ALUMINUM PHOSPHIDE POISONING

Dr Aniruddha Ghose
Associate Professor
Chittagong Medical College
• Increasing world population: pressure on grain production

• Use of increasing no of pesticides

• Improved quantity and quality of crops: better availability of food grains to the population(!?)

• Misused as agents of self-harm
• Fumigants are pesticides used to control rodents, insects, weed seeds, and fungi, typically for storage (silos) and transport (ships, containers, or railcars)

• Comprise a diverse group of compounds and exist in solid (aluminum phosphide), liquid (formaldehyde), and gaseous (ethylene oxide) forms
Phosphides (aluminum, zinc, calcium, and magnesium) are used worldwide as grain fumigants and rodenticides.

- Highly efficacious in killing rodents and insects
- Inexpensive and simple to manufacture
- No toxic residue
- No adverse effect on the seed viability
Aluminium phosphide (ALP): used since the 1940s (registered as a pesticide in 1958)

- Easily available: Bangladesh, India.

- Trade names: Celphos, Alphos, Quickphos, Synfume, Phosfume, Quickfume etc.

Local name: ‘Gas tablet’, ‘Rice tablet’.
Incidences

- AlP was found to be the most common suicidal poison, causing 68.4 % of total deaths due to poisoning between 1977 and 2002: autopsy study of unnatural deaths in Northwest India
- 1977 - 1987: Barbs (33.3 %), OPs (23.8 %), and Cu SO4 (14.3 %)
- 1987 – 1997: OPs (45 %), AlP (26.5 %).
- Peak incidence of suicidal death: 18.2% in 1992-97, when AlP became available on the free market
Iran

AlP poisoning

• 471 cases: between 2000 and 2007
• 146 (31 %) were fatal
• ! AlP has been banned for marketing in Iran!
Other countries

- Suicide: Sri Lanka, Iran, Jordan, Morocco
- Developed countries: rare
  - Suicidal: Denmark, Germany, France, and the UK.
  - Accidental: Australia, Germany
Bangladesh

• Ingestion:
  – Bogura (N 50)
  – Cumilla (N 25)

• Inhalation: Chattogram (N 7)
Physical Properties

• Tabs, pellets, granules, dust
• Tablets: greenish gray
  – 3 g (56 % AlP, 44 % ammonium carbonate)
• Release of PH3 (1gm) when it comes in contact with moisture or gastric HCL.
  – ‘decaying fishlike‘/ garliclike odour: substituted phosphines, diphosphines, and arsine
  – Pure phosphine is a colorless and odorless gas.
• Flammable: spontaneous ignition
Routes of exposure

• Inhalation: between 1900 and 1960: accidental

• Ingestion: DSH

• Dermal and ocular absorption: reported*

Toxic Dose

• Safe level of occupational exposure to phosphine gas at the workplace is less than 0.3 ppm for up to 10 h per day (The US National Institute of Occupational Safety and Health)

• 50 ppm: immediate threat to life
• 600 ppm for 30 min could be lethal

• Death following ingestion: 500 mg of aluminum phosphide, 4 g of zinc phosphide
• After ingestion PH3 is liberated upon contact with moisture in the oral cavity, majority upon reaching the acidic stomach juices

• PH3 is rapidly absorbed from the mucous membranes in the GIT.

• Highly soluble: widely distributed to all organs
Pathophysiology

• A cellular toxin

• Several mechs of action: proposed and debated

• Various organs are affected in different ways
Mehrpour O, et al. ALUMINIUM PHOSPHIDE POISONING
Arh Hig Rada Toksikol 2012;63:61-73
Evidence suggesting diffuse endothelial dysfunction leading to systemic capillary leak characterized by ascites, as well as pleural and pericardial effusion.
Clinical Presentation

• Depend on the route, the dose, and the interval between ingestion and presentation

• Concealment of information about dose, the nature of the ingestion, and the elapsed time since exposure

• Maintain a high index of suspicion with this demographic

• Inhalation of phosphine is a difficult clinical diagnosis
<table>
<thead>
<tr>
<th>Following ingestion</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal</td>
<td>Nausea, vomiting, epigastric discomfort, retrosternal burning, diarrhea</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Hypotension, shock, arrhythmias</td>
</tr>
<tr>
<td>Respiratory</td>
<td>Tachypnea, cyanosis, ARDS</td>
</tr>
<tr>
<td>Hepatic</td>
<td>Tender hepatomegaly, jaundice, elevated Transaminases</td>
</tr>
<tr>
<td>Renal</td>
<td>Oliguria, acute renal failure</td>
</tr>
<tr>
<td>Central nervous</td>
<td>Altered sensorium, restlessness, coma</td>
</tr>
<tr>
<td>system</td>
<td></td>
</tr>
<tr>
<td>Metabolic</td>
<td>Metabolic acidosis, hypomagnesemia, hypermagnesemia, hypokalemia</td>
</tr>
<tr>
<td>Signs of capillary leak</td>
<td>Ascites, pleural effusion and ARDS</td>
</tr>
<tr>
<td>------------------------</td>
<td>-----------------------------------</td>
</tr>
<tr>
<td>Others</td>
<td>DIC, intravascular hemolysis, gastrointestinal bleeding, fulminant hepatic failure, congestive heart failure, and, rarely, pericarditis</td>
</tr>
</tbody>
</table>
‘A study on epidemiology, clinical presentation and outcome of Aluminum phosphide poisoning.’

