Radiation Injury Treatment Network®

Fact Sheet for Health Care Professionals on Mustard Agents ("Mustard Gas")

Mustard agents were first employed as chemical warfare during World War I. At that time, mustard agents were used in their vaporous or gaseous forms, and hence the term "mustard gas" has entered the popular vocabulary. Although the use of mustard agents in warfare has been banned by international treaties, they could still be used in conventional or terrorist attacks. As part of an ongoing contingency plan to treat casualties resulting from untoward events, the Radiation Injury Treatment Network (RITN), National Marrow Donor Program (NMDP) and the U.S. Navy have developed this fact sheet on mustard agents.

The goal of this fact sheet is to provide medical professionals who manage patients with bone marrow toxicity with facts about the short- and long-term effects of mustard agents and the basic elements of clinical care for mustard agent casualties. Although it is not a common reaction, some casualties exposed to mustard agents will have bone marrow damage. Therefore, RITN may be asked to provide care or guidance for some casualties, and a small percentage may even be considered for hematopoietic cell transplantation.

Properties of mustard agents

Mustard agents are organic molecules composed of carbon, hydrogen, chlorine, and either a sulfur atom (sulfur mustards) or a nitrogen atom (nitrogen mustards). There are several varieties of each form: sulfur mustard varieties are given the military designations H, HD, and HT; nitrogen mustards are designated HN-1, HN-2, and HN-3. Because treatment after exposure to either nitrogen or sulfur mustard is very similar, the general term mustard agent will be used throughout this fact sheet.

Mustard agents are alkylating agents and vesicants. In their pure form, mustard agents are colorless, oily liquids that will slowly evaporate at room temperature. In use, mustard agents have a yellow to brown tint due to impurities and a slight scent of garlic or mustard. Mustard agents are only minimally soluble in water, but will readily mix in fats, oils, and organic solvents.

To be effective in chemical warfare, mustard agents must come into contact with a victim's skin or mucous membranes (including the eyes). Mustard agents belong to the category of "blistering agents" and the physical damage they cause results from burning of the skin or mucous membranes. Inhalation, ingestion, and physical contact are all ways that mustard agents can harm a victim. Mustard agents are not usually fatal, except at high levels of exposure. When used in chemical warfare, mustard agents are intended to incapacitate and demoralize combatants and to overwhelm the enemy's medical resources. Many of the long-term effects of mustard agents have not been clearly identified, although they are known to be carcinogenic.

Clinical symptoms of mustard agent casualties

Clinical presentations by mustard agent casualties vary depending on the means of contact with the agent and whether the agent was absorbed systemically. Mustard agents in all forms (vapor,

liquid, and solid) can be absorbed through the skin, eyes, and mucous membranes. Vaporous mustard agents can be inhaled, and solid and liquid mustard agents can be ingested if they have been placed in food and water.

- Skin exposure: Redness, swelling and itching of the skin will occur in as little as one hour after exposure, but may not develop for up to 48 hours. This initial skin reaction will be followed by a yellow blistering of the skin. Contact with high levels of mustard agents will cause second- and third-degree burns.
- Eye exposure: Mustard agents contacting the eyes will lead to inflammation, swelling, pain, burns, corneal damage, and, if the contact is severe, blindness may result.
- Inhalation: Inhaling mustard agents can damage the cells lining the lungs, pharynx, and the mucous membranes in the nasal and sinus passages. Inhalation of mustard agents can also result in chronic respiratory disease, shortness of breath, and repeated respiratory infections such as pneumonia.
- Ingestion: Ingestion of mustard agents may cause local and systemic effects such as diarrhea, nausea, vomiting, and burns to the lining of the mouth, esophagus and stomach.

Mustard agents can also be absorbed systemically via any of the exposure routes outlined above, which can lead to damage of the immune system and bone marrow. However, such systemic damage usually occurs only after severe exposures, so only a minority of casualties of a mustard agent attack would typically be at risk for bone marrow toxicity and immunosuppression.

