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

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The chemical risk is consistently present in our society

Seveso Dioxine 10 July 1976
Bhopal 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

Number of victims

Acute accident
Subacute accident

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

Primary Pollutants
- CO, CO₂
- SO₂, NO, NO₂
- Most hydrocarbons
- Most suspended particles

Secondary Pollutants
- SO₂, HNO₃, H₂SO₄
- H₂O₂, O₃, PANs
- Most NO₃⁻ and SO₄²⁻ salts

Sources
- Natural
- Stationary
- Mobile

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

<table>
<thead>
<tr>
<th>Toxicant</th>
<th>Site of Action</th>
<th>Acute Effect</th>
<th>Chronic Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ammonia</td>
<td>Upper Airways</td>
<td>Bronchitis</td>
<td></td>
</tr>
<tr>
<td>Atomic</td>
<td>Upper Airways</td>
<td>Bronchitis, irritation, pharyngitis</td>
<td></td>
</tr>
<tr>
<td>Asbestos</td>
<td>Lung</td>
<td>-</td>
<td>Fibrosis, cancer</td>
</tr>
<tr>
<td>Chlorine</td>
<td>Upper Airways</td>
<td>Cough, irritation, asphyxiation (by aspiration)</td>
<td></td>
</tr>
<tr>
<td>Isocyanate</td>
<td>Upper Airways</td>
<td>Bronchitis, pulmonary edema, asthma</td>
<td></td>
</tr>
<tr>
<td>Nickel</td>
<td>Alveoli</td>
<td>Edema (delayed symptoms)</td>
<td></td>
</tr>
<tr>
<td>Phosgene</td>
<td>Alveoli</td>
<td>Edema</td>
<td></td>
</tr>
<tr>
<td>Toluene</td>
<td>Upper Airways</td>
<td>Bronchitis, edema, bronchoconstriction</td>
<td></td>
</tr>
<tr>
<td>Xylene</td>
<td>Lower Airways</td>
<td>Edema, bronchoconstriction</td>
<td></td>
</tr>
</tbody>
</table>

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 choking agents

- Primary irritants: local toxicity, effects depending on aqueous solubility
  - Highly soluble gases: affect mostly eyes and oro/nasopharynx
    Ex. NH₃, chlorine, HCl, HNO₃, H₂SO₄, SO₂
  - Low solubility gases: affect mostly deep pulmonary structures (alveoli)
    Ex. NO₂, O₃, phosgene
- Secondary irritants: local + general toxicity
  Ex. Hydrogen sulfide (H₂S), H₃P, CS₂

Asphyxiant gas

- Simple effect: reduction of FiO₂
  Ex. inert gas like CO₂, N₂, alcanes (methane...)
- Chemical effect: reduction of transport, extraction and use of O₂
  Ex. CO, HCN, ClCN, acetonitrile

Gas with other systemic activity than asphyxia
Ex. Arsenic (AsH₃)

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

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
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 exposure) 80%
- Late death (post-exposure) 20%

Smoke composition
Polyintoxication: combustion or pyrolosis products in fire smokes

Compounds responsible of direct cellular anoxic toxicity:
- Carbon dioxide (CO₂)
- Carbon monoxide (CO)
- Hydrogen cyanide (HCN)
- Anhydro-derivatives: sulfur dioxide, hydrogen sulfide
- Nitric oxide (NO)
- Carbon halogenated oxides: phosgene, chlorine

Compounds responsible of mucous membrane irritant toxicity:
- Soot (particulates of polycyclic nitric and carbon compounds)
- Aldehydes: acrolein, formaldehyde, butyraldehyde, acetaldehyde, ...
- Nitrous derivatives: nitric oxide and ammonia, isocyanides and amines
- Mineral acids: hydrochloric, hydrofluoric, hydrobromic acids, ...
- Water vapors

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: 8–12 h

Teige et al. Z Rechtsmedizin 1977

Pathophysiology of CO poisoning

- CO affinity to hemoglobin is 240 times greater than Hb-O₂ affinity.
- CO-Hb binding causes leftward shift in the O₂-Hb dissociation curve, impeding O₂ delivery to tissues.
- CO binds to myoglobin, cytochromes a and a₃, and cytochrome c oxidase, impeding O₂ utilization and worsening cellular dysxia.
- 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.

