Chemical Emergency Medical Guideline

Information and recommendations for healthcare professionals

Dimethyl sulfate

CAS No.: 77-78-1

GHS symbols:

GHS05
Corrosive

GHS06
Acute toxicity

GHS08
Health hazard

Signal word: Danger

Hazard statements:

H301	Toxic if swallowed.
H314	Causes severe skin burns and serious eye damage.
H317	May cause allergic skin reactions.
H330	Fatal if inhaled.
H341	May cause genetic defects.
H350	May cause cancer.

Overview

- There is no danger from contact with patients who have only been exposed to dimethyl sulfate vapors. However, a patient who is wet with liquid dimethyl sulfate or whose clothing is wet with it may endanger other people through direct contact or through evaporating dimethyl sulfate.
- Dimethyl sulfate may cause irritation to the eyes, skin and respiratory tract. Signs of pulmonary oedema (shortness of breath, cyanosis, sputum, coughing) may occur more than 12 hours after exposure. Skin reactions may also occur with a delay and heal very slowly.
- Inhalation and skin contact can lead to systemic absorption of dimethyl sulfate, which can cause headaches, nausea, vomiting, abdominal pain, and lung, liver and kidney damage.
- There is no known specific antidote. Treatment depends on the extent of exposure and the symptoms.

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1. Information about the substance

Dimethyl sulfate: $(CH_3)_2SO_4$, CAS 77-78-1
Synonyms: DMS, sulfuric acid dimethyl ester
Dimethyl sulfate is a colorless and largely odorless (slight onion smell) oily liquid with a melting point of approximately -32° C and a boiling point of 188°C. It is non-flammable and non-explosive; the flash point is 83°C and the vapor pressure is low at 65 Pa at 20°C. Dimethyl sulfate is slightly soluble in water but soluble in alcohols, ethers and aromatic hydrocarbons. It hydrolyses rapidly in sulfuric acid and methanol. Dimethyl sulfate is mainly used as an intermediate for the methylation of various organic chemicals (e.g. amines, carboxylic acids, thiols and phenols) in industry and in the laboratory. It is used in the manufacture of paints, perfumes and pharmaceuticals and for the separation and analysis of mineral oils. It also has sulfating properties.

2. Exposition

2.1. Inhalation

Exposure to dimethyl sulfate occurs mainly through inhalation. Dimethyl sulfate is largely odorless (possibly with a slight onion smell) and does not provide sufficient warning of dangerous exposure.

2.2. Skin/eye contact

Dimethyl sulfate can be absorbed through the skin or eyes as a vapor or liquid. Direct contact with dimethyl sulfate vapors or concentrated solutions can cause severe chemical burns.

2.3. Ingestion

Accidental ingestion of dimethyl sulfate is unlikely.

3. Acute health effects

3.1. Dose-response relationship

Concentration of dimethyl sulfate		Effect/effects
0.1 ppm	-	TLV-TWA (ACGIH, USA)
1 ppm	-	PEL (OSHA, USA)
1 ppm	-	Burning sensation in the eyes, nose and throat; dyspnea, coughing
7 ppm	-	IDLH (NIOSH, USA)
97 ppm	-	LCLO (10 min)

TLV: Threshold limit value → Air concentration below which it is assumed that almost all workers can be repeatedly exposed to this concentration day after day throughout their working lives without this leading to harmful effects on their health.
TWA: Time weighted average
ACGIH: American Conference of Governmental Industrial Hygienists
PEL: Permissible Exposure Limits → Limit value for the amount or concentration of a substance in the air. This is usually based on a time-weighted average (TWA) over eight hours.
OSHA: Occupational Safety and Health Administration
IDLH: Immediately Dangerous to Life and Health
NIOSH: National Institute for Occupational Safety and Health
LCLO: lowest concentration of a substance that has been shown to cause death in humans or animals after exposure

3.2. Respiratory tract

Exposure to dimethyl sulfate concentrations greater than 1ppm may cause irritation to the eyes, nose and throat. Higher concentrations may cause pulmonary oedema even more than 12 hours after exposure.