Dr. Md. Rashadul Kabir, Shaheed Ziaur Rahman Medical college, Bogura. 2011
Following inhalation

Chest tightness, cough, shortness of breath, dizziness, diplopia, weakness, paresthesias, tremors and pulmonary edema if severe exposure
<table>
<thead>
<tr>
<th>Name</th>
<th>Age (yr)</th>
<th>Jo 18</th>
<th>Mi 22</th>
<th>Mo 30</th>
<th>ASA 24</th>
<th>Sa 28</th>
<th>Sh 15</th>
<th>Bi 28</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dizziness</td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Fatigue</td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Chest tightness</td>
<td></td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Headache</td>
<td></td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Nausea</td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Vomiting</td>
<td></td>
<td>3</td>
<td>5</td>
<td>3</td>
<td>&gt; 10</td>
<td>&gt; 20</td>
<td>8–9</td>
<td>4</td>
</tr>
</tbody>
</table>

**Signs**

| Anaemia  |        | -     | Mild | -     | Mild   | -     | -     | -     |
| Cyanosis |        | -     | -    | -     | -      | -     | -     | -     |
| Resp. rate |      | 28    | 20   | 22    | 34     | 20    | 22    | 20    |
| Pulse/min |       | 120   | 80   | 80    | 124 AF | 108   | 88    | 60    |
| BP mm Hg  |         | 90/50 | 120/90 | 95/60 | 70/40 | 100/70 | 110/60 | 130/80 |
| Temp (°F) |         | 101   | N    | N     | N      | 101   | N     | N     |
| GCS      |         | 15    | 15   | 15    | 15     | 15    | 15    | 15    |
| Ataxia   |         | +     | +    | +     | +      | +     | -     | -     |
| Tremor   |         | +     | +    | -     | +      | +     | -     | -     |
Chronic poisoning

• Usually those who work in silos
• Cough, dyspnoea, chest pain, drowsiness, loss of appetite, and epigastric pain.
• Toothache and mandibular swelling and necrosis (phossy jaw).
• Chronic dermal exposure to 0.4 mg L$^{-1}$ (0.4 ppm) of phosphine gas may cause dermal congestion and sensitivity.
Associated sequel

One-third of the patients presents with dysphagia

- Esophageal stricture
- Tracheo-esophageal fistula
## ECG changes

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Arrhythmias</strong></td>
<td>Sinus tachycardia, bradycardia, supraventricular ectopics, VEs, AF, VF</td>
</tr>
<tr>
<td><strong>Conduction defects</strong></td>
<td>Wide QRS complex, A-V conduction defects, bundle branch block, complete heart block</td>
</tr>
<tr>
<td><strong>ST-T changes</strong></td>
<td>ST depression, ST elevation, T-wave changes</td>
</tr>
</tbody>
</table>
‘A study on epidemiology, clinical presentation and outcome of Aluminum phosphide poisoning.’
Dr. Md. Rashadul, Kabir Shaheed Ziaur Rahman Medical college, Bogura. 2011

VT in 40%
VF in 23.3%,
SVT in 46.7%
Atrial flutter/fibrillation in 20%
Hypotension: 76% to 100%.
Outcome

• Correlates best with
  – number of vomiting episodes after ingestion and
  – severity of the patient’s hypotension and acidosis
• Reported 40-80%

• The majority of deaths: 12–24 hr: refractory hypotension and dysrhythmias.
• Deaths after 24 h: ARDS, liver failure, renal failure, or other complications
• Bogura: 50%; Cumilla: 80%
Diagnosis

• History of ingestion
• Symptoms and signs compatible with aluminum phosphide ingestion
  – Emesis with vomitus smelling like decaying fish or garlic
  – Severe hypotension or shock
  – Metabolic acidosis
  – Abnormalities in cardiac rate or rhythm
• The diagnosis of phosphide exposure can be confirmed through detection of phosphine in exhaled air or stomach aspirate using the silver nitrate test

• Neither phosphine nor its metabolites can be reliably detected in urine or blood

• Breath phosphine: phosphine detector tubes, gas chromatography with nitrogen phosphorus detection (GC-NPD)
Other Invs

- ABG
- CXR
- ECG
- Echocardiography
- Serum electrolytes
- Blood sugar
- LFTs
- Renal function
Management

