemic, the population expects the determination of competent and relevant bodies and institutions that are (and will be) responsible for strategic communication and crisis management. From these institutions and bodies, the population expects to

receive necessary information, instructions, and assurances about correct behavior, and measures that must be taken for their protection. Therefore, strategic and crisis communication, in the event of a pandemic, is a critical factor in dealing with such a deadly and widespread crisis. Insufficient, late, partial, or incorrectly formed or directed messages, with different content and instructions, can cause public concern, panic, wrong behavior, wrong decision-making, major economic disruptions, and even social upheavals. At the same time, they open the door for disinformation to appear and be influential. Effective and timely strategic and crisis communication by competent and relevant bodies and institutions can significantly contribute to the reduction of numerous social, health, security, and economic problems caused by the pandemic.

The pandemic crisis caused by the SARS-CoV-2 virus strongly influenced societies and states, forcing them to change and adapt previous patterns of crisis management to the new reality. Since the beginning of World War II, the world has not faced such a crisis. The appearance of this crisis was completely different from previous crises to which we had become accustomed, with more or less success in dealing with them. Previous crises, such as (a) terrorist attacks; (b) the emergence of radicalism, violence, and extremism; (c) natural disasters (earthquakes, floods, droughts); (d) attacks on critical infrastructure, technical incidents, and accidents; (e) energy and political crises, were mainly characterized by an intense and sharp effect, with a short duration in a specific geographical location. They did not hurt the entire population, and not everyone was affected by their negative consequences. The number and speed of the spread of disinformation related to those crises (causes and consequences) were negligible. Considering the nature of these crises, the security and defense systems focused their capabilities on the development of two groups of activities: crisis prevention and the development of capabilities for quick and complete recovery after a crisis event, i.e., post-crisis actions and resiliency.

The COVID-19 pandemic has become a multi-year, global, all-encompassing crisis (counting the time since the appearance of the disease, the duration of the pandemic, and the post-pandemic period in which many people have had to face the post-COVID consequences). The pandemic has hurt all domains of human existence, revealing that no one is immune to its negative consequences. It quickly spread throughout the world, thanks to globalization processes that enable fast travel and the movement of people and goods. Therefore, one of the essential differences compared to all previous crises is related to the population: the management of this crisis required the active participation of the population to achieve the general goals of protecting the population, slowing down, and finally stopping the spread of the deadly disease. Competent and relevant state and international organizations demanded that the population change the previous rules of behavior, adapt to the new reality, play an active role in crisis management with an emphasis on the implementation of protective measures and activities, and fight against the spread of numerous disinformation disseminated in the information environment. The overall effectiveness of the crisis management depended on the citizens' reactions to the messages that came from the competent institutions, as well as the disinformation.

This crisis has necessitated the definition of new paradigms in numerous human activities: (a) the integration of abilities and knowledge from different scientific fields (medical, social, technical, and other relevant scientific fields); (b) the establishment of a whole-of-society approach (homeland security concept) in the fight against emerging security challenges; (c) the development and implementation of effective strategic and crisis communication management; (d) strong and intensive cooperation at the national and international levels; (e) the equalization of protective measures and activities at the supranational level; (f) the fight against the negative influence of disinformation and the misuse of existing information and communication channels and technologies.

Institutions and organizations of the state and society were mostly unprepared for effective crisis management at the beginning of the pandemic. Crisis and strategic communication skills were at a low level. Disinformation appeared quite quickly in the first days and weeks after the beginning of the crisis. Regarding its causes and consequences, the crisis began to be interpreted by numerous people for whom the knowledge about the cause-and-effect relationship of the pandemic was beyond their horizon of knowledge and professional experience. This often led to negative consequences, such as increased confusion, vagueness of messages disseminated to the public, and different "medical" measures suggested as a "solution." The cacophony of messages (information overload or infodemic and poisoning the information environment with malicious disinformation or intoxication) has reduced the ability of society and the state to defend itself effectively and quickly against the negative consequences of disinformation.

Different countries have reacted differently to this kind of security challenges, especially in the first stages of the crisis, during the process of procurement and delivery of protective means and equipment, medical instrumentation, and devices, and later the procurement and distribution of medicines. The complexity and demanding nature of the challenges in dealing with a pandemic, as well as the sudden change in usual security practices and procedures, immediately open an area of activities for a malign attacker. A clear example is the very dangerous and intensive cyber-attack launched by Iran on Israel in April 2020 (8). Some states almost completely engaged their repressive apparatus in strengthening the resilience of the state and society. Israel, with an emphasis on agencies from the intelligence community (9, 10, 11), immediately began to use them in the fight against pandemic consequences at all levels. They were engaged in observing, recognizing, and monitoring trends of infection spreading, conducting surveillance of infected persons, as well as persons who were in various forms of isolation, procurement and ensuring the delivery, storage, and distribution of protective materials, medical equipment, and instrumentation, and later medicines. They were also more active in the fight against potential opponents who were trying to use the extraordinary situation for their interests, which were directed against the interests of Israel, including the fight against the negative influence of disinformation (10, 11, 12).

The USA had a slightly different position. The USA focused on identifying the cause, place, time, and manner of the virus's outbreak and its spread, combating the negative impact of disinformation, identifying its authors and the communication channels used for their spread, and analyzing the negative consequences on global geopolitical, strategic, security, and economic aspects (12). The German response to the crisis was very demanding. Namely, Germany, considering its decentralization of state repressive institutions, approached this problem quite differently (12).

Organizations such as the EU, UN, and NATO (13, 14, 15) have also begun to equalize practices in the fight against the pandemic. Special emphasis was placed on combating the negative consequences of disinformation: recognizing patterns, identifying possible authors and spreaders, and analyzing the use of various media communication channels (16), as well as truthfully informing the public and developing unified platforms to fulfill the identified goals.

Examples of disinformation in the Croatian media space

The Croatian information environment and the associated corpus of public knowledge were (and still are) systematically exposed to numerous instances of disinformation. Information attackers exploited the fact that (a) Slavic languages are relatively similar, (b) there are numerous connections between different people living in different countries, which accelerates and facilitates mutual communication and the spread of various disinformation, (c) there are numerous (especially online media) that are visited by members of different countries, as well as the fact that numerous media outlets are interestingly networked at the national and supranational level (1, 5, 16, 17, 18). The Hybrid Warfare Research Institute has been actively involved in countering disinformation activities even before the outbreak of the pandemic.

In the initial weeks of the rapid spread of the disease, the media environment in Croatia, especially social media and mobile communication applications, was flooded with numerous pieces of disinformation. This phenomenon in Croatia somewhat flew under the radar until the release of an audio recording in which an unknown woman conveys a disturbing message, referring to herself as a "reliable source close to the Prime Minister" (19, 20). Using a dramatic voice, she warned the audience and spread disinformation about the false behavior and actions of the Croatian government and state institutions in managing the pandemic. Soon, new disinformation appeared in public (5), claiming that "the virus dies/disappears at a temperature of 26-27° C and that, as the air temperature increases, the virus will disappear by itself"; "the need to perform exercises that people should do to independently determine whether they are infected with the coronavirus or not and what they should do, beyond the instructions of the competent health institutions, to help themselves", and the spread of defeatist claims such as "we are guinea pigs in the games of the powerful," "we are being tested for the virus without our consent, and they have a vaccine they won't give us," "this is how they are trying to save pension funds in all countries from collapse," and "this government should be replaced, even if it requires violence on the streets." Interestingly, messages with very similar, almost identical content entered the information environment of Croatia, Slovakia, Slovenia, Serbia, Bosnia and Herzegovina, Italy, Germany, and Austria, and even the English-speaking population in some other countries (Israel, and Belgium) in a very short time.

The first disinformation tends to be, as a rule, somewhat more benign in content and is not aimed at directly causing divisions and more serious problems. Each subsequent piece of disinformation contains more and more dangerous messages (considering the possible consequences for human health if they are accepted as true) and becomes increasingly difficult to identify undeniably as disinformation to the public. Many unrecognized instances of disinformation can additionally encourage some target audiences to express distrust and dissatisfaction against the institutions of the state, introducing divisions and inducing protests that could lead to the creation of a state of disorder and chaos, ultimately producing political upheavals by force. Their cumulative impact, if not recognized in time, can be very destructive to the stability of every society and state.

In addition to textual disinformation, numerous photo and video documents with manipulated content have appeared. They quickly became available to the general audience through dissemination on social networks and mobile communication applications. For example:

> Train photographed in September 2019 in Kansas, USA, with the inscription: COVID-19 (5)
>
> Photo taken in front of a hospital in Zagreb after the earthquake that struck the City of Zagreb (Croatia) on March 22, 2020, falsely attributed to being taken in front of a hospital in Italy (21).
>
> Photo of an anti-COVID-19 protester in Belgrade holding a banner with the written text: „The measures of the crisis headquarters are from Ustasha origin. We do not want a COVID concentration camp" (22).

AIM

This paper aims to (a) examine the hypothesis that disinformation activities distributed across various countries related to the SARS-CoV-2 virus are interconnected to some extent; (b) affirm that they appeared with the intent of maliciously influencing crisis and communication management; (c) establish a cause-and-effect relationship that can pinpoint the real authors and drivers of this disinformation; and (d) identify the intended malicious consequences sought to be achieved through its distribution.

MATERIALS AND METHODS

Considering the numerous disinformation instances that appeared during and after the pandemic, it was necessary to conduct a quantitative and qualitative analysis of selected (representative) information influence operations that entered the Croatian media space. Most of the disinformation examples were distributed in Slavic-speaking countries, despite the incompleteness and inaccuracy of the machine translations into individual languages, primarily from the Russian language.

For this analysis, we selected disinformation that appeared almost simultaneously in several different countries and societies with the same or very similar content. To obtain relevant samples, we contacted colleagues who are experts in intelligence studies, security and defense topics, and information-communication sciences from several countries gathered within the Zagreb Security Forum (Austria, Belgium, Bosnia and Herzegovina, Germany, Greece, Italy, Israel, Serbia, Slovakia, Slovenia). For our analysis, we chose a few examples of disinformation that were most frequently received (more than 75% of received messages and links) by members of our Institute via mobile communication applications (WhatsApp, Viber, Telegram) as information content or as a link to some social networks such as Facebook or Instagram in the last week of February and the first week of March 2020 (23). These examples, translated into English (where necessary), were sent to our colleagues to check their possible appearance and presence in their home countries. In their responses, they confirmed that disinformation, of the same or similar content appeared in their national information environment (they received it in the same way as we did). Our colleagues have confirmed that, during that time frame, this disinformation was among the most numerous they received. In almost all countries, the disinformation "cited" "doctors/experts" from Italy, China, and the USA (the choice of institutions' names was intentional to enhance the relevance of the disinformation content). Selected examples are listed and described on our website (23).

Those cases remind us of the deliberate spread of disinformation connected with the AIDS virus when the secret services of the former Soviet Union deliberately produced and disseminated much disinformation on a global level (24). Therefore, we applied intelligence analysis methodology (24) to extract truth from the received information contents in these cases.

RESULTS

In our study, we identified three main groups of disinformation spreaders:

Those who are aware of all the negative consequences of these activities and know that they are dealing with disinformation.

Those who were not aware of all the negative consequences but, working in good faith (bona fide), still spread them. In other words, they are not aware that they are spreading disinformation. In that case, by the definition of information-communication sciences, as well as intelligence studies, they were spreading misinformation.

Those who spread them as an example of good jokes, emphasizing the harmfulness of accepting disinformation over real and true knowledge.

In all three instances, the dissemination of disinformation resulted in negative and (un)intended malicious effects.

It has also been determined that disinformation of the same or very similar content is disseminated in the same timeframe across different languages in various countries, to achieve objectives that are more precisely outlined and described in the following chapter.

DISCUSSION

In today's strongly interconnected world, a large part of communication takes place on the Internet, especially in social networks and applications for mobile communication. During the pandemic crisis, there were numerous instances of disinformation in the public information environment. Their negative influence is still present, as seen in numerous conspiracy theories related to the origin and circulation of the SARS-CoV-2 virus, medical procedures, and the use of vaccines. By analyzing the content of the disinformation that entered the Croatian (as well as other states that were part of our research) information environment in the first weeks and months of the pandemic, we recognized their interconnection. We also noticed several different goals that they intended to achieve:

Decreasing trust, i.e. encouraging mistrust in the competent and relevant health and first responders' institutions and authorities that were designated to manage the crisis and communicate with the public.

Preventing an understanding of the complexity of the situation, encouraging frivolous and irresponsible individual and group behavior.

Reducing population trust in the government and state institutions on a general level encourages mistrust, insecurity, social instability, radicalization, and extremism of the opinions and behavior of individuals and groups, creating the necessary preconditions for organizing public protests and their transformation into violence.

Decreasing trust in the vaccine as preventive medicine and vaccination as a process. As a result, the population experiences a decline in vaccination rates, resulting in an elevated vulnerability to the disease, particularly among at-risk groups.

By increasing the number of infected and isolated people, the economic, social, defense, security, and overall capacities of both society and the state are significantly reduced. That situation triggers additional internal crisis and instability, especially when there is a lack of resources, primarily financial, to help the state navigate through the crisis period and prevent malign and unwanted processes and possible political changes caused by violent actions.

Reducing the effectiveness of the health system by overburdening it, leads to numerous other negative consequences as a logical consequence of the cascading of the crisis into other critical infrastructures of society and the state.

Overburdening the health system not only diminishes its effectiveness, but also leads to various adverse consequences. This is a logical outcome of the crisis cascading into other critical infrastructures within both society and the state.

One of the outcomes of this pandemic is the need for changes and adaptations in the analysis of existing and future hybrid risks and threats. Rare but highly impactful crises, often referred to as Low Probability - High Impact events, should not be overlooked. The repercussions of disinformation during crises significantly impact the psychological stability, health, and safety of individuals and communities. It can lead individuals to adopt radicalized views and interpretations of processes and events in society. In today's strongly interconnected world, consequences manifest simultaneously in vari-

ous areas. The disinformation instances observed in the analyzed examples were quite similar, and in some cases, identical.

In future pandemics (it's not a question of whether there will be one, but when, where it will start, how fast it will spread, and the consequences it will bring), disinformation will again play an important role defined by the information attacker. It will occur at both national and supranational levels. If we find ourselves unprepared for the emergence of disinformation, history may repeat itself, potentially with even more severe consequences compared to those caused by the COVID-19 pandemic.

This consideration is essential for future planning in the effective battle against various forms of disinformation, ensuring that, with the best intentions, no harmful effects are produced. The fight against disinformation and its harmful consequences cannot be confined to a single level. Sole reliance on professionals within specific scientific or professional domains is inadequate for effective resolution. Combating disinformation requires the active engagement of both society and the state, the homeland security concept, or a comprehensive whole-of-society approach.

The pandemic has highlighted that addressing pandemics is no longer the exclusive responsibility of medical science and professionals. Due to numerous disinformation policies and the dissemination of false information, the state and society's capability to confront these health challenges effectively and swiftly was compromised.

It is imperative to conduct detailed and in-depth analyses of all factors and processes that contributed to the declaration of a pandemic.

How can the unhindered flow of scientific information and knowledge be facilitated from totalitarian societies and countries in the event of an unknown, or known but incurable (or highly lethal) pathogen appearing, which has the potential to spread rapidly?

What measures and activities can democratic societies and states undertake to prevent the swift spread of deadly diseases without jeopardizing the fundamental tenets of democracy?

How should democratic societies and states, founded on the principles of the right and freedom of expression, deal with individuals who intentionally disseminate disinformation to undermine the defense capabilities of society, thereby increasing the vulnerability of the population and the mortality of infected persons?

These are serious issues that require an interdisciplinary approach at the societal level and involvement from organizations such as the UN, WHO, and EU.

Trivializing numerous instances of disinformation circulated during the pandemic can be an effective way to debunk them. The best example is the claim that "Covid-19 vaccines contain microchips, and that the population is forcibly and non-consensually chipped to be governed maliciously." Those who believe in such disinformation should be confronted with a series of questions: How many microchips would need to be inserted into a vial from which six vaccination doses are extracted to ensure at least one microchip per dose? What is the cost of these "invisible to the human eye" microchips, and what is the price of a bottle containing all these microchips? What is the cumulative cost of all the vials? And who can produce such a vast quantity of microchips in such a short time?

There are numerous examples of counter-disinformation activities, often disseminated on social networks and other media:

> Widely circulated "college liberal meme" conveys the message: "Takes LSD from strangers in a concert parking lot but won't take vaccines because she doesn't trust the source" (26).

> Visual representation of the data-information-knowledge-insight-wisdom hierarchy with a supplemented conspiracy theory (27).

> Message: People who think vaccination changes their DNA, should consider it as an opportunity" (28).

Understanding, recognizing, and leveraging the experiences gained during the COVID-19 pandemic are crucial for generating better and more effective responses to similar situations in the future. High-quality analyses and studies authored by experts across various domains and at both national and supranational levels serve as excellent educational resources. Every crisis is simultaneously an opportunity, especially for learning from mistakes—a process known as Lessons Identified – Lessons Learned (LI-LL). The learning process, particularly from identified errors, should

be highly motivating. To effectively address anticipated risks and threats, science must consistently stay ahead, distinguishing between risk as the possibility of an unwanted event or process with harmful consequences, and threat as the realization or transformation of the risk into reality. In the face of unpreparedness for unexpected threats, the capabilities of the entire society need to be swiftly reorganized. Learning processes should transcend political or geographical divisions, occurring on a supranational and global level, especially when dealing with global threats. A unified approach in applying agreed-upon measures to combat new global threats is essential. In this context, efforts should focus on educating specially trained multidisciplinary crisis management experts who, when the need arises, should be capable of integrating the defense capabilities of society and the state in a relevant, reliable, safe, and credible manner, fostering international cooperation.

Given that facing such challenges requires active participation from the entire population, a special role should be dedicated to the distribution of truthful and accurate information to the public. Simultaneously, there should be efforts to combat disinformation using strategic communication abilities. Another crucial group to be educated for crisis management and action in such situations is political decision-makers. There will be instances where decisions proposed by competent experts may not be accepted or may be implemented in a modified content and context due to political considerations regarding potential negative impacts on the decision maker's political rating. Decision-makers must possess the strength and courage to make decisions that might be temporarily unpopular, but benefit the entire society in the mid-and long-term, especially in crises like the one experienced. These challenging decisions distinguish between a mere politician and a true statesman.

CONCLUSION

In the pursuit of strengthening all capacities within society and the state to combat modern security challenges, including the early detection of disinformation, enhancing social resilience to its harmful influence, as well as identifying the authors and distributors of disinformation, various activities need to be undertaken, such as:

Supporting the efforts of public authorities and optimizing communication resources with local, regional, and national public health partners and institutions.

Disseminating pertinent pandemic information (public health information) to educate the public and vulnerable non-health sectors.

Mitigating social and economic disruptions.

As a primary objective, both during and after the pandemic outbreak, sustaining and enhancing public trust in the work of health authorities.

Proactively, promptly, and comprehensively addressing the adverse impacts of disinformation with the help of all relevant bodies, institutions, organizations, and companies from the private, public, state, media, civil and academic sectors.

The examination of contemporary crises and conflicts encountered in recent decades highlights a distinct characteristic: the integration, creation, and simultaneous management of multiple crises. A comprehensive and proactive approach to addressing modern security challenges is the sole assurance of fostering society's resilience to these challenges. This is exemplified by the crisis caused by the SARS-CoV-2 virus.

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S A Ž E T A K

DEZINFORMACIJSKE AKTIVNOSTI POVEZANE SA ZARAZNIM BOLESTIMA – SLUČAJ COVID-19

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Pojava i brzo širenje virusa SARS-CoV-2, uzročnika bolesti COVID-19, dovela je do globalne i masovne pojave brojnih i različitih, ali ipak sličnih zlonamjernih informacijskih operacija utjecaja. Glavno sredstvo u provođenju tih operacija utjecaja su protuobavijesti, plasirane na nacionalnoj i međunarodnoj razini. Namjerno širenje protuobavijesti povezanih s pandemijom ima sva obilježja pretvaranja rizika hibridne prirode u hibridne prijetnje u odnosu na napadnuta društva i države. Modus operandi na nacionalnoj i međunarodnoj razini bio je prilično sličan. To dokazuju i analize koje smo napravili u prvih nekoliko tjedana nakon pojave virusa. U ovom radu prikazat ćemo nekoliko karakterističnih slučajeva koji se u budućnosti mogu iskoristiti kao obrazac za prepoznavanje nadolazećih prijetnji. Navedeni primjeri ukazuju na organizirano i usmjereno zlonamjerno djelovanje protiv različitih ciljanih publika s ciljem iskorištavanja (poticanja, produbljivanja) postojećih te stvaranja novih ranjivosti, poticanja emocija koje uzrokuju društvene podjele, izazivanja osjećaja nesigurnosti, defetizma, nemoći, beznađa, sumnjičavosti, poremećenosti i kolapsa demokratskih struktura i procesa, uključujući zdravstvenu infrastrukturu. Ove su aktivnosti bile usmjerene na slabljenje obrambenih sposobnosti te pokušaj kontrole funkcioniranja obrambenog sustava društva i države. Društvene mreže, različiti (osobito internetski) forumi kao i mobilne aplikacije za razmjenu poruka identificirane su kao mediji koji se najčešće koriste za širenje protuobavijesti.

Ključne riječi: COVID-19, protuobavijesti, hibridne prijetnje, društvene mreže, internet

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WHAT THE DEBATE ON THE ORIGIN OF COVID-19 HAS TOLD US ABOUT LABORATORY SAFETY AND SECURITY*

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Abstract

The world has witnessed the most devastating pandemic facing humankind in more than a century. A critical question remains as to the origin of the virus responsible for this tragedy. Two theories have been put forward; that the virus spilled over from wild animals and infected humans who then spread the new virus to others, or that the virus somehow escaped a research laboratory. Both theories are plausible. While there is no direct evidence to suggest that the virus originated from a laboratory, the theory does offer an opportunity to review safety and security protocols that are designed to keep biocontainment facilities and the staff that work within them safe and secure. Advances in science and technology are greatly outpacing our ability to establish policies to mitigate risks in life science research and solutions will require international consensus building, sustained commitment, and effective collaborations.

Key Words: COVID-19, SARS-CoV-2, Laboratory Biosafety, Biosecurity, Pandemic origin

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INTRODUCTION

We have all witnessed the most devastating pandemic to face humankind in more than a century. As the world begins to transition from the global pandemic of COVID-19 disease caused by the SARS-CoV-2 virus, a pathogen new to science, we are now faced with learning how to manage this still very dangerous virus as an endemic threat, one that will likely be with us for many years to come. At the same time, we must prepare to recognize and respond to future threats as new infectious diseases arise. While some countries had made limited preparations for a possible pandemic, thought likely to be caused by the influenza virus, no country was prepared to face the massive suffering and loss of life caused by this new virus, one that none of us had seen previously and one to which we were all susceptible. As a result, about 7 million people have died, and probably many, many more that were not officially counted. Today, the vast majority of us have been infected and/or been vaccinated and some are still suffering from associated lingering illnesses that are yet to be fully understood.

METHODS

The pandemic was first recognized in Wuhan, China in late 2019. The source of the SARS-CoV-2 virus remains unknown; however, two theories regarding its origin have been put forward. These include that the virus spilled over from wild animals and infected humans who then spread the new virus to others. This may have occurred in one or more live animal markets that were in operation in Wuhan before the start of the pandemic. Early human cases of COVID-19 clustered

near the Huanan Seafood Market in Wuhan where the market sold live animals, including those known to be susceptible to SARS-like coronaviruses such as raccoon dogs, palm civets, and others. Environmental sampling after the start of the pandemic found specimens positive for the SARS-CoV-2 virus and the live virus was isolated from some samples (1, 2). However, it could not be determined with certainty if the virus detected was from wild animals or reflected infection among humans entering the market as the pandemic began. Some specimens collected at the market had genomic signatures of both SARS CoV-2 virus and animals sold there (3, 4). The spillover of a naturally occurring coronavirus from wild animals to humans is generally accepted as the way the original SARS coronavirus emerged in late 2002 and is thought by many experts as the likely route of introduction of the new virus into humans (5, 6).

The second theory is that the virus may have emerged from a laboratory accident, perhaps involving studies of naturally occurring bat-associated coronaviruses or created in the lab by recombining elements from existing viruses or manipulating sequences. Bat-associated coronaviruses were the likely source of the original SARS virus and another newly emerged coronavirus that causes Middle East Respiratory Syndrome (MERS). Viruses sharing significant genetic similarity to the SARS-CoV-2 virus were found among field-collected specimens obtained from wild-caught bats in southern China (7). Some of this work was done at the Wuhan Institute of Virology and perhaps elsewhere in China. As more information became available, the theory that the virus may have been created by molecular manipulation of an existing virus or created *de novo* has generally been discounted by most molecular biologists; however, the theory highlights an emerging challenge as technological advances make such studies increasingly feasible.

RESULTS

Both the natural spillover and the lab-associated theories are plausible; however, there is currently not sufficient evidence from inside China to draw firm conclusions on the origin of the pandemic (8). Nonetheless, there are several lessons to be considered that could reduce the risk of future pandemics. The focus of discussion here will be on those aspects of laboratory biosafety, biosecurity, and operations that if implemented might lessen the risk of future pandemics.

DISCUSSION

The first question is, "How might the activities of a virus research laboratory be associated with the introduction of a new virus into the community?" Bat-associated coronaviruses are known to exist in free-living bat colonies in China and field teams from the Wuhan Institute of Virology and perhaps other laboratories actively captured bats in southern China and obtained samples from them to look for bat-associated coronaviruses in the laboratory. Infection risks for humans involved in field studies are present from airborne droplets that might be inhaled while inside bat caves and field technicians may have inhaled infectious viruses while collecting bats and become infected. Bat guano is also potentially infectious and could have been a source of human infection. Humans may have been bitten or scratched by bats as they were being captured or handled, or as blood and other samples were obtained. Potentially infectious specimens may have leaked or spilled while being packed or in shipment, potentially leading to human infection as the field-collected specimens were transferred to the laboratory. A small cluster of cases of a disease some speculated was due to a bat-associated coronavirus infection occurred several years before the pandemic among persons working in or near a cave where bats were present, but the cause of these infections was never identified. Thus, a naturally occurring virus similar or identical to the SARS-CoV-2 virus may have infected a human while working near bat colonies, collecting field samples from bats, or while specimens were being transported to the laboratory. Such an infected person might then travel to Wuhan where they could have infected others in the laboratory or the community. Importantly, there is no evidence to suggest that any of these possibilities occurred.

Bat-associated coronaviruses very similar to the SARS-CoV-2 virus were studied at the Wuhan Institute of Virology, at the regional China Centers for Disease Control in Wuhan, and perhaps in other laboratories. Details of the exact work being undertaken in laboratories working with bat-associated coronaviruses are not well known; however, it is known that bat-associated coronaviruses are difficult to grow in cultures. Potentially risky research may have taken place to modify the virus to make it easier to grow and study in the laboratory; however, it is not clear that such risky research was ever actually attempted.

If the SARS-CoV-2 virus or a close relative was in a laboratory in Wuhan, a scientist or technician might

have infected themselves or others while trying to grow the virus from samples collected from bats or from a strain that was modified to allow it to more easily infect mammalian cells. Perhaps a laboratory accident occurred such as a needle stick, exposure to infectious aerosol following a spill, or other incidents that could lead to symptomatic or asymptomatic infections of staff. An equipment or system failure might have led to the release of infectious virus into the laboratory or the local community, or infectious waste may have not been fully inactivated, leading to the release of infectious virus into the environment. The infectious virus might have been stolen or intentionally released by a disgruntled employee or bad actor, potentially exposing an individual or the entire community. Importantly, there is no evidence to suggest that the SARS-CoV-2 virus was intentionally created or released to cause the pandemic, or indeed that any of these potential accidents even occurred. Nonetheless, several possible events may have happened during routine laboratory investigations of bat-associated coronaviruses that could have led to human infections or release into the surrounding community.

A systematic review of laboratory operations and records might shed light on possible ways that a SARS-CoV-2-like virus might have escaped laboratory containment. Questions that the laboratory director or others might ask while investigating the possible origin of the virus from a research laboratory are listed below, along with comments on the type of information or records that could be reviewed to help determine areas of possible concern.

Questions about laboratory personnel

- Were staff appropriately trained in biosafety and biosecurity precautions and procedures?

  To do this, one might examine training records for each person working in the laboratory.

- Were lab workers or support staff sick with an illness that could be COVID-19?

  A medical surveillance program could provide a record of acute illnesses among staff, and a serum bank in which regularly collected samples were stored could provide critically important specimens to allow serological testing that could document infection at a particular time.

- Was there a laboratory accident?

  A program to document and record potential breaks in containment, needle sticks, spills, or other possible staff exposures could provide important information.

- Was appropriate PPE available and used correctly by staff?

  A record of PPE supplies and use could provide important information to assure that PPE was present and training records could suggest that they were likely appropriately used. Aerosols are not the only means of becoming infected. In addition to needle sticks, these viruses are prone to infection by mucosal contamination. Contaminated hands rubbed into the eyes or nose can lead to infections. Wearing masks or powered air-purifying respirators (PAPRs) inhibits this. What was the practice in the labs?

- Was there a disgruntled employee associated with the laboratory who may have had access to infectious material that could be misused?

  Personnel records could provide important information to help identify individuals for special consideration.

Questions about laboratory biocontainment and security

- Was there evidence of theft of infectious material?

  A review of physical security for the laboratory and records of controlled access to infectious material could provide important information to determine if a virus sample was lost or stolen.

- What level of biocontainment was being used when potentially infectious specimens were being handled?

  A review of research protocols could show where work with SARS-CoV-2-like viruses was done, by whom, and what biocontainment precautions were in place.

- Were laboratory containment systems functioning correctly?

  Biosafety cabinets are the first line of defense for an individual handling potentially infectious material. A record of annual inspections and certification of

filters and air flow could document that these were in good working order.

Air handling and filtration systems ensure that any aerosolized infectious material is captured through filtration and removed before the air exits the facility. Inspections and maintenance records could provide evidence that these systems were functioning appropriately.

Laboratory equipment and instrumentation, including centrifuges and other mechanical devices that might be a source of potentially infectious aerosols, could serve as a source of infections. Having documentation of staff training on the standard operating procedures for the safe use of such equipment, a record of individuals using each piece of equipment, and a review of scheduled maintenance and servicing records could reduce the risk of accidents and potential release of infectious material.

Autoclaves and other equipment to inactivate infectious material. Documentation of staff training on the proper use of autoclaves and records of use, including a written record that documents that critical temperatures were reached to fully inactivate infectious material during each run would confirm that waste material was fully inactivated before leaving biocontainment.

A systematic approach allowing for careful examination and formal records of inspections, including specific examination of the many safeguards in place for the entire waste stream operations, records of maintenance of air handling systems, documentation of inspection and replacement as needed of filters and others would ensure that infectious material never leaves biocontainment.

Global surveillance of infectious diseases

Regardless of the controversy surrounding the origin of the SARS-CoV-2 virus, two major agendas should be addressed going forward (9). First, governments must improve their intelligence about infectious disease threats occurring both in their own country and in coordination with others around the world. Such situational awareness is critical for rapid recognition and coordinated, effective response to outbreaks before they become international tragedies. Heretofore we have relied on national governments to provide timely and complete reporting. Although there was early reporting and sharing of sequence information, subsequent sequestration and suppression of information seemed to replace early openness. Under these circumstances, the system failed decisively and it is clear that we need an alternative. The need for transnational biomedical surveillance, with open communications, clarity, and implementation by strong national systems is essential. The pandemic has spotlighted the need for better surveillance and situational awareness about emerging infectious diseases. The One Health approach that recognizes the interconnection between human and animal health and the interface with environmental conditions has helped to identify sites where spillover events might occur and is an especially valuable model for many countries to incorporate as they work towards implementing improved surveillance activities.

Laboratories play an important role in generating the data needed for effective global surveillance by identifying and characterizing pathogens found in nature or as causes of human infections. Genomic characterization of these pathogens and rapid sharing of specimens and sequence information is critical for the development of diagnostic tests, vaccines, and therapeutics, as well as for the implementation of targeted preventive measures. There will be a need to assist some countries in obtaining the technical skills and capabilities needed to allow national laboratories to meaningfully contribute to global surveillance efforts and strategies, along with resources that will need to be identified to support the creation of such a system. All laboratories will need to adapt and sustain a strong foundation in biosafety and biosecurity as global surveillance of emerging infectious diseases is advancing.

How information is to be assimilated and distributed internationally must be refined. The World Health Organization is the obvious organization to undertake this critical role; however, it is clear from the COVID-19 pandemic response that a tremendous amount of work still must be done to establish an accurate, timely, and equitable global surveillance system that is supported by all countries and free of political interference.

Regulation of "risky research"

Second, we need a large, multinational effort to regulate "risky research." Risky research includes experiments

that might intentionally or unintentionally enhance the transmissibility of a microbe, increase its natural host range, enhance pathogenicity, or further its ability to overcome natural or vaccine-induced immunity or the efficacy of proven therapeutics. Through the National Science Advisory Board for Biosecurity (NSABB), the United States government has proposed guidelines to reduce the risk of experiments dealing with or creating pathogens of pandemic potential. These guidelines are well-reasoned but are limited in scope in that they only address research undertaken within the United States or supported by the United States government when conducted by international grantees. These or similar guidelines must be discussed and incorporated into internationally accepted standards to reduce the risk of accidental or intentional creation of novel pathogens of pandemic potential. Such guidance must include ensuring that appropriate biosafety and biosecurity programs are in place wherever dangerous pathogens are being handled. It will be challenging to ensure that these safeguards are in place, but an essential first step will be to ensure that potentially risky research is fully vetted and assessed by qualified individuals and their host institutions *before* potentially risky studies are even begun.

Among the issues that must be considered are dual-use research of concern and gain of function research of concern, both of which can involve molecular modification of otherwise non-threatening microbes to create pathogens that might impact human health, animal welfare, or plant production. Gain of function studies are critical to modern virology and we need to ensure that efforts to reduce risk from these studies do not hinder beneficial research. Gain of function research of concern includes genetic modification of a potential pathogen that may result in increased transmissibility, enhanced virulence, or evasion of immunity or therapeutics. Substantial overlap exists with dual-use research of concern. Widespread concern was first raised following modifications made to avian influenza viruses in 2011 when two separate laboratories attempted to identify the molecular changes needed to allow avian influenza viruses to be efficiently transmitted among mammals. This led to a pause in some research supported by the US government and resulted in a comprehensive set of recommendations prepared by the NSABB that are included in the *Framework for guiding funding decisions involving pathogens of pandemic potential* (10).