3.3. Skin contact

Skin contact with dimethyl sulfate as a vapor or liquid may cause irritation with reddening of the skin, blistering, itching and pain. Skin reactions may occur with a delay of 1 to 2 hours, and it may take more than 12 hours for the full symptoms to develop. Skin reactions heal very slowly. Dimethyl sulfate is a skin allergen.
High concentrations of vapor or splashes of concentrated solutions can cause tearing and redness of the eyes as well as corneal damage.
Both inhalation and skin contact can cause systemic absorption, which can lead to severe headaches, nausea, vomiting, abdominal pain and damage to the lungs, liver and kidneys.

3.4. Possible consequences

Survivors of severe inhalation damage may suffer from chronic lung disease and a predisposition to repeated respiratory tract infections. After pronounced systemic exposure, liver or kidney damage may remain.

3.5. Carcinogenicity and mutagenicity

Dimethyl sulfate is classified as carcinogenic based on animal studies as follows: - Directive EC 1272/2008: Carc. 1B (may cause cancer). IARC Group 2A (probably carcinogenic to humans).
Dimethyl sulfate may cause germ cell mutations (Muta. 2 - Substances that may cause heritable mutations in human germ cells. There is some evidence from appropriate animal studies, but it is not sufficient to classify a substance in Category 1).

4. Measures

4.1. Self-protection of first aiders

If there is a suspicion that the area the helper must enter contains dimethyl sulfate, a self-contained breathing apparatus and a chemical protection suit must be worn.
There is no danger from contact with patients who have only been exposed to dimethyl sulfate vapors. A patient who is wet with liquid dimethyl sulfate or whose clothing is wet with liquid dimethyl sulfate, may endanger other people through direct contact or through dimethyl sulfate gas emissions.

4.2. Rescue

Patients should be removed from the danger zone immediately. If they are unable to walk unaided, they should be removed from the danger zone quickly using appropriate means, taking care to protect themselves. The "A, B, C procedure" has absolute priority.

A) Clear the airways (check for blockages caused by the tongue or foreign objects)
B) Ventilation (check the patient's breathing, if necessary, begin ventilation with adequate self-protection, e.g. breathing mask)
C) Circulation (begin resuscitation for any person who does not respond to verbal commands and is not breathing normally)

4.3. Cleaning

Patients who have been exposed to dimethyl sulfate vapors or liquid require special cleaning measures even if there are no signs of skin or eye irritation. If possible, patients should assist in their own cleaning.
If liquid dimethyl sulfate has been exposed and clothing is contaminated, it must be removed and securely wrapped.
Rinse affected skin and hair with water for at least 15 minutes. Protect eyes while rinsing.
In case of exposure to dimethyl sulfate, rinse eyes with water or neutral saline solution for at least 15 minutes. Remove contact lenses, if present and if possible, without additional risk to the eye. Continue other important emergency measures in the meantime.

4.4. Initial treatment (preclinical or clinical)

Empirical therapy; no specific antidote available.
All asymptomatic patients exposed to dimethyl sulfate concentrations of 0.1ppm or more should be given 8 sprays of beclomethasone (800µg beclomethasone dipropionate) from a metered dose inhaler. Patients should be monitored for an appropriate period and re-examined repeatedly.

The following measures are recommended if the exposure concentration is 1ppm or more, if symptoms such as eye irritation or pulmonary symptoms are present, or if the exposure concentration cannot be estimated but exposure is considered highly likely:

- Oxygen administration
- Administration of 8 puffs of beclomethasone (800µg beclomethasone dipropionate) from a metered dose inhaler.

If there are signs of airway constriction (e.g. bronchospasm or stridor)

- Nebulization of adrenalin (epinephrine): mix 2mg adrenalin (2ml) with 3ml NaCl 0.9% and administer via a nebulizer mask
- Administration of a ß2-selective adrenoceptor agonist, e.g. four puffs of terbutaline or salbutamol or fenoterol (one puff usually contains 0.25mg terbutaline sulfate; or 0.1mg salbutamol; or 0.2mg fenoterol); this can be repeated once after 10 minutes.

