
Information and recommendations for doctors at hospitals/emergency departments

- Patients exposed only to dimethyl sulfate vapor do not pose a significant risk of secondary contamination. Patients whose clothing or skin is contaminated with liquid dimethyl sulfate can secondarily contaminate rescue and medical personnel by direct contact or through evaporation of dimethyl sulfate.
 - Dimethyl sulfate can produce eye, skin, and respiratory tract irritation. Signs of pulmonary edema (shortness of breath, cyanosis, expectoration, cough) may evolve 12 hours or more after exposure. Skin reactions may be delayed and may heal very slowly.
 - Inhalation and skin contact may result in systemic absorption resulting in headache, nausea, vomiting, abdominal pain, lung, liver, and kidney damage.
 - There is no antidote to be administered to counteract the effects of dimethyl sulfate. Treatment consists of supportive measures.
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1. Substance information

Dimethyl sulfate (CH₃)₂SO₄ CAS 77-78-1

Synonyms: DMS, sulfuric acid dimethyl ester.

Dimethyl sulfate is a color- and odorless (to faint onion odor) oily liquid with a melting point of about -32°C and a boiling point of 188 (-25,6°F, 370 °F respectively). It is not flammable and not explosive. The flash point is 83 °C 181 °F and the vapor pressure is low with 65 Pa at 20 °C (68 °F). It is slightly soluble in water; soluble in alcohols, ether, and aromatic hydrocarbons. It rapidly hydrolyzes in the presence of water to produce sulfuric acid and methanol.

Dimethyl sulfate is mainly used as a chemical intermediate. Its major applications are as a methylating agent of many organic chemicals (e.g. amines, carbon acids, thiols and phenols) both in industry and in laboratories. DMS is used, for example, in the manufacturing of dyes, perfumes, pharmaceuticals, for the separation of mineral oils and for the analysis of automobile fluids. The substance has also sulphating properties.

2. Routes of exposure

Inhalation

Inhalation is a major route of dimethyl sulfate exposure. Dimethyl sulfate is odorless (to faint onion odor) and is considered to have poor warning properties of hazardous exposure.

Skin/eye contact

Dimethyl sulfate vapor or liquids may be absorbed through the skin and eyes; however, direct contact with dimethyl sulfate vapor or concentrated solutions may cause severe chemical burns.

Ingestion

Involuntary ingestion of dimethyl sulfate is unlikely.

3. Acute health effects

Exposure to dimethyl sulfate concentrations of more than 1 ppm may produce irritation of the eyes, nose, and throat. Higher concentrations may cause pulmonary edema up to 12 hours or more after exposure.

Skin contact with dimethyl sulfate vapor or liquid may cause irritation with redness of the skin, blistering, itching, and pain. **Skin reactions may have a 1 to 2 hour delay before onset of symptoms, and the full effects may be delayed up to 12 hours or more after exposure and may heal very slowly.**

Dimethyl sulfate is a skin sensitizer.

High vapor concentrations or splashes of concentrated solutions can cause tearing and redness of the eye, and corneal injury.

Both inhalation and skin contact may lead to systemic absorption causing severe headache, nausea, vomiting, abdominal pain, and lung, liver and kidney injury.

Dose-effect relationships

Dose-effect relationships are as follows:

<u>Dimethyl sulfate concentration</u>	<u>Effect</u>
0.1 ppm	- TLV-TWA (ACGIH, USA)
1 ppm	- PEL (OSHA, USA)
1 ppm	- Burning of eyes, nose, and throat, dyspnea, coughing
7 ppm	- IDLH (NIOSH, USA)
97 ppm	- LC _{Lo} (10 min)

Potential sequelae

Survivors of severe inhalation injury may suffer residual chronic lung disease or recurrent respiratory tract infections. Permanent liver or kidney damage may result from high systemic exposure.

Carcinogenicity

Dimethyl sulfate is classified as a carcinogen on the basis of animal evidence as follows:

- EC directive 1272/2008, Carc. 1B (known or presumed human carcinogen);
- IARC Group 2A (probably carcinogenic to humans).

4. Actions

Decontamination

Patients exposed only to dimethyl sulfate vapor do not pose a significant risk of secondary contamination. Patients whose clothing or skin is contaminated with liquid dimethyl sulfate can secondarily contaminate other people by direct contact or through evaporation of dimethyl sulfate. Patients who are able and cooperative may assist with their own decontamination. If the exposure involved liquid dimethyl sulfate and if clothing is contaminated, remove and double-bag the clothing.

Assure that skin and hair exposed to liquid containing dimethyl sulfate 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 dimethyl sulfate.

All asymptomatic patients potentially exposed to an airborne dimethyl sulfate concentration of 1 ppm or more should take 8 puffs of beclomethasone (800 µg beclomethasone dipropionate) from a metered dose inhaler, if not already done. Thereafter, 4 puffs every 2 hours for 24 hours.

The following measures are recommended if the airborne exposure concentration is 1 ppm or more and/or if patients have respiratory complaints or evidence of systemic toxic effects after inhalation of dimethyl sulfate:

- 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 β₂-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 dimethyl sulfate 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.

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, hepatic and renal function parameters, glucose and electrolyte determinations.

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 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.

Further evaluation and treatment

*Patient release/
follow-up instructions*

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

Consider hemodialysis in case of significant systemic absorption of dimethyl sulfate with impairment of liver and/or kidney function.

Clinically asymptomatic patients exposed to a concentration of **less than 1 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 dimethyl sulfate 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 dimethyl sulfate.
- 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 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 after 24 hours. For those patients with inhalation injury, 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 dimethyl sulfate. 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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