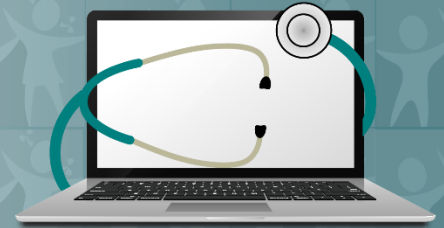




PEHSU NATIONAL CLASSROOM

Pediatric Environmental Health Specialty Units



www.pehsu.net/nationalclassroom.html



Webinars

Series of scientific webinars that provide a forum for discourse on scientific issues.

Live and On-Demand

Case Conferences
Journal Clubs
Grand Rounds

CE Available



Online Courses

Evidence-based online courses on a variety of children's environmental health topics.

Interactive and Self-Paced

CE Available



Resource Catalog

Fact sheets, journal publications, reports, and other resources for parents, community members, patients and healthcare professionals

Topics included:
Air Quality, Pesticides, Natural Disasters, BPA, Mold, Lead, Mercury



Phosphine Reminds Us That Children are Not Little Adults

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Medical Director
Texas Panhandle Poison Center
PEHSU Region 6

Objectives

- Describe danger of improper phosphide application in community
- Identify vulnerable age group and why
- Describe PPE required for providers
- Describe manifestations of PH_3 poisoning
- Describe treatment of PH_3 poisoning
- Describe challenges in declaring exposure site safe for reoccupancy

1/1/17 Amarillo, Texas

- Family of 10 seen at local health care facility for complaints of nausea, vomiting, diarrhea and abdominal pain.
- They were diagnosed with gastroenteritis, treated symptomatically
- Unknown if ED staff were told that father had laid pesticide under home
- PC not consulted

Family's Residence



1/2/17 Amarillo, Texas

- EMS called to home of severely ill family
- Hospital told carbon monoxide suspected
- One child in cardiac arrest, ACLS initiated
- 2nd very ill small child transported code 1
- 2 parents, 6 siblings transported with less severe signs and symptoms

Family MCI Possible Causes

- Infectious agents
- Inhaled toxins
 - Carbon Monoxide – most likely, especially winter.
- Ingested toxins
 - Next mostly likely to poison family
- Dermally absorbed toxins
 - Mainly liquids, less likely powder

Toxic Gas Dermal Absorption

- In vitro model using human donor skin
- Undamaged human skin is a good barrier
- Phosphine - up to 1000 ppm
- Hydrogen sulphide - up to 800 ppm
- At concentrations that would be lethal via inhalation, similar results for: methyl bromide, sulfuryl fluoride & chloropicrin
- Toxicol Ind Health 2017 PM 26939834, 28196457

Toxic Inhalant Mechanisms

- Physical Asphyxia
- Tissue Hypoxemia
- Systemic Toxicity
- Airway Irritation
- Deep Lung Damage

**“The Poison Is In
The Dose”
Paracelsus**

Inhalant Exposure Dose

- Concentration x
- Duration x
- Minute Ventilation x
- Bioavailability

ER Course

- 7 yo M declared dead in field
- 11 yo M declared dead in ED
 - Arrived with bloody pulmonary edema
 - COHgb undetectable
- Others: AAO, c/o stomach ache
- EMS found superwarfarin rodenticide
 - Anticoagulants don't cause sudden death
 - Bleeding only seen in one patient

