

Toxic Industrial Chemicals

Introduction

The first chemical warfare agent of the modern era, chlorine, was released with devastating effect on 22 April 1915 at Ypres, Belgium. Along a 4 mile front, German soldiers opened the valves of 1,600 large and 4,130 small cylinders containing 168 tons of chlorine. The gas formed a thick white cloud that crossed the first allied trenches in less than a minute. The allied line broke, allowing the Germans to advance deep into allied territory. If the Germans had been fully prepared to exploit this breakthrough, the course and possibly the outcome of WWI may have been very different.

Chlorine is a commodity industrial chemical with hundreds of legitimate uses; it is not a "purpose designed" chemical warfare agent. Phosgene, another commodity industrial chemical, accounted for 80% of the chemical fatalities during WWI. Other industrial chemicals, most notably hydrogen cyanide and cyanogen chloride, were also used during WWI. More recently, both sides in the Bosnian civil war threatened to use chlorine as a "weapon of opportunity".

Industrial chemicals include chlorine, ammonia, phosgene, hydrogen cyanide, acids, solvents, pesticides, herbicides, fertilisers, fuels, petrochemicals, and intermediates used in the manufacture of plastics. Industrial chemicals are legitimate articles of commerce which are traded in very large volumes and are not subjected to the same regulations or export controls as chemical warfare agents. Industrial chemicals are available in bulk quantities during production, in storage prior to use or shipment, or during their transport from one

location to another. Depending on the available routes of movement, and quantity of chemical to be moved, transport can occur by truck or rail tank cars, over water by barge or boat, over land through above- or below-ground pipelines and by air.

Toxic chemicals may be produced by the burning of materials (e.g., the burning of Teflon produces perfluoroisobutylene) or by their reaction if spilled into water (e.g. silanes produce hydrogen chloride and cyanides, hydrogen cyanide).

Toxic Industrial Chemicals (TICs)

A Toxic Industrial Chemical (TIC) is defined as:

an industrial chemical which has a LCt50 value of less than 100,000 mg.min/m³ in any mammalian species and is produced in quantities exceeding 30 tonnes per year at one production facility.

This definition differentiates TICs from highly toxic speciality chemicals which are produced in very limited volumes. However, there are still thousands of potential TICs. In many operational situations, the number of potential TICs can be further reduced by considering only those compounds that produced an acute inhalation effect. However, effects from chronic exposures and the effects of percutaneous exposure should not be ignored.

Toxic Industrial Chemicals and Military Missions

NATO forces are deployed in a variety of military missions including (Figure 23):

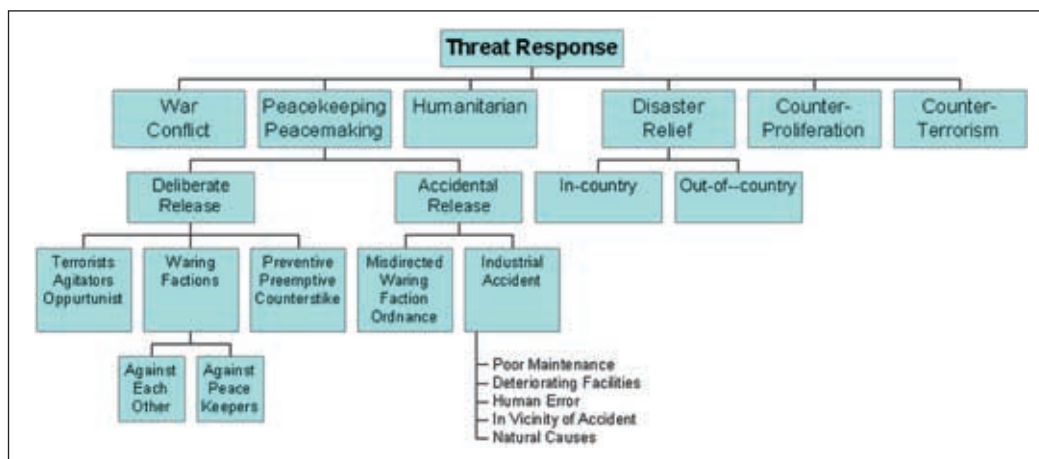


Fig 23. Industrial chemical releases could impact on these missions.