• No Antidote

• Several agents or approaches tried: has been debated against
<table>
<thead>
<tr>
<th>Treatment</th>
<th>Experimental model</th>
<th>Dose/route of AIP</th>
<th>Dose/route</th>
<th>Main findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnesium sulfate</td>
<td>Human study</td>
<td>–</td>
<td>0.1-2 mM</td>
<td>Improved oxidative stress status</td>
</tr>
<tr>
<td>Melatonin</td>
<td><em>In vitro</em> (Rat brain homogenate)</td>
<td>0.25-2 mM</td>
<td>0.1-2 mM</td>
<td>Antioxidant activity</td>
</tr>
<tr>
<td></td>
<td>Animal study (Rats)</td>
<td>4 mg/kg IP</td>
<td>10 mg/kg IP</td>
<td>Increased ATP production</td>
</tr>
<tr>
<td></td>
<td>Animal study (Rats)</td>
<td>16.7 mg/kg</td>
<td>40-50 mg/kg</td>
<td>Prevention of apoptosis</td>
</tr>
<tr>
<td></td>
<td>Animal study (Rats)</td>
<td>2 mg/kg</td>
<td>10 mg/kg IP</td>
<td></td>
</tr>
<tr>
<td>Coconut oil</td>
<td>Human study</td>
<td>12 g</td>
<td>Oral</td>
<td>Increased survival rate</td>
</tr>
<tr>
<td>N-acetyl cysteine</td>
<td>Animal study (Mice)</td>
<td>10-20-40 mg/kg IP</td>
<td>50-100 mg/kg</td>
<td>Delaying the latency of death</td>
</tr>
<tr>
<td></td>
<td>Animal study (Rats)</td>
<td>12.5 mg/kg</td>
<td>6.25 mg/kg/min infusion for 30 min</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Human study</td>
<td>–</td>
<td>140 mg/kg infusion (loading dose) followed by 70 mg/kg/IV infusion every 4 h</td>
<td>Prevention of hepatic necrosis Reduction of the duration of hospitalization and mechanical ventilation Decrement of mortality rate</td>
</tr>
<tr>
<td>Sodium selenite</td>
<td>Animal study (Mice)</td>
<td>10-20-40 mg/kg IP</td>
<td>300 mg/kg infusion for 20 h</td>
<td></td>
</tr>
<tr>
<td>Vitamin E</td>
<td>Case report</td>
<td>–</td>
<td>3 mg/kg</td>
<td>Improvement of cardiac alteration</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>400 units IM</td>
<td>Reduction of pulmonary and liver complications</td>
</tr>
<tr>
<td>Triiodothyronine</td>
<td>Animal study (Rats)</td>
<td>12 mg/kg</td>
<td>3 μg/kg</td>
<td>Decrement of mechanical ventilation duration</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Reduction of the mortality</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Improvement of cardiovascular complications</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Decrement of oxidative stress</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Increment of ATP</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Decrement of apoptosis rate</td>
</tr>
<tr>
<td>Liothyronine</td>
<td>Human study</td>
<td>–</td>
<td>50 μg oral</td>
<td>Amelioration of cardiac complications and oxidative stress</td>
</tr>
<tr>
<td>Vasopressin</td>
<td>Animal study (Rats)</td>
<td>12.5 mg/kg</td>
<td>2 IU/kg IP</td>
<td>Cardio protective effects</td>
</tr>
<tr>
<td></td>
<td></td>
<td>gavage</td>
<td></td>
<td>Increment of ATP</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12.5 mg/kg</td>
<td>0.25 mg/kg</td>
<td>Decrement of oxidative damage and apoptosis</td>
</tr>
<tr>
<td>Milrinone</td>
<td>Animal study (Rats)</td>
<td>58 mg/l</td>
<td>25, 50, 100 and 200 mg/l</td>
<td></td>
</tr>
<tr>
<td><em>Laurus nobilis</em></td>
<td><em>In vitro</em> (Cultured human blood cells)</td>
<td></td>
<td></td>
<td>Decrement of oxidative stress</td>
</tr>
<tr>
<td></td>
<td>Animal study (Rats)</td>
<td>–</td>
<td>200 mg/kg for 14 days, IP</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Decrement of DNA damage</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Suppression of genetic damage</td>
</tr>
<tr>
<td>6-aminonicotinamide</td>
<td><em>In vitro</em> (Isolated rat hepatocyte)</td>
<td>–</td>
<td>3 μg/ml</td>
<td>Decrement of oxidative stress</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>for 2 h</td>
<td>Decrement of ROS formation and lipid peroxidation</td>
</tr>
<tr>
<td>Boric acid</td>
<td><em>In vitro</em> (Distilled water, activated charcoal, and saturated boric acid solution)</td>
<td>1 g/200 ml</td>
<td>Saturated boric acid solution</td>
<td></td>
</tr>
<tr>
<td>Acetyl-l-carnitine</td>
<td>Animal study (Rats)</td>
<td>–</td>
<td>100, 200, 300 mg/kg, IP</td>
<td>Increment of cytochrome oxidase and ATP production Decrement of oxidative stress Decrement of apoptosis</td>
</tr>
</tbody>
</table>
Take history of AlP tablet ingestion or inhalation
(establish place and label of the purchased tablet/ time of ingestion/ signs and symptoms on admission/ vital signs and VBG)

Gastrointestinal signs/symptoms/acidosis/decreased blood pressure or CO level >10 (62) or positive silver nitrate paper test (27)

Yes

GI decontamination (in the 1st post-ingestion hour) with NaHCO₃ gavage (two 44-meq vials [100 mL] per L) and KMnO₄ (1/10000/1 g per 10 L)
- protect the airways (consider RSI)
- establish central IV access
- perform biochemistry, ECG, chest x-ray, ABG, or echocardiography (27)

