Sector 2a. Chemical Threats

(Number at the end of the presentation title is the abstract number in the printed abstract book)

1. **Dr. Zdravko Lovrić**, Head of the Risk Assessment Department, Croatian Institute of Public Health, Croatia – **"**Legislation on Chemical Safety Management" (64)
2. **Maja Knepr Šegina, mag. edu. biol. et mag. biol.,** Head of Section, Division for Toxicology at Croatian Institute of Public Health, Croatia - "Education on protection and decontamination of the general population in cases of CBRN Mass Casualties Events" (32)
3. **Dr. Todd Myers,** United States Army Medical Research Institute of Chemical Defense, USA - **"**Synthetic Opioid Poisoning: Primate Models to Advance Improved Emergency Medicines" (29)
4. **Dr. Laura Cochrane,** Vice President Global Government Procurement, Emergent BioSolutions - "Evaluation of Decontamination Efficacy of the RSDL® Kit againts Incapacitating Agents [Pepper Spray (OC), MACE™ (CN), And CS]" (40)
5. **Dr. Matthias Berger,** Bundeswehr Research Institute for Protective Technologies and CBRN Protection, Chemistry Department, Germany – *"*Analysis of VX and its degradation products in conjunction with plasma decontamination" (54)

Sector 2b. Chemical Threats

1. **Dr. Faraidoun Moradi,** School of Public Health and Community Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Sweden - "Respiratory function 34 years after sulfur mustard exposure in survivors in Sweden" (16)
2. **Dr. Shahriar Khateri,** MD, Ph.D, Medical Toxicologist, W. Nikan Hospital, Tehran-Iran - "Are we prepared? Medical response to incidents involving toxic chemicals; The OPCW and strengthening preparedness and response capacity of its member states" (12)
3. **Dr. Laura Cochrane**, Vice President Global Government Procurement, Emergent BioSolutions - "Analytical Estimation of Novichok Exposure Risk and Economic Consequences Using an SCR Vertex Mathematical Model" (41)
4. **Dr. Ondrej Soukup,** University of Defence, Faculty of Military Health Sciences, Department of Toxicology and Military Pharmacy, Czech Republic - "The cytotoxicity and reactivation efficacy of oxime reactivators against Novichok inhibited acetylcholinesterase" (21)
5. **Prof. Jaroslav Pejchal,** University of Defence, Faculty of Military Health Sciences, Department of Toxicology and Military Pharmacy, Czech Republic - "Evaluation of new modified bisquarternary pyridinium oximes K1651–K1654" (44)
6. **Mr. Robert J. Malone,** US Army Futures Command DEVCOM Chemical Biological Center, Aberdeen Proving Ground, MD, USA - "Compact Rapid Chemical Agent Neutralization System: A Rapidly Deployable Method for Large Scale Chemical Agent Destruction" (28)
7. **Donna Vadlja**, Ministry of Defense, Battalion for nuclear-biological-chemical defense, Croatia **-** "Remote controlled systems for first responds" (48)

64. Legislation on Chemical Safety Management

Dr. Zdravko Lovrić,

Head of the Risk Assessment Department, Croatian Institute of Public Health, Croatia, e-mail: zdravko.lovric6@gmail.com

Abstract

Jurisdiction on chemical legislation is under different directorate general in European Union. Same situation is in Republic of Croatia. Competent authority for manufacturing, putting on market and use of chemicals is Ministry of Health, for chemical weapons is Ministry of Economy and Sustainable Development, for pesticides and mineral fertilizer is Ministry of Agriculture, for accidents and waste is Ministry of Physical Planning, Construction and State Assets, for transport are Ministry of the Sea, Transport and Infrastructure, and Ministry of Interior, for water protection permissions is Ministry of Regional Development and EU Funds, etc. That means that horizontal cooperation is the most important. From the point of health, the most important legislative act is Regulation concerning he Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) and its amendment Regulation on classification, labelling and packaging of substances and mixtures (CLP). Two more regulations are also important such are Biocidal Product Regulation (BPR) and Regulation concerning the export and import of hazardous chemicals based on Rotterdam convention on the prior informed consent procedure for certain hazardous chemicals and pesticides in international trade.