Smoke inhalation

The two fundamental signs are:
1) Soot in the airways (nose, mouth, throats)
2) Neurological impairment (Headaches, dizziness, confusion, seizures, changes in mental status, coma)

Vital signs in pure CO poisoning

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>CO (mmol/l)</th>
<th>SBP (mmHg)</th>
<th>HR (/min)</th>
<th>RR (/min)</th>
<th>Lactates (mmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe (n=54)</td>
<td>2.87 ± 2.15</td>
<td>124 ± 19</td>
<td>88 ± 19</td>
<td>19 ± 4</td>
<td>3.2 ± 1.7</td>
</tr>
<tr>
<td>Moderate (n=12)</td>
<td>0.84 ± 0.82</td>
<td>126 ± 18</td>
<td>85 ± 20</td>
<td>19 ± 3</td>
<td>2.3 ± 1.2</td>
</tr>
<tr>
<td>Mild (n=8)</td>
<td>0.43 ± 0.56</td>
<td>125 ± 18</td>
<td>82 ± 13</td>
<td>19 ± 5</td>
<td>1.9 ± 0.9</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>0.38 ± 0.45</td>
<td>128 ± 19</td>
<td>80 ± 6</td>
<td>17 ± 4</td>
<td>1.9 ± 0.7</td>
</tr>
<tr>
<td>p-value</td>
<td>0.9</td>
<td>0.07</td>
<td>0.6</td>
<td>&lt; 0.0001</td>
<td></td>
</tr>
</tbody>
</table>

Correlation between blood cyanide & lactate concentrations

Factors contributing to lactic acidosis:
- Cardiovascular failure
- Apnea
- Seizures
- Acute liver failure
- Catecholamine rush
- Mitochondrial dysfunction

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
Polynea, wide ventilation, hypopnea or apnea

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

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

<table>
<thead>
<tr>
<th>Signs and symptoms</th>
<th>CO (%)</th>
<th>CN (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>64</td>
<td>6</td>
</tr>
<tr>
<td>Dizziness</td>
<td>56</td>
<td>6</td>
</tr>
<tr>
<td>Gastro-intestinal</td>
<td>43</td>
<td>33</td>
</tr>
<tr>
<td>Altered mental status</td>
<td>15</td>
<td>13</td>
</tr>
<tr>
<td>Loss of consciousness</td>
<td>31</td>
<td>NR</td>
</tr>
<tr>
<td>Coma</td>
<td>25</td>
<td>70</td>
</tr>
<tr>
<td>Dilated pupils</td>
<td>6</td>
<td>77</td>
</tr>
<tr>
<td>Seizures</td>
<td>3</td>
<td>34</td>
</tr>
<tr>
<td>Abnormal respiratory pattern</td>
<td>23</td>
<td>93</td>
</tr>
<tr>
<td>Pulmonary edema</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Hypotension/shock</td>
<td>7</td>
<td>61</td>
</tr>
<tr>
<td>Plasma lactate (mM) + coma</td>
<td>2.8</td>
<td>13.4</td>
</tr>
</tbody>
</table>

Baud FJ, Crit Care Med 2002

Baud FJ, NEJM 1991

Carbon monoxide intoxication
Sensitivity (%) | Specificity (%) | Positive predictive value (%) | Negative predictive value (%)
--- | --- | --- | ---
83 | 63 | 43 | 92

Cyanide intoxication
Sensitivity (%) | Specificity (%) | Positive predictive value (%) | Negative predictive value (%)
--- | --- | --- | ---
98 | 56 | 28 | 99

Sensitivity
Specificity
Positive predictive value
Negative predictive value
Toxic irritant gas syndrome

Responsible toxicants: multiple and not individualized
- C \(\rightarrow\) aldehydes
- N \(\rightarrow\) nitric oxide, amines
- S \(\rightarrow\) sulfur oxide
- Cl \(\rightarrow\) Cl\(_2\), HCl, COCl\(_2\), ...

Irritation-related symptoms:
- Ocular
- Respiratory
They participate in the incapacitating action. Their effects could be delayed (till > 48 hours).

Pathophysiology of tracheobronchial injury

Chemicals in Smoke

- Bronchoconstriction
- Phospholipase activation
- Alveolar M cell activation
- Chemotaxin release
- \(O_2\) Species
- Neutrophil activation
- Exudative 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

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.

Assessments (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 CO-Hb and hydroxocobalamin

Assessments (2)

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.

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

- Some studies demonstrated a reduction in CNS symptoms and quicker recovery if CO poisoning
- Indications and availability vary depending on the institution and region.

Winter PM. JAMA 1976
Metaanalysis of usefulness of hyperbaric O₂ in CO poisoning

Buckley NA. Cochrane Database Syst Rev 2011

When to suspect cyanide poisoning?