Suspected Toxin

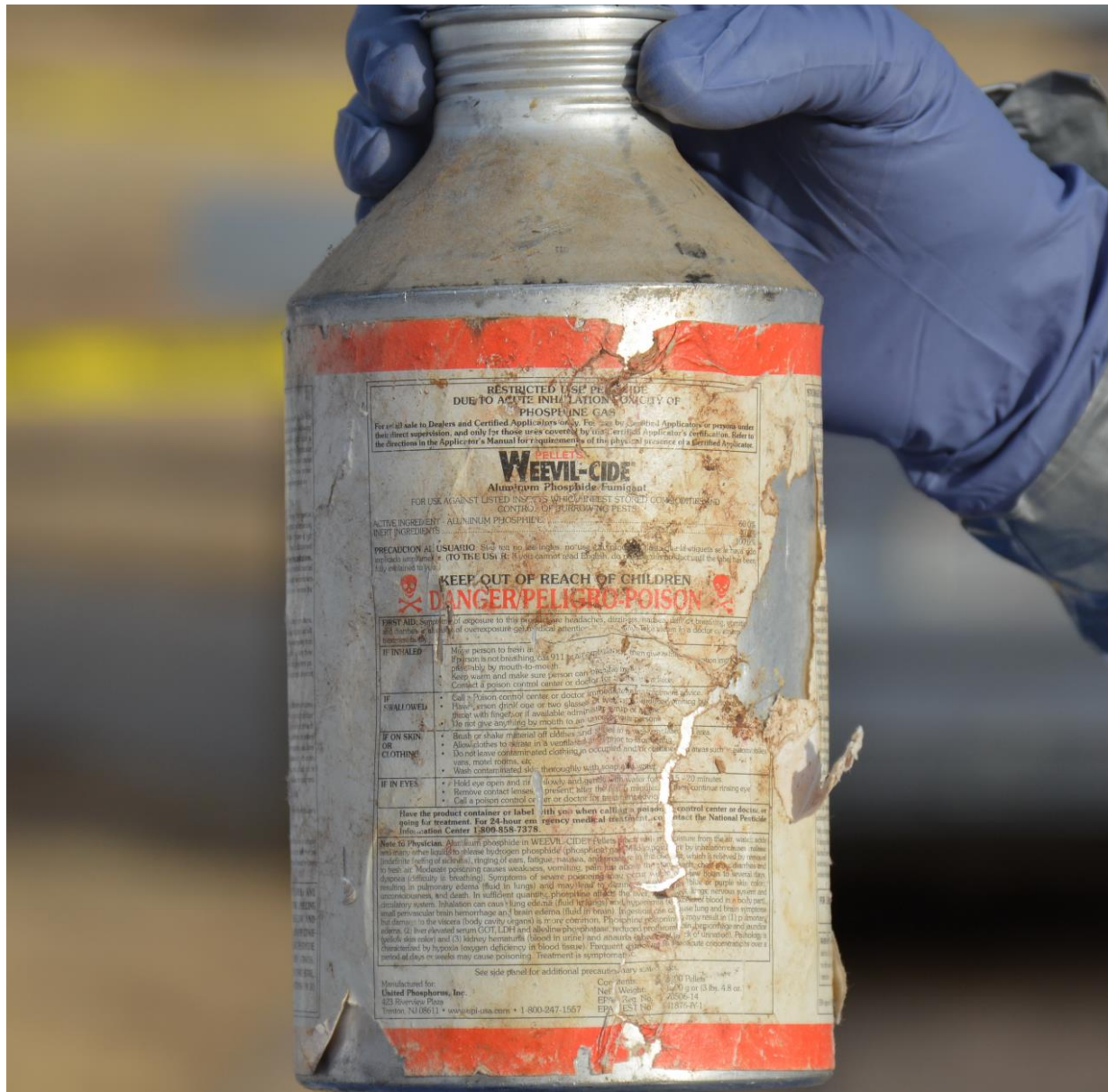
- Father placed pesticide tablets under prefabricated home, several days earlier
- Family became ill and did not improve after HCF visit.
- Therefore, father “got rid of tablets”
- Dissolved tablets with garden hose water
- Phosphine poisoning first suspected!

Weevil-Cide Tablets

WEEVIL-CIDE®



Container at Scene



Health Care Provider Safety?

- Exposure risk: ingestion vs inhalation
- Many providers/administrators came to ED
- Did patients need decontamination?
- Nurses wanted to know if they were safe
- Administrators wanted to know if ED safe
- Hospitalists wanted everyone to done PPE but unsure what level of PPE was required
- Pathologists wanted to know if PPE needed

ED Course, Continued

- 9 yo M deteriorated quickly, transferred to PICU
 - Expired in PICU despite aggressive ACLS
- 17 yo F deteriorated more gradually, CX-ray: white out, shock refractory to triple pressors/fluids, expired in ED
- 45 yo F deteriorated even more gradually, transferred to MICU, Impella inserted in cath lab
- PC identified and facilitated aeromedical transport to nearest accepting ECMO facility

Phosphide Pesticides

- Highly effective outdoor and indoor insecticide and rodenticide
- A solid fumigant used for:
 - Fumigation of agricultural products, animal feed
 - For pest control in agricultural fields
- Cheap, effective, free from toxic residue and does not affect seed viability PM 1452567
- Due to PH_3 flammability, usually combined with ammonium carbamate.

