Gas and volatile toxicants: mechanisms of toxicity, clinical consequences and principles of management

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Circumstances of poisoning with gaseous toxicants

The chemical risk is consistently present in our society


Work

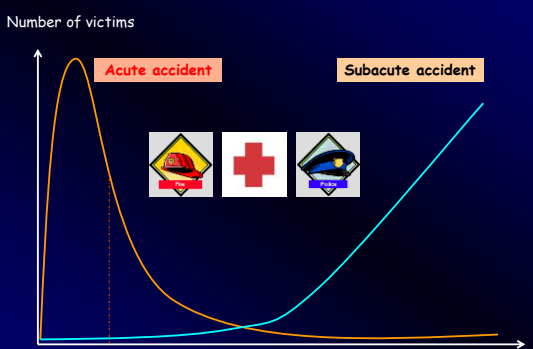

Environnement


Military


Terrorism

Seveso	Dioxine	10 July 1976
Bophal	Isocyanate of methyl	3 December 1984
Tokyo metro	Saran gas	20 March 1995
AZF in Toulouse	Ammonium nitrate	21 September 2001
World Trade Centre	Fumes and smokes	11 September 2001

Kinetics of massive intoxication

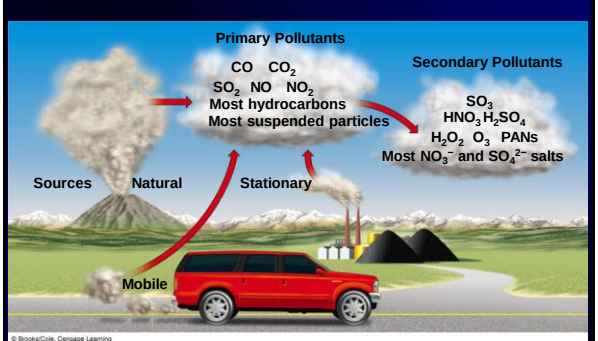


Air Pollution: a serious worldwide issue


Shanghai, China

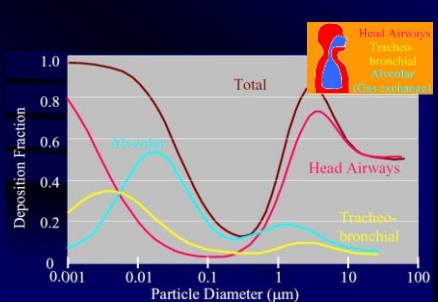
Five Major Pollutants:
1) Carbon Monoxide
2) Sulfur Dioxide
3) Nitrogen Dioxide
4) Particulate Matter
5) Ground Level Ozone

Origin of outdoor air pollutants



Behavior of airborne particles

The air we breathe always contains solid particles or droplets (from natural sources or man-made sources) and is therefore an aerosol



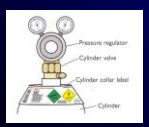
Industrial toxicants at the workplace that produce respiratory diseases

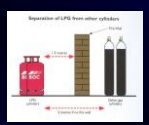
Toxicant	Site of Action	Acute Effect	Chronic Effect
Ammonia	Upper Airways	Irritation, edema	Bronchitis
Arsenic	Upper Airways	Bronchitis, irritation, pharyngitis	Cancer, bronchitis, laryngitis
Asbestos	Lung parenchyma	--	Fibrosis, cancer
Chlorine	Upper airways	Cough, irritation, asphyxiant (by muscle cramps in larynx)	--
Isocyanates	Lower airways, alveoli	Bronchitis, pulmonary edema, asthma	--
Nickel Carbony	Alveoli	Edema (delayed symptoms)	--
Ozone	Bronchi, alveoli	Irritation, edema, hemorrhage	Emphysema, bronchitis
Phosgene	Alveoli	Edema	Bronchitis, fibrosis, pneumonia
Toluene	Upper airways	Bronchitis, edema, bronchospasm	--
Xylene	Lower airways	Edema, hemorrhage	--

Prevention and control measures (detection)

- Wear appropriate Personal Protective Equipment (PPE)
- Ensure adequate ventilation
- Ensure suitable physical environment for dispensing (liquid nitrogen)
- Consider fixed point gas detection monitors / alarms
- Ensure emergency procedures
- Ensure the correct storage: regulators, segregation between flammable/non-flammable gases, full/empty cylinders
- Ensure the correct manual handling of cylinders and vessels