- Neurological:
  - Dizziness
  - Restlessness
  - Anxiety
  - Confusion
  - Coma
  - Seizures
- Respiratory:
  - Hyperpnea
  - Central apnea
  - Pulmonary edema
- Cardiovascular:
  - Hypertension
  - Shock
  - Cardiac arrest
- Metabolic:
  - Blood glucose
  - Lactate
  - Metabolic acidosis
  - Rhabdomyolysis
  - Renal failure

Abnormal respiratory pattern
Abnormal arterial pressure
Lactates >10 mmol/l

Hydroxocobalamin (Cyanokit®)
- Currently used in Europe and more recently in the USA
- 50 g bind 1 g of CN
- Dose: 5 g, to be repeated according to seriousness
- Ability to pass through the BBB
- Side effects: reddish discoloration of skin and urine, allergic reactions

Other CN antidotes
- Sodium thiosulfate: efficient, safe, delayed action
- MethHb forming agents: potent improvement of O₂ delivery
- Cobalt EDTA: very potent, immediate action effective if late

Cardiac disorders in smoke inhalation-associated CN poisoning

- Smoke inhalation incident
- Evaluate: vital signs, airway, breathing, circulation of exposed smoke inhalation
- Administer O₂ 100%
- Severe poisoning: GCS ≤ 9
- Intermediate poisoning: GCS 10-13 and/or abnormal vital signs
- No neurological or severe hemodynamic symptoms: GCS ≤ 4
- Collect blood samples, if possible
- Hydroxocobalamin 50 mg, 150 mg²
- Monitoring
- Transfer to hospital

EeSEA guidelines 2012

Pre-hospital algorithm

Fortin JL. J Emerg Med 2010

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 antiproteinase: antiproteinase consumption
- PAF antagonists: ROI generation, membrane lipid peroxidation
- Whole body hypothermia
- ECMO

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

Complications and sequelae

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

Complications and sequelae

- Post-anoxic encephalopathy
- CO-related post-interval syndrome
- ON-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 putami and globi pallidi; but respect of hippocampi

2- Natural toxicant

Hydrogen sulfide (H₂S)

- Colorless, highly flammable and explosive gas, characteristic rotten-egg odor (sense of smell for H₂S 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

<table>
<thead>
<tr>
<th>Clinical effects</th>
<th>Concentration (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye irritation</td>
<td>4 – 100</td>
</tr>
<tr>
<td>Respiratory irritation, pulmonary edema</td>
<td>50 – 800</td>
</tr>
<tr>
<td>Bronchitis, ARDS</td>
<td>250 for 24-72h</td>
</tr>
<tr>
<td>Symptomatic</td>
<td>50 for 0.5 h</td>
</tr>
<tr>
<td>Severely toxic</td>
<td>200 for 1 min</td>
</tr>
<tr>
<td>Coma and death</td>
<td>500 – 1000</td>
</tr>
<tr>
<td>Fatal</td>
<td>800 immediate, 600, 30 min</td>
</tr>
<tr>
<td>Immediate collapse</td>
<td>1050</td>
</tr>
</tbody>
</table>
Management of \( \text{H}_2\text{S} \) 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 ??

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**AsH\(_3\) Toxicity**

Acute toxicity: symptoms and onset delay vary with poisoning severity

- **Mild**:
  - Fatigue, headaches, nausea, weakness, lumbago
  - Urine « pork » 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 arsineosis

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**Management of AsH\(_3\) poisoning**

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

- **No validated antidote**
  - Dimercaprol (BAL\(_3\)): 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 arsenic intoxication (example: neurological disturbances)

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**Chemical Warfare Agents**

**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

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**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)

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**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-capillary 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

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**3- Industrial toxicant**
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

<table>
<thead>
<tr>
<th>Organophosphorus Compound</th>
<th>Aging Half time (h)</th>
<th>Spontaneous reactivation Half time (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paraoxon-ethyl</td>
<td>31.2</td>
<td>31.2</td>
</tr>
<tr>
<td>Paraoxon-methyl</td>
<td>3.7</td>
<td>0.69</td>
</tr>
<tr>
<td>RVX</td>
<td>138.6</td>
<td>17.8</td>
</tr>
<tr>
<td>VX</td>
<td>36.5</td>
<td>33.0</td>
</tr>
<tr>
<td>Tabun</td>
<td>19</td>
<td>-</td>
</tr>
<tr>
<td>GF</td>
<td>7.0</td>
<td>-</td>
</tr>
<tr>
<td>Sarin</td>
<td>3.0</td>
<td>-</td>
</tr>
<tr>
<td>Soman</td>
<td>0.1</td>
<td>-</td>
</tr>
</tbody>
</table>

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 Fio₂ is one major mechanism of toxicity. Management is mainly supportive. Prevention and detection are mandatory.

QUESTIONS?