ALUMINIUM PHOSPHIDE POISONING

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Metal phosphides (aluminum, zinc, magnesium, and calcium) have long been used as rodenticides and fumigants around the world.

The metal phosphides are advantageous due to their low cost, high effectiveness in destroying harmful insects and rodents, freedom from toxic residue, and lack of adverse effect on seed viability.
• Upon exposure to ambient moisture, the metal phosphides release phosphine gas (\(\text{PH}_3\)).
• Exposure to water results in rapid release highlighting the concern for their use as chemical weapons.
Aluminum phosphide (AlP) poisoning is now one of the commonest causes of poisoning in agricultural societies, such as those found in India, Sri Lanka, Iran, Jordan, and Morocco.

The incidence of phosphide poisoning is rare in Europe and North America.
• Commercially, AlP is most widely available as a greenish-gray tablet that has a garlic odor.

• The tablets usually contain 3 g of AlP (56%), ammonium carbamate, and urea.
In the presence of moisture, phosphide is converted to gaseous PH₃ (hydrogen phosphide, phosphorus trihydride), ammonia, and carbon dioxide:
• ALP+3 H2O = ALOH + PH3

• ALP+3 HCL = ALCL3 + PH3
TOXICOkinetics

• Following ingestion, the most common route of exposure, metal phosphides react with acidic fluid in the gastrointestinal (GI) tract to release PH3, which is rapidly absorbed.
• Phosphides may be absorbed as microscopic particles of unhydrolyzed salt and subsequently converted to PH₃.

• PH₃ can be absorbed from respiratory tract mucosa if inhaled.

• Dermal and ocular absorption occurs.
TOXICODYNAMICS

- PH3 is a protoplasmic toxin that interferes with enzymatic function and synthesis of proteins.
- The mechanism of toxicity includes blocking the electron transport chain and oxidative phosphorylation through noncompetitive inhibition of cytochrome-c oxidase.
• This inhibits cellular respiration and leads to the formation of highly reactive hydroxyl radicals that cause additional damage.

• PH3 also inhibits catalase, induces superoxide dismutase, and reduces the glutathione (GSH) concentration.
• All of these effects combine to result in lipid peroxidation and protein denaturation of cell membranes, leading to widespread cellular damage and ion channel dysfunction.
TOXIC DOSE

- Ingestion of 1 g of ZnP can cause toxicity in humans and death has been reported after ingestion of 4 g.

- Ingestion of 500 mg of AlP can be fatal.
CLINICAL MANIFESTATIONS

• The smell of garlic or decaying fish on the breath is a common finding and can be the result of oral or inhalational poisoning with phosphides and PH3.

• The clinical manifestations are dependent on the dose, route of entry, and time since exposure.
• In patients with mild poisoning, nausea, repeated vomiting, diarrhea, abdominal discomfort or pain, especially epigastric pain, and tachycardia are common clinical manifestations.

• In those with moderate to severe effects, GI manifestations, refractory hypotension and shock, palpitations, cardiovascular collapse, dysrhythmias, tachypnea, and ARDS occur early.
• Restlessness, anxiety, dizziness, ataxia, numbness, paresthesias, and tremor are universally observed, but central nervous system (CNS) manifestations are not prominent until a secondary event, such as hypoxia occurs.
• Following limited PH3 inhalational exposure, patients commonly have airway irritation and breathlessness.

• Other features may include dizziness, tightness in the chest, headache, nausea, vomiting, diarrhea, ataxia, numbness, paresthesias, tremor, muscle weakness, and Diplopia.
Uncommon complications

- of phosphides and PH3 poisoning include gastroduodenitis, hepatitis, ascites, pancreatitis, myocardial infarction, acute pericarditis, pleural effusion, skeletal muscle damage and rhabdomyolysis, acute tubular necrosis, adrenocortical congestion, hemorrhage and/or necrosis, and delayed esophageal stricture or tracheoesophageal fistula.
- Hepatic and kidney failure, as well as (DIC), may occur following acute poisoning.
DIAGNOSTIC TESTING

- Initial investigations should include (ECG) and continuous cardiac monitoring, chest radiograph, blood glucose, blood gases, serum electrolytes, complete blood count, and liver and kidney function studies.
• Hypokalemia is common after oral poisoning and is probably due to vomiting, although this effect may be catecholamine related.

• Magnesium concentrations may be normal, increased, or decreased.
• Hypoglycemia as a result of impaired gluconeogenesis, glycogenolysis, and possibly due to adrenal insufficiency is common and may be severe and persistent.