Fig 24. Bhopal, India. The release of methyl isocyanate on 3rd December 1984 led to the deaths of approximately 3800 people.

- War/Armed Conflict.
- Peace-keeping.
- Peace-making (Enforcement).
- Humanitarian and Civic Assistance.
- Disaster Relief.
- Counter-proliferation.
- Counter-terrorism.

TICs were the original CW agents and were very successfully used during WWI. Consequently, TICs are still attractive as improvised chemical weapons fills and have potential for inclusion in clandestine weapons programs or contingency plans. During military operations TICs could be released from industrial plants or storage depots through battle damage, as consequence of a strike against a particular facility, or deliberately as a desperation measure. TICs are particularly attractive to terrorists because of their ready availability.

The release of TICs through industrial accidents is common in lesser developed countries (Figure 24).

The safety, environmental, maintenance and transportation standards for industrial sites, manufacturing facilities and shipping containers are usually substantially less stringent than in NATO countries. In these areas, common causes of industrial accidents are human error, poorly maintained equipment, and deteriorating facilities. Natural causes such as earthquakes and atmospheric phenomena can also cause accidental releases, especially where sub-

standard construction codes were followed.

In Operations Other Than War (OOTW), the commander may be expected to obey civilian health and safety standards when dealing with TICs.

Ranking of Toxic Industrial Chemicals

The TICs of greatest concern are those which pose an acute inhalation hazard. For a given TIC to present a hazard in a given military situation, the TIC must be present in sufficient quantity in the area of concern, must exhibit sufficient toxicity by inhalation and must normally exist in a state which could give rise to an inhalation hazard.

A general hazard ranking for TICs can be developed by estimating the:

- probability that a given TIC would be present in an area of concern by considering the geographical distribution of countries producing the TIC, the number of countries producing it and the number of producers.
- potential inhalation hazard as determined by the vapour pressure of the TIC - the higher the vapour pressure the greater the potential inhalation hazard.
- the toxicity of the TIC to humans as measured by an appropriate toxicity parameter (e.g., Immediately Dangerous to the Life and Health (IDLH) value).

A Hazard Index (HI) is the product of four factors and used to rank TICs.

Table 6. Hazard Index Parameters.

Distribution		No. of Producers (NP)		Toxicity (IDLH in ppm)		State (VP in torr)	
Continents >5	5	NP >100	5	IDLH <1	5	Gas	5
Continents = 4	4	50 < NP < 99	4	1 < IDLH < 10	4	Liquid: VP > 400	4
Continents = 3	3	25 < NP < 49	3	11 < IDLH < 100	3	Liquid: 100 < VP < 400	3
Continents = 2	2	5 < NP < 24	2	101 < IDLH < 500	2	Liquid: 10 < VP < 100	2
Continents = 1	1	NP < 5	1	IDLH > 500	1	Liquid : vp < 10	1

Table 7. Characteristics of Toxic Industrial Chemicals of Greatest Concern (in order of Hazard Index).

