

Nitrogen Oxides (NO, NO₂, and others)
CAS 10102-43-9; UN 1660 (NO)
CAS 10102-44-0; UN 1067 (NO₂)
UN 1975 (Mixture)

Synonyms for nitric oxide (NO) include mononitrogen monoxide and nitrogen monoxide. Synonyms for nitrogen dioxide (NO₂) include dinitrogen tetroxide, nitrogen peroxide, nitrogen tetroxide, and NTO. Synonyms for mixtures of nitrogen oxides include nitrogen fumes and nitrous fumes.

- **Persons exposed only to nitrogen oxide gases do not pose substantial secondary contamination risks. Persons whose clothing is contaminated with liquid nitrogen oxides can secondarily contaminate others by direct contact or through off-gassing vapors.**
- **Nitric oxide and nitrogen dioxide are nonflammable liquids or gases; however, they will accelerate the burning of combustible materials. Odor generally provides an adequate warning of acute exposure providing the higher oxides (NO₂, N₂O₄ and N₂O₅) are present. Nitric oxide (NO) is odorless and nitrous oxide (N₂O) has only a very faint odor.**
- **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. On contact with moisture, nitrogen dioxide forms a mixture of nitric and nitrous acids.**

Description

Nitrogen oxides represent a mixture of gases designated by the formula NO_x. The mixture includes nitric oxide (NO), nitrogen dioxide (NO₂), nitrogen trioxide (N₂O₃), nitrogen tetroxide (N₂O₄), and nitrogen pentoxide (N₂O₅). The toxicity of nitrous oxide (N₂O) or laughing gas, which is used as an anesthetic, is different from that of the other nitrogen oxides and is not discussed in this protocol.

The most hazardous of the nitrogen oxides are nitric oxide and nitrogen dioxide; the latter exists in equilibrium with its dimer, nitrogen tetroxide. Nitric oxide is a colorless gas at room temperature, very sparingly soluble in water. Nitrogen dioxide is a colorless to brown liquid at room temperature and a reddish-brown gas above 70 °F poorly soluble in water. Nitric oxide is rapidly oxidized in air at high concentrations to form nitrogen dioxide.

Routes of Exposure

Inhalation

Nitrogen oxides (NO₂, N₂O₄, N₂O₃ and N₂O₅) are 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. Odor is generally an adequate warning property for acute

exposures. Nitrogen dioxide is heavier than air, such that exposure in poorly ventilated, enclosed, or low-lying areas can result in asphyxiation.

Children exposed to the same levels of nitrogen oxides as adults may receive larger doses because they have greater lung surface area:body weight ratios and increased minute volumes:weight ratios. In addition, they may be exposed to higher levels of nitrogen dioxide than adults in the same location because of their short stature and the higher levels of nitrogen dioxide found nearer to the ground.

Skin/Eye Contact

Exposure to relatively high air concentrations can produce eye irritation and inflammation.

Children are more vulnerable to toxicants affecting the skin because of their relatively larger surface area:body weight ratio.

Ingestion

Both nitrogen dioxide and nitric oxide are gases at room temperature. However, nitrogen dioxide exists as a liquid below 21 °C and, if ingested, will cause gastrointestinal irritation or burns.

Sources/Uses

Nitrogen oxides form naturally during the oxidation of nitrogen-containing compounds such as coal, diesel fuel, and silage. Nitrogen oxides are also formed during arc welding, electroplating, engraving, dynamite blasting, as components of rocket fuel, and nitration reactions such as in the production of nitro-explosives, including gun-cotton, dynamite and TNT. They are produced commercially, usually as the first step in the production of nitric acid, either by the direct oxidation of atmospheric nitrogen in the electric arc (Birkeland-Eyder Process) or by the catalytic oxidation of anhydrous ammonia (Oswald Process). Trace metal impurities most likely cause nitrogen oxides to form in nitric acid and its solutions. Nitrogen oxides are intermediates in the production of lacquers, dyes, and other chemicals and are important components of photo-oxidant smog.