Mechanisms of gas toxicity

Irritant, blister (vesicant) and chocking agents

- Primary irritants : local toxicity; effects depending on aqueous solubility
  - + Highly soluble gases: affect mostly eyes and oro/nasopharynx
    Ex. NH_3, chlorine, HCl, HNO_3, H_2SO_4, SO_2
  - + Low solubility gases: affect mostly deep pulmonary structures (alveoli)
    Ex. NO_2, O_3, phosgene
- Secondary irritants: local + general toxicity
  Ex. Hydrogen sulfide (H_2S), H_3P, CS_2

Asphyxiant gas

- Simple effect : reduction of FiO_2
  Ex. inert gas like CO_2, H_2, N_2, alcanes (methane…)
- Chemical effect : reduction of transport, extraction and use of O_2
  Ex. CO, HCN, ClCN, acetonitrile

Gas with other systemic activity than asphyxia

Ex. Arsine (AsH_3)

Gas toxicokinetics : Haber's rule

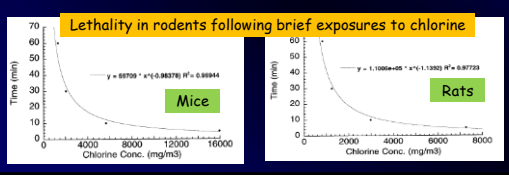
The relationship between the concentration of a poisonous gas and how long the gas must be breathed to produce death or toxic effect

$$C \times t = k \quad \text{or} \quad \int C dt = k$$

C = concentration of the gas (mass per unit volume)
t = amount of time necessary to breathe the gas to produce a given toxicity
k = a constant, depending on both the gas and the effect

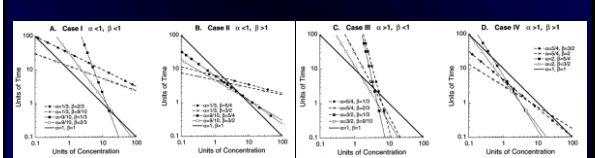
The relationship between C and t is linear on a log-log scale

Lethality in rodents following brief exposures to chlorine



Haber's rule: a special case in a family of curves relating concentration and duration of exposure to a fixed level of response for a given endpoint

General power law family, $C^{\alpha} \times t^{\beta} = k$
Haber's rule corresponding to $\alpha = \beta = 1$
Baxter's formula corresponding to $\beta = 1$



Miller FJ. Toxicology 2000

Principles of gas poisoning management

TRIAGE ++++ exposition ≠ intoxication

- Identification of life-threatening presentations
- Determination of the event circumstances
- Clinical examination + Biological tests/imaging
- Therapeutic indications
  1- Supportive care
  2- Decontamination
  3- Elimination enhancement techniques
  4- Antidotes
- Toxicological analysis

Clinical syndromes and readily available biomarkers are more useful than analytical results for emergent decisions

1- Fire scene

Smoke inhalation

Fire may expose to 3 dangers:

- Thermal risk (flames, heated gases)
- Traumatic risk (blast, defenestration)
- Chemical risk

Smoke inhalation associates:

- Neurological and cardiac anoxic systemic injuries
- Ocular and respiratory irritant injuries

~ 80% of deaths are related to toxic smoke inhalation:

- Early death (*per* exposition) 80%
- Late death (*post*-exposition) 20%

Smoke composition

Polyintoxication: combustion or pyrolosis products in fire smokes

Compounds responsible of direct cellular anoxic toxicity :

- Carbon dioxide (CO_2)
- Carbon monoxide (CO)
- Hydrogen cyanide (HCN)
- Anhydro- derivates : sulfur dioxide, hydrogen sulfide
- Nitric oxide (NO)

Compounds responsible of mucous membrane irritant toxicity :

- Soot (particulates of polycyclic nitric and carbon compounds)
- Aldehydes : acrolein, formaldehyde, butyraldehyde, acetaldehyde, …
- Nitrous derivates : nitric oxide and ammonia, isocyanides and amines
- Mineral acids : hydrochloric, hydrofluoric, hydrobromic acids, …
- Carbon halogenated oxides : phosgene, chlorine
- Water vapors

Composition varies with environment

CN: residential fires, including pipe and furniture, organic materials, plastics (polyurethane), and melanine resines

Consequences of ↘ FiO2 and CO

FiO_2	Consequences
21 %	Normal
17 %	Symptoms
12 %	Dizziness, headaches
9 %	Consciousness loss
6 %	Death in 6-8 min