Chemical	Appearance	Odour	IDLH (ppm)	Hazard Index	Specific Treatment
Chlorine (Cl ₂)	greenish-yellow gas; nonflammable	strong swimming-pool	10	500	no
Ammonia (NH ₃)	colourless gas; nonflammable	pungent	300	375	no
Formaldehyde (CH ₂ O)	colourless gas; combustible	pungent, suffocating	20	375	no
Ethylene Oxide (C ₂ H ₄ O)	colourless gas; flammable	ether-like	800	300	no
Sulfur Dioxide (SO ₂)	colourless gas; nonflammable	irritating, pungent	100	300	no
Phosgene (COCl ₂)	colourless gas; noncombustible	suffocating, musty hay	2	240	no
Hydrogen Fluoride (HF)	colourless gas or fuming liquid	strong irritating	30	225	no
Arsine (AsH ₃)	colourless gas; flammable	mild, garlic	3	160	no
Nitric Acid (HNO ₃)	colourless, yellow or red fuming liquid	acidic, suffocating	25	160	no
Boron Trichloride (BCl ₃)	colourless gas	hydrochloric acid-like	ND	<150	no
Phosphorus Trichloride (PCl ₃)	colourless to yellow fuming liquid	hydrochloric acid-like	25	144	no
Hydrogen Cyanide (HCN)	colourless-pale blue gas or liquid; flammable	bitter, almond	50	135	yes
Fluorine (F ₂)	pale yellow-greenish gas; nonflammable	pungent, irritating	25	120	no
Hydrogen Sulfide (H ₂ S)	colourless gas; flammable	rotten eggs	100	120	no
Sulfuric Acid (H ₂ SO ₄)	colourless to dark brown oily liquid	odourless	4	100	no
Boron Trifluoride (BF ₃)	colourless gas; nonflammable	pungent, suffocating	25	90	no
Diborane (B ₂ H ₆)	colourless gas; flammable	repulsive, sweet	15	90	no
Hydrogen Bromide (HBr)	colourless gas; nonflammable	sharp, irritating	30	90	no
Hydrogen Chloride (HCl)	colourless-light yellow gas; nonflammable	pungent, irritating	50	90	no

HI = (toxicity)x(state)x(distribution)x (producers) = maximum value of 625.

This approach with the ranking factors given in Table 6 allows the TICs of highest concern to be identified. TICs of Highest Concern and their properties are in Table 7.

Once the TICs of Highest Concern have been identified, their civilian sector Toxicity Levels and Protection Levels can be obtained from standard HAZMAT references. The TICs of Highest Concern are the bulk commodity chemicals: chlorine and ammonia. Chlorine, the original CW agent which was extensively used in World War I, is now of great concern as an improvised munition fill and weapon of opportunity in OOTW and terrorist situations.

Although the approach outlined above allows the identification of TICs of Highest Concern, it can never replace good pre-deployment intelligence and assessment. This assessment will determine which TICs are produced, used, stored and transported

through the area of operation and will consider not only the final products but all precursors and intermediates and combustion products.

Antiplant Agents

Antiplant agents are industrial chemicals used to destroy the enemy's food supply and deny him concealment by foliage or vegetation. Antiplant chemicals can be classified as herbicides, defoliants and growth suppressants or inhibitors.

Herbicides kill or inhibit the growth of plants. They are divided into two main groups:

1. Selective herbicides kill only certain plant species and have little or no effect on others. They are generally organic compounds such as derivatives of phenoxyacetic acid (2,4-D and 2,4,5-T), triazines and urea compounds.
2. Non-selective herbicides which kill all

Table 8. Recommended Hazard Distances from Representative Chemical Storage Sites.

Chemicals	Quantity	Day	Night
Chlorine	Up to 100 tonnes	2.5 km	5 km
Phosgene	Up to 50 tonnes		
Ammonia	Up to 500 tonnes		
Hydrogen Cyanide in Hot Climates	Up to 50 tonnes		
Hydrogen Sulphide	Up to 50 tonnes		
Hydrogen Cyanide in Cold Climates	Up to 50 tonnes	1 km	2.5 km
Hydrogen Fluoride	Up to 100 tonnes		
Hydrogen Chloride	Up to 50 tonnes		
Ammonia	Up to 100 tonnes		

plant life are usually inorganic compounds such as sodium arsenite, dimethylarsenic acid (cacodylic acid) and sodium chloride.

Defoliants cause trees, shrubs and other plants to shed their leaves prematurely. Herbicides normally do not constitute an acute inhalation hazard. However, they do constitute a hazard if inadvertently or deliberately ingested. Further absorption should be prevented by gastric lavage or inducing emesis and administration of activated charcoal. Supportive therapy should be given.

Scenarios for Toxic Industrial Chemicals

Scenario analysis indicates that the major hazard is from massive releases from storage/transport containers of liquified, pressurized gaseous TICs. Hazard distances from chemical production or storage sites, within which a lethal exposure level could be reached if a massive release occurs, are given in Table 8.

The most important action in the case of a massive release of an industrial chemical is immediate evacuation. It is vitally important that commanders and troops be made aware that the best defence against toxic industrial chemical releases is to escape the path of the toxic chemical immediately. The respirator can provide limited protection and should only be used to escape the hazard area.

