

Information and recommendations for doctors at hospitals/emergency departments

- These guidelines are based on information about the aliphatic amines mono-, di-, trimethylamine, and mono-, di-, triethylamine. Recommendations for other aliphatic amines might be similar. However, these guidelines do not cover special features potentially related to other aliphatic amines.
- Patients exposed only to gas/vapor of aliphatic amines do not pose a significant risk of secondary contamination. Victims whose clothing or skin is contaminated with liquid aliphatic amines can secondarily contaminate rescue and medical personnel by direct contact or through off-gassing/evaporation of aliphatic amines.
- Gas, vapor or liquid of aliphatic amines is highly irritating and can cause serious injuries to eyes or skin.
- Irritation of the respiratory tract can result in rhinorrhea, coughing, and dyspnea. Laryngospasm and signs of pulmonary edema (shortness of breath, cyanosis, expectoration) may occur.
- There is no antidote to be administered to counteract the effects of aliphatic amines. Treatment consists of supportive measures.

1. Substance information

Aliphatic amines: (Mono-)methylamine (CH_3NH_2) CAS 74-89-5, dimethylamine ($(\text{CH}_3)_2\text{NH}$) CAS 124-40-3, trimethylamine ($(\text{CH}_3)_3\text{N}$) CAS 75-50-3, (mono-)ethylamine ($\text{CH}_2\text{CH}_2\text{NH}_2$) CAS 75-04-7, diethylamine ($(\text{CH}_3\text{CH}_2)_2\text{NH}$) CAS 109-89-7, triethylamine ($(\text{CH}_3\text{CH}_2)_3\text{N}$) (CAS 121-44-8)

The lower aliphatic amines discussed here are alkyl derivatives of ammonia where one, two, or three of the hydrogen atoms are replaced by methyl or ethyl groups. At room temperature, methylamine and ethylamine are colorless gasses, the other aliphatic amines are volatile liquids. These aliphatic amines are soluble to slightly soluble in water. They all have a distinctly unpleasant odor. In high concentrations their odor is like ammonia, in lower concentrations their odor is fishlike. Aliphatic amines are widely used as basic materials for chemical syntheses, as intermediates and as solvents in the manufacture of plastics, crop protection products, explosives, dyes, surfactants, catalysts and other chemicals.

2. Routes of exposure

Inhalation

Inhalation is a significant route of exposure. Aliphatic amines' odor and irritant properties may provide adequate warning of hazardous concentrations. However, olfactory fatigue may occur, making their presence difficult to detect with prolonged exposure.

Skin/eye contact

Fairly low concentrations of aliphatic amines produce rapid irritation of the eye and moist skin. **Direct contact with liquid aliphatic amines or concentrated gas/vapor on moist skin or eyes causes severe chemical injuries.**

Ingestion

Accidental ingestion of aliphatic amines is unlikely. Aliphatic amines solutions may cause corrosive injury to the mouth, throat, and stomach if ingested.

3. Acute health effects

Aliphatic amines exposure usually causes eye, nose, and throat irritation. Respiratory distress with coughing, dyspnea, upper airway obstruction, bronchitis, pneumonitis, and pulmonary edema may occur.

If the skin is wet or moist, contact with the gas or vapor of aliphatic amines can cause burning pain, inflammation, blisters, and ulceration. Contact with liquid aliphatic amines under pressure can result in frostbite.

Low gas/vapor concentrations can cause edema of the corneal epithelium without pain accompanied by hazing of vision, blue/gray vision and halos. After exposure to higher concentrations or liquid aliphatic amines, conjunctival hemorrhages, corneal opacities, and keratitis may occur. Additional symptoms like burning discomfort, spasmodic blinking or involuntary closing of the eyelids, redness, and tearing may result.

After inhalation, transient headache, nausea, faintness, and anxiety may occur.