↘ FiO2

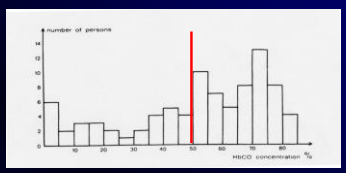
Concentration	Consequences
< 100 ppm	Headaches
500 ppm	Dizziness, headaches, vomiting
1000 ppm	Consciousness loss
2000 ppm	Coma then death
5000 ppm	Death in minutes

CO concentrations

Smoke inhalation ≠ CO poisoning

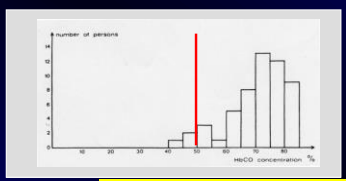
Post-mortem HbCO in 57 fire victims

Exposition duration: 30 min



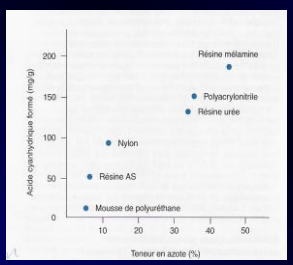
Post-mortem HbCO in 54 cases of fatal CO poisoning

Exposition duration: 8 à 12 h



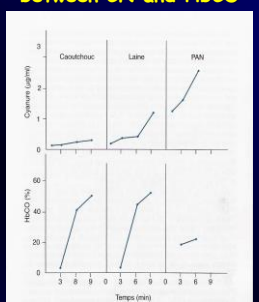
Teige et al. Z Rechtsmedizin 1977

Relationship between N content and CN production



Ballentyne B. Clinical and experimental toxicology of cyanides, 1987

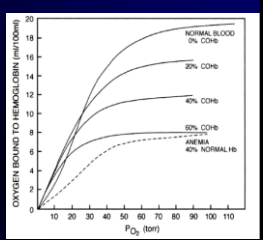
Relationship in vivo between CN and HbCO

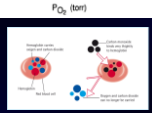


Bertol E. *Forens Sci Int* 1983

Pathophysiology of CO poisoning

- CO affinity to hemoglobin is 240 times greater than Hb-O_2 affinity.
- CO-Hb binding causes leftward shift in the O_2-Hb dissociation curve, impeding O_2 delivery to tissues.
- CO binds to myoglobin, *cytochromes a* and a_3, and *cytochrome c oxidase*, impeding O_2 utilization and worsening cellular dysoxia.
- CO toxicity at the level of mitochondrial cytochromes is synergistically amplified by concomitant CN exposure.

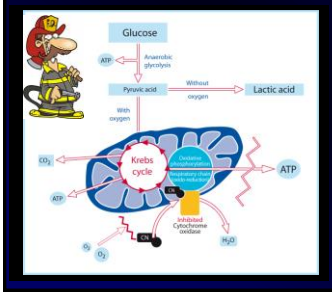




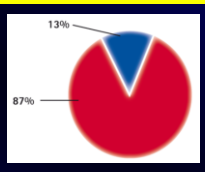
Pathways of cyanide toxicity

A potent intracellular poison, with attachment to the ferric form of necessary enzymes (cytochrome oxidase, succinic dehydrogenase, SOD)

CN poisoning results in tissue hypoxia, acidosis and death.



CN levels in fire-related deaths



Toxic cyanide levels (> 1 mg/l or > 39 µmol/l)
Non-toxic cyanide levels

Smoke inhalation

Positive diagnosis

The two fundamental signs are :

1)- Soot in the airways (nostrils, mouth, throats)

2)- Neurological impairment (Headaches, dizziness, confusion, seizures, changes in mental status, coma)

	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Carbon monoxide intoxication	83	63	43	92
Cyanide intoxication	98	56	28	99

Vital signs in pure CO poisoning

Symptoms	*CO (mmol/l)*	*SBP (mmHg)*	*HR (/min)*	RR (/min)	Lactates (mmol/1)
Severe (n= 54)	2.87 ± 2.15	124 ± 19	88 ± 15	19 ± 4	3.2 ± 1.7
Moderate (n= 12)	0.84 ± 0.82	126 ± 18	85 ± 20	19 ± 3	2.3 ± 1.2
Mild (n= 65)	0.43 ± 0.56	125 ± 18	82 ± 13	19 ± 5	1.9 ± 0.9
Asymptomatic (n=15)	0.38 ± 0.45	128 ± 19	80 ± 6	17 ± 4	1.9 ± 0.7
p value		0.9	0.07	0.6	< 0.0001