Standards and Guidelines

Nitric Oxide: OSHA PEL (permissible exposure limit) = 25 ppm
(averaged over an 8-hour workshift)

NIOSH IDLH (immediately dangerous to life or health) = 100 ppm

Nitrogen Dioxide: OSHA PEL (permissible exposure limit) = 5 ppm
(Ceiling)

NIOSH IDLH (immediately dangerous to life or health) = 20 ppm

Nitrogen Dioxide AIHA ERPG-2 (maximum airborne concentration below which it is believed that nearly all persons could be exposed for up to 1 hour without experiencing or developing irreversible or other serious health effects or symptoms that could impair their abilities to take protective action) = 15 ppm

Physical Properties	Nitric Oxide	Nitrogen Dioxide
<i>Description:</i>	Colorless gas	Yellow-brown liquid or red-brown gas
<i>Warning properties:</i>	Non-irritating, odorless and colorless gas; no adequate warning for acute exposure unless accompanied by NO ₂ or another higher oxide as is usual.	Irritating, sharp odor at 1–5 ppm; adequate warning for acute exposure; inadequate warning for chronic exposure.
<i>Molecular weight:</i>	30.0 daltons	46.0 daltons
<i>Boiling point (760 mm Hg):</i>	-241 °F (-152 °C)	70 °F (21 °C)
<i>Freezing point:</i>	-263 °F (-164 °C)	12 °F (-11 °C)
<i>Vapor pressure:</i>	>760 mm Hg at 68 °F (20 °C)	720 mm Hg at 68 °F (20 °C)
<i>Gas density:</i>	1.0 (air = 1)	1.5 (air = 1)
<i>Water solubility:</i>	Water soluble	Highly soluble, but reacts with water to form a mixture of nitric and nitrous acids.
<i>Flammability:</i>	Not flammable, but will accelerate burning of combustible materials	Not flammable, but will accelerate burning of combustible materials
Incompatibilities	Nitrogen dioxide and nitric acid react with combustible materials, chlorinated hydrocarbons, carbon disulfide, and ammonia. May react violently with cyclohexane, fluorine, formaldehyde and alcohol, nitrobenzene, petroleum, and toluene.	

Health Effects

- **Most of the higher oxides of nitrogen are eye, skin, and respiratory tract irritants. Nitrogen dioxide is a corrosive substance that forms nitric and nitrous acids upon contact with water; it is more acutely toxic than nitric oxide, except at lethal concentrations when nitric oxide may kill more rapidly.**
- **Nitric oxide is a potent and rapid inducer of methemoglobinemia.**
- **Exposure to nitrogen oxides may result in changes of the pulmonary system including pulmonary edema, pneumonitis, bronchitis, bronchiolitis, emphysema, and possibly methemoglobinemia. Cough, hyperpnea, and dyspnea may be seen after some delay.**
- **Damage to, and subsequent scarring of, the bronchioles may result in a life-threatening episode several weeks following exposure involving cough, rapid, shallow breathing, rapid heartbeat, and inadequate oxygenation of the tissues.**
- **Populations that may be particularly sensitive to nitrogen oxides include asthmatics and those with chronic obstructive pulmonary disease or heart disease.**

Acute Exposure

Nitrogen dioxide is thought to damage lungs in three ways: (1) it is converted to nitric and nitrous acids in the distal airways, which directly damages certain structural and functional lung cells; (2) it initiates free radical generation, which results in protein oxidation, lipid peroxidation, and cell membrane damage; and (3) it reduces resistance to infection by altering macrophage and immune function. There may be an immediate response to exposure to nitrogen oxide vapors that may include coughing, fatigue, nausea, choking, headache, abdominal pain, and difficulty breathing. A symptom-free period of 3 to 30 hours may then be followed by the onset of pulmonary edema with anxiety, mental confusion, lethargy, and loss of consciousness. If survived, this episode may be followed by bronchiolitis obliterans (fibrous obstruction of the bronchioles) several weeks later. Any of these phases can be fatal.

Children do not always respond to chemicals in the same way that adults do. Different protocols for managing their care may be needed.

