ATSDR Department of Health and Human Services
Agency for Toxic Substances & Disease Registry

Nitrogen Mustards
Fact Sheet

Description

Nitrogen mustards are vesicants and alkylating agents. They are colorless to pale yellow, oily liquids that evaporate slowly. HN-1 has a faint, fishy or musty odor. It is sparingly soluble in water but miscible with acetone and other organic solvents. At temperatures greater than 194ºC, it decomposes.

HN-2 has a fruity odor at high concentrations and a soapy odor at low concentrations. Its solubility is similar to HN-1.

HN-3 is odorless when pure but has been reported to have a butter almond odor. It is the most stable of the nitrogen mustards but decomposes at temperatures greater than 256ºC. It has a much lower vapor pressure than HN-1 or HN-2 and is insoluble in water.

Routes of Exposure

Inhalation

Inhalation is an important route of exposure. Nitrogen mustard vapors are heavier than air. The LCt_{50} (the product of concentration times time that is lethal to 50% of the exposed population by inhalation) is approximately 1,500 mg-min/m³ for HN-1 and HN-3, and 3,000 mg-min/m³ for HN-2.

Skin/Eye Contact

Exposure to nitrogen mustard vapor can cause injury to the eyes, skin, and mucous membranes at low concentrations. Direct contact with the liquid can cause skin and eye burns. The median incapacitating dose for the eyes is 100 mg-min/m³ for HN-2 and 200 mg-min/m³ for HN-1 and HN-3. Absorption may occur after skin or eye exposure to liquid or vapor nitrogen mustard and may cause systemic toxicity.

Ingestion

Ingestion is an uncommon route for exposure but can lead to local effects such as esophageal or gastrointestinal burns and systemic absorption.

Sources/Uses

Nitrogen mustards were first developed in the late 1920s and early 1930s. HN-1 was originally designed to remove warts but was later identified as a potential chemical warfare agent; HN-2 was designed as a military agent but was later used in chemotherapy; HN-3 was developed as a military agent. None of the nitrogen mustards have been used on the battlefield, and none are included in U.S. stockpiles.

Physical Properties

Incompatibilities

HN-1 is corrosive to ferrous alloys at temperatures of 149ºF (68ºC) and higher. HN-2 and HN-3 do not have any incompatible actions on metals or other materials.

Health Effects

- Nitrogen mustards are vesicants causing skin, eye, and respiratory tract injury. Although these agents cause cellular changes within several minutes of contact, the onset of pain and other clinical effects is delayed for hours.

- Nitrogen mustards are alkylating agents that may cause bone marrow suppression and neurologic toxicity.

Acute Exposure

Nitrogen mustards are vesicants and alkylating agents; however, the mechanisms of action are not clearly understood. They are highly reactive and combine rapidly with proteins, DNA, or other molecules. Therefore, within minutes following exposure intact mustard or its reactive metabolites are not found in tissue or biological fluids.

- **CNS - High doses of nitrogen mustards have caused tremors, seizures, incoordination, ataxia, and coma in laboratory animals.**

- **Respiratory - Damage to the mucosa of the airways begins within hours and may progress over several days. Nasal and sinus pain or discomfort, pharyngitis, laryngitis, cough, and dyspnea may occur. Pulmonary edema is uncommon.**

- **Gastrointestinal - Ingestion may cause chemical burns of the GI tract and hemorrhagic diarrhea. Nausea and vomiting may occur following ingestion, dermal, or inhalation exposure.**

- **Ocular - Exposure to nitrogen mustard vapor or liquid may cause intense conjunctival and scleral inflammation, pain, swelling, lacrimation, photophobia, and corneal damage. High concentrations can cause burns and blindness.**

- **Dermal - Direct skin exposure to nitrogen mustards causes erythema and blistering. Generally, a rash will develop within several hours, followed by blistering within 6 to 12 hours. Prolonged contact, or short contact with large amounts, may result in second- and third-degree chemical burns.**

- **Hematopoietic - Systemic absorption of nitrogen mustard may induce bone marrow suppression and an increased risk for fatal complicating infections, hemorrhage, and anemia.**

Delayed Effects

Chemotherapeutic doses of HN-2 have been associated with menstrual irregularities, alopecia, hearing loss, tinnitus, jaundice, impaired spermatogenesis, generalized swelling, and hyperpigmentation.

Chronic Exposure

In laboratory animal studies, prolonged or repeated exposures to nitrogen mustards have caused cancer, developmental and reproductive effects, and hepatic toxicity. Repeated exposures result in cumulative effects because mustards are not naturally detoxified by the body.

- Carcinogenicity - The International Agency for Research on Cancer (IARC) has classified nitrogen mustard as probably carcinogenic to humans (Group 2A). There is some evidence that it causes leukemia in humans, and it has been shown to cause leukemia and cancers of the lung, liver, uterus, and large intestine in animals.

- Reproductive and Developmental Effects Nitrogen mustards may decrease fertility. A few case reports have linked treatment with HN-2 to fetal abnormalities in humans. Nitrogen mustards have produced developmental effects in animals.

Prehospital Management

- Victims whose skin or clothing is contaminated with liquid nitrogen mustard can contaminate rescuers by direct contact or through off-gassing vapor.

- Nitrogen mustards are extremely toxic and may damage the eyes, skin, and respiratory tract and suppress the immune system. Although these agents cause cellular changes within minutes of contact, the onset of pain and other symptoms is delayed.