Benaissa ML. *Intensive Care Med* 2003

Diagnosis of cyanide poisoning

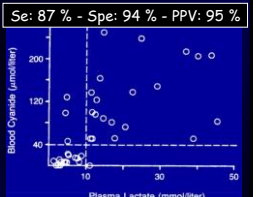
1- Cardiovascular impairment

Hypotension, collapse, shock, or cardiac arrest
Transient reversible cardiomyopathy

2- Abnormal respiratory pattern

Polypnea, wide ventilation, hypopnea or apnea

Se: 87 % - Spe: 94 % - PPV: 95 %



3- Metabolic impairment

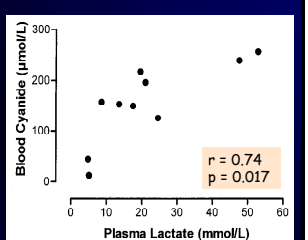
Lactate concentration > 10 mmol/l in the presence of smoke inhalation without severe burns is strongly suggestive of CN (≥ 40 µmol/l) intoxication.

Baud FJ. *NEJM* 1991

Correlation between blood cyanide & lactate concentrations

Factors contributing to lactic acidosis

- Cardiovascular failure
- Apnea
- Seizures
- Acute liver failure
- Catecholamine rush
- Mitochondrial dysfunction



Baud FJ. *Crit Care Med* 2002

Occurrence of signs and symptoms in cases of CO and CN poisonings

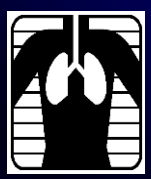
Signs and symptoms	CO (%)	CN (%)
Headache	64	6
Dizziness	56	6
Gastro-intestinal	43	33
Altered mental status	15	13
Loss of consciousness	31	NR
Coma	25	70
Dilated pupils	6	77
Seizures	3	34
Abnormal respiratory pattern	23	95
Pulmonary oedema	6	6
Hypotension/shock	7	61
Plasma lactate (mM) + coma	2.8	13.4

Irritant chemical injury

Toxic irritant gas syndrome

Responsible toxicants : multiple and not individualized

- C → aldehydes
- N → nitric oxide, amines
- S → Sulfur oxide
- Cl → Cl_2, HCl, $COCl_2$, ...



Irritation-related symptoms:

- Ocular
- Respiratory

They participate in the incapacitating action.

Their effects could be delayed (till > 48 hours).

1- Ocular symptoms

- Red eyes
- Cornea burns

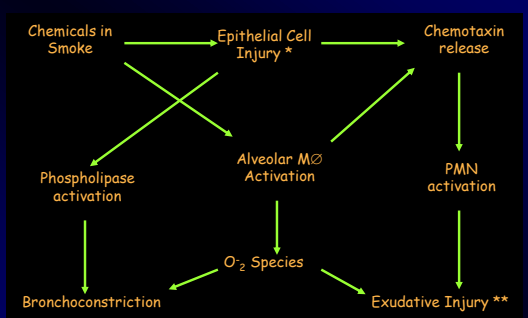
Persistent conjunctivitis on hospital admission is predictive of an associated respiratory injury.

2- Respiratory symptoms

- Dysphonia + inspiratory dyspnea = obstructive laryngitis
- Expiratory dyspnea + wheezing = bronchospasm
- Rapid breathing + crackles = chemical bronchopneumonia

Dysphonia and rhonchi are associated with a longer hospital stay.

Pathophysiology of tracheobronchial injury



* Loss of ciliary action, mucosal edema, diminished surfactant activity, atelectasis
** Resulting in necrotizing bronchiolitis, alveolar pulmonary edema, hyaline membrane formation, and intra-alveolar hemorrhage

Patient management

Assessments

On the scene

1- Pulse oximetry may not distinguish between O_2-Hb and CO-Hb, resulting in inaccurate SpO_2.

2- Pulse CO oximetry or atmospheric CO measurement.

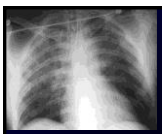
3- Blood sampling for CO-Hb or CO measurement (if possible immediately after O_2 administration).

4- Blood sampling for further CN concentration determination.

5- Arterial blood gases.

