

Information and recommendations for doctors at hospitals/emergency departments

- These guidelines are based on information about the diisocyanates toluene diisocyanate (TDI), diphenylmethane diisocyanate (MDI), and hexamethylene diisocyanate (HDI). Recommendations for other isocyanates might be similar. However, these guidelines do not cover special features potentially related to other isocyanates.
- Patients exposed only to diisocyanates vapor do not pose a significant risk of secondary contamination. Patients whose clothing or skin is contaminated with liquid diisocyanates or solvents containing diisocyanates can secondarily contaminate rescue and medical personnel by direct contact or evaporation of diisocyanates.
- Diisocyanates are severely irritating to all tissues, in particular to the respiratory tract. Exposure may result in eye and skin irritation, coughing, chest pain, dyspnea. Laryngospasm and signs of pulmonary edema (shortness of breath, cyanosis, expectoration, cough) may occur.
- Asthmatic attacks may occur after exposure to very low diisocyanate concentrations.
- There is no antidote to be administered to counteract the effects of diisocyanates. Treatment consists of supportive measures.

1. Substance information

Diisocyanates: TDI - $\text{CH}_3\text{C}_6\text{H}_3[\text{NCO}]_2$, CAS 26471-62-5 (mixture), CAS 584-84-9 (2,4-isomer), CAS 91-08-7 (2,6-isomer);

MDI - $\text{CH}_2(\text{C}_6\text{H}_4[\text{NCO}])_2$, CAS 144490-96-0 (mixture), CAS 5873-54-1 (2,4'-isomer), CAS 101-68-8 (4,4'-isomer);

HDI - $\text{C}_6\text{H}_{12}(\text{NCO})_2$, CAS 822-06-0

Synonyms: TDI, diisocyanatotoluene, tolylene diisocyanate;

MDI, methylenediphenyl diisocyanate, methylene bis(phenylisocyanate);

HDI, hexamethylene diisocyanate, diisocyanatohexane

At room temperature, TDI and HDI are colorless to straw-colored liquids while MDI monomer is a colorless solid. Diisocyanates have a fruity, pungent odor. Diisocyanates are highly reactive even to hydroxyl and amino groups in human body cells. When heated to decomposition, they emit toxic fumes of nitrogen oxides.

The major application of diisocyanates is the manufacture of polyurethane foams, various plastic materials, and elastomers. In addition, diisocyanates are used as hardeners for paints, coatings, and adhesives.

2. Routes of exposure

Inhalation

Inhalation is the major route of diisocyanate exposure. The odor does not provide adequate warning of hazardous diisocyanate concentrations. Irritation of the respiratory tract and asthmatic attacks (constriction of the bronchi with severe dyspnea) can occur even at very low concentrations.

Skin/eye contact

Direct contact with diisocyanate liquids and vapor can cause severe irritation to skin or eyes.

Ingestion

Involuntary ingestion of diisocyanates is unlikely but could cause chemical burns of the mouth, throat, esophagus, and stomach.

3. Acute health effects

Diisocyanate exposure causes irritation of all tissues. However, often throat and lung irritation are predominant and may lead to chest tightness, coughing, shortness of breath, and blood-streaked sputum.

Non-specific airway hyperresponsiveness may occur and persist after cessation of exposure.

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Asthmatic attacks may occur after exposure to very low diisocyanate concentrations. They can be immediate, delayed up to about 8 hours, or both.

Toxic pneumonitis as well as pulmonary edema may develop and may be delayed up to 24 hours after a severe exposure.

Euphoria, ataxia, memory loss, and muscle pain can occur after inhalation exposure.

Skin contact with diisocyanates can cause irritation and redness with blister formation.

Eye contact may result in severe irritation with immediate pain, lacrimation, lid edema, inflammation of conjunctiva and cornea, clouding of the eye surface, and secondary glaucoma.

Dose-effect relationships

Dose-effect relationships are as follows:

<u>Diisocyanate concentration</u>	<u>Effect</u>
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, coughing
0.4 ppm	- Odor detection
>1.0 ppm	- Severe irritative and inflammatory reactions with persistent effects possible: bronchial hyperresponsiveness, pneumonitis, pulmonary edema
>2.5 ppm	- Immediately dangerous to life

Potential sequelae

After one high-concentration exposure individuals may exhibit persistent asthma and non-specific bronchial hyperresponsiveness. Diisocyanates are potent sensitizers. Reduction in lung function and respiratory symptoms related to narrowing of the bronchi may persist.

4. Actions

Decontamination

Patients exposed only to diisocyanate vapor do not pose a significant risk of secondary contamination. Patients whose clothing or skin is contaminated with liquid diisocyanates or solvents containing diisocyanates can secondarily contaminate other people by direct contact or through evaporation of diisocyanates.

Patients who are able and cooperative may assist with their own decontamination. If the exposure involved liquid diisocyanates or solvents containing diisocyanates and if clothing is contaminated, remove and double-bag the clothing.

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. 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 diisocyanates.

The following measures are recommended if the airborne exposure concentration is 1.0 ppm or greater, if symptoms have developed, or if no exposure concentration can be estimated but exposure has possibly occurred:

- 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.

If diisocyanates were in contact with the skin or eyes 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.

All asymptomatic patients potentially exposed to a diisocyanate concentration of 0.1 ppm or more should take 8 puffs of beclomethasone from a metered dose inhaler. Thereafter, 4 puffs should be administered every 2 hours for 8 hours. These patients should be observed for at least 8 hours.

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 possible exposure to an airborne concentration of 1.0 ppm or greater should be observed for a minimum of 8 hours and reexamined frequently before confirming the absence of toxic effects.

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*

Patients exposed to an airborne concentration of **less than 0.1 ppm who have no signs or symptoms of toxicity** as well as patients exposed to a concentration of **0.1 ppm or more who have a normal examination and no signs or symptoms of toxicity** may be discharged from the emergency department after an appropriate observation period in the following circumstances:

- a) The evaluating physician is experienced in the evaluation of individuals with diisocyanate 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 diisocyanate and the provided follow-up instructions.
- d) Site medical is notified, so that the patient may be contacted at regular intervals in the 24-hour period following release.
- 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 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 in assessing the condition and managing the treatment of patients exposed to diisocyanates. 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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