Implementation of the 2017 NSABB Framework found that the recommendations were incomplete and that additional conditions were needed to further ensure the safety surrounding research activities on pathogens of pandemic potential. In March 2023, a reconvened NSABB released a new report, *Proposed Biosecurity Oversight Framework for the Future of Science* (11). The new report expanded the scope to include research that may enhance the transmissibility or virulence of *any* pathogen (recommendation 6) "likely to pose severe threats to human health, food security, economic security, or national security by its impacts on animals or plants or to animal or plant products." Further, it called for an integrated approach to research oversight that includes a "bottom-up" review involving investigators and institutions where the work is to be undertaken. This places greater responsibility on individual investigators, their parent institutions, and their associated biosafety review committees (recommendation 10.2) "Investigators and institutions should be aware of the potential risks of such research". The report further recommends (recommendation 3.2) "institutional compliance procedures must be better harmonized, strengthened…". The guidance is limited to research that is funded by the United States government; however, the need for international collaborations and consistent guidance throughout the global research community is recognized (recommendation 7): "Commitments to international engagement to harmonize and strengthen international norms, standards, education, and training related to biosafety and biosecurity must be renewed". Progress in science and technology is accelerating daily while our policy guidance to mitigate risks in life sciences research is failing to keep pace. There is a critical need for international collaborations and cooperation to establish norms and standards to effectively address "risky research". The 2023 NSABB report offers valuable recommendations to reduce the threat of "risky research" and to strengthen international biosafety and biosecurity.

The global proliferation of biocontainment laboratories

Today we are witnessing a global proliferation of biocontainment laboratories. There are about 70 maximum containment (Biosafety Level 4) laboratories in operation or advanced stages of planning or construction around the world (12). When operational, investigators in these laboratories will be handling the most dangerous pathogens known and potentially considering "risky research" that could lead to the creation

of novel pathogens able to initiate another pandemic. There is a clear need for internationally accepted norms and standards of operations, biosafety, and biosecurity in biocontainment laboratories. Before the construction of a biocontainment laboratory, national leaders should consider the following:

- What will be the mission of the laboratory?

  Will it be strictly research-focused, provide clinical services such as diagnostics, or be involved in product development, for example?

- How will success be measured?

  Criteria might include the number and quality of scientific publications, the products developed, or the services rendered.

- Who will provide external oversight of the facility including safety, security, and standards of operation?

  Options might include the national government, a private business, or an academic enterprise. A reference framework of internationally agreed-upon standards for safe and secure laboratory operations could be helpful.

- How will construction costs be managed? Who will be responsible for the sustained operations costs?

  It is often easier to obtain one-time funding to build a facility than it is to be assured that the costs of routine operations and maintenance will be available year after year. These recurrent costs can approach 10% of the original cost of construction in some instances.

- Who will use the laboratory? Who will be the responsible person for directing the laboratory?

  Work in modern biocontainment laboratories requires not only technical skills in the field of research to be pursued, but also strong leadership, specialized training in biosafety and biosecurity, and a robust cadre of support personnel. Leaders who communicate effectively with both their staff and the local community are essential to the success of the laboratory (13). They must create a culture of safety and security that is the foundation of successful operations for the laboratory. Access to such skilled personnel may be challenging.

- How will the security of the lab be maintained?

  Assuring that dangerous pathogens are securely stored with limited access to only qualified personnel is expensive, but essential.

- Reliable supply chains for reagents, equipment, maintenance parts, supplies, and services are needed for the successful operations of the laboratory.

  Having access to these critical elements may be challenging in some parts of the world.

- Will laboratory animals be used?

  A host of special needs and regulatory requirements must be met if laboratory animals are to be used in research. This adds significantly to operations costs and manpower requirements.

- How will potentially infectious waste be managed?

  The safety of the surrounding community demands that infectious waste is completely inactivated prior to release into local sewage systems or solid waste management facilities. Ensuring that this is done safely and efficiently is essential.

- Is the power supply reliable and is there a system in place to provide backup power? Biocontainment at all levels depends on a secure power source to maintain negative pressure and directional airflow, in addition to operations of all the associated laboratory equipment, instrumentation, and security systems.

Finally, the overarching question is: What is the most appropriate level of biocontainment required to meet the needs of the organization?

CONCLUSION

Advances in science and technology are greatly outpacing our ability to establish policies to mitigate risks in life science research. Solutions will require international consensus building sustained commitment and effective collaborations. Overseeing risky research relies on a leadership culture committed to safety and security, and the individual researchers that accept and practice this culture. A "bottom-up" approach to ensure a critical review of proposed research by qualified local

investigators and institutional officials before it is initiated is essential to reduce the risks from risky research. Laboratories with staff that have a strong safety culture, that don't view safety as a box-checking exercise, will be safer, more productive, and more rewarding places in which to work.

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S A Ž E T A K

ŠTO NAM JE RASPRAVA O PODRIJETLU COVID-19 OTKRILA O SIGURNOSTI I ZAŠTITI U LABORATORIJIMA*

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Sažetak

Svijet je svjedočio najrazornijoj pandemiji s kojom se čovječanstvo suočio u više od jednog stoljeća. Ostaje ključno pitanje podrijetla virusa odgovornog za ovu tragediju. Iznesene su dvije teorije; da se virus proširio s divljih životinja na ljude koji su zatim širili novi virus na druge ili da se virus proširio iz istraživačkog laboratorija. Obje teorije su moguće. Iako nema izravnih dokaza koji bi upućivali na to da je virus potekao iz laboratorija, teorija nudi priliku za pregled sigurnosnih i zaštitnih protokola koji su osmišljeni da bioistraživački instituti i osoblje koje u njima radi budu sigurni i zaštićeni. Napredak u znanosti i tehnologiji uvelike nadmašuje našu sposobnost uspostavljanja protokola koji bi uzeli u obzir rizike prilikom bioloških istraživanja, a rješenja će zahtijevati izgradnju međunarodnog konsenzusa, trajnu predanost i učinkovitu suradnju.

Ključne riječi: **COVID-19, SARS-CoV-2, biološka sigurnost u laboratoriju, biozaštita, podrijetlo pandemije**

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GENETICS, BIOSECURITY AND THE BIOECONOMY: LOOKING TO THE TWENTY-FIRST CENTURY AND THE AGE OF BIOLOGY

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Abstract

As the "Century of Biology" advances, multiple technologies are converging in the development of creative new approaches to sustainability in manufacturing. Genetics, artificial intelligence, engineering, and chemistry are combining to solve many of the world's pressing problems in agriculture, food, medicine, and the environment. Here we summarize some of these developments to illustrate the kind of advances in bio-manufacturing that exemplify new approaches to sustainable manufacturing. Accompanying these developments are concerns with the possible dual-use aspects of some of these technologies. We discuss some of the approaches within the biotechnology field to allay such concerns.

Keywords: **genetics, biosecurity, bioeconomy, dual-use**

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INTRODUCTION

The bioeconomy commonly refers to the phasing out of non-renewable, polluting resources and replacing them with biological, renewable alternatives (1). Simply, the bioeconomy is an economy based on biologically-sourced goods and services, also known as bioresources. The bioeconomy encompasses the sustainable production and conversion of biological materials, such as crops, forests, marine resources, and microorganisms into a wide range of products like food, feed, biofuels, chemicals, pharmaceuticals, and more. Nearly 60% of the physical inputs to the global economy could, in principle, be produced biologically. The bioeconomy emphasizes sustainability and minimization of environmental impact, to promote long-term availability of resources. A primary goal is to reduce reliance on fossil fuels. It encourages research and innovation in biotechnology, as detailed below. The bioeconomy aligns with the concept of "circular economy", whereby waste and by-products are minimized, and materials are reused or recycled whenever possible. Finally, the global bioeconomy plays a role in addressing global challenges including food security and climate change facilitating a transition to more sustainable industrial practices. The global bioeconomy is estimated to process up to $4 trillion US dollars per year globally over the next 10 years.

Role of biotechnology

Biotechnology plays a central and transformative role in the emerging bioeconomy, serving as a key driver in innovation and sustainability. Bioprocessing and biomanufacturing rely heavily on biotechnological innovation. In agriculture and crop improvement, biotechnology is employed to create high-yield and/or pest-resistant crops. Biotechnology is instrumental in drug discovery, vaccine development, and personalized medicine. Remediation and waste conversion methods offer solutions to environmental problems and rely on biotechnological tools and techniques. Finally, synthetic biology enables the design of biological systems and organisms for specific applications. Here, we describe several examples of the use of synthetic biology, to solve a range of problems in industrial manufacturing, agriculture, medicine, and environmental protection.

Synthetic Biology (SynBio)

Remarkable advances in genetics over the last decade have led to the ability to read, write, and modify DNA inexpensively and with great precision. These developments opened the door to SynBio, a multidisciplinary field of science that focuses on living systems and organisms, and it applies engineering principles to develop new biological parts, devices, and systems. SynBio relies on the rapid advances in multiple fields, including chemistry, microbiology, genetics, engineering, mathematics, physics, social sciences, computer science, and bioinformatics. The approach is based on the iterative and circular engineering principles of "Design-Build-Test-Redesign"(2). A simplified description of the process has the following steps:

1. Design: Scientists start by identifying a biological function they want to create or modify. This could involve designing a new protein, pathway, or even an entire organism.

2. DNA Manipulation: The genetic information needed to implement the desired function is encoded in DNA. Researchers can manipulate DNA through techniques like gene synthesis, polymerase chain reaction (PCR), or gene editing using a variety of tools such as CRISPR-Cas9.

3. Assembly: The modified DNA sequences are then assembled into a plasmid, which is a small, circular piece of DNA that can be inserted into a host organism such as a bacterium, yeast, or mammalian cells.

   These "host" organisms serve as "factories" to produce the desired biological product.

4. Testing and Iteration: The engineered organism is tested to see if it exhibits the desired function. If the test fails, the system can be further modified, and the process is repeated until the desired result is achieved.

Applications

The final engineered organism or system can be applied in various fields, such as medicine, agriculture, energy production, and environmental remediation. The applications of synthetic biology range from creating new biofuels and pharmaceuticals to novel organisms that clean up pollution or produce sustainable/biodegradable materials. The promise and opportunity of SynBio are best described with specific examples such as those below.

Microbial production of biofuels:

Scientists at LanzaTech in Illinois (https://lanzatech.com/) identified an organism that can synthesize ethanol from industrial waste gases. The bacterium was further refined with additional genes to maximize efficiency and expand its repertoire; LanzaTech's first commercial plant in China has produced millions of gallons of ethanol from steel mill emissions. The ethanol can be converted into jet fuel and other products (3).

Drought resistance:

Cytokinin is a plant hormone that under dry conditions signals to the plant to close pores to retain water and slow growth. Synthesis of the hormone is expensive. To circumvent using the hormone to induce pore closure, scientists developed tomato plants with novel receptors that respond to fungicide instead of cytokinin, making the plants more resilient under drought conditions. In related work, scientists at the Salk Institute have identified the genetic pathways that promote deep root growth in a plant's root system. These genes can prompt the development of deeper roots, enabling crops to resist stress, sequester more carbon, and enrich the soil. These are two examples of SynBio holding great promise in increasing agricultural yields (4).

Built-in fertilizer:

Most plants must acquire nitrogen from the soil or from chemical fertilizers to synthesize proteins and other components. Legumes have microbes associated with their roots that can remove nitrogen from the atmosphere and "fix" it into a form that can then be taken up by plants to make cell components. Fertilizer is produced mainly from fossil fuels and contribute to both greenhouse gas emissions and eutrophication. Pivot Bio, a California company (https://www.pivotbio.com/), engineered a microbe that lives on the roots of corn, wheat, and rice plants with genes from the nitrogen-fixing bacteria, to enable the crops' microbes to extract nitrogen from the atmosphere and supply it to the plant. In field tests, its nitrogen-producing microbe for corn yielded 7.7 bushels per acre more than chemically fertilized fields (5).

Sustainable foods:

Impossible Foods' plant-based burger (https://impossiblefoods.com/) contains synthesized heme protein, the iron-containing molecule found in animals and plants. Scientists added the plant gene encoding heme to yeast, which, after fermentation, produced large quantities of the heme protein. Impossible Burger uses 75 percent less water and 95 percent less land than a regular beef burger and produces 87 percent fewer greenhouse gas emissions (6).

As the demand for seafood grows globally (fishing stocks are already 90 percent overfished), so does the need for fishmeal, the protein pellets made of ground-up small fish and grain that feed farmed fish and livestock. California-based NovoNutrients (https://www.novonutrients.com/) uses CO_2 from industrial emissions to provide carbon to engineered bacteria, which then produce protein similar to the amino acids fish get by eating smaller fish and fishmeal. The bacteria replace the fishmeal, providing the fish with protein and other nutrients (7).

Cement/concrete:

Traditional cement production accounts for 8% of global carbon dioxide emissions. Global demand continues to grow with enormous environmental impact. If the cement industry were a country, it would be the third largest carbon dioxide emitter in the world with up to 2.8 bn tons, surpassed only by China and the US. Companies such as Biomason (https://biomason.com/) have developed a system to create new building materials by placing sand in molds and injecting them with bacteria. Calcium ions are used by the bacteria to produce a calcium carbonate shell with the bacteria's cell walls, causing the particles to stick together. A brick grows in three to five days (8). These cement bricks can be used in construction and landscaping.

Textiles and dyes:

DNA synthesis is used to create genes that encode enzymes tailored to produce different pigments. No petroleum products or chemicals are used and only one-fifth of the water of regular dyes is required. Spider silk is one of nature's strongest materials as it is elastic, durable, and soft (9). Companies such as Bolt Threads (https://boltthreads.com) are using engineered genes from spider DNA and expressing them in yeast. Then the yeast cells are grown in large fermentation tanks to produce large quantities of liquid silk proteins. The silk protein is then spun into fibers, which can be made into renewable Microsilk.

Risks and benefits: Dual-use

It is possible to imagine malicious uses that could lead to events that might threaten the health and safety of citizens, destabilize governments, disrupt social enterprises, destroy agriculture and the global economy, and imperil the very survival of the planet. The risk of malevolent use of technology is often referred to as the "dual use conundrum":

> "Life sciences research that, based on current understanding, can be reasonably anticipated to provide knowledge, products, or technologies that could be directly misapplied by others to pose a threat to public health and safety, crops and other plants, animals, the environment, or material."

-National Science Advisory Board for Biosecurity (10)

Essential to the oversight of potentially dangerous research are the processes of biosafety and biosecurity, and the terms are interrelated. The National Institute of Standards and Technology (NIST) published a bioeconomy lexicon (https://www.nist.gov/bioscience/nist-bioeconomy-lexicon) that defines biosafety as "practices, controls, and containment infrastructure that reduce the risk of unintentional exposure to, contamination with, release of, or harm from pathogens, toxins, and biological materials," and biosecurity as "security measures designed to prevent the loss, theft, misuse, diversion, unauthorized possession or material introduction, or intentional release of pathogens, toxins, biological materials, and related information and/or technology." In the context of biomanufacturing and the potential creation of entirely new organisms, it is clear that these terms will need to be expanded in their reach to think about biosecurity broadly, to include any kind of action with intent to cause harm that uses biological systems or data. The recognition of the potential risks of applications of advanced genetic and other technologies has led to a resurgence of interest in applied biosafety research. For the most part, this resurgence has focused on laboratory containment techniques, specifically with human or zoonotic pathogens.

Governance – what are we doing, what can be done, and what should we do?

Accompanying the need for biosafety and biosecurity processes to keep pace with the rapid pace of biotech development is the need for governance and oversight. Different governance tools and mechanisms are needed to achieve diverse goals and engage different stakeholders (11). They include laws and regulations, standards, guidelines, best practices, codes of ethics, research review processes, awareness-raising activities, training, and education (12).

The collective process of creating an international governance mechanism for research and applications with the potential for harmful application requires the standardization of language and concepts. Frameworks – decision models - help clarify and standardize the approach being used. Frameworks can ensure that estimates include all the components that the collaborating decision makers believe are important, and second, they enable comparisons across multiple estimates. Developing shared frameworks increases the usefulness of estimates of risk and allows comparison across national and conceptual boundaries. Several frameworks, or decision trees, have been elaborated for analysis of the risks and benefits of research with dual-use potential (13). Qualitative frameworks serve as a tool to evaluate risks and benefits and determine how to address them both. The process of using the frameworks to discuss scientific and technological capabilities organizes information in ways that illuminate unstated assumptions, clarify areas of agreement and disagreement, bring forward questions, and facilitate productive discussions. In this way, the frameworks enable potential security risks to be assessed in a systematic way to inform policymakers and support the goal of evidence-informed policy.

A compelling example of an international body contributing to dual-use governance is *The International Genetic Engineering Machine Competition* (iGEM) (14). iGEM was started twenty years ago in the USA and now has yearly participants from 66 countries and regions with 6,000 students competing each year in 400+ teams. Multidisciplinary students work together in teams to identify problems to be solved, designing solutions using synthetic biology and engaging in self-organization to address societal problems safely and securely. Intrinsic to the iGEM process of project development is a dedicated biosafety and biosecurity program (15). The iGEM Safety and Security Committee comprises a team of specialists from a range of fields with expertise in biosafety, biosecurity, and risk assessment. Its members represent multiple sectors of industry, academia, and government. The committee oversees iGEM's safety and security programs, offering guidance on potential safety and security concerns and systematically reviewing each of the proposals. The competition has a number of checks for dual use along the life cycle of the projects: the parameters for evaluation also include human practices and rules for communication and transfers of microorganisms. Thus, students who compete in iGEM have early career exposure to the basics of responsible science. Over 40,000 students, instructors, and judges have passed through the iGEM system since 2004 and spread across the field of biotechnology.

CONCLUSION

Global biomanufacturing is at the beginning of a true revolution. Multiple problems facing humanity can likely be solved using genetic technologies such as those described in this article. Sustainable and circular approaches to the generation of goods and products are necessary to protect the natural resources of the planet, under severe threat from overuse and climate crisis. However, any technologies in the life sciences have the potential for dual-use applications. Each has the potential to make substantial improvements in or lead to possible harm to human, animal, plant, and environmental health. The risks that accompany many of these technologies must be addressed by biosafety and biosecurity governance mechanisms that represent a moving target. Applied research into biosafety and biosecurity practices can be used to standardize across regions as appropriate. Existing and future governance structures will need to be adapted to be relevant to changing environments, advances in technology, and novel applications, and in some cases, where existing governance structures are inadequate, new structures and ways of limiting harm are urgently needed.

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S A Ž E T A K

GENETIKA, BIOSIGURNOST I BIOEKONOMIJA: GLEDAJUĆI PREMA DVADESET PRVOM STOLJEĆU I DOBU BIOLOGIJE

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Sažetak

Kako „Stoljeće biologije“ napreduje, više se tehnologija istovremeno razvija i međusobno povezuje u stvaranju kreativnih novih pristupa održivoj proizvodnji. Genetika, umjetna inteligencija, inženjerstvo i kemija udružuju se kako bi riješile mnoge od gorućih svjetskih problema u poljoprivredi, prehrani, medicini i zaštiti okoliša. U ovom radu sažimamo neka od tih dostignuća kako bismo ilustrirali napredak u bio-proizvodnji koji predstavlja nove pristupe održivoj proizvodnji. Uz ove razvojne procese javljaju se i zabrinutosti zbog moguće dvostruke namjene nekih od tih tehnologija. Raspravljamo o nekim pristupima unutar biotehnološkog sektora koji nastoje umanjiti te zabrinutosti.

Ključne riječi: **genetika, biosigurnost, bioekonomija, dvostruka namjena**

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THE IDF AND THE COVID-19 EPIDEMIC

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Abstract

The COVID-19 epidemic was a global surprise and during 2020, militaries were deployed around the world to engage in the campaign against COVID-19. These engagements took various forms.

The Israel Defense Force's experience and cooperation in large-scale national emergencies have been tested in natural disasters, security or health-related situations. The military's engagements were instrumental as well in addressing the COVID-19 pandemic due to its resources and hierarchical discipline, especially in light of its centrality in Israel.

The purpose of the article is to describe the manner and extent of the involvement of the IDF in the national fight against Corona, to examine the lessons that can be learned from this, and to answer the question of whether, even in a future crisis, the Israeli government will assign a central role in dealing with the epidemic to the IDF, or whether it would be more appropriate to strengthen the civilian bodies so that they can cope with the challenges in the future.

Keywords: COVID-19, IDF, Home front command, Directorate of Military Intelligence, Vaccination, Ministry of Health

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INTRODUCTION

The COVID-19 epidemic was a global surprise. COVID-19 entered Israel on February 21, 2020, when 11 Israelis aboard a cruise ship returned home and entered quarantine in Israel's first coronavirus ward at Sheba Medical Center. That same day, doctors discovered that one of the travelers had the virus. Then, Israel began its fight against the COVID-19 (1).

The Ministry of Health in Israel was responsible at the national level for dealing with the COVID-19 epidemic but it did not have the operative tools to manage the crisis and to enforce government policy on the matter and the Israel Defense Forces (IDF) was soon called upon to assist in the fight against COVID-19.

Ever since its establishment, the IDF has been involved in civilian missions. Given its logistical, technological, and operational capabilities, it was only natural that the IDF would be extensively involved in the country's response to the COVID-19 pandemic. The government declared a national state of emergency in March 2020, following the high infection rates and it was both legitimate and legal to use the IDF.

On July 23, 2020, Israeli Prime Minister Benjamin Netanyahu appointed a "Corona Project Manager", whose main goal was to lead and manage the national program to fight COVID-19 by integrating professional and executive bodies. Professor Roni Gamzu took on the position of Israel's first coronavirus coordinator in late July 2020. Gamzu established Israel's coronavirus headquarters, recruited the Home Front Command, and built a system to increase testing, decentralizing it from the Central Virology Laboratory at Sheba. He also increased efforts to cut the chain of infection and helped design the protocol that enabled Israel to focus on super-spreaders instead of everyone with a positive COVID test result. He also established desks to deal with the ultra-Orthodox, Arab, and senior citizen communities and their diverse needs (1).

As part of the war against the COVID-19 epidemic, the IDF had to act on two levels at the same time:

1. To protect the soldiers from the COVID-19 epidemic in order to maintain the army's ability to fulfill its security tasks.
2. To help the various authorities of the state to fight the COVID-19 epidemic at the national level.

AIM

During 2020, militaries were deployed around the world to engage in the campaign against COVID-19. These engagements took various forms. As the comparative analysis of Stuart Cohen and Meir Elran indicated that the IDF were deployed more extensively relative to other democracies' militaries to address COVID-19 (2).

IDF's experience and cooperation in large-scale national emergencies have been tested in natural disasters, security or health-related situations. The military's engagements were instrumental as well in addressing the COVID-19 pandemic due to its resources and hierarchical discipline, especially in light of its centrality in Israel. However, problems remain concerning this deployment. For example, it should be taken into account that the IDF may be busy with its main task of protecting the State of Israel from its enemies and will not be able, under these circumstances, to allocate considerable resources to a civilian mission.

The purpose of the article is to describe the manner and extent of the involvement of the IDF in the national fight against Corona, to examine the lessons that can be learned from this, and to answer the question of whether, even in a future crisis, the Israeli government will assign a central role in dealing with the epidemic to the IDF, or whether it would be more appropriate to strengthen the civilian bodies so that they can cope with the challenges in the future.

METHODS

Methodologically, the military involvement and deployment can be seen as part of the 'securitization of COVID-19'. The concept of "securitization" was initially developed by Ole Waever to make a major contribution to the so-called "widening–deepening" debate in security studies, which had begun in the 1980s and intensified with the end of the Cold War. The "widening" dimension was defined as the extension of security to issues or sectors other than the military, such as global health, the environment, or the economy (3).

Global political leaders have referred to the pandemic situation as both a threat and a war, positioning COVID-19 within a security discourse. The methods of labeling the virus as a security issue range from merely identifying COVID-19 as a threat, to declaring war. Therefore, the construction of threat justified the use of exceptional measures at both domestic and international levels. In this case, securitizing the pandemic meant that states adopted a security discourse framing COVID-19 as a high national security threat, and therefore, among other means, they deployed their armed forces (4).

The article draws on official reports (IDF website), articles, news, and policy texts from the case of Israel.

RESULTS

The central role played by the IDF in the State of Israel's fight against COVID-19 and how the decision-makers in Israel also adopted the security terminology regarding the fight against COVID-19 indicate that Israel's case study is indeed compatible with the concept of "securitization".

The IDF's efficient and quick response to these needs contributed greatly to the success of the State of Israel in dealing with the COVID-19 pandemic, but it must be remembered that the IDF has other missions and tasks and it should not be assumed that it will be able to contribute its capabilities and resources to civilian tasks at any time of crisis.

The key takeaway from the COVID-19 crisis is to develop a comprehensive methodology of national crisis management and to set up a new national virus protection system in order to minimize any future virus situations impacting both the national as well as civilian levels.

DISCUSSION

The efforts to protect the IDF against the COVID-19

The main task of the IDF is to protect the sovereignty of the country, the security of its residents,

and its strategic interests. Therefore, the IDF had to protect its forces from the COVID-19 epidemic to maintain the army's ability to fulfill its missions.

It could be expected that when the entire world is dealing with an epidemic, the terrorist organizations will refrain from carrying out attacks, however, the Palestinian terrorist organizations did not stop the attacks against Israel and the IDF had to respond to the terrorist threats during this period.

In 2020 Hamas and other terrorist groups including the Palestinian Islamic Jihad (PIJ) launched rockets from Gaza toward Israel, some of which landed in civilian areas. According to the IDF the "Iron Dome ", Israel's air defense system, intercepted many of the rockets. The West Bank saw 60 terror attacks in 2020, up from 51 in 2019.

The IDF's priorities were clearly defined - above all, to maintain IDF's operational readiness to protect Israel (5). The IDF has implemented the following essential policies to limit the spread of COVID-19 and maintain its operational capabilities (6):

Any soldier suspected of coming into contact with someone who has tested positive for COVID-19 was placed in a 14-day home quarantine.

All meetings in the IDF were limited to 10 people, gatherings in closed spaces were limited to 50 people, and gatherings in open spaces were limited to 100.

All soldiers were expected to maintain a distance of at least 2 meters from one another.

All soldiers were required to wear masks in all civilian and military situations.

Units reduced the sizes of shifts as much as possible, including gatherings and meetings.

Commanding officers were strictly separated into two shifts.

Since March 2020, the IDF operated an alternative transport system for military personnel. In order to maintain maximum operational capacity, 260 buses drove between bases across the country Sundays through Thursdays and followed strict guidelines to ensure the health of the soldiers aboard (7).

The vaccination of the IDF soldiers

The Israeli government realized at an early stage of the epidemic that the solution would be found in vaccinating the people and the IDF was the priority. The highlight of Israel's successful efforts came at the end of December 2020, when it managed to secure enough Pfizer vaccines for all citizens and then inoculate them in only months.

Israel launched its COVID-19 vaccination campaign on December 20th, but preparations for it began months earlier. Throughout 2020, Israel signed vaccine purchase contracts with several pharmaceutical companies at the forefront of COVID-19 vaccine development (8).

The purpose of the IDF's vaccination campaign was to vaccinate all military personnel in the shortest amount of time from the moment Israel received its first doses and to carry out the campaign in an efficient, safe, and professional manner.

All IDF service members received the Pfizer-BioNTech COVID-19 vaccine, administered by staff from the IDF Medical Corps who trained at the School of Military Medicine under the supervision of certified nurses. Vaccines were available across 22 complexes throughout the country in order for each unit to have access to its nearest compound.

In March 2021, with 83% of IDF soldiers vaccinated and zero IDF deaths from COVID-19, the IDF reached its goal as the first military and the largest organization in the world to be vaccinated against COVID-19 (9).

The IDF supports civilian authorities in fighting the COVID-19 epidemic

Since the outbreak of COVID-19 in early 2020, the IDF has been the leading force in the battle against the virus in Israel. The IDF successfully fulfilled a wide variety of tasks that should have been carried out by other ministries and organizations of the Israeli government.

The Home Front Command

Much of the military support was provided or coordinated by the Home Front Command (HFC), the arm of the IDF specializing in civilian protection, usually in

times of conflict, and experienced in cooperating with local authorities.

HFC provided logistical support to civilian authorities that supplied aid to the civilian population, such as food, medication, and essential services to the elderly.

Throughout the pandemic, the IDF has managed and facilitated the use of six hotels across the country to host COVID-19 patients who display only mild symptoms of the virus. Of these hotels, four hosted people who have tested positive for the virus, and two hosted quarantined civilians (6). The HFC has also been operating several COVID-19 "drive-through" testing locations across the country, making testing more accessible for civilians, in addition to initially being charged with operating hotels for recovering COVID-19 patients who did not require medical support (10). At the end of March 2020, the Israeli government decided to allocate 1,400 soldiers of the HFC to assist the police in enforcing lockdowns and maintaining public order (11).

In July 2020, when it became apparent that the Ministry of Health was unable to operate an effective system of epidemiological investigations, the HFC was charged with the task and established the "Alon" (Oak) Coronavirus Command Center, as well as the "Ella" (Terebinth) Unit. The latter uses a special digital system, developed by the IDF's SIGINT Agency, Unit 8200, and the Cyber Defense Directorate.

On September 21, 2020, Israeli Minister of Defense Benny Gantz together with Chief of the General Staff Lt. Gen. Aviv Kohavi approved the establishment of the "Ella" Unit for Epidemiological Investigation. Approximately 600 soldiers and dozens of reservists were allocated to the unit to help reinforce and extend the epidemiological investigation efforts under the command of the "Alon" Task Force of the Home Front Command (12).

During 2021 these units performed 706,271 investigations, carried out 13,540,000 PCR tests, and operated 28 hotels for quarantine purposes. In no other democracy have the armed forces been tasked with similar missions (13).

In the field of public information, the HFC operated a call center that provided guidelines and other necessary information regarding COVID-19 for civilians, and its troops distributed leaflets in several languages (in Arabic, Russian, and Amharic as well as Hebrew and English), explaining the significance of complying with the government instructions (14).

The Directorate of Military Intelligence (DMI)

The involvement of the Directorate of Military Intelligence (DMI) in the COVID-19 crisis was multidimensional (15). Conscripts and some reservists from Israel's elite 8200 intelligence unit, and the high-level technological Unit 81, have been engaged to help find solutions to some of the tremendous medical challenges posed by COVID-19.

The DMI's technological unit created information management software for the coronavirus testing labs and conducted epidemiological analysis of COVID-19 patients to determine hotspots where the infection spread in order to help the local authorities focus their efforts on preventing the disease from spreading in their vicinity.

Additionally, the DMI established the National Information and Knowledge Center for the Fight against COVID-19. The central task of the center was to analyze the spread of the virus and identify risks and opportunities, in addition to providing governmental organizations with data analysis, global information, and recommendations to assist policy formulation. The center was headed by an officer with the rank of colonel and included a team of officers and soldiers of the technological arena of the research division at the DMI. During its activity, the center published 748 reports on various topics, including reports on the level of morbidity about the means and capabilities available to the state.

The technological unit of DMI, known as Unit 81, was responsible for designing sophisticated gadgets, such as monitors for remote control operations, personal protection gear, and designated ambulances.

The unit has worked with the Ministry of Health, Magen David Adom—Israel's Emergency Medical Services—and hospitals across the nation to find innovative solutions to some of the medical challenges Israel has faced during the COVID-19 pandemic. Unit 81 has adapted thousands of BiPAP home ventilation devices into ventilators for COVID-19 patients in Sheba Hospital and manufactured up to 1,000 protective masks a day for military and civilian medical teams to counter the shortage of masks in Israel. The unit also developed special shields and sepa-

rate air conditioning systems in approximately 50 ambulances, to enable drivers to evacuate COVID-19 patients without endangering themselves (16).

The DMI's secret units were also called to support the crisis response. In April 2020, The Israeli Navy Marine Commando Unit, Shayetet 13, developed a solution to increase limited oxygen supplies for civilians. The unit has converted an operational production line into a medical oxygen compressing system that follows required health protocols (16).

The IDF Medical Corps

The main mission of the IDF Medical Corps was to maintain the health of the army, but despite the burden on the IDF medical system, it also helped the civilian system.

In collaboration with the Ministry of Health and Rambam Hospital in Haifa, the IDF established two hospital wards dedicated to treating patients with moderate symptoms of COVID-19. This was the first time in history that the IDF was formally tasked with providing medical care for Israeli civilians. Dozens of patients were treated by personnel from the IDF Medical Corps (14).

The IDF played an important role in vaccinating the Israeli public by utilizing military doctors and nurses. The HFC also has been tasked with the mission of coordinating vaccination campaigns in schools and vaccination sites in local authorities, to make the vaccines as accessible as possible to the Israeli public.

Assistance to special communities

Israel is a small country but holds great demographic and geographic diversity. Therefore, every region, town, and municipality faced very different battles in the fight against COVID-19.

The support to ultra-orthodox Jewish populations

Soldiers from elite combat reconnaissance units have been deployed to the ultra-Orthodox city of Bnei Brak, which the government has declared a "restricted zone". This step was taken after unsuccessful efforts to make its residents comply with the nationwide shelter-at-home and social distancing regulations, which have caused the city, one of the most densely populated in Israel, to become a major hot spot for COVID-19.

In Bnei Brak, soldiers were helping evacuate the elderly into hotels facilitated and managed by the IDF and provided additional assistance such as distributing food and medication and providing welfare and logistical assistance (11).

The support to the Israeli Arab population

To help Israeli Muslims prepare for the month of Ramadan, the IDF Home Front Command has launched a public awareness campaign in Arabic to provide instructions to the Israeli Muslim public on how to celebrate Ramadan while adhering to medical guidelines. Arabic-speaking reservists have assisted in various Israeli Arab municipalities across the country (11). The IDF also delivered food and essential supplies to Muslim families across the country.

The IDF has worked closely with the Ministry of Health and Bedouin community leaders to initiate a variety of efforts to assist the Bedouin community in fighting the virus. The efforts included sending information via text messages, providing informational pamphlets, visiting homes and mosques, giving appropriate guidance to hospitals, and transferring sick patients from authorities to designated recovery hotels (14).

The IDF's support to Palestinians in Gaza and Judea in Samaria

The Palestinian Authority was responsible for the health and health care of Palestinian residents of Gaza and the West Bank. This included responsibility for providing vaccinations against COVID-19. Since the beginning of the COVID-19 outbreak, the IDF Coordinator of Government Activities in the Territories (COGAT) cooperated with the Palestinian Authority to facilitate the transfer of critical medical equipment to Palestinians in Judea Samaria and Gaza (15).

In addition to the thousands of COVID-19 test kits and PPE gear that have been transferred into the Palestinian territories, COGAT has also coordinated joint medi-

cal workshops and online tutorials for Palestinian and Israeli medical personnel (6).

Although the Gaza Strip is controlled by the terrorist organization Hamas, which strives to destroy the State of Israel, the IDF allowed the COVID-19 epidemic the transfer of humanitarian aid and medical equipment to the Palestinian population in the Gaza Strip. The IDF worked closely with the World Health Organization (WHO) and the United Nations (UN) to deliver essential supplies—including testing kits, PPEs, disinfectant materials, lab equipment, fuel and food—into Gaza.

SUMMARY AND CONCLUSIONS

Lessons learned from three years of the COVID-19 pandemic in the country should ensure Israel is more prepared for the next public health emergency, whatever that may be, said COVID-19 coordinator Prof. Salman Zarka. "We need to formalize the processes we developed for managing COVID-19, so we can roll them out again," he said (1).

Since the outbreak of COVID-19 in early 2020, the IDF has been the leading force in the battle against the virus in Israel. The IDF successfully fulfilled a wide variety of tasks that should have been carried out by other ministries and organizations of the Israeli government.

The central role played by the IDF in the State of Israel's fight against COVID-19 and how the decision-makers in Israel also adopted the security terminology regarding the fight against COVID-19 indicate that Israel's case study is indeed compatible with the concept of "securitization".