Phosphide Preparations

- 3.0 g tablets: AlP (56%), carbamate(44%)
- Celphos, Alphos, Quickphos, Phosfume, Phostoxin, Talunex, Degesch, Synfume, Chemfume, Phostek & Delicia
- Tablets contain other agents such as methanethiol, diphosphine and other impurities, which give a decaying-fish or garlic-like smell.

Phosphine Sources

- Most common forms
 - Aluminum phosphide (AlP)
 - Zinc phosphide (Zn_3P_2)
- Less common forms
 - Ca_3P_2 , Mg_3P_2
- Compressed gas (PH_3)
- Meth labs using red phosphorus method

Phosphine Exposure Limits

- OSHA PEL/ACGIH TLV: 0.3 ppm (0.4 mg/m³)
- ACGIH/OSHA STEL: 1 ppm (1.4 mg/m³)
- NIOSH IDLH: 50 ppm
- 400–600 ppm lethal within half an hour
- > 1000 ppm lethal after a few breaths

Phosphine Mortality

- Most common cause (81%) of fatal toxic suicides in NW India 1992 – 2002 PM15275009
- Mortality rate 37% to 100% overall
 - > 60% when treated by experienced clinicians at well-equipped hospitals
 - > 75% if refractory myocardial depression occurs
- In unintentional exposures to families, children invariably most severely poisoned!

Routes of Exposure

- Oral ingestion - suicide attempts
 - Majority of cases
 - Developing countries
- Inhalation – occupational or unintentional
 - Industrial countries

Pharmacology

- Gas released upon contact with acid/water
 - $\text{AlP} + 3 \text{H}_2\text{O} \rightarrow \text{Al}(\text{OH})_3 + \text{PH}_3$
 - $\text{AlP} + 3 \text{HCl} \rightarrow \text{AlCl}_3 + \text{PH}_3$
 - PH_3 is colorless and odorless
- Absorbed through gastric mucosa and lungs
- Oxidized to oxyacids then excreted in urine as hypophosphite or through lungs unchanged.

