BASF Chemical Emergency Medical Guidelines

Ethylene oxide ($[CH_2]_2O$) C 1

Information and recommendations for doctors at hospitals/emergency departments

- **Patients exposed only to ethylene oxide gas do not pose a significant risk of secondary contamination. Patients whose clothing or skin is contaminated with ethylene oxide liquid or solution can secondarily contaminate rescue and medical personnel by direct contact or through off-gassing ethylene oxide.**
- **Ethylene oxide can produce CNS depression and immediate eye, skin, and respiratory tract irritation and may lead to seizures, coma, or respiratory paralysis. Signs of pulmonary edema (shortness of breath, cyanosis, expectoration, cough) may evolve 12 hours or more after exposure.**
- **There is no antidote to be administered to counteract the effects of ethylene oxide. Treatment consists of supportive measures.**

1. Substance information

Ethylene oxide ($[CH_2]_2O$), CAS 75-21-8
Synonyms: epoxyethane, ETO, oxirane
Ethylene oxide is a colorless gas at room temperature and a colorless liquid below 11°C (51°F, respectively). It is highly reactive and water soluble. Both the gas and liquid are potential fire and explosion hazards. Ethylene oxide has a sweet ether-like odor at air concentrations of 500 ppm and above. However, dangerous exposures may occur at levels too low to smell.
Ethylene oxide is an important industrial solvent, plasticizer, and chemical intermediate. Ethylene oxide is used in the sterilization of hospital supplies, foods, and cosmetics, as a fumigant for spices, tobacco, furs, bedding, etc., and in the manufacture of antifreeze and other chemicals. It reacts with strong acids, alkalis and oxidizers.

2. Routes of exposure

Inhalation

Inhalation is a major route of ethylene oxide exposure. Ethylene oxide's odor is not a reliable indicator of any level of exposure and provides insufficient warning of hazardous exposure. The gas is heavier than air; exposure will be higher in enclosed, poorly ventilated, or low-lying areas.

Skin/eye contact

Ethylene oxide gas or liquids may be absorbed through the skin and eyes; however, direct contact with ethylene oxide gas or concentrated solutions may cause severe chemical burns.

Ingestion

Ingestion of ethylene oxide is unlikely because it is a gas at room temperature.

3. Acute health effects

Respiratory

Initially, ethylene oxide affects the nasopharynx. Concentrations as low as 200 ppm produce rapid onset of nose and throat irritation. Higher concentrations may cause inflammation of the trachea and bronchi, bronchoconstriction, and atelectasis. Acute pulmonary edema may evolve up to 12 hours or more after exposure.

Dermal

Skin contact with concentrated ethylene oxide gas or aqueous solutions may cause irritation with redness of the skin, blistering, and crusted ulcerations. Skin reactions may be delayed up to 12 hours or more after exposure. Contact with liquefied ethylene oxide can result in frostbite.

Inhalation and skin exposure may cause allergic and immune-mediated sensitization leading to contact dermatitis, urticaria, and anaphylactic reactions.

Ocular	Exposure to high levels of ethylene oxide gas or eye splashes of concentrated solutions can cause eye irritation and inflammation, and with more intense exposure, corneal burns.
CNS	Ethylene oxide is a CNS depressant. High-dose exposures can result in diverse neurologic manifestations including seizures and coma. Onset of neurologic signs and symptoms may be delayed up to 12 hours ore more after exposure. Respiratory paralysis and delayed peripheral neuropathy have been reported after massive exposure.
Gastrointestinal	Exposure to even low gas concentrations of ethylene oxide can result in nausea and vomiting, often delayed.
Cardiovascular	Dysrhythmias may occur after a severe inhalation exposure.
Potential sequelae	Survivors of severe inhalation injury may suffer residual chronic lung disease.
Carcinogenicity	According to EC directive 1272/2008 ethylene oxide 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

Decontamination	Patients exposed only to ethylene oxide gas do not pose a significant risk of secondary contamination. Patients whose clothing or skin is contaminated with liquid ethylene oxide (ambient temperature below 11°C) can secondarily contaminate other people by direct contact or through off-gassing ethylene oxide. Patients who are able and cooperative may assist with their own decontamination. If the exposure involved liquid ethylene oxide (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 ethylene oxide 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 exposed or irritated eyes 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 ethylene oxide. The following measures are recommended if patients have respiratory complaints and/or evidence of systemic toxic effects after inhalation of ethylene oxide: - **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 ethylene oxide was in contact with the skin, 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.
After eye exposure chemical burns may result; treat as thermal burns. Immediately consult an ophthalmologist.

Further evaluation and treatment

Add pulse oximetry monitoring and a PA chest X-ray to the standard intake history, physical examination, and vital signs add. Spirometry should be performed. **Routine laboratory studies should include a complete blood count, hepatic and renal function parameters, glucose and electrolyte determinations.**
Because neurologic and 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 12 hours or later after exposure. The chest X-ray is typically normal on first presentation to the emergency department even with severe exposures.**
If blood gasses begin to show deterioration and/or if the chest X-ray begins to show pulmonary edema start oxygen supplementation.
In case of worsening clinical signs (especially tachypnea >30/min with a simultaneous decrease of the partial pressure of carbon dioxide) CPAP-therapy (Continuous Positive Airway Pressure Ventilation) should be started within the first 24 hours after exposure.
In case of a 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 methylprednisolone (or an equivalent steroid) should be continued in intervals of 8-12 hours.

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

C 4

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 ethylene oxide 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 ethylene oxide 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 eye exposures 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.

BASF SE
Corporate Health Management
Carl-Bosch-Straße 38
67056 Ludwigshafen
Germany

BASF Corporation
Medical Department
100 Campus Drive, M/S F 221
Florham Park, NJ 07932
USA