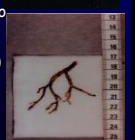
Useful in smoke inhalation mass casualty incidents without dermal burns

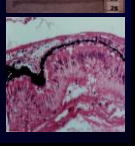
Goh SH. Eur J Emerg Med 2006



Assessments (2)

After hospital admission





1- Chest X-Ray: low specificity and predictive value; initially normal despite symptoms; to be repeated to look for delayed lung injury.

2- Sputum microbiology: high incidence of aspiration (38%)

3- Bronchoscopy:

In burnt patient: predict severity, ARDS, mortality

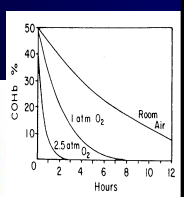
In non-burnt patients: no correlation with PaO_2/FiO_2 ratio, infection, X-ray features, ICU stay duration.

No evaluation of its therapeutic interest (toilet).

4- Bedside continuous CO-oximetry: interference between COHb and hydroxocobalamin

Treatment of CO poisoning

- Normobaric oxygen
- Hyperbaric oxygen (60-90 min à 2.5 ATA, compression chamber)
  - Consciousness loss
  - Coma
  - Neurological deficiency
  - Coronary insufficiency
  - Children
  - Pregnant women

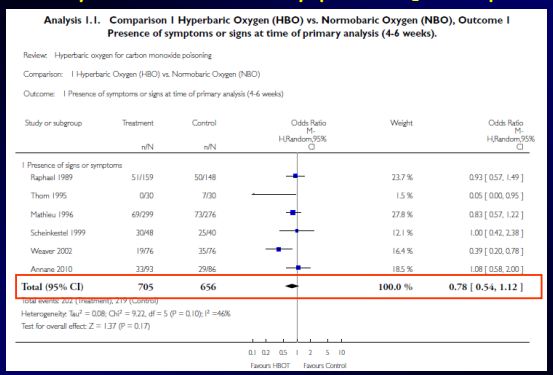


Winter PM. *JAMA 1976*

- Some studies demonstrated a reduction in CNS symptoms and quicker recovery if CO poisoning

- Indications and availability vary depending on the institution and region

Metaanalysis of usefulness of hyeprbaric O_2 in CO poisoning



Analysis 1.1. Comparison 1 Hyperbaric Oxygen (HBO) vs. Normobaric Oxygen (NBO), Outcome 1 Presence of symptoms or signs at time of primary analysis (4-6 weeks).

Review: Hyperbaric oxygen for carbon monoxide poisoning

Comparison: 1 Hyperbaric Oxygen (HBO) vs. Normobaric Oxygen (NBO)

Outcome: 1 Presence of symptoms or signs at time of primary analysis (4-6 weeks)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 Presence of signs or symptoms					
Raphael 1989	51/159	50/148		23.7 %	0.93 [0.57, 1.49]
Thom 1995	0/30	7/30		1.5 %	0.05 [0.00, 0.95]
Mathieu 1996	69/299	73/276		27.8 %	0.83 [0.57, 1.22]
Scheinkestel 1999	30/48	25/40		12.1 %	1.00 [0.42, 2.38]
Weaver 2002	19/76	35/76		16.4 %	0.39 [0.20, 0.78]
Annane 2010	33/93	29/86		18.5 %	1.08 [0.58, 2.00]
Total (95% CI)	**705**	**656**		**100.0 %**	**0.78 [0.54, 1.12]**

Total events: 202 (Treatment), 219 (Control)

Heterogeneity: $Tau^2 = 0.08$; $Chi^2 = 9.22$, df = 5 (P = 0.10); I^2 =46%

Test for overall effect: Z = 1.37 (P = 0.17)

0.1 0.2 0.5 1 2 5 10

Favours HBOT Favours Control

Buckley NA. *Cochrane Database Syst Rev* 2011

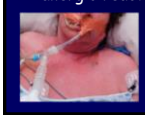
When to suspect cyanide poisoning ?

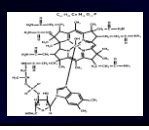
Neurological	Respiratory	Cardiovascular	Metabolic
Dizziness Restlessness Anxiety ↓ Confusion ↓ Coma Seizures	Hyperpnea ↓ Central apnea ± Pulmonary edema	Hypertension ↓ Shock ↓ Cardiac arrest	↗Blood glucose ↗Lactate Metabolic acidosis Rhabdomyolysis Renal failure
↓	Abnormal respiratory pattern	or Abnormal arterial pressure	or Lactates > 10 mmol/l
CO and CN	↺ CN	↺ CN	↺ CN

Hydroxocobalamin (Cyanokit®)

- Currently used in Europe and more recently in the USA
- 50 g bind 1 g of CN
- Dose: 5 g, to be repe… according to se…
- Ability … ugh the BBB
- … ts: reddish … loration of skin and urine, allergic reactions

First-line antidote





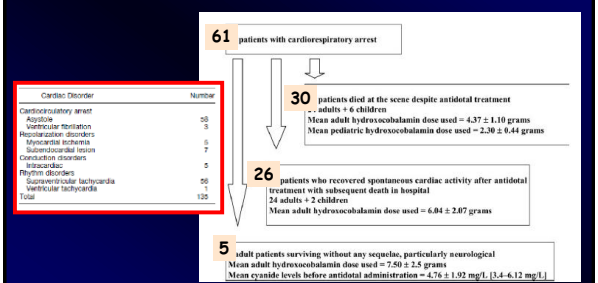
Other CN antidotes

Sodium thiosulfate:
efficient - safe
dela… action

MetHb fo…ing agents:
potent
impairme… O_2 delivery

Cobalt … EDTA:
very potent
immediate action
effective if late
numerous side effects

Cardiac disorders in smoke inhalation-associated CN poisoning



Cardiac Disorder	Number
Cardiocirculatory arrest	
Asystole	58
Ventricular fibrillation	5
Repolarization disorders	
Myocardial ischemia	5
Subendocardial lesion	7
Conduction disorders	
Intracardiac	5
Rhythm disorders	
Supraventricular tachycardia	56
Ventricular tachycardia	1
Total	135

61 patients with cardiorespiratory arrest

30 patients died at the scene despite antidotal treatment
… adults + 6 children
Mean adult hydroxocobalamin dose used = 4.37 ± 1.10 grams
Mean pediatric hydroxocobalamin dose used = 2.30 ± 0.44 grams

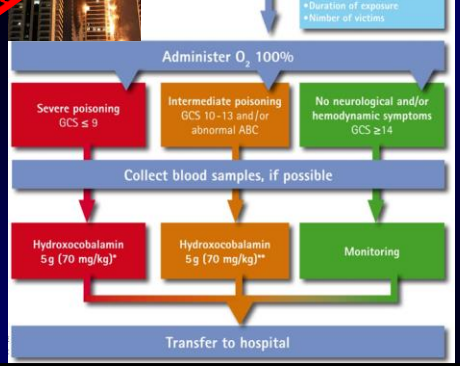
26 patients who recovered spontaneous cardiac activity after antidotal treatment with subsequent death in hospital
24 adults + 2 children
Mean adult hydroxocobalamin dose used = 6.04 ± 2.07 grams

5 adult patients surviving without any sequelae, particularly neurological
Mean adult hydroxocobalamin dose used = 7.50 ± 2.5 grams
Mean cyanide levels before antidotal administration = 4.76 ± 1.92 mg/L [3.4–6.12 mg/L]

Fortin JL. J Emerg Med 2010

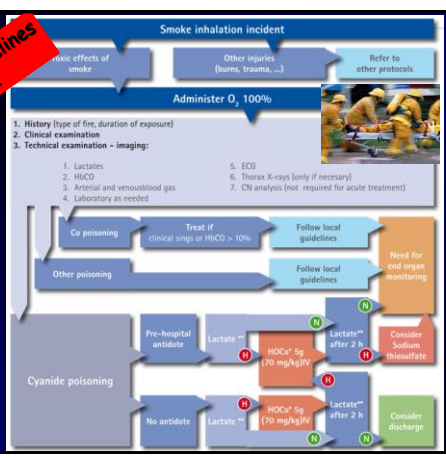
EuSEM guidelines 2012

Pre-hospital algorithm



EuSEM guidelines 2012

Hospital algorithm



Inhalation injury therapy and airway Management

- Humidified Oxygen
- Bronchodilators (IV or nebulized)
- Mucolytics and/or expectorants
- Intubation, mechanical ventilation, PEEP, HFO
- Pulmonary edema: role of fluid therapy
- Antibiotics: gram+ versus gram- coverage
- Corticosteroids controversial
- Investigational adjuncts:
  - Aerosolized Heparin: endobronchial fibrin-mucus casts
  - Exosurf: surfactant inactivation
  - Exogenous antiprotease: antiprotease consumption
  - PAF antagonists: ROI generation, membrane lipid peroxidation
  - Whole body hypothermia
  - ECMO

Enkhbaatar P. Crit Car Med 2007

Other toxic gases ?