Alternatively, 2.5mg salbutamol and 0.5mg ipratropium bromide can be administered via a nebulizer mask.
If inhalation is not possible, administer terbutaline sulfate (0.25mg to 0.5mg) subcutaneously or salbutamol (0.2mg to 0.4mg over 15 minutes) intravenously. Intravenous administration of 250mg methylprednisolone (or an equivalent steroid dose).

If there are signs of toxic pulmonary oedema (e.g. frothy sputum, moist rales)

- CPAP therapy
- Intravenous administration of 1000mg methylprednisolone (or an equivalent steroid dose)
  In case of (increasing) respiratory insufficiency, advanced airway management, e.g. endotracheal intubation or coniotomy if necessary.

Note: The efficacy of corticosteroid administration has not yet been proven in controlled clinical trials.

Skin contact with dimethyl sulfate can cause severe damage; this should be treated as burns: adequate fluid administration, analgesic therapy, maintenance of body temperature, covering the affected skin area with sterile dressing. Exposure of the eyes can also result in severe damage; this should also be treated as a burn. Consult an ophthalmologist immediately.

Patients who have been exposed to a concentration of 7ppm (IDLH value) or more or who have swallowed dimethyl sulfate, as well as patients without exposure measurements but with suspected relevant exposure, should be transported immediately to a hospital with intensive care facilities.

4.5. Further action and treatment

In addition to medical history, physical examination and vital signs, pulse oximetry, a p.a. chest X-ray and spirometry should be performed.
Routine laboratory tests should include a complete blood count, liver and kidney function parameters, glucose and electrolytes. Inpatient observation of patients with signs of systemic toxicity should be considered regardless of the route of exposure.
Radiologically clear signs of pulmonary oedema – enlargement of the hili, typical, centrally emphasized, patchy shadows on the chest X-ray – are late signs that only become apparent 12 hours or more after exposure. The X-ray is typically still normal at initial presentation at the hospital, even after inhalation of a relevant dose.

If oxygen saturation falls below 90%, arterial blood gas concentrations must be checked immediately and the chest X-ray repeated.
If blood gas concentrations deteriorate and/or the chest X-ray shows signs of toxic pulmonary oedema, oxygen should be administered via a mask. If deterioration manifests (especially in the case of tachypnoea (>30/min) and a simultaneous decrease in carbon dioxide partial pressure), CPAP therapy should be started within the first 24 hours after exposure.
In the event of pulmonary oedema developing, fluid intake and excretion as well as electrolytes should be closely monitored. A positive balance should be avoided. To optimize fluid management, the insertion of a central venous catheter should be considered.
If signs of pulmonary oedema persist, intravenous administration of methylprednisolone (or an equivalent steroid) should be continued at intervals of 8 to 12 hours.
Prophylactic antibiotic administration is not routinely recommended but may be considered based on the results of sputum cultures. Pneumonia may occur as a complication of severe pulmonary edema.

In the event of significant systemic absorption of dimethyl sulfate with impaired liver and/or kidney function, hemodialysis may be considered.

4.6. Discharge of the patient / instructions for further rules of conduct

Clinically asymptomatic patients who have been exposed to a dimethyl sulfate concentration of less than 1ppm (depending on the duration of exposure) and who show no abnormal clinical findings and no signs of toxic effects after an appropriate follow-up period may be discharged under the following circumstances:

- Information and recommendations for patients with instructions for further action were provided verbally and in writing. The patient was advised to seek immediate medical attention if any health problems arise.
- The patient is aware of and understands the toxic effects of dimethyl sulfate.
- The attending physician has been informed that regular contact between the patient and the physician is possible in the following 24 hours.
- Heavy physical work should not be done in the following 24 hours.
- Do not smoke or be exposed to cigarette smoke for at least 72 hours; smoke can impair lung function.
- Patients with eye exposure should be re-examined after 24 hours.
- Spirometry should be repeated at regular intervals after discharge until the values have returned to the patient's baseline values prior to exposure.

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Administrative Information

Document Type	Chemical Emergency Medical Guideline
Version Number	DE.1.0.0
Initial Publication	01.01.2026
Next Revision	2029
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