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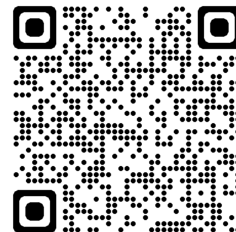

Chemical Emergency Medical Guideline

Information and recommendations for healthcare professionals

Isocyanates

CAS No.: 26471-62-5; 584-84-9; 91-08-7; 144490-96-0; 5873-54-1; 101-68-8; 822-06-0

GHS symbols:

GHS06
Acute toxicity

GHS08
Health hazard

Signal word: Danger

Hazard statements:

For detailed information on the H statements for the individual substances within this group, it is recommended to consult the relevant safety data sheets provided by the distributor or official databases (e.g. https://echa.europa.eu/de/search-for-chemicals).

Overview

- These guidelines are based on information about the diisocyanates toluene diisocyanate (TDI), diphenylmethane diisocyanate (MDI) and hexamethylene diisocyanate (HDI). Recommendations for other isocyanates are similar in many respects. However, these guidelines do not cover the specific characteristics of other isocyanates that may need to be considered.
- Before the paramedic/emergency doctor on site approaches a patient, who has been or is exposed to diisocyanates, it must be ensured that there is no danger to themselves from diisocyanates.
- There is no danger from contact with patients who have only been exposed to diisocyanate vapors. However, a patient who is wet with liquid diisocyanates or diisocyanate solutions, or whose clothing is wet with them, may endanger other people through direct contact or through outgassing diisocyanates.
- Diisocyanates are highly irritating to all tissues, especially the respiratory tract. Exposure can result in eye and skin irritation, coughing, chest pain and shortness of breath. Bronchospasm and signs of toxic pulmonary oedema (shortness of breath, cyanosis, sputum and coughing) may occur.
- Asthma attacks can also occur after exposure to very low concentrations of diisocyanates.
- There is no known specific antidote. Treatment depends on the extent of exposure and the symptoms.

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1. Information on the substance

Diisocyanates: TDI - $CH_3C_6H_3[NCO]_2$, CAS: 26471-62-5 (mixture), CAS: 584-84-9 (2,4-isomer), CAS: 91-08-7 (2,6-isomer); MDI - $CH_2(C_6H_4[NCO])_2$, CAS: 144490-96-0 (mixture), CAS: 5873-54-1 (2,4'-isomer), CAS: 101-68-8 (4,4'-isomer); HDI - $C_6H_{12}(NCO)_2$, CAS: 822-06-0
Synonyms:
TDI, diisocyanatotoluene, toluene diisocyanate
MDI, methylenediphenyl diisocyanate, methylene bis(phenyl isocyanate)
HDI, hexamethylene diisocyanate, diisocyanatohexane

TDI and HDI are colourless to straw-yellow liquids at room temperature, while MDI monomer is a colorless solid. Diisocyanates have a fruity, pungent odor. They are highly reactive, even with hydroxyl and amino groups in human body cells. When heated to decomposition, toxic nitrogen oxide vapors are released. An important application of diisocyanates is the manufacture of polyurethane foams, various plastics and elastomers. Diisocyanates are also used as hardeners for paints, coatings and adhesives.

2. Exposition

2.1. Inhalation

Exposure to diisocyanates occurs mainly through inhalation. The odor of diisocyanates does not provide a clear warning of dangerous concentrations. Respiratory tract irritation and asthma attacks (constriction of the bronchi with severe breathing difficulties) can occur even at very low concentrations.

2.2. Skin/eye contact

Direct contact with liquid diisocyanates or vapors can cause severe skin or eye irritation.

2.3. Ingestion

Accidental ingestion of diisocyanates is unlikely, but can cause chemical burns to the mouth, throat, oesophagus and stomach.

3. Acute health effects

Exposure to diisocyanates causes irritation of all tissues.

3.1. Dose-response relationship

Diisocyanate concentration		Effect/effects
0.0001 ppm	-	Asthmatic reactions in sensitized individuals possible
0.05 – 1.0 ppm	-	Irritation of skin, eyes, upper respiratory tract with conjunctivitis, sore throat, cough
0.4 ppm	-	Odor threshold
> 1.0 ppm	-	Severe irritative and inflammatory reactions, bronchial hypersensitivity, pneumonia, pulmonary oedema
> 2.5 ppm	-	Immediate danger to life

3.2. Respiratory tract

Irritation of the throat and lungs is often prominent and can lead to chest tightness, coughing, shortness of breath and bloody sputum. Non-specific respiratory hypersensitivity may occur and persist even after exposure has ended.
Asthma attacks can occur even after exposure to very low concentrations of diisocyanates. They can occur immediately or up to 8 hours after exposure.
Toxic pneumonia may develop, as may pulmonary oedema, and may occur up to 24 hours after severe exposure.