In a prospective study (54 fire victims versus 116 controls), 15 volatile organic compounds were associated with death in fire victims

- ethyl acetate
- acrylonitrile
- propionitrile
- tetrahydrofuran
- toluene
- benzene
- o-xylene
- p-xylene
- ethylbenzene
- nitromethane
- trichlorofluoromethane
- indene
- trichloroethylene
- 2 pentanone
- acetaldehyde

Three (benzene, nitromethane, ethyl acetate) are remarkable in regard to their detection in blood with an elevated incidence and correlation with CO.

Houeto P. Unpublished data

Complications and sequellae

Early complications :

- Barotrauma injuries
- Hospital-acquired pulmonary infections

Late complications :

- Tracheal or bronchial stenosis
- Non-specific bronchial reactivity (Brooks syndrome)
- Bronchiolitis obliterans
- Bronchiectasis
- Chronic bronchitis
- Pulmonary fibrosis

Neurological sequellae :

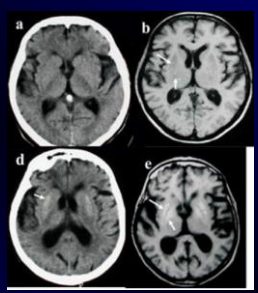
- Smoke inhalation is a cause of post-interval syndrome
- Persistent hoarseness of the voice (surgical treatment)

Complications and sequellae

- Post-anoxic encephalopathy
- CO-related post-interval syndrome
- CN-related brain injuries

F 50 years, comatose, pulseless and apneic, CPR + 2.5 g HCob +HBO
Blood cyanide (68 µM) HBCO (10.9%)

- Extrapyramidal hypertonia, choreo-athetotic movements
- MRI: increased cerebral atrophy, in the white matter, hemorrhagic putamini and globi pallidi; but respect of hippocampi



Baud FJ. *BMJ Case Reports* 2011

2- Natural toxicant

Hydrogen sulfide (H_2S)

- Colorless, highly flammable and explosive gas, characteristic rotten-egg odor (sense of smell for H_2S fatigues in seconds)
- Naturally produced from putrefaction of organic substances, off-gassing of volcanos, and by certain industrial processes (oil)
- Irritant toxicity on mucous membranes and distal airway injury (exfoliation)
- Asphyxiant toxicity from interaction with metalloproteins including cytochrome oxidase + inhibition of succinic dehydrogenase by reducing disulfide bridges

➔ Knockdown effect
➔ Pulmonary effects
➔ Cardiovascular effects
➔ Neurological effects
➔ Lactic acidosis

Hydrogen sulfide Toxicity

Clinical effects	Concentration (ppm)
Eye irritation	4 – 100
Respiratory irritation, pulmonary edema	50 - 500
Bronchitis, ARDS	250 for 24-72h
Symptomatic	50 for 0.5 h
Severely toxic	200 for 1 min
Coma and death	500 - 1000
Fatal	800 immediate, 600, 30 min
Immediate collapse	1000

Management of H_2S poisoning

- Supportive care
- Removal from exposure
- Oxygen (avoid mouth-to-mouth)
- Irrigation of exposed skin and eyes with normal saline
- Ventilatory support, anticonvulsants, antibiotics, …

- Specific treatments
- if persistent acidosis, coma, life-threatening arrhythmias
- Methemoglobin induction: Cyanide antidote kit: amyl nitrate (gauze pad) + sodium nitrite (IV)
- Hyperbaric oxygen
- Hydroxocobalamine ??

3- Industrial toxicant

Arsine (AsH_3)

- Inorganic, flammable, pyrophoric and highly toxic gas (PE = - 63°C)
- Colorless, denser-than-air gas, soluble in water (20%, 20°C) and organic solvents
- Smell a slight garlic or fish-like scent when present above 0.5 ppm

- Use in the semiconductor industry and synthesis of organoarsenic compounds

- Liposoluble and able to cross alveolar-capillar and red cell membrane (hemolysis)

Relationship between exposure and toxicity
- Exposure to arsine concentrations of 250 ppm is rapidly fatal
- Concentrations of 25–30 ppm are fatal for 30 min exposure
- Concentrations of 10 ppm can be fatal at longer exposure times
- Symptoms of poisoning appear after exposure to concentrations of 0.5 ppm