Consider HD or CRRT in case of severe persistent acidosis/ overload/ or renal failure (29)

- serum bicarbonate is <15 or pH is <7.2 (68)
- bicarbonate deficit = (20- serum bicarbonate level of the patient ) x 0.4 / patient's weight

No

- consider NAC (as antioxidant) at 50-100 mg kg⁻¹ day⁻¹ (TDS) (62)
- consider vitamin E (as antioxidant) at 400 IU every 12 h (82)
- consider steroids in patients in shock or to lower inotrope dosage (93)
- consider diuretics in non-hypotensive patients with pulmonary oedema (57)

Abbreviations: GI: gastrointestinal; NaHCO₃: sodium bicarbonate; KMnO₄: potassium permanganate; ECG: electrocardiogram; ABG: arterial blood gases; IABP: intra-aortic balloon pump; PAWP: pulmonary artery wedge pressure; SBP: systolic blood pressure; CVP: central venous pressure; HIE: hyperinsulinemia-hypoglycemia; HD: haemodialysis; CRRT: continuous renal replacement therapy; MgSO₄: magnesium sulphate; ARDS: acute respiratory distress syndrome; NAC: N-acetyl cysteine
Take history of AP tablet ingestion or inhalation
(establish place and label of the purchased tablet/ time of ingestion/ signs and symptoms on admission/ vital signs and VBG)

Gastrointestinal signs/symptoms/acidity/decreased blood pressure or CO level >10 (62) or positive silver nitrate paper test (27)

Yes

GI decontamination (in the 1st post-ingestion hour) with NaHCO₃ gavage (two 44 meq vials [100 mL] per l) and KMnO₄, (1/10000/1 g per 10 L)
- protect the airways (consider RSI)
- establish central IV access
- perform biochemistry, ECG, chest x-ray, ABG, or...

No

Admission / follow with serial VBGs

Acidosis / other symptoms of poisoning

- consider NAC (as antioxidant) at 50-100 mg kg⁻¹ day⁻¹ (TDS) (62)
- consider vitamin E (as antioxidant) at 400 IU every 12 h (82)
- consider steroids in patients in shock or to lower inotrope dosage (93)
- consider diuretics in non-hypotensive patients with pulmonary oedema (57)

If hypotension develops (SBP<90 mmHg):
- insert CV line to check CVP
- give N/S or ringer (2x10 mL kg⁻¹)
- give norepinephrine (2-4 µg min⁻¹) or phenylephrine (4-6 µg min⁻¹) to keep SBP >90 mmHg and urination at 0.5-1 mL kg⁻¹ h⁻¹
- anti-arrhythmics / DC cardioversion available

Consider bicarbonate therapy if:
- serum bicarbonate is <15 or pH is <7.2 (68)
- bicarbonate deficit = (20 - serum bicarbonate level of the patient) x 0.4 x patient’s weight

Consider HD or CRRT in case of severe persistent acidosis/ overload/ or renal failure (29)

Abbreviations: GI: gastrointestinal; NaHCO₃: sodium bicarbonate; KMnO₄: potassium permanganate; ECG: electrocardiogram; ABG: arterial blood gases; IABP: intra-aortic balloon pump; PAWP: pulmonary artery wedge pressure; SBP: systolic blood pressure; CVP: central venous pressure; HIE: hyperviscosityosaemia-angioedema; HD: haemodialysis; CRRT: continuous renal replacement therapy; MgSO₄: magnesium sulphate; ARDS: acute respiratory distress syndrome; NAC: N-acetyl cysteine
Take history of API tablet ingestion or inhalation
(establish place and label of the purchased tablet/ time of ingestion/ signs and symptoms on admission/ vital signs and VBG)

Gastrointestinal signs/symptoms/acidosis/decreased blood pressure or CO level >10 (62) or positive silver nitrate paper test (27)

Yes

GI decontamination (in the 1st post-ingestion hour) with NaHCO₃ gavage (two 44 meq vials [100 mL] per L) and KMnO₄ (1/10000/1 g per 10 L)
- protect the airways (consider RSI)
- establish central IV access
- perform biochemistry, ECG, chest x-ray, ABG, or echocardiography (27)

Admission / follow with serial VBGs

No

Acidosis / other symptoms of poisoning

Consider administration of MgSO₄ (as antioxidant) at 1 g stat, followed by 1 g qh for 3 h and then 1 g every 6 h (7)

- consider NAC (as antioxidant) at 50-100 mg kg⁻¹ day⁻¹ (TDS) (62)
- consider vitamin E (as antioxidant) at 400 IU every 12 h (82)
- consider steroids in patients in shock or to lower inotrope dosage (93)
- consider diuretics in non-hypotensive patients with pulmonary oedema (57)

