# R7DHRE Hazardous Materials Guideline: Nitrogen Oxides (Nox)

Region VII Disaster Health Response Ecosystem

# REGION VII DISASTER HEALTH RESPONSE ECOSYSTEM (R7DHRE)

## CHEMICAL SPECIALTY TEAM

## Call Your Poison Center for Immediate Assistance: 1-800-222-1222

# Hazardous Materials Guideline: Nitrogen Oxides (Nox)

**This document is intended as a supplement for discussion with your local poison center or toxicologist.**

## 1.0 BACKGROUND

**1.1** Description: **Nitrogen oxides are a mixture of gases** designated by the formula NOx. The mixture includes nitric oxide (NO), nitrogen dioxide (NO2), nitrogen trioxide (N2O3), nitrogen tetroxide (N2O4), and nitrogen pentoxide (N2O5). NO is odorless. Odor generally provides an adequate warning of acute exposure of NO2, N2O4 and N2O5. **The most hazardous of the nitrogen oxides are nitric oxide (NO) and nitrogen dioxide (NO2)**. Both NO and NO2 are nonflammable liquids or gases, but they will accelerate the burning of combustible materials. The higher oxides of nitrogen are irritants to the eye, skin, and respiratory tract; with the **primary site of toxicity being the lower respiratory tract**. Both nitric oxide and nitrogen dioxide are frequently transported in cylinders as a liquefied compressed gas; contact with liquid NO or NO2 may result in frostbite injury.

**1.1.1** The toxicity of nitrous oxide (N2O), the inhaled anesthetic, is not discussed in this guideline.

**1.2** Mechanism of Injury:

**Nitric oxide (NO)** is a colorless gas at room temperature, and at high concentrations is rapidly oxidized in air to form nitrogen dioxide. Nitric oxide is a potent and rapid **inducer of methemoglobinemia.**

***Nitrogen dioxide ($NO_2$)*** is a colorless to yellow-brown liquid at room temperature and a reddish-brown gas above 70°F. $NO_2$ is heavier than air and can accumulate in poorly ventilated, enclosed, or low-lying areas. $NO_2$ gas is irritating and has a sharp odor which does provide adequate warning for acute exposure. **Nitrogen dioxide is corrosive** and is more acutely toxic than nitric oxide, except at lethal concentrations when nitric oxide may kill more rapidly. **On contact with moisture, $NO_2$ forms a mixture of nitric and nitrous acids**. **Nitrogen dioxide damages lungs** in three ways: (1) it is converted to nitric and nitrous acids in the distal airways, directly damaging lung tissue; (2) it initiates free radical generation; and (3) it reduces resistance to infection by altering macrophage and immune function.

**1.3** Routes of Exposure: **Inhalation**, Ocular, Dermal, Ingestion.

## 2.0 PROVIDER SAFETY

**2.1** Personal Protective Equipment (PPE) – Decontamination Team: Personnel decontaminating patients must wear **full-body chemical-resistant clothing and respiratory protection**. Respiratory protection may consist of either:

**2.1.1** A positive pressure air or oxygen source, such as an air-line respirator or a Self-Contained Breathing Apparatus (SCBA) or

**2.1.2** A filtered air respirator (including Powered Air Purifying Respirators (PAPRs)) with filters capable of adsorbing ALL nitrogen oxides.

**2.1.3** A positive pressure air or oxygen source is preferred if there is doubt as to the identity of the chemical in question or if there may be exposure to a level of nitrogen oxides which would overwhelm the filter.

**2.2** Personal Protective Equipment (PPE) – Treatment Team: Personnel treating patients who have been adequately decontaminated need no additional PPE other than **universal precautions** since there is no serious risk of secondary contamination.

**2.2.1** The vomitus from persons who have ingested solutions containing nitrogen oxides (i.e., solutions containing nitric acid and nitrous acid) is hazardous because it may off-gas nitrogen oxide vapors or contaminate those coming in contact with the vomit. Prepare treatment areas for rapid clean up in case the patient vomits.

**2.3** Patient Decontamination:

**2.3.1** Persons exposed only to nitrogen oxide gases who have no eye or skin irritation still need decontamination as irritation may not become evident until washing commences. Patients exposed to only nitrogen oxide gasses and have dry skin and clothes do not pose a significant risk of secondary contamination.

