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Chemical Emergency Medical Guideline

Information and recommendations for healthcare professionals

Maleic acid / Phthalic anhydride

CAS No.: 108-31-6 / 85-44-9

GHS symbols:

GHS05
Corrosive

GHS07
Acute toxicity

GHS08
Health hazard

Signal word: Danger

Hazard statements:

H302	Harmful if swallowed.
H314	Causes severe skin burns and serious eye damage.
H317	May cause allergic skin reactions.
H334	May cause allergy, asthma-like symptoms or breathing difficulties if inhaled.
H372	Causes damage to organs (respiratory system) through prolonged or repeated exposure (inhalation).

Overview

- Before emergency medical personnel/emergency doctors approach a patient, who has been or is exposed to acid anhydrides or their dusts, they must ensure that there is no danger to themselves from acid anhydrides.
- Acid anhydrides and their dusts and vapors are irritating to the eyes, skin and upper respiratory tract and cause symptoms such as coughing, dryness of the nose and throat, and sneezing. Chest tightness and breathing difficulties with chest pain and shortness of breath may occur.
- Swallowing acid anhydrides can cause irritation to the lips, mouth, throat, esophagus and stomach.
- Immediate cleaning is the most important measure: first remove solid acid anhydride, then rinse the affected eyes, skin and hair thoroughly.
- 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

Maleic anhydride ($C_4H_2O_3$), CAS 108-31-6
Synonym: 2,5-furandione
At room temperature, maleic anhydride is a white, crystalline solid with a pungent odor. Maleic anhydride is soluble in acetone, ethyl acetate, chloroform and benzene. The vapor pressure is 25Pa at 25°C. Maleic anhydride reacts violently with water.

Phthalic anhydride ($C_8H_4O_3$), CAS 85-44-9
Synonym: 1,2-benzenedicarboxylic acid anhydride
At room temperature, phthalic anhydride is a white, crystalline solid with a characteristic odor. Phthalic anhydride is soluble in alcohol and slightly soluble in ether. The vapor pressure is <0.3Pa at 20°C. When exposed to moisture, phthalic anhydride reacts to form phthalic acid.

2. Exposition

2.1. Inhalation

Inhalation of dust and vapors is a relevant route of exposure. The irritant effect of acid anhydrides does not provide adequate protection against hazardous concentrations. Allergic/sensitized individuals may react to very low concentrations.

2.2. Skin/eye contact

The most common route of exposure to acid anhydrides is through skin contact. Direct contact of the eyes or skin with solid acid anhydrides or dust causes irritation of the skin and eyes.

2.3. Ingestion

Ingestion of acid anhydrides can cause irritation to the lips, mouth, throat, esophagus and stomach.

3. Acute health effects

3.1. Dose-response relationship

Maleic anhydride concentration		**Effect/effects**
0.4 mg/m³	-	Occupational exposure limit (AGS, Germany)
1.0 mg/m³	-	Odor threshold
1.5 mg/m³	-	Mucous membrane irritation
2.5 mg/m³	-	Strongly irritating effect
10 mg/m³	-	IDLH (NIOSH, USA)

Phthalic anhydride concentration		**Effect/effects**
6 mg/m³	-	TLV (NIOSH, USA)
0.32 mg/m³	-	Odor threshold
25 mg/m³	-	Mucous membrane irritation
30 mg/m³	-	Conjunctivitis
60 mg/m³	-	IDLH (NIOSH, USA)

IDLH: Immediately Dangerous to Life and Health
NIOSH: National Institute for Occupational Safety and Health
Occupational exposure limit AGW: According to the Hazardous Substances Ordinance, the occupational exposure limit (AGW) is the limit value for the time-weighted average concentration of a substance in the air at the workplace in relation to a given reference period. It specifies the concentration of a substance at which acute or chronic harmful effects on health are generally not to be expected.
AGS: Committee for Hazardous Substances
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 health.

3.2. Respiratory tract

Exposure to acid anhydrides usually causes coughing, dryness of the nose and throat, and sneezing. Inhalation can lead to airway obstruction and breathing difficulties with chest pain and shortness of breath. Various cases of asthma have been reported.

3.3. Skin contact

Contact with acid anhydrides can cause burning pain, redness and inflammation of the skin and mucous membranes. Skin allergies with urticaria and eczema may occur.

3.4. Eye contact

Eye irritation with painful sensations, spasmodic blinking or involuntary closing of the eyelids, redness and tearing may be caused by acid anhydrides.