Additional data on downwind hazard distances for a variety of TICs can be obtained from HAZMAT manuals such as the 2000 Emergency Response Guidebook which is available on the Internet at www.tc.gc.ca/canutec.

Deploying Military Forces

Following a TICs release, the toxic cloud will tend to remain concentrated downwind from the release point and in low-lying areas (e.g., valleys, ravines or cellars). High concentrations could be found in buildings, woods, or any place where there is little air circulation. Subject to overriding operational considerations, the preferred positions for locating static military facilities - in a area where TICs are a consideration - are at higher elevation, on open ground and

upwind or away from the sources of industrial chemicals.

Exclusion Areas for TICs

A safety exclusion area around TIC facilities commensurate with current intelligence and technical assessment should be established:

- If the location of the source is defined and no release has occurred, a minimum safety exclusion zone of a 1 km radius around the TIC facility shall be established. NATO forces shall only enter this exclusion area when operational requirements dictate. Encampment of mobile units within a 5 km radius and fixed semi-permanent and permanent encampments within 10 km of the facility shall be avoided. NATO forces within these safety radii shall have military respiratory protection on their person. Aviation assets may only transit the exclusion zone observing a minimum flight level of 150 m.
- If a TIC release has occurred from the facility, all NATO forces must be evacuated from the area and a 5 km safety exclusion zone establish until a TICs hazard prediction is produced. Only units appropriately equipped and protected against the relevant TIC hazards can be ordered, if necessary to remain in the dangerous area. Once the prediction is produced, NATO forces shall not enter this zone until appropriate follow-on actions are taken. Encampment of all units within a 10 km radius of the centre of the hazard release shall be avoided.

Detection and Protection of Toxic Industrial Chemicals

Military detection, protection and decontamination equipment was not designed for TICs. Providing the TICs have an adequate vapour pressure, in service detection and monitoring systems based on mass spectrometry (MS) or ion mobility spectrometry (IMS) (e.g., the Chemical Agent Monitor) can, in principle, be re-programmed to detect it. Detection systems such as the Draeger detector system can be used for detecting and determining the concentration of a large number of dangerous chemicals in the gas, vapour or particulate state.



Fig 25. A chemical spill exercise.

In-service respirators should only be used to evacuate the immediate hazard zone resulting from a TICs release because NBC respirators were not designed to give protection and have not been tested against the majority of TICs. ***Self-contained breathing apparatus must be used in the immediate hazard zone because of the potential lack of oxygen and the very high challenge levels likely to be encountered.*** In service protective clothing was not designed or tested against TICs releases.

Civilian sector protective equipment can be used with TICs (Figure 25). The TICs of Highest Concern require encapsulated clothing (Civilian Level A) or non-encapsulated protective with a supplied breathing atmosphere (Level B).

Medical Management of Toxic Industrial Chemical Exposures

General

Certain procedures are common for all chemical exposures. Unfortunately, antidotes are available for relatively few substances. Good patient support with maintenance of vital signs is essential and rescuers should wear chemical resistant impervious clothing, boots, gloves and self contained breathing apparatus. Patient care personnel should wear chemical resistant impervious clothing, boots, gloves and self contained breathing apparatus unless the patient has undergone full field decontamination.

Basic Life Support

- The most important part of THERAPY is support of vital functions. Ensure an adequate airway.
- Remove from contaminated area or atmosphere as soon as possible.
- Evacuate to fresh air when a person has been overcome by fumes or exposed to a gaseous poison. Administer oxygen, 10-12L by a non-rebreather mask.
- Conduct primary survey.
- Remove and isolate contaminated clothing.
- After eye exposure, thoroughly flush the eyes with water and continue to do so until arrival at hospital or pH has returned to normal.
- Conduct complete secondary survey.
- Decontaminate skin if the patient has been exposed to something that will burn the skin or penetrate through it. Use large amounts of water and non-caustic soap.
- If swallowed, administer a glass of water to dilute the agent, unless the patient is comatose, convulsing or has no gag reflex.
- Save all vomitus and bring to hospital should spontaneous vomiting occur.
- Manage skin exposure of injuries.