The IDF's efficient and quick response to these needs contributed greatly to the success of the State of Israel in dealing with the COVID-19 pandemic, but it must be remembered that the IDF has other missions and tasks and it should not be assumed that it will be able to contribute its capabilities and resources to civilian tasks at any time of crisis.

The Home Front Command is the only entity in the IDF whose main mission is to assist the civilian sector during war, and therefore this entity will be able to fulfill the tasks it performed during the COVID-19 epidemic in the future if required.

The key takeaway from the COVID-19 crisis is to develop a comprehensive methodology of national crisis management and to set up a new national virus protection system in order to minimize any future virus situations impacting both the national as well as civilian levels.

The government should take all necessary steps to develop the bodies and operational methods to deal with national crisis situations such as the COVID-19 crisis and make sure that the system that will be built will maintain its ability to respond to unexpected challenges in the future.

A transition plan needs to be in place for moving from "routine" to "emergency" mode of decision-making and government operations and following successful virus containment to restore routine life as soon as possible. This includes the establishment of an ad-hoc cabinet to manage the crisis, aided by a dedicated operations headquarters.

The establishment of ad-hoc intelligence capabilities in the Ministry of Health is needed. Just as in military conflict, it is vital to gather and analyze all information available to deal with the crisis, in conditions of great uncertainty. This is the situation always faced by intelligence services.

The Ministry of Health has stated that "as part of learning lessons from the COVID-19 epidemic it was decided to establish a National Information and Knowledge Center in the Ministry of Health that will assist in research and gathering relevant information for warning and dealing with national health crises, and replace the DMI's Information and Knowledge Center.

The crisis ought to be managed 24/7 from a central operations room or command headquarters, headed by a prominent official such as the head of the National Security Council. This will best coordinate the activities of all relevant agencies. An advisory board should operate alongside this headquarters, tasked with thinking ahead and preventing the tendency to deal mainly with urgent matters rather than with the most important issues.

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S A Ž E T A K

IDF I EPIDEMIJA COVID-19

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Epidemija COVID-19 bila je globalno iznenađenje, a tijekom 2020. godine vojske su bile angažirane diljem svijeta u borbi protiv COVID-19. Ti angažmani su se odvijali u različitim oblicima. Iskustvo i suradnja Izraelskih obrambenih snaga (IDF) u situacijama velikih nacionalnih izvanrednih stanja testirani su u prirodnim katastrofama, sigurnosnim i zdravstvenim krizama. Vojni angažman pokazao se ključnim i u suočavanju s pandemijom COVID-19 zahvaljujući svojim resursima i hijerarhijskoj disciplini, osobito s obzirom na središnju ulogu IDF-a u izraelskom društvu. Cilj ovog članka je opisati način i opseg uključenosti IDF-a u nacionalnu borbu protiv koronavirusa, ispitati koje se pouke mogu izvući iz tog iskustva te odgovoriti na pitanje hoće li izraelska vlada i u budućim krizama IDF-u dodijeliti središnju ulogu u upravljanju epidemijama ili bi bilo prikladnije jačati civilne institucije kako bi mogle samostalno odgovarati na buduće izazove.

Ključne riječi: **COVID-19, IDF, Zapovjedništvo domovinske obrane, Uprava vojne obavještajne službe, cijepljenje, Ministarstvo zdravstva**

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BLOOD-BORNE VIRAL HEPATITIS MARKERS AMONG PEOPLE WHO INJECT DRUGS IN CROATIA: PREVALENCE AND RISK FACTORS

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ABSTRACT

People who inject drugs (PWID) represent a high-risk and high-prevalence group for both hepatitis C (HCV) and hepatitis B virus (HBV) infection. A total of 224 PWID from three geographically distant Croatian regions (three continental counties and one county located on the Adriatic Coast) were tested for the presence of blood-borne hepatitis markers: hepatitis B surface antigen (HBsAg), hepatitis B core total antibodies (anti-HBc) and hepatitis C (anti-HCV) antibodies. Study participants were recruited from the psychiatry hospital ward (19.6%) and outpatient counseling centers (80.4%). Serologic tests were performed using a commercial enzyme-linked fluorescent assay. Initially, reactive anti-HCV samples were confirmed using a third-generation line immunoassay. The overall prevalence of HBsAg, anti-HBc and anti-HCV was 0.9% (95%CI=0.1-3.2), 22.8% (95%CI=17.4-28.2), and 55.8% (95%CI=49.0-62.4), respectively. There were significant regional differences in both anti-HBc (17.9-38.8%, p=0.01) and anti-HCV prevalence (49.1-75.5%, p=0.007). Anti-HBc prevalence increased gradually with age from 21.3% to 64.3%, starting with the 30-39 age group (p<0.001). In contrast, a sharp increase in anti-HCV seroprevalence was observed from 24.6% in PWID less than 30 years to 59.6% in the 30-39 age group. Thereafter, there was a steady increase to 92.9% in PWID above 50 (p<0.001). Sharing injection equipment correlated strongly with HBV and HCV seropositivity. Significantly higher seroprevalence rates were found in PWID who reported sharing syringes/needles frequently or occasionally (anti-HBc 34.7%/23.5% *vs* 14.9%, p=0.009; anti-HCV 87.8%/63.5%% *vs* 8.7%, p<0.001). Residents of urban areas were more often seropositive compared to residents of suburban/rural areas (anti-HBc 25.3% *vs* 6.7%, p=0.033; anti-HCV 58.8% *vs* 36.7%, p=0.03). Heterosexual individuals had higher HCV prevalence rates compared to homo/bisexual individuals (60.1% *vs* 25.0%; p=0.03). Gender, educational level, marital status, employment status, history of imprisonment, tattooing, and traveling, as well as sexual risk factors, were not associated with HBV or HCV seropositivity.

Keywords: Hepatitis B, hepatitis C, people who inject drugs, seroprevalence, risk factors, Croatia

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INTRODUCTION

Viral hepatitis B and C represent global public health problems. According to the World Health Organization estimates, 58 million people worldwide are chronically infected with the hepatitis C virus (HCV) and approximately 1.5 million new infections occur each year (1). Although most acute HCV infections are subclinical, 80-85% of patients become chronically infected and are at risk of developing liver disease including cirrhosis and hepatocellular carcinoma (2). Regarding hepatitis B virus (HBV) infection, it is estimated that one-third of the world's population has a history of exposure to HBV and 296 million people have chronic infection (3). HBV is transmitted by percutaneous or per mucosal exposure to infected blood and other body fluids, mainly semen and vaginal secretions. The primary transmission mechanism of HCV is through significant or repeated direct percutaneous exposure to infected blood or blood products (4).

In the European region, people who inject drugs (PWID) represent a high-risk and high-prevalence group for both HCV and HBV infection due to many factors, including sharing injection equipment and lack of awareness about hepatitis transmission (5). PWID may account for up to 60% of new HCV infections in developed countries (2). In addition, HCV/HBV co-infection is common in this risk group. The prevalence of HBV and HCV infection among PWID varies widely across European countries (6-10).

In Croatia, there are several published studies on the prevalence of viral hepatitis in the general population (11) and some specific population groups such as prisoners (12), groups with high-risk sexual behavior (13, 14), and pregnant women (15). Some regional studies addressed HCV infection in PWID (16-18), however, there is very little data on the HBV prevalence in this population group (17). The seropositivity varies according to the population tested. The HBV seroprevalence ranges from 7.0% in the general population to 38.8% among PWID, depending on the region. Similarly, the HCV seroprevalence of HCV is highest among PWID (up to 75%) compared with the general population (0.9%) (19).

This study aimed to analyze the prevalence, sociodemographic characteristics, and risk factors for HBV and HCV infection among PWID in three geographically distant continental and coastal Croatian regions.

MATERIALS AND METHODS

Study population

The study included 224 PWID from four Croatian counties: the City of Zagreb/Zagreb County (north-western continental), Brod-Posavina (north-eastern continental), and Istria County (northern coastal) tested in the period from 2014 to 2018. Among study participants, 44 (19.6%) were recruited from the psychiatry hospital ward and 180 (80.4%) from outpatient counseling centers. After obtaining informed consent, each participant completed a questionnaire regarding the sociodemographic characteristics (age, gender, marital status, educational level, employment status, place of residence) and potential risk factors (injecting and sexual risk behaviors, history of imprisonment, traveling, tattooing).

Serological testing

Hepatitis B surface antigen (HBsAg), hepatitis B core total antibodies (anti-HBc), and hepatitis C antibodies (anti-HCV) were detected using an automated enzyme-linked fluorescent assay (ELFA; Vidas, bioMérieux, Marcy l'Etoile, France). The results were interpreted according to the manufacturer's recommendations as follows: HBsAg Long protocol test value <0.10 negative; ≥0.10 positive, anti-HBc test value<1 positive; ≥1-≤1.4 equivocal; ≥1.4 negative, anti-HCV antibodies test value <1.00 negative, ≥1.00 positive. Samples repeatedly reactive for HBsAg were further analyzed using a confirmation test with neutralizing antibodies (Vidas, bioMérieux, Marcy l'Etoile, France). HBV serologic results were classified as follows: active HBV infection (HBsAg positive), past infection (anti-HBc positive). Initially, reactive samples for anti-HCV antibodies were confirmed using a third-generation LIA test (Fujirebio EUROPE N.V., Ghent, Belgium).

Statistical analysis

The difference between groups of nominal variables was assessed using chi-square or Fisher exact test. The difference between groups of ordinal variables was assessed using the Mann-Whitney U test. The strength of the association was assessed using logistic regression. Statistical analysis was performed using STATA/IC 15.1 for Windows (StataCorp LP, USA). The level of statistical significance was chosen to be $\alpha=0.05$.

RESULTS

Participants' demographic characteristics and risk behaviors

The majority of participants were males (91.5%). The median age was 35 (range 18-62) years. Of all participants included in the study, 26.9% had elementary school or lesser education, 59.6% were single/divorced, 59.8% were unemployed and 18.8% reported a history of imprisonment. Regarding injecting risk behavior, 37.9% and 21.9% of participants reported sharing injecting equipment occasionally or frequently. Among risk sexual behavior factors, 2.2% reported homosexual/bisexual orientation, 3.1% history of sexually transmitted diseases (STDs), and 11.6% paid sex. About one-half of the participants (48.7%) reported being tattooed and 34.4% reported a history of traveling or long stays abroad.

Seroprevalence results

The overall prevalence of HBsAg, anti-HBc and anti-HCV was 0.9% (95%CI=0.1-3.2), 22.8% (95%CI=17.4-28.2), and 55.8% (95%CI=49.0-62.4), respectively. There were significant differences in seropositivity among regions. Both anti-HBc and anti-HCV seroprevalence were significantly higher in Istria County compared to Brod-Posavina County and the City of Zagreb/Zagreb County: anti-HBc 38.8%, 18.8%, and 17.9% (p=0.01), anti-HCV 75.5%, 52.2% and 49.1%, respectively (p=0.007) (Table 1). The prevalence of anti-HBc and anti-HCV according to the characteristics of participants is presented in Table 2. Anti-HBc seropositivity increased gradually with age from 21.3% to 64.3% starting with the 30-39 age group (p<0.001). A sharp increase in anti-HCV seroprevalence was observed from 24.6% in PWID less than 30 years to 59.6% in the 30-39 age group. Thereafter, seropositivity increased steadily to 92.9% in PWID above 50 (p<0.001).

The rate of sharing injecting equipment in Croatian PWID was 59.8% and correlated strongly with both HBV and HCV seropositivity. Anti-HBc prevalence in PWID who did not share equipment was reported to be 14.9% compared to 23.5% and 34.7% in PWID who shared equipment occasionally and frequently (p=0.009). Anti-HCV seropositivity increased from 28.7% in those who reported no sharing equipment to 63.5%/87.8% in those who reported sharing equipment occasionally/frequently (p<0.001). Residents of urban areas were more often seropositive than residents of suburban and rural areas (anti-HBc 25.3% *vs* 6.7%, p=0.033; anti-HCV 58.8% *vs* 36.7%, p=0.03). Although unemployed PWID showed higher anti-HCV seroprevalence (59.0%) than employed participants (40.9%), this difference did not reach statistical significance (p=0.054).

Regarding sexual orientation, anti-HCV prevalence was higher in heterosexuals (60.1%) than in homo/bisexuals (25.0%, p=0.03). Other sexual risk factors (paying for sex, and history of STDs) were not associated with anti-HBc or anti-HCV positivity.

Gender, marital status, educational level, history of imprisonment, tattooing, setting of recruitment, and traveling/long staying in endemic countries were not associated with HBV and HCV prevalence.

Results of the logistic regression showed that older age, frequency of sharing injecting equipment and living in urban areas were factors significantly associated with anti-HBc and anti-HCV prevalence (Table 3).

Table 1. *Prevalence of HBsAg, anti-HBc and anti-HCV among people who inject drugs in Croatia*

	The City of Zagreb / Zagreb County (N=106)		Brod-Posavina County (N=69)		Istria County (N=49)		
Serologic marker	N (%)	95%CI	N (%)	95%CI	N (%)	95%CI	P
HBsAg	1 (0.9)	0 - 5.2	0 (0)	0 - 5.2	1 (2.0)	0.1 - 10.9	0.509
Anti-HBc	19 (17.9)	11.2 - 26.6	13 (18.8)	10.4 - 30.1	19 (38.8)	25.2 - 53.8	0.01
Anti-HCV	52 (49.1)	39.2 - 59.0	36 (52.2)	39.8 - 64.4	37 (75.5)	61.1 - 86.7	0.007

CI=Confidence interval

Table 2. *Seroprevalence of anti-HBc and anti-HCV according to participants' characteristics*

		Anti-HBc			Anti-HCV		
Characteristic	N tested	N (%)	95%CI	p	N (%)	95%CI	p
Gender				0.576			0.631
Male	205	48 (23.4)	17.8 - 29.8		113 (55.1)	48.0 - 62.1	
Female	19	3 (15.8)	3.4 - 39.6		12 (63.2)	38.4 - 83.7	
Age (years)				<0.001*			< 0.001*
< 30	65	0 (0)	0 - 5.5		16 (24.6)	14.8 - 36.9	
30 - 39	94	20 (21.3)	13.5 - 30.9		56 (59.6)	49.0 - 70.0	
40 - 49	51	22 (43.1)	29.3 - 57.8		40 (78.4)	64.7 - 88.7	
50+	14	9 (64.3)	35.1 - 87.2		13 (92.9)	66.1 - 99.8	
Marital status				0.282			0.264
Single	101	17 (16.8)	10.1 - 25.6		50 (49.5)	39.4 - 59.6	
Married	29	8 (27.6)	12.7 - 47.2		19 (65.5)	45.7 - 82.1	
Steady relationships	61	17 (27.9)	17.1 - 40.8		34 (55.7)	42.4 - 68.5	
Divorced/widowed	32	9 (28.1)	13.7 - 46.7		21 (65.6)	46.8 - 81.4	
Educational level				0.389			0.081
≤ Primary school	60	10 (16.7)	8.3 - 28.5		26 (43.3)	30.6 - 56.8	
High school	145	37 (25.5)	18.6 - 33.4		87 (60.0)	51.1 - 68.0	
> High school	18	4 (22.2)	6.4 - 47.6		11 (61.1)	35.7 - 82.7	
Employment status				0.527			0.054
Employed	44	11 (25.0)	13.2 - 40.3		18 (40.9)	50.1 - 67.4	
Unemployed	134	27 (20.1)	13.7 - 27.9		73 (59.0)	26.3 - 56.8	
Area of residence				0.033*			0.03*
Urban	194	49 (25.3)	19.3 - 32.0		114 (58.8)	51.5 - 65.8	
Suburban/rural	30	2 (6.7)	0.8 - 22.1		11 (36.7)	19.9 - 56.1	
Sampling site				0.235			0.735
Inpatients (hospital ward)	44	13 (29.5)	16.8 - 45.2		26 (59.1)	43.2 - 73.6	
Outpatient settings	180	38 (21.1)	15.4 - 27.8		99 (55.0)	47.4 - 62.4	
History of imprisonment				0.068			0.084
Yes	42	5 (11.9)	4.0 - 25.6		18 (42.9)	27.7 - 59.0	
No	182	46 (25.3)	19.1 - 32.2		107 (58.8)	51.3 - 66.0	
Sharing injection equipment				0.009*			<0.001*
No	87	13 (14.9)	8.2 - 24.2		25 (28.7)	19.5 - 39.4	
Occasionally	85	20 (23.5)	15.0 - 34.0		54 (63.5)	52.4 - 73.7	
Frequently	49	17 (34.7)	21.7 - 49.6		43 (87.8)	75.2 - 95.4	
Sexual orientation				0.49			0.03*

		Anti-HBc			Anti-HCV		
Characteristic	N tested	N (%)	95%CI	p	N (%)	95%CI	p
Heterosexual	143	34 (23.8)	17.1 - 31.6		86 (60.1)	51.6 - 68.2	
Homosexual/bisexual	12	4 (33.3)	9.9 - 65.1		3 (25.0)	5.5 - 57.2	
History of STDs				0.196			0.468
Yes	7	3 (42.9)	9.9 - 81.6		5 (71.4)	29.0 - 96.3	
No	217	48 (22.1)	16.8 - 28.2		120 (55.3)	48.4 - 62.0	
History of paid sex				0.458			0.537
Yes	26	4 (15.4)	4.4 - 34.9		13 (50.0)	29.9 - 70.1	
No	198	47 (23.7)	18.0 - 30.3		112 (56.6)	49.4 - 59.2	
Tattooing				0.867			0.646
Yes	69	14 (20.3)	11.6 - 31.7		37 (53.6)	41.2 - 75.7	
No	109	21 (19.3)	12.3 - 27.9		54 (49.5)	39.8 - 59.2	
History of traveling				0.868			0.261
Yes	77	18 (23.4)	14.5 - 34.4		47 (61.0)	49.2 - 72.0	
No	147	33 (22.4)	16.0 - 30.1		78 (53.1)	44.7 - 61.3	

CI=Confidence interval; STD=Sexually transmitted diseases; *Significant at 0.05 level

Table 3. *Logistic regression for the risk of anti-HBc and anti-HCV seropositivity*

	Anti-HBc				Anti-HCV			
Characteristic	OR	95%CI	AOR[a]	95%CI	OR	95%CI	AOR	95%CI
Male vs. female gender	1.63	0.46 - 5.83	-	-	0.72	0.27 - 1.89	-	-
Age group (one-year increase)	1.14*	1.09 - 1.20	-	-	1.15*	1.1 - 1.21	-	-
Marital status								
Single	1		1		1		1	
Married	1.88	0.72 - 4.95	0.98	0.31 - 3.16	1.94	0.82 - 4.58	1.37	0.52 - 3.59
Steady relationships	1.91	0.89 - 4.10	2.85*	1.18 - 6.88	1.28	0.68 - 2.43	1.74	0.84 - 3.60
Divorced/widowed	1.93	0.76 - 4.90	0.63	0.20 - 2.0	1.95	0.85 - 4.45	0.77	0.29 - 2.08
Educational level								
≤ Primary school	1		1		1		1	
High school	1.71	0.79 - 3.72	1.12	0.46 - 2.69	1.96*	1.07 - 3.61	1.39	0.70 - 2.74
> High school	1.43	0.39 - 5.25	0.43	0.09 - 2.06	2.05	0.70 - 6.03	0.98	0.28 - 3.39
Employed vs unemployed	1.32	0.59 - 2.95	1.86	0.76 - 4.60	0.48*	0.24 - 0.96	0.45*	0.21 - 0.99
Imprisonment (yes vs no)	0.40	0.15 - 1.08	0.64	0.22 - 1.85	0.53	0.27 - 1.04	0.86	0.10 - 1.84

	Anti-HBc				Anti-HCV			
Characteristic	OR	95%CI	AOR[a]	95%CI	OR	95%CI	AOR	95%CI
Sharing injection equipment								
No	1		1		1		1	
Occasionally	1.75	0.81 - 3.80	1.36	0.57 - 3.26	4.32*	2.28 - 8.20	4.6*	2.21 - 9.57
Frequently	3.02	1.32 - 6.95	2.34	0.92 - 5.94	17.77*	6.72 - 46.99	21.18*	7.27 - 61.64
Sexual orientation (heterosexual vs. homo/ bisexual)	1.60	0.45 - 5.65	4.3*	1.01 - 18.27	0.22*	0.06 - 0.85	0.28	0.06 - 1.22
Risk sexual behavior (yes vs no)	0.83	0.42 - 1.67	1.47	0.66 - 3.31	0.55*	0.31 - 0.98	0.89	0.46 - 1.71
Tattooing (yes vs no)	1.07	0.50 - 2.27	2.38	0.93 - 6.11	1.18	0.64 - 2.15	1.93	0.94 - 3.96
Traveling (yes vs no)	1.05	0.55 - 2.03	0.71	0.34 - 1.51	1.39	0.79 - 2.43	1.08	0.58 - 2.03

aAOR=adjusted for age and gender; *Significant at 0.05 level

DISCUSSION

After the introduction of HCV testing in 1992, PWID represent the group with the highest HCV prevalence in Croatia. Studies across Europe showed a wide range of prevalence rates from 34%-78% in Slovakia (20), 40% in Slovenia (8), 42.3-75% in Germany (21), 43.3%-61.3% in Greece (22), 48% in Sweden (23) 52.5% in Bosnia and Herzegovina (24), 53% in Montenegro (25), 59% in Poland (26), 66.8% in Denmark (9), 68.3%-83.2% in Italy (7, 27), 70.5% in Portugal (28), 71.4%-81.3% in Luxembourg (29, 30), 73.9% in Bulgaria (31), 80% in Lithuania (32), 84.2%-88% in Spain (33, 34), 86.5% in Sweden (35), 88.9% in Romania (36), 94.6% in Russia (37) to 96,2% in Estonia (10).

In Croatia, several regional studies conducted from 2001 to 2010 addressed the seroprevalence of HCV in PWID which differed greatly. Significantly higher prevalence was reported in the Split region (65%) (38) compared to Zadar (59%) (16), Zagreb (51.3%) (18), and Rijeka (29%) (38). As in previous Croatian studies, this study found significant geographical differences in HCV prevalence. The highest seroprevalence rate (75.5%) was found in Istria County (Pula) compared to 49.1% in the City of Zagreb/Zagreb County and 52.2% in Brod-Posavina County. According to the data from the National Register of Persons Treated for Psychoactive Drug Abuse (2019), the highest rate of addiction per 100,000 inhabitants was recorded in Istria County (505.7), which reported the highest HCV seropositivity in this study. In the City of Zagreb, Zagreb County, and Brod-Posavina County, addiction rates were 348.3, 131.8, and 105.1, respectively (39). Pula is a tourist destination located on the Adriatic coast with a higher movement of people and goods, which may be the reason for the higher HCV seroprevalence rate compared to continental areas of the country.

Regarding the anti-HBc prevalence, the prevalence of 22.8% among Croatian PWID is comparable to that of Slovenia (17.5%) (8) and Luxembourg (21.6%) (29). In the number of European countries, higher prevalence rates were reported from 40.2%-53% in Germany (40-42), 50% in Switzerland (43), 50.2% in Denmark (9), 55.6% in Romania (36), 70.4% in Italy (7) to a very high of 85.1% in Estonia (10). Similar to the prevalence of HCV infection, there were also significant geographical differences in HBV prevalence in Croatia (17.9%-38.8%). Compared with a previous Croatian study, this study showed a higher anti-HBc prevalence in the Zagreb region (17.7% *vs* 13%). In Rijeka and Split, prevalence rates were 9% and 31%, respectively (38).

Active HBV infection (HBsAg positive) was found in 0.9% of Croatian PWID. A wide range of HBsAg prevalence was reported in other European countries: 0.8% in Bosnia and Herzegovina (24), 0.9% in Denmark (9), 1.4% in Montenegro (25), 2.5% in Slovenia (8), 7% in Spain (34), and 21.3% in Estonia (10).

As reported in other studies (8, 23, 30), both anti-HBc and anti-HCV prevalence in Croatia increased significantly with age. While anti-HBc positivity increased gradually, anti-HCV positivity increased sharply from

24.6% in PWID less than 30 years to 59.6% in PWID aged 30-39 years, with a further continuous increase of up to 92.9% in PWID older than 50 years.

In addition, seroprevalence rates correlated with injecting risk behaviors. Statistically significant differences in prevalence were found in PWID who reported sharing equipment (anti-HBc 23.5%-34.7% *vs* 14.9%, anti-HCV 63.5%-87.8% *vs* 28.7%). PWID from urban areas was more often seropositive (anti-HBc 25.3%, anti-HCV 58.8%) than PWID from suburban/rural areas (anti-HBc 6.7%, anti-HCV 36.7%). The higher seroprevalence in urban areas may be explained by better drug availability.

Educational level was not associated with the prevalence of HBV and HCV markers in the Croatian PWID cohort, whereas in Sweden lower educational level was found to be a risk factor for HCV seropositivity (23).

Some studies have found a higher prevalence of HBV or HCV infection in PWID with a history of imprisonment (30, 40, 44). In a large European multicenter study, a correlation between HCV seropositivity and history of incarceration was observed with HCV prevalence rates reaching 91.4% in individuals who reported staying in prison (45). In contrast, our study found no difference in anti-HBc and anti-HCV among PWID who reported staying in prison and those who did not.

Regarding sexual risk behaviors, a significant association was found between anti-HCV prevalence in heterosexuals compared to homo/bisexuals (60.1% *vs* 25.0%). Although higher prevalence rates were reported in PWID with a history of STDs (anti-HBc 42.9% *vs* 22.1%, anti-HCV 71.4% *vs* 55.3%), the small numbers did not allow to reach the statistical difference.

Tattoos are very common among PWID (48.7% of Croatian PWID reported tattooing), which may also contribute to HBV and HCV transmission (46). Our results showed no significant difference in the seroprevalence rates in PWID who had been tattooed.

Another possible risk factor for HBV and HCV acquisition may be traveling to areas where these infections are endemic. In a study from San Francisco conducted among young PWID, travelers were more likely to be HCV-positive than non-travelers (47). This study showed no significant difference in HBV and HCV seropositivity between PWID with a history of traveling and long stays abroad and those who denied traveling.

An earlier Croatian study from Brod-Posavina County (2002-2009) showed significantly higher prevalence rates of HBV and HCV markers among PWID treated in therapeutic communities compared to outpatients (HBsAg 3.28% *vs* 1.16%, anti-HCV 60.66% *vs* 41.86%) (17). This study showed no significant difference in anti-HBc or anti-HCV positivity among patients treated at psychiatric hospital wards and outpatients.

The logistic regression results showed that among Croatian PWID, both HCV and HBV infections were significantly associated with increasing age, needle-sharing behaviors, and residence in an urban area.

CONCLUSIONS

The results of this study showed that PWID still represents a high-risk group for both HBV and HCV infection in Croatia. Prevalence rates differed significantly between regions and correlated strongly with age and syringe/needle sharing frequency.

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S A Ž E T A K

BILJEZI KRVLJU PRENOSIVIH VIRUSA HEPATITISA U INTRAVENSKIH KORISNIKA DROGA U HRVATSKOJ: PREVALENCIJA I RIZIČNI FAKTORI

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Intravenski korisnici droga (engl. *people who inject drugs*; PWID) predstavljaju visoko rizičnu skupinu za infekciju virusom hepatitisa C (HCV) i hepatitisa B (HBV). Ukupno 224 PWID iz tri geografski udaljene hrvatske regije (tri kontinentalne i jedne primorske županije) testirano je na biljege krvlju prenosivih virusa hepatitisa: hepatitis B površinski antigen (HBsAg), protutijela na hepatitis B core antigen (anti-HBc) te protutijela na HCV (anti-HCV). Probir bolesnika i uključenje u istraživanje učinjeni su na psihijatrijskim bolničkim odjelima (19,6%) te centrima za dobrovoljno HIV savjetovanje i testiranje (80,4%). Serološko testiranje učinjeno je pomoću komercijalnog imunoeznimskog testa s fluorescentnom detekcijom. Uzorci opetovano reaktivni na HBsAg dodatno su testirani metodom s "neutralizacijskim protutijelima". Početno reaktivni anti-HCV uzorci seruma su potvrđeni pomoću immunoblot testa treće generacije. Ukupna prevalencija HBsAg, anti-HBc i anti-HCV iznosila je 0,9% (95%CI=0,1-3,2); 22,8% (95%CI=17,4-28,2) te 55,8% (95%CI=49,0-62,4). Uočene su značajne regionalne razlike kako u prevalenciji anti-HBc (17.9-38.8%, p=0.01), tako i u prevalenciji anti-HCV (49,1-75,5%, p=0,007). Prevalencija anti-HBc je rasla postupno s porastom dobi od 21,3% do 64,3%, počevši s dobnom skupinom od 30 do 39 godina (p<0,001). Za razliku od postupnog porasta seroprevalencije HBV-a, uočen je nagli porast anti-HCV seroprevalencije od 24,6% u PWID mlađih od 30 godina do 59,6% u dobnoj skupini 30-39 godina, nakon čega je daljnji porast seropozitiviteta bio postupan do 92,9% u PWID starijih od 50 godina (p<0,001). Zajedničko korištenje pribora za i.v. korištenje droga je značajno koreliralo s HBV i HCV seropozitivitetom. Statistički značajno više stope seroprevalencije dokazane su u PWID koji su naveli podatak o čestom ili povremenom dijeljenju pribora za i.v. korištenje droga (anti-HBc 34,7/23,5% naspram 14,9%, p=0,009; anti-HCV 87,8/63,5% naspram 8,7%, p<0,001). Ispitanici iz gradskih područja su bili češće seropozitivni u odnosu na ispitanike iz prigradskih/seoskih područja (anti-HBc 25,3% naspram 6,7%, p=0,033; anti-HCV 58,8% naspram 36,7%, p=0,03). Heteroseksualne osobe su imale višu HCV seroprevalenciju u odnosu na homo/biseksualne odnose (60,1% naspram 25,0%; p=0,03). Spol, stručna sprema, bračni status, radni status, boravak u zatvoru, tetoviranje te putovanja izvan Hrvatske kao i rizično spolno ponašanje nisu bili povezani s HBV i HCV seropozitivitetom.

Ključne riječi: Hepatitis B, hepatitis C, osobe koje injiciraju droge, seroprevalencija, rizični faktori, Hrvatska.

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SAŽETAK

Zarazne bolesti i u moderno doba predstavljaju važan izvor morbiditeta i mortaliteta kako u razvijenim, tako i u nerazvijenim zemljama. Važan način prekograničnog prijenosa mikroorganizama jesu migracije ljudi, životinja i vektora. Mobilnost ljudi obuhvaća širok dijapazon kretanja, od turističkih putovanja, socioekonomski uvjetovanih selidbi, do silom uvjetovanih razmještanja ljudi zbog prirodnih katastrofa ili ratnih, odnosno oružanih sukoba. Nažalost, posljednjih godina imamo brojne primjere prisilne migracije ljudi, od sada već dugogodišnjeg priljeva migranata u Europu do razmještaja izbjeglica iz ratom pogođene Ukrajine. Ovakve migracije mogu direktno pogodovati širenju zaraznih bolesti zbog povećanog rizika za obolijevanjem u migrantskoj populaciji te uvođenja mikroorganizama u podneblja s povoljnijom epidemiološkom situacijom. Nadalje, nisu samo migracije ljudi važan način širenja zaraznih bolesti, već je isto slučaj i za migracije životinja koje su domaćini različitih patogena te vektora, prijenosnika bolesti, na što značajno mogu utjecati i aktualne klimatske promjene. Zbog sve većih migracija ljudi potrebno je pratiti epidemiološku situaciju u svijetu te nadzirati prekogranično širenje bolesti.

Ključne riječi: Migracije, biosigurnost, pandemije, zarazne bolesti, vektori

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UVOD

Zarazne bolesti te njihovi uzročnici od pamtivijeka značajno utječu na morbiditet i mortalitet ljudi. Od deset glavnih uzroka smrti globalno u 2019. godini čak tri se odnose na zarazne bolesti, uključujući infekcije donjeg dijela dišnog sustava, dijarealne bolesti te stanja povezana s neonatalnom smrtnosti. Međutim, ako pogledamo statistiku vodećih uzroka smrtnosti u zemljama s niskim socioekonomskim statusom, tada se čak njih šest od deset odnosi na zarazne bolesti (1). Radi sve većih mogućnosti kretanja ljudi, važno je poznavati epidemiološke prilike u različitim regijama svijeta te pratiti prekogranično širenje zaraznih bolesti.

Danas, nakon intenzivnog razdoblja globalne pandemije bolesti COVID-19, znamo da i samo jedan uzročnik zarazne bolesti može zaustaviti cijeli svijet te u kratkom vremenu ubiti milijune ljudi. Jasno je da za ovakav utjecaj moramo imati ispunjene određene uvjete, od virulentnosti i zaraznosti uzročnika te prijemčivosti domaćina, jednostavnog načina prenošenja, nemogućnosti sprječavanja širenja patogena i zaraze ljudi do nedostupnosti učinkovite prevencije i specifičnog liječenja. U današnje vrijeme globalne mobilnosti pandemijski ili epidemijski potencijal određenih patogena osobito dolaze do izražaja zbog brzog širenja iz države u državu te s kontinenta na kontinent. I sama zaraza SARS-CoV-2, koja je započela kao lokalna epidemija u Kini, ubrzo se proširila na ostatak svijeta upravo zbog sve veće mobilnosti ljudi. Naravno da COVID-19 nije prva pandemija koja je pogodila čovječanstvo, ali zasigurno je najvažnija koja se dogodila u posljednjih 100 godina (Tablica 1.). Nakon što je Svjetska zdravstvena organizacija proglasila kraj pandemije u svibnju 2023. godine predstoji nam vrijeme razmišljanja o naučenim lekcijama te u radu na našoj boljoj spremnosti za buduće ugroze (2). Osobito treba naglasiti da spremnost ne smijemo graditi samo za visokopatogene uzročnike s pandemijskim potencijalom, već i za svakodnevne prijetnje širenja pojedinih zaraznih bolesti zbog sve češćih migracija ljudi.

Nadalje, nisu samo migracije ljudi pod rizikom širenja zaraznih bolesti, već je isto slučaj i za migracije životinja koje su domaćini pojedinih patogena te vektora, prijenosnika bolesti, na što značajno mogu utjecati i aktualne klimatske promjene.