3.5. Gastrointestinal tract

Abdominal pain, nausea and vomiting may occur. If swallowed, diffuse irritation of the mucous membrane may affect the entire gastrointestinal tract.

3.6. Effect on the hematopoietic system

Hemolytic anemia and pulmonary hemorrhage have been observed after exposure, but a link with acid anhydrides has not been conclusively proven.

3.7. Possible consequences

Skin and respiratory allergies may occur.

4. Measures

4.1 Self-protection of first aiders

If there is a suspicion that the area the helper must enter contains acid anhydride dust/vapor, a self-contained breathing apparatus and a chemical protection suit must be worn. Contaminated equipment should not be used. A patient who is contaminated with acid anhydrides, or whose clothing is contaminated, may endanger other people through direct contact.

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 only been exposed to acid anhydride vapors and show no signs of skin or eye irritation do not require any special cleaning measures, unlike all others.

If possible, patients should assist with their own cleaning. If they have been exposed to acid anhydrides and their clothing is contaminated, it must be removed and securely wrapped.

If solid acid anhydride is present on a patient's skin, hair or clothing, carefully remove it with a brush, for example, before rinsing. It is essential to ensure adequate self-protection and protection of the patient's eyes.
Then rinse the affected skin and hair with water for at least 15 minutes. Continue other important first aid measures during this time. Immediate cleaning is the most important measure.
In the event of exposure to acid anhydride, rinse the eyes with water or neutral saline solution for at least 15 minutes until the pH value of the conjunctival fluid returns to normal (pH=7.0). Continue other important first aid measures during this time.

If rinsing is impeded by eyelid spasm, the use of a local anesthetic solution (e.g. lidocaine, oxybuprocaine) may be considered. Remove any contact lenses, if possible, without causing additional danger to the eye.

4.4. Initial treatment (preclinical or clinical)

Empirical therapy; no specific antidote available.
The following measures are recommended if the exposure concentration is 1.5mg/m³ (maleic acid) or 30mg/m³ (phthalic acid) or more, if symptoms such as eye irritation or pulmonary symptoms are present, or if no exposure concentration can be estimated but relevant exposure is likely:

- Oxygen administration
- Administration of 8 sprays 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 sulphate; 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 sulphate (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.

If acid anhydrides are swallowed, do not induce vomiting under any circumstances. If there are signs or symptoms of esophageal irritation or burns, the patient should be taken to an endoscopy center as soon as possible. An endoscopy should be considered to determine the extent of the damage (suspected gastrointestinal necrosis or perforation?).
Skin contact with acid anhydrides may cause irritation; this should be treated symptomatically.
Exposure to the eyes may cause irritation; this should also be treated symptomatically. Consult an ophthalmologist.
Patients who have been exposed to concentrations of 1.5mg/m³ (maleic acid) or 30mg/m³ (phthalic acid) or more, or who have swallowed acid anhydrides, as well as patients without exposure measurements but with a high degree of suspicion of significant exposure, should be transported immediately to a hospital with intensive care facilities.

4.6. Further procedure 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 complete blood count, glucose and electrolytes. Arterial blood gases and methemoglobin concentrations should be determined in symptomatic patients to determine the extent of any acidosis or methemoglobinemia.

Radiological signs of pulmonary oedema – enlargement of the hila, typical, centrally accentuated, patchy shadows on the chest X-ray – are late signs that often cannot be detected until 24 hours after exposure. The X-ray is typically normal on initial presentation at the hospital, even after inhalation of a relevant dose.

Patients with possible exposure or with significant complaints or symptoms should be monitored for an appropriate period and re-examined repeatedly before any consequential damage to health can be ruled out. Delayed effects in patients with only mild, rapidly subsiding upper respiratory tract symptoms (mild burning or coughing) are unlikely.
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 becomes apparent (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.

Irritation or chemical burns should be re-examined at short intervals during the first 24 hours after exposure. Damage to the skin and gastrointestinal tract can continue to progress for days after exposure and significantly impair fluid balance.

4.7. Discharge of the patient / instructions for further action

Asymptomatic patients who have been exposed to concentrations of less than 0.4mg/m^3 (maleic acid) or 6mg/m^3 (phthalic acid) and who show no abnormal examination 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 acid anhydrides.
- 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 serious skin or eye injuries should be re-examined after 24 hours.

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