Ethylenimine (C_2H_5N) C 1

Information and recommendations for doctors at hospitals/emergency departments

- **Patients exposed only to ethylenimine vapor do not pose a significant risk of secondary contamination. Patients whose clothing or skin is contaminated with ethylenimine liquid can secondarily contaminate rescue and medical personnel by direct contact or through evaporation of ethylenimine.**
- **Ethylenimine can produce immediate eye, skin, and respiratory tract irritation and may cause nausea and vomiting. These symptoms as well as signs of pulmonary edema (shortness of breath, cyanosis, expectoration, cough) may be delayed for more than 3 hours after exposure.**
- **Immediate decontamination by flushing of exposed skin and eyes with copious amounts of water is required in order to avoid irreversible damage.**
- **There is no antidote to be administered to counteract the effects of ethylenimine. Treatment consists of supportive measures.**

1. Substance information

Ethylenimine (C_2H_5N), CAS 151-56-4
Synonyms: azacyclopropane, aziridine, dimethylenimine
Ethylenimine is a colorless liquid at room temperature with a boiling point of 56°C (133°F, respectively). Both the vapor and liquid are potential fire and explosion hazards. Ethylenimine has an ammonia-like odor at air concentrations of 1.5 ppm and above. However, dangerous exposures may occur at levels too low to smell.
Ethylenimine is a highly reactive chemical, used as an intermediate and monomer for oil additive compounds, ion exchange resins, coating resins, pharmaceuticals, adhesives, polymer stabilizers, and surfactants. Polymerization products of ethylenimine are used in the manufacture of paper.

2. Routes of exposure

Inhalation

Inhalation of vapor is a relevant route of ethylenimine exposure. Eye and nose irritations have been reported to occur at concentrations of 100 ppm and above. **Ethylenimine's odor is not a reliable indicator of exposure and provides insufficient warning of hazardous exposure.**

Skin/eye contact

Liquid ethylenimine is absorbed readily through the skin and eyes. It is a potent irritant and vesicant. Fatal ethylenimine intoxication caused mainly by skin absorption has been observed. Percutaneous absorption of vapor probably does not occur, but ethylenimine vapors severely irritate the eyes and may irritate moist skin.

Ingestion

Involuntary ingestion of ethylenimine is unlikely.

3. Acute health effects

Respiratory

Exposure to ethylenimine vapors may produce immediate, severe, local irritation of the nose, throat, and lungs, and moist skin; clinical effects usually occur between 30 and 120 minutes after inhalation exposure. Higher concentrations may cause inflammation of the trachea and bronchi, bronchoconstriction, and laryngeal edema. Acute pulmonary edema may evolve up to 3 hours or more after exposure. Cough may be delayed in onset.

Dermal

After a very brief period of contact, liquid ethylenimine results in skin irritation. Depending on the concentration and length of exposure, the skin irritation may be evident within 5 minutes or not noticed until after several days. Skin contact with ethylenimine may cause inflammation and redness of the skin, blistering, and slowly healing necrotic burns.

	Dermal sensitization leading to contact dermatitis, urticaria, and anaphylactic reactions may occur.
Ocular	Exposure to both ethylenimine liquid and vapor can cause tearing and redness of the eye, and with more intense exposure, severe corneal injury.
Other	Neurologic signs and symptoms of excitation may occur as well as damage to the liver and the kidneys. Exposure to even low vapor concentrations of ethylenimine can result in nausea and vomiting, often delayed.
Potential sequelae	Skin contact with liquid ethylenimine may cause slowly healing/necrotic burns. Irreversible corneal damage may develop after a serious eye exposure. Survivors of severe inhalation injury may suffer residual chronic lung disease. Cough and inflammation may be persistent for months after exposure. Damage to the liver and the kidneys (renal tubular damage with proteinuria and elevated blood nitrogen) may occur after massive exposure.
Carcinogenicity	According to EC directive 1272/2008 ethylenimine is classified as follows: Carc. 1B (known or presumed human carcinogen, classification is largely based on animal evidence) Muta. 1B (known or to induce or to be regarded as if they induce heritable mutations in the germ cell of humans, classification is is based on positive results from in vivo mutagenicity tests in mammals)

4. Actions

Self-protection	Patients exposed only to ethylenimine vapor do not pose a significant risk of secondary contamination. Patients whose clothing or skin is contaminated with liquid ethylenimine (ambient temperature below 11°C) can secondarily contaminate other people by direct contact or through evaporation of ethylenimine.
Decontamination	Patients who are able and cooperative may assist with their own decontamination. If the exposure involved liquid ethylenimine (ambient temperature below 11°C) and if clothing is contaminated, remove and double-bag the clothing. **Assure that skin and hair exposed to liquid containing ethylenimine have been flushed with plain water for at least 15 minutes.** If not, continue flushing during other basic care. Protect eyes during flushing of skin and hair. **Assure that eyes exposed to liquid containing ethylenimine have been irrigated with plain water or saline for at least 15 minutes.** If not, continue eye irrigation during other basic care. Remove contact lenses if present and easily removable without additional trauma to the eye.
Initial treatment	Therapy will be empiric; there is no antidote to be administered to counteract the effects of ethylenimine. The following measures are recommended if patients have respiratory complaints and/or evidence of systemic toxic effects after inhalation of ethylenimine: - **Administration of oxygen** - **Administration of 8 puffs of beclomethasone (800 µg beclomethasone dipropionate) from a metered dose inhaler.** **Patients with severe clinical respiratory symptoms (e.g. bronchospasms, stridor) should be treated as follows:** a) Nebulization of adrenaline (epinephrine): 2 mg adrenaline (2 ml) with 3 ml NaCl 0.9% and inhale through a nebulizer mask.