Beside the laws on implementation of these regulations in Croatian legislation, we strength some important characteristic points by Law on Chemicals. This act provides measures and conditions for environmental standards and protection of the environment and population, chemical management, classifying, labelling and packaging of chemicals, manufacturing, trading, importing and exporting chemicals, controlling and monitoring of chemicals. Measures of this act are also to be applied on biocide products and import and export of hazardous chemicals. Law on chemicals is supported by four main ordinances: Ordinance on Conditions for the Manufacturing, Placing on the Market and Use of Dangerous Chemicals that covers majority of Law on chemicals; Ordinance on the Manner of Keeping the Register on Chemicals and Manner and Deadline for Submitting the Data from Register; Ordinance on the Conditions and the Manner for Acquiring and Verification of Knowledge About Protection from Dangerous Chemicals; Ordinance on the Storage of Dangerous Chemicals Which Act in Gaseous Phase.

Biography - Dr. Zdravko Lovrić

Education
1982 – graduated chemistry on Faculty of science and mathematics on University of Zagreb and 2010 – university magister of toxicology
Employment
1982-1984 – assistant on Faculty of Science and Mathematics
1985-1998 – chemical analyst in Centre of Medical Science Zagreb
1998-2007 – head of Division and Department for Documentation and Evidence in Croatian Institute for Toxicology
2012-2018 – director of Croatian Institute for Toxicology
2019-2023 – assistant director of Croatian Institute of Public Health
Activities
Member of Croatian chemical society and Croatian Toxicological society
Memeber of croatia tim for screening of Croatian legislation compatibility with EU akqui
Expert reviwer of croatian translations of EU chemical legislation
Publications
5 CC papers

3 coauthors of educational books
3 educational handbooks

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32. Education on protection and decontamination of the general population in cases of CBRN Mass Casualties Events

Maja Knepr Šegina, mag. educ. biol. et mag. biol.

Croatian Institute for Public Health, Toxicology Service, Head of the chemicals documentation department, Craoatia (maja.knepr-segina@hzjz.hr)

Abstract

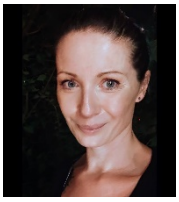
The risk of chemical, biological, radiological and nuclear (CBRN) incidents has increased in recent years and because of that we need to provide good and secure protection and decontamination to mass population in case of mass CBRN event. The risk of Mass Casualties Events comes from technological advance and increased possibility of unconventional weapons usage. All basic actions that first emergency responders are able to use in such events must be in some way introduced to mass public as well.

There are two basic ways to inform public about actions that should be taken: pre-incident information or ad hoc during the event. Pre-incident information will enhance the reaction speed in case of emergency and can save more lives. In this case public can take action to reduce their own risk before any of emergency responders arrive on scene. Certain research papers suggest that pre-incident information provision will not be very effective since people are not usually willing to engage in that type of education. However, there is a difference between population that have been involved in some kind of CBRN event and population with really low CBRN risk.

Main methods of providing pre-incident information could be various: television, commercial billboards in well-populated areas, online adverts or even implemented in school curriculum. On the other hand, ad hoc information (e.g early warning system) would be useful in the moment and more people would be interested, but reaction time would be much longer. Nevertheless, any information given is better than nothing.

Croatia is, for now, low risk country, but we do provide basic information about chemical danger implemented in school curriculum, and all workers that handle chemicals must take courses on how to safely work with chemicals and how to properly protect themselves. Each year, approximately 8000 individuals complete the courses.

Biography - Maja Knepr Šegina



Maja Knepr Šegina, mag. educ. biol et mag. biol., born on November 1, 1980 in Bjelovar. She graduated from the Faculty of Science and Mathematics, Biology Department, University of Zagreb in 2005 as a professor then at the beginning of 2006 as an engineer, and obtained the diplomas of then graduate professor of biology and engineer of biology - majoring in ecology.

After completing her education, she worked as an expert consultant in the sale and marketing of laboratory materials, and then as an environmental protection specialist, an occupational safety specialist and a person responsible for hazardous chemicals.

In 2017, she came to the then Croatian Institute for Toxicology and Anti-Doping (CITA) as an expert associate, and in 2019 she became the Head of the Chemicals Documentation Department, after CITA joined the Croatian Institute for Public Health as the Department of Toxicology.

Since 2018, she has been involved in the work of the Anti-Explosion Service of the Administration for Public Order and Security, as an external collaborator for the chemical part of CBRN issues. She participated in various meetings, workshops and congresses that include the issue of chemicals as part of the REACH and CPL Regulations, chemical risk assessment and CBRN.

During the SARS-CoV-2 pandemic, she coordinated the work of the 113 call centre, and since 2020 she has been leading the JA TERROR project as an expert coordinator and collaborator on several work packages. She also participated as a collaborator on some of the SHARP JA work packages.

