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Chemical Emergency Medical Guideline

Information and recommendations for healthcare professionals

Aniline

CAS No: 62-53-3

GHS symbols:

GHS05
Corrosive

GHS06
Acute toxicity

GHS08
Health hazard

Signal word: Danger

Hazard statements:

H317	May cause allergic skin reactions.
H318	Causes serious eye damage.
H341	May cause genetic defects.
H351	May cause cancer.
H372	Damages organs through prolonged or repeated exposure.
H301+H311+H331	Toxic if swallowed, in contact with skin or if inhaled.

Overview

- A patient who is covered in Aniline or whose clothing is covered in Aniline may endanger other people through direct contact or through Aniline vapors.
- Aniline is rapidly absorbed systemically after inhalation, ingestion and even through intact skin.
- Aniline can significantly impair and even destroy the function of red blood cells (erythrocytes). This leads to a reduced oxygen transport capacity in the blood. In severe cases of poisoning, central nervous system functions may also be impaired. In the worst case, cardiovascular arrest may occur.
- Immediate treatment after exposure to Aniline includes close monitoring and maintenance of cardiovascular function as well as intravenous injection of the antidote toluidine blue or methylene blue.

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1. Information on the substance

Aniline ($C_6H_5NH_2$), CAS 62-53-3
Synonyms: aminobenzene, phenylamine
At room temperature, Aniline has low vapor pressure and is a clear to slightly yellowish oily liquid that turns brownish upon contact with air. Aniline is moderately soluble in water. Aniline has a sweetish to fishy odor. Aniline is obtained by reducing nitrobenzene with hydrogen or by ammonolysis of phenol. It is used in the synthesis of a variety of products such as polyurethane foams, photographic chemicals, rubber chemicals, dyes and pesticides.

2. Exposition

2.1. Inhalation

When inhaled, Aniline is rapidly absorbed by the lungs and can then have a systemic toxic effect. Usually, the smell of Aniline provides sufficient warning of dangerous concentrations. As Aniline vapors are heavier than air, there is a risk of suffocation in poorly ventilated, low-lying or enclosed spaces.

2.2. Skin/eye contact

Contact with liquid Aniline generally causes only slight eye irritation. However, liquid Aniline or Aniline vapors are readily absorbed through the skin and can then affect the whole body.

2.3. Ingestion

Accidental ingestion of Aniline is unlikely. Toxic effects occur rapidly after ingestion.

3. Acute health effects

Exposure to Aniline can cause methemoglobinemia and hemolysis, thereby severely impairing the transport of oxygen in the bloodstream to the tissues.
Aniline concentrations of up to 30 to 50ppm over several hours cause only minor discomfort. Concentrations above 100ppm over an hour can result in significant health impairments.

The complaints and symptoms that can be expected at different methemoglobin levels are shown in the table below. Patients with relevant underlying diseases (especially anemia) may develop complaints and symptoms even at lower methemoglobin levels. Methemoglobin levels of up to 5% can be caused by smoking.

Acute exposure to Aniline can cause dysuria, hematuria and acute renal failure. The absorption of large amounts of Aniline can result in liver damage with jaundice.

Eye, nose and throat irritation caused by Aniline generally results in only mild symptoms.

Methemoglobin levels between 15% and 30% can cause a bluish skin color (cyanosis) in patients, but this is due to the darker color of methemoglobin and not to insufficient oxygen saturation of the blood. Methemoglobin levels above 90% are considered fatal.

Acute or delayed hemolytic anemia may occur due to exposure to Aniline. Individuals with glucose-6-phosphate dehydrogenase deficiency are at increased risk of Aniline-induced hemolysis.

3.1. Dose-response relationship

Methemoglobin (in %)		Effect/effects
15 - 30	-	Grey-blue skin color
30 - 50	-	Headache, fatigue, dizziness, tachycardia, mild shortness of breath
50 - 70	-	Stupor, bradycardia, respiratory depression, cardiac arrhythmia, acid-base balance disorders
60 - 70	-	Cardiac arrest, unconsciousness, coma
> 90	-	Fatal

Aniline converts Fe^{2+} in hemoglobin in red blood pigment to Fe^{3+}. Exposure to Aniline can cause methemoglobinemia and hemolysis, thereby impairing the transport of oxygen to the tissues. Methemoglobinemia following exposure to Aniline can develop gradually, and symptoms may be delayed for several hours. The formation of methemoglobin can continue for 12 to 24 hours after exposure.

3.2. Cardiovascular system

The reduced transport of oxygen to the tissues after exposure to Aniline can result in cardiac effects such as cardiac arrhythmia or acute heart failure. Fatal Aniline poisoning is the result of cardiovascular failure.

3.3. Skin contact

Skin contact with liquid Aniline or Aniline vapors can result in systemic toxic effects. Patients with significant methemoglobinemia may appear grey, bronze or bluish even at normal pO_2levels.

3.4. Central nervous system

Acute exposure to Aniline can lead to disturbances of consciousness and motor functions, dizziness, seizures and coma.

3.5. Kidneys and liver

Acute exposure to Aniline can cause dysuria and hematuria (presence of blood, hemoglobin or methemoglobin in the urine) as well as impaired kidney function, up to and including acute kidney failure. Absorption of large amounts of Aniline can result in liver damage with jaundice.