Advanced Life Support

- Determine the level of consciousness. ***The most important part of THERAPY is support of vital functions.*** Ensure an adequate airway. Check for airway obstruction. Intubate if necessary.
- In the event of respiratory difficulties arterial blood gases should be obtained to assess the adequacy of ventilation and oxygenation (if possible). Support

- ventilation as necessary.
- If the patient is in shock, administer normal saline or Ringer's Lactate, IV, 200-300 ml/h for adults. Apply pneumatic trousers as necessary. Place patient in Trendelenburg position, avoid vasopressors, if possible.
 - If not in shock, initiate IV dextrose, 5% in water to keep vein open.
 - If cardiac or pulmonary problems occur, apply appropriate treatment protocols.
 - If swallowed, initiate emesis with Syrup of IPECAC, only under medical supervision. Syrup of IPECAC should not be used the following ingestion of strong acids or bases or when the patient is unconscious, has lost gag reflex or is fitting.
 - Activated charcoal and saline cathartic should follow gastric evacuation.
 - Seizures may be alleviated by administering diazepam; adult dosage, IV bolus slowly (5mg/min) 5-10 mg. This may be repeated at 10-15 minute intervals up to a maximum dose of 30 mg. Monitor vital signs closely. If diazepam is not achieving desired results, administer phenobarbital sodium IV at 200-230 mg over 10-15 minutes.
 - Observe for pulmonary oedema; observe for circulatory collapse.
 - If the TIC has been positively identified, apply treatment protocol specific for that TIC. Consult the HAZMAT reference manual.

Decontamination

All clothing should be removed and contained for disposal or decontamination. If the material is in solid form, carefully brush as much as possible off the victim prior to removing the clothing. The patient should be washed with a copious amount of water; use of a mild detergent is appropriate.

Lung Damaging Agents (Choking Agents)

GENERAL

Introduction

Lung damaging agents are chemical agents, which produce a toxic inhalational injury – they attack lung tissue and primarily cause pulmonary oedema. Whether produced for military or industrial use, these chemical agents pose a very real threat to military personnel.

The term choking agents has been traditionally applied to the use of certain lung damaging agents as chemical weapons, and includes phosgene (CG), diphosgene (DP), chlorine (CL), and chloropicrin (PS). Phosgene accounted for 80% of all chemical fatalities in World War I, but at least 14 different respiratory agents were used, as well as obscurants (smokes), harassing agents (chloracetone), and vesicants (mustard) that could cause pulmonary injury.

Today, only a handful of such pulmonary toxicants still exist in stockpiles around the world. Several however, such as chlorine and phosgene, are currently produced in large quantities for industrial purposes; other toxic industrial chemicals which may cause toxic inhalational injury include ammonia, isocyanates, mineral acids etc.

Other lung damaging materials – although not likely to be used as CW agents – are still likely to be encountered on the battlefield. Perfluoroisobutylene (PFIB) is a toxic pyrolysis product of tetrafluoroethylene polymers encountered in military materiel (e.g., Teflon®, found in the interior of many military vehicles). The oxides of nitrogen (NO_x) are components of blast weapons or may be toxic decomposition products. Smokes (e.g. HC) contain toxic compounds that cause the same effects as phosgene. Similar substances encountered in fires, e.g. PFIB, isocyanates, phosgene, and HCl may also produce lung damage. Chemical fire extinguishers containing carbon dioxide should not be used in confined spaces to extinguish thermite or magnesium types of incendiaries – carbon tetrachloride in contact with flame or hot metal produces a mixture of phosgene, chlorine, carbon monoxide and hydrochloric acid.

Physical and Chemical Properties

Choking agents are usually true gases in field environments, and stored and transported as a liquid under pressure. Other less volatile

lung damaging materials injury such as those in smoke or products of combustion may cause toxic inhalational injury following the generation of particulate aerosols.