The Göttingen Minipig for Medical Countermeasure Development: Benefits and Capabilities

Dr. Todd Myers
United States Army Medical Research Institute of Chemical Defense (USAMRICD)

Abstract

Despite efforts to reduce reliance upon the use of animals, animal research continues to serve a critical role in the testing and development of medical countermeasures. The continued use of non-human primate models is unsustainable due to ethical concerns, reduced availability, and skyrocketing costs.

The Göttingen minipig was developed for laboratory research and could be capable of providing comparable or possibly superior attributes for many research questions within medical chemical defense. Targeted development of the Göttingen minipig model could improve study design, statistical power, and throughput to advance medical countermeasures for regulatory approval and fielding. Of course, studies must be designed, funded, and completed to meet this goal.

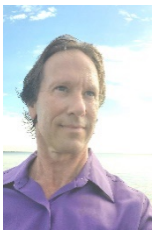
In this vein, we completed foundational studies regarding the pharmacokinetics and physiological safety of intramuscularly administered atropine sulfate, pralidoxime chloride (2-PAM), and diazepam across a broad range of doses using adult male Göttingen minipigs surgically implanted with vascular access ports and telemetric devices to monitor cardiovascular, respiratory, arterial pressure, and temperature signals. Pharmacokinetic data were orderly and largely mirrored available human data at comparably scaled doses. Atropine sulfate dose-dependently increased the magnitude and duration of tachycardia and decreased the PR and ST intervals (consistent with findings obtained from other species).

To further advance our safety assessment capabilities, two behavioral tests from the FDA's Operant Test Battery commonly used in primates were adapted to swine using a custom-built apparatus. Göttingen minipigs were capable of learning and performing both tests at high levels of proficiency and consistency, setting the stage for behavioral drug safety testing.

This work was supported by the Defense Threat Reduction Agency, Medical S&T Division.

The experimental protocol was approved by the Animal Care and Use Committee at the United States Army Medical Research Institute of Chemical Defense, and all procedures were conducted in accordance with the principles stated in the Guide for the Care and Use of Laboratory Animals (National Research Council, 2011) and the Animal Welfare Act of 1966 (P.L. 89-544), as amended.

Biography – Dr. Todd Myers



Dr. Todd Myers is a Research Toxicologist who has dedicated his professional career to furthering medical chemical defense. As a scientist, he has elaborated methods for assessing the safety and efficacy of medical countermeasures against the most potent poisons in the world, from toxic industrial chemicals to nerve agents, pesticides, and synthetic opioids. His work has enabled scientists within his institute to evaluate behavioral perturbation ranging from subtle to profound, in species including mice, rats, guinea pigs, ferrets, swine, and monkeys. He has advanced the African green monkey and the Göttingen minipig as alternative large animal models for pharmacological and behavioral assessment. In addition to understanding threat agent toxicity, he has also explored and elaborated improved acetylcholinesterase reactivators, anticholinergic drugs, first-line and adjunct anticonvulsants, as well as novel scavengers capable of detoxifying threat agents in vivo. As a subject matter expert, Dr. Myers serves on domestic and international working groups to guide animal model selection, the design of laboratory studies, product development decisions, and regulatory approval, with an eye toward optimizing human emergency use and clinical practice guidelines for fielded medical countermeasures. His recent body of work has focused on countering the threat posed by synthetic opioid poisoning by utilizing non-human primate models of physiology, pharmacokinetics, and behavior to study existing and evolving medical countermeasures.

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40. Evaluation of Decontamination Efficacy of the RSDL® Kit against Incapacitating Agents [Pepper Spray (OC), MACE™ (CN), AND CS]

M. Fentabil[1], M. Gebremedhin[1], **Laura Cochrane***[2], and D. Toth[1]

[1]*Emergent BioSolutions Canada Inc., Winnipeg, MB, Canada*
[2]*Emergent BioSolutions UK, Chiswick, UK*

*Corresponding Author: *Laura Cochrane,* cochranel@ebsi.com

Abstract

Objective:
To evaluate the efficacy of RSDL® (Reactive Skin Decontamination Lotion Kit) in decontaminating the incapacitating agents capsaicin (OC), commonly referred to as Pepper Spray; 2-chloroacetophenone (CN), commonly referred to as MaceTM; and 2-chlorobenzalmalononitrile (CS), typically used in military training exercises.

Methods:
The current study was designed to specifically investigate the reactivity component of the RSDL lotion with OC, CN, and CS in vitro. The RSDL lotion was mixed with each incapacitating agent at different molar ratios of the lotion's active ingredient. The reactivity of the lotion with the incapacitating agent was observed for one hour, while 10 µL samples were quenched and analyzed for residual incapacitating agent using liquid chromatography-mass spectrometry.