MIGRACIJE U PROŠLOSTI

Kroz povijest kretanje ljudi imalo je ključnu ulogu u prijenosu zaraznih bolesti te su migracije stanovništva mahom bile uzrokovane trgovinom, ratovima te iseljavanjem zbog gladi i neimaštine. Kako su se migracije povećavale te sve veći broj ljudi putovao, tako je i potencijal širenja zaraznih bolesti rastao. Jedan od najvažnijih patogena u povijesti, *Yersinia pestis* – uzročnik kuge, uzrokovao je nekoliko smrtonosnih pandemija (3). Prva jasno opisana pandemija kuge bila je Justinijanova kuga u 6. stoljeću, koja je najvjerojatnije krenula iz Egipta te se trgovačkim putevima širila na zapad do Europe. Pandemija je najviše zahvatila područja sjeverne Afrike, Europe te južne i središnje Azije ubivši 50 – 60 % stanovništva. Druga pandemija kuge, također poznata kao Crna smrt ili Velika kuga, pojavila se u 14. stoljeću u Kini, a zatim se proširila na zapad velikim kopnenim i morskim trgovačkim putovima. Mongoli su također pretrpjeli velike žrtve zbog kuge te su morali odustati od opsade grada Kafe na Krimu, koji je u to vrijeme bio đenoveška kolonija. Prije napuštanja svojih položaja Mongoli su preko zidina katapultirali tijela umrlih od kuge i gnijezda štakora, što je dovelo do izbijanja zaraze unutar grada. Godine 1347. trgovci iz Genove i Venecije prenijeli su posljedično kugu i u sredozemne luke. Bolest se polako i neizbježno širila od grada do grada preko zaraženih štakora i ljudi te na kraju dovela do smrti 20 do 30 milijuna ljudi samo u Europi. Već je tada, i prije otkrića mikroorganizama kao uzročnika bolesti, primijećeno da su za širenje bolesti odgovorni putnici koji su bolest donosili iz drugih područja svijeta te su se lučki i trgovački gradovi pokušali zaštititi od prijenosa zaraze na svoje stanovništvo. S obzirom na to da specifične zaštite od zaraze te liječenje nisu bili dostupni, jedini način sprječavanja bolesti bio je smanjiti izloženost ljudima i robom koji su potencijalno bili inficirani, odnosno kontaminirani. Karantena (od talijanskog „*quaranta*“, što znači 40) je prvi put uvedena 1377. godine u Dubrovniku, a označavala je izolaciju ljudi i robe izvan grada na 40 dana kako bi se omogućio razvoj bolesti u slučaju perioda inkubacije te dezinfekcija predmeta. Također se pratilo izbijanje bolesti u drugim regijama te su u slučaju javljanja epidemije gradovi bili zatvoreni za brodove i trgovce iz zahvaćenih regija.

Nakon otkrivanja Novog svijeta 1492. godine Europljani su na domicilno stanovništvo Sjeverne Amerike prenijeli difteriju, gripu, ospice, zaušnjake, šarlah, velike boginje, tifus i žutu groznicu, što je dovelo do smrti više od polovice nativnog američkog stanovništva (4).

Tijekom ranog 19. stoljeća kolera se iz sjeveroistočne Indije proširila na Cejlon, Afganistan i Nepal. Tijekom narednih godina proširila se na Europu, Kanadu i SAD te uzrokovala nekoliko velikih pandemija s milijunima žrtava, od kojih posljednja, 7. pandemija, još uvijek traje (5).

Tablica 1. *Najvažniji uzročnici epidemija/pandemija kroz povijest*

Bolest	Uzročnik	Razdoblje	Broj žrtava (u milijunima)
Kuga	*Yersinia pestis*	2. stoljeće	5
		6. stoljeće	25
		14. stoljeće	75 – 200
Kolera	*Vibrio cholerae*	1817. – 1824. (1. pandemija)	3
		1852. – 1860. (3. pandemija)	1
		1910. – 1911. (6. pandemija)	1
Gripa	virus influence	Španjolska gripa, 1918.	20 – 50
		Azijska gripa, 1956. – 1958.	2
		Hong Kong, 1968.	1
AIDS	HIV	1980 –	40
COVID-19	SARS-CoV-2	21. stoljeće	6

Najvažnije pandemije u posljednjih 100 godina mahom su uzrokovane virusima. Najrazornija pandemija 20. stoljeća, epidemija španjolske gripe 1918. i 1919. godine, ubila je više od 50 milijuna ljudi diljem svijeta, značajno više nego što je bilo umrlih u Prvom svjetskom ratu (6). Uz virus gripe koji je u narednom razdoblju uzrokovao još nekoliko značajnih epidemija, još je jedan virus postao važan javnozdravstveni problem, virus humane imunodeficijencije (HIV), koji se u krakom vremenu iz Sjedinjenih Američkih Država (SAD) proširio na cijeli svijet.

MIGRACIJE DANAS

Mobilnost ljudi obuhvaća širok spektar kretanja, od turističkih putovanja, socioekonomski uvjetovanih selidbi, do silom uvjetovanih razmještanja ljudi zbog prirodnih katastrofa ili ratnih, odnosno oružanih sukoba. Trenutna je procjena Ujedinjenih naroda da globalno danas u svijetu imamo oko 281 milijun međunarodnih migranata, što odgovara 3,6 % svjetske populacije (7). Ove su brojke za 128 milijuna više nego 1990. godine i više od tri puta veće od procijenjenog broja 1970. godine. S druge strane, broj međunarodnih turističkih dolazaka diljem svijeta udvostručio se u 2022. godini u odnosu na prethodnu godinu, s najvećim brojem dolaznih putnika u Europi, koji se procjenjuje na 594,5 milijuna (8). Isto tako, građani Europske unije (EU) putuju u druge dijelove svijeta, što sa sobom nosi određene medicinske rizike ovisno o odredišnoj zemlji i lokalnoj epidemiološkoj situaciji. Najbolji primjer kako putovanja mogu utjecati na prijenos zaraznih bolesti imamo od COVID-19 pandemije, kada se virus zaraženim putnicima ubrzo proširio iz Kine u sve ostale dijelove svijeta. Čak ni stroge epidemiološke mjere koje su bile na snazi u pojedinim državama nisu uspjele spriječiti širenje SARS-CoV-2 virusa. Nadalje, nedavna agresija Rusije na Ukrajinu uvjetovala je jedan od najvećih migrantskih valova posljednjih godina te se procjenjuje da je iz Ukrajine u vrlo kratkom vremenu izbjeglo više od šest milijuna ljudi, najvećim dijelom u države EU-a, uključujući i Hrvatsku. Također, sve veći zahtjevi za radnom snagom uvjetovali su priljev stranih radnika iz mahom nerazvijenih zemalja, što također nosi sa sobom određene rizike vezane za unos određenih zaraznih bolesti koje su endemske u zemljama odlaska. Visokorazvijene zemlje već se dugi niz godina bore s izazovom otvaranja svog tržišta rada stranim radnicima, a uz zahtjev održavanja javnog zdravstva te sprječavanja širenja pojedinih zaraznih bolesti. Prije odobravanja dozvole boravka navedene zemlje traže medicinske potvrde te preglede kako bi se isključile najvažnije zarazne bolesti od javnozdravstvenog interesa. Sam pristup probiru razlikuje se od zemlje do zemlje, ovisno o testovima koji se koriste te roku testiranja, ovisno o tome traže li se rezultati testiranja prije dobivanja dozvole ili nakon preseljenja (9). Hrvatska je tek nedavno počela širom otvarati svoje tržište stranoj radnoj snazi te smo, primjerice, ne tako davne 2017. godine izdali samo 7000 radnih dozvola za strance. Od kada su ukinute kvote stranih radnika u siječnju 2021. godine, ta se brojka značajno promijenila te je u Hrvatskoj samo u prva tri i pol mjeseca 2023. godine već izdano 47 tisuća radnih dozvola za strane radnike (10). Od ukupnog broja radnih dozvola iz inozemstva njih oko 60 % još se uvijek odnosi na zemlje iz regije, međutim broj radnika iz dalekih zemalja porastao je na gotovo 40 %. Ovakve promjene u broju stranih državljana koji borave na području Republike Hrvatske na duže vrijeme sa sobom nose potencijalni rizik širenja pojedinih zaraznih bolesti. Osim stranih radnika koji službeno dolaze u razvijenije zemlje radi zapošljavanja, veliki izazov za organizacijom zdravstvene skrbi predstavljaju i ilegalni migranti koji na područje Europe dolaze putem nekoliko migrantskih ruta. Prema podacima Frontexa, Agencije za europsku graničnu i obalnu stražu, većina migranata koji ilegalno prelaze granicu prema EU-u zabilježena je na srednjoj sredozemnoj ruti, koja uključuje zemlje poput Italije i Malte (11). Za Hrvatsku je najvažnija Balkanska ruta, koja prolazi kroz Grčku i Tursku prema zemljama zapadne Europe. Ilegalni migranti pod povećanim su rizikom obolijevanja od brojnih bolesti, uključujući zarazne bolesti. Brojni su razlozi zašto je ova skupina osobito podložna zaraznim bolestima, od rizičnih faktora koji utječu na zaražavanje prije puta, preko uvjeta tijekom migracije do faktora koji utječu na razvoj zaraznih bolesti u zemlji dolaska (12). Od rizičnih faktora prije migracije, najvažniji su prevalencija određene zarazne bolesti u matičnoj zemlji te razvijenost javnozdravstvenog sustava, što utječe na razinu zdravstvene skrbi te procijepljenost stanovništva. Tijekom migracije rizični faktori uključuju pothranjenosti i stres, nedostupnost preventivne medicine i zaziranje od traženja zdravstvene skrbi, prenapučenost u kampovima ili drugim privremenim skloništima, nisku razinu higijene, nasilje (osobito seksualno nasilje) te neadekvatnu kontrolu mogućih kroničnih stanja (npr. dijabetes). Neregularne migracije koje su povezane s nesigurnim uvjetima putovanja povećavaju rizik od izloženosti nasilju, trgovini ljudima, prenapučenim životnim uvjetima i prijenosu infekcija izravnim kontaktom, krvlju i zrakom, a regu-

larne migracije s planiranim kretanjem imaju niži rizik od izloženosti zaraznim bolestima tijekom tranzita.

Nakon nastanjenja u zemlju dolaska na zdravlje migranta mogu utjecati kulturna uvjerenja, stigmatizacija i marginalizacija, jezična barijera te dostupnost zdravstvene skrbi. Treba naglasiti da povećani rizik zaražavanja postoji i u narednom razdoblju nakon smještaja zbog povremenih putovanja u matične zemlje u posjet prijateljima ili rodbini, osobito za malu djecu koja nemaju imunitet za određene endemske zarazne bolesti.

Zarazne bolesti koje se najviše spominju kao važne u planiranju održavanja zdravlja migranata su tuberkuloza, hepatitis B i C, HIV te pojedine zarazne bolesti koje se mogu spriječiti cijepljenjem, kao što su polio i ospice (13). Zbog svega navedenoga, migrantska kriza potaknula je žustre lokalne, nacionalne i međunarodne rasprave o riziku od zaraznih bolesti koji migranti predstavljaju za zemlje i građane koji im pružaju utočište. Doseljavanje stranaca u brojnim je zemljama promijenilo dotadašnju epidemiološku situaciju, tako da su određene zarazne bolesti u domicilnom stanovništvu postale rijetkost, ali njihov je broj u doseljenicima visok. Tako je primjerice broj oboljelih od tuberkuloze u osoba rođenih u primjerice Danskoj ili Luksemburgu u odnosu na sve prijavljene u tim državama nizak (14). Naime, u Luksemburgu je više od 90 % slučajeva tuberkuloze otkriveno u stranih državljana. Nadalje, infekcija HIV-om u migrantskoj populaciji u pojedinim je zemljama EU-a visoka, pa primjerice u Francuskoj 68 % svih novootkrivenih HIV zaraženih osoba otpada na osobe koje su rođene izvan Francuske. Kako bi se aktivno pristupilo smanjenju učestalosti pojedinih zaraznih bolesti od javnozdravstvenog interesa, brojne zemlje imaju organizirane programe probira. Tako primjerice Australija, Kanada, Novi Zeland, Ujedinjeno Kraljevstvo i SAD zahtijevaju probir prije dolaska i liječenje aktivne tuberkuloze za sve podnositelje zahtjeva za useljenike. Ovakvi su programi aktivnog probira na tuberkulozu u SAD-u i Ujedinjenom Kraljevstvu rezultirali smanjenom stopom aktivne tuberkuloze među migrantima u prvoj godini nakon dolaska.

Ne manje važan problem predstavlja doseljavanje osoba za koje nije poznat cjepni status ili nisu cijepljene protiv zaraznih bolesti. Prema nedavnim podacima o seroprevalenciji, kod izbjeglica koje žive u Njemačkoj, iako su uočene visoke stope imuniteta među odraslima, djeca uglavnom nisu imuna na glavne infekcije koje se mogu spriječiti cjepivom (15). Cjepni status novopridošlih migranata često nije dostupan zbog nedostatka dokaza o prethodnom cijepljenju, stoga većina zemalja domaćina preporučuje cijepljenje migranata protiv ospica, rubele, difterije, tetanusa, dječje paralize i *Haemophilusa influenzae* tipa b (Hib) na prihvatnim mjestima kako bi se spriječile i ograničile epidemije.

MIGRACIJE ŽIVOTINJA

Uz migracije ljudi, rizik za prijenosom zaraznih bolesti postoji i kod migracija i/ili selidbe divljih i domaćih životinja koje su domaćini određenim virusima, bakterijama ili parazitima. Odnos životinja i ljudi u prijenosu bolesti od iznimno je velike važnosti te se procjenjuje da je 60 % infektivnih bolesti zoonotskog podrijetla (16). Već je odavno poznato kako pojedine životinjske vrste mogu proputovati i više desetaka tisuća kilometara godišnje radi osiguravanja hrane i sigurne lokacije za razmnožavanje i podizanje mladunčadi. Migracije životinja u više su navrata povezane sa širenjem infektivnih bolesti, uključujući epidemije Ebola virusa, virusa Zapadnog Nila, virusa gripe i borelioze (17). Ptice su životinjska vrsta koja ima visoki zoonotski potencijal te svojim kretanjima mogu pogodovati širenju zaraznih bolesti. Naime, tijekom migracija ptice se često zaustavljaju na određenim područjima radi odmora i hranjenja. Ovakva okupljališta velikog broja i vrsta ptica u kratkom vremenu otvaraju mogućnost širenja zaraze među istim, ali i prijenosa zaraze na druge vrste ptica. Tako je primjerice zaljev Delaware, koji se nalazi na sjeveroistoku SAD-a, često stanište migratornih ptica koje svake godine migriraju između arktičkih područja i Južne Amerike te se godišnje tamo okuplja više od 1,5 milijuna ptica. Prevalencija ptičjih virusa gripe u ovoj je ekološkoj niši čak 17 puta veća nego u sličnim nadzornim punktovima u svijetu (18). Radi sve veće urbanizacije i ekspanzije poljoprivrede, ptice na svojim migratornim putevima imaju na raspolaganju sve manji broj lokacija zaustavljanja, što dovodi do povećane gustoće ptica na preostalim lokacijama te većoj mogućnosti prijenosa zaraze. Nadalje, sve veće prodiranje ljudi u staništa divljih životinja povećava mogućnost kontakta te infekcije ljudi i domaćih životinja.

Možda najbolji primjer širenja zarazne bolesti putem migracije životinja predstavlja širenje virusa Zapadnog Nila na području Sjeverne Amerike, koji je pratio glavni koridor za ptice selice od New Yorka do obale Atlantika od 1999. do 2000. godine (19). Zaraza virusom Zapadnog Nila do tada nije bila opisana na području zapadne hemisfere, a već dvije godine nakon širenja u

SAD-u infekcije su potvrđene u Kanadi i Meksiku. Prije pojave prvih ljudskih slučajeva zaraze primijećeno je značajno ugibanje ptica, osobito vrana, i to u blizini zoološkog vrta u četvrti Bronx u New Yorku. Uz divlje ptice, uginuća su opisana i u više vrsta ptica u samom zoološkom vrtu. Premda izvor epidemije nije sa sigurnošću potvrđen, vjeruje se kako su to bile ptice selice. Kao što je to bio slučaj i u nekoliko europskih epidemija, kao glavni vektor zaraze u New Yorku prepoznat je ornitofilni komarac *Culex pipiens*.

Uz migracije ptica, zoonotski potencijal opisan je i za migratorna kretanja šišmiša koji se hrane voćem. Naime, vjeruje se kako je uzrok epidemije virusa Ebole koja je zahvatila Demokratsku Republiku Kongo 2007. godine kontakt domicilnog stanovništva s migratornim voćnim šišmišima (20). Epidemiološkim izvidom prikupljene su informacije o neobično velikom broju ove vrste šišmiša koji su na to područje došli na putu migracije prema jugoistoku. Ovi su šišmiši cijenjena hrana među domicilnim stanovništvom, koje ih tijekom perioda obitavanja na tom području masovno izlovljava. Prva ljudska žrtva epidemije bio je seljanin koji je kupio svježe ubijene šišmiše od lokalnog lovca. U razdoblju od svibnja do studenog 2007. godine otkriveno je 260 slučajeva zaraze, a nažalost kod 186 pacijenata došlo je do smrtnog ishoda.

MIGRACIJE VEKTORA

Kukci, osim što su molestanti, mogu biti i važni prenosioci zaraznih bolesti. U ovu grupu vektora spadaju brojne vrste kukaca, ali medicinski su najznačajniji komarci i krpelji. Patogeni koji se prenose putem vektora ograničeni su na određena endemska područja koja podržavaju život i razmnožavanje pojedinih kukaca. Klimatske promjene značajno utječu na preživljavanje vektora te globalno zatopljenje direktno utječe na njihovu rasprostranjenost i brojnost (21). Porast temperature okoliša, uz podržavanje razmnožavanja i preživljavanja vektora, može utjecati i na ubrzanu replikaciju vektora te posljedično poduprijeti prijenos zaraze, stoga ne čudi što je posljednjih godina opisan povećani broj zoonoza koje se prenose vektorima. Nadalje, došlo je širenja određenih zoonoza na područje europskog kontinenta, koje su ranije bile ograničene na tropske dijelove svijeta. Takav su primjer pojava virusnih zoonoza groznice dengue, chikungunya i Zika koje prenose komarci iz roda *Aedes*, a posljednjih godina pojavljuju se i u Europi. Ispunjenje uvjeta za prijenos ovih bolesti omogućilo je nastanjivanje komaraca *Aedes albopictus,* poznatog i kao tigrasti komarac, iz Afrike u Europu putem automobilskih guma (22). Međutim, njihovo se stanište u posljednje vrijeme širi iz toplijih dijelova južne Europe prema sjeveru te su pronađeni i u Belgiji, Nizozemskoj i Velikoj Britaniji (23). Među prije navedenim virusnim bolestima koje se prenose vektorima, najvažnija je dengue groznica, od koje godišnje oboli oko 400 milijuna ljudi, pretežito u tropskim i suptropskim regijama svijeta. Međutim, 2010. godine otkriveni su prvi slučajevi autohtonog prijenosa ove virusne zoonoze na području Europe s nekoliko opisanih slučajeva u Francuskoj i Hrvatskoj (24, 25). Nažalost, ova se bolest nastavila širiti na europskom tlu te je 2012. godine došlo do izbijanja velike epidemije dengue groznice u regiji Madeira u Portugalu, gdje je zabilježeno čak 2000 oboljelih.

Chikungunya virus ima sličan obrazac prijenosa kao i virus dengue te dijele zajednički vektor, komarce roda *Aedes*. Kao što je to bio slučaj i za virus dengue, i chikungunya virus mahom je uzrokovao epidemije u Africi i Aziji, ali je nažalost na područje Europe uveden 2007. godine (26). Epidemija je započela u kolovozu 2007. godine u Italiji u dva mala grada u okolici Ravene, u pokrajini Emilia Romagna, na jadranskoj obali. Virus je unio putnik koji se vratio iz jugozapadne Indije te se virus brzo lokalno proširio. Potvrđeno je više od 200 oboljelih osoba. Od tada endemski prijenos zaraze opisan je i u drugim zemljama Europe te broj prijavljenih slučajeva raste iz godine u godinu.

Tako su tijekom 2010. i 2014. godine prijavljeni autohtoni slučajevi i u Francuskoj, a 2017. godine opisana je nova epidemija u Italiji s više od 400 zaraženih (27).

Rizik od širenja virusa chikungunya u EU-u visok je zbog mogućeg unosa putem zaraženih putnika, prisutnosti kompetentnih vektora u mnogim zemljama (osobito oko obale Sredozemnog mora) i osjetljivosti stanovništva.

S obzirom na to da na području Europe imamo ispunjene sve kriterije za epidemijsko pojavljivanje spomenutih virusnih groznica, uz daljnji rast temperatura okoliša za očekivati je sve češće izbijanje vektorskih zoonotskih zaraza u budućnosti.

Dok su zasad komarci najvažniji prijenosnici brojnih zaraznih bolesti u tropskim krajevima, na području Europe najvažniji vektori su krpelji. Brojnost krpelja sve je veća zbog ljudskog djelovanja i klimatskih promjena te se oni danas mogu naći na višim nadmorskim visi-

nama nego je to bio slučaj u prošlosti. Krimsko-kongoanska hemoragijska groznica prenosi se putem krpelja te je jedna od najčešćih virusnih zoonoza koju prenose ovi vektori. Tradicionalno se ova bolest javljala na području Balkana i pojedinim istočnoeuropskim zemljama. Međutim, postoji trend širenja endemskog područja te je lokalni prijenos dokazan i u Portugalu, Španjolskoj, Nizozemskoj i Njemačkoj (28).

Uz klimatske promjene koje pogoduju širenju i razmnožavanju vektora sve češći prijevoz životinja i migracije ljudi mogu dovesti do infekcije postojećih vektora na nekom području. Tako je primjerice epidemija malarije u Grčkoj u razdoblju od 2009. do 2011. godine započela prvim slučajevima infekcije parazitom *Plasmodium vivax* kod dvoje pacijenata koji su dolazili iz endemskih zemalja (Pakistan i Afghanistan) te se zaraza posljedično širila zaražavanjem lokalnih komaraca (29). Grčka je bila proglašena zemljom bez malarije još davne 1973. godine, kada je bio zabilježen zadnji autohtoni prijenos zaraze, premda su zbog velikog broja migranata svake godine bilježili oko 40 importiranih slučajeva. Upravo radi ovog primjera važno je uspostaviti pojačani nadzor nad populacijom komaraca te uspostaviti mjere suzbijanja vektora. Ne manje važno, potrebno je u diferencijalnoj dijagnostici razmišljati i o bolestima koje do sada nisu bile endemske na području Europe kako bi se napravila brza dijagnostika te spriječilo širenje zaraze.

ZAKLJUČAK

Mobilnost i migracije ljudi, životinja i vektora važan su čimbenik u širenju zaraznih bolesti. Radi jednostavnog prekograničnog prijenosa infektivnih bolesti od javnozdravstvenog interesa važno je nadzirati i pratiti rizik širenja zaraze na nacionalnoj i međunarodnoj razini, stoga svaka država mora imati razrađene standardne postupke prilikom doseljavanja ljudi te mogućnost detekcije i otkrivanja ne samo zaraznih bolesti koje se endemski pojavljuju u toj državi, već i ostalih infektivnih bolesti koje se migracijom ljudi mogu pojaviti u određenoj populaciji.

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SUMMARY

THE IMPACT OF MIGRATION ON THE SPREAD OF INFECTIOUS DISEASES

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Even in modern times, infectious diseases represent an important source of global morbidity and mortality in both developed and underdeveloped countries. Namely, of the ten leading causes of death globally in 2019, three were attributed to infectious diseases. An important mode of cross-border transmission of infectious diseases is the migration of people, animals and vectors. According to the current estimate by the United Nations, there are approximately 281 million international migrants globally, which corresponds to 3.6 % of the world's population. Throughout history, numerous epidemics and pandemics that spread over different continents have been described. However, today, the pandemic or epidemic potential of certain pathogens is particularly emphasized due to the possibility of fast the spread of disease around the world. The SARS-CoV-2 infection itself, which started as a local epidemic in China, soon spread to the rest of the world precisely because of the increasing possibilities of human migration. In earlier times, pandemics were mostly caused by bacterial pathogens. However, with the improvement in hygiene standards and the progress in the field of medicine in the last 100 years, especially with the discovery of antibiotics, epidemics have primarily been caused by viruses. Furthermore, the risk of spreading infectious diseases is not only attributed to migrations of people, but the same is true for migrations of animals that are reservoirs of certain pathogens and vectors, carriers of diseases. The relationship between animals and humans in disease transmission is extremely important, and it is estimated that 60% of infectious diseases are of zoonotic origin. Animal migrations, especially migrations of birds and bats, have been repeatedly linked to the spread of infectious diseases, including outbreaks of the Ebola virus, West Nile virus and influenza virus.

Insects, in addition to being a nuisance, can also be important vectors of infectious diseases. This group of vectors includes numerous insect species, but the most medically significant are mosquitoes and ticks. Vector-borne pathogens are limited to specific endemic areas that support the life and reproduction of individual insects. Climate change significantly affects the survival of vectors, and global warming directly affects their distribution and abundance.

Due to the ever-increasing migration of people, it is necessary to closely follow the epidemiological situation in the world and monitor the cross-border spread of diseases.

Keywords: migration, biosecurity, pandemics, infectious diseases, vectors

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ZAŠTITA PITKE VODE OD BIOTERORIZMA

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Sažetak:

Bioterorizam, odnosno raznovrsni napadi biološkim agensima, događa se još od antičkih vremena te je realna opasnost i u suvremenom svijetu. Vodoopskrbni sustavi direktno i indirektno utječu na život svih građana, a o kvaliteti pitke vode izravno ovisi kvaliteta života svakog pojedinca i zajednice. Sigurnosna zaštita cijelog vodoopskrbnog sustava ključni je dio upravljanja rizicima, a efektivne zaštitne mjere nužne su kako bi se preveniralo izvođenje terorističkih akata u ovoj domeni.

Teroristički napadi otrovnim, toksičnim i zaraznim agensima mogu ostaviti velike posljedice na društvo, gubici života mogu biti veliki, a zdravstvena ugroza može imati masovne razmjere. Psihološke traume koje ostaju kao posljedica ovakvih akata značajno smanjuju kvalitetu života svih pojedinaca koji su direktno ili indirektno bili izloženi ovakvim napadima.

Zadaća je sigurnosnih profesionalaca utvrditi rizike, anticipirati ih te testirati sigurnosne sustave vodoopskrbe kako bi se utvrdilo stvarno stanje sigurnosti. Sukladno tome potrebno je kreirati akcijske planove putem kojih će se navedeni rizici umanjiti, odnosno pitka voda zaštititi. Vodoopskrba je jedan od ključnih elemenata svakodnevice svih građana, stoga se na sigurnost iste mora konstantno obraćati posebna pozornost.

Ključne riječi: **bioterorizam, vodoopskrba, sigurnost, zaštita.**

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UVOD

Čista i pitka voda od velike je važnosti za funkcioniranje suvremenog demokratskog društva. Sigurna vodoopskrba građana i poslovnog sektora osigurava nesmetanost svakodnevnog života i pridonosi ekonomskom rastu. U 2020. godini preko 5,8 milijardi ljudi imalo je siguran pristup pitkoj vodi (oko 74 % globalne populacije) (1). Preostale dvije milijarde ljudi imaju ograničen, otežan ili nesiguran pristup pitkoj vodi (2).

Voda je, dakle, nesporno krucijalan dio ljudske svakodnevice jer gotovo je svaki pojedinac koristi nekoliko desetaka puta u danu, a dio je gotovo svih ekonomskih i poslovnih procesa. Osim za piće i pripremu jela, koristi se i za druge kućanske poslove i potrebe (pr. pranje, sanitarni čvorovi i dr.). Također, voda je važan dio agrikulturnog sustava, proizvodnje električne energije, turizma, transporta te generalno industrije. Sukladno tome, sigurnost (pitke) vode od krucijalne je važnosti za svako suvremeno društvo.

Sigurnosni rizici povezani s vodom mogu se manifestirati na mnogo načina, primjerice od prekida vodoopskrbe zbog nenajavljenih kvarova sustava pa sve do pojedinačnog pucanja cijevi u stambenoj zgradi (3). Osim velikih sigurnosnih rizika uzrokovanih slučajnim akcidentima, za državu i društvo od velikog su interesa namjerni napadi i teroristički akti protiv pitke vode, a posebice protiv sustava kojima se prenosi pitka voda od izvora do kućanstava i poslovnih subjekata. Jedan od takvih sigurnosnih rizika jest bioterorizam.

Prema Interpolu, „bioterorizam je namjerno puštanje virusa, bakterija, toksina i drugih štetnih agenasa kako bi se uzrokovala bolest ili smrt ljudi, životinja ili biljaka" (4). Rječnik Merriam-Webster bioterorizam definira kao „terorizam koji uključuje korištenje biološkog oružja" (5). Bioteroristički napadi mogu imati „političke, religiozne, ideološke ili kriminalne motivacije" te ih također mogu unaprijed planirati grupe ili individualci (6). Ove definicije u skladu su s općim definicijama terorizma, iako valja napomenuti kako trenutno ne postoji

unificirana i jednoznačna definicija što je to terorizam. No većina definicija terorizma u svom sadržaju uključuje i naglašava namjeru, nanošenje ozljeda ili smrtnih ishoda, destrukciju i političke, religiozne ili ideološke motive (7). Brojne vladine, nevladine i institucije civilnog društva (pr. američki Savezni ured za istrage (engl. *Federal Bureau of Investigation* – FBI), američki Centar za kontrolu i prevenciju bolesti (engl. *Centers for Disease Control and Prevention* – CDC), NATO savez, Europska unija, Crveni križ i dr.) bioterorizam prepoznaju kao realnu prijetnju suvremenom društvu te naglašavaju važnost pripreme za slučaj takvog incidenta.

1. Povijest korištenja biološkog oružja

Moderni napredak mikrobiologije tijekom kasnog 19. stoljeća predstavlja ključni trenutak u evoluciji biološkog oružja. Napredak znanosti omogućio je sustavnu identifikaciju i razvoj odgovarajućih kapaciteta za širu proizvodnju štetnih patogena. Ratni sukobi u 20. stoljeću pretvorili su (nekoć rijetko, kompleksno i nestabilno) biološko oružje u ono „gabarita" sličnih konvencionalnom oružju, koje mogu masovno koristiti vojne snage. Zabrinutost zbog te činjenice postojala je od samih početaka masovnog korištenja biološkog oružja, ali ista je postala još izraženija nakon Drugog svjetskog rata, kada su osim vojnih snaga država i manje nevladine i/ili paravojne organizacije stekle znanje i sposobnost za korištenje bioloških agensa i toksina kao oružja (8).

Biološko oružje korišteno je mnogo prije modernog doba i pojave modernog načina ratovanja. Još u 14. stoljeću prije Krista Hetiti su svojim neprijateljima slali životinje zaražene tularemijom. Otprilike deset stoljeća kasnije zabilježeno je namjerno zaražavanje vojnih strijela uranjajući ih u leševe koji su bili u stadiju raspada. U 14. stoljeću Mongoli su bacali mrtva tijela zaraženih žrtava preko zidina gradova u Bohemiji, a Španjolci u kasnim dijelovima 15. stoljeća miješaju vino i krv pacijenata zaraženih gubom te ga takvog prodaju Francuzima (8). Korištenje biološkog oružja nije nova suvremena ideja, ali i dalje je aktualna i danas – te napadi ovog tipa uz dobru pripremu mogu biti iznimno pogubni.

Tijekom Drugog svjetskog rata Japan je provodio opsežna istraživanja mogućeg korištenja biološkog oružja. Program je uključivao eksperimentiranje na više od 10 000 zarobljenika. Korišteni su različiti patogeni koji su izazivali bolesti kao što su antraks, meningitis, kolera i dizenterija. Sjedinjenje Američke Države tijekom tog perioda također su ubrzano razvijale svoj napadački biološki kapacitet. Tijekom trajanja programa proizvedeno je oko 5000 komada streljiva koje je sadržavalo biološke agense, ali budući da je proizvodnja naišla na ograničenja iz sigurnosnih razloga, odustalo se od masovne proizvodnje (9).

Zbog spoznaje opasnosti i velikih rizika vezanih za biološko oružje, 1972. godine donesena je Konvencija o biološkom oružju (*The Biological Weapons Convention* – BWC). Ona predstavlja ključnu prekretnicu u globalnim naporima sprječavanja uporabe biološkog i toksinskog oružja. Prije spomenute Konvencije Ženevski protokol iz 1925. predstavljao je rani pokušaj zabrane uporabe biološkog oružja. Rezerviranost i oprez država potpisnica spriječili su njegovu učinkovitost kao sveobuhvatne zabrane. Konvencija o biološkom oružju službeno je stupila na snagu 26. ožujka 1975., nakon što su Konvenciju ratificirale dvadeset i dvije svjetske vlade, uključujući Ujedinjeno Kraljevstvo, Sjedinjene Američke Države i Sovjetski Savez, te i dan danas ostaje ključni međunarodni dokument koji promiče razoružanje i sprječavanje posljedice biološkog ratovanja (10).

2. Kategorizacija agenasa u kontekstu bioterorizma

Generalno gledajući, bioteroristički napadi mogu se izvesti gotovo svim patogenim mikroorganizmima. Kako bi pak taj napad bio učinkovit, biološki agens, između ostaloga, mora biti relativno visoko koncentriran, štetan po čovjekovo zdravlje i visoko zarazan. Također, faktor koji utječe na uspješnost takvog napada jest predvidljivost inkubacijskog perioda koji u idealnom slučaju mora biti kratak (11).

Američki Centar za kontrolu i prevenciju bolesti (CDC) klasificira biološko oružje u tri kategorije: kategoriju A, kategoriju B i kategoriju C, i to na temelju njihovog potencijalnog utjecaja na javno zdravlje.

Agensi kategorije A predstavljaju bioagense koji se mogu koristiti kao najopasnije biološko oružje. Kategorija A uključuje patogene koji predstavljaju ozbiljnu prijetnju javnom zdravlju, lako se prenose i imaju potencijal za visoku stopu smrtnosti. Primjeri uzročnika kategorije A uključuju antraks, botulizam i male boginje. Uzročnici kategorije B uključuju patogene koji se umjereno lako šire i rezultiraju umjerenom bolešću. Primjeri uzročnika kategorije B uključuju Q groznicu i brucelozu. Agensi

kategorije C uključuju patogene u nastajanju koji imaju potencijal kao sredstvo napada bioterorista, ali još nisu dobro proučeni ili shvaćeni. Primjeri uključuju Nipah virus i hantavirus (13).

CDC-ov sustav klasifikacije pomaže pri upravljanju javnozdravstvenim i hitnim odgovorima na ovakve biološke prijetnje. Agensi kategorije A predstavljaju najveću zabrinutost i zahtijevaju najveću spremnost i planiranje adekvatnog odgovora zbog njihovog potencijala za izazivanje masovnih žrtava. Navedeni sustav klasifikacije također usmjerava prioritete znanstvenih i kliničkih istraživanja, osiguravajući odgovarajuću raspodjelu novčanih i drugih resursa za praćenje, otkrivanje i odgovor na potencijalne biološke prijetnje, bile one prirodnog podrijetla ili namjerno izazvane.

Agensi koji se koriste kao biološko oružje većinski su prilagođeni za diseminaciju zrakom, odnosno putem aerosola. Većina njih može biti efektivno dozirana za transmisiju putem vode, no postoje određeni agensi koje voda neutralizira. Biološki patogeni i toksini predstavljaju dvije vrste bioloških prijetnji. Patogeni su živi organizmi (bakterije, virusi, protoze i sl.), dok su biotoksini kemikalije koje su nastale u i koje su izuzete iz živih organizama (najčešće iz bakterija i gljiva). Biotoksini se definiraju kao agensi koji „izazivaju kemijsku toksičnost koja rezultira bolešću i/ili smrtnim ishodom". Uzgajanje pojedinih patogena van profesionalnih laboratorija ne zahtijeva velike novčane resurse niti visoko specijalizirano i profesionalno znanje (13).

U nastavku teksta prikazane su dvije tablice s popisom bioloških agensa i biotoksina u kontekstu pitke vode. Svaki bioagens drugačije reagira na vodu, odnosno na kemikalije koje se nalaze unutar vode. Neki su otporni, neki nestabilni pa se „deaktiviraju" prilikom kontakta s vodom i kemikalijama kojima se tretira pitka voda. Isto tako, svaki agens ima različitu infektivnu dozu i drugačiju stabilnost u pitkoj vodi.