Respiratory

The higher nitrogen oxides are respiratory irritants. The primary site of toxicity is the lower respiratory tract. Low concentrations initially may cause mild shortness of breath and cough; then, after a period of hours to days, victims may suffer bronchospasm and

pulmonary edema. Inhalation of very high concentrations can rapidly cause burns, spasms, swelling of tissues in the throat, upper airway obstruction, and death.

Exposure to certain chemicals can lead to Reactive Airway Dysfunction Syndrome (RADS), a chemically- or irritant-induced type of asthma.

Children may be more vulnerable to corrosive agents than adults because of the relatively smaller diameter of their airways. Children also may be more vulnerable because of relatively increased minute ventilation per kg and failure to evacuate an area promptly when exposed.

Cardiovascular

Absorption of nitrogen oxides can lead to a weak rapid pulse, dilated heart, chest congestion, and circulatory collapse.

Hematologic

High-dose exposure may convert Fe^{+2} in hemoglobin to Fe^{+3} , by virtue of the presence of nitric oxide (NO), causing methemoglobinemia and impaired oxygen transport.

Dermal

Higher nitrogen oxides are skin irritants and corrosives. Skin moisture in contact with liquid nitrogen dioxide or high concentrations of its vapor can result in nitric acid formation, which may lead to second- and third-degree skin burns. Nitric acid may also cause yellowing of the skin and erosion of dental enamel.

Because of their relatively larger surface area:body weight ratio, children are more vulnerable to toxicants affecting the skin.

Ocular

Liquid nitrogen oxides cause severe eye burns after brief contact. High concentrations of the gas cause irritation and, after prolonged exposure, may cause clouding of the eye surface and blindness.

Potential Sequelae

Obstruction of the bronchioles may develop days to weeks after severe exposure. Patients suffer malaise, weakness, fever, chills, progressive shortness of breath, cough, hemorrhage of the lungs or bronchioles, blue or purple coloring of the skin, and respiratory failure. This condition may be confused with the adult respiratory distress syndrome secondary to infectious diseases such as miliary tuberculosis.

Victims of inhalation exposure may suffer reactive airways dysfunction syndrome (RADS) after a single acute, high-dose exposure.

Chronic Exposure

Chronic exposure to nitrogen oxides is associated with increased risk of respiratory infections in children. Permanent restrictive and obstructive lung disease from bronchiolar damage may occur.

Carcinogenicity Reproductive and Developmental Effects

Nitrogen oxides have not been classified for carcinogenic effects.

Nitric oxide and nitrogen dioxide are not included in *Reproductive and Developmental Toxicants*, a 1991 report published by the U.S. General Accounting Office (GAO) that lists 30 chemicals of concern because of widely acknowledged reproductive and developmental consequences. Methemoglobin inducers are considered harmful to the fetus and nitrogen dioxide has been shown to be fetotoxic in rats and has affected behavior and growth statistics in newborn mice. Nitrogen dioxide also causes DNA damage, mutations, sister chromatid exchanges, and other DNA aberrations.

Special consideration regarding the exposure of pregnant women may be warranted, since nitrogen oxides have been shown to be mutagenic and clastogenic, and fetotoxic in rats; thus, medical counseling is recommended for the acutely exposed pregnant woman.

Prehospital Management

- **Victims exposed only to nitrogen oxide gases do not pose risks of secondary contamination to rescuers. Victims whose clothing or skin is contaminated with liquid nitrogen oxides or nitric acid can secondarily contaminate response personnel by direct contact or through off-gassing vapors.**
- **Most of the higher nitrogen oxides are eye, skin, and respiratory tract irritants. Initial respiratory symptoms after exposure to nitrogen oxides may be mild, but progressive inflammation of the lungs may develop several hours to days after exposure. Noncardiogenic pulmonary edema may develop even if initial pulmonary signs were minimal. Exposures may result in methemoglobinemia, depending upon the presence of nitric oxide (NO) in the gas mixture.**
- **There is no antidote for nitrogen oxides. Primary treatment consists of respiratory and cardiovascular support. Methylene blue may be necessary to treat methemoglobinemia.**

Hot Zone

Rescuers should be trained and appropriately attired before entering the Hot Zone. If the proper equipment is not available, or if rescuers have not been trained in its use, assistance should be obtained from a local or regional HAZMAT team or other properly equipped response organization.