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**2.3.2** Remove contact lenses if it can be done without additional trauma to the eye. **Irrigate eyes for a minimum of 20 minutes.** Continue irrigation until eye pH is neutral (7 to 8).

**2.3.3** Remove ALL clothing and jewelry. Double bag clothing and jewelry to prevent off-gassing.

**2.3.4** Decontamination is best **accomplished by irrigation with copious amounts of water**. Wash skin and hair with plain water for a minimum of 20 minutes and then wash twice with soap & water after washing with plain water. Washing with water alone (for a longer period of time) is acceptable if soap is not available. **Neutralization is NOT recommended**.

**2.3.5** Watch for hypothermia (1) in children and the elderly, (2) when decontamination is done with un-heated water, or (3) during cold weather.

**2.3.6** *Frostbite Considerations*: Handle frostbitten skin and eyes with caution. Re-warm the affected area in the same manner as for environmentally-induced frostbite. For eyes, use lukewarm water or saline to irrigate & re-warm eyes, as appropriate.

## 3.0 SIGNS & SYMPTOMS

**3.1** Severity of symptoms will depend upon the concentration of the nitrogen oxides to which the person is exposed and the duration of exposure.

**3.2** *General*: The primary route of exposure to nitrogen oxides is by inhalation, but exposure by any route can cause systemic effects. Nitrogen oxides are **irritating** to the eyes, skin, mucous membranes, and respiratory tract. Nitric oxide is a potent and rapid **inducer of methemoglobinemia**.

**3.2.1** *Methemoglobinemia*: Nitric oxide (NO) induces methemoglobinemia (MetHb), which impairs the delivery of oxygen to tissues.

| Methemoglobin Level | Signs and Symptoms |
|---|---|
| **30-50%** | Headache, fatigue, dizziness, tachycardia, mild shortness of breath. |
| **50-70%** | Stupor, bradycardia, respiratory depression, irregular heart rhythm, metabolic acidosis. |
| **60-70%** | Cardiac arrest, loss of consciousness, coma, death. |
| Methemoglobin levels exceeding 70% are potentially lethal if untreated. | |
| Patients who have underlying diseases may develop signs and symptoms at lower methemoglobin levels | |

**3.2.2** When MetHb levels are 15% to 30%, the patient's skin may become bluish in color, which is due to the dark color of MetHb and not to inadequate oxygen in the blood. Methemoglobin blood itself has a chocolate-brown appearance.

**3.2.2** *Pulse Oximetry and Co-Oximetry*: Methemoglobin causes absorption interference with standard pulse oximetry reading, making standard pulse oximetry unreliable. Accurate oxygen saturation determinations require co-oximeter measurements. A co-oximeter is also needed to determine the MetHb level in the patient's blood.

**3.3** Inhalation: Nitrogen oxides are very irritating to the upper respiratory tract and lungs even at low concentrations. Only one or two breaths of a very high concentration can cause severe toxicity.

**3.3.1** Exposure to low concentrations may initially cause mild shortness of breath, cough, hyperpnea, choking, fatigue and other non-specific systemic symptoms. After a symptom-free period of 3 to 30 hours, progressive inflammation in the lungs may lead to bronchospasm and life-threatening pulmonary edema. Non-cardiogenic pulmonary edema may develop even if initial pulmonary signs were minimal.

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**3.3.2** Inhalation of very high concentrations can rapidly cause burns, laryngospasm, laryngeal edema, upper airway obstruction, and death.

**3.3.3** Bronchiolitis obliterans may develop several weeks following exposure.

**3.3.4** Reactive Airway Dysfunction Syndrome (RADS) may develop after a single acute, high-dose exposure.

**3.4** Dermal: Nitrogen oxides are skin irritants and corrosives. Skin moisture in contact with either liquid nitrogen dioxide or high concentrations of $NO_2$ vapor can result in nitric acid formation, which may cause second-and third-degree skin burns. Nitric acid may also cause yellowing of the skin and erosion of dental enamel.

**3.5** Ocular: Exposure to high air concentrations can produce eye irritation and inflammation. Prolonged exposure to NOx may cause clouding of the eye surface and blindness. Liquid nitrogen oxides cause severe eye burns after brief contact.