- There is no antidote for nitrogen mustard toxicity. Decontamination of all potentially exposed areas within minutes after exposure is the only effective means of decreasing tissue damage.

Hot Zone

Rescuers should be trained and appropriately attired before entering the Hot Zone. If the proper equipment is not available, or if the rescuers have not been trained in its use, call for assistance from the U.S. Soldier and Biological Chemical Command-Edgewood Research Development and Engineering Center (from 0700-1630 EST call 410-671-4411, and from 1630-0700 EST call 410-278-5201; ask for the Staff Duty Officer).

Rescuer Protection

Nitrogen mustard vapor and liquid are readily absorbed by inhalation and ocular and dermal contact.

- *Respiratory Protection*: Pressure-demand, self-contained breathing apparatus (SCBA) is recommended in response situations that involve exposure to any amount of nitrogen mustard.

- *Skin/Ocular Protection*: Personal protective equipment (PPE) and butyl rubber chemical protective gloves are recommended at all times when these chemicals are suspected to be involved.

Multi-Casualty Triage

Chemical casualty triage is based on walking feasibility, respiratory status, age, and additional conventional injuries. The triage officer must know the natural course of a given injury, the medical resources immediately available, the current and likely casualty flow, and the medical evacuation capabilities. General principles of triage for chemical exposures are presented in the box on the following page. There are four triage categories: immediate (priority 1), delayed (priority 2), minimal (priority 3), and expectant (priority 4).

Before transport, all casualties must be decontaminated. If needed, consult with the base station physician or the regional poison control center for advise concerning management of multiple casualties.

Because most signs and symptoms of nitrogen mustard exposure do not occur for several hours postexposure, patients should be observed for at least 6 hours or sent home with instructions to return immediately if

symptoms develop. Patients who develop significant dermal, ocular, or airway injury and patients who have ingested nitrogen mustard should be transported to a medical facility for evaluation.

Symptoms may not develop for 24 hours. Patients with mild symptoms who are seen long enough after exposure to minimize the likelihood that the lesions will worsen may be sent home after their names, addresses, and telephone numbers have been recorded. They should be advised to rest and to seek medical care promptly if additional symptoms develop

Consult with the base station physician or closest Metropolitan Medical Response System, or the regional poison control center for advice regarding triage of multiple victims.

General principles of triage for chemical exposures are as follows:

- Check triage tag/card for any previous treatment or triage.
- Survey for evidence of associated traumatic/blast injuries.
- Observe for sweating, labored breathing, coughing/vomiting, secretions.
- Severe casualty triaged as immediate if assisted breathing is required.
- Blast injuries or other trauma, where there is question whether there is chemical exposure, victims must be tagged as immediate in most cases. Blast victims evidence delayed effects such as ARDS, etc.
- Mild/moderate casualty: self/buddy aid, triaged as delayed or minimal and release is based on strict follow up and instructions.
- If there are chemical exposure situations which may cause delayed but serious signs and symptoms, then overtriage is considered appropriate to the proper facilities that can observe and manage any delayed onset symptoms. *For nitrogen mustards, potentially exposed individuals should be observed for 6 - 8 hours and, if signs or symptoms appear, be sent to the hospital.*
- Expectant categories in multi-casualty events are those victims who have experienced a cardiac arrest, respiratory arrest, or continued seizures immediately. Resources should not be expended on these casualties if there are large numbers of casualties requiring care and transport with minimal or scant resources available.

    1. *Immediate*: casualties who require lifesaving care within a short time, when that care is available and of short duration. This care may be a procedure that can be done within minutes at an emergency treatment station (e.g., relief of an airway obstruction, administering antidotes) or may be acute lifesaving surgery.

    2. *Delayed*: casualties with severe injuries who are in need of major or prolonged surgery or other care and who will require hospitalization, but delay of this care will not adversely affect the outcome of the injury (e.g., fixation of a stable fracture).

    3. *Minimal*: casualties who have minor injuries, can be helped by nonphysician medical personnel, and will not require hospitalization.

    4. *Expectant*: casualties with severe life-threatening injuries who would not survive with optimal medical care, or casualties whose injuries are so severe that their chance of survival does not justify expenditure of limited resources. As circumstances permit, casualties in this category may be reexamined and possibly be retriaged to a higher category.

ABC Reminders

Quickly ensure that the victim has a patent airway. Maintain adequate circulation. If trauma is suspected, maintain cervical immobilization manually and apply a cervical collar and a backboard when feasible. Apply direct pressure to stop arterial bleeding, if present.

Victim Removal

If victims can walk, lead them out of the Hot Zone to the Decontamination Zone. Victims who are unable to walk may be removed on backboards or gurneys. If these are not available, carefully carry or drag victims to safety.

Decontamination Zone

Decontamination within 1 or 2 minutes following exposure is the only effective means for decreasing tissue damage. Later decontamination is not likely to improve the victim's condition but will protect other personnel from exposure. Decontaminable gurneys and back boards should be used if available when managing casualties in a contaminated area. Decontaminable gurneys are made of a monofilament polypropylene fabric that allows drainage of liquids, does not absorb chemical agents, and is easily decontaminated. Fiberglass back boards have been developed specifically for use in HAZMAT incidents. These are nonpermeable and readily decontaminated. The **Chemical Resuscitation Device** is a bag-valve mask equipped with a chemical agent cannister that can be used to ventilate casualties in a contaminated environment.