Rescuer Protection

Nitrogen oxides are severe respiratory tract irritants.

Respiratory Protection: Positive-pressure, self-contained breathing apparatus (SCBA) is recommended in response situations that involve exposure to potentially unsafe levels of nitrogen oxides.

Skin Protection: Chemical-protective clothing is recommended when repeated or prolonged contact with liquids of nitrogen oxides or with high concentrations of nitrogen oxide vapors is anticipated because skin irritation or burns may occur.

ABC Reminders

Quickly access for a patent airway, ensure adequate respiration and pulse. If trauma is suspected, maintain cervical immobilization manually and apply a cervical collar and a backboard when feasible.

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.

Consider appropriate management of chemically contaminated children, such as measures to reduce separation anxiety if a child is separated from a parent or other adult.

Decontamination Zone

Victims exposed only to nitrogen oxide gases may appear to have no skin or eye irritation. However, they should still be decontaminated as described below as irritation may not become evident until washing commences.

Rescuer Protection

If exposure levels are determined to be safe, decontamination may be conducted by personnel wearing a lower level of protection than that worn in the Hot Zone (described above).

ABC Reminders

Quickly access for a patent airway, ensure adequate respiration and pulse. Stabilize the cervical spine with a collar and a backboard if trauma is suspected. Administer supplemental oxygen as required. Assist ventilation with a bag-valve-mask device if necessary.

Basic Decontamination

Victims who are able may assist with their own decontamination. Remove and double-bag contaminated clothing and personal belongings.

Flush exposed skin and hair with water for 20 minutes. Use caution to avoid hypothermia when decontaminating children or the elderly. Use blankets or warmers when appropriate.

Immediately begin irrigation of exposed or irritated eyes with plain water or saline and continue for at least 20 minutes. Remove contact lenses if easily removable without additional trauma. Continue eye irrigation during other basic care and transport.

If the victim has ingested a solution of nitrogen oxides or nitric acid, **do not induce emesis.** Do not administer activated charcoal. Victims who are conscious and able to swallow should be given 4 to 8 ounces of water or milk.

Consider appropriate management of chemically contaminated children at the exposure site. Also, provide reassurance to the child during decontamination, especially if separation from a parent occurs. If possible, seek assistance from a child separation expert.

Transfer to Support Zone

As soon as decontamination is complete, move the victim to the Support Zone.

Support Zone

Be certain that victims have been decontaminated properly (see *Decontamination Zone* above). Victims who have undergone decontamination pose no serious risks of secondary contamination to rescuers. In such cases, Support Zone personnel require no specialized protective gear.

ABC Reminders

Quickly access for a patent airway. If trauma is suspected, maintain cervical immobilization manually and apply a cervical collar and a backboard when feasible. Ensure adequate respiration and pulse. Administer supplemental oxygen as required and establish intravenous access if necessary. Place on a cardiac monitor.

Additional Decontamination

Continue irrigating exposed skin and eyes, as appropriate.

If the patient has ingested a solution of nitrogen oxides or nitric acid, **do not induce emesis**. Do not administer activated charcoal. Patients who are able to swallow should be given 4 to 8 ounces of water or milk, if not provided previously.

Advanced Treatment

In cases of respiratory compromise secure airway and respiration via endotracheal intubation. If not possible, perform cricothyroidotomy if equipped and trained to do so.

Treat patients who have bronchospasm with aerosolized bronchodilators. The use of bronchial sensitizing agents in situations of multiple chemical exposures may pose additional risks. Consider the health of the myocardium before choosing which type of bronchodilator should be administered. Cardiac sensitizing agents may be appropriate; however, the use of cardiac sensitizing agents after exposure to certain chemicals may pose enhanced risk of cardiac arrhythmias (especially in the elderly).