3.6. Possible consequences

In most cases, the symptoms subside after a few days to weeks. However, survivors of severe Aniline poisoning may suffer from chronic symptoms due to irreversible damage to the brain, kidneys or liver, especially if significant hypoxia has developed.

4. Measures

4.1 Self-protection of first responders

If there is a suspicion that the area that the helper must enter may be affected by dangerous concentrations of Aniline vapors (10ppm or more) or that there may be contact with liquid Aniline, a self-contained breathing apparatus and a chemical protection suit must be worn. Contaminated equipment must not be used. For rescue operations, short-term exposure to Aniline concentrations below 10ppm without protective measures may be acceptable.

A patient who is covered in Aniline or whose clothing is contaminated with Aniline may endanger other people through direct contact or through Aniline vapors.
Adequate protective gloves must be worn, e.g. butyl rubber or latex gloves with a thickness of more than 1mm (*note: nitrile gloves generally used by medical personnel do not provide adequate protection*).

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 yourself. 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

Unlike all other patients, those who have only been exposed to Aniline vapors and show no signs of eye irritation do not require any special cleaning measures.
If possible, patients should assist with their own cleaning. If liquid Aniline has come into contact with clothing, it must be removed and securely wrapped.
It must be ensured that the eyes are rinsed with water or neutral saline solution for at least 15 minutes in the event of Aniline exposure. Remove any contact lenses, if possible, without additional risk to the eye. Other important emergency measures must be continued during this time.
Rinse affected skin and hair with water for at least 15 minutes. Other important first aid measures must be continued during this time. Protect eyes while rinsing.

4.4. Estimation of inhaled dose

Severe methemoglobinemia can be recognized directly in the patient due to brownish-bluish skin discoloration. Methemoglobin levels can be measured non-invasively with special pulse oximeters. Methemoglobin levels of up to 5% can be caused by smoking.

4.5. Initial treatment (preclinical or clinical)

Administer oxygen if there are signs of hypoxia.
In case of respiratory insufficiency, perform endotracheal intubation or alternative airway management. If this is not feasible, perform coniotomy if necessary.
The following measures are recommended for patients with symptoms (not only cyanosis, but also headache, fatigue, dizziness, rapid or irregular heartbeat, shortness of breath) that indicate a methemoglobin level above 30% or if pulse oximetry detects relevant methemoglobinemia.

4.6. Antidote treatment

Intravenous access and intravenous administration of toluidine blue over 5 to 10 minutes (2-4mg/kg body weight, i.e. 0.07 to 0.14ml/kg body weight of a 3% solution). If toluidine blue is not available, methylene blue should be injected intravenously at a dose of 1-2mg/kg body weight (0.1 to 0.2ml/kg body weight of a 1% solution) over 5 to 10 minutes.
Note: In individuals with known glucose-6-phosphate dehydrogenase deficiency, the administration of both toluidine blue and methylene blue has no therapeutic benefit and may cause further hemolysis.

All patients who have been exposed to Aniline concentrations of 30 ppm or more or who have had significant dermal exposure (more than 100cm^2 of skin affected) should be transported immediately to a hospital with intensive care facilities.
Toluidine blue can be administered once after 30 minutes and methylene blue after 60 minutes, depending on the methemoglobin level and the patient's clinical condition. The total initial dose of toluidine blue should not exceed 7mg/kg of body weight. (A dose above 15mg/kg of body weight can cause hemolysis.)
Possible side effects include nausea, vomiting, chest/abdominal pain, dizziness, sweating and dysuria.
Positive end-expiratory pressure (PEEP) therapy and exchange transfusion should be considered in life-threatening poisoned patients whose condition deteriorates despite antidote therapy or who have severe glucose-6-phosphate dehydrogenase deficiency.

4.7. Further procedure and treatment

All patients who have been exposed to Aniline concentrations of 30ppm or more or who have had significant dermal exposure (affecting more than 100cm^2 of skin) should be examined as follows:

In addition to medical history, physical examination and vital signs, complete blood count, hemoglobin, methemoglobin and glucose measurements, and urinalysis should be performed. Fluid intake and output as well as electrolytes should be closely monitored. Arterial blood gas concentrations, a chest X-ray and an ECG should be performed in cases of cyanosis or dyspnea. Additional tests for patients exposed to Aniline include a peripheral blood smear, kidney function tests and determination of unconjugated bilirubin.

Patients should be observed for an appropriate period and undergo repeated follow-up examinations. Repeated measurements of methemoglobin levels and arterial blood gas concentrations are advisable. Pulse oximetry is unreliable under these conditions. Methemoglobin levels should be monitored regularly until they fall below 15%.
Hemolysis may also occur more than 24 hours after exposure. Watch for signs of acute renal failure and cardiac arrhythmias.

4.8. Biomonitoring

Biomonitoring with determination of the Aniline concentration in urine can be performed to estimate the systemic dose absorbed after exposure.

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

Asymptomatic patients who have been exposed to a concentration of less than 30 ppm and have no relevant dermal exposure, as well as patients who, after an appropriate follow-up period, have a methemoglobin level of less than 15% and have remained asymptomatic, 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 Aniline.
- 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 for at least 72 hours and avoid cigarette smoke; smoke can impair lung function.

5. References

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