

# A Case of Toxic Gas Exposure

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## The Case

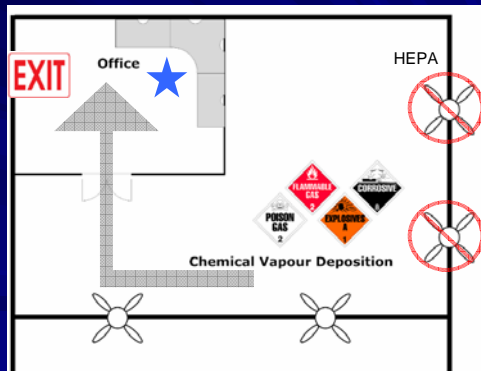
M/27  
Good PH  
Employee - Semiconductor raw material  
manufacturing industry in China  
Work process: Junction formation  
Headache / dizziness during work  
?Gas inhalation

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## Working Environment



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## Clinical Exam

SBP108 P78 RR18 SpO<sub>2</sub>100(RA)  
PERL T36 Skin normal  
No resp irritation  
Erythematous LT eye  
Systemic exam: NAD  
ECG CXR NAD  
Admitted EMW



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What could be the possible culprit?



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## Semiconductor Manufacturing

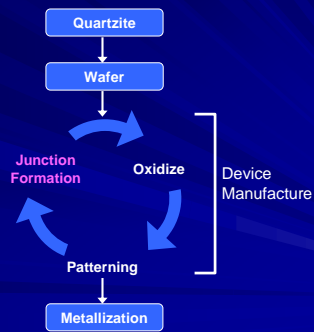
“Clean” and “light”  
Hazards: large number & variety  
Complex, rapidly changing  
Lack of info to health care providers  
Trade secrets

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## Manufacturing Process

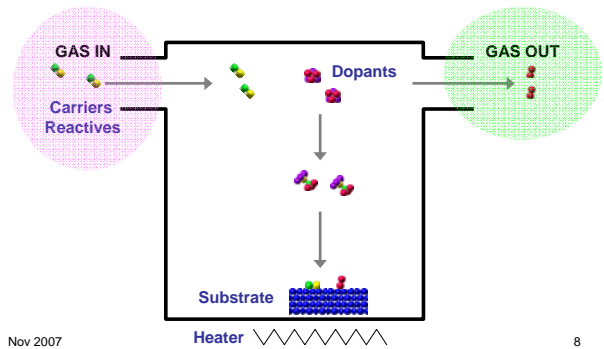


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## Chemical Vapor Deposition (CVD)



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## Gaseous Hazards

### Dopants

Arsine ( $\text{AsH}_3$ ),  $\text{AsH}_5$   
 Diborane ( $\text{B}_2\text{H}_6$ ),  $\text{BF}_3$   
 Phosphine ( $\text{PH}_3$ ),  $\text{PF}_3$

### Carriers

$\text{Si}$  ( $-\text{H}_4$ ,  $-\text{H}_2\text{Cl}_2$ ,  $-\text{Cl}_3$ ,  $-\text{Cl}_4$ )  
 Asphyxiants:  $\text{H}_2$ ,  $\text{N}_2$ , Ar, He

### Reactives

Corrosive:  $\text{HCl}$ ,  $\text{HF}$ ,  $\text{H}_3\text{PO}_4$ ,  $\text{NH}_3$ ,  $\text{NO}_2$

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## Dopants – extremely toxic

### Phosphine ( $\text{PH}_3$ )

Oxidative phosphorylation  
 Myocardial Ischemic, pump failure, NCPO, shock

### Arsine ( $\text{AsH}_3$ )

Non-irritant  
 Hemolysis, ARF

### Diborane ( $\text{B}_2\text{H}_6$ )

Highly water soluble irritant  
 Lower airway: noncardiogenic PO

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## Case Summary

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

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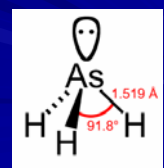
## Arsine 砷化三氢

Arsenic-containing ores/metals + acid

➔ Arsine gas

n-Dopant in semiconductor industry

Manufacture of crystals for computer chips  
 and fiber optics



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## Arsenicals *Industrial Uses*