If CO level is >18:
- start HIE protocol (1 U kg⁻¹ insulin stat, followed by 0.5 U kg⁻¹ h⁻¹ infusions; can be increased to 10 U kg⁻¹ h⁻¹) + 0.5-1 g kg⁻¹ dextrose stat, followed by 0.5-1 g kg⁻¹ h⁻¹
- maintain BS between 100 and 150 mg dL⁻¹
- maintain K between 2.8 and 3.2 meq L⁻¹ (62)
- consider pacemaker and IABP (72, 75)
- CVP/PAWP-guided fluid therapy (27)

balloon pump; PAPW: pulmonary artery wedge pressure; SBP: systolic blood pressure; CVP: central venous pressure; HIE: hyperinsulinaemia-hypoglycaemia HD: haemodialysis; CRRT: continuous renal replacement therapy; MgSO₄: magnesium sulphate; ARDS: acute respiratory distress syndrome; NAC: N-acetyl cysteine
Take history of AP tablet ingestion or inhalation
(establish place and label of the purchased tablet/time of ingestion/signs and symptoms on admission/vital signs and VBG)

Gastrointestinal signs/symptoms/acidosis/decreased blood pressure or CO level >10 (62) or positive silver nitrate paper test (27)

Yes

- GI decontamination (in the 1st post-ingestion hour) with NaHCO₃ gavage (two 44-meq vials [100 mL] per L) and KMnO₄ (1/10000/1 g per 10 L)
  - protect the airways (consider RSI)
  - establish central IV access
  - perform biochemistry, ECG, chest X-ray, ABG, or echocardiography (27)

If hypotension develops (SBP-90 mmHg):
- insert N/S or ringer (2x10 mL kg⁻¹)
- give norepinephrine (2-4 µg min⁻¹) or phenylephrine (4-6 µg min⁻¹) to keep SBP >90 mmHg and urine output at 0.5-1 mL kg⁻¹ h⁻¹
- anti-arrhythmics/DC cardioversion available

If CO level is ≥18:
- start HIE protocol (1 U kg⁻¹ min stat, followed by 0.5 U kg⁻¹ h⁻¹ infusions; can be increased to 10 U kg⁻¹ h⁻¹) + 0.5-1 g kg⁻¹ dextrose stat, followed by 0.5-1 g kg⁻¹ h⁻¹
- maintain BS between 100 and 150 mg dL⁻¹
- maintain K between 2.8 and 3.2 meq L⁻¹ (62)
- consider pacemaker and IABP (72, 75)

- consider NAC (as antioxidant) at 50-100 mg kg⁻¹ day⁻¹ (TDS) (62)
- consider vitamin E (as antioxidant) at 400 IU every 12 h (82)
- consider steroids in patients in shock or to lower inotrope dosage (93)
- consider diuretics in non-hypotensive patients with pulmonary oedema (57)

No

- Admission/follow with serial VBGs

Acidosis/other symptoms of poisoning

Consider administration of MgSO₄ (as antioxidant) at 1 g stat, followed by 1 g qh for 3 h and then 1 g every 6 h (7)

In case of toxic myocarditis or persistent hypovolemic shock or arrhythmia consider:
- IABP (72)
- extracorporeal membrane oxygenation (ECMO) (76)

If acute lung injury or ARDS develops:
- treat ARDS
- provide ventilatory support (27)
- consider methaemoglobinemia in persistent cyanosis and administer 2 mg kg⁻¹ methylene blue over 5 min (35)

Consider HD or CRRT in case of severe persistent acidosis/overload or renal failure (29)

Abbreviations: GI: gastrointestinal; NaHCO₃: sodium bicarbonate; KMnO₄: potassium permanganate; ECG: electrocardiogram; ABG: arterial blood gases; IABP: intra-aortic balloon pump; PAWP: pulmonary artery wedge pressure; SBP: systolic blood pressure; CVP: central venous pressure; HIE: hyperinsulinaemia-hyperglycaemia; HD: haemodialysis; CRRT: continuous renal replacement therapy; MgSO₄: magnesium sulphate; ARDS: acute respiratory distress syndrome; NAC: N-acetyl cysteine
Take history of AIP tablet ingestion or inhalation
(establish place and label of the purchased tablet/ time of ingestion/ signs and symptoms on admission/ vital signs and VBG)

Gastrointestinal signs/symptoms/acidosis/decreased blood pressure or CO level >10 (62) or positive silver nitrate paper test (27)

Yes

GI decontamination (in the 1st post-ingestion hour) with NaHCO₃, gavage (two 44-meq vials [100 mL] per L) and KMnO₄, (1/10000/1 g per 10 L)
- protect the airways (consider RSI)
- establish central IV access
- perform biochemistry, ECG, chest x-ray, ABG, or echocardiography (27)

If hypotension develops (SBP<90 mmHg):
- insert CV line to check CVP
- give N/S or ringer (2x10 mL kg⁻¹)
- give norepinephrine (2-4 µg min⁻¹) or phenylephrine (4-6 µg min⁻¹) to keep SBP>90 mmHg and maintain at 0.5-1 mL kg⁻¹ h⁻¹
- anti-arrhythmias / DC cardioversion available

If CO level is >18:
- start HIE protocol (1U kg⁻¹ insulins stat, followed by 0.5U kg⁻¹ h⁻¹ infusions; can be increased to 10 U kg⁻¹ h⁻¹ + 0.5-1 g kg⁻¹ dextrose s.l. kg h⁻¹
- maintain BS between 100 and
- maintain K between 2.5 and
- consider pacemaker and IABP
- CVP/PAWP-guided fluid therapy