Dose-effect relationships

Dose-effect relationships are as follows:

<u>Aliphatic amines concentration</u>	<u>Effect</u>
0.01-20 ppm	- Fishlike odor detection (some tolerance develops)
5-25 ppm	- Slight visual disturbances
10-100 ppm	- Transient mucous membrane irritation
100-200 ppm	- Odor becomes ammoniacal
>50-500 ppm	- Marked irritation of skin, eyes, upper respiratory tract with conjunctivitis, sore throat, coughing

Potential sequelae

For most exposed individuals symptoms will clear over several weeks or months. Survivors of severe inhalation injury, especially if chest x-ray and pulmonary function abnormalities are associated, may suffer residual chronic lung disease. In cases of eye contact with liquid aliphatic amines, permanent damage and impairment of vision can result.

4. Actions

Self-protection

Patients exposed only to aliphatic amines gas do not pose a significant risk of secondary contamination. Victims whose clothing or skin is contaminated with liquid aliphatic amines can secondarily contaminate other people by direct contact or through off-gassing aliphatic amines.

Decontamination

Victims exposed only to aliphatic amines gas who have no evidence of skin or eye irritation do not need decontamination. All others require decontamination.

Victims who are able and cooperative may assist with their own decontamination. If the exposure involved liquid aliphatic amines and if clothing is contaminated, remove and double-bag the clothing.

Assure that exposed or irritated eyes have been irrigated with plain water or saline for at least 20 minutes, and that the pH of the conjunctival fluid has returned to normal (7.0). If not, continue eye irrigation during other basic care and transport. If eye irrigation is impaired by blepharospasm, one to two drops of oxybuprocaine 0.4% may be instilled into affected eyes to allow adequate irrigation.

Remove contact lenses if present and easily removable without additional trauma to the eye.

Assure that exposed skin and hair have been flushed with plain water for at least 15 minutes. If not, continue flushing during other basic care and transport. Protect eyes during flushing of skin and hair.

Initial treatment

Therapy will be empiric; there is no antidote to be administered to counteract the effects of aliphatic amines.

After eye exposure chemical burns may result; treat as thermal burns. Immediately consult an ophthalmologist.

Any facial exposure to liquid aliphatic amines and any burns affecting more than 100 cm² (15 square inches) of skin should be considered as a serious exposure.

If aliphatic amines have been 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. If contact of the skin with liquid aliphatic amines under pressure has occurred, evaluate for the presence of frostbite.

The following measures are recommended if the exposure concentration is 100 ppm or greater and if symptoms, e. g. eye irritation or pulmonary symptoms, have developed:

- 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 β 2-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.

In case of ingestion of aliphatic amines, **do not induce emesis. If signs or symptoms of esophageal irritation or burns are present, consider endoscopy to determine the extent of the injury; in severe cases surgical intervention should be considered if gastrointestinal necrosis or perforation is suspected.**

Only if a large dose has been ingested less than 30 minutes before evaluation of the patient's condition and if a perforation can be excluded, consider immediate gastric lavage with a small-bore tube.

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.

Evidence of pulmonary edema - hilar enlargement and ill-defined, central-patch infiltrates on chest radiography - is a late finding that may occur 6 to 8 hours or later after exposure. The chest X-ray is typically normal on first presentation to the emergency department even with severe exposures.

Patients who have been exposed to a concentration of 100 ppm or greater, or who develop serious signs or symptoms, should be

observed for a minimum of 24 hours and reexamined frequently. Delayed effects are unlikely in patients who have minor upper respiratory symptoms (mild burning or a slight cough) that resolve quickly. 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. 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.

*Patient release/
follow-up instructions*

Clinically asymptomatic patients exposed to a concentration of **less than 100 ppm** (depending on the period of time exposed) **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 aliphatic amines 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 aliphatic amines.
- d) Site medical is notified, so that the patient may be contacted at regular intervals in the 24-hour period following release from the emergency department.
- e) Heavy physical work should be precluded for 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 or serious skin injuries should be reexamined in 24 hours.

Post discharge spirometry should be repeated until values return to the patient's baseline values.

In this document BASF has made a diligent effort to ensure the accuracy and currency of the information presented but makes no claim that the document comprehensively addresses all possible situations related to this topic. This document is intended as an additional resource for doctors at hospitals/emergency departments in assessing the condition and managing the treatment of patients exposed to aliphatic amines. It is not, however, a substitute for the professional judgement of a doctor and must be interpreted in the light of specific information regarding the patient available to such a doctor and in conjunction with other sources of authority.

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