Consider racemic epinephrine aerosol for children who develop stridor. Dose 0.25–0.75 mL of 2.25% racemic epinephrine solution in 2.5 cc water, repeat every 20 minutes as needed, cautioning for myocardial variability.

Patients who are comatose, hypotensive, or are having seizures or cardiac arrhythmias should be treated according to advanced life support (ALS) protocols.

If evidence of shock or hypotension is observed begin fluid administration. For adults, bolus 1,000 mL/hour intravenous saline or lactated Ringer's solution if blood pressure is under 80 mm Hg; if systolic pressure is over 90 mm Hg, an infusion rate of 150 to 200 mL/hour is sufficient. For children with compromised perfusion

administer a 20 mL/kg bolus of normal saline over 10 to 20 minutes, then infuse at 2 to 3 mL/kg/hour.

Transport to Medical Facility

Only decontaminated patients or patients not requiring decontamination should be transported to a medical facility. “Body bags” are not recommended.

Report to the base station and the receiving medical facility the condition of the patient, treatment given, and estimated time of arrival at the medical facility.

If a solution of nitrogen oxides, which means in effect a mixture of nitric (HNO₃) and nitrous (HNO₂) acids, has been ingested, prepare the ambulance in case the victim vomits toxic material. Have ready several towels and open plastic bags to quickly clean up and isolate vomitus.

Multi-Casualty Triage

Consult with the base station physician or regional poison control center for advice regarding triage of multiple victims. Because delayed respiratory compromise may occur even with minimal initial symptoms, all patients who have histories or evidence of exposure should be transported to a medical facility for evaluation. Because of the danger of acute, though delayed, onset of severe, life-threatening pulmonary edema from 3 to 30 hours after what may appear to have been quite a trivial exposure it is important that exposed subjects be maintained under medical surveillance for the first 48 hours post-exposure. If such are allowed to return home and acute pulmonary edema develops in a home environment during sleep it may not be possible to get the patient to resuscitative medical treatment in time. Others may be discharged at the scene after their names, addresses, and telephone numbers are recorded. Those discharged should be advised to seek medical care promptly if symptoms develop (see *Patient Information Sheet* below).

Emergency Department Management

- **Patients exposed only to nitrogen oxide gases do not pose risks of secondary contamination to rescuers. Patients whose clothing or skin is contaminated with liquid nitrogen oxides or nitric acid can secondarily contaminate response personnel by direct contact or through off-gassing vapors.**
- **Most of the higher nitrogen oxides are eye, skin, and respiratory tract irritants. Initial respiratory symptoms after exposure to nitrogen oxides may be mild, but progressive inflammation of the lungs may develop several hours to days after exposure. Noncardiogenic pulmonary edema may develop even if initial pulmonary signs were minimal. Exposures may result in methemoglobinemia, depending upon the presence of nitric oxide (NO) in the gas mixture.**
- **There is no antidote for nitrogen oxides. Treatment consists of respiratory and cardiovascular support. Methylene blue may be necessary to treat methemoglobinemia.**

Decontamination Area

Previously decontaminated patients may be transferred immediately to the Critical Care Area. Others require decontamination as described below.

Be aware that use of protective equipment by the provider may cause fear in children, resulting in decreased compliance with further management efforts.

Because of their relatively larger surface area:body weight ratio, children are more vulnerable to toxicants absorbed affecting the skin. Also, emergency room personnel should examine children's mouths because of the frequency of hand-to-mouth activity among children.

ABC Reminders

Evaluate and support airway, breathing, and circulation. Administer supplemental oxygen as required. Children may be more vulnerable to corrosive agents than adults because of the relatively smaller diameter of their airways. In cases of respiratory compromise secure airway and respiration via endotracheal intubation. If not possible, surgically create an airway.

Treat patients who have bronchospasm with aerosolized bronchodilators. The use of bronchial sensitizing agents in situations of multiple chemical exposures may pose additional risks. Consider the health of the myocardium before choosing which type of bronchodilator should be administered. Cardiac sensitizing agents may be appropriate; however, the use of cardiac sensitizing agents

after exposure to certain chemicals may pose enhanced risk of cardiac arrhythmias (especially in the elderly).