Consider HD or CRRT in case acidosis/ overload/ or renal failure

No

Admission / follow with serial VBGs

Acidosis / other symptoms of poisoning

Consider administration of MgSO₄ (as antioxidant) at 1 g stat, followed by 1 g qh for 3 h and then 1 g every 6 h (7)

In case of toxic myocarditis or persistent hypovolemic shock or arrhythmia consider:
- IABP (72)
- extracorporeal membrane oxygenation (ECMO) (76)

Consider bicarbonate therapy if:
- serum bicarbonate is <15 or pH is <7.2 (68)
- bicarbonate deficit = (20- serum bicarbonate level of the patient ) ×0.4×patient's weight

Take history of AP tablet ingestion or inhalation (establish place and label of the purchased tablet/ time of ingestion/ signs and symptoms on admission/ vital signs and VBG)

Gastrointestinal signs/symptoms/acidosis/decreased blood pressure or CO level >10 (62) or positive silver nitrate paper test (27)

- Yes
  - GI decontamination (in the 1st post-ingestion hour) with NaHCO3 gavage (two 44-meq vials [100 mL] per l) and KMnO4 (1/10000 g per 1 L)
  - protect the airways (consider RSI)
  - establish central IV access
  - perform biochemistry, ECG, chest x-ray, ABG, or echocardiography (27)

- No
  - Admission / follow with serial VBGs
  - Acidosis / other symptoms of poisoning

If hypotension develops:
- insert CV line to check CO
- give N/S or ringer (2x10)
- give norepinephrine (2-4 (4-6 µg min^-1) to keep SBP at 0.5-1 mL kg^-1 h^-1
- anti-arrhythmics / DC cardioversion

If CO level is >18:
- start HIE protocol (1U kg^-1 h^-1 + 0.5 U kg^-1 h^-1 infusion; can be titrated to keep SBP at 100 mm Hg)
- maintain BS between 100 and 120
- maintain K between 2.5 and 3.0
- consider pacemaker and IABP (72, 75)
- CVP/PAWP-guided fluid therapy (27)

Consider bicarbonate therapy if:
- serum bicarbonate is <15 or pH is <7.2 (68)
- bicarbonate deficit = (20 - serum bicarbonate level of the patient) x 0.4 x patient’s weight

Consider HD or CRRT in case of severe persistent acidosis/ overload/ or renal failure (29)

If acute lung injury or ARDS develops:
- treat ARDS
- provide ventilatory support (27)
- consider methaemoglobinemia in persistent cyanosis and administer 2 mg kg^-1 methylene blue over 5 min (35)

Abbreviations: GI: gastrointestinal; NaHCO3: sodium bicarbonate; KMnO4: potassium permanganate; ECG: electrocardiogram; ABG: arterial blood gases; IABP: intra-aortic balloon pump; PAWP: pulmonary artery wedge pressure; SBP: systolic blood pressure; CVP: central venous pressure; HIE: hyperinsulinemia-angiotensinemia HD: haemodialysis; CRRT: continuous renal replacement therapy; MgSO4: magnesium sulphate; ARDS: acute respiratory distress syndrome; NAC: N-acetyl cysteine
Take history of AIP tablet ingestion or inhalation
(establish place and label of the purchased tablet/ time of ingestion/ signs and symptoms on admission/ vital signs and VBG)

Gastrointestinal signs/symptoms/acidosis/decreased blood pressure or CO level >10 (62) or positive silver nitrate paper test (27)

**Yes**

- GI decontamination (in the 1st post-ingestion hour) with NaHCO₃, gavage/syne 4L, Na₂S₂O₃ (100 ml) and KMnO₄ (1/10)
- protect the airways
- establish central IV
- perform biochemical echocardiography (27)

**No**

- Admission / follow with serial VBGs

If hypotension develops:
- insert CV line to check CO
- give N/S or ringer (1 L)
- give norepinephrine (4-6 μg min⁻¹) to keep CO at 5-1 ml kg⁻¹ h⁻¹
- anti-arrhythmics (27)

If CO level is >18:
- start HIE protocol (1 U kg⁻¹ inastin stat, followed by 0.5 U kg⁻¹ h⁻¹ infusions; can be increased to 10 U kg⁻¹ h⁻¹ + 0.5-1 g kg⁻¹ dextrose stat, followed by 0.5-1 g kg⁻¹ h⁻¹
- maintain BS between 100 and 150 mg dl⁻¹
- maintain K between 2.8 and 3.2 meq L⁻¹ (62)
- consider pacemaker and IABP (72, 75)
- CVP/PAWP-guided fluid therapy (27)

Consider HD or CRRT in case of severe persistent acidosis/ overload/ or renal failure (29)

If acute lung injury or ARDS develops:
- treat ARDS
- provide ventilatory support (27)
- consider methaemoglobinemia in persistent cyanosis and administer 2 mg kg⁻¹ methylene blue over 5 min (35)

In case of toxic myocarditis or persistent hypovolemic shock or arrhythmia consider:
- IABP (72)
- extracorporeal membrane oxygenation (ECMO) (76)

If acute lung injury or ARDS develops:
- serum bicarbonate is <15 or pH is <7.2 (68)
- bicarbonate deficit = (20- serum bicarbonate level of the patient) × 0.4 × patient’s weight

Abbreviations: GI: gastrointestinal; NaHCO₃: sodium bicarbonate; KMnO₄: potassium permanganate; ECG: electrocardiogram; ABG: arterial blood gases; IABP: intra-aortic balloon pump; PAWP: pulmonary artery wedge pressure; SBP: systolic blood pressure; CVP: central venous pressure; HIE: hypoxia-ischaemia-eneglycaemia syndrome; ARDS: acute respiratory distress syndrome; NAC: N-acetyl cysteine
Take history of AlP tablet ingestion or inhalation (establish place and label of the purchased tablet/ time of ingestion/ signs and symptoms on admission/ vital signs and VBG)

Gastrointestinal signs/symptoms/acidosis/decreased blood pressure or CO level >10 (62) or positive silver nitrate paper test (27)

Yes

GI decontamination (in the 1st post-ingestion hour) with NaHCO₃, gavage (1/1) and KMnO₄ (1/10)
- protect the airways
- establish central IV
- perform biochemistry/ echocardiography (2)

If hypotension develops (CO <60 mmHg):
- insert CV line to check CVP
- give N/S or ringer (2x10 mL kg⁻¹)
- give norepinephrine (2-4 μg min⁻¹) or phenylephrine (4-6 μg min⁻¹) to keep SBP 90 mmHg and urine output 0.5-1 mL kg⁻¹ h⁻¹
- anti-arrhythmics/ DC cardioversion available

If CO level is <18:
- start HIE protocol (1 U kg⁻¹ intramuscular stat, followed by 0.5 U kg⁻¹ h⁻¹; infusions can be increased to 10 U kg⁻¹ h⁻¹) + 0.5-1 g kg⁻¹ dextrose stat, followed by 0.5-1 g kg⁻¹ h⁻¹
- maintain BS between 100 and 150 mg dL⁻¹
- maintain K between 2.8 and 3.2 meq L⁻¹ (62)
- consider pacemaker and IABP (72, 75)
- CVP/PAWP-guided fluid therapy (27)

Consider HD or CRRT in case of severe persistent acidosis/ overload/ or renal failure (29)

Consider administration of MgSO₄ (as antioxidant) at 1 g stat, followed by 1 g qh for 3 h and then 1 g every 6 h (7)

No

Admission / follow with serial VBGs

In case of toxic myocarditis or persistent hypovolemic shock or arrhythmia consider:
- IABP (72)
- extracorporeal membrane oxygenation (ECMO) (76)

If acute lung injury or ARDS develops:
- treat ARDS
- provide ventilatory support (27)
- consider methaemoglobinemia in persistent cyanosis and administer 2 mg kg⁻¹ methylene blue over 5 min (35)

Consider bicarbonate therapy if:
- serum bicarbonate is <15 or pH is <7.2 (68)
- bicarbonate deficit = (20- serum bicarbonate level of the patient ) × 0.4 × patient’s weight

Abbreviations: GI: gastrointestinal; NaHCO₃: sodium bicarbonate; KMnO₄: potassium permanganate; ECG: electrocardiogram; ABG: arterial blood gases; IABP: intra-aortic balloon pump; PAWP: pulmonary artery wedge pressure; SBP: systolic blood pressure; CVP: central venous pressure; HIE: hyperperfusionemia-encephalopathy; HD: haemodialysis; CRRT: continuous renal replacement therapy; MgSO₄: magnesium sulphate; ARDS: acute respiratory distress syndrome; NAC: N-acetyl cysteine
Take history of AIP tablet ingestion or inhalation
(establish place and label of the purchased tablet/ time of ingestion/ signs and symptoms on admission/ vital signs and VBG)

Gastrointestinal signs/symptoms/acidosis/decreased blood pressure or CO level >10 (62) or positive silver nitrate paper test (27)

Yes

GI decontamination (in the 1st post-ingestion hour) with NaHCO₃ gavage (2 x 44-meq vials [100 mL] per l) and KMnO₄ (1/10000/1 g per 10 L)
- protect the airways (consider RSI)
- establish central IV access
- perform biochemistry, ECG, chest x-ray, ABG, or echocardiography (27)

If hypotension develops (SBP<90 mmHg):
- insert CV line to check CVP
- give N/S or ringer (2 x 10 mL kg⁻¹)
- give norepinephrine (2-4 μg min⁻¹) or phenylephrine (4-6 μg min⁻¹) to keep SBP>90 mmHg and urine output>0.5-1 mL kg⁻¹ h⁻¹
- anti-arrhythmics / DC cardioversion available

If CO level is >18:
- start HIE protocol (1 U kg⁻¹ insulin stat, followed by 0.5 U kg⁻¹ h⁻¹ infusions; can be increased to 10 U kg⁻¹ h⁻¹) + 0.5-1 g kg⁻¹ dextrose stat, followed by 0.5-1 g kg⁻¹ h⁻¹
- maintain BS between 100 and 150 mg dL⁻¹
- maintain K between 2.5 and 3.2 meq L⁻¹ (62)
- consider pacemaker and IABP (72, 75)
- CVP/PAWP-guided fluid therapy (27)