Solid Phosphide
Pellets / Tablets

+

Water or Acid



Phosphine Gas

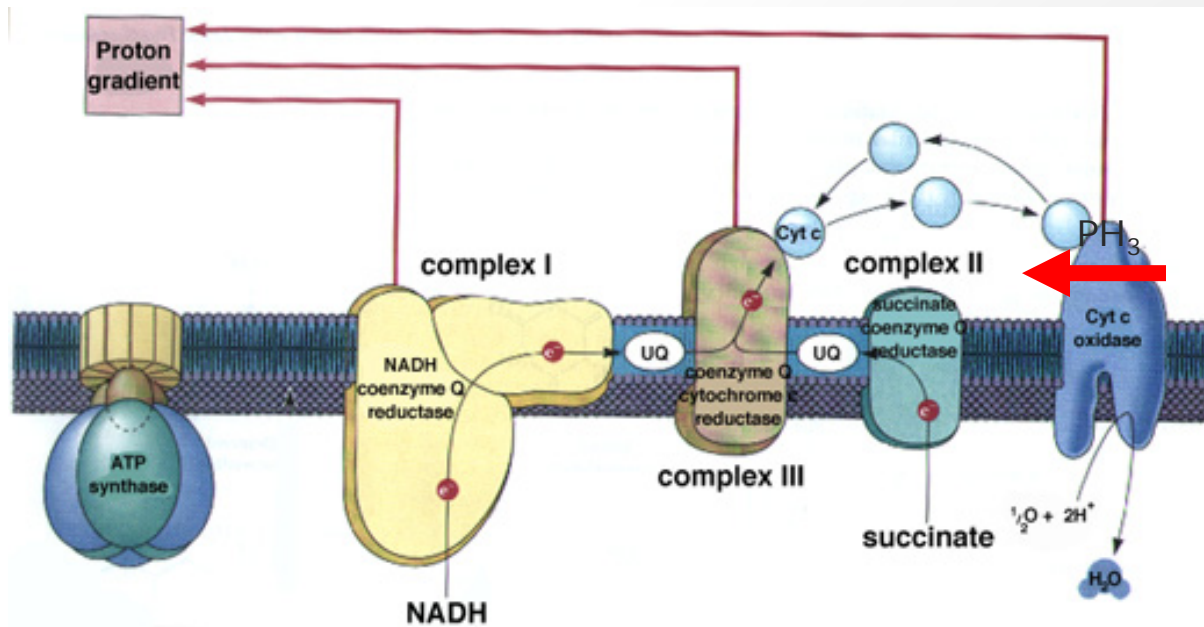
Mechanisms of Toxicity

- Inhibit Cytochrome C Oxidase
- Free Radical Generation
- Oxidize Hemoglobin
- Local Effects

Phosphine Toxicology

- Phosphine gas
 - Blocks mitochondrial oxidative metabolism
 - Inhibition of cytochrome c oxidase
 - Degradation of hydrogen ion gradient needed to drive ATP production

Mitochondrion



Inhibit Cytochrome C Oxidase

- *In vitro* - PH_3 inhibits cytochrome C oxidase
 - Proposed as primary mechanism
- *In vivo* – only 45% decrease in activity
 - No significant differences in survival
 - Similar decreases in hemorrhagic & septic shock
- Inhibits mitochondrial respirations
- Relative importance debatable

Free Radical Generation

- Forms highly reactive hydroxyl radicals
- Cellular injury from lipid peroxidation
- Decrease catalase & increase superoxide dismutase activity
- Reduces glutathione in tissues
 - (Glutathione catalyzes peroxides)
- Oxidative stress peaks within 48 h

Oxidize Hemoglobin

- Methemoglobinemia has been implicated
- Intravascular hemolysis reported with severe cases in G6PD deficient patients
- Probably a consequence of GI decon with potassium permanganate, a routine measure in some areas.

Local Effects

- Esophageal & gastric corrosion
- During inhalation or exhalation, injures alveolar capillary membrane

Clinical Manifestation

- Nausea, vomiting, diarrhea, dizziness, headache, retrosternal/epigastric pain within minutes followed by dyspnea, anxiousness, tremor, agitation and weakness
- Tachycardia, hypotension, ventricular hypokinesia and metabolic acidosis may occur within 1-2 hr
- In severe cases: acute lung injury, cardiac injury, cardiac arrhythmias, convulsion, coma, DIC, hepatotoxicity, nephrotoxicity, death

Clinical Manifestation Cont.

- Intentional ingestions usually more severe than unintentional inhalations
- Ingestion:
 - Esophageal/gastric corrosion, esophageal stricture or tracheoesophageal fistula
- Inhalation:
 - Airway irritation and breathlessness
 - Very high concentrations kill within seconds
- Either: systemic toxicity may occur rapidly

Troubling Case Reports

- Family of 6 suffered AIP poisoning in home. At 36 h, 4 yo died quickly. 15 mo died hrs later from refractory shock.
 - Pediatr Emerg Care 2011 PM: 21926889
- 29/31 crew aboard grain freighter became acutely ill from AIP fumes. One child was DOA at heliport. 4 yo developed severe shock but survived.
 - JAMA 1980 PM: 7382074
- Family of 5 had home fumigated with AIP. 8 yo expired within few hrs in ED from severe shock. 5 yo died 3 d later.
 - J Col Surg Pakistan 2015

More Troubling Cases

- Another family had home fumigated. Next morning 3 yo died within hrs in ED. 1 yo survived despite severe shock.
 - J Col Surg Pakistan 2015
- 2 children (2 yo & 4 yo) played on top of wheat pile fumigated with PH_3 . Both died within 18 hrs.
 - Eur J Toxicol Environ Hyg 1976 1278248
- Family of 4 used AIP in home to kill bedbugs. Within a day, all became ill, 2 yo died while 3 adults survived.
 - 2007 Lubbock, TX
- Interesting documentary with similar pediatric poisonings in Saudi Arabia posted on YouTube:
<https://youtu.be/H9KIL2KIwTs>

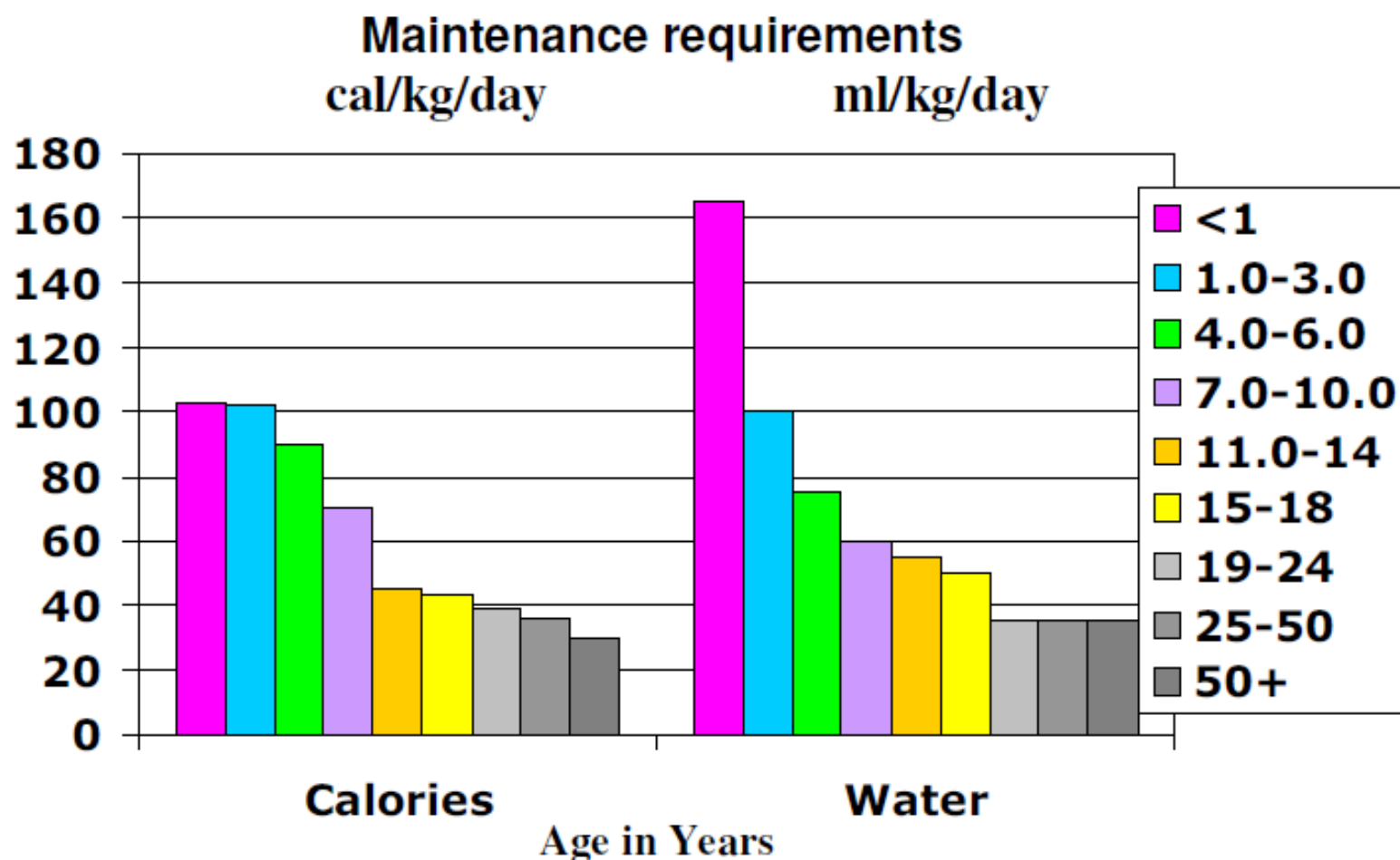
Children more Vulnerable?

- Often, children are affected most severely.
- They play on floors where PH_3 settles.
- They have higher metabolic rates.
- They have higher minute ventilation.
- They have greater body surface area.
- They have slower xenobiotic metabolism.