AsH_3 Toxicity

Acute toxicity: symptoms and onset delay vary with poisoning severity

▪ ***Mild:***
- Fatigue, headaches, nausea, weakness, lumbago
- Urine « porto » and garlic scent

▪ ***Moderate:***
- Headaches, vertigo, shivering, nausea, vomiting, abdominal cramps, lumbar pain
- Intravascular hemolysis (DIC, hyperkalemia, metabolic acidosis, shock, pulmonary edema, renal failure, anemia)

▪ ***Severe:***
- Consciousness loss/syncope/coma,
- Circulatory failure, MOF, death

Little information on the chronic toxicity of arsine, although it is reasonable to assume that a long-term exposure could lead to arsenicosis

Management of AsH_3 poisoning

- Supportive care
- Treatment of metabolic acidosis and shock
- Red cell transfusion
- Exsanguino-transfusion.
- Extracorporeal replacement (antidotes are not useful if renal injury)

- No validated antidote
Dimercaprol (BAL®): inefficient to reverse but may prevent the risk of delayed inorganic arsenic toxicity , before acute renal failure onset

- Monitoring of acute toxicity:
- Non-symptomatic patients : 6 h (first signs of hemolysis)
- Symptomatic patients: 48 h

- Follow-up:
- Acute renal failure
- Delayed arsenical intoxication (example : neurological disturbances)

4- Terrorism and war

Scenarios of an attack with Chemical Warfare Agents

World War

Saddam Hussein bombing the Kurds

Syria Civil War

Tokyo tube attack by Aum Shinrikyo sect

Life-threatening effects of Organophosphorus Compounds

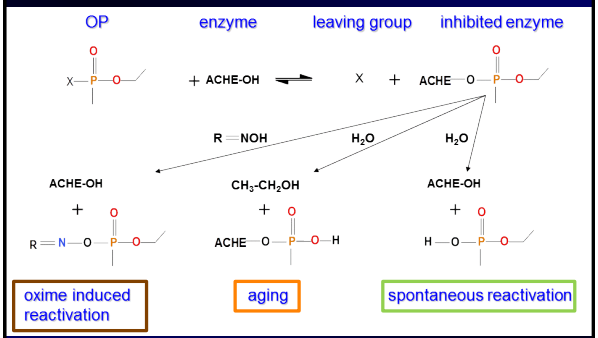
Mechanisms of toxicity:
- Inhibition of AChE
- Accumulation of ACh
- Disturbance of cholinergic functions

Lethal effects:
- Bronchoconstriction/Bronchorrhoea (M)
- Central respiratory arrest (M, N)
- Peripheral respiratory muscle paralysis (N)
- Inhalation and ARDS (solvent)

Diagnosis

Clinical Diagnosis: Signs and symptoms, circumstances
Confirmation with simple and easy to use laboratory methods

Reactions occurring at AchE with an OP and an oxime



Aging half-time of RBC-AChE-OP-conjugates

Organophosphorus Compound	Aging Half time (h)	Spontaneous reactivation Half time (h)
Paraoxon-ethyl	31.2	31.2
Paraoxon-methyl	3.7	0.69
RVX	138.6	17.8
VX	36.5	33.0
Tabun	19	-
GF	7.0	-
Sarin	3.0	-
Soman	0.1	-

Worek et al. Biochem Pharmacol 2004

Therapeutic approach in Nerve Agent-poisoning

Self protection: Utmost important due to serious threat of percutaneous and inhalational poisoning

Treatment of muscarinic signs and symptoms by atropine

Treatment and/or prevention of seizures by benzodiazepines

Prompt reactivation of inhibited AChE
- Even in the absence of severe signs by effective oximes
- Prolonged oxime treatment is expected to be mandatory in most patients

+ Supportive therapy: artificial ventilation, sedation, cardiovascular stabilisation

Conclusions

- Gas may be responsible for acute life-threatening systemic and irritant respiratory toxicity as well as chronic disease resulting in respiratory and neurological functional disabilities.
- Smoke inhalation must be viewed as a polyintoxication. Cyanide plays an important role. While not uniformly present, it may often contribute to toxicity and lethality. Other gases than CO and CN, like volatile organic compounds should be considered. Hydroxocobalamin is recommended as first-line antidote due to its safety and assessed efficiency, in association with oxygen and supportive treatment, administered as rapidly as possible.
- Many various gas could be involved at the workplace. Reduction in FiO_2 is one major mechanism of toxicity. Management is mainly supportive. Prevention and detection are mandatory.