• Hyperglycemia has also been reported.
• Metabolic acidosis or mixed metabolic acidosis and respiratory alkalosis are common.
• Intravascular hemolysis, methemoglobinemia, and microangiopathic hemolysis are unusual complications of phosphide poisoning.
• ECG abnormalities are very common, but highly variable, and include rhythm disturbances, ST segment and T wave changes, and conduction defects.

• During the first 3 to 6 hours after poisoning, sinus tachycardia is predominant, followed over the next 6 to 12 hours by ST segment and T wave changes, conduction disturbances, and dysrhythmias.
• Ventricular tachycardia, ventricular fibrillation, supraventricular tachycardia, and atrial flutter/fibrillation are the most common consequential dysrhythmias.

• Echocardiography may reveal dysfunction, dilation, and hypokinesia or akinesia of the left ventricle that typically resolves over several days.
TOXICOLOGICAL ANALYSES.

- Chemical analysis for PH3 in blood or urine is not recommended and is not typically helpful as PH3 is rapidly oxidized to phosphite and hypophosphite.

- Gas chromatography with a nitrogen-phosphorous detector is the most specific and sensitive test.
PROGNOSIS

- The mortality rate following metal phosphide ingestion is 31% to 77%.

- Most of the deaths occur within 12 to 24 hours and are due to cardiovascular collapse.
PROGNOSIS

- After 24 hours, most of the deaths are due to refractory shock, severe acidemia, and ARDS.

- Fulminant hepatic failure may develop within 72 hours after poisoning and may be another cause of death.
**PROGNOSIS**

- A high Acute Physiology and Chronic Health Evaluation Score, a high Simplified Acute Physiology Score, shock, decreased level of consciousness, lack of vomiting after ingestion, acidemia, hyperglycemia, uremia, hemoconcentration, leukocytosis, and ECG abnormalities are all poor prognostic factors
TREATMENT

- The victim of PH inhalation should immediately be removed to fresh air and supplemental oxygen should be provided as needed.

- Clinical staff and other health care professionals should use universal precautions, including gloves and masks with the understanding that a particulate mask will not protect against PH3.
• As PH3 may be absorbed by the cutaneous route, the patient’s clothes should be removed and their skin and eyes decontaminated with water as early as possible.
• GI decontamination may be useful if it is done within 1 to 2 hours of ingestion.

• The acidic content of stomach assists the conversion of phosphide to PH$_3$, and some have suggested the oral administration of sodium bicarbonate, but this is not supported by experimental evidence. Potassium permanganate (1:10,000) has also been suggested in case reports as an adjunct to gastric lavage to oxidize PH$_3$ to nontoxic phosphate.
There is limited evidence that activated charcoal (AC) 100 g may reduce GI absorption if the patient arrives within 1 hour after ingestion of a large amount of poison.
• Standard supportive care to address ventilatory and vital sign abnormalities should be administered.

• If necessary, norepinephrine or phenylephrine should be employed.
• Vasopressors with greater $\beta$-receptor agonist action like dopamine and dobutamine should be used cautiously as they are prone to induce dysrhythmias.
As there is no known specific antidote, management remains primarily intensive monitoring and supportive treatment, to allow the toxin to be eliminated. ARDS, hypoglycemia, hypokalemia, and metabolic acidosis should be managed conventionally.
• Dysrhythmias should be treated with standard antidysrhythmics.

• Recently, a few studies hypothesized that treatment with digoxin could have beneficial effects on myocardial contractility and blood pressure.
The benefit of hyperinsulinemia-euglycemia treatment is suggested by preliminary investigations in that insulin promotes energy production from carbohydrates, restores calcium flux, and improves myocardial contractility.
- N-acetylcysteine (NAC) has been shown in an experimental animal model and human study to be beneficial.

- Experimental data show that hyperbaric oxygenation may improve the survival time of poisoned rats, with no change in the mortality rate.
- Magnesium sulfate acts as a cell membrane stabilization factor and, possibly by this mechanism, reduces the incidence of fatal dysrhythmias.

- Magnesium also has antioxidant effects and combats free radicals due to PH3.

Although likely of low risk, the use of magnesium sulfate in phosphides/PH3 poisoning is controversial.
Hemodialysis is not very effective in removing PH3, although it may be useful in the setting of a patient with acute kidney failure, severe metabolic acidosis, or fluid overload.