b) Administration of a ß2-selective adrenoceptor agonist, e.g., four strokes of terbutaline or salbutamol or fenoterol (one stroke usually contains 0.25 mg of terbutaline sulfate; or 0.1 mg of salbutamol; or 0.2 mg of fenoterol); this may be repeated once after 10 minutes. Alternatively, 2.5 mg salbutamol and 0.5 mg atrovent may be administered by nebulizer mask.
If inhalation is not possible, administration of terbutaline sulfate (0.25 mg to 0.5 mg) subcutaneously or salbutamol (0.2 mg to 0.4 mg over 15 minutes) intravenously.

c) Intravenous administration of 250 mg methylprednisolone (or equivalent steroid dose).

Patients with clinical signs of a toxic lung edema (e.g. foamy sputum, wet crackles) should be treated as follows:

a) Start CPAP-therapy (Continuous Positive Airway Pressure Ventilation).
b) Intravenous administration of 1000 mg methylprednisolone (or an equivalent steroid dose) is recommended.

Intubation of the trachea or an alternative airway management should be considered in cases of respiratory compromise. When the patient's condition precludes this, consider cricothyrotomy if equipped and trained to do so.

Note: Efficacy of corticosteroid administration has not yet been proven in controlled clinical studies.

If ethylenimine was in contact with the skin, severe chemical burns may result; treat as thermal burns: adequate fluid resuscitation and administration of analgesics, maintenance of the body temperature, covering of the burn with a sterile pad or clean sheet. If relevant dermal absorption with the risk of systemic toxic effects cannot be excluded, add routine laboratory studies as described below to the standard intake. These patients should be observed for at least 12 hours.
After eye exposure severe chemical burns may result; treat as thermal burns. Immediately consult an ophthalmologist.
All asymptomatic patients with an exposure history consistent with significant potential for inhalation of ethylenimine should take 8 puffs of beclomethasone from a metered dose inhaler. Thereafter, 4 puffs should be administered every 2 hours for 12 hours. These patients should be observed for at least 12 hours.

Further evaluation and treatment

To the standard intake history, physical examination, and vital signs add pulse oximetry monitoring and a PA chest X-ray.
Spirometry should be performed. Routine laboratory studies should include a complete blood count, blood glucose and electrolyte determinations.
Routine laboratory studies should include a complete blood count, hepatic and renal function parameters, glucose and electrolyte determinations.
Because respiratory signs and symptoms may not be evident for as long as 12 hours after exposure, patients suspected to have serious exposure should be observed and reexamined periodically. Consider hospitalization of patients who have evidence of systemic toxicity from any route of exposure.
Evidence of pulmonary edema - hilar enlargement and ill-defined, central-patch infiltrates on chest radiography - **is a late finding that may occur 3 hours or later after exposure. The chest X-ray is typically**

normal on first presentation to the emergency department even with severe exposures.
If oxygen saturation is less than 90 % or if it appears to drop, immediately check arterial blood gasses and repeat the chest X-ray. If blood gasses begin to show deterioration and/or if the chest X-ray begins to show pulmonary edema start oxygen supplementation. **Should it become clear that pulmonary edema is worsening positive end-expiratory pressure (PEEP) therapy should be started** within the first 24 hours after exposure even if oxygenation can be maintained by mask.

Early indication for PEEP therapy is tachypnea (>30/min) with a simultaneous decrease of the partial pressure of carbon dioxide.
An inadequate increase or a relative decrease of the partial pressure of oxygen despite hyperventilation indicates the development of pulmonary edema. Fluid intake/output and electrolytes should be monitored closely. Avoid net positive fluid balance. Central line or Swan-Ganz catheterization might be considered, to optimize fluid management.
As long as signs of pulmonary edema are present, intravenous administration of 1 g methylprednisolone (or an equivalent steroid dose) should be continued in intervals of 8-12 hours.
Patients with bronchospasms should be treated as follows:

Prophylactic antibiotics are not routinely recommended, but may be used based on the results of sputum cultures. Pneumonia can complicate severe pulmonary edema.

Patient release/ follow-up instructions

Clinically asymptomatic patients as well as patients **who have a normal clinical examination and no signs or symptoms of toxicity** may be discharged **after an appropriate observation period** in the following circumstances:

a) The evaluating physician is experienced in the evaluation of individuals with ethylenimine exposure.
b) Information and recommendations for patients with follow-up instructions are provided verbally and in writing. Patients are advised to seek medical care promptly if symptoms develop or recur.
c) The physician is comfortable that the patient understands the health effects of ethylenimine and the provided follow-up instructions.
d) Site medical is notified, so that the patient may be contacted at regular intervals in the 24-hour period following release.
e) Heavy physical work should be precluded for up to 24 hours.
f) Exposure to cigarette smoke should be avoided for 72 hours; the smoke may worsen the condition of the lungs.

Patients who have skin or eye exposure should be reexamined in 24 hours.
For those patients with inhalation injury, post discharge spirometry should be repeated until values return to the patient's baseline values.

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