A Case of Toxic Gas Exposure

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The Case

M/27
Good PH
Employee - Semiconductor raw material manufacturing industry in China
Work process: Junction formation
Headache / dizziness during work
?Gas inhalation

Working Environment

Clinical Exam

sbp108  p78  RR18  SpO2100(RA)
PERL  t36 Skin normal
No resp irritation
Erythematous LT eye
Systemic exam: NAD
ECG CXR NAD
Admitted EMW

What could be the possible culprit?

Semiconductor Manufacturing

“Clean” and “light”
Hazards: large number & variety
Complex, rapidly changing
Lack of info to health care providers
Trade secrets
### Manufacturing Process

- Quartzite
- Water
- Junction Formation
- Oxidize
- Patterning
- Device Manufacture
- Metallization

### Chemical Vapor Deposition (CVD)

- Gas In
- Reagents
- Reactives
- Dopants
- Gas Out
- Substrate
- Heater

### Gaseous Hazards

**Dopants**
- Arsine (AsH₃), AsH₅
- Diborane (B₃H₆), BF₃
- Phosphine (PH₃), PF₃

**Carriers**
- Si(H₂, -H₂Cl₂, -Cl₃, -Cl₄)
- Asphyxiants: H₂, N₂, Ar, He

**Reactives**
- Corrosive: HCl, HF, H₃PO₄, NH₃, NO₂

### Dopants – extremely toxic

**Phosphine (PH₃)**
- Oxidative phosphorylation
- Myocardial ischemic, pump failure, NCPO, shock

**Arsine (AsH₃)**
- Non-irritant
- Hemolysis, ARF

**Diborane (B₃H₆)**
- Highly water soluble irritant
- Lower airway: noncardiogenic PO

### Case Summary

**Work with CVD**
- Rapid onset
- s/s headache dizziness
- No resp irritation
- No corrosive injuries
- No cardiopulmonary manifestation

### Arsine 砷化三氫

Arsenic-containing ores/metals + acid ➔ Arsine gas
n-Dopant in semiconductor industry
Manufacture of crystals for computer chips and fiber optics
Arsenicals  *Industrial Uses*

**Arsenic acid (H₃AsO₄)**
- wood preservative, biocide, metal finishing agent

**Arsenic trioxide (As₂O₃)**
- herbicide, pesticide, and rodenticide, pharmaceuticals and veterinary products

**Arsine (Arsenic Trihydride AsH₃)**
- synthesis of semiconducting materials

**Cadmium arsenide (Cd₃As₂)**
- infrared detectors, pressure sensors, photodetectors

**Gallium arsenide (GaAs)**
- semiconductor, MMICs, diodes, solar cells

**Lead hydrogen arsenate (PbH₂AsO₄)**
- insecticide

**Properties - Arsine**
- Colorless, nonirritating
- 2.5x denser than air
- Water soluble, garlic/fishy odor
- Explosive, irritant, systemic toxicant
- Odor threshold 10-x greater than OSHA permissible exposure limit

**Industries**

- Aniline work
- Bronzing
- Dye manufacturer
- Electronics
- Etching
- Fertilizer making
- Galvanizing
- Jeweler making
- Lead burning
- Paper production
- Plumbing
- Semiconductor
- Submarine work
- Tin production

**Mechanism of Toxicity**

**Hemoglobin**
- primary subcellular target
- formation of colloidal arsenic within RBC
- formation of hydrogen peroxide
- Na/K-ATPase pump
- increase heme release from oxyHb
- oxidative stress
- increased levels of circulating MHb and reduced glutathione in RBC

**Renal Failure**
- Arsine- Haptoglobin complex
- Pigment nephropathy
- Toxic to cortical epithelial cells

**Skin**
- Bronze tint
- Hemolysis + Hb deposits

**Toxicity**
- **Human**
  - Fatal at 50 ppm (30 min)
  - Around 750 reported exposures, 1/5 resulting in death
  - Human and animal toxicity is very similar to production models
- **Animal**
  - Similar toxic effects seen in mice, rats, and hamsters
  - RBC toxicity at 3-12 ppm exposure
  - Li filters in treatment with long-term 5 ppm exposure
  - Kidney toxicity at higher exposure
  - Fatal at 30-50 ppm
Acute Effects

**Pre-hemolysis phase** (30-60 min or delayed)
- Asymptomatic, garlicky odour, red conjunctiva

**Hemolysis phase**
- Weakness, headache, abdominal pain, hypotension
- Free Hb, Hburia, hematuria

**Post-hemolysis phase**
- Renal impairment and shutdown
- Jaundice

Laboratory Findings

- Intravascular hemolysis
- Blood arsenic level
- Urine spot & 24-hr arsenic
- Free Hb level
  - >1.2 - 1.5 g/dL for ET
- Mobilization test

Bronze Skin, Black Plasma, Red Urine

Treatments

- Remove patient, O2, treat bronchospasm
- IVF + furosemide
- Hypotension: dopamine, norepinephrine
- Hemolysis: urine alkalinization
- Major hemolysis: ET >> hemodialysis
  - ?NAC
- Chelation: not advised

Pullen-James S 2006

OELs

1. **Time-weighted Average (OEL-TWA)**
   - conc exposed over an 8-hr workday and a 40-hr workweek, without adverse health effects
2. **Short-term Exposure Limit (OEL-STEL)**
   - conc exposed not > 15 mins and not > 4 times (> 60 mins between successive exposures) in workday
3. **Ceiling (OEL-C)**
   - conc that should not be exceeded during any part of working exposure

Occupational Exposure Limits (OELs)

- LC values of 25 ppm (30 min) and 300 ppm (5 min)
- TWA 0.05ppm or 0.2mg/m³ (US OSHA)
- NIOSH REL: Ca C 0.002 mg/m³ [15-minute]
- TWA 0.05ppm or 0.16mg/m³ (HKSAR OSHB, Labour Department)
- STEL/Ceiling not listed
- Odour threshold 0.5ppm
- 3ppm immediately dangerous to life (NIOSH)
### Workup

**RFT NAD**  
Hb 14.5 Bil 15 LDH 261  
PH 7.38 Bicarb 28.0 BE 1.9  
Urine m’six – ve Hb – ve

### Progress

**IVF given**  
Good U/O  
No signs of hemolysis  
D/C LOS 20hrs

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### Approach - Industrial Gas Poisoning

- Occupational survey  
- Hazardous exposures  
- Known health effects  
- Workplace monitoring & control  

### Occupational Survey

- Type of industry  
- Duration of employment  
- Location, hours, shift  
- Work process & adjacent work process  
- Occasional unusual activities
Hazardous Exposures

Physical hazards
Chemical hazards
  Solvents- HCs, alcohols, ketones, peroxides
  Metals- Pb, Hg, Ca
Gases- toxic, combustion, irritant, asphyxiants
Dusts- asbestos, silica
Biological hazards
Radiological

Health Effects

Clinical features
Temporality
Affected coworkers
Known risk factors

Workplace Monitoring and Control

Area air monitoring
Medical surveillance records
Exposure control
  Administrative control
  Process engineering: enclosure, shielding, ventilation
  Personal protective equipment

Information Resources

Poison control center - HKPIC
Employers / Insurance carriers
Labour Unions — respective industries
Government agencies
  Local: OSH branch, Labour Department
  US: OSHA, NIOSH, ATSDR
Online databases
  EPA, TOXNET, Poisondex
Thank you!