Consider bicarbonate therapy if:
- serum bicarbonate is <15 or pH is <7.2 (68)
- bicarbonate deficit = (20- serum bicarbonate level of the patient) x 0.4 x patient's weight

Admission / follow with serial VBGs

Acidosis / other symptoms of poisoning

- consider NAC (as antioxidant) at 50-100 mg kg⁻¹ day⁻¹ (TDS) (62)
- consider vitamin E (as antioxidant) at 400 IU every 12 h (82)
- consider steroids in patients in shock or to lower inotrope dosage (93)
- consider diuretics in non-hypotensive patients with pulmonary oedema (67)

Consider administ:
1 g stat, followed by 6 h (7)

In case of toxic my shock or arrhythmias
- IABP (72)
- extracorporeal me

If acute lung injury
- treat ARDS
- provide ventilator
- consider methaemoglobin and admit over 5 min (35)

Consider HD or CRRT in case of severe persistent acidosis/ overload/ or renal failure (29)

Abbreviations: GI: gastrointestinal; NaHCO₃: sodium bicarbonate; KMnO₄: potassium permanganate; ECG: electrocardiogram; ABG: arterial blood gases; IABP: intra-aortic balloon pump; PAWP: pulmonary artery wedge pressure; SBP: systolic blood pressure; CVP: central venous pressure; HIE: hyperinsulinemia-anginaemia HD: haemodialysis; CRRT: continuous renal replacement therapy; MgSO₄: magnesium sulphate; ARDS: acute respiratory distress syndrome; NAC: N-acetyl cysteine
Take history of AIP tablet ingestion or inhalation (establish place and label of the purchased tablet/ time of ingestion/ signs and symptoms on admission/ vital signs and VBG)

Gastrointestinal signs/symptoms/acidosid/decreased blood pressure or CO level >10 (62) or positive silver nitrate paper test (27)

Yes

- establish central IV access
- perform biochemistry, ECG, chest x-ray, ABG, or echocardiography (27)

If hypotension develops (SBP<90 mmHg):
- insert CV line to check CVP
- give N/S or ringer (2x10 mL kg⁻¹)
- give norepinephrine (2-4 µg min⁻¹) or phenylephrine (4-6 µg min⁻¹) to keep SBP>90 mmHg and urine output 0.5-1 mL kg⁻¹ h⁻¹
- anti-arrhythmics / DC cardioversion available

If CO level is >18:
- start HIE protocol (1 U kg⁻¹ insulin stat, followed by 0.5 U kg⁻¹ h⁻¹ infusion; can be increased to 10 U kg⁻¹ h⁻¹) + 0.5-1 g kg⁻¹ dextrose stat, followed by 0.5-1 g kg⁻¹ h⁻¹
- maintain BS between 100 and 150 mg dL⁻¹
- maintain K between 2.8 and 3.2 meq L⁻¹ (62)
- consider pacemaker and IABP (72, 75)
- CVP/PAWP-guided fluid therapy (27)

Consider HD or CRRT in case of severe persistent acidosis/ overload/ or renal failure (29)

No

Consider administration of N 1 g stat, followed by 1 g qh for 6 h (7)

In case of toxic myocarditis, shock or arrhythmias consider:
- IABP (72)
- extracorporeal membrane oxygenation (ECMO) (76)

Acidosis / other symptoms of poisoning

If acute lung injury or ARDS develops:
- treat ARDS
- provide ventilatory support (27)
- consider methaemoglobinemia in persistent cyanosis and administer 2 mg kg⁻¹ methylene blue over 5 min (35)

Consider bicarbonate therapy if:
- serum bicarbonate is <15 or pH is <7.2 (68)
- bicarbonate deficit = (20 - serum bicarbonate level of the patient) × 0.4 / patient’s weight

Abbreviations: GI: gastrointestinal; NaHCO₃: sodium bicarbonate; KMnO₄: potassium permanganate; ECG: electrocardiogram; ABG: arterial blood gases; IABP: intra-arterial balloon pump; PAWP: pulmonary artery wedge pressure; SBP: systolic blood pressure; CVP: central venous pressure; HIE: hypernatremia-auglycaemia HD: haemodialysis; CRRT: continuous renal replacement therapy; MgSO₄: magnesium sulphate; ARDS: acute respiratory distress syndrome; NAC: N-acetyl cysteine
Prognosis

• Predictors of poor prognosis:
  – Low arterial pH
  – Low sodium bicarbonate levels
  – Hypotension (SBP < 90 mmHg)
  – Altered mental status

SAPS II score > 24.5
APACHE II score > 8.5
SOFA score > 7.5
Prevention

• Better regulated supply of ALP

• Legislative and administrative measures to restrict and modify its supply

• Changes in formulation to granules: helped in reducing human mortality

Conclusion

• A deadly toxin
• Increasing number of patients
• No antidote: Optimum organ support
• Guidelines for attending physicians
• Legislation/regulation to contain