3.3. Skin/eye contact

Skin contact with diisocyanates can cause irritation and redness with blistering. Eye contact can result in severe irritation with immediate pain, tearing, eyelid oedema, inflammation of the conjunctiva and cornea, clouding of the eye surface and secondary glaucoma.

3.4. Possible consequences

After exposure to high concentrations, some individuals may develop asthma or non-specific bronchial hypersensitivity. Diisocyanates are potent allergens. Impaired lung function and respiratory symptoms due to bronchial constriction may persist.

4. Measures

4.1. Self-protection of first aiders

If there is a suspicion that the area which the helper must enter contains diisocyanates in potentially dangerous concentrations (see above), 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 diisocyanate vapors. A patient who is wet with liquid diisocyanates or diisocyanate solutions, or whose clothing is wet with them, may endanger other persons through direct contact or through outgassing diisocyanates.

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 suitable means, taking care to protect themselves. The "A, B, C procedure" has absolute priority in this case.

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 diisocyanate 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 liquid diisocyanates or diisocyanate solutions have been exposed and clothing is contaminated, it must be removed and securely wrapped.
Rinse affected skin areas with water for at least 15 minutes. Other important first aid measures must be continued during this time. Protect eyes while rinsing.
In case of diisocyanate exposure, 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 first aid measures during this time.

4.4. Initial treatment (preclinical or clinical)

Empirical therapy; no specific antidote available.

The following measures are recommended if the exposure concentration of diisocyanates is 1.0ppm or more, if symptoms such as eye irritation or pulmonary symptoms are present, or if the exposure concentration cannot be estimated but exposure is likely to have occurred:

- 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 adrenaline (epinephrine): mix 2mg adrenaline (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.

After inhalation of diisocyanates, administer humidified air or oxygen. If there are signs of hypoxia, administer oxygen.
In case of respiratory insufficiency, perform endotracheal intubation or alternative airway management. If this is not feasible, perform coniotomy if necessary.

Skin contact with diisocyanates 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 a sterile dressing.
Exposure of the eyes can also cause severe damage; this should also be treated as a burn. Consult an ophthalmologist immediately.

For all asymptomatic patients who have likely been exposed to a diisocyanate concentration of 0.1ppm or more, consider administering 5 puffs of beclomethasone from a metered dose inhaler. The administration can then be repeated every 10 minutes with 2 puffs. These patients should be monitored for an appropriate period.

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

4.5. Further procedure and treatment

In addition to taking medical history, performing a physical examination and checking vital signs, pulse oximetry, a chest X-ray and spirometry should be carried out.
Routine laboratory tests should include complete blood count, glucose and electrolytes.
Radiological signs of pulmonary oedema – enlargement of the hilar regions, typical, centrally accentuated, patchy opacities in the chest X-ray – are late signs that only become apparent 6 to 8 hours or even later after exposure. The X-ray is typically still normal at the initial presentation at the hospital, even after inhalation of a relevant dose.

Patients with a possible exposure concentration of 1.0ppm or more should be monitored for an appropriate period and re-examined repeatedly before any consequential damage to health can be ruled out.

If oxygen saturation falls below 90%, arterial blood gas concentrations should 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.

4.6. Biomonitoring

To estimate the systemic dose absorbed after exposure to 2,4- (CAS No. 91-08-7) or 2,6-toluene diisocyanate (CAS No. 584-84-9), biomonitoring can be performed by determining the concentration of 2,4- or 2,6-toluene diamine in urine.
To estimate the systemic dose absorbed after exposure to methylenediphenyl-4,4'-diisocyanate (CAS No. 101-68-8), biomonitoring can be carried out to determine the concentration of 4,4'-methylenedianiline in urine.
To estimate the systemic dose absorbed after exposure to hexamethylene-1,6-diisocyanate (CAS No. 822-06-0), biomonitoring can be carried out to determine the concentration of hexamethylene-1,6-diamine in urine.

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

Clinically asymptomatic patients who have been exposed to a diisocyanate concentration of less than 0.1ppm (depending on the duration of exposure), have normal clinical 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 diisocyanates.
- 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 carried out in the following 24 hours.
- Do not smoke and avoid cigarette smoke for at least 72 hours; smoke can impair lung function.
- Patients with eye damage should be examined again 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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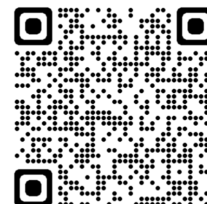

BASF has taken every possible care to ensure that the information presented in this document is accurate and up to date but does not claim that this document comprehensively covers all possible situations in this regard. This document is intended as an additional source of information for doctors in hospitals and is designed to assist in the assessment of the condition and treatment of patients exposed to isocyanates. However, it does not replace the professional assessment of the respective situation by physicians in hospitals and must be interpreted in accordance with legal regulations and provisions as well as specific information available about the respective patients.