**3.6** Ingestion: Both nitric oxide and nitrogen dioxide are gases at room temperature, but nitrogen dioxide exists as a liquid below 70$^{o}$F. If ingested, solutions of nitrogen dioxide (including nitrous acid and nitric acid) will cause gastrointestinal irritation or burns with nausea, vomiting, hematemesis, drooling and abdominal pain.

## 4.0 DIAGNOSTICS

**4.1** Nitrogen oxide poisoning is a clinical diagnosis and there is no specific diagnostic testing. Any diagnostic evaluation should be based on signs and symptoms.

**4.2** Pulse oximetry should be used in symptomatic patients to evaluate the need for supplemental oxygen and additional monitoring.

**4.2.1** Co-oximetry and blood methemoglobin levels should be measured if there is any evidence of cyanosis or hypoxia.

**4.3** Consider a chest x-ray in patients with persistent symptoms and hypoxia.

**4.4** Considerations For Delayed-Onset Pulmonary Symptoms:

**4.4.1** Because of the risk of a delayed onset of severe, life-threatening pulmonary edema from what may appear to have been a trivial exposure, it is important that exposed subjects be maintained under medical surveillance for the first 48 hours post-exposure.

**4.4.2** All patients determined to have been exposed to nitrogen oxides should be advised that life-threatening symptoms (i.e., bronchiolitis obliterans) may develop as late as several weeks after the exposure.

## 5.0 TREATMENT

**5.1** General: **Treatment is mainly decontamination and supportive care** including basic and advanced life support. There is no specific antidote for exposure to nitrogen oxides unless there is development of methemoglobinemia. **In cases of methemoglobinemia, methylene blue may be necessary**.

**5.1.1** *Antidote: Methylene Blue*

**5.1.1.1** Indications: Patients with methemoglobinemia who have cardiopulmonary symptoms, signs and symptoms of hypoxia (other than cyanosis) or MetHb level >30%. Cyanosis alone does not require treatment.

**5.1.1.2** Side Effects: nausea, vomiting, abdominal and chest pain, dizziness, diaphoresis, and dysuria.

**5.1.1.3** Dosing: 1 to 2 mg per kg of body weight (0.1 to 0.2 mL/kg of a 1% solution) over 5 to 10 minutes, repeated in one hour if needed.

**5.1.1.4** Clinical response is usually observed within 30 to 60 minutes. The total dose over a 24-hour period should not exceed 7 mg/kg, as methylene blue itself can cause hemolysis at greater doses.

**5.1.1.5** In patients with G6PD deficiency, methylene blue may not be effective and may cause hemolysis.

**5.1.1.6** May consider hyperbaric oxygen therapy in patients whose methemoglobin levels are refractory to methylene blue therapy and may consider exchange transfusions for severely poisoned patients who are deteriorating clinically despite methylene blue treatment.

**5.2** Inhalation: **Maintain the patient's airway as necessary. Support oxygenation and ventilation as necessary**. Use standard treatments for pulmonary edema and bronchospasm.

**5.2.1** Because of the risk of a delayed onset of severe, life-threatening pulmonary edema after what may appear to have been a trivial exposure, it is important that exposed subjects be maintained under medical surveillance for the first 48 hours post-exposure.

**5.3** Dermal: Treatment is the same as that for thermal burns. If frostbite is present, rewarm the affected area in the same manner as for environmentally induced frostbite.

**5.4** Ocular: **Irrigate eyes to a neutral pH**. Perform a thorough eye exam: test visual acuity and perform fluorescein and slit lamp examinations. Ophthalmology consultation may be necessary. Immediately consult an ophthalmologist for patients who have corneal injuries.

**5.5** Ingestion: Do NOT give activated charcoal or induce emesis. Consider dilution by giving 2 to 4 ounces of milk or water orally ONLY to patients who are conscious, able to swallow, and are able to protect their airway. Endoscopic evaluation may be necessary.

**Disclaimer:** This guideline is intended to be an informational reference only and should not be used as a substitute for consultation with a poison center or toxicologist, and/or the clinical judgement of the bedside team.

Initial author: Edward Bottei, MD, FACMT; revised by Dan McCabe, MD and the R7DHRE Chemical Specialty Team

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