Consider racemic epinephrine aerosol for children who develop stridor. Dose 0.25–0.75 mL of 2.25% racemic epinephrine solution in 2.5 cc water, repeat every 20 minutes as needed, cautioning for myocardial variability.

Patients who are comatose, hypotensive, or have seizures or ventricular arrhythmias should be treated in the conventional manner.

Basic Decontamination

Patients who are able may assist with their own decontamination. If the patient's clothing is wet with nitrogen oxides or nitric acid, remove and double-bag the contaminated clothing and all personal belongings.

Flush exposed skin and hair with water for 20 minutes (preferably under a shower). Use caution to avoid hypothermia when decontaminating children or the elderly. Use blankets or warmers when appropriate.

Begin irrigation of exposed eyes **immediately** and continue for at least 20 minutes. Remove contact lenses if easily removable without additional trauma to the eye. Continue irrigation while transporting the patient to the Critical Care Area.

If the patient has ingested a solution of nitrogen oxides or nitric acid, **do not induce emesis**. Do not administer activated charcoal. Activated charcoal is unlikely to be of benefit and may obscure endoscopic findings if GI tract irritation or burns are present. Patients who are conscious and able to swallow should be given 4 to 8 ounces of water or milk if not provided earlier.

Critical Care Area

Be certain that appropriate decontamination has been carried out (see *Decontamination Area* above).

ABC Reminders

Evaluate and support airway, breathing, and circulation as in *ABC Reminders* above. Administer supplemental oxygen as required. Children may be more vulnerable to corrosive agents than adults because of the relatively smaller diameter of their airways. Establish intravenous access in seriously symptomatic patients. Continuously monitor cardiac rhythm.

Patients who are comatose, hypotensive, or have seizures or ventricular arrhythmias should be treated in the conventional manner.

Inhalation Exposure

Administer supplemental oxygen by mask to patients who have respiratory symptoms. Treat patients who have bronchospasm with aerosolized bronchodilators. The use of bronchial sensitizing agents in situations of multiple chemical exposures may pose additional risks. Consider the health of the myocardium before choosing which type of bronchodilator should be administered. Cardiac sensitizing agents may be appropriate; however, the use of cardiac sensitizing agents after exposure to certain chemicals may pose enhanced risk of cardiac arrhythmias (especially in the elderly). Some clinicians recommend high doses of corticosteroids for seriously symptomatic patients, especially with severe bronchospasm; in patients with acute respiratory failure without bronchospasm, the value of steroids is unproven.

Consider racemic epinephrine aerosol for children who develop stridor. Dose 0.25–0.75 mL of 2.25% racemic epinephrine solution in 2.5 cc water, repeat every 20 minutes as needed, cautioning for myocardial variability.

Skin Exposure

If the skin was in contact with liquid nitrogen oxides or their solutions, chemical burns may occur; treat as thermal burns.

Because of their relatively larger surface area:body weight ratio, children are more vulnerable to toxicants affecting the skin.

Eye Exposure

Continue irrigation for at least 20 minutes. If liquid nitrogen oxides or nitric acid has been splashed in the eyes, irrigate until the pH of the conjunctival fluid has returned to normal. Test visual acuity. Examine the eyes for corneal damage and treat appropriately. Immediately consult an ophthalmologist for patients who have severe corneal injuries.

Ingestion Exposure

If the patient has ingested a solution of nitrogen oxides or nitric acid, **do not induce emesis**. Do not administer activated charcoal. Patients who are conscious and able to swallow should be given 4 to 8 ounces of water or milk if not provided earlier.

Consider endoscopy to evaluate the extent of gastrointestinal tract injury. Extreme throat swelling may require endotracheal intubation or cricothyroidotomy. Gastric lavage is useful in certain circumstances to remove caustic material and prepare for endoscopic examination. Consider gastric lavage with a small nasogastric tube if: (1) a large dose has been ingested; (2) the patient's condition is evaluated within 30 minutes; (3) the patient has oral lesions or persistent esophageal discomfort; and (4) the lavage can be administered within 1 hour of ingestion. Care must be taken when placing the gastric tube because blind gastric tube

placement may further injure the chemically damaged esophagus or stomach.