Military dispersion of phosgene during World War I followed the explosion of liquid filled shells with subsequent rapid evaporation and formation of a white cloud due to its slight solubility in an aqueous environment. It spontaneously converted to a colourless, low-lying gas four times as dense as air. Because of its relatively low boiling point (7.5°C), phosgene was often mixed with other substances. Chlorine was released from pressurised cylinders to form a pungent greenish-yellow gas that was heavier than air.

Detection

Although field-detection equipment for classical choking agents is currently employed by some nations, and various commercial industrial detectors are available for the wider of lung damaging agents, there are no automatic detectors in service. The characteristic odour of some lung damaging agents may be unreliable as a sure means of detection. For example, in low concentration phosgene has a smell resembling new mown hay, but the odour may be faint or lost after accommodation. There is also considerable variation in the sense of smell between individuals.

Similarly the eye irritation, coughing, sneezing, hoarseness, and other central respiratory effects seen after exposure to high concentrations of some pulmonary toxicants are also unreliable indicators of exposure, as these may be transient or entirely absent at lower but still potentially lethal concentrations. This is particularly true in the case of phosgene.

Protection

The activated charcoal in the canister of the chemical protective mask adsorbs phosgene, and in-service respirators afford full protection from this and other choking agents. However, only limited or temporary protection against toxic products of combustion or smoke can be assumed, and may be complicated in addition by the presence of oxygen-depleted air.

Decontamination

No decontamination is required following exposure to classic choking agents or other lung damaging agents in gas or vapour form.



Fig 26. Phosgene induced injury to pig lungs.

Mechanism of Action

Chemicals that are highly reactive and/or highly soluble in aqueous solutions tend to act in the conducting, or central compartment of the respiratory tract. Centrally-acting irritants such as sulphur mustard, ammonia, and hydrochloric acid, cause pronounced irritation of the epithelial cells lining the upper airway. Additionally, at low concentrations, centrally-acting compounds are essentially consumed by deposition and reaction in the conducting airways before they reach the peripheral portion of the respiratory tract.

In contrast, most of the pulmonary agents, such as phosgene, oxides of nitrogen, and PFIB, are relatively insoluble and nonreactive, readily penetrating to the level of the respiratory bronchioles and the alveoli. There they undergo acylation reactions and are essentially consumed at that site, causing the damage that may eventually lead to pulmonary oedema.

Chemically induced, acute lung injury by these peripherally-acting agents involves a permeability defect in the blood-air barrier (the alveolar-capillary membrane); however, the precise mechanisms of toxicity remain largely unknown. Leakage of fluid from capillaries into the pulmonary interstitium is normally compensated by lymphatic drainage from the parenchyma, but as the fluid leakage increases, normal drainage mechanisms become progressively overwhelmed. After an asymptomatic or latent period of 20 min to 24 h (depending on the exposed dose), fluid leakage into the pulmonary interstitium decreases compliance producing a stiff lung and increasing complaint of tight chest, shortness of breath, and dyspnoea. Fluid eventually invades the alveoli and produces clinically evident pulmonary oedema.

The distinction between centrally and peripherally acting agents is not strict.

Following exposure to high concentrations of centrally acting irritants, sufficient agent may penetrate into the peripheral lung to cause pulmonary oedema. Similarly, high concentrations of peripherally-acting agents can release enough hydrochloric acid to cause significant central airway irritation and epithelial damage. Because chlorine is intermediate in its solubility and reactivity, chlorine-exposed soldiers in World War I usually exhibited both central airway damage and pulmonary oedema, even from moderate concentrations of the gas. Phosgene is only slightly soluble in water and aqueous solutions; once dissolved, it rapidly hydrolyses to form carbon dioxide and hydrochloric acid. The early-onset ocular, nasopharyngeal, and central airway irritation from high concentrations of phosgene appears to result from the release of hydrochloric acid during phosgene hydrolysis by water in the upper airways.