### Arsenic acid ( $H_3AsO_4$ )

wood preservative, biocide, metal finishing agent

### Arsenic trioxide ( $As_2O_3$ )

herbicide, pesticide, and rodenticide, pharmaceuticals and veterinary products

### Arsine (Arsenic Trihydride $AsH_3$ )

synthesis of semiconducting materials

### Cadmium arsenide ( $Cd_3As_2$ )

infrared detectors, pressure sensors, photodetectors

### Gallium arsenide (GaAs)

semiconductor, MMICs, diodes, solar cells

### Lead hydrogen arsenate ( $PbHAsO_4$ ) -insecticide

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## 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

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## Industries

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

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## Mechanism of Toxicity

**Hemoglobin** - primary subcellular target *Hattelid 1995*

1. formation of colloidal arsenic within RBC
2. formation of hydrogen peroxide
3. ?Na/K-ATPase pump
4. increase heme release from oxyHb *Rael LT 2006*
5. oxidative stress - increased levels of circulating MHb and reduced *glutathione* in RBC *Blair 1990*

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## Mechanism of Toxicity

RBC *Arsine- Hb complex*

Prone to oxidant stress → hemolysis

Renal Failure *Arsine- Haptoglobin complex*

Pigment nephropathy

Toxic to cortical epithelial cells *Ayala-Fierro F 2000*

Skin – Bronze tint

Hemolysis + Hb deposits

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## Toxicity

### $AsH_3$ TOXICITY



#### Hematologic

• RBC lysis

• (1 - 10 ppm)

#### Kidneys

• Hemoglobinuria

• Toxic to nephron

• RENAL FAILURE IS CAUSE OF DEATH

#### Central and Peripheral Nervous System

• hallucinations

• headaches

• neural degeneration

• sensory loss

#### Abdominal pain

• diarrhea

• vomiting

• unknown mechanism (GI toxicity?)

#### Liver

• Liver toxicity

• Altered hepatic function

#### HUMAN



• Fatal at 50 ppm (30 min)

• Around 750 reported exposures,

1/3 resulting in death

• Human and animal toxicity is

very similar ? predictive models

#### ANIMAL



• Similar toxic effects seen in mice,

rats, and hamsters

• RBC lysis at 3-12 ppm exposure

• Liver and spleen enlargement with

long-term 5 ppm exposure

• Kidney toxicity at higher exposure

• Fatal at 30-50 ppm

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NSF/SRC Engineering Research Center for Environmentally Benign Semiconductor Manufacturing 7

18

## Acute Effects

- Pre-hemolysis phase** (30-60min 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

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## Laboratory Findings

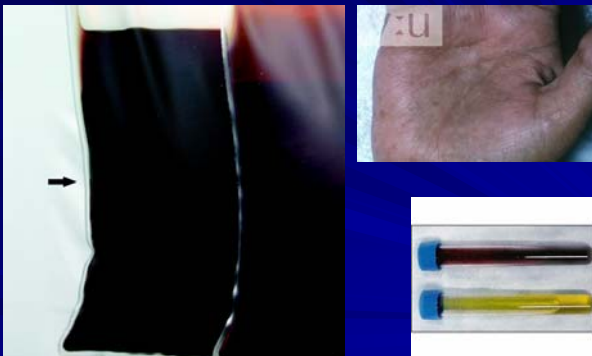
- Intravascular hemolysis  
Blood arsenic level  
Urine spot & 24-hr arsenic  
Free Hb level  
>1.2 -1.5 g/dL for ET  
Mobilization test

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## Bronze Skin, Black Plasma, Red Urine



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## Treatments

- Remove patient, O<sub>2</sub>, treat bronchospasm  
IVF + furosemide  
Hypotension: dopamine, norepinephrine  
Hemolysis: urine alkalinization  
Major hemolysis: ET >> hemodialysis  
?NAC  
Chelation: not advised

*Pullen-James S 2006*

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## 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

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## Occupational Exposure Limits (OELs)

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

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## Lethal Dose

TABLE 2. ACUTE TOXICITY VALUES FOR ARSINE POISONING IN HUMANS

Toxicity Value	C x t (ppm-min)	Comments	Reference
30-min LC <sub>50</sub> : 25 ppm	750	fatal within 30 minutes	RTECS, 1986
5-min LC <sub>50</sub> : 300 ppm	1,500		RTECS, 1986
30-min LC <sub>50</sub> : 250 ppm	7,500		Henderson and Haggard, 1943
30-min LC <sub>50</sub> : 250 ppm	7,500		Flury and Zernik, 1931
30 to 60-min LC <sub>50</sub> : 15.5 ppm	465-930		Flury and Zernik, 1931
30 to 60-min LC <sub>50</sub> : 6.25 ppm	188-375	"dangerous to life"	Flury and Zernik, 1931
6-hr NOAEL: 3.1 ppm	19	no symptoms reported following this 6-hr exposure	Flury and Zernik, 1931

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Authors	Sources	Onset	Clinical features	Treatments
Hesdorffer 1986	Metal reduction with HCl	6 hours	Hemolysis, renal shutdown, marrow suppression	HDx4 ET
Phoon 1984 (5 cases)	Tin smelting	3 hours	Hemolysis, renal impairment	ET(3) PD(2)
Williams 1981	Cleaning paintings		Non-specific	Nil
Risk 1991	Automotive transmission repair	Repeated episodes	LL neurology	Penicillimine
Romeo 1997	Shoe cleaning	90 mins	Asthenia, paresthesias, hemolysis	HD + ET BAL
Teitelbaum 1969 (5 cases)	?Pipe cleaning	30 mins	1 died; 3 hemolysis; 1 renal failure	ET + HD BAL no use
Kleinfeld 1980	Exposed to arsine cylinder	1-2 mins	Hemolysis	IVF, transfusion

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## Workup

RFT NAD  
 Hb 14.5 Bil 15 LDH 261  
 pH 7.38 Bicarb 28.0 BE 1.9  
 Urine m'stix -ve Hb -ve

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## 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

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## Occupational Survey

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

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## 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

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Industries	Gases exposures	Examples
<b>Furniture manufacturing</b>	Preservative, pesticide, glues, finishing products	HCs, glycols, phenols, copper arsenate, creosote, formaldehyde
<b>Chemical manufacturing</b>	Simple and chemical asphyxiants, irritant	HCs, CO, CN, H <sub>2</sub> S, formaldehyde, ethylene oxide
<b>Mining</b>	Mine gases	Oxygen, Nitrogen, H <sub>2</sub> S, CO, Methane, SO <sub>2</sub> , HCl, CO <sub>2</sub> , H <sub>2</sub> , Radon gas
<b>Paper Industry</b>	Pulping, fire-retardants, bleaches	Ammonias, Nitrogen oxides, SO <sub>2</sub> , H <sub>2</sub> S, Cl <sub>2</sub> , - ClO <sub>2</sub> , formaldehyde
<b>Textile industry</b>	Water repellents, antistatic, antimicrobial agents, softeners	Fluorocarbons, silicones, glycols, ammoniums
<b>Plastics industry</b>	Thermal decomposition products	HCs, CO, CO <sub>2</sub> , formaldehyde, styrene, chlorine, NO <sub>2</sub> , HCN, NH <sub>3</sub> , benzene, phosgene, HCl
<b>Jewelers</b>	Gases, metal fumes, vapors	NH <sub>3</sub> , CO, arsine, Cl <sub>2</sub> , H <sub>2</sub> S, NO <sub>2</sub> , HCN, Al, Cd, Cu, Pb, Mn, Hg, Ni, Zn, Ag
<b>Sewage</b>	Simple and chemical asphyxiants, irritant	CO <sub>2</sub> , methane, H <sub>2</sub> S, CO, HCN, Ammonia, chlorine

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## Health Effects

Clinical features

Temporality

Affected coworkers

Known risk factors

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## Workplace Monitoring and Control

Area air monitoring

Medical surveillance records

Exposure control

Administrative control

Process engineering: enclosure, shielding, ventilation

Personal protective equipment

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## Multi-Gas Detector



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35

## 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, Poisonsindex

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Thank you!