Tablica 1. *Potencijal prijetnje replicirajućih agensa* (14)*

***Uzročnik (agens) /* bolest**	**Može biti oružje**	**Prijetnja za pitku vodu**	**Infektivna doza**	**Stabilan u vodi**	**Tolerancija na klor**
Antraks	Da	Da	6000 spora (inh*)	2 godine (spore)	Spore su otporne
Bruceloza	Da	Vjerojatno	10 000 organizama (gut**)	20 – 72 dana	Nepoznato
Kolera	Nepoznato	Da	1000 organizama (gut)	Preživljava dobro	Lako ih se ubija
Clostridium perfringens	Vjerojatno	Vjerojatno	10^8 organizama (ing)	Uobičajeno u kanalizaciji	Otporne
Maleus (sakagija)	Vjerojatno	Malo vjerojatno	3,2 x 10^6 organizama (gut)	Do 30 dana	Nepoznato
Melioidoza	Moguće	Malo vjerojatno	Nepoznato	Nepoznato	Nepoznato
Kuga	Vjerojatno	Da	500 organizama (inh)	16 dana	Nepoznato
Psitakoza	Moguće	Moguće	Nepoznato	18 – 24 sata, more	Nepoznato
Q groznica	Da	Moguće	25 organizama (gut)	Nepoznato	Nepoznato
Salmonela	Nepoznato	Da	10^4 organizama (ing)	8 dana, svježa voda	Deaktivirane
Šigeloza	Nepoznato	Da	10^4 organizama (ing)	2 – 3 dana	Deaktivirane, 0,05 ppm klora, 10 minuta
Tularemija	Da	Da	10^8 organizama (ing)	Do 90 dana	Deaktivirane, 1 ppm klora, 5 minuta

***Uzročnik (agens)* / bolest**	**Može biti oružje**	**Prijetnja za pitku vodu**	**Infektivna doza**	**Stabilan u vodi**	**Tolerancija na klor**
Tifus	Vjerojatno	Malo vjerojatno	10 organizama (gut)	Nepoznato	Nepoznato
Encefalomijelitis	Vjerojatno	Malo vjerojatno	25 čestica (aer***)	Nepoznato	Nepoznato
Enterički virusi	Nepoznato	Da	6 čestica (ing)	8 – 32 dana	Lako se inaktivira (rotavirus)
Hemoragijska groznica	Vjerojatno	Malo vjerojatno	10^5 čestica (ing)	Nepoznato	Nepoznato
Velike boginje	Moguće	Moguće	10 čestica (gut)	Nepoznato	Nepoznato
Kriptosporidioza	Nepoznato	Da	132 oociste (gut)	Stabilan danima ili više dana	Otporne

Inh* = izloženost inhalacijom; Gut** = izloženost gutanjem; Aer*** = izloženost aerosolu

Tablica 2. *Potencijal prijetnji biotoksina* (14)*

Biotoksin	**Može biti oružje**	**Prijetnja za pitku vodu**	**NOAEL*, 2 L/dan****	**Stabilan u vodi**	**Tolerancija na klor**
Aflatoksin	Da	Da	75 pg/L*	Vjerojatno stabilan	Vjerojatno tolerantan
Anatoksin A	Nepoznato	Vjerojatno	Nepoznato	Deaktiviran nakon nekoliko dana	Vjerojatno tolerantan
Botulinum toksin	Da	Da	0,0004 pg/L	Stabilan	Deaktiviran, 6 ppm, 20 min
Mikrocistini	Moguće	Da	1,0 pg/L	Vjerojatno stabilan	Otporan na 100 ppm
Ricin	Da	Da	15 pg/L	Stabilan	Otporan na 10 ppm
Saksitoksin	Moguće	Da	0,4 pg/L	Stabilan	Otporan na 10 ppm
Enterotoksini stafilokoka	Moguće	Da	0,1 pg/L	Vjerojatno stabilan	Nepoznato
T-2 mikotoksin	Moguće	Da	65 pg/L	Stabilan	Nepoznato
Tetrodotoksin	Moguće	Da	1 pg/L	Vjerojatno stabilan	Deaktiviran, 50 ppm

*NOAEL je kratica za *No Observed Adverse Effect Level* (hrv. nema uočenih štetnih učinaka). To je termin koji se koristi u toksikologiji te predstavlja najvišu dozu ili razinu izloženosti tvari (u ovom slučaju, biotoksinu) pri kojoj nisu primijećeni štetni učinci ili toksični učinci u eksperimentalnim studijama ili procjenama na ljudima.

**2 L/dan: Ovaj dio oznake označava procijenjeni dnevni unos ili razinu izloženosti koja se razmatra u kontekstu sigurnosti biotoksina. NOAEL se temelji na dnevnom unosu od 2 litre vode kontaminirane biotoksinom.

*** pg/L: pikogram po litri

U kontekstu zaštite pitke vode od bioterorizma, funkcioniranja suvremenih urbanih vodoopskrbnih sustava te biološkog potencijala samog agensa, prilikom analize mogućnosti korištenja pojedinog agensa (ili biotoksina) kao sredstva bioterorističkog napada u uvjetima prisutnosti vode potrebno je obratiti pozornost na sljedeće:

- može li se biološki agens ili biotoksin pretvoriti u oružje
- je li agens prijetnja za pitku vodu
- kolika je infektivna doza agensa
- koja je stabilnost biološkog agensa u vodi
- je li agens otporan na klor.

Pretvaranje biološkog agensa u biološko oružje može, između ostalog, uključivati sljedeće: povećavanje infektivnosti (može uključivati genetičke mutacije koje doprinose vjerojatnosti da se ciljana meta zarazi), povećanje stabilnosti (modificiranje tako da biološko oružje izdrži transport, skladištenje i diseminaciju), smanjivanje vjerojatnosti detekcije, povećanje otpornosti na poznate lijekove i tretmane i ostalo (15).

U kontekstu otpora agensa prema kloru nužno je spomenuti da se u određenim dijelovima vodoopskrbnog sustava voda za piće tretira klorom. Prema Nastavnom zavodu za javno zdravstvo Dr. Andrija Štampar, „dezinfekcija je zadnja faza priprave vode sa svrhom eliminacije tj. smanjivanja broja mikroorganizama u njoj. Većinom se za kemijsku dezinfekciju koristi klor, klor dioksid ili ozon." (16) Klor nije učinkovit protiv svih bioloških agensa, već njegova učinkovitost ovisi o prirodnom otporu agensa na klor, doziranju agensa te ostalim faktorima.

Kemijsko oružje kao sredstvo počinjenja terorističkih akata

Kemijsko oružje uključuje uglavnom sintetičke tvari i materijale koje otpuštaju toksične kemikalije. Ono često ima trenutni učinak na žrtve koje dođu u kontakt s istim te se ne prenose s osobe na osobu kao što je to slučaj s biološkim agensima (pr. bakterije, virusi). Trenutno postoji oko 70 održivih kemijskih agensa koji se mogu koristiti kao kemijsko oružje. Oni se dijele na (17):

- krvne agense (blokiraju transport kisika u krvi)
- agense koji stvaraju mjehuriće
- agense koji uzrokuju gušenje
- nervne agense
- sredstva za onesposobljavanje (izmijenjeno stanje svijesti).

I biološko i kemijskog oružje može se diseminirati različitim metodama, uključujući kazetne bombe iz malih projektila, helikoptera, niskoletećih zaprašivača, dronova i sprejeva različite veličine. Sukladno toj činjenici, postoje sličnosti u načinima diseminacije za obje vrste oružja (17). Također, oba tipa oružja mogu se raspršiti jednostavnim metodama poput ulijevanja u vodu, ispuštanjem u ventilacijske sustave i dr.

Međutim, bitno je napomenuti da učinkovitost i specifični mehanizmi diseminacije mogu varirati ovisno o vrsti korištenog agensa (biološkog ili kemijskog), ciljanim metama napada i ostalim faktorima.

3. Sustav vodoopskrbe u kontekstu bioterorizma

Pitka voda ključan je prirodni resurs kojeg svakodnevno koristi šire građanstvo i širi poduzetnički sektor svake države. Može se pronaći na izvorištima, unutar kućanstava (voda iz slavine), u trgovinama (voda u bocama), na javnim mjestima (fontane, javne slavine), bunarima, raznoraznim vodospremama i drugim mjestima. Većina vode koja se konzumira danas, na bilo koji od načina, do krajnjeg potrošača dolazi sustavom vodoopskrbe.

Javna vodoopskrba predstavlja djelatnost koja se primarno bavi zahvaćanjem vode (podzemne ili površinske), njenom kemijskom obradom i pripremom za konzumaciju (18). Sustav vodoopskrbe kompleksan je sustav, a njegova operativnost razlikuje se od države do države, odnosno od lokaliteta do lokaliteta – te ovisi o konfiguraciji terena, razvijenosti same regije, potrebnim kapacitetima i dr. Njega čine građevine, uređaji i instalacije koje za svrhu imaju dovođenje (pitke) vode do krajnjeg korisnika (18). Generalno, u slučajevima urbanih sredina, vodoopskrbni sustav sadržava sve ili neke od sljedećih komponenata: izvor/vodocrpilišta; postrojenja za obradu sirove vode (kondicioniranje); cjevovode; crpne stanice; vodospreme/vodotornjeve; lokalnu vodovodnu mrežu.

U kontekstu bioterorizma i napada ovakve vrste svaki pojedini dio sustava može biti meta napada (odnosno ulazna točka u koju napadač ubacuje biološki agens ili

biotoksin), odnosno napad može biti obavljen na više podsustava istovremeno.

Izvor je mjesto na kojem podzemna voda trajno ili povremeno izbija na površinu. Ona može biti različitih biokemijskih parametara prije nego dođe do postrojenja za obradu sirove vode.

Postrojenje za obradu sirove vode (kondicioniranje) postoji u sustavu vodoopskrbnih sustava na kojima kakvoća sirove vode ne zadovoljava standarde i zdravstvene parametre. Ova postrojenja najčešće rade jednu ili više zadaća: koagulaciju, flokulaciju, sedimentaciju, filtraciju ili dezinfekciju.

Cjevovod predstavlja skup posebno dizajniranih cijevi koje služe za transport pitke vode do krajnjeg korisnika. Razne varijante cijevi koje čine cjevovod uključuju široke cijevi koje od izvorišta prenose vodu do vodosprema te manje ogranke koje od vodosprema prenose vodu do krajnjih korisnika (19).

Crpna stanica je postrojenje koje se koristi za „podizanje energetske razine vode unutar vodoopskrbne distributivne mreže i objekata vodoopskrbnog sustava koji su priključeni na mrežu". Ona se sastoji primarno od pumpnog agregata koji je smješten unutar samostojećeg objekta (18).

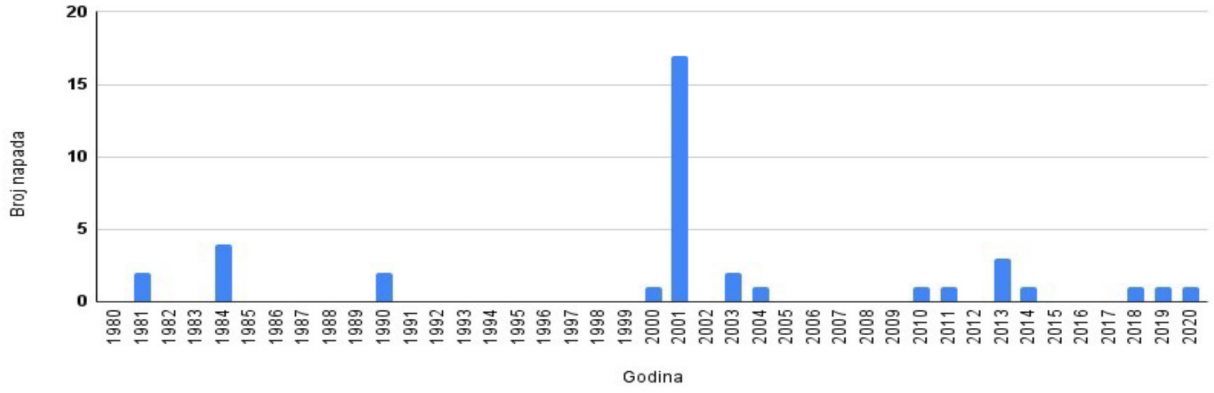
Vodosprema (vodotoranj) je objekt u kojem se akumuliraju velike količine vode koje se potom distribuiraju do krajnjih korisnika. Većinom su locirane polupodzemno te se nalaze unutar nekog samostojećeg objekta (kako bi se spriječio izravan pristup pitkoj vodi).

Lokalna vodovodna mreža u ovom kontekstu predstavlja skup cijevi koje dolaze do krajnjih potrošača.

Cijevi su različitih dimenzija, a najčešće njihov put započinje od vodospreme.

4. Bioteroristički napadi i terorističke grupe

Kao izvor podataka o količini i vremenu kada su počinjeni teroristički napadi, odnosno informacijama o pojedinom terorističkom napadu, korištena je službena baza podataka Globalne baze podataka o terorizmu (eng. *Global Terrorism Database*; skraćeno GTD). U tražilici spomenute baze zadani su sljedeći kriteriji: godina izvršenja terorističkih napada od 1970. – 2020. (baza podataka nije osvježena za 2021., 2022. i 2023. godinu) te oružje napada: biološko. Prema navedenim kriterijima u bazi podataka identificirano je 38 terorističkih napada, svi počinjeni od 1980. do 2020. godine (20). Važno je napomenuti da su među ovih 38 incidenata uvršteni i dovršeni bioteroristički napadi i bioteroristički napadi u pokušaju. U svrhu pojednostavljenja prikaza rezultata, unutar grafikona 1. prikazan je vremenski period od 1980. do 2020. godine (u periodu od 1970. do 1979. nije bio (zabilježenih) bioterorističkih napada. Limiti ove baze podataka ogledaju se u tome što ne postoje rezultati za period prije 1970. godine, odnosno postoji mogućnost da određeni teroristički napadi nisu popisani (pr. nije jasan kriterij je li neki događaj teroristički napad ili nije i dr.).



Slika 1. *Broj terorističkih napada biološkim agensima za period od 1980. do 2020. (20).*

Analizom podataka utvrđeno je kako je najviše bioteroristčkih napada počinjeno 2001. godine (u jeku napada Al-Qaide na teritorij Sjedinjenih Američkih Država). U periodu od 1980. do 1999. godine počinjeno je ukupno osam bioterorističkih napada, a u periodu od 2010. do 2020. izvršeno je deset bioterorističkih napada. Najaktivnije razdoblje bioterorizma je ono između 2000. i 2005. godine, kada je ukupno počinjen 21 bioteroristčki napad diljem svijeta (20).

Daljnjom analizom podataka, sada prema kriteriju države počinjenja bioterorističkih napada, utvrđeno je da su čak 24 napada počinjena na području SAD-a, 3 napada na području Kenije, 2 na području Ujedinjenog Kraljevstva i Pakistana te po 1 u Japanu, Čileu, Kolumbiji, Izraelu, Rusiji i Tunisu (20).

Analizom meta bioterorističkih napada ističu se generalno napadi na vladine objekte i vladine dužnosnike (kojih je najviše), potom napadi na medije i novinare, napadi na poslovne subjekte, privatne osobe, zračne luke i zrakoplove, edukacijske institucije i turiste (20). Ako na ove podatke gledamo s aspekta agensa korištenog za bioteroristički napad, korišteni su: antraks (najviše); salmonela; ricin; materija fecesa; botulinum toksin; HIV (navodno).

Analizom iste baze podataka utvrđeno je da je do kraja 2020. godine upisano 209 706 terorističkih incidenata. Udio bioterorističkih napada u ukupnom broju je iznimno nizak, svega 0,02 %. No bioteroristički napadi imaju jednu posebnu značajku, a to je da prosječno nanose više ozljeda nego ostali teroristički akti kombinirano. Primjerice, srednja stopa ozljeda od eksploziva u terorističkim napadima približno je 4 ozljede po napadu, dok bioteroristički napad ima srednju stopu od 28,8 ozljeda po napadu. Važno je napomenuti da specifične stope ozljeda u terorističkim napadima mogu uvelike varirati ovisno o različitim čimbenicima kao što su: vrsta upotrijebljenog oružja, cilj, lokacija i učinkovitost sigurnosnih mjera (21). Također, zbog tajnosti pripreme i samog napada moguća je veća vjerojatnost da bioteroristički napadi ostanu neprepoznati.

Skupine koje koriste biološko oružje za terorističke napade

Analizom baze podataka GTD (20), vezane uz kriterije povezane s bioterorističkim napadima, popisane su skupine (i pojedinci) koji su tijekom svojeg postojanja koristile bioterorističke agense i biotoksine kao sredstvo napada kako je to opisano dalje u tekstu.

1. Pokret Rajneesh – religijska sekta koju je osnovao Bhagwan Shree Rajneesh (kasnije poznat kao Osho). Njegovi su sljedbenici 1984. godine u Oregonu počinili najmasovniji bioteroristički napad korištenjem salmonele. Napadi su počinjeni kontaminiranom salatom koja je posluživana u nekoliko desetaka lokalnih restorana, a ukupno je zaraženo preko 700 osoba (22).

2. Aum Shinrikyo – grupu je osnovao Shoko Asahara 1987. godine. Grupa vjeruje u neizbježnu apokalipsu, a sukladno tome njihova tranzicija na nasilje uključuje korištenje kemijskog i biološkog oružja, kao i fizičke obračune i ubojstva. Grupa je 1993. godine u Tokiju izvela napad korištenjem antraksa. U napadu nije bilo žrtava (23).

3. Justice Department – grupa za zaštitu prava životinja koja je tijekom svog aktivnog perioda koristila nasilne metode za postizanje svojih ciljeva (24). Bili su glavni osumnjičeni za korištenje HIV-a kao bioterorističkog agensa kada su na Sveučilište u Los Angelesu poslali žilete umočene u krv HIV pozitivnog pacijenta. Meta napada bio je liječnik koji je radio vivisekcije. Službena analiza nije potvrdila da je krv bila zaražena (20).

4. Ekstremisti pojedinci koji su protiv kontrole oružja – pojedinci koji se protive bilo kakvoj državnoj kontroli oružja. U konkretnom slučaju jedna osoba poslala je pismo koje je sadržavalo biotoksin ricin. Meta napada je bio gradonačelnik New Yorka, Michael Bloomberg. Pismo nikad nije došlo do Bloomberga, već je ricin detektiran na vrijeme (20).

5. Ekstremisti koji su direktno protiv Donalda Trumpa – ekstremisti koji ne podržavaju Donalda Trumpa sudjelovali su u slanju pisama koja su sadržavala ricin. Pisma nikad nisu došla do Donalda Trumpa jer su ih presreli pripadnici osiguranja (20).

6. Pojedinci – tzv. „vukovi samotnjaci“ – unutar baze podataka GTD-a zabilježen je niz bioterorističkih napada koje su izveli pojedinci. Vukovi samotnjaci opasni su zbog toga što je njihove akcije teško predvidjeti, odnosno prevencija takvih napada je teška (20).

7. Islamski ekstremisti (nije službeno potvrđeno) – u Tunisu su državna sigurnosna tijela presrela 19

pisama koja su sadržavala otrovnu tvar. Pisma su bila upućena novinarima, političarima i sindikalistima. Nisu prijavljene žrtve, a nijedna skupina nije preuzela odgovornost za incident (napad je pripisan islamskim ekstremistima) (20).

8. Grupa SERB (nije službeno potvrđeno) – jugoistočni radikalni blok je nacionalistička ruska radikalna skupina s antiglobalističkim stavovima koja je u svojim obračunima koristila određene elemente kemijskog i biološkog oružja (20).

9. Revolucionarne oružane snage Kolumbije (nije službeno potvrđeno) (eng. *Revolutionary Armed Forces of Colombia – People's Army*; skraćeno FARC) – pobunjenička grupa koja djeluje na području Kolumbije. Američki State Department proglasio ju je terorističkom skupinom koja je sposobna izvesti terorističke napade na međunarodnoj razini (25). Iako nema službene potvrde, izvori povezuju ovu skupinu s napadom u kojem je korišten feces (20).

Tijekom godina različite skupine i pojedinci pribjegavali su bioterorizmu kao sredstvu za promicanje svojih ideoloških, političkih ili vjerskih uvjerenja. Incidenti dokumentirani u Globalnoj bazi podataka o terorizmu (GTD) naglašavaju raznolikost aktera, i to u rasponu od vjerskih sekti do ekstremista koji se suprotstavljaju političarima. Također je evidentno da svi napadi nisu rezultirali velikim brojem žrtava, međutim, psihološki utjecaj i potencijal za razaranje velikih razmjera ostaju značajni i prisutni. Zabrinjavajuća opažanja usmjerena su k napadima tzv. „vukova samotnjaka" ili izoliranih pojedinaca koji djeluju bez izravne povezanosti s većim skupinama. Njihova nepredvidljivost čini ih posebno opasnima. Dok je za neke incidente potvrđeno da su ih izvršile točno određene skupine, neki incidenti, poput onih koje su potencijalno orkestrirali islamski ekstremisti ili FARC, ostaju bez službene potvrde. Navedeno ukazuje na širi izazov bioterorizma – poteškoće u detekciji podrijetla napada i pripisivanju odgovornosti točno određenim skupinama.

Teroristički napadi kemijskim oružjem na pitku vodu

Zbog analogije i sličnosti diseminacije biološkog i kemijskog oružja te zbog dosad neprijavljenih terorističkih napada biološkim oružjem na pitku vodu dalje se prikazuje kratki presjek terorističkih napada kemijskim oružjem na pitku vodu.

Analizom relevantne baze terorističkih napada (GTD) za razdoblje od 1970. do 2020., analizirajući kriterij kemijskog oružja kao vrste oružja koje se koristilo prilikom napada, pronađeno je 425 terorističkih incidenata koji odgovaraju spomenutim kriterijima. Većina napada dogodila se između 1995. i 2020. godine., a ogledan je i rapidan porast kemijskih napada od 2012. do danas.

Uključivanjem dodatnog kriterija – mete napada, u ovom slučaju opskrbe hrane i vode (fiksno zadani kriterij prema GTD-u), rezultati su suženi na 13 incidenata. Najznačajniji teroristički napad kemijskim oružjem na vodnu infrastrukturu dogodio se u Somaliji 2017. godine kada je grupa Al-Shabaab otrovala bunar, prilikom čega su smrtno stradale 32, a ranjeno je 10 osoba (20).

Pokušaj hakerovog trovanja vode vodoopskrbnog sustava na Floridi dogodio se u veljači 2021. godine, što ukazuje na naglašenu ranjivost kritične infrastrukture na kibernetičke napade ovog tipa. Haker je manipulirao razinama natrijevog hidroksida u sustavu za obradu vode. Iako je direktna prijetnja izbjegnuta te nije bilo žrtava, ovaj incident služi kao podsjetnik na potrebu za pojačanim mjerama kibernetičke sigurnosti (26).

5. Pitka voda i bioterorizam u Republici Hrvatskoj

Iako u RH nisu registrirani bioteroristički napadi povezani s pitkom vodom i vodoopskrbnim sustavima, prijetnja i dalje ostaje realna i moguća (tim više što u domeni kemijskih napada postoji suvremeni trend istih). Terorističke prijetnje mijenjaju svoj oblik iz godine u godinu, a pojavom novih tehnologija moguće su i drugačije metode izvršenja bioterorističkih napada, odnosno oni mogu biti usmjereni prema vodoopskrbnim sustavima i pitkoj vodi.

Uspješnost bioterorističkog napada na pitku vodu, odnosno korištenje vode kao medija napada, ovisi o puno faktora kao što su to: vrsta agensa ili biotoksina, njegova otpornost, infektivna doza te u konačnici količina agensa ili biotoksina koju je teroristička skupina ili pojedinac sposoban proizvesti. Bioteroristički akti ne moraju biti izvršeni isključivo protiv velikih sustava. Osim što se mogu izvršiti na komponente sustava vodoopskrbe, mogu se vršiti protiv pojedinaca i manjih skupina (pr. biološki agensi u bocama, bazenima, kupalištima i dr.). Uspješnost bioterorističkog

napada uvelike ovisi i o mjerama sigurnosne zaštite na objektima vodoopskrbe, odnosno na objektima u kojima se nalaze mete samog bioterorističkog napada (pr. grupe ili pojedinci). Bioteroristi imaju dva zadatka, a to je svladati sigurnosnu zaštitu (ako ona postoji) te uspješno pretvoriti biološke agense u oružje koje će biti stabilno i očuvano do ulaska u tijelo žrtve.

Popisivanjem bioloških agenasa i biotoksina utvrđeno je da nemali broj njih može preživjeti u pitkoj vodi, i to unatoč kemijskog zaštiti koju pruža klor. Vjerojatno moguću prijetnju za pitku vodu tako predstavljaju: antraks, Clostridium perfringens, kuga, kriptosporidioza, aflatoksin, anatoksin A, mikrocistini, ricin, tetrodotoksin i ostali. U praksi se način diseminacije i ubacivanja samog biološkog oružja u sustav vodoopskrbe može razlikovati te o tome može ovisiti i konačni učinak samog bioagensa.

Sigurnosna zaštita vodoopskrbnih sustava od bioterorističkog napada

Vodoopskrbni sustavi razlikuju se po komponentama koje ih sačinjavaju, odnosno s obzirom na to o kakvim se objektima radi. Pojedine države u svijetu vode veću brigu o sigurnosti vodoopskrbnih sustava te su isti objekti „tvrdo" čuvani kombinacijom tjelesne, tehničke i mehaničke zaštite. U kontekstu Republike Hrvatske, vodama se gospodari i upravlja sukladno Zakonu o vodama, kojim se uređuje pravni status vode.

U Republici Hrvatskoj vode su opće dobro i imaju osobitu zaštitu Republike Hrvatske. Vode u tijelima površinskih i podzemnih voda ne mogu biti objektom prava vlasništva i drugih stvarnih prava. Upravljanje vodoopskrbnim sustavima povjereno je jedinicama lokalne i područne (regionalne) samouprave. Sukladno pozitivnoj pravnoj regulativi RH, trenutno ne postoje zakonom propisane minimalne standardizirane mjere sigurnosne zaštite za objekte i procese sustava vodoopskrbe. Sigurnosna zaštita objekata, postrojenja, procesa i svega ostalog što je povezano sa sustavom vodoopskrbe u Republici Hrvatskoj počiva na sigurnosnoj svijesti društva (tvrtke) koje upravlja pojedinim vodoopskrbnim sustavom, odnosno na sigurnosnoj svijesti lokalne i regionalne samouprave.

Sukladno navedenom, ali i na temelju praktičnih iskustava autora rada u domeni zaštite vodoopskrbnih sustava, može se utvrditi da postoji nejednakost u:

- stupnju sigurnosne zaštite vodoopskrbnih sustava koji su pod upravljanjem različitih jedinica lokalne i područne (regionalne) samouprave u Republici Hrvatskoj
- stupnju sigurnosne zaštite pojedinih dijelova i objekata unutar jednog vodoopskrbnog sustava pod upravljanjem društva koje je osnovala jedinica lokalne i područne (regionalne) samouprave
- stupnju sigurnosne svijesti čelnih (i rukovodećih) osoba društava koje upravljaju vodoopskrbnim sustavima.

Mjere sigurnosne zaštite u kontekstu vodoopskrbnih sustava

Sigurnosna zaštita relativno je širok pojam te obuhvaća različite kategorije sigurnosne zaštite. U kontekstu vodoopskrbnih sustava sigurnosna zaštita može uključivati sljedeće:

- izradu sigurnosnih procjena rizika vodoopskrbnih sustava s akcijskim planovima otklanjanja uočenih nedostataka i sigurnosnih manjkavosti;
- ograđivanje perimetra postrojenja ili objekta tako da se oteža pristup napadačima
- instalaciju sveobuhvatnog sustava videonadzora te razmatranje nadogradnje računalnim programima koji koriste benefite umjetne inteligencije ili strojnog učenja
- angažiranje sigurnosnog osoblja (pr. zaštitara) na samim postrojenjima ili objektima
- osiguranje kontrole pristupa objektima putem ID kartica, otisaka prstiju i sl.
- nadogradnju sigurnosnih mjera u prostorijama u kojima se nalaze skladišta kemijskih tvari
- ugradnju alarmnih sustava (pr. protuprovala)
- ugradnju adekvatnih pomičnih barijera za vozila na ulazu u postrojenja
- provođenje redovitih i izvanrednih sigurnosnih obilazaka svih postrojenja i objekata
- mehaničko osiguranje svih potencijalnih ulaza u objekte (pr. prozori)
- maksimiziranje kibernetičke zaštite poduzeća koja upravljaju vodoopskrbnim sustavima
- dodatne češće kontrole kvalitete vode

- učestalo održavanje sigurnosnih edukacija za sve zaposlenike
- edukaciju javnosti o prijetnjama i rizicima koje sa sobom donosi bioterorizam
- edukaciju donositelja odluka o rizicima bioterorizma
- usku suradnju s državnim sigurnosnim institucijama.

Sigurnosna procjena rizika može se izrađivati kao formalni dokument te uključuje identifikaciju i procjenu rizika. U kontekstu vodoopskrbnih sustava i bioterorizma sigurnosna procjena rizika može uključivati sljedeće:

- identifikaciju segmenata vodoopskrbnog sustava te popisivanje mjera sigurnosne zaštite
- procjenu ranjivosti pojedinih segmenata vodoopskrbnog sustava (mogući proboji, sabotaže, diverzije, neutralizacija sigurnosnog sustava, lakoća dolaska do pitke vode i sl.)
- identifikaciju potencijalnih terorističkih skupina i izradu profila individualaca koji bi potencijalno mogli izvesti bioteroristički napad (ponajprije radi preventivnih aktivnosti)
- procjenu utjecaja bioterorističkog napada (procjena broja žrtava pri različitim scenarijima)
- procedure za nadopunu sigurnosne procjene rizika
- akcijski plan za otklanjanje uočenih sigurnosnih manjkavosti.

ZAKLJUČAK

Zaštita pitke vode od potencijalnih prijetnji bioterorizma imperativ je i zadaća koja zahtijeva multidisciplinarni pristup koji uključuje znanstvena istraživanja, razvoj proaktivnih politika zaštite te usku suradnju brojnih različitih dionika.

Iako su učinjeni značajni pomaci u razumijevanju potencijalnih prijetnji i razvoju strategija otkrivanja i ublažavanja, nedvojbeno je potreban kontinuiran oprez i ulaganja kako bi se išlo ispred prijetnji bioterorizma u budućnosti. To uključuje povećanje svijesti cjelokupnog društva o fenomenu bioterorizma i ponašanju potencijalnih patogena, poboljšanje sustava nadzora te usavršavanje sustava zaštite i protokola odgovora.

Štoviše, međunarodna suradnja i razmjena informacija ključni su u rješavanju ovog globalnog sigurnosnog izazova. Zajednički napori država, organizacija, znanstvenika i praktičara mogu pomoći u stvaranju snažne obrane od bioterorizma u području zaštite pitke vode. U tom je smislu neophodno poticati zajednički rad država na razmjeni znanja, najboljih praksi i resursa za jačanje globalne sigurnosti.

Zajednička predanost zaštiti pitke vode od bioterorizma nije samo pitanje javnog zdravlja, već i vitalna komponenta nacionalne i globalne sigurnosti. Zadržavanjem proaktivnog stava, ulaganjem u istraživanje i razvoj te poticanjem međunarodne suradnje može se osigurati sigurnost i dostupnost čiste pitke vode za generacije koje dolaze.

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6. Popis priloga

Tablica 1. Potencijal prijetnje replicirajućih agensa* (14) *(tablica je prevedena na hrvatski jezik te je kao takva zadržala izvorni oblik)

Inh* = izloženost inhalacijom; Gut** = izloženost gutanjem; Aer*** = izloženost aerosolu

Tablica 2. Potencijal prijetnji biotoksina* (14) *(tablica je prevedena na hrvatski jezik te je kao takva zadržala izvorni oblik)

*NOAEL je kratica za *No Observed Adverse Effect Level* (hrv. nema uočenih štetnih učinaka). To je termin koji se koristi u toksikologiji te predstavlja najvišu dozu ili razinu izloženosti tvari (u ovom slučaju, biotoksinu) pri kojoj nisu primijećeni štetni učinci ili toksični učinci u eksperimentalnim studijama ili procjenama na ljudima.

**2 L/dan: Ovaj dio oznake označava procijenjeni dnevni unos ili razinu izloženosti koja se razmatra u kontekstu sigurnosti biotoksina. NOAEL se temelji na dnevnom unosu od 2 litre vode kontaminirane biotoksinom.

*** pg/L: pikogram po litri

Slika 1. Broj terorističkih napada biološkim agensima za period od 1980. do 2020. (20).

S U M M A R Y

PROTECTION OF DRINKING WATER FROM BIOTERRORISM

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Abstract:
Bioterrorism, or diverse attacks with biological agents, has been occurring since ancient times and is a real danger in the modern world. Water supply systems directly and indirectly affect the lives of all citizens, and the quality of drinking water directly determines the quality of life of every individual and community. Security protection of the entire water supply system is a key part of risk management, and effective protective measures are essential to prevent the execution of terrorist acts in this domain.
Terrorist attacks with poisonous, toxic, and infectious agents can have significant consequences on society, the loss of life can be considerable, and the health threat can have massive proportions. The psychological traumas that remain as a result of such acts significantly reduce the quality of life of all individuals who were directly or indirectly exposed to such attacks.
The task of security professionals is to determine the risks, anticipate them, and test the security systems of the water supply to ascertain the actual state of security. Accordingly, it is necessary to create action plans through which the mentioned risks will be reduced, or, in other words, drinking water will be protected. The water supply is one of the essential elements of the daily life of all citizens, so constant special attention must be paid to its security.

Keywords: bioterrorism, water supply, security, protection

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EDUKACIJA O BIOSIGURNOSTI I BIOZAŠTITI U HRVATSKOM OBRAZOVNOM SUSTAVU

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SAŽETAK

Hrvatski obrazovni sustav od školske godine 2020./2021. godine ima sustavnu edukaciju učenika, učitelja, nastavnika, stručnih suradnika i ravnatelja o biosigurnosti i biozaštiti. Projekt je pokrenula OŠ „Vijenac" iz Osijeka uz potporu Hrvatskog društva za biosigurnost i biozaštitu, Klinike za infektivne bolesti „Dr. Fran Mihaljević", Hrvatskog zavoda za javno zdravstvo, Akademije medicinskih znanosti Hrvatske, Ministarstva znanosti i obrazovanja te Agencije za odgoj i obrazovanje. Virus SARS-CoV-2 pokazao je važnost dodatne edukacije učenika, učitelja, nastavnika stručnih suradnika i ravnatelja o navedenom problemu. Važnost promicanja vrijednosti očuvanja ljudskog zdravlja i prevencije zaraznih bolesti bila je glavni poticaj za pokretanje ovog projekta. Glavni su ciljevi projekta upoznavanje učenika s važnošću stručnog, znanstvenog, globalnog i osobnog pristupa u sprječavanju širenja zaraznih bolesti; upoznavanje s opasnim uzročnicima i njihovim načinom djelovanja; usvajanje odgovornog ponašanja prema svome i tuđem zdravlju; analiziranje potencijalnih opasnosti biougroze i načina prevencije; popularizacija znanosti i istraživanja u STEM području (od engl. *science, technology, engineering, and mathematics*) kroz istraživački projekt učenika; razvijanje interesa za znanost; razvijanje suradničkog odnosa; razvijanje i usavršavanje digitalnih kompetencija; poticanje komunikacijskih i prezentacijskih vještina te stručno usavršavanje učitelja. Broj je učenika uključenih u projekt tijekom tri godine blizu broja 12 000, a ukupno je odrađeno 25 095 sati nastave u više od 300 škola. Učenici svoje istraživačke projekte prezentiraju na Smotri učeničkih radova koju organizira Agencija za odgoj i obrazovanje, a radovi se svake godine prezentiraju na izložbi koju organizira Hrvatsko društvo za biosigurnost i biozaštitu.