Children are not little adults

2. DYNAMIC DEVELOPMENTAL PHYSIOLOGY

CALORIE AND WATER NEEDS



Children are not little adults

2. DYNAMIC DEVELOPMENTAL PHYSIOLOGY

OXYGEN DEMAND

Minute ventilation per kg body weight/day



Cardiac Toxicity

- In one study with holter monitoring, the frequency of ventricular tachycardia was 40%, ventricular fibrillation 23.3%, supraventricular tachycardia 46.7% and atrial flutter/fibrillation 20%. PM 12152839
- In another review, the frequency of hypotension varied from 76% to 100%.

PH₃ Diagnostic Tests

- Diluted gastric contents heated to 50°C for 15 min with silver nitrate paper in vapor stream.
- If PH₃ present, paper will turn black due to silver phosphate. PM 1282918
- Head space analysis via gas chromatography/ nitrogen-phosphorus detector PM 18294792

Ingestion: GI Decon

- *in vitro* - liquid paraffin and vegetable oils inhibit PH_3 release
- castor oil may also accelerate GI motility and enhance GI elimination
- Emesis may off gas PH_3 , seal it in containers
- KMnO_4 (1:10,000) irrigation to oxidize PH_3 to nontoxic phosphate is not recommended.

Inhalation: External Decon

- There is no evidence of significant secondary exposure to health care providers from exhalation of PH_3 or off gassing from skin or clothing
- There is no need for health care provider personal protective equipment when treating inhalation exposures.



Patient Decontamination in a Mass Chemical Exposure Incident: National Planning Guidance for Communities



MCI: Decision To Decontaminate

- Signs and symptoms of exposure
- Visible evidence of contamination
- Proximity to source of toxin
- Toxin detected on the patient using appropriate detection technology
- Toxin: physical state & properties, absorption routes, spectrum of toxicity
- Request by patient for decontamination

OSHA BEST PRACTICES

for

HOSPITAL-BASED FIRST RECEIVERS OF VICTIMS from Mass Casualty Incidents Involving the Release of Hazardous Substances



January 2005

OSHA Recommendations

- Removal of victim's clothing may have a marked effect on the quantity of contaminant that first receivers encounter.
- Removing contaminated clothing can reduce the quantity of contaminant associated with victims by 75-90%

PH₃ Poisoning Management

- There is no antidote for PH₃ poisoning.
- Aggressive supportive care is the mainstay of therapy.
- Cases given adequate (heroic) care may survive severe toxicity with complete recovery.
- In many areas heroic care not available.

PH₃ Induced CV Shock

- Elevated lactate levels give early warning.
- Correct significant hypo Ca and hypo K
- Refractory hypotension may not respond to even massive crystalloid therapy.
- Vasopressors (dopamine, norepinephrine, phenylephrine, etc.) are second line therapy of shock, but have with limited success.

Unproven Therapies

- N-Acetylcysteine (NAC)
- L-Carnitine
- Hyperinsulin Euglycemia
- IV Lipid Emulsion
- Circulatory Assist Devices
 - IABP, Impella, ECLS (VA-ECMO)

Can Family Reoccupy Residence?

- HazMat Team did not try to ID phosphine
- Special equipment, personnel were required for thorough air monitoring in and around home
- EPA reference concentration (RfC) (safe for home to be reoccupied) for PH_3 was below level of detection for OSHA approved method.
- Can furnishing and surfaces off gas PH_3 ?
- Can home ever be declared safe to reoccupy?

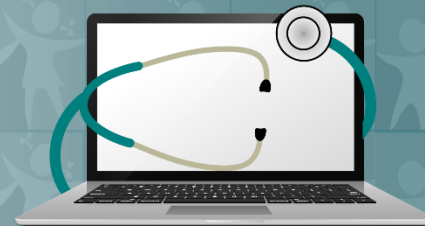
Summary Points

- Intentional and unintentional fatal PH_3 poisoning is common in developing countries
- Developed countries: mainly unintentional
- Severe myocardial depression is main effect
- Children are definitely most vulnerable
- Aggressive resuscitation may be lifesaving
- Deaths continue to occur despite regulated use because of thriving black market use!



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