Because children do not ingest large amounts of corrosive materials, and because of the risk of perforation from NG intubation, lavage is discouraged in children unless intubation is performed under endoscopic guidance.

Toxic vomitus or gastric washings should be isolated, e.g., by attaching the lavage tube to isolated wall suction or another closed container.

*Antidotes and
Other Treatments*

There are no antidotes for nitrogen oxide poisoning. Methylene blue (tetramethylthionine chloride) should be considered for patients who have signs and symptoms of hypoxia (other than cyanosis) or for patients who have methemoglobin levels >30%. Cyanosis alone does not require treatment. Methylene blue may not be effective in patients who have G6PD deficiency and may cause hemolysis.

The standard dose of methylene blue is 1 to 2 mg/kg body weight (0.1 to 0.2 mL/kg of a 1% solution) intravenously over 5 to 10 minutes, repeated in 1 hour if needed. The total initial dose should not exceed 7 mg/kg. (Doses greater than 15 mg/kg may cause hemolysis.) Clinical response to methylene blue treatment is usually observed within 30 to 60 minutes. Side effects include nausea, vomiting, abdominal and chest pain, dizziness, diaphoresis, and dysuria.

Consider exchange transfusion in severely poisoned patients who are deteriorating clinically in spite of methylene blue treatment. Intravenous ascorbic acid administered to severely poisoned patients has not proved to be effective.

Administration of steroids is thought by some physicians to reduce the likelihood of the development of bronchiolitis obliterans by reducing inflammation and therefore lung damage. Steroids should be started soon after exposure and continued for 8 weeks, then tapered gradually. The data on steroid use to prevent late sequelae (bronchiolitis obliterans) is anecdotal and somewhat controversial.

Laboratory Tests

The diagnosis of acute nitrogen oxide toxicity is primarily based on respiratory symptoms and establishing a history of exposure to nitrogen oxides. Routine laboratory studies for all exposed patients include CBC, glucose, and electrolyte determinations. Additional studies for patients exposed to nitrous oxides include determination

of methemoglobin levels. The condition of victims who have respiratory complaints should be evaluated with pulse oximetry (or ABG measurements), chest radiography, spirometry, and peak flow measurements. Pulse oximetry is not reliable if methemoglobin is present.

NO and NO₂ are metabolized to nitrite (NO₂⁻) and nitrate (NO₃⁻) and are excreted in the urine. The levels of these urinary metabolites are not medically useful but may be helpful in documenting exposure.

Disposition and Follow-up

Consider hospitalizing patients who have histories of significant inhalation exposure and are symptomatic.

Delayed Effects

Symptomatic patients should be observed in a controlled setting for 48 hours for delayed noncardiogenic pulmonary edema. All patients determined to have been exposed to nitrogen oxides should be advised that life-threatening symptoms may develop as late as several weeks after the exposure.

Patient Release

Patients who have been observed for several hours after minimal exposure and remain asymptomatic may be treated as outpatients. They should be advised to seek medical care promptly if symptoms develop (see *Nitrogen Oxides—Patient Information Sheet*). A patient whose symptoms resolve within 24 to 36 hours may be released with a follow-up appointment to assess pulmonary status.

Follow-up

Obtain the name of the patient's primary care physician so that the hospital can send a copy of the ED visit to the patient's doctor.

Close outpatient follow-up should be continued in patients who experienced significant respiratory compromise because these patients are at high risk of developing bronchiolitis obliterans within several weeks.

Patients who have corneal injuries should be reexamined within 24 hours.

Reporting

If a work-related incident has occurred, you may be legally required to file a report; contact your state or local health department.

Other persons may still be at risk in the setting where this incident occurred. If the incident occurred in the workplace, discussing it with company personnel may prevent future incidents. If a public health risk exists, notify your state or local health department or other responsible public agency. When appropriate, inform patients that they may request an evaluation of their workplace from OSHA

or NIOSH. See Appendices III and IV for a list of agencies that may be of assistance.

Nitrogen Oxides Patient Information Sheet

This handout provides information and follow-up instructions for persons who have been exposed to nitrogen oxides.

What are nitrogen oxides?

Nitrogen oxides are a mixture of gases that each contain nitrogen and oxygen. Nitrogen oxides are formed naturally when fossil fuels (e.g., coal, oil, gas, kerosene) are burned and when silage containing nitrate fertilizer ferments in storage silos. They are also formed during electric arc welding, electroplating, and engraving. They are part of airborne smog and are partly indirectly responsible for the burning eyes, nose, and throat caused by air pollution, through formation of the intensely irritating compound peroxyacetylnitrate, PAN.

What immediate health effects can be caused by exposure to nitrogen oxides?

Breathing low levels of nitrogen oxides may cause brief, nonspecific symptoms such as cough, shortness of breath, tiredness, and nausea. However, even if removed from exposure, a person who has breathed nitrogen oxides can develop more serious lung injury over the next 1 to 2 days. Exposure to massive concentrations can cause sudden death due to lung injury and suffocation or choking. Generally, the more serious the exposure, the more severe the symptoms.

Can nitrogen oxide poisoning be treated?

There is no antidote for nitrogen oxide poisoning. Treatment for exposure usually involves giving the patient oxygen and medications to make breathing easier.

Are any future health effects likely to occur?

A single small exposure from which a person recovers quickly may not cause delayed or long-term effects. After a serious exposure or repeated exposures, a patient may develop asthma or other lung conditions.

What tests can be done if a person has been exposed to nitrogen oxides?

Specific tests for the presence of nitrogen oxides in blood or urine generally are not useful to the doctor. If a severe exposure has occurred, blood and urine analyses and other tests may show whether damage has been done to the lungs, heart, and brain. Testing is not needed in every case.

Where can more information about nitrogen oxides be found?

More information about nitrogen oxides can be obtained from your regional poison control center; your state, county, or local health department; the Agency for Toxic Substances and Disease Registry (ATSDR); your doctor; or a clinic in your area that specializes in occupational and environmental health. If the exposure happened at work, you may wish to discuss it with your employer, the Occupational Safety and Health Administration (OSHA), or the National Institute for Occupational Safety and Health (NIOSH). Ask the person who gave you this form for help in locating these telephone numbers.

Follow-up Instructions

Keep this page and take it with you to your next appointment. Follow *only* the instructions checked below.

Call your doctor or the Emergency Department if you develop any unusual signs or symptoms within the next 48 to 72 hours, especially:

- coughing or wheezing
- difficulty breathing, shortness of breath, or chest pain
- weakness, fatigue, or flu-like symptoms
- increased redness or pain or a pus-like discharge in the area of a skin burn

No follow-up appointment is necessary unless you develop any of the symptoms listed above.

Call for an appointment with Dr. _____ in the practice of _____.

When you call for your appointment, please say that you were treated in the Emergency Department at _____ Hospital by _____ and were advised to be seen again in _____ days.

Return to the Emergency Department/ _____ Clinic on (date) _____ at _____ AM/PM for a follow-up examination.

Do not perform vigorous physical activities for 1 to 2 days.

You may resume everyday activities including driving and operating machinery.

Do not return to work for _____ days.

You may return to work on a limited basis. See instructions below.

Avoid exposure to cigarette smoke for 72 hours; smoke may worsen the condition of your lungs.

Avoid drinking alcoholic beverages for at least 24 hours; alcohol may worsen injury to your stomach or have other effects.

Avoid taking the following medications: _____

You may continue taking the following medication(s) that your doctor(s) prescribed for you: _____

Other instructions: _____

• Provide the Emergency Department with the name and the number of your primary care physician so that the ED can send him or her a record of your emergency department visit.

• You or your physician can get more information on the chemical by contacting: _____ or _____, or by checking out the following Internet Web sites: _____; _____.

Signature of patient _____ Date _____

Signature of physician _____ Date _____