(0-300 μM, 1-24 hours). We found that SM degraded laminin-5 and its two subunits β3 and γ2, but not α3. Preincubation of cells with a serine protease inhibitor (PMSF), or a metalloprotease inhibitor (1, 10-phenanthroline) prior to SM exposure partially prevented SM-induced degradation of laminin-5 subunits, β3 and γ2.

Regarding specificity, laminin-5 γ2 was degraded due to a bifunctional mustard compound like SM, but not due to the other alkylating agents tested.

Our results support that laminin-5 degradation is an important mechanism of SM injury as well as a useful biomarker of SM exposure.

This knowledge of the mechanism of laminin-5 degradation due to SM has potential application in developing cutaneous therapeutics against SM.

Key words: sulfur mustard, vesicant effect, laminin 5, protease inhibitors

44. CELL DEATH MECHANISMS IN SULFUR MUSTARD INJURY: BASIS FOR THERAPEUTICS DEVELOPMENT *(4)*

[1]**Dr. Radharaman Ray**, [1]Dr. Brian Keyser, [1]Ms. Betty Benton, [2]Dr. Dean S. Rosenthal
[1]Cell and Molecular Biology Branch, Research Division, US Army Medical Research Institute of Chemical Defense, APG, MD 21010-5400, USA
[2]Department of Biochemistry and Molecular Biology Georgetown University School of Medicine Washington D.C. 20007, **USA**

Sulfur mustard (SM, bis-(2-chloroethyl) sulfide), commonly called mustard gas, is a vesicant chemical warfare agent and a potential terrorism agent. SM is relatively easy to make and to deploy, which makes this chemical most likely to be used. SM exposure causes debilitating skin blisters (vesication) and injury to the eyes and the respiratory tract.

Therefore, developing an effective medical countermeasure to protect against the dermal, ocular and airway injuries due to this dreaded chemical agent is an urgent priority of the US Army.

SM pathophysiology is consistent with epithelial cell damage, particularly basal cell apoptosis. SM-induced apoptosis may occur via multiple pathways dependent on one or more of the following: (a) abnormal Ca^{2+} homeostasis, (b) disturbed cellular bioenergetics, and (c) Fas (death receptor) response.

Apoptosis pathways are characterized by the involvement of the pathway-specific caspases (cysteine aspartase). We determined caspase activity by assay of fluorogenic caspase type-specific peptide substrate hydrolysis. We studied caspase processing, i.e., proteolytic conversion of procaspase to active caspase by immunoblot analyses utilizing caspase type-specific antibodies.

Our results in cell culture models of both human epidermal keratinocytes and human airway epithelial cells indicated that SM activates (a) caspase-9, an indicator of the Ca^{2+}/CaM-mediated mitochondrial pathway, (b) caspase-8, a marker for the Fas-mediated pathway, and (c) caspase-3, the executioner caspase involved in both pathways.

A peptide caspase inhibitor, specific for caspase-3 (AC-DEVD-CHO), added to cells prior to SM decreased apoptosis.

These observations suggest apoptosis as a mechanism of SM toxicity and caspase inhibitors as prospective medical countermeasures.

Key words: sulfur mustard, vesicant, chemical warfare agent, terrorism agent, apoptosis, therapeutics

45. SANITARY ASSESSMENT OF HAZARDOUS MATERIALS EXPOSED TO HIGHLY TOXIC CHEMICAL COMPOUNDS *(14)*

Dr. Vladimir Rembovskiy, Elena Ermolaeva
Research Institute of Hygiene, Occupational Pathology and Human Ecology (RIHOPHE)
p/o Kuzmolovsky, Leningradsky Region, 188663
Russian Federation

Industrial or terroristic accidents in which toxic chemicals (TC) are the main or attendant damaging factors should be regarded as a new challenge for experts, because of little knowledge on the methodology to estimating the long-term risk for humans due to contamination of the building materials and environment.

In the Russian Federation, there appeared to be a kind of model systems for developing an algorithm for solving these or similar problems. Under dismantling and liquidation of the former facilities for chemical weapon production (FCWP) the building materials are regarded as potential waste products the fate of which (processing, warehousing, utilization, and destruction) is dependent on their possible hazard for human population and environment.

The standard approaches for hazard assessment of waste products of the FCWP turned out to be insufficient. When conducting the present work, the following problems have been solved:

1. Selection of representative samples taking into consideration a diversity of construction materials, great quantities of potentially toxic waste materials, information on the production conditions, breakdowns in the process of production, accidents, composition of the decontaminators used, decontamination frequency, etc.

