BASF Chemical Emergency Medical Guidelines

Dimethylformamide $(CH_3)_2N$-CHO C 1

Information and recommendations for doctors at hospitals/emergency departments

- **Patients exposed only to dimethylformamide vapor do not pose a significant risk of secondary contamination. Patients whose clothing or skin is contaminated with liquid dimethylformamide (boiling point 153°C, 307°F respectively) can secondarily contaminate rescue and medical personnel by direct contact or evaporation of dimethylformamide.**
- **Dimethylformamide is irritating when it comes in contact with the eyes, skin, and throat and causes headache, nausea, vertigo, dizziness, weakness, disorientation, and hypotension. Liver toxicity and alcohol intolerance have been noted.**
- **There is no antidote to be administered to counteract the effects of dimethylformamide. Treatment consists of supportive measures.**

1. Substance information

Dimethylformamide ($(CH_3)_2N$-CHO), CAS 68-12-2
Synonyms: DMF, formyldimethylamine
Dimethylformamide is, at room temperature, a colorless to very slightly yellow liquid with a faint amine or "fishy" odor. Though stable at normal temperatures and storage conditions, dimethylformamide may react violently with halogens, alkyl halides, strong oxidizers, and polyhalogenated compounds in the presence of iron. Decomposition products include toxic gases and vapors such as dimethylamine and carbon monoxide. It is water-soluble.
Dimethylformamide is an organic solvent with a slow evaporation rate used for polar polymers and resins, adhesives, cleaners, zinc electroplating, protective coatings, inks, film, paint removers, and in selective gas absorption. It is used in Orlon® and acrylic fiber spinning, synthetic leather, polyurethanes, wire enamels, chemical manufacturing and pharmaceutical production.

2. Routes of exposure

Inhalation

Exposures may occur by inhalation. Dimethylformamide is readily absorbed by the respiratory tract.

Skin/eye contact

Most exposures occur by direct contact. It is readily absorbed through the skin, causing systemic effects

Ingestion

Dimethylformamide is readily absorbed from the gastrointestinal tract. However, ingestion is uncommon in occupational settings.

3. Acute health effects

Systemic

Dimethylformamide causes headache, nausea, vertigo, dizziness, weakness, disorientation, and hypotension. Liver toxicity with jaundice and altered liver enzymes and alcohol intolerance has been noted. Dimethylformamide poisoning may cause unconsciousness, respiratory and cardiovascular failure.

Respiratory

Irritation of the upper respiratory tract may be caused by dimethylformamide.

Dermal

Irritation of the skin, including itching and desquamation, may be caused by direct contact to liquid dimethylformamide.

Ocular

Eye contact to vapor or liquid dimethylformamide cause burning discomfort, spasmodic blinking or involuntary closing of the eyelids, redness, and tearing.

Gastrointestinal — **Liver toxicity with jaundice and altered liver enzymes and alcohol intolerance has occurred after exposure via inhalation or skin contact.** Anorexia, taste loss and various digestive disturbances, including nausea, epigastric pain, vomiting, constipation, diarrhea, and colic may also occur.

Dose-effect relationships — Dose-effect relationships are as follows:

Dimethylformamide concentration		Effect
0.47 - 100 ppm	-	Odor detection
10 ppm	-	Alcohol intolerance
25 - 60 ppm	-	Increase of liver enzymes
500 - 3000 ppm	-	Immediately dangerous to life
10 g per oral	-	Estimated lethal dose in humans

Potential sequelae — If the patient survives the initial 48 hours after inhalation exposure, recovery is likely. After acute exposure, pulmonary function usually returns to normal in 7 to 14 days. Complete recovery is usual; however, symptoms and pulmonary deficits may persist. Airways hyperreactivity to non-specific irritants may persist, resulting in bronchospasm and chronic inflammation of the bronchi; reactive airways dysfunction syndrome has been reported to persist for years. Sequelae of the pulmonary tissue destruction and scarring may lead to chronic dilation of the bronchi and increased susceptibility to infection. **In case of ingestion or skin absorption, gastrointestinal, cardiovascular, nervous system, and hepatic necrosis have been observed.**

Carcinogenicity — According to EC directive 1272/2008 dimethylformamide is classified as follows:
Repr. 1B (known or presumed human reproductive toxicant, classification is largely based on data from animal studies)

4. Actions

Decontamination — Patients exposed to dimethylformamide require decontamination. Patients who are able and cooperative may assist with their own decontamination. If clothing is contaminated, remove and double-bag the clothing.
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.
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.

Initial treatment — **In case of suspected dimethylformamide poisoning by ingestion or skin absorption immediate supportive measures are required, including establishment of intravenous access.**
There is no specific antidote to counteract the effects of dimethyl-formamide.
If inhalation exposure is 100 ppm or greater (depending on time exposed), if symptoms, e. g. eye irritation or pulmonary symptoms have developed, or if the exposure concentration cannot 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 ß2-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.

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If dimethylformamide vapor or liquid dimethylformamide has been in contact with the skin, irritation may result; treat as thermal burns.
After eye exposure, irritation may result; treat as thermal burns. Consult an ophthalmologist.

Note: Any facial exposure to liquid dimethylformamide should be considered as a serious exposure.

Laboratory tests

The diagnosis of acute dimethylformamide toxicity is primarily a clinical one, based on the presence of irritation, CNS effects, and liver toxicity together with known or strongly suspected dimethylformamide exposure

Further evaluation and treatment

To the standard intake history, physical examination, and vital signs add spirometry.
Routine laboratory studies should include a complete blood count, liver enzymes, renal function tests, and blood glucose and electrolyte determinations. To check for acute liver failure thromboplastin time should be determined. Elevated CPK levels and hypercholesterolemia may also occur with exposure.
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.
As N-acetylcysteine (NAC) is generally used in hepatic failure administration of NAC in a dosage equivalent to the treatment in paracetamol poisoning may be considered. Transfer to a specialized unit for hepatic disorders should be considered if jaundice, elevation of liver enzymes and clotting disorders occur.

Patient release/ follow-up instructions

Clinically asymptomatic patients exposed to a concentration of **less than 10 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 dimethylformamide 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 dimethylformamide.
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) **Drinking of alcohol beverages should be strictly forbidden for at least 72 hours. Alcohol intolerance has been noted.**
f) Heavy physical work should be precluded for 24 hours.
g) Exposure to cigarette smoke should be avoided for 72 hours; the smoke may worsen the condition of the lungs.

Patients who have serious skin or eye injuries should be reexamined in 24 hours.
Post discharge spirometry should be repeated until values return to the patient's baseline values.

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