Treatment of mustard agent casualties

The information in this section is intended to inform specialists in the care of hematologic diseases about the basic clinical care of mustard agent casualties. It is not meant to provide comprehensive medical information on the treatment of mustard agent exposure. The triage and decontamination of casualties at the site of a mustard agent attack are also outside the scope of this fact sheet.

No specific treatment exists for skin and mucous membrane lesions caused by exposure to mustard agents. Treatment is therefore designed to relieve symptoms, prevent infections, and promote healing. Most skin burns from mustard agent exposure will be second-degree burns, although liquid exposure may cause third-degree burns. Blister fluid does not contain mustard agents or other toxic substances. Irrigation of the burned areas is indicated followed by the liberal application of a topical antibiotic. Casualties with large areas of second- or third-degree burns should be cared for in a burn unit using standard burn treatments.

Eye lesions from mustard agent exposure can range from mild conjunctivitis to severe damage to the cornea, including perforation. Mild cases can be treated with topical antibiotics and over-the-counter saline solutions. Healing can be expected in about two weeks. More severe lesions may require hospitalization and specialized care.

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Inhalation of vapor and the subsequent damage (including infections) to the airways is the leading cause of death in mustard agent casualties. Systemic antibiotics are typically administered when signs of infection are evident and tailored once infectious organisms are identified. Patients with damage below the pharynx require care in a Critical Care Unit by a physician experienced in pulmonary injuries and infections. Intubation is commonly necessary in these patients, both for ventilatory support and for airway protection.

Ingested mustard agents can cause further damage if emesis is induced, so emetic compounds are not recommended. Orogastric lavage may be useful if performed within an hour or less after exposure, but this treatment is controversial because it carries the risk of bleeding and perforation. Treatment for mustard agent ingestion is usually limited to supportive care.

The roles of RITN and the NMDP

A small percentage of mustard agent casualties may have bone marrow suppression. The clinical course of hematologic toxicity from mustard agent exposure is expected to parallel the course observed in patients treated with high doses of therapeutic nitrogen mustards (*e.g.* melphalan, cyclophosphamide). If the bone marrow has been damaged, white blood cell counts in the peripheral blood will begin to decline 3-5 days after exposure. Often, recovery occurs without any intervention. Myeloid cytokines (*e.g.* G-CSF, GM-CSF) have been used as a treatment for bone marrow suppression caused by mustard agent exposure and may shorten the duration and reduce the severity of neutropenia. After a large-scale mustard agent attack, RITN centers may be asked to accept casualties with marrow toxicity. Guidelines for management of these casualties parallel those for casualties of an untoward radiation event (e.g. a nuclear detonation), which are available at: www.ritn.net. In addition, extensive guidelines for post-event management are available through the Radiation Emergency Medical Management website (www.remm.nlm.gov) maintained by the National Library of Medicine.

A very small percentage of casualties exposed to mustard agents could experience myeloablation and be considered for hematopoietic cell transplantation. The efficacy of hematopoietic cell transplantation in this setting is currently unknown. However, the NMDP expects that any mustard agent attack resulting in significant casualties will lead to an increase in registry searches and donor activations. The NMDP and the U.S. Navy have contingency plans in place to accommodate this increased activity. If any casualties of a mustard agent attack ultimately require a stem cell transplant, the NMDP is prepared to search its Registry to find matched donors. As of November 2010, the NMDP Registry contained over 8.5 million potential stem cell donors and more than 140,000 cord blood units, the largest source of blood stem cell donors in the world.

Further information

Web sites:

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Radiation Injury Treatment Network Web site: www.ritn.net

Radiation Emergency Medical Management Web site: www.remm.nlm.gov

U.S. Centers for Disease Control and Prevention (CDC) Web site: www.cdc.gov

Agency for Toxic Substances and Disease Registry (ATSDR) Web site: www.atsdr.cdc.gov

World Health Organization – Radiation Emergency Preparedness and Assistance Network (REMPAN) Web site: www.who.int/ionizing_radiation/a_e/rempan/en/

Radiation Emergency Assistance Center/Training Site (REAC/TS) Web site: http://orise.orau.gov/reacts/

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