2. Analysis of TC in composite matrixes complicated by the following problems: extraction, masking effects of concomitant components during indirect analysis, lack of certified methods of direct analysis of TC, discrepancy of results of GC and direct GCMS analysis, low sensitivity of GCMS analysis, big volume of samples (more than 0.5 kg), heterogeneity of physical-chemical properties

of different matrixes influencing the process of degradation of TC.

3. Hazard assessment of the wastes in toxic-and-sanitary experiment relying on non-specific signs of intoxication due to relatively low percentage of TC and masking effects of various matrix components. Application of the integral toxicity tests with soil-and-plant microflora and hydrocoles.

4. Development of non-standard methodical approaches when determining and interpreting the hazard classes of the wastes, containing high toxic compounds such as nerve gases. In particular, disembodied methods applied for solving the tasks of assessment of chemical compounds toxicity were summarized, as well as a uniform scheme of experimental toxicological assessment of TC of a high risk is presented. A system of quantitative assessment of the TC risk is developed on the basis of integral coefficient of risk (K_{TC}), thus simplifying decision making after toxicological testing. Calculation of the coefficient of the TC risk is based on logarithm of ratio of toxicometry parameters to the value of identical parameters determining affiliation of the TC to the 1st class of risk (extreme risk).

Due to the methodology developed in our Institute, we have for the first time estimated the class of toxicity of a highly complicated industrial system.

46. RADIATION RISK ASSOCIATED WITH LOW DOSES OF IONIZING RADIATION: IRRATIONAL FEAR OR REAL DANGER? *(14)*

Dr. Vladimir Rembovskiy, Dr. Vladimir Reshetin
Joint Institute for Power and Nuclear Research
National Academy of Sciences of Belarus
Sosny-Minsk, 220109, **Belarus**

The established worldwide practice of protecting people from radiation based on the assessments of radiation risk received in the researches carried out earlier costs hundreds of billions of dollars a year to implement. In the opinion of the well-known experts, the maintenance of the existing radiation protection regulations or moreover acceptance of more tough regulations can influence the development of nuclear power engineering.

The accepted practice of assessment of human health risk from radiation may also significantly affect our perception of threats of radiation terrorism. In this work, the critical analysis of publications on the assessment of the effects of small doses of radiation on human health is carried out. In our analysis, we especially emphasize the data on cancer mortality among survivors of the atomic bombing of Hiroshima and Nagasaki who received instantaneous radiation doses of less than 200 mSv including the data on leukemia and solid cancer, as well as epidemiological studies in the regions of India and China with high level of natural radiation.

Since the investigations of radiation risk is a base for formulating modern radiation protection regulations, their reliability and validity are of great importance. As follows from the analysis, the subsequent, during three decades, toughening of radiation protection regulations has already led to exceedingly prohibitive standards and impractical recommendations the science-based validity of which can cause serious doubts.

Now, a number of world-wide known scientists and authoritative international organizations call for revision of these standards and of the radiation safety concept itself.

Key words: Radiation protection, Low dose, Epidemiological study, Atomic bombing, Safety

47. THE INTEGRATION OF A SMALL THERMAL DESORPTION (TD) SYSTEM FOR AIR MONITORING INTO A MOBILE ANALYTICAL LABORATORY IN FRANCE USED BY THE NRBC EMERGENCY FIRST RESPONDER POLICE ORGANIZATION *(10)*

Dr. Gareth M. Roberts
Markes International Ltd, Gwaun Elia, Medi Science Campus, Llantrisant, South Wales, CF72 8XL, **UK**

A mobile analytical laboratory has been developed in France by Thales Security Systems in conjunction with the French department of defense (DGA) to rapidly identify the composition of toxic substances released accidentally or by terrorist activity at a location of high civilian population density.

Accurate and fast identification of toxic material is critical for first responder teams that attend an incident site. Based on this analysis defined decontamination protocols for contaminated people can be implemented, and specific medical treatment can be administered to those worst affected.

Analysing samples with high technology instrumentation close to the point of release is therefore highly advantageous and is only possible with mobile analytical platforms. Transporting samples back to a central laboratory for analysis is not realistic due to time limitations.

This paper looks at one particular aspect of analysis performed in this mobile multi-technique laboratory namely air monitoring for CW or TIC compounds. Air sampling and pre concentration is achieved using a small, innovative Thermal Desorption system (Unity^{tm}) in combination with a gas chromatograph-mass spectroscopy system for the detection and identification of specific analytes.

Implementation of the Unity TD system in the confines of this small mobile environment will be reviewed in this paper.