Toxicity

The odour threshold for phosgene is about 1.5 mg/m^3 , and phosgene irritates mucous membranes at 4 mg/m^3 . The LCt₅₀ of phosgene is approximately $3200 \text{ mg}\cdot\text{min}\cdot\text{m}^{-3}$, which is half the LCt₅₀ ($6,000 \text{ mg}\cdot\text{min}\cdot\text{m}^{-3}$) of chlorine, the first gas used on a large scale in World War I. Phosgene is twice as toxic as chlorine; although it is less potent than almost all of the subsequently developed chemical warfare agents, this should not lead to an underestimation of its danger - deaths have occurred after the inhalation of only a few breaths of high concentrations of phosgene. Perfluoroisobutylene (PFIB) is said to be ten times more toxic than phosgene.

CLINICAL-PATHOLOGICAL EFFECTS

Pathology

The outstanding feature of acute lung injury caused by lung damaging agents is massive pulmonary oedema. This is preceded by damage to the bronchiolar epithelium, development of patchy areas of emphysema, partial atelectasis, and oedema of the perivascular connective tissue. The trachea and bronchi are usually normal in appearance. This contrasts with the findings in chlorine and chloropicrin poisoning in which both structures may show serious damage to the epithelial lining with desquamation. The lungs are large, oedematous and darkly congested. Oedema fluid, usually frothy, pours from the bronchi and may be seen escaping from the mouth and nostrils (Figure 26). With exposure to very high concentrations, death may occur within several hours; in most fatal cases pulmonary oedema reaches a maximum in

12h, followed by death in 24 to 48h. If the casualty survives, resolution commences within 48h and, in the absence of complicating infection, there may be little or no residual damage.

Clinical Effects

Exposure to high concentrations of lung damaging agent may irritate moist mucous membranes, depending on their reactivity and solubility in water. Transient burning sensation in the eyes with lacrimation may coexist with early onset cough and a substernal ache with a sensation of pressure. Irritation of the larynx by very large concentrations of the agent may lead to sudden laryngeal spasm and death.

Pulmonary oedema follows a clinically latent period of variable length that depends primarily on the intensity of exposure (i.e., the Ct), but also partly on the physical activity of the exposed individual. This is particularly true for phosgene. After the latent period, the patient experiences worsening respiratory distress that at first is unaccompanied by objectively verifiable signs of pulmonary damage, but may progress relentlessly to pulmonary oedema and death.

The most prominent symptom following the clinical latent period is dyspnoea, perceived as shortness of breath, with or without chest tightness, and in the initial stages there may be no objectively verifiable signs of pulmonary damage. These sensations reflect hypoxemia, increased ventilatory drive, and decreased lung compliance, all of which result from the accumulation of fluid in the pulmonary interstitium and peripheral airways. Fine crackles appear at the lung bases, but these may not be clearly audible unless auscultation is conducted after a forced expiration. Later, auscultation reveals coarse crackles and râles in all lung fields, and increasing quantities of thin, watery secretions are noted. The build-up of fluid in the lungs has two clinically pertinent effects.

1. Developing pulmonary oedema interferes with oxygen delivery to alveolar capillaries and may lead to hypoxemia. If a sufficient percentage of haemoglobin is unoxygenated, cyanosis will become apparent.
2. The sequestration of plasma-derived fluid in the lungs (up to one litre per hour) may lead to hypovolemia and hypotension. Death results from respiratory failure, hypoxemia, hypovolemia, or a combination of these factors. Hypoxia and hypotension may progress particularly rapidly and suggest a poor prognosis.

The development of symptoms and signs of pulmonary oedema within four hours of exposure is an especially accurate indicator of a poor prognosis; in the absence of immediately available intensive medical

support, such patients are at high risk of death. Complications include infection of damaged lungs and delayed deaths following such respiratory infections.

Condition of Exposed Tissues

Pre-existing airway damage (such as that caused by prior exposure to a lung damaging agent) may seriously compromise the respiratory system's normal protection and clearance mechanisms. Cigarette smoking may severely compromise airway function with respect to both airway patency and clearance mechanisms. Hyper-reactive airways (asthma in varying degrees) are seen in up to 15% of the adult population. Exposures to pulmonary intoxicants may trigger bronchospasm in these individuals. This bronchospasm may delay the clearance of the agent, interfering further with gas transport. The development of an acute interstitial process (e.g. phosgene-related pulmonary oedema) may also trigger bronchospasm. Individuals with any of the following characteristics should be considered likely to develