
Information and recommendations for doctors at hospitals/emergency departments

- Patients whose clothing or skin is contaminated with aniline can secondarily contaminate rescue and medical personnel by direct contact or through evaporation of aniline.
 - Aniline is rapidly absorbed after inhalation and ingestion as well as through intact skin.
 - Aniline exposure can cause methemoglobinemia and red blood cell hemolysis, which impairs the delivery of oxygen to tissues. Depression of the central nervous system and cardiovascular collapse may result.
 - Immediate treatment for aniline overexposure consists of cardiorespiratory support and intravenous administration of the antidote toluidine blue. If toluidine blue is not available, methylene blue is the recommended antidote.
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1. Substance information

Aniline (C₆H₅NH₂), CAS 62-53-3

Synonyms: aminobenzene, aminophen, phenylamine.

At room temperature, aniline has a low vapor pressure and is a clear to slightly yellow, oily liquid that darkens to brown color on exposure to air. It is slightly soluble in water. Aniline has an aromatic or fishy odor.

Aniline is synthesized by catalytic hydrogenation of nitrobenzene or by ammonolysis of phenol. It is used in the synthesis of a variety of products including polyurethane foam, photographic developers, rubber, dyes, and crop protection products.

2. Routes of exposure

Inhalation

Inhaled aniline is rapidly and significantly absorbed from the lungs, leading to systemic toxicity. Aniline's odor usually provides an adequate warning of hazardous concentrations. Aniline vapor is heavier than air and may cause asphyxiation in poorly ventilated, low-lying or enclosed spaces.

Skin/eye contact

Contact with liquid aniline usually causes only mild irritation of the eyes. **However, liquid aniline or aniline vapor are absorbed very well through the skin and may cause systemic toxicity.**

Ingestion

Involuntary ingestion of aniline is unlikely. Ingestion can lead rapidly to severe systemic toxicity.

3. Acute health effects

Aniline converts the Fe²⁺ in hemoglobin to Fe³⁺. Aniline exposure can cause methemoglobinemia and hemolysis, which impairs the delivery of oxygen to tissues. Methemoglobin formation from aniline exposure may develop insidiously, and onset of symptoms may be delayed for hours. Production of methemoglobin may continue for up to 12-24 hours after exposure.

Aniline concentrations up to 30-50 ppm over several hours caused only minor health disturbances while concentrations greater than 100 ppm could not be tolerated over more than 1 hour without major adverse health effects.

Signs and symptoms expected at various percentages of methemoglobin formation are outlined below. Patients who have underlying diseases may develop signs and symptoms at even lower methemoglobin percentages. Methemoglobin levels of about 5% may be caused by smoking.

<u>Methemoglobin percentages</u>	<u>Signs and symptoms</u>
15-30	- Gray to bluish color of the skin
30-50	- Headache, fatigue, dizziness, rapid heart rate, mild shortness of breath
50-70	- Stupor, slow heart rate, respiratory depression, irregular heart rhythm, acid-base imbalance
60-70	- Cardiac arrest, loss of consciousness, coma
> 90	- Death

When methemoglobin levels are 15 % to 30 %, the patient may become bluish in color, which is due to the dark color of methemoglobin and not to inadequate oxygen in the blood. Methemoglobin levels exceeding 90% are usually fatal.

Acute or delayed hemolytic anemia caused by destruction of red blood cells may result from aniline exposure. **Persons with glucose-6-phosphate dehydrogenase deficiency are at increased risk of aniline-induced hemolysis.**

Cardiovascular

Cardiac effects of acute aniline exposure, such as arrhythmia and acute congestive heart failure, may be caused by decreased oxygen delivery to the tissues. Death is usually due to cardiovascular collapse.

CNS

Acute aniline exposure can cause changes in the level of consciousness and motor control, dizziness, convulsions, and coma. These effects are usually transitory.

Renal/hepatic

Acute aniline exposure can cause dysuria; blood, hemoglobin or methemoglobin in the urine; scant urine production; and acute kidney failure. Absorption of high amounts of aniline might lead to liver damage and jaundice.

Dermal

Systemic effects can result from skin contact with aniline vapor or liquid. Patients who have methemoglobinemia can appear gray, bronze, or blue even though PO₂ is normal.

Other

Aniline exposure usually causes only mild eye, nose, and throat irritation.

Potential sequelae

For most exposed individuals symptoms will clear over several days or weeks. Survivors of severe intoxication, especially if significant hypoxia had developed, may have chronic effects due to irreversible damage to the brain, heart, kidneys, and liver.

4. Actions

Self-protection

Patients whose clothing or skin is contaminated with aniline can secondarily contaminate other people by direct contact or through evaporation of aniline.

Decontamination

Patients exposed only to aniline vapor who have no evidence of eye irritation do not need decontamination. All others require decontamination.

Patients who are able and cooperative may assist with their own decontamination. If the exposure involved liquid aniline and 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 and transport.

Remove contact lenses if present and easily removable without additional trauma to the eye.

Assure that exposed skin and hair have been flushed with soap and water for at least 15 minutes. If not, continue flushing during other basic care and transport. Protect eyes during flushing of skin and hair.

If signs of hypoxemia are present, supplemental oxygen should be administered.

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.

Methemoglobinemia can be detected at the bedside by the characteristic chocolate-brown color that it imparts to blood. Methemoglobin levels greater than 10 % can usually be detected by comparing a drop of the patient's blood with a drop of normal blood on white filter paper or gauze.

The following measures are recommended for patients who demonstrate symptoms (not only cyanosis, but also headache, fatigue, dizziness, rapid or irregular heart rate, respiratory distress) suggesting a methemoglobin level of more than 30%:

If not already done, initially, establishment of intravenous access and intravenous administration of toluidine blue or, if not available, of methylene blue. In persons with glucose-6-phosphate dehydrogenase deficiency, toluidine blue or methylene blue might not be useful but cause additional hemolysis.

The standard dose of toluidine blue is 2 to 4 mg/kg body weight (0.07 to 0.14 ml/kg body weight of a 3% solution) intravenously over 5 to 10 minutes. Administration of toluidine blue may be repeated once after 30 minutes, depending upon the methemoglobin level and the clinical condition of the patient. Side effects include nausea and vomiting.

Alternatively, the standard dose of methylene blue is 1 to 2 mg/kg body weight (0.1 to 0.2 ml/kg body weight of a 1% solution) intravenously over 5 to 10 minutes. Administration of methylene blue may be repeated once after 60 minutes, depending upon the methemoglobin level and the clinical condition of the patient. The total initial dose should not exceed 7 mg/kg body weight. (Doses greater than 15 mg/kg body weight may cause hemolysis.) Side effects include nausea, vomiting, abdominal and chest pain, dizziness, diaphoresis, and dysuria.

Consider positive end-expiratory pressure (PEEP) therapy and exchange transfusion therapy for severely poisoned patients who are deteriorating clinically in spite of antidotal therapy and for severely poisoned patients with glucose-6-phosphate dehydrogenase deficiency.

All patients who might have been exposed to aniline concentrations greater than 30 ppm or who have significant dermal exposure affecting more than 100 cm² (15 square inches) of skin should be examined as follows:

To the standard intake history, physical examination, and vital signs add monitoring of complete blood count, hemoglobin, methemoglobin, glucose, and a urine analysis. Fluid intake/output and electrolytes should be monitored closely. Arterial blood gases measurements, PA chest X-ray, and ECG should be performed if

*Initial treatment
of methemoglobinemia*

Antidotal treatment

Further evaluation and treatment

cyanosis or dyspnea is present. Additional studies for patients exposed to aniline include peripheral blood smear, renal function tests, and determination of unconjugated bilirubin levels.

Patients should be observed for a minimum of 6 hours and reexamined frequently.

Repeated determinations of the methemoglobin levels and the arterial blood gases are advisable. Pulse oximetry is unreliable in this setting. Measurement of methemoglobin should be repeated every 3 hours to ensure that the level is decreasing to less than 15%. Hemolysis may begin up to 24 hours or more after exposure. Observe hospitalized patients for signs of acute renal failure and dysrhythmias.

*Patient release/
follow-up instructions*

Patients remaining **asymptomatic up to 6 hours after measurement of a methemoglobin level lower than 15%** may be discharged in the following circumstances:

- a) The evaluating physician is experienced in the evaluation of individuals with aniline 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 aniline.
- 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) 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 and methemoglobinemia.

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 at hospitals/emergency departments in assessing the condition and managing the treatment of patients exposed to aniline. 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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