Results:
CN was effectively degraded at 90% within 2 minutes at a molar ratio of 2:1 (active lotion:compound),. Degradation of more than 68% of CS was achieved at a 20:1 molar ratio within 1 hour reaction time. No degradation of OC was observed with the lotion, irrespective of the relatively higher molar ratios of up to 20:1 and longer reaction time of up to one hour.

Conclusion:
This study evaluated the direct effect of the liquid phase reaction of the incapacitating agents with the RSDL lotion in the absence of any physical removal action by the sponge. The lotion was highly effective in degrading CN and moderately effective in degrading CS. The lack of reactivity of OC by the lotion alone suggests that physical removal by the sponge plays a significant role in achieving decontamination.

Keywords: RSDL; Incapacitating Agents; Decontamination

Biography - Laura Cochrane

Laura is supporting activities in Biological and Chemical Threat medical preparedness as Vice President of Medical affairs for the health protection and medical countermeasures across partnerships with industry, government, research and academia. Her early background was in Chemical and Materials engineering from the Royal Military College of Canada, furthered education at St. Andrews University, has an extensive background in Defence Research, and a specialized career in support of medical clinical operations for government agencies around the globe.

She has focused her area of expertise for the last 20+ years in medical applications to support CBRN and Health research programs, published across peer review publications, with primary focus on the development of medical countermeasures to high impact events, such as pandemics, intentional events or epidemics.

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54. Analysis of VX and its degradation products in conjunction with plasma decontamination

Dr. Matthias Berger*[1], A. Ficks[1]

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*Corresponding Author: *Dr. Berger, Matthias,* matthias2berger@bundeswehr.org

Abstract

VX (S-{2-[Di(propan-2-yl)amino]ethyl} O-ethyl methylphosphonothioate) is one of the deadliest and most persistent nerve agent known. Furthermore, it is one of the most challenging chemical warfare agents to decontaminate using vacuum technology due to its low vapour pressure and high boiling point. A relatively novel approach in decontamination of sensitive equipment is the application of plasma. Reasonable priced vacuum plasma chambers, originally designed for the microchip industry, have become commercially available in recent years. By utilising such a plasma chamber, we have investigated the reaction of VX with different types of plasma (air, oxygen) and ozone. The principle idea is that the reactive plasma species/ozone breaks up the chemical bonds in the structure of VX to yield smaller and, thus, more volatile and less toxic substances.

The presented investigation was carried out utilising GC-HRMS (High Resolution Mass Spectrometry) and LC-HRMS analytical techniques. We were able to identify the structures of multiple toxic and non-toxic degradation products after plasma decontamination of a VX contaminated model surface. The investigation has led to multiple benefits; on the one hand, various chemical substances with relation to VX were registered and subsequently added to our in-house databases, which may facilitate future analysis of environmental samples of our OPCW-designated laboratory. On the other hand, compounds like EA 2192 were identified, which represent very toxic stable degradation products of VX and

highlights the need for investigating reaction processes with modern analytical instrumentals in order to decide whether a decontamination process was successful or not.

Keywords: Plasma, Decontamination, VX

Biography - Dr. Matthias Berger (will be added**)**

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16. Respiratory function 34 years after sulphur mustard exposure in survivors in Sweden

Dr. Faraidoun Moradi[1]***,** Sanna Kjellberg[1], Ying Li[1], Bledar Daka[1], and Anna-Carin Olin[1]

[1]*School of Public Health and Community Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Sweden*
* Correspondence: Faraidoun Moradi, faraidoun.moradi@gmail.com, E-mail: moradi.faraidoun@gu.se

Abstract

Background:
Sulfur mustard (SM) exposure causes acute and chronic respiratory diseases. The extent of small airway dysfunction (SAD) in individuals exposed to SM is unclear. This study evaluated and compared SAD in SM-exposed versus SM-unexposed participants using non-invasive lung function tests assessing small airway function.

Methods:
This retrospective cohort study involved SM-exposed (n=15, mean age: 53±8 years) and SM-unexposed (n=15, mean age: 53±7 years) Kurdish-Swedish individuals in Sweden. Small airway resistance and reactance were assessed using impulse oscillometry (IOS). Nitrogen (N_2) multiple breath washout (MBW) was used to assess lung ventilation inhomogeneity. The gas-exchanging capacity of the lung was assessed using the diffusing capacity of the lungs for carbon monoxide test. Lung function outcomes were reported as absolute values and z-scores. Group comparisons were performed using the Mann-Whitney U test.

Results:
No statistically significant differences in age, height, or body mass index were observed between the two groups. IOS identified significantly increased small airway resistance, while N_2 MBW identified significantly increased global and small airway ventilation inhomogeneity in SM-exposed compared to non-exposed individuals. SAD was identified in 13/15 SM-exposed individuals, defined as at least one abnormal IOS (FDR and/or AX) or N_2 MBW (S_{acin}) outcome. Out of these 13 individuals, only four individuals demonstrated concordant findings across the IOS and N_2 MBW tests.

Conclusions:
Exposure to SM was associated with long-term impairment of respiratory tract function in the small airways in the majority of previously SM-exposed individuals in the present study. Whether they are at risk of further deterioration and lung disease is unknown, but to explore this would be of great interest. IOS and N2 MBW seems however to give complementary information hence both should be employed to detect SAD in SM-exposed survivors. To identify and characterize the remaining pathology of the small airways in SM survivors is a first step towards improved treatment and follow up.

Keywords: Small airways, Oscillometry, Multiple Breath washout, Pulmonary Disease, Sulfur Mustard, Halabja

Biography – Dr. Faraidoun Moradi

I am a clinician-researcher at the Institute of Medicine and is also connected to a Centre for disaster medicine, Kunskapscentrum katastrofmedicin väst, based at the Institute of Clinical Sciences, Sahlgrenska Academy at the University of Gothenburg. I obtained my medical degree from the prestigious University of Gothenburg in 2012, specializing in Family Medicine. I also hold a license as a pharmacist from the renowned University of Uppsala in 2006. With a passion for research, I embarked on a Ph.D. journey investigating sulfur mustard's long-term effects. My research involves conducting interviews, surveys, and medical examinations to gather comprehensive data on the survivors' experiences and health outcomes. Using a combination of qualitative and quantitative approaches, my research aims to shed light on the long-term consequences of exposure to sulfur mustard. Specifically, I am dedicated to examining the firsthand experiences, mental well-being, quality of life, and respiratory function of individuals exposed to sulfur mustard in Kurdistan-Iraq and Sweden.

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12. Are we prepared? Medical response to incidents involving toxic chemicals; The OPCW and strengthening preparedness and response capacity of its member states

Dr. Shahriar Khateri, MD, PhD

Medical Toxicologist, Chemical Emergency Response Expert, Nikan Hospital, Tehran-Iran

Abstract

As long as there is a possibility of the use or threat of use of chemical weapons, deliberate release or incidents involving toxic chemicals, there will be a need to maintain and improve the protective capabilities of all countries in terms of their domestic preparedness and response and their ability to assist other countries. Such enhanced capabilities exert an important deterrent effect. Medical response as an integrated part of chemical emergency response has to be included in any capacity building program to ensure preparedness of medical responders and medical facilities to deal with chemical emergencies particularly in mass casualty incidents. Even tough medical responders are expected to be able to provide care for patients during chemical incidents however; they should also know how to protect themselves as the first priority to prevent their own exposure as well as secondary contamination, this would require sufficient training and equipment. Medical facilities and emergency departments should also be prepared for dealing with chemical casualties including decontamination station and a comprehensive disaster plan to include a CBRN component. Once these tasks are taken care of, in the higher level of preparedness, the key questions are: have responsibilities for the chemical emergency tasks including medical care of casualties been assigned through legislation or other binding policy, are the institutions having such responsibility aware of their role? Have the institutions with responsibility for medical response practiced their role? And if so, have they identified any capacity gaps or unresolved challenges to carrying out their legal mandate? If so, what are they? The Organisation for the Prohibition of chemical weapons provides support to its member states to enhance their capability on chemical emergency response through capacity building programs as well as providing expert and technical advice. The organisation also works closely with several regional and sub-regional organisations to enhance their capacity to respond effectively to chemical emergencies. This presentation is going to provide an overview on the role of the OPCW as an international organization in strengthening capacity of its member states in preparedness and responding to incidents involving chemical warfare agents and other toxic chemical.

Biography - Dr. Shahriar Khateri

Dr. Shahriar Khateri is a physician and "Chemical Emergency Response" specialist currently based in Tehran-Iran. He has extensive experience in clinical aspects of long term health effects of exposure to CW agents, medical management of CW casualties as well as rehabilitation of the CW victims. Dr. Khateri received his MD degree from Beheshti University of medical sciences in Tehran-Iran and his PhD in Medical Toxicology from Institute of Cellular Medicine, Newcastle University, United Kingdom. He worked for the Organization for the Prohibition of Chemical Weapons (OPCW) in the Hague as Senior Program Officer, International Cooperation and Assistance Division from 2014 to 2021. Currently he in charge of organizing national and international trainings courses on medical management of chemical casualties as well as providing expert advice on CBRN emergency response. Before joining the OPCW, he worked in the field of "war and Public health" for over 15 years dealing with the war related injuries among the survivors of Iran-Iraq war with focus on chemical warfare survivors. As senior researcher and head or research unit on CW health impacts at JMERC, he was involved in various clinical and epidemiological research projects addressing the long-term health impacts of chemical warfare agents as well as victims assistance programs, He has also been involved in local and international NGO activities including on CW victims' support, peace and disarmament. He is co-founder and head of International relations of the Tehran Peace Museum, a non-governmental organization with the aim of raising public awareness about the effect of chemical weapons as well as providing support for victims of chemical warfare. Dr. Khateri has several publications on health and environmental impacts of war with focus on chemical weapons and landmines.

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41. Analytical Estimation of Novichok Exposure Risk and Economic Consequences Using an SCR Vertex Mathematical Model

Tristan Learoyd*[1], **Laura Cochrane**[1]

[1]*Emergent BioSolutions UK Ltd, Building 3, Chiswick Park, 566 Chiswick, High Road Chiswick, London W4 5AY, United Kingdom*

*Corresponding Author: *Tristan Learoyd,* learoydt@ebsi.com

Abstract

The low volatile nerve agent Novichok (Nx) represents a significant health risk combining rapid onset of symptoms and the potential to purposefully expose civilian, first responder, and health care professional populations. An intentional use mathematical SCR (Susceptible-Contaminated-Removed) scenario, with parameters based on 11 existing Nx reports (e.g., case fatality ratio, time to death, first response and hospital treatment variations), was adapted to a vertex model with causal linear time event decision trees, which factored for actor competency when applied to an at-risk civilian population (n=750). A further itemized direct, indirect, and productive cost analysis was formed using the scenario's parameters. Direct treatments were taken from case studies, and respective best prices and/or national formulary price. Indirect costs for administration, decontamination, equipment loss, and loss to host enterprise turnover were computed. Local economy losses of 10% reduced visitor loss in the annum to a metropole of size 1.25M were additionally factored. Productive costs were expressed as a function of half national life expectancy and median hourly GDP per capita, with assumed injury duration of three months and 10% carer accumulation cost. The model forecasted an event of 356.25 civilian casualties, 48.66 responder casualties, and total deaths of 114.73. Direct costs of $75.15M, and total incident including indirect and productive costs of $828.17M were calculated. The adaptable vertex model with underlying cost analysis offers a template to identify positive preparatory measures and forecast human loss and economic values.

Keywords: Low Volatile Chemical Agents, Exposure, Patient Populations

21. The cytotoxicity and reactivation efficacy of oxime reactivators against novichok inhibited acetylcholinesterase

Ondrej Soukup[2],

V. Hepnarova [1], M. Hrabinova [1], L. Pulkrabkova[2], L. Muckova[2], J. Korabecny[1,2], Daniel Jun[1]
[1] *University of Defence, Faculty of Military Health Sciences, Department of Toxicology and Military Pharmacy, Trebesska 1575, 500 01 Hradec Kralove, Czech Republic*
[2] *University Hospital, Biomedical Research Centre, Sokolska 581, 500 05 Hradec Kralove, Czech Republic*

*Corresponding Author: Ondrej, Soukup, ondrej.soukup@fnhk.cz

Abstract

In recent years, so-called Novichoks receive worldwide attention. There are several types of novichok agent (e.g. A-234, A-232 etc). One type of Novichok was evaluated in our laboratory and its physical-chemical and biological properties were compared to well-known nerve agents such as sarin or VX.

Inhibition kinetics of human acetylcholinesterase and butyrylcholinesterase was determined. Further, the ability of standard oxime reactivators like HI-6, obiodoxime, methoxime etc. to restore the activity of both acetylcholinesterase and butyrylcholinesterase was assessed.

The results showed that low capability of currently available oximes to reactivate novichok-inhibited cholinesterase in vitro and some effect in vivo. Such result highlights the necessity of further development of effective antidotes or alternative approaches for post exposure therapy against novichok.

Considering the cytotoxic effect of organophosphates, the mechanism of cytotoxicity of the NAs, including A-agents, was confirmed to be ascribed rather to non-specific effects of OPs than to AChE-mediated effects and must be addressed in further research.

Keywords: Organophospahtes, novichoks, oxime reactivators

Biography - Ondrej Soukup

Ondrej obtained his PhD in 2011 at the University of Defence in Hradec Kralove. He became Assoc prof. and Professor in Toxicology in 2018 and 2023 respectively with the special focused on the military toxicology and fore mostly on nerve agent poisoning ant its treatment. Currently, he is the head of Biomedical Research Center (BRC), University Hospital Hradec Kralove, solving many research projects on various clinical topics as well as in the field of drug-development.

In particular, his research is focused on the evaluation of new therapeutics for Alzheimer's disease and organophosphorus poisoning, where biological properties of the new compounds, pharmacological and toxicological profile both *in vitro* and *in vivo* are determined. He is author or co-author of 180+ research articles with over 2700 citations up-to-date.

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44. Evaluation of new modified bisquarternary pyridinium oximes K1651–K1654

Jaroslav Pejchal[1*], K. Musilek[2], M. Hrabinova[1], E. Prchalova[2], D. Malinak[2], R. Andrys[2], and J. Zdarova Karasova[1]

1 University of Defence, Faculty of Military Health Sciences, Department of Toxicology and Military Pharmacy, Hradec Kralove, Czech Republic
2 University of Hradec Kralove, Faculty of Science, Department of Chemistry, Hradec Kralove, Czech Republic

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Abstract

Oxime reactivators are causal antidotes for organophosphate (OP) poisoning, restoring acetylcholinesterase (AChE) physiological functions. These compounds are more or less effective. However, none has proved the ability to sufficiently reactivate AChE inhibited by various OPs regardless of their chemical structure.

Research of new oximes is therefore still ongoing. Our study aimed to assess new modified bisquarternary pyridinium oximes K1651, K1652, K1653, and K1654. Firstly, we conducted reactivation screening and determined the reactivation kinetics of K1651, K1652, K1653, and K1654 using human recombinant AChE (*hr*AChE) inhibited by nerve agent surrogates and paraoxon. Based on *in vitro* results, the maximum tolerated dose (MTD) for rats was established only for K1653 and K1654.

Subsequently, we conducted reactivation experiments *in vivo* against sarin and VX and established protective indices against VX. K1654 showed the highest reactivation ability, while both K1653 and K1654 exhibited superior reactivation kinetics against nitrophenyl isopropyl methylphosphonate- (sarin surrogate) and nitrophenyl ethyl methylphosphonate (VX surrogate)-inhibited *hr*AChE. MTD of K1653 and K1654 was established at 150 and 50 mg/kg, respectively. K1653 significantly reactivated blood and brain cholinesterases in VX-poisoned rats, while K1654 significantly reactivated blood cholinesterases in sarin-poisoned animals and brain cholinesterases in VX-intoxicated rats. Oxime K1653 provided higher protection against VX in rats than asoxime or obidoxime. K1653 seems promising for further testing.
This work was supported by the Czech Science Foundation (no. 21-03000S).

Keywords: oxime; organophosphate; therapy

Biography - Jaroslav Pejchal

Assoc. Prof., M.D., Ph.D. et Ph.D.

Jaroslav Pejchal is a researcher in the field of toxicology. His background also covers medicine and military radiobiology. He has published as an author and co-author of over 80 papers in highly regarded, peer-reviewed journals.

He has been twice assigned to the NATO CBRN Joint Assessment Team, was twice a member of NATO working groups, and once served as a medical manager on a half-year mission abroad.

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28. Compact Rapid Chemical Agent Neutralization System: A Rapidly Deployable Method for Large Scale Chemical Agent Destruction

T. Blades[1], **Robert J. Malone*[1]**, M. Marinelli[1]

US Army Futures Command DEVCOM Chemical Biological Center, Aberdeen Proving Ground, MD, USA

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Abstract

The Compact Rapid Chemical Agent Neutralization System (CRaCANS) is a patent-pending chemical agent neutralization technology under development at the US Army Chemical Biological Center since 2021. Modeled after the Field Deployable Hydrolysis System (FDHS) neutralization process that was used to destroy the Syrian Chemical Agent Stockpile in 2014, the CRaCANS is designed to be a chemical agent destruction technology that is more rapid and flexible than those historically used for large stockpiles. The CRaCANS deploys on a single 463L NATO pallet (108"x88"x80") and is designed to destroy more than two tons of bulk or 48 projectiles/mortars (when paired with an access system) of chemical agent in 24 hours. With minimal logistical support requirements due to its onboard power source, heaters, air compressor and waste containers, the CRaCANS is fabricated to effectively destroy agent whilst maximizing the ease of operation, transportability, and ruggedness of the equipment. The US Army Chemical Biological Center is currently live agent testing the CRaCANS at Aberdeen Proving Ground to prove its capability to deploy and destroy chemical agents, including H, GB, VX, HD/L, and L.
Approved for public release: distribution unlimited

Keywords: Chemical Weapon; Chemical Agent; Destruction; Disposal; Mobile; Portable

Biography - Robert J. Malone

Plans and Assessments Chief

Robert Malone is a subject matter expert in chemical agent operations, secondary waste processing, treatment technology selection, facility closure planning / implementation, field sampling and site remediation. His career includes leadership roles as both a government civilian for the U.S. Army and as a contractor for Science Applications International Corporation. Rob currently serves as a Program Manager and Chief of the Plans and Assessments Team for Chemical Biological Applications and Risk Reduction (CBARR). His work has led to the technology selection, fabrication and delivery of the Field Deployable Hydrolysis System (FDHS) a first-of-akind deployable chemical agent destruction system developed under a rapid acquisition process to satisfy the first Joint Emergent Operational Needs Statement (JEONS) issued. Mr. Malone has worked the project planning for both land-based and ship-board FDHS operations. He served aboard the Cape Ray throughout the construction, operation and demobilization phase of the Syrian chemical weapons destruction mission. Rob previously served as the Associate Site Project Manager for the Tooele Chemical Agent Disposal Facility (TOCDF), responsible for both technical and contractual management. TOCDF, in Tooele Utah has destroyed the largest and most diverse stockpile of chemical agent munitions in the world. Rob chaired the Integrated Risk and Schedule Management IPT for the Deseret Chemical Depot utilizing his knowledge of

acquisition lifecycle management, demilitarization, chemical operations, and closure to lead the integrated team of government and contractor personnel through a first-ofa-kind process that quantifies risks to project schedule execution, calculates milestone confidence and identifies solutions for risk avoidance or mitigation to the Project Managers. Prior to TOCDF, Rob was the Closure and Remediation Department Manager and the Johnston Atoll Chemical Agent Disposal System (JACADS) Project Manager for SAIC. JACADS was the first full-scale chemical agent demilitarization plant in the U.S. Mr. Malone holds a Masters of Science degree from The Johns Hopkins University in Environmental Science and Policy and a Bachelors of Science degree from the University of Maryland at College Park in Natural Resources Management. He is a PMI certified Project Management Professional since 2007 and is a Registered Environmental Manager with the NREP. Rob was awarded the Superior Civilian Service Award in 2013 and 2014 for his work at TOCDF and the Syria Cape Ray mission respectively. He received the Commanders Award in 2011 and 2012 for his work at JACADS and TOCDF.

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48. Remote controlled systems for first responds

Donna Vadlja*[1], D. Tušek[2], Z. Orehovec[3]

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Abstract

With the development of new technologies, unmanned air and ground vehicles (UGV, UAV) have found their irreplaceable purpose in the daily performance of military and civilian activities. The synergy of system and man is visible in the design and use od UGV and UAV. These systems are still not fully automated and depend on human management, and cannot perform complex, autonomous tasks without operator supervision. In order to better develop algorithms for the cognitive mode of operation of the system, cognitive task analysis (CTA) was used. UGV/UAV systems must replace the human role in responding to threats, where they can be life- threatening.

Natural disasters, CBRN threats are just some f the challenges for designing an optima system. The main tasks in which such systems would be used are; removal of obstacles in the way of intervention, research, disposal of dangerous objects during and after incident itself, transport of necessary substances and equipment to the CBRN dangerous area and assessment and medical evacuation of the injured. Operating in highly contaminated area presents a special kind of challenge.

Reconnaissance detection and identification require a number of specialized detectors, containers and compartments to be located on the system. The communication network, as all components that systems to the operator, can be potential targets of cyberattacks.
The systems are most vulnerable precisely in this area because the information that can be obtained from these systems can be very valuable.

Keywords: UAV/UGV; CBRN; Cognitive Tasks Analysis – CTA; Cyber protection

Biography - Donna Vadlja

Donna Vadlja was born in Osijek in 1993, where she completed undergraduate and graduate studies in medical laboratory diagnostics at the Faculty of Medicine in Osijek in 2017.

The Armed Forces of the Republic of Croatia joined in 2018. as a soldier in the Nuclear-Biological-Chemical Defense Battalion. He will complete his basic officer training in 2020. at the Croatian Military Academy, after which he assumed the duties of platoon commander.

In 2023, he assumed the position of commander of the 1st company in the NBC Defense Battalion.

In parallel with his work in the Armed Forces, he enrolled in postgraduate studies at the University of J.J. Strossmayer in Osijek - Molecular biosciences, majoring in biomedicine, where he is still at today as part of the CellToxTargets project. In the past two years, he and his collaborators have published international reviews on the topic of N-alkyl quaternary quinuclidinium compounds.