Ključne riječi: biosigurnost, biozaštita, zdravstvena pismenost, edukacija učenika i odgojno-obrazovnih djelatnika

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UVOD

U hrvatskom obrazovnom sustavu do izbijanja pandemije bolesti COVID-19 nije postojala sustavna edukacija o području biosigurnosti i biozaštite. Neki segmenti biosigurnosnih kompetencija i vještina svladavali su se u okviru nastavnih sadržaja Prirode i društva u nižim razredima osnovne škole, s naglaskom na razvijanje higijenskih navika djece, a u višim razredima osnovne škole edukacija se provodila u okviru nastave Prirode i Biologije bazirana na higijenskih navikama, patogenim mikroorganizmima i osnovnim infektivnim bolestima. Srednja škola (osobito strukovne škole) imala je zadane sadržaje isključivo u sklopu predmeta Biologija izuzev srednjih škola s biomedicinskim usmjerenjem. Određeni sadržaji obrađivali su se u sklopu međupredmetne teme Zdravlje u svim ciklusima predviđenim Nacionalnim kurikulumom, s naglaskom na higijenske navike te zdravlje općenito.

Pojava pandemije pokazala je da je potrebna dodatna edukacija o ovom području koja obuhvaća ne samo učenike, nego i učitelje, nastavnike, stručne suradnike i ravnatelje osnovnih i srednjih škola. Tu je potrebu prepoznalo Hrvatsko društvo za biosigurnost i biozaštitu Hrvatskog liječničkog zbora još od svoga osnutka 2014. godine. Pandemija SARS-CoV-2 bila je okidač koji je pokrenuo proces uvođenja sustavnog poučavanja biosigurnosti i biozaštite u hrvatske škole. Mnoštvo neznanstveno utemeljenih, konfuznih informacija

u medijima i na društvenim mrežama te neadekvatan odaziv na cijepljenje tijekom pandemije SARS-CoV-2 pokazali su da edukacija o biosigurnosti i biozaštiti nije samo potreba, već da su takve edukacije nužne i zbog eventualnih budućih biosigurnosnih ugroza koje su svakodnevna prijetnja suvremenog čovjeka. Hrvatsko društvo za biosigurnost i biozaštitu u suradnji s Osnovnom školom Vijenac iz Osijeka osmislilo je Kurikulum izvannastavne aktivnosti Biosigurnost i biozaštita za osnovne i srednje škole, koji je svjetlo dana ugledao već u lipnju 2020. godine tijekom pandemijske *online* nastave. Ovaj projekt podržala je i Klinika za infektivne bolesti „Dr. Fran Mihaljević" iz Zagreba, Hrvatski zavod za javno zdravstvo te Hrvatska akademija medicinskih znanosti Hrvatske. Uvidjevši važnost brzog djelovanja na području edukacije školske djece i školskih djelatnika o biosigurnosnim ugrozama, Ministarstvo znanosti i obrazovanja Republike Hrvatske te Agencija za odgoj i obrazovanje izdali su odobrenje i preporuku za provođenje projekta u Hrvatskom obrazovnom sustavu te je izvannastavna aktivnost Biosigurnost i biozaštita uz velik interes škola uvedena već u školskoj godini 2020./2021.

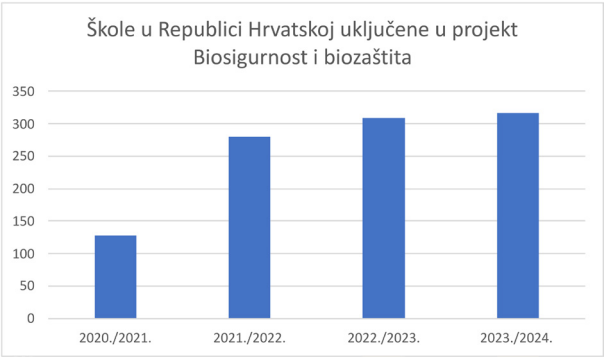
1. Način provedbe projekta „Biosigurnost i biozaštita" u osnovnim i srednjim školama u Hrvatskoj

Projekt „Biosigurnost i biozaštita" provodi se kao izvannastavna aktivnost u osnovnim i srednjim školama u Hrvatskoj. U nekim osnovnim i srednjim školama kurikulumska se područja obrađuju u okviru dodatne nastavne Prirode ili Biologije odnosno kao fakultativni programi ili kao školski projekti u kojima škola sudjeluje na nacionalnoj razini.

Biosigurnost i biozaštita poučavaju se na tri razine. Prva razina namijenjena je učenicima 5. i 6. razreda osnovne škole, a druga razina obuhvaća učenike 7. i 8. razreda. Zbog različitog trajanja srednjoškolskog obrazovanja u Hrvatskoj, s ciljem da se uz gimnazije mogu obuhvatiti i strukovne te petogodišnje medicinske škole, treća razina poučavanja jedinstvena je za sve srednje škole. Neke srednje škole u Hrvatskoj uvele su Biosigurnost i biozaštitu kao fakultativni predmet. Učenici na sve tri razine poučavanja sukladno svojoj dobi čine kombinirane odgojno-obrazovne skupine od 8 – 20 učenika pod vodstvom učitelja/nastavnika mentora. Ovisno o broju učenika na školskoj razini te o iskazanom interesu učenika za ovaj program u nekim školama postoji više odgojno-obrazovnih skupina i više mentora.

Mentori su u najvećem broju učitelji i nastavnici STEM (*Science, Technology, Engineering, and Mathematics*) područja te stručni suradnici poput knjižničara, pedagoga i psihologa. Svi su mentori prošli edukaciju o biosigurnosti i biozaštiti za učitelje, nastavnike i stručne suradnike u organizaciji Hrvatskog društva za biosigurnost i biozaštitu Hrvatskog liječničkog zbora te institucija partnera. U školskoj godini 2022./2023. deset učitelja i nastavnika prošlo je poseban oblik edukacije te su stekli status učitelja-edukatora iz područja biosigurnosti i biozaštite.

U suradnji s institucijama nositeljima projekta Ministarstvo znanosti i obrazovanja prije početka nove školske godine na svojim internetskim stranicama objavljuje Javni poziv za sudjelovanje osnovnih i srednjih škola u projektu „Biosigurnost i biozaštita" te se na taj način škole prijavljuju za sudjelovanje.



Slika 1. *Broj škola uključenih u projekt „Biosigurnost i biozaštita" u osnovnim i srednjim školama u Republici Hrvatskoj tijekom prve tri godine provođenja*

Prva slika pokazuje uzlazni trend interesa škola za sudjelovanje u projektu „Biosigurnost i biozaštita". U drugoj školskoj godini provođenja projekta broj uključenih škola povećao se za 54,27 %. U trećoj godini provođenja projekta porast u odnosu na prvu godinu iznosi 58,76 %, a 9,39 % u odnosu na školsku godinu 2021./2022.

Porastu škola uključenih u projekt doprinijela je velika medijska pozornost koju je projekt dobio, preporuka Ministarstva znanosti i obrazovanja te uloga Agencije za odgoj i obrazovanje u popularizaciji projekta putem organizacije stručnog usavršavanja djelatnika osnovnih i srednjih škola te organizacije smotre istraživačkih projekata.

Slika 2. *Udio odgojno-obrazovnih skupina učenika u projektu „Biosigurnost i biozaštita“*

Druga slika pokazuje da su srednje škole zastupljene s 50 %, a najmanje je učenika 5. i 6. razreda. U kontekstu popularizacije biomedicinskih znanosti (jednog od ciljeva projekta) ovo su pozitivni pokazatelji jer odgojno-obrazovni ishodi biosigurnosti i biozaštite više su zastupljeni u ovoj dobi, a učenici lakše svladavaju biosigurnosne vještine zbog stečenih predznanja s nižih razina poučavanja. S druge strane, pozitivno je da se i određeni broj učenika od 5. do 6. razreda susreće s usvajanjem biosigurnosnih vještina i kompetencija na odgovarajućoj razini.

Uvođenjem projekta „Biosigurnost i biozaštita“ kao izvannastavne aktivnosti u osnovnim i srednjim školama povećana je i satnica poučavanja STEM područja, osobito područja biomedicinskih znanosti. Broj učenika uključenih u projekt tijekom tri godine blizu je broja 12 000. U 5. i 6. razredu učenici sudionici projekta imaju u prosjeku 7,4 % više sadržaja iz područja biomedicinskih znanosti, a učenici 7. i 8. razreda 6,8 %. Na nacionalnoj razini ukupan broj sati provođenja biosigurnosti i biozaštite u školskoj godini 2020./2021. iznosio je 4480 na nacionalnoj razini, 2021./2022. 9800 sati, a u školskoj godini 2022./2023 ukupno 10 815 sati. Ukupno je provedeno 25 095 sati. Ovome treba dodati i sate koje učenici ostvaruju sa svojim mentorima u pripremi učeničkih istraživačkih projekata te sudjelovanje na zajedničkim edukacijama.

Učitelji i nastavnici provode kurikulum Biosigurnosti i biozaštite u fondu od 35 ili 70 sati godišnje.

Pri kreiranju kurikuluma Biosigurnosti i biozaštite za osnovne i srednje škole polazišna je točka bila sveobuhvatan pristup i korelacija sa sadržajima koji se poučavaju u drugim nastavnim predmetima i međupredmetnim temama. Poučavanje sadržaja Biosigurnosti i biozaštite u osnovnim i srednjim školama koristi multidisciplinarni pristup kroz korelaciju biomedicinskih znanosti, informacijsko-komunikacijske tehnologije, povijesti, ekologije, matematike i umjetnosti vodeći se načelom aktualizacije. Biosigurnost i biozaštita dio je poučavanja STEM područja te se velikim dijelom provodi u korelaciji s predmetnim kurikulumom Biologije, Kemije, Matematike, Fizike, Geografije, Povijesti i Informatike.

Usvajanje vještina vezanih za ovo područje pridonosi ostvarivanju svih temeljnih vrijednosti hrvatskog odgojno-obrazovnog sustava. Temeljne vrijednosti i načela na kojima počiva poučavanje biosigurnosti i biozaštite su: znanstvena utemeljenost, načelo aktualizacije, ekološke vrijednosti, očuvanje vlastitog zdravlja i zdravlja drugih ljudi, etičnost, suradnički odnos, kritičko mišljenje, kreativno izražavanje i sl.

Kurikulum Biosigurnosti i biozaštite kreiran je tako da usvajanjem ishoda učenici ovladaju temeljnim biosigurnosnim znanjima i kompetencijama. Područja poučavanja biosigurnosti i biozaštite u osnovnim i srednjim školama su sljedeća: biosigurnost i biozaštita, zarazne bolesti i njihovi uzročnici, epidemiološki – Vogralicov lanac, emergentne i reemergentne bolesti, koronavirusi – pošast 21. stoljeća, velike svjetske pandemije, „Jedno zdravlje“ te biosigurnost – međunarodne organizacije i Hrvatska. Kurikulumska područja, odgojno-obrazovni ishodi i područja kurikuluma jednaki su za sve tri razine poučavanja. Razlike su vidljive u razradi ishoda koji su primjereni dobi učenika i nacionalnom kurikulumu.

U prvom poglavlju kurikuluma Biosigurnosti i biozaštite od učenika se očekuje svladavanje sljedećih ishoda: navodi definiciju biosigurnosti i biozaštite, opisuje područja biosigurnosti i biozaštite, objašnjava svrhu učenja i poučavanja biosigurnosti i biozaštite, objašnjava načine zaštite od prijenosa zaraznih bolesti, prepoznaje simbol za biološku opasnost (biohazard), opisuje uvjete za rad s biološkim materijalom u biosigurnosnim laboratorijima (BSL) kao i izolacijske prostore u zdravstvenim ustanovama, opisuje zaštitnu opremu za rad s opasnim uzročnicima, razlikuje vrste zaštitnih maski i njihovu različitu uporabu, navodi primjere poznatih slučajeva bioterorizma te primjenjuje stečena znanja i vještine u svakodnevnom životu. Drugo poglavlje vezano je uz patogene mikroorganizme kao uzročnike zaraznih bolesti, a od učenika se očekuje da opisuje, navodi i razlikuje osnovne vrste patogenih mikroorganizama, objašnjava način djelovanja patogena u ljudskom

organizmu, objašnjava osnovne principe imunološkog odgovora, analizira učestalost zaraznih bolesti u Hrvatskoj i njihovih uzročnika, objašnjava nastanak zoonoza, opisuje ulogu cijepljenja kao važne javnozdravstvene mjere, navodi primjere eradiciranih zaraznih bolesti te objašnjava kalendar cijepljenja u Republici Hrvatskoj. Treće poglavlje se odnosi na znanja i vještine vezane uz sastavnice i povezanost u epidemiološkom (Vogralikovom) lancu, a ishodi koje učenici svladavaju su: navodi i opisuje izvore zaraze, analizira putove prijenosa i širenja zaraze, razlikuje ulazna mjesta zaraze, objašnjava dostatnu količinu i virulenciju uzročnika, analizira osjetljivost ili dispoziciju domaćina na određenu bolest, objašnjava povezanost i međuodnos karika u lancu te grafički prikazuje Vogralikov lanac. Četvrto poglavlje bazira se na uzrocima i pojmu emergentnih i reemergentnih bolesti te učenik nakon svladanih ishoda objašnjava pojam emergentnih i reemergentnih bolesti, ekološke, demografske, socijalne i političke uzroke nastanka emergentnih i reemergentnih bolesti, analizira geografsku rasprostranjenost emergentnih i reemergentnih bolesti, izrađuje kartogram emergentnih i reemergentnih bolesti u svijetu, opisuje opasnost od bioterorizma i upotrebe znanosti u neetične svrhe, objašnjava i analizira emergentne i reemergentne bolesti u kontekstu nacionalno-sigurnosnih ugroza. Peto poglavlje odnosi se na koronaviruse u 21. stoljeću i njihove posljedice na zdravlje čovjeka i svjetsku ekonomiju. Učenik opisuje nastanak i tijek pandemija SARS, MERS i SARS-CoV-2, objašnjava posljedice pandemije na zdravlje ljudi i smrtnost stanovništva, analizira utjecaj pandemije na svjetsko gospodarstvo, objašnjava preventivne mjere protiv širenja zaraznih bolesti, primjenjuje način zaštite od prijenosa zaraznih bolesti, opisuje uzročno-posljedične odnose suvremenog načina života i širenja bolesti (prednosti i nedostatke), grafički prikazuje statističke podatke o broju oboljelih i umrlih u Hrvatskoj po županijama i analizira ih i uspoređuje, grafički prikazuje statističke podatke o broju oboljelih i umrlih u svijetu i analizira ih i uspoređuje, analizira važnost pojedinca kao odgovornog člana društva u suzbijanju širenja zaraznih bolesti na primjeru SARS-COV-2 te vrednuje informacije iz znanstvenih i medijskih izvora u kontekstu pandemije i zaštite zdravlja. Šesto poglavlje kurikuluma u korelaciji s Povijesti temelji se na primjerima velikih svjetskih pandemija te njihovog utjecaja na čovječanstvo. Zadatak učenika je da nakon ovoga poglavlja navodi i opisuje velike svjetske pandemije, opisuje pandemiju kuge i način širenja po svijetu, opisuje pandemiju španjolske gripe i uzroke velike smrtnosti, objašnjava pojavu i raširenost AIDS-a (*Acquired Immunodeficiency Syndrome* – sindrom stečene imunodeficijencije) u svijetu, uspoređuje karakteristike velikih svjetskih pandemija, njihovu geografsku rasprostranjenost, broj oboljelih i umrlih te utjecaj na čovječanstvo i opisuje spomenike povezane uz pandemije; npr. Kugin spomenik u Osijeku; spomenik Robertu Kochu na Brijunima. Želja je autora projekta da se učenici upoznaju s konceptom „Jedno zdravlje" te se sedmo poglavlje kurikuluma odnosi na važnost ovog koncepta na lokalnoj, nacionalnoj i globalnoj razini te nakon svladanih ishoda učenik: navodi, opisuje i definira pojam „Jedno zdravlje", objašnjava važnost njegova pristupa na primjeru Vennovog dijagrama, primjenjuje znanja i vještine o emergentnim i reemergentnim bolestima u kontekstu pristupa „Jedno zdravlje", navodi primjer pojave, praćenja i nadzora emergentnih i reemergentnih arbovirusa u Republici Hrvatskoj u kontekstu pristupa „Jedno zdravlje". Posljednje, osmo poglavlje, odnosi se na međunarodne organizacije s područja biosigurnosti i biozaštite u Hrvatskoj i svijetu te doprinos hrvatske medicine i domaćih stručnjaka ovome području.

Izvannastavna aktivnost i dodatni program Biosigurnost i biozaštita kroz svoj kurikulum u potpunosti je implementirala sve dijelove nacionalnog kurikuluma međupredmetnih tema. Područje informacijsko-komunikacijske tehnologije zastupljeno je kroz izradu postera u različitim digitalnim alatima, prikupljanje znanstveno utemeljenih informacija putem internetskih pretraživača, izradu kvizova, stripova, igrica i drugih edukativnih materijala. Kroz sve aktivnosti učenici uče pravilno postaviti problem koji će proučavati kako bi s pomoću raspoloživih resursa pronašli rješenje. Na taj način učvršćuju i razvijaju područje građanskog odgoja i obrazovanja. Istražujući ponuđene teme u kurikulumu Biosigurnosti i biozaštite, učenici uče kako unaprijediti i zaštititi svoje zdravlje, a samim time i razvijati nove poduzetničke ideje koje nastaju kao rezultat istraživačkih radova učenika. Kreativnost, samopouzdanje, razvoj komunikacijskih i socijalnih vještina temelj su timskog rada koji njegujemo u području Biosigurnosti i biozaštite, a tako učenici doprinose napretku svog osobnog i socijalnog razvoja. Održivi razvoj načelo je koje se poštuje kroz cijelu edukaciju, a tema „Učiti kako učiti" kroz svoje različite načine i oblike poučavanja temelj je kurikuluma Biosigurnosti i biozaštite.

Kako bi se osigurala znanstvena utemeljenost izvannastavnih sadržaja, za potrebe provedbe projekta Hrvatsko društvo za biosigurnost i biozaštitu je pripremilo sve obrazovne sadržaje u obliku digitalnih platformi za sve tri razine poučavanja prema propisanom Kurikulumu.

Svi obrazovni sadržaji na digitalnoj platformi prošli su znanstvenu i stručnu recenziju. Također su javno dostupni i digitalni priručnici za učitelje i nastavnike mentore s uputama i odgojno-obrazovnim materijalima za obradu sadržaja. Posebna je pozornost usmjerena i na učenike s teškoćama te su i za njih napravljene prilagodbe kako bi mogli sudjelovati u projektu s ostalim učenicima.

2. Dosadašnja postignuća projekta „Biosigurnost i biozaštita"

Upravo je pandemija bolesti COVID-19 pokazala nedostatak zdravstvene pismenosti, čije je podizanje glavni cilj provedbe projekta „Biosigurnost i biozaštita". Edukacija od najranije dobi najbolje je sredstvo za postizanje željenih rezultata. Glavni ciljevi projekta „Biosigurnost i biozaštita" u osnovnim i srednjim školama su: upoznavanje učenika s važnošću stručnog, znanstvenog, globalnog i osobnog pristupa u sprječavanju širenja zaraznih bolesti, analiziranje potencijalnih opasnosti biougroza i načina njihove prevencije, upoznavanje učenika s opasnim uzročnicima i njihovim načinom djelovanja, razvijanje odgovornog ponašanje prema svome i tuđem zdravlju u školi, obiteljskom domu i prirodi, razvijanje ekološke svijesti učenika u kontekstu održivog razvoja, razvijanje zdravih navika učenika, osposobljavanje učenika za prosuđivanje i vrednovanje informacija u javnom medijskom prostoru. Biosigurnost i biozaštita dio su STEM područja te projekt doprinosi popularizaciji znanosti i istraživanju kroz istraživački rad, osobito u STEM području.

Ciljevi projekta odnose se i na razvijanje socijalno-komunikacijskih vještina učenika kao što su razvijanje suradničkog odnosa među učenicima te učenicima i mentorima, razvijanje komunikacijskih i prezentacijskih vještina i kreativnog načina izražavanja. Kao dodatni cilj naglašeno je razvijanje i usavršavanje digitalnih kompetencija učenika putem izrade digitalnih videomaterijala i audiomaterijala, prezentacija, slika i kvizova.

Biosigurnost i biozaštita u osnovnim i srednjim školama potiče stručno usavršavanje ravnatelja, učitelja, nastavnika i stručnih suradnika u školi u suradnji sa znanstvenim institucijama i stručnjacima u Republici Hrvatskoj te Agencijom za odgoj i obrazovanje u sklopu cjeloživotnog učenja kroz organizaciju stručnih skupova, *webinara* i digitalnih platformi za poučavanje. U želji da su edukacije dostupne što većem broju odgojno-obrazovnih djelatnika omogućen je pristup svim odgojno-obrazovnim djelatnicima Hrvatske. Edukacije se organiziraju tri puta godišnje na državnoj i međužupanijskoj razini. Od kolovoza 2023. pristup edukacijama omogućen je i učiteljima i nastavnicima iz Bosne i Hercegovine. Na internetskoj stranici projekta www.biosigurnost.eu dostupne su teme s dosadašnjih stručnih skupova. Prosječan broj učitelja prisutnih na edukacijama kreće se oko 500, a prosječna ocjena sudionika o izboru tema, gostima predavačima i organizaciji skupova je iznad 4,9, što ove edukacije svrstava među najuspješnije u suorganizaciji Agencije za odgoj i obrazovanje.

Cilj je uključivanje što više znanstvenih institucija u projekt te njihova suradnja, kao i uspostava suradnje osnovnih i srednjih škola sa znanstvenim institucijama. Svoja vrata učeničkom istraživačkom radu otvorile su brojne institucije poput Klinike za infektivne bolesti „Dr. Fran Mihaljević", Hrvatski zavod za javno zdravstvo, Veterinarski fakultet, Nastavni zavodi za javno zdravstvo, biološki odsjeci pri fakultetima odgojno-obrazovnih znanosti i dr.

Izvannastavna aktivnost Biosigurnost i biozaštita za ostvarenje odgojno-obrazovnih ciljeva i usvajanje ishoda planiranih kurikulumom Biosigurnosti i biozaštite naglašava provedbu aktivnosti i metoda kao što su: istraživačka nastava, učenje putem rješavanja problema, učenje putem videomaterijala, praktični rad, unos, obrada i analiza podataka, *online* učenje, rješavanje *online* kvizova i upitnika, izrada grafičkih priloga (slika i kartograma), fotografiranje svih faza projekta, izrada plakata i prezentacija, sudjelovanje u edukacijama i radionicama te vrednovanju projekta.

U svrhu ostvarivanja zadanih ciljeva koji se odnose na popularizaciju znanosti i usvajanja biosigurnosnih te odgojno-obrazovnih ciljeva projekta, organizira se Smotra biosigurnosti i biozaštite u organizaciji Ministarstva znanosti i obrazovanja i Agencije za odgoj i obrazovanje u suorganizaciji s ostalim nositeljima projekta. Smotra biosigurnosti i biozaštite smotra je istraživačkih radova učenika osnovnih i srednjih škola koje sudjeluju u projektu „Biosigurnost i biozaštita" u vidu izvannastavne aktivnosti. Ravnopravna je sa svim ostalim natjecanjima i smotrama u Republici Hrvatskoj. Učenici u sklopu izvannastavne aktivnosti i projektne nastave provode istraživanje i izrađuju male znanstvene postere koje prezentiraju na međužupanijskoj smotri, a oni najuspješniji i na državnoj razini. Za Smotru biosigurnosti i biozaštite za 2023. godinu prijavili su se učenici i mentori iz 128 osnovnih i srednjih škola. Dosad su u protekle tri godine na smotrama sudjelovali učenici

iz 333 tima sa svojim mentorima (Slika 3.). Posteri svih učenika koji su izrađeni tijekom projekta izloženi su na Nacionalnoj izložbi učeničkih radova otvorenoj za javnost u organizaciji Hrvatskog društva za biosigurnost i biozaštitu.

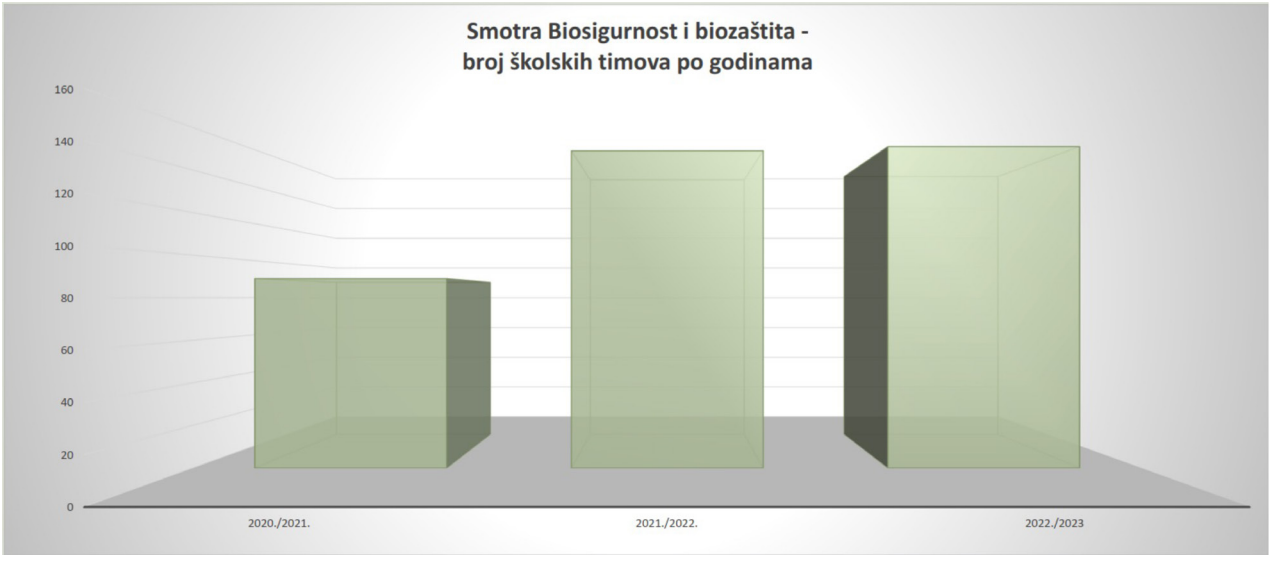
Istraživački rad ima veliku važnost u području obrazovanja jer njime se u smislu akademskog napredovanja dobivaju mnogi benefiti. Područje tehnologije, medicine, prirodnih i društvenih znanosti nezamislivo je bez istraživačkog rada na osnovi kojeg se dolazi do novih spoznaja, analiziraju postojeći i donose zaključci u cilju poboljšanja i unaprjeđenja određenih područja. Učenicima je istraživački rad neophodan za stvaranje novih spoznaja kroz utvrđene etape, a kao prirodoslovnu pismenost učenici uče kako formulirati istraživačko pitanje, postaviti hipotezu, odabrati potreban materijal i pribor za provođenje istraživanja, matematički prikazati rezultate te, najvažnije, razlikovati opažanje od zaključaka. Razvoj novih tehnologija oslanja se na istraživanja, a rezultati doprinose unaprjeđenju kvalitete života i općenito napretku u znanosti. U školama se nastoji potaknuti zanimanje za STEM područje u svakodnevnim aktivnostima, ali i u izvannastavnim aktivnostima. Biosigurnost i biozaštita izvannastavna je aktivnost koja je bazirana na istraživačkom radu i kao takva doprinosi razvoju kompetencija učenika koje se involviraju u sve ostale predmete gdje je takav rad neophodan.

Primjer Hrvatske u poučavanju sadržaja Biosigurnosti i biozaštite slijedi i Bosna i Hercegovina, koja je u pripreme projekta te se očekuje implementacija u škole tijekom 2024. godine, a svoj interes iskazale su Švedska i Mađarska.

ZAKLJUČAK

Nakon uspješno provedenog projekta u posljednje tri godine na osnovi vrednovanja ostvarenih ishoda ispunjeni su sljedeći očekivani rezultati: oblikovan način razmišljanja i ponašanja učenika kao odgovornih članova društva vezanih uz osobno zdravlje i zdravlje drugih ljudi, primjena znanja o opasnim uzročnicima, prevenciji i zaštiti od istih, razvijena ekološka svijest učenika i interes za ekologiju, razvijen interes za istraživački rad i STEM područje, razvijene digitalne kompetencije vezane uz programiranje, mjerenje, unos, obradu, analizu i prezentaciju podataka, razvijen suradnički odnos učenika i mentora te razvijene komunikacijske i prezentacijske vještine.

Veliki broj učitelja, nastavnika i stručnih suradnika koji su prihvatili kurikulum Biosigurnosti i biozaštite u osnovnim i srednjim školama u Republici Hrvatskoj i ostvaruju njegove ishode pokazuje kako su ovakva poučavanja potrebna, ali i djeci zanimljiva. Danas je ovaj projekt dobro prihvaćen u velikom broju škola, a Hrvatska je jedina zemlja u Europi koja ima sustavno razrađeno poučavanje o biosigurnosnim ugrozama, čiji primjer počinju slijediti i druge zemlje.



Slika 3. *Broj školskih timova sudionika smotre Biosigurnosti i biozaštite po godinama*

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S U M M A R Y

EDUCATION ON BIOSAFETY AND BIOSECURITY IN THE CROATIAN EDUCATION SYSTEM

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Abstract:
The Croatian education system from the school year 2020/2021 has had a systematic education of students, teachers, professional associates, and principals on biosafety and biosecurity. The project was initiated by Elementary School Vijenac from Osijek with the support of the Croatian Society for Biosafety and Biosecurity, the University Hospital for Infectious Diseases "Dr. Fran Mihaljević", the Croatian Institute of Public Health, the Croatian Academy of Medical Sciences, the Ministry of Science and Education of the Republic of Croatia and the Education and Teacher Training Agency. The SARS-CoV-2 virus has shown the importance of additional education for students, teachers, mentors, professional associates, and principals about the aforementioned problem. The importance of promoting the value of preserving human health and preventing infectious diseases was the main aim for starting this project. The main goals of the project were to familiarize students with the importance of a professional, scientific, global, and personal approach to preventing the spread of infectious diseases; familiar with dangerous agents and their mode of action; adoption of responsible behavior towards one's own and others' health; analyzing potential dangers of biothreats and methods of prevention; popularization of science and research in the STEM field (science, technology, engineering and mathematics) through a student research project; developing interest in science; developing a collaborative relationship; development and improvement of digital competences; encouragement of communication and presentation skills and professional training of teachers. The number of students involved in the project over three years is close to 12,000, and a total of 25,095 hours of teaching have been completed in more than 300 schools. Students present their research projects at the Exhibition of Student Works organized by the Education and Teacher Training Agency, and the works are presented every year at the Annual exhibition organized by the Croatian Society for Biosafety and Biosecurity.

Keywords: biosafety, biosecurity, health literacy, student and teacher education

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BIOSIGURNOST U ORGANIZACIJI COVID STACIONARA ARENA TIJEKOM PANDEMIJE COVID-19 BOLESTI – KAKO OD SPORTSKE DVORANE USPJEŠNO NAPRAVITI BOLNICU?

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SAŽETAK

Tijekom pandemije COVID-19 bolesti zdravstveni sustav doživio je preopterećenja koja su zahtijevala organizacijske promjene. Veliki i temeljni izazov organizacijskih promjena bili su oboljeli koji su zahtijevali stacionarno bolničko liječenje u jedinicama intenzivne skrbi i COVID odjelima.

Vršna popunjenost bolničkih kreveta i opterećenje zdravstvenog osoblja bilo je najveće tijekom drugog i trećeg vala pandemije. Zbog potrebe za dodatnim bolničkim krevetima u uvjetima popunjenosti akutnih COVID bolnica, Klinike za infektivne bolesti „Dr. Fran Mihaljević" i Kliničke bolnice Dubrava, te po potrebi i u ostalim bolnicama koje su imale organizirane odjele za skrb o oboljelima od COVID-19 bolesti, u studenom 2020. godine u zdravstveni je sustav Republike Hrvatske integrirana sportska dvorana Arena u Zagrebu. Svrha organizacije i pokretanja bila je smještaj pacijenta koji su bili pri kraju bolničkog liječenja i pacijenata s blažim i srednje teškim oblikom bolesti koji su zahtijevali bolničko liječenje.

Klinički bolnički centar Sestre milosrdnice bio je zadužen za organizaciju rada stacionara u Areni. Krajem listopada 2020. godine ustrojen je Operativni stožer s glavnim koordinatorom i koordinatorima za liječnike, sestrinstvo i kontrolu infekcija povezanih sa zdravstvenom skrbi. Dio stožera bili su pripadnici Glavnog stožera OSRH-a (Obrambenih snaga Republike Hrvatske) za zdravstvo, Civilna zaštita RH i uprava dvorane. U rad su uključeni djelatnici informatičke službe, Sektora financijsko-ekonomskih i tehničkih poslova, ljekarne, biokemijskog laboratorija i po potrebi ostale djelatnosti KBC Sestre milosrdnice. Čišćenje i dezinfekciju obavljao je vanjski servis, a usluge prehrane Pleter-Usluge d. o. o.

Operativni stožer održavao je svakodnevne sastanke. Prije otvaranja napisani su postupnici rada, provedeno početno čišćenje i dezinfekcija, provjeren vodovodni sustav na prisutnost *Legionella* sp., uvježbani djelatnici za postupke čišćenja te su provedene pokazne vježbe.

Stacionar je podijeljen u prostorno i ventilacijski odvojene zone. Bolesnička zona sa 100 kreveta opremljena je laboratorijem, RTG uređajem, prostorom za reanimaciju i ljekarnom. Stacionar je umrežen među zonama i s matičnom bolnicom. Prije izmjene djelatnika održavan je edukacijski dan. U stacionaru je radilo 30 liječnika iz KBC-a Sestre milosrdnice i 6 liječnika iz MORH-a te 112 medicinskih sestara/tehničara iz zagrebačkih bolnica i MORH-a. Ukupno je zbrinuto 282 bolesnika iz zagrebačkih bolnica te iz Petrinje i Siska nakon potresa. Tijekom rada nije bilo podjele na zdravstvene i nezdravstvene djelatnike. Stacionar je prestao s radom u svibnju 2021. godine.

Kohezijska snaga svih službi uključenih u djelovanje stacionara pokazala je sposobnost stvoriti učinkovitu i sigurnu bolnicu u prostoru nenamijenjenom za pružanje zdravstvene skrbi

Ključne riječi: COVID-19, bolnica, sportska dvorana, zdravstveni sustav, biosigurnost

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UVOD

Pandemija COVID-19 bolesti stavila je na kušnju mogućnosti zdravstvenih sustava diljem svijeta u pružanju skrbi pacijentima oboljelim od nove virusne bolesti i obavljanju svakodnevne zdravstvene skrbi u non-COVID-19 populaciji. Prvi izvještaji o pojavi grupiranja slučajeva pacijenata oboljelih od atipične pneumonije nepoznatog uzročnika koja se brzo širila u gradu Wuhanu u pokrajini Hubei u Kini u prosincu 2019. godine govorili su o sve većem broju oboljelih koji su zahtijevali bolničko liječenje. Do kraja siječnja 2020. godine virus se proširio diljem svijeta u 20 različitih zemalja te je Svjetska zdravstvena organizacija (SZO) 30. siječnja 2020. godine proglasila javnozdravstvenu prijetnju od međunarodnog značaja (engl. *Public Health Emergency of International Concern – PHEIC*), što je bio signal za akciju globalnog odgovora na prijetnju biosigurnosti (1 – 2).

U Republici Hrvatskoj (RH) 31. siječnja 2020. godine aktiviran je Krizni stožer Ministarstva zdravstva koji je imao zadaću koordinacije zdravstvenog sustava i organizaciju protokola za postupanje u kriznim situacijama vezanim za pojavu nove bolesti koja je već tijekom siječnja pokazala potencijal brzog širenja (3). Nakon toga odlukom Vlade RH 20. veljače 2020. godine osnovan je i Stožer civilne zaštite Republike Hrvatske na čelu s potpredsjednikom Vlade RH i ministrom unutarnjih poslova Davorom Božinovićem. U radu Stožera, koji je osnovan na temelju Zakona o sustavu civilne zaštite, sudjelovali su predstavnici različitih ministarstava, Hrvatskog zavoda za javno zdravstvo (HZJZ), Civilne zaštite i predstavnici institucija uključenih u odgovor na novonastalu biološku ugrozu stanovništva (4 – 6). Pripreme preporuka o sprječavanju širenja bolesti i smjernice za postupanje prilikom hospitalizacije novooboljelih bile su javno dostupne u razdoblju prije proglašenja pandemije 11. ožujka 2020. godine. U prvom pandemijskom valu u proljeće i ljeto 2020. g. u RH broj novooboljelih koji su zahtijevali bolničko liječenje nije zahtijevao otvaranje dodatnih stacionara s bolesničkim krevetima osim postojećih u bolničkim ustanovama.

U rujnu 2020. godine broj oboljelih počinje rasti razvijajući drugi pandemijski val. Dinamiku rasta broja zaraženih osoba pratila je dinamika potreba za bolničkim krevetima u jedinicama intenzivnog liječenja i u COVID odjelima bolničkih ustanova. Tjedni broj novohospitaliziranih pacijenata bio je 522 u trećem tjednu listopada, uz tendenciju rasta svaki tjedan od sredine rujna (7). Pritisak za potrebom novih bolničkih kreveta u gradu Zagrebu dodatno je bio otežan činjenicom da su u Zagrebu najveće ustanove tercijarne zdravstvene skrbi koje su pružale zdravstvenu skrb pacijentima oboljelim od ostalih bolesti i koje su za održavanje te djelatnosti trebale imati osigurane bolesničke krevete i dovoljan broj zdravstvenih djelatnika koji skrbe o njima.

Krajem listopada 2020. g. počinju pripreme za osiguravanje dodatnih stacionarnih kreveta za smještaj oboljelih s oblicima bolesti koji zahtijevaju bolničko liječenje.

CILJ

Cilj je ovog rada prikazati način planiranja, organizaciju i provođenja zdravstvene skrbi u COVID-19 Stacionaru Arena koji je organiziran u sportskoj dvorani Arena u Zagrebu za liječenje oboljelih od COVID-19 bolesti.

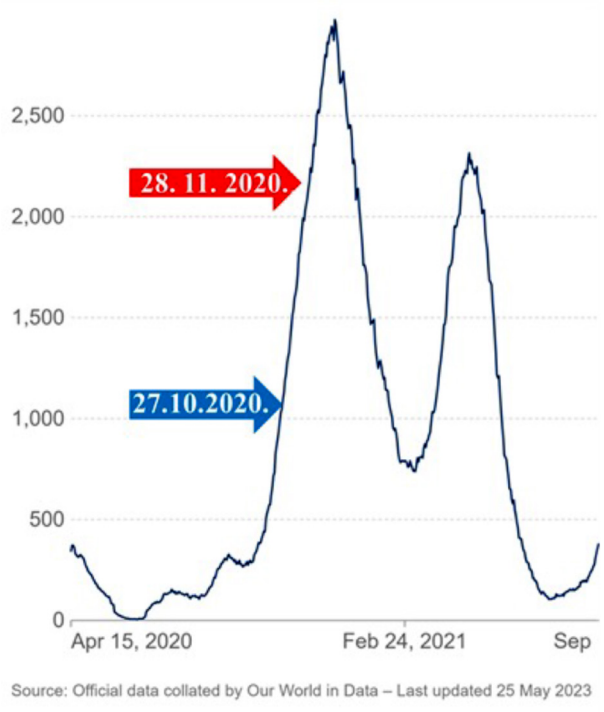
Pitanja na koja želimo dati odgovor jesu koje su aktivnosti provedene tijekom djelovanja stacionara, kako su provedene, tko je sudjelovao u njima i s kojim uspjehom.

METODE

Metode rada uključuju opise početka planiranja, način postavljanja u rad COVID-19 Stacionara Arena, aktivnosti koje su se provodile u provođenju zdravstvene i nezdravstvene skrbi, način osiguranja sigurnosti pacijenata u Stacionaru te način koordinacije djelatnika zdravstvenih i nezdravstvenih struka koji su sudjelovali u njegovom osnivanju, postavljanju, djelovanju i zatvaranju.

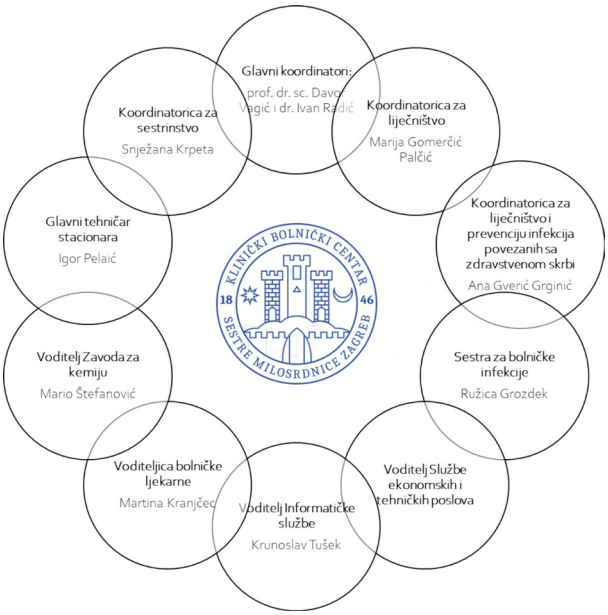
REZULTATI

Tijekom jesenskog pandemijskog vala, zbog rasta broja novozaraženih i novooboljelih koji su zahtijevali bolničko liječenje kao je prikazano na Slici 1., odlukom Stožera Civilne zaštite i ministra zdravstva krenula je priprema COVID-19 Stacionara u sportskoj Dvorani Arena. Sportska dvorana Arena nalazi se u Zagrebu u gradskom naselju Lanište, ima prostorni kapacitet *brutto* površine 90 500 četvornih metara, što uključuje parter s gledalištem, prvi, drugi, treći kat i natkriveno parkiralište te se nalazi uz Jadransku aveniju koja spaja Zagreb s autocestama.



Slika 1. *Broj hospitaliziranih pacijenata u jesenskom pandemijskom valu s vremenom početka pripreme i otvaranja Stacionara*

Za organizaciju rada COVID-19 Stacionara Arena odgovoran je bio Klinički bolnički centar Sestre milosrdnice. Prema odredbi ministra zdravstva od 27. listopada 2020. godine, u Kliničkom bolničkom centru Sestre milosrdnice održan je inicijalni sastanak Operativnog stožera Arena. Na tom prvom sastanku ravnatelj KBC-a Sestre milosrdnice prof. dr. sc. Mario Zovak ustrojio je Operativni stožer Arena koji su vodili glavni koordinatori prof. dr. sc. Davor Vagić i dr. Ivan Radić i koordinatori za aktivnosti u provođenju zdravstvene skrbi i osiguranju sigurnosti pacijenata, što je uključivalo koordinatore za liječnike, sestrinstvo i kontrolu infekcija povezanih sa zdravstvenom skrbi. U rad Operativnog stožera bili su uključeni djelatnici bolničke ljekarne, biokemijskog laboratorija, informatičke službe, Sektora financijsko-ekonomskih i tehničkih poslova i po potrebi ostali djelatnici KBC-a Sestre milosrdnice (Slika 2.).



Slika 2. *Koordinacija Operativnog stožera Arena iz KBC-a Sestre milosrdnice*

Uz članove Operativnog stožera koji su bili zaposlenici KBC-a Sestre milosrdnice, dijelom Operativnog stožera bili su pripadnici Glavnog stožera OSRH-a za zdravstvo, Civilna zaštita RH i uprava dvorane (Slika 3.).

Slika 3. *Koordinacija Operativnog stožera Arena izvan KBC-a Sestre milosrdnice*

Čišćenje i dezinfekciju obavljao je vanjski servis, a usluge prehrane Pleter-Usluge d. o. o.

Operativni stožer održavao je svakodnevne koordinacijske sastanke ujutro u 8 sati u svim razdobljima aktivnosti stacionara, što je uključivalo razdoblje pripreme, aktivnosti i zatvaranja stacionara. Prije otvaranja napisani su postupnici rada svih uključenih službi, provedeno početno čišćenje i dezinfekcija, provjeren vodovodni sustav na prisutnost *Legionella* sp., uvježbani su djelatnici vanjskog servisa za postupke čišćenja i dezinfekcije pod kontrolom sestre za prevenciju infekcija povezanih sa zdravstvenom skrbi, a Stacionar je opremljen potrebnim aparatima i opremom za obavljanje zdravstvene skrbi. U pripremnom razdoblju, nakon što su ustanovljeni putevi kretanja pacijenta i djelatnika i određeni postupnici aktivnosti, svakodnevno su provođene pokazne vježbe uz primjenu korektivnih mjera. Provođenje završne pokazne vježbe održano je dan prije otvaranja Stacionara 28. studenog 2020. godine (Slika 1).

Prvi pacijenti premješteni su u Stacionar iz Klinike za infektivne bolesti „Dr. Fran Mihaljević", KB-a Dubrava i KBC-a Sestre Milosrdnice.

Napisani postupnici rada uključivali su postupak prijema i indikacije za prijem (pacijenti na završetku bolničkog liječenja kojim je još bilo potrebno stacionarno liječenje), provođenje svakodnevne zdravstvene skrbi i njege, ulazak i sigurni izlazak djelatnika u prostore, mjere za sprječavanje širenja višestruko otpornih organizama među bolesnicima i sprječavanje infekcija povezanih sa zdravstvenom skrbi, čišćenje i dezinfekciju prostora, zbrinjavanje zaraznog otpada, otpust bolesnika i umrlih te postupnik u slučaju pojave simptoma COVID-19 bolesti kod djelatnika.

Prije svake izmjene smjena svi djelatnici imali su poseban edukacijski dan prije ulaska u prostor, u kojem su upoznati s prostorom, postupnicima i planom evakuacije. Određen je kućni red u zoni za djelatnike i u zoni za bolesnike. Kućni red u zoni za djelatnike uključivao je obavezno nošenje maske (medicinska maska ili FFP2), održavanje udaljenosti od dva metra za vrijeme odmora, obavezno provođenje higijene ruku nakon kontakta s potencijalno kontaminiranim površinama (tipkovnice), u slučaju pojave simptoma koji mogu upućivati na COVID-19 (temperatura, zimice, grlobolja, suhi kašalj, gubitak osjeta njuha i okusa, glavobolja, proljev i povraćanje uz temperaturu) obavještavanje nadležnog koordinatora (broj telefona i e-mail u mapi Arena javno na svim računalima) i odlazak kući. Kućni red u bolesničkoj zoni uključivao je zabranu primjene otvorenog plamena (upaljači) i zabranjeno pušenje zbog prisutnosti eksplozivnih plinova. Svi postupnici i kućni red bili su dostupni na svim računalima u Stacionaru. Stacionar je putem svih računala u bolesničkoj zoni, zoni za djelatnike i administraciji umrežen s matičnim KBC-a Sestre milosrdnice.

Stacionar je podijeljen u prostorno i ventilacijski odvojene zone za boravak djelatnika („čiste") i bolesničke („nečiste") zone s posebnim ulazima i putevima kretanja pacijenta i djelatnika. Svaka zona imala je odvojen ventilacijski sustavi s maksimalnim izmjenama vanjskog i unutarnjeg zraka, što je prema zahtjevima Operativnog stožera omogućila tehnička služba dvorane Arena.

„Čista" zona sastojala se od ulaznog hodnika odvojenog za djelatnike, prostora za administraciju u prizemlju i prostora za djelatnike na 2. katu (Slika 4. i 5.). Lože za gledatelje na 2. katu pretvorene su u prostorije za odmor i spavanje djelatnika, garderobe izvođača iskorištene su za skladišta čistih uniformi za djelatnike. Središnji prostor za oblačenje osobne zaštitne opreme postao je šank za prodaju pića za vrijeme utakmica i koncerata. Prijašnji prostor za tiskovne konferencije prenamijenjen je u veliku liječničku sobu za sastanke i administrativni rad. Već postojeći dvoranski restoran prilagođen je epidemiološkim mjerama s odvojenim stolovima za jednu osobu i dezinficijensom za ruke i površine na svakom stolu.

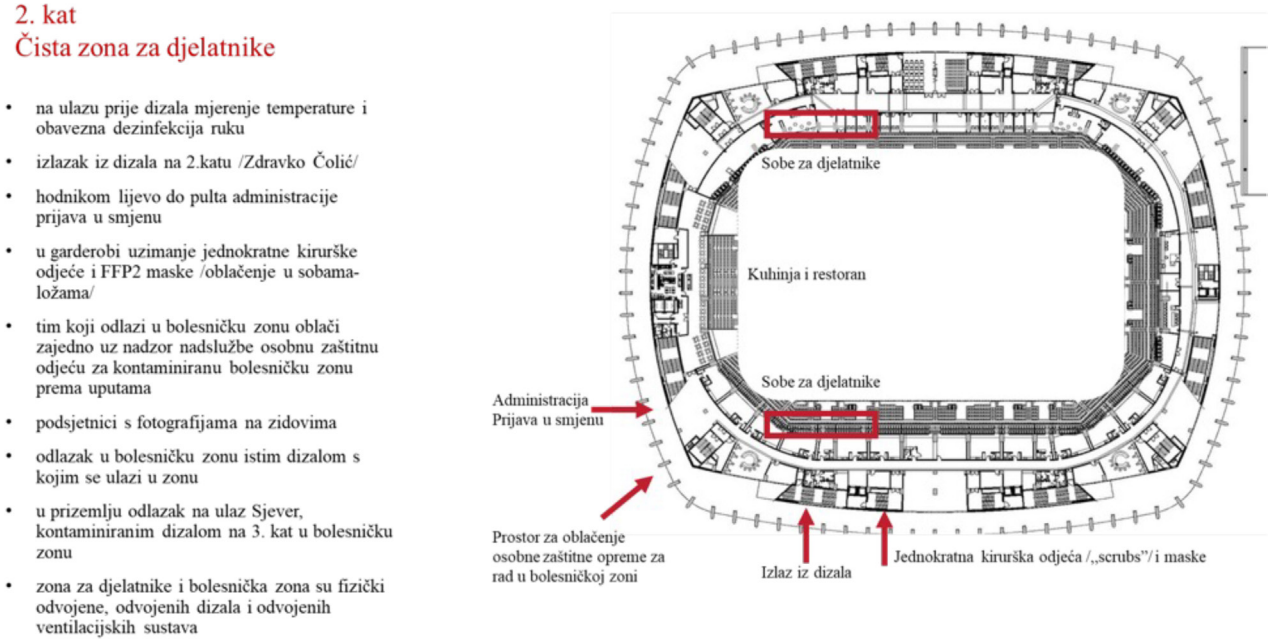
„Nečista" bolesnička zona nalazila se na 3. katu i podijeljena je prema kategorijama bolesnika ovisno o njihovim komorbiditetima. U različitom zonama bili su smješteni internistički, neurološki i kirurški pacijenti. Imala je 100 kreveta, od kojih su 62 kreveta bila opremljena 50-litarskim bocama za kisik.

U bolesničkoj zoni nalazio se biokemijski laboratorij u kojem su se određivali dijagnostički testovi (kompletna krvna slika, CRP i arterijski acido-bazni status), RTG uređaj, potpuno opremljen prostor za reanimaciju i bolnička ljekarna (Slika 6. i 7.).

Izvan zona odvojen je prostor za svlačenje osobne zaštitne opreme. Nalazio se u vanjskom prostoru parkirališta radi sprječavanja mogućeg prijenosa kontaminiranom opremom (Slika 7.).

U tom dijelu zaštićenog i ograđenog parkirališta nalazilo se sekundarno odlagalište zaraznog otpada s velikim spremnicima iz kojih se otpad odvozio svakodnevno.

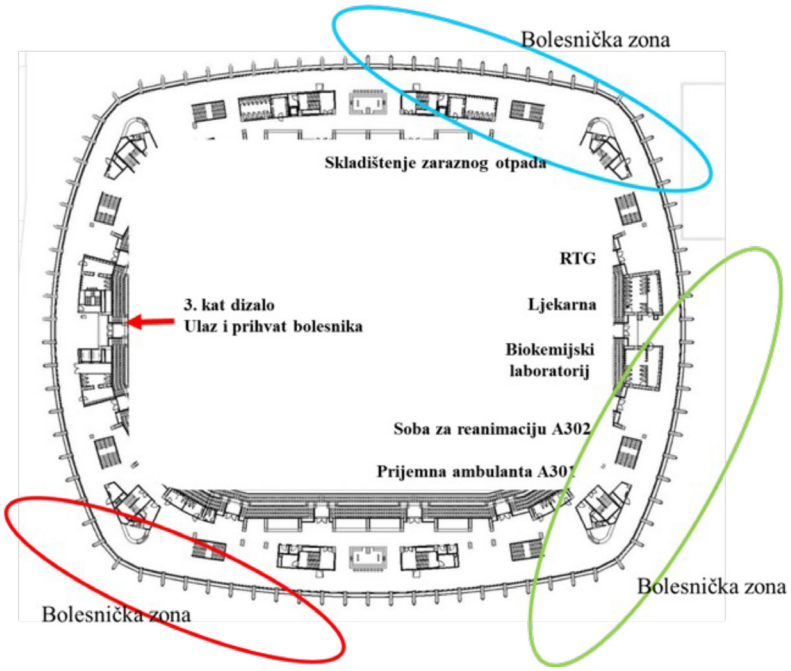
Slika 4. *Ulazni prostor za djelatnike u „čistu" zonu i odvojeni ulaz za pacijente u „nečistu" zonu*



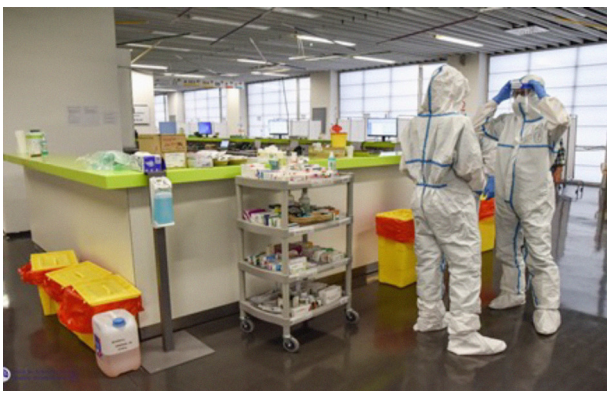
Slika 5. *Zona za djelatnike („čista zona")*

3. kat
kontaminirana bolesnička zona

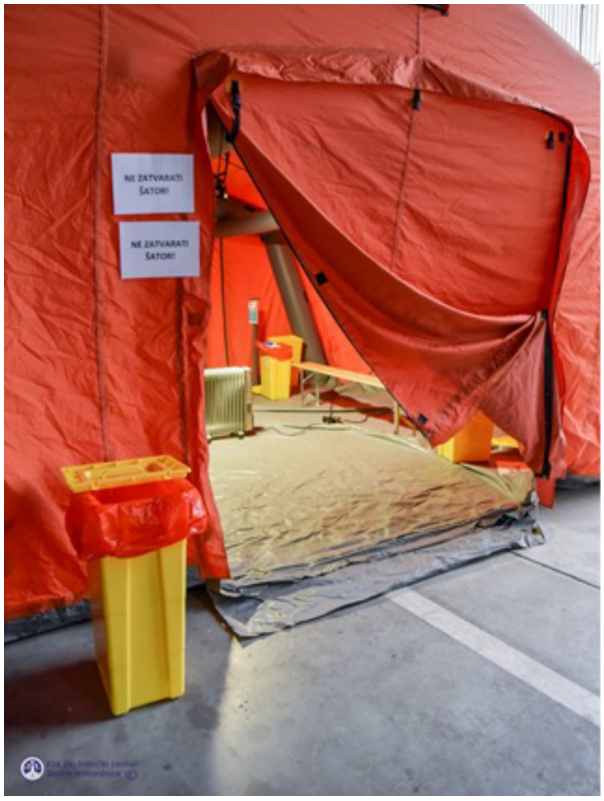
- ulazak bolesnika s djelatnicima saniteta na 3. kat kontaminiranim dizalom
- medicinska sestra prihvaća bolesnika /premještaj u Arenu dogovara nadslužba-liječnik specijalist iz središnjeg pulta/
- transport bolesnika u prijemnu ambulantu
- liječnički pregled, pregled dokumentacije i odluka o smještaju u određenu zonu
- zone za bolesnike s pultovima u boji: CRVENA, ZELENA I PLAVA zona ovisno o težini kliničke slike
- o kategorizaciji u zone detaljne upute koordinatora za liječničku službu doc. dr. sc. M. Gomerčić Palčić
- **Središnji ZELENI pult**
- posebne oznake za prijemnu ambulantu, biokemijski laboratorij, RTG, sobu za reanimaciju, ljekarnu i skladištenje infektivnog otpada



Slika 6. *Bolesnička zona („nečista zona“)*



Slika 7. *Bolesnička zona („nečista zona“)*



Slika 8. *Prostor za skidanje i odlaganje osobne zaštitne opreme*

Sveukupno je 36 liječnika i 112 medicinskih sestara i tehničara skrbilo o pacijentima tijekom djelovanja Stacionara. Trideset liječnika KBC-a Sestre milosrdnice specijalista internista, kardiologa, specijalist hitne medicine, specijalisti kirurgije, otorinolaringologije, urologije, ginekologije, fizikalne medicine, neurologije i specijalizanti različitih specijalnosti dragovoljno su se javili za rad u Stacionaru Arena. Hrvatska vojska sudjelovala je u pružanju skrbi s medicinskim timom od triju liječnika i šest medicinskih sestara/tehničara i logističkim timom od šest vojnika. Veliki broj medicinskih sestara i tehničara je, osim iz KBC-a Sestre milosrdnice, bio iz KBC-a Zagreb, Psihijatrijske bolnice Sv. Ivan i Klinike za psihijatriju Vrapče (Slika 9.).

Smjene djelatnika trajale su 12 sati dan, 12 sati noć i 24 sata slobodno u timovima koji su bili raspoređeni u stacionaru po mjesec dana. U jednom mjesečnom timu u smjenama se razmjenjivalo 18 liječnika i 50 medicinskih sestara/tehničara.

Tijekom razdoblja u kojem je bio aktivan, iz Kliničke bolnice Dubrava, Klinike za zarazne bolesti i iz KBC-a Sestre milosrdnice u stacionaru je liječeno 282 pacijenata. Taj broj uključuje i pacijente primljene nakon potresa koji je razorio Petrinju i Sisak. Smanjenjem pojavnosti COVID-19 bolesti smanjio se broj hospitaliziranih bolesnika te su 18. siječnja otpušteni zadnji bolesnici iz Arena stacionara, koji je ostao u pripravnosti u slučaju ponovnog širenja pandemije. Tijekom cjelokupnog razdoblja aktivnosti Stacionara nije bilo prijenosa virusa među bolesnicima i djelatnicima niti među djelatnicima.

Slika 9. *Zdravstveni djelatnici u prostoru „čiste zone“*

Priljev oboljelih u bolnički sustav u proljetnom valu epidemije 2021. godine nije zahtijevao ponovno otvaranje stacionara, stoga smo iz Arena stacionara uklonili sve što je korišteno da od sportske dvorane napravimo bolnicu, slučajnošću na simboličan datum 12. svibnja 2021. godine, Međunarodni dan sestrinstva.

RASPRAVA

Osnovni razlog organizacije i aktivacije COVID-19 Stacionara u sportskoj dvorani Arena u gradu Zagrebu za vrijeme drugog pandemijskog vala bio je rasterećenje zagrebačkih bolničkih ustanova i oslobađanje potrebnih kreveta za liječenje novooboljelih s teškim oblikom bolesti u bolnicama. S obzirom na to da je prema podacima tijekom listopada 2020. godine tjedni broj novooboljelih koji su hospitalizirani bio od 232 do 1082 i imao je trend rasta, potreba za bolničkim krevetima u bolnicama koje su skrbile o hospitaliziranim COVID-19 pacijentima povećavala se svakim danom (7). Pojavom nove virusne bolesti nije prestala pojavnost kroničkih nezaraznih bolesti i ostalih zaraznih bolesti. Prema Zdravstveno-statističkom ljetopisu grada Zagreba iz 2019. godine u pretpandemijskoj godini u zagrebačkim se bolnicama liječilo 254 268 pacijenta (8). U zdravstvenom sustavu trebalo je osigurati bolesničke krevete za sve pacijente kojima je potrebna zdravstvena skrb.

U Zagrebu je početkom 2020. godine, uz Kliniku za infektivne bolesti „Dr. Fran Mihaljević" osnovana i dodatna COVID-19 bolnica u prostorima Kliničke bolnice Dubrava. Ostale bolnice u Zagrebu osnovale su COVID-19 odjele i intenzivne jedinice te su uz to nastavile pružati skrb ostalim pacijentima iz područja grada Zagreba, okolnih županija, ali i ostalih područja Republike Hrvatske s obzirom na to da se radi o kliničkim ustanovama od kojih su neke i tercijarna razina zdravstvene skrbi.

To je u vrijeme najvećeg opterećenja na bolnički sustav stvorilo potrebu za otvaranjem dodatnog prostora za prihvat i liječenje COVID-19 bolesnika kojima je liječenje bilo pri kraju i kojima nije bila potrebna invazivna i neinvazivna strojna potpora disanju.

Način aktivacije Stacionara uključivao je osnivanje manjeg upravljačkog i koordinacijskog tijela koje se sastojalo od 5 do 10 stručnjaka za unaprijed definirana područja budućeg rada. Svakodnevnim koordinacijskim sastancima s vođenjem zapisnika o podijeljenim zadacima i svakodnevnom provjerom učinjenog, planiranje, uvježbavanje, pisane protokole i provjerom pridržavanja protokola postignuta je brza i učinkovita priprema Stacionara.

Članica tima zadužena za liječništvo nadzirala je raspored i zaduženja liječnika u stacionaru te je sudjelovala u procesu dogovora prijema, liječenja, potrebne dijagnostike i odluke o otpustu pacijenata iz stacionara. Glavna sestra i glavni tehničar stacionara sudjelovali su u održavanju rasporeda medicinskih sestara i tehničara i u procesu kontrole pružanja zdravstvene njege. Sestra za bolničke infekcije i liječnica zadužena za sprječavanje infekcija povezanih sa zdravstvenom skrbi svakodnevnim su izvidima i potrebnim korektivnim mjerama sudjelovale u postavljanju postupnika koji su omogućili sigurnost pacijenata i djelatnika stacionara.

Svakodnevna prisutnost visokomotiviranog i unaprijed educiranog i uvježbanog osoblja među pacijentima, a ne samo u dvorani za sastanke, osnova je učinkovitosti rada stacionara. Učinkovitost stacionara vidljiva je iz nekoliko mjerljivih ishoda. Uz činjenicu da se ni u jednom danu drugog pandemijskog vala s najvećim vršnim opterećenjima bolničkog sustava, koji je dodatno bio opterećen s primitkom pacijenata iz bolničkih ustanova u Petrinji i Sisku nakon potresa, nije dogodilo da bolesnik koji zahtjeva hospitalizaciju nije primljen u bolnicu, još je nekoliko dodatnih pokazatelja ishoda Stacionara Arena. Jedan je od njih činjenica da nije bilo prijenosa bolesti između zaraženih pacijenata i zdravstvenog i nezdravstvenog osoblja.

Sve navedeno u radu dragocjene su lekcije naučene tijekom postavljanja i djelovanja Stacionara Arena za vrijeme pandemije COVID-19 bolesti. Prema sličnim iskustvima u svijetu i one se temelje na interdisciplinarnom pristupu u suočavanju s biološkim ugrozama (9). Prve bolnice izvan bolnica, odnosno terenske privremene bolnice (engl. *field hospitals*) nakon početka pandemije COVID-bolesti ustanovljene su u Kini već u veljači 2020. godine. Nazvane su Fangcang skloništa (riječ Fangcang zvuči slično kao Noina arka u kineskom jeziku), izgrađene su na stadionima, u sportskim i sajamskim dvoranama te je u njima pružana zdravstvena skrb u izolacijskim uvjetima oboljelima s blagim i umjerenim oblikom COVID-19 bolesti. Koncept je preuzet iz vojne prakse, a glavne prednosti predstavljaju mogućnost brzog uspostavljanja, masovni prihvat oboljelih zbog velikog broja kreveta i niski troškovi. Terenske bolnice uspostavljene su u državama širom svijeta. Uz kineske Fangcung bolnice, najpoznatije su bile u Ujedinjenom Kraljevstvu (Nightingale Hospitals), Sjedinjenim Američkim Državama (Javits Centar u New Yorku) i Brazilu (Pacaembu Stadium u São Paulu). Glavna zadaća bila je preuzeti skrb o bolesnicima s lakšim oblikom bolesti i time omogućiti bolnicama pružanje skrbi teško oboljelima koji su zahtijevali kompleksniju i intenzivnu zdravstvenu skrb. Objavljene studije učinkovitosti i analize tokova i koristi terenskih bolnica pokazala su ekonomsku vrijednost ovakvih javnozdravstvenih intervencija u usporedbi s pružanjem standardne skrbi u prenapučenim bolnicama u zemljama u kojima su provedene.

Naša iskustva u postavljanju i radu Stacionara Arena temelj su intervencija u mogućim budućim zdravstvenim krizama uzrokovanim zaraznim bolestima.

ZAKLJUČAK

Kohezijska snaga svih službi uključenih u djelovanje stacionara pokazala je sposobnost stvoriti učinkovitu i sigurnu bolnicu u prostoru koji nema prostornih normativa za pružanje zdravstvene skrbi.

Na tom novostečenom znanju i iskustvu pandemijskog odgovora trebamo temeljiti svoju buduću spremnost za moguće biougroze i osiguravanje javnog zdravlja.

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SUMMARY

BIOSAFETY IN THE ORGANIZATION OF THE COVID ARENA FIELD HOSPITAL DURING THE COVID-19 PANDEMIC – HOW TO SUCCESSFULLY TURN A SPORTS HALL INTO A HOSPITAL?

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During the COVID-19 pandemic, healthcare systems all over the world experienced burdens that required organizational adjustments and changes. The increased number of patients requiring inpatient hospital treatment in intensive care units and designated COVID isolation departments was one of the main challenges in the Croatian healthcare system reorganization. The peak occupancy of hospital beds and the workload of health personnel were highest during the second and third waves of the pandemic. Due to the need for hospital beds in conditions of overcrowded acute COVID hospitals in Zagreb, Clinic for Infectious Diseases and Dubrava Clinical Hospital, and other hospitals that had organized isolation departments for the care of COVID-19 patients, in November 2020, the sports hall Arena was integrated into the health system of the Republic of Croatia. The purpose of this field hospital was to admit patients who were at the end of hospital treatment and patients with a mild and moderately severe form of the disease who required hospital treatment. The Sisters of Charity Hospital. was in charge of the organization of Arena stationery. At the end of October 2020, the Operational Arena Headquarters was established. The general coordinator appointed by the Minister of Health established coordination for doctors, nursing, and healthcare-associated infection control with designated coordinators. Additional members of headquarters were members of the Croatian general staff of the Armed Forces, Croatian Civil Protection, and administration of the hall. IT service, the Department of Financial-Economic and Technical Affairs, the pharmacy, the biochemical laboratory, the radiology department, and other services of University Hospital Centre Sestre milosrdnice participated in the preparation of the field hospital. Cleaning and disinfection and catering services for patients and medical staff were performed by an external outsourced service. Operational headquarters held daily meetings and briefings. Before the opening, and admission of the first patient, all procedures and guidelines were written, initial cleaning and disinfection were carried out, the water system was checked for the presence of *Legionella* spp., employees of outsourced services were trained in cleaning and disinfection procedures, and demonstration exercises were carried out daily. The arena field hospital was divided into clean and contaminated zones, both spatially and by different ventilation systems. The patient area had 100 patient beds and was equipped with a resuscitation area, biochemical laboratory, X-ray machine, and a pharmacy. Arena Hospital was connected by a hospital information system with Sisters of Charity Hospital., and the connection was established with other two main COVID hospitals in Zagreb. Before every change of medical staff, an educational day was held. Thirty medical doctors were employed in Sisters of Charity Hospital., 6 medical doctors from the Ministry of Defence and 112 nurses/technicians from several hospitals in Zagreb and the Ministry of Defence worked in the inpatient unit. A total of 282 patients from Zagreb, Petrinja, and Sisak were treated in Arena. No transmission accidents and hospital-acquired infections by SARS-CoV-2 virus between patients and medical staff or among medical staff were recorded. Arena field hospital ceased activation in May 2021. The cohesive strength of all medical and non-medical services involved demonstrated the ability to create an efficient and safe hospital in an area not intended for the provision of healthcare.

Keywords: COVID-19, hospital, sports hall, healthcare system, biosafety

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NAJZNAČAJNIJI BIOLOŠKI EFEKTI I SIGURNOST PRI OSLIKAVANJU MAGNETSKOM REZONANCIJOM

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SAŽETAK

Magnetska rezonancija (MR) ima nadmoćan kontrast mekih tkiva u usporedbi s drugim radiološkim modalitetima snimanja te se smatra sigurnom metodom zbog nepostojanja ionizirajućeg zračenja. Cilj je ovog članka prikazati pregled sigurnosnih rizika povezanih s trima elektromagnetskim poljima koja se koriste u MR snimanju: statičko magnetsko polje, radiofrekvencijsko polje i vremenski promjenjivo gradijentno magnetsko polje.

Statičko magnetsko polje MR uređaja privlači feromagnetske predmete i ubrzava ih prema središtu tunela, što može dovesti do projektilskih incidenata. Biomedicinski implantati i taloženje topline također mogu predstavljati opasnost za pacijenta. Biološki učinci statičkog magnetskog polja uključuju osjetilne efekte poput mučnine, vrtoglavice, metalnog okusa i pojave magnetofosfena (svjetlosne senzacije izazvane magnetskim poljem).

Radiofrekvencijsko polje, koje se koristi za pobuđivanje tkiva pacijenta i stvaranje MR signala potrebnih za dobivanje slike, odgovorno je za opekline koje se mogu dogoditi ako elektronički uređaji budu u izravnom kontaktu s kožom, ako postoji kontakt koža-koža ili ako je odjeća pacijenta izrađena od mikrofibera sa srebrnim vlaknima koja nisu vidljiva oku.

Gradijentno magnetsko polje, koje služi za prostornu lokalizaciju u procesu rekonstrukcije slike, često se uključuje i isključuje. Ova vremenska promjena inducira električno polje u pacijentu koje može stimulirati živce i mišiće, pa čak i uzrokovati srčanu stimulaciju. Akustička buka i oštećenje sluha priznati su kao specifične opasnosti MR-a. Korištenje slušne zaštite tijekom MR pretrage obavezno je i mora biti pravilno postavljeno.

Preporučuje se definiranje četiriju zona oko MR uređaja. Pristup tim zonama ograničen je, a granice svake zone određene su udaljenošću od uređaja i funkcionalnom namjenom.

MR snimanje tijekom bilo kojeg tromjesečja trudnoće prema trenutačno dostupnim studijama nije povezano sa štetnim učincima na embrij/fetus, no potrebno je provesti prospektivne i longitudinalne studije. Primjena kontrastnih sredstava na bazi gadolinija tijekom trudnoće treba se provoditi s oprezom i samo kada se očekuje da korist nadmašuje potencijalni rizik za fetus.

Medicinsko osoblje koje ulazi u prostor MR uređaja treba biti informirano i educirano o hitnim postupcima u različitim MR zonama.

Ključne riječi: magnetska rezonancija, biološki efekti, sigurnost pri oslikavanju

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UVOD

Zbog visoke kontrastnosti u oslikavanja mekih tkiva i nekorištenja ionizirajućeg zračenja, magnetska rezonancija (MR) široko je primijenjena dijagnostička metoda u svijetu (1). Tri elektromagnetska polja koja se koriste u oslikavanju (statičko magnetsko polje, radiofrekventno magnetsko polje i prostorno te vremenski promjenjivo gradijentno magnetsko polje) stvaraju rizike za sigurnost pacijenata i djelatnika te ih je potrebno dobro poznavati kako bi se izbjegli neželjeni efekti. Radiolozi i radiološki tehnolozi odgovorni su za procjenu kompatibilnosti implantata i drugih medicinskih uređaja kao što su elektrostimulatori srca i sl. Sile snažnog magnetskog polja mogu djelovati na feromagnetske implantate tako da izazovu njihovo pomicanje, što može dovesti do teških ozljeda pacijenta, pa čak i smrti. Isto tako, izlaga-

nje magnetskom polju može uzrokovati disfunkciju nekih medicinskih uređaja. Vanjski feromagnetski objekti koji nisu u tijelu pacijenta, ali su u blizini uređaja, kao što su metalne boce s kisikom i sl. također mogu biti pod utjecajem snažnog magnetskog polja, pri čemu se mogu vrlo brzo kretati prema izocentru magneta, što se naziva efektom projektila. Na taj način mogu uzrokovati ozljede pacijenata i osoblja te oštećenje uređaja (2). Rizici povezani s radiofrekventnim poljem (engl. *Radiofrequency Field – RF*) odnose se na apsorpciju RF energije koja se mjeri specifičnom brzinom apsorpcije (engl. *Specific Absorption Rate – SAR*) u kablovima i žicama, kožnim režnjevima te velikim tetovažama, što može izazvati zagrijavanje i opekotine visokog stupnja. (2). Akustička buka također predstavlja rizik za pacijente koji nemaju pravilnu zaštitu upotrebom slušalica ili tehnologije za redukciju buke.

CILJ RADA

Cilj je ovog rada sustavni pregled literature i najnovijih podataka o biološkim efektima i sigurnosti pacijenata pri dijagnostičkom oslikavanju MR-om. Obuhvaćene su smjernice Američkog društva radiologa (engl. *American College of Radiology – ACR*) te Međunarodne komisije za zaštitu od neionizirajućeg zračenja (engl. *International Commission on Non-Ionizing Radiation Protection – ICNIRP*) koje se odnose na postupnike za dobru i sigurnu praksu u primjeni uređaja za MR.

STATIČKO MAGNETSKO POLJE (B_0)

Donedavno je magnetska indukcija statičkog magnetskog polja uređaja korištenih u kliničkoj praksi bila 1,5 Tesla (T), ali u posljednje vrijeme sve su više u upotrebi uređaji magnetske indukcije 3 T. Snažniji magneti imaju bolju efikasnost i kvalitetu slike, ali i dodatne sigurnosne rizike u prostorijama za oslikavanje. To uključuje veći broj incidenata zbog efekta projektila (3). Ulaskom u statičko magnetsko polje velike magnetske indukcije, feromagnetski objekti, dolaze pod utjecaj snažne privlačne sile, što uzrokuje efekt projektila usmjerenog prema kućištu uređaja (3). Magnetska sila povezana je s brojnim neželjenim događajima, koji se javljaju u svakodnevnom radu, a mogu se odnositi na privlačenje nehotice ostavljenih metalnih predmeta uz pacijenta, kao što su hvataljke i škare ili nepažnjom ostavljenih metalnih boca kisika.

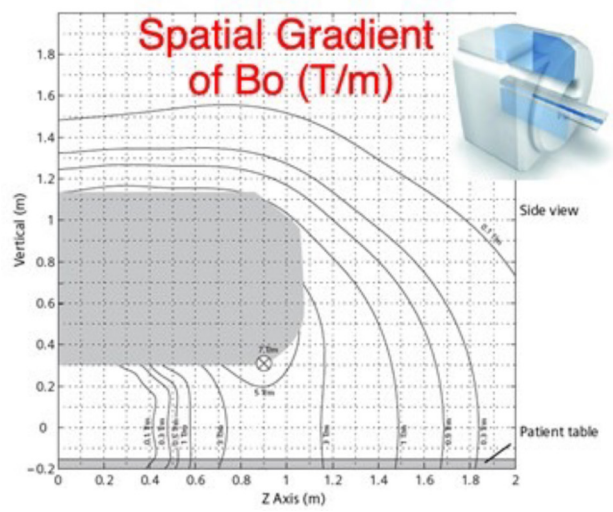
Kako bi se moglo ujednačiti i olakšati razlikovanje objekata koji su sigurni za MR snimanje, Američko društvo za testiranje i materijale (engl. *American Society of Testing and Materials – ASTM*) 2005. godine publiciralo je sustav označavanja podijeljen u tri kategorije: „MR sigurni", „MR uvjetno sigurni" i „MR nesigurni" objekti, a uz svaku oznaku pridružena je odgovarajuća ikona (Slika 1.) (4).

Slika 1.: *Oznake za implantate, medicinske uređaje i ostalu opremu koja se koristi kod MR oslikavanja (preuzeto od Food and Drug Administration (FDA) Understanding MRI Safety Labeling,https://www.fda.gov/media/101221/download)*

Kod predmeta označenih kao „MR uvjetno sigurnih" treba prije primjene uzeti u obzir ograničenje magnetske indukcije i maksimalnog prostornog gradijenta magnetskog polja (engl. *Spatial Gradient Magnetic Field – SGMF*), kao i uvjete pod kojima je izvršeno ispitivanje i testiranje navedenog predmeta (4).

B_0 se trodimenzionalno prostire oko tunela uređaja i njegova magnetska indukcija varira ovisno od udaljenosti od uređaja. Promjena u intenzitetu koja ovisi o udaljenosti poznata je kao prostorni gradijent magnetskog polja (dB/dx) i mjeri se u T/m (5). Magnetska sila proporcionalna je vrijednosti dB/dx i najjača je u točki gdje je SGMF najveći, a to je ulaz u kućište MR uređaja (5).

Za svaki model uređaja postoje izrađene specifične SGMF mape. Proizvođači uređaja dužni su kod isporuke uređaja dostaviti medicinskoj ustanovi navedene mape, na kojima su označene promjene statičkog magnetskog polja u odnosu na udaljenost od kućišta. Isto tako, na mapama je prikazana točka maksimalnog prostornog gradijenta (Slika 2.). Radiološki tehnolozi koji rukuju uređajem obavezno moraju obaviti obuku koju vode certificirani edukatori da mogu ispravno interpretirati SGMF mape i definirati prostorno ograničenje prije snimanja pacijenata koji imaju ugrađene medicinske sprave, kao i poziciju anesteziološkog uređaja u slučaju potrebe za anestezijom pacijenta (5).



Slika 2.: *Primjer dijagrama Spatial Gradient Magnetic Field – SGMF mape s označenim promjenama statičkog polja u odnosu na udaljenost od kućišta (preuzeto s https://mriquestions.com/most-dangerous-place.html)*

Kada vlastito magnetsko polje feromagnetskih objekata u polju magnetske indukcije B_0 nije poravnato s glavnim magnetskim poljem, javlja se moment sile koji uzrokuje rotaciju objekta. Predmeti se rotiraju kako bi se uskladili sa smjerom glavnog magnetskog polja, što u kombinaciji s translacijskom komponentom privlačne sile može dovesti do teških oštećenja pacijenta, pa i do smrti, bilo zbog pomicanja implantata ili prestanka rada medicinskih sprava i uređaja. U literaturi su opisani pomaci metalnih zavojnica za aneurizme, prestanak rada elektrostimulatora srca i infuzijskih pumpi, što je dovelo do životnog ugrožavanja pacijenata (6,7).

Teške ozljede orbite događale su se kod neželjenih pomicanja nedetektiranih intraorbitalnih stranih tijela, što je rezultiralo sljepoćom (8,9). ACR smjernice preporučuju da vrata prostorije u kojoj se nalazi uređaj budu stalno zatvorena, osim prilikom ulaska pacijenta koji će se snimati ili osoblja koje rukuje uređajem ili ga održava. Također sugeriraju da, ako vrata ostaju otvorena, na samom ulasku bude plastični lanac s odgovarajućim upozorenjem o zabranjenom ulazu da bi se spriječili neželjeni događaji (10).

Detaljna povijest bolesti i razgovor s pacijentom prije snimanja neophodni su kako bi se identificirali mogući metalni objekti zaostali od prethodnih operativnih zahvata ili ranjavanja. S obzirom na to da se sve više različitih implantata i sprava ugrađuje u tijelo ljudi, moraju postojati relevantne informacije o vrsti materijala od kojih su sastavljeni i pripadaju li MR sigurnim objektima.

BIOEFEKTI POVEZANI SA STATIČKIM MAGNETSKIM POLJEM (B_0)

U ovu skupinu bioefekata pripadaju prolazni senzorni efekti, kao što su metalni okus u ustima, magnetofosfeni, mučnina i vrtoglavica. Udruženi su s gibanjem kroz statičko magnetsko polje i smatra se da su uzrokovani induciranim naponom stvorenim ovim gibanjem (prema Faradayevom zakonu o indukciji) (3). Magnetofosfeni su definirani kao bljeskovi slabih, treperećih vizualnih senzacija u perifernom vidnom polju i generirani su stimulacijom retine i mozga. U potpunosti su biološki reverzibilni te se smatraju neškodljivima (11.) Prolazna mučnina i povraćanje u osoba izloženih mangnetskom polju indukcije 2 T i više opisani su u više istraživanja (12,13), a nastaju zbog podražaja labirinta i potiskivanja endolimfe u semicirkularne kanale. Obično traju manje od jedne minute i ne ostavljaju nikakve posljedice (13,14).

RADIOFREKVENTNO MAGNETSKO POLJE (B_1)

Za nastajanje snimaka na uređaju za MR u sustav je potrebno dodati energiju. Energija potrebna za postizanje rezonancije na određenoj frekvenciji postiže se sklopom zavojnica koje predstavljaju odašiljačke zavojnice, a one koje detektiraju signal predstavljaju prijemne zavojnice (15).

Specifična brzina apsorpcije (engl. *Specific Absorption Rate – SAR*) je dozimetrijska veličina kojom se određuje snaga elektromagnetskog polja apsorbirana u jediničnoj masi tkiva i izražava se u jedinici Watt po kilogramu (W/kg). Apsorbirana se energija u ljudskom tijelu transformira u toplinu, pa tijekom snimanja dolazi do povišenja tjelesne temperature (15). Za SAR 4 W/kg i vrijeme skeniranja od 20 – 30 minuta povećanje temperature cijelog tijela može iznositi do 0,6 stupnjeva Celzija (5).

Biološki efekti uzrokovani RF poljem mogu se klasificirati u:

- netermalne efekte zbog izravne interakcije između magnetskog polja i tkiva
- termalne efekte zbog zagrijavanja tkiva.

Netermalni efekti manje su proučavani, a pripisuju se električnom međudjelovanju radiofrekventnog polja s tkivom (15). Termalni efekti detaljnije su ispitani, pogotovo zbog mogućnosti nastanka površinskih ili dublje smještenih opekotina u humanim tkivima i organima (15). Termalni

efekti javljaju se kao posljedica vrtložnih električnih struja u tkivu, induciranih visokofrekventnim magnetskim poljem (15). Kontakt kože s kožom i pri tome nastale električne petlje kod pacijenta (na primjer priljubljeni dlanovi ili ruke priljubljene uz trup) mogu dovesti do fokusiranog i lokaliziranog zagrijavanja, što također stvara opekline.

Isto tako, ako nepažnjom pacijent ne skine svu odjeću sa sebe, moguće je da određene tkanine, koje sadrže srebro u mikrovlaknima, imaju provodljiva svojstva te mogu dovesti do stvaranja opeklina II. i III. stupnja, što je opisano u istraživanjima Pietryga i Vatarija (16,17).

Neki transdermalni flasteri, kao oni koji se koriste protiv bolova ili nikotinski flasteri mogu sadržavati metalne čestice. Oni mogu izazvati zagrijavanje površinskih tkiva i opekline. Britanska regulatorna agencija (engl. *The United Kingdom Medicines and Healthcare Products Regulatory Agency – MHRA*) preporučuje odstranjivanje svih medicinskih flastera u pacijenata prije snimanja u MR uređaju (18). Tetovaže i trajni kozmetički produkti koji sadrže metalne komponente također predstavljaju rizik reakcije pigmenta koji sadrži čestice željeznog oksida i može uzrokovati bezbolni edem koji prolazi unutar 48 sati (18).

Slika 3. *Poster koji su kreirali FDA i Society for Magnetic Resonance Technologists (SMRT) s napomenama za prevenciju nastanka opekotina pri MR oslikavanju. Dostupno na https://www.fda.gov/radiation-emitting-products/mri-magnetic-resonance-imaging/mri-safety-posters*

U suradnji s Američkim društvom radioloških tehnologa koji rade u MR dijagnostici (engl. *Society for Magnetic Resonance Technologists – SMRT*), FDA je kreirala seriju postera koji na jednostavan i slikovit način prikazuju postupke koje treba učiniti da bi se spriječio nastanak opeklina pri oslikavanju MR-om (Slika 3.) (4).

Pacijenti prije snimanja moraju s tijela odstraniti sve predmete koji sadrže metal (nakit, flastere koji mogu imati metalne čestice). Potrebno je upotrijebiti izolacijsku tkaninu kako bi se spriječio kontakt kože s kožom i dodirivanje dijelova tijela. Pacijent na sebi treba imati samo ogrtač koji je specijalno predviđen za pretragu i koji dobiva u zdravstvenoj ustanovi. Svi implantati i sprave (elektrode, elektrostimulatori) moraju biti provjereni i njihova kompatibilnost tj. MR sigurnost mora biti potvrđena (19).

ZAGRIJAVANJE IMPLANTATA

Implantati, medicinski uređaji i sprave iz Sjedinjenih Američkih Država i Europske unije koji su proizvedeni u posljednja tri desetljeća napravljeni su od neferomagnetskih materijala i nose oznaku „MR sigurnih" ili „MR uvjetno sigurnih" objekata (19). Ostali implantati moraju se smatrati „MR nesigurnima" i kontraindicirani su za upućivanje pacijenta na skeniranje. Interakcija tih objekata i RF polja može dovesti do stvaranja opsežnih artefakata i prekomjernog zagrijavanja tkiva (20). Zbog niskog unutarnjeg otpora metalnih implantata očekuje se pojačano zagrijavanje zbog snažnih vrtložnih struja induciranih u metalu (21).

Analiza porasta temperature kod prisutnosti metalnih implantata različitih veličina, oblika i sastava u tijeku MR pregleda vršena je u više istraživanja korištenjem *ex vivo* tehnika (22). Rezultati su pokazali da se manje promjene temperature, koje ne predstavljaju značajnu opasnost niti izazivaju ozljede pacijenata, javljaju kod relativno malih, tzv. „pasivnih" metalnih implantata (odnosi se na uređaje koji nisu elektronički aktivirani). To su na primjer stentovi u koronarnim i perifernim arterijama, vaskularni pristupni portovi, aneurizmatske i hemostatske „kopče" (22). Nasuprot tome, značajan porast temperature i potencijalno veće

oštećenje tkiva kod pacijenata može nastati kod implantata izduženog oblika ili oblika „petlje" (22). Čimbenici koji utječu na zagrijavanje jesu: vrsta RF zavojnice koja se koristi pri pregledu, SAR te konfiguracija implantata i njegova orijentacija u odnosu na RF zavojnicu.

Shellock i suradnici su u *ex-vivo* istraživanju prikazali da se značajno manje zagrijavanje postiže na uređaju magnetske indukcije 3T/128 MHz (SAR za cijelo tijelo iznosio je 3 W/kg), nego na uređaju magnetske indukcije 1,5 T/64 MHz (SAR za cijelo tijelo 1,4 W/kg), za elektrodni kateter elektrostimulatora srca koji nije bio povezan s pulsnim generatorom (20). Ovaj fenomen manjeg zagrijavanja pri 128 MHz u odnosu na 64 MHz zabilježen je kod vanjskih fiksacijskih uređaja, Foley katetera s temperaturnim senzorima, neurostimulacijskih sustava i duljih perifernih vaskularnih stentova (20, 22),

stoga je značajno provođenje *ex-vivo* testiranja različitih implantata i uređaja prije izlaganja samog pacijenta kako bi se ispravno odredio stupanj zagrijavanja pri MR pregledu i identificirali „MR nesigurni" objekti.

GRADIJENTNO MAGNETSKO POLJE

Tijekom pregleda MR-om, gradijentno magnetsko polje koje služi za prostornu lokalizaciju u procesu rekonstrukcije slike često se uključuje i isključuje. Gradijenti stvaraju vremenski promjenjivo magnetsko polje s mogućim biološkim efektima koji uključuju stimulaciju perifernih živaca i mišića, kardijalnu stimulaciju i čak ventrikularnu fibrilaciju (5). Stimulacija perifernih živaca može uzrokovati osjećaj nelagode, a u ekstremnim slučajevima bolnost i nevoljne pokrete ekstremiteta. Ljudsko tijelo osjetljivo je na fibrilaciju u rasponu frekvencija od 10 do 100 Hz, a na stimulaciju perifernih živaca do 5 KHz. Ispod navedenih frekvencija živčane i mišićne stanice daju manji odgovor na električnu stimulaciju (21).

Oštećenje sluha i tinnitus opisani su kao specifični MR hazard (10). Međunarodna elektrotehnička komisija (engl. *International Electrotechnical Commision – IEC*) propisuje da se zaštita sluha mora primijeniti kada je izlaganje akustičkoj buci veće od 99dB (10). S obzirom na to da većina MR sustava prelazi ovu granicu, primjena slušalica obavezna je i mora biti pravilno izvedena kod osoba koje ostaju u sobi za pregled tijekom snimanja na MR uređaju (10).

SIGURNOST DIJAGNOSTIKE MAGNETSKOM REZONANCIJOM TIJEKOM TRUDNOĆE

Interakcija magnetskih polja na staničnoj razini detaljno je istražena, osobito na matičnim stanicama (22, 23). Istraživanja su pokazala da MR polja mogu utjecati na staničnu migraciju, diferencijaciju i proliferaciju putem stanične signalizacije *in vitro*, ali te je procese teško dokazati *in vivo* (23, 24). Zagrijavanje tkiva i moguć utjecaj na razvoj kongenitalnih anomalija pod djelovanjem radiofrekventnog pulsa treba također uzeti u obzir zbog povezanosti s majčinom hipertermijom (25, 26). Depozicija energije i zagrijavanje najveći su na površini tijela majke, a kod protokola oslikavanja pri korištenju standardne zavojnice za tijelo, fetalni SAR iznosi oko 40 – 70 % majčinog (27).

Dosad nema dokazanog teratogenog efekta MR-a koji bi bio prikazan na animalnom modelu (28). Novija retrospektivna istraživanja (Strizek 2015; Ray 2016; Chartier 2019) nisu utvrdila razliku u porođajnoj težini ili stopi perinatalne smrti za fetuse izložene MR-u tijekom trudnoće majke (29, 30, 31).

Oštećenje sluha fetusa jedno je od važnih područja istraživanja. Akustička buka koju stvara MR u rasponu je od 80 – 110 dB (31). Nije poznat stupanj do kojeg majčino tkivo i amnionska tekućina mogu atenuirati intenzitet zvuka kojem je izložen fetus. Istraživanja učinjena pri izlaganju žena tijekom trudnoće buci na radnom mjestu (Selander, 2016.; Nieuwenhuijsen, 2017) i utjecaju na sluh neonatusa pokazala su mješovite rezultate (29). Retrospektivne studije koje se temelje na probiru sluha u novorođenčadi nisu pokazale razliku između neonatusa koji su bili izloženi MR pregledu i onih koji nisu (29,32). Bouyssi i suradnici proveli su prospektivnu studiju kod sedamdeset i dvoje djece koja su bila izložena standardnom MR pregledu tijekom drugog ili trećeg trimestra. Praćena su u intervalu od dvije godine. U tom razdoblju nije bilo utvrđenog gubitka ili oštećenja sluha kod navedene djece, iako je studija bila limitirana nedostatkom kontrolne skupine (33).

Magnetska indukcija MR-a jedno je od najvećih uzroka zabrinutosti za sigurnost fetusa. SAR je proporcionalan s kvadratom magnetske indukcije statičnog magnetskog polja (B_0), što znači da se u kliničkoj praksi prenosi u četverostruko povećanje depozita energije između pregleda na uređaju od 1,5 T i 3 T (28). Istraživanje Chartiera i sur., koje je uključilo osamdeset i jednog neonatusa izloženog MR-u indukcije 3 T i stotinu šezdeset i dvoje neizloženih neonatusa, nije utvrdila oštećenja sluha u ispitivanoj skupini (30).

ACR je u svojim smjernicama naveo da zasad ne postoji dokazan rizik od izlaganja fetusa MR-u, ali da se odluka donosi individualno za svaku pacijenticu, osobito kod akutnog abdominalnog bola i novonastale glavobolje (33, 34). Slično ACR-u, American College of Obstetrics and Gynecology (ACOG) također navodi da nema dokazanog rizika izlaganja fetusa MR-u, ali ipak ga treba primjenjivati s oprezom (35).

UPOTREBA GADOLINIJSKIH KONTRASTNIH SREDSTAVA U TRUDNOĆI

Sposobnost prijenosa gadolinijskih kontrastnih sredstava kroz placentu potvrđena je na animalnim modelima (35,36). Nedavno provođena istraživanja na miševima i nehumanim primatima, koja su evaluirala transplacentarnu farmakokinetiku, pokazala su da mala, ali mjerljiva količina gadolinium helata može biti detektirana u amnionskoj tekućini i fetalnom tkivu, unutar 24 – 48 sati od aplikacije (37,38). Istraživanja koja su uključivala miševe, štakore i pse dala su mješovite rezultate. Neka istraživanja pokazala su visoku stopu spontanih abortusa, nisku srednju porođajnu težinu i različite kongenitalne anomalije, čak i kod supraklničkih, dnevnih doza, dok neka istraživanja čak i kod doza značajno viših od terapijskih nisu dokazala nikakve štetne efekte (39, 40).

Opći je zaključak da gadolinijska kontrastna sredstva nose mali ili nikakav rizik za trudnice. Međutim, ne postoji jasan zaključak o sigurnosti primjene za fetus. Dosad nema publiciranih velikih kohortnih studija koje bi pokazale povezanost pregleda MR-om i neonatalne smrti (41). Smjernice ACR-a preporučuju da se gadolinijska kontrastna sredstva upotrijebe u tijeku trudnoće ako je benefit za majku veći od potencijalnog rizika za fetus, kao što su na primjer trudnice s malignom bolešću (42).

MR ZONE

ACR u svojim smjernicama definira četiri različite zone oko MR uređaja (10). Ulaz u navedene zone ograničen je i određen prema udaljenosti od samog tunela uređaja (15).

Zona I. uključuje sva područja u kojima je slobodan ulaz osoblja i pacijenata, u kojem nema nikakvih opasnosti od MR polja (15).

Zona II. smještena je između zone I. i značajno restriktivnije zone III. U zoni II. osoblje kontrolira kretanje pacijenata. Ta zona uključuje prijam pacijenta, ulazak u sobe za presvlačenje i razgovor s pacijentom te ispunjavanje obaviještenog pristanka kao i utvrđivanje može li pacijent pristupiti pregledu (3).

Zona III. je područje s restrikcijom ulaska i fizičkim barijerama, kao što su vrata s kodiranim pristupom. U tu zonu može ući samo ovlašteno osoblje i pacijenti koji će biti skenirani u pratnji radiološkog tehnologa ili radiologa. Kontrolna soba za MR uređaj nalazi se u toj zoni (3).

Zona IV. je prostorija u kojoj se nalazi MR uređaj. Ulaz u tu zonu moguć je samo kroz zonu III., unutar koje se ona i nalazi. Ova zona mora biti označena kao potencijalno opasna zona zbog prisutnosti jakog magnetskog polja i to crvenim svjetlom i natpisom na kojem je jasno naznačeno da je magnet uključen (3).

PRIMJENA POSTUPNIKA MR SIGURNOSTI U ZDRAVSTVENIM USTANOVAMA

ACR periodično revidira postupnike i u 2023. godini kreiran je nacrt u *web* formatu kako bi mogao biti revidiran i nadopunjen. Europske smjernice o MR sigurnosti datiraju iz 2013. godine. U zdravstvenim ustanovama u Hrvatskoj primjenjuju se smjernice EU-a. Američki i europski postupnici navode da bi svaka država trebala donijeti svoje postupnike, koji bi se kontinuirano revidirali (43, 44). Ti bi se postupnici morali primijenjivati u prostorijama u kojima se provodi znanstveno-istraživačka djelatnost i klinička uporaba.

U postupnicima moraju biti navedene apsolutne i relativne kontraindikacije za ulaz u MR prostoriju (osobito u zonu IV.), postupanje kod pacijenata s elektrostimulatorima srca, pravila o ispunjavanju obaviještenog pristanka i probira pacijenata koji smiju pristupiti snimanju. Nadalje, moraju sadržavati detaljan opis zona i restrikciju ulaska osoblja i pacijenata u pojedine zone uz objašnjenje razloga zbog kojeg postoje.

Potencijalni rizici i opasnosti moraju biti ukratko opisani: oni koji se odnose na statičko magnetsko polje i radiofrekventno magnetsko polje te bioefekti. Tzv. „kriogeni rizik" koji nastaje zbog iznenadnog, nepredviđenog gašenja magnetskog polja (engl. *quench*) također mora biti opisan, jer zbog pretvaranja tekućeg helija u plinovito stanje može doći do ulaska plina u prostoriju za snimanje i asfiksije (25). Zbog akustične buke svi pacijenti moraju dobiti čepiće za uši ili slušalice i bez toga se skeniranje ne smije učiniti.

U slučaju hitnih stanja (zastoja rada srca, anafilaktičkog šoka i sl.) mora postojati jasno napisan protokol postupanja s opisom odgovarajuće opreme. Pacijent mora biti prenesen u zonu II. ili III., gdje se nastavlja postupak oživljavanja i hitna medicinska intervencija. Detaljan opis i redoslijed postupaka u slučaju pojave požara i naglog gašenja uređaja mora biti naveden, s precizno definiranom ulogom pojedinih članova tima. Poseban dio postupnika treba se odnositi na sigurnu primjenu MR-a u trudnoći i primjenu kontrasta na bazi gadolinija u trudnica, prema važećim smjernicama (43, 44). Sve osoblje trebalo bi proći edukaciju o primjenama mjera sigurnosti tijekom MR dijagnostike.

ZAKLJUČAK

Razvojem uređaja za MR tijekom protekla tri desetljeća i rastućim brojem pretraga za sve dobne skupine, počevši od embrija i fetusa, povećava se potreba za istraživanjem i utvrđivanjem sigurnosti i potencijalnih bioefekata na humana tkiva i organe pri snimanju ovim uređajem. Feromagnetski objekti, implantati i uređaji dijele se u tri kategorije: „MR sigurni", „MR uvjetno sigurni" i „MR nesigurni", pri čemu za svaku kategoriju postoje posebne oznake kreirane 2005. godine. Detaljnom analizom povijesti bolesti pacijenta i razgovorom s pacijentom može se prevenirati snimanje pacijenata s različitim feromagnetskim metalnim stranim objektima u tijelu, zaostalim od ranijih operativnih zahvata ili ranjavanja. Senzorni efekti, kao što su metalan okus, magnetofosfeni, mučnina i vrtoglavica prolazni su i ne ostavljaju trajne posljedice. Opekline kože i površnih tkiva jedan su od najčešćih neželjenih efekata snimanja MR-om. Mogu biti uzrokovani elektronički kontroliranim uređajima koji se nalaze uz pacijenta. Opekline također mogu nastati prilikom kontakta kože pacijenta s dijelovima uređaja unutar tunela ili kontaktom kože s kožom kod spojenih dlanova ili ekstremiteta priljubljenih uz tijelo. Prema dosadašnjim istraživanjima, nativni MR sigurna je metoda u sva tri trimestra trudnoće majke za embrio/fetus. Primjena kontrastnih sredstava na bazi gadolinija u trudnoći limitirana je samo na slučajeve u kojima se očekuje da će potencijalna korist biti veća od mogućeg potencijalnog štetnog efekta. Prema smjernicama ACR-a definirane su četiri zone sigurnosti u prostorijama u kojima se nalazi MR uređaj, uz opis sigurnosti pacijenata i osoblja u pojedinoj zoni. Svaka ustanova koja koristi uređaj za MR trebala bi primjenjivati smjernice i postupnike za MR sigurnost.

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S U M M A R Y

THE MOST IMPORTANT BIOLOGICAL EFFECTS AND SAFETY IN MAGNETIC RESONANCE IMAGING

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Magnetic Resonance Imaging (MRI) has a superior soft-tissue contrast compared to other radiologic imaging modalities and has been regarded as a safe imaging modality due to the lack of use of ionizing irradiation. The objective of this article is to give an overview of the safety risks of the three electromagnetic fields used in MR imaging: the static magnetic field, the radiofrequency field, and the time-varying gradient magnetic field. The static magnetic field of an MRI machine attracts ferromagnetic objects and accelerates them toward the center of the bore, which can cause several projectile incidents. Biomedical implants and heat deposition have the potential to cause harm to patients. Bioeffects of static magnetic field comprise some sensory effects such as nausea, vertigo, metallic taste, and magnetophosphens.

The radiofrequency field, which is used to excite the patient's tissue and produce MR signals required for image acquisition is responsible for burns that may occur if electronically controlled devices are in direct contact with the skin, then if skin-to-skin contact in the patient occurs or if invisible silver-embedded microfibers are present in patients' clothing.

The gradient magnetic field serves for spatial localization in the image reconstruction process and is often switched on and off. This time variation induces an electric field in the patient that could stimulate nerves and muscles and generate cardiac stimulation. Acoustic noise and hearing damage are recognized as a specific MRI hazard. Hearing protection during the MRI scan is mandatory and must be correctly used.

Four MRI zones are suggested around the MRI scanner. The access to these zones is restricted and the boundary of each zone is defined by its distance from the MRI scanner and by its purpose.

MRI during any trimester of pregnancy has not shown any harm to the embryo/fetus, based on currently published studies, but prospective and longitudinal studies should be performed. The use of gadolinium-based contrast agents during pregnancy should be administrated with caution and only when it is expected that the potential benefits justify the potential risk to the fetus.

Medical personnel entering the MRI suite need to be informed and trained in emergency procedures in different MRI zones.

Keywords: magnetic resonance, biological effects, magnetic resonance imaging safety

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UPUTE AUTORIMA

Časopis ACTA MEDICA CROATICA objavljuje uvodnike, izvorne radove, preglede, klinička zapažanja, osvrte, primjere iz kontinuirane medicinske edukacije, sažetke radova s kongresa i simpozija, pisma uredništvu, prikaze knjiga i drugo. Objavljuje i tematske brojeve časopisa uz gosta-urednika. Prihvaćanje kategoriziranog članka obvezuje autora da isti članak ne smije objaviti na drugome mjestu bez dozvole Uredništva.

Upute autorima u skladu su s tekstom "International Committee of Medical Journals of Editors. Uniform Re-quirements for Manuscripts Submitted to Biomedical Journals (N Engl J Med 1997; 336: 305-15)".

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Članci i svi prilozi dostavljaju se na hrvatskom jeziku u tri istovjetna primjerka i na CD/DVD u Wordu. Rad ne smije imati više od 20 stranica, tipkanih dvostrukim proredom (najviše 30 redaka na jednoj stranici). S obje strane teksta valja ostaviti bijeli rub širine 3,6 cm.

Izvorni radovi sadrže ove dijelove: uvod, cilj rada, metode rada, rezultati, rasprava i zaključci. Uvod je kratak i jasan prikaz problema, cilj sadrži kratak opis svrhe istraživanja. Metode se prikazuju tako da čitatelju omoguće ponavljanje opisana istraživanja. Poznate se metode ne opisuju, nego se navode izvorni literaturni podatci. Ako se navode lijekovi, rabe se njihova generička imena (u zagradi se može navesti njihovo tvorničko ime). Rezultate treba prikazati jasno i logički, a njihovu značajnost potvrditi odgovarajućim statističkim metodama. U raspravi se tumače dobiveni rezultati i uspoređuju s postojećim spoznajama na tom području. Zaključci moraju odgovoriti postavljenom cilju rada.

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Sažetak na hrvatskom jeziku prilaže se u obimu od najviše 200 riječi na posebnom listu papira.

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Popis literature piše se na posebnom papiru s rednim brojevima prema redoslijedu kojim se citat pojavljuje u tekstu. Literatura se citira prema dogovoru postignutom u Vancouveru, a za naslove časopisa treba rabiti kraticu navedenu u Index medicus/Medline/Pubmed. Uz rad je obvezno priložiti izjavu o suglasnosti koautora o publiciranju rada te o nepostojanju uskoba interesa.

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Disertacija ili magistarski rad

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Djelmiš J, Ivanišević M, Mrzljak A. Sadržaj lipida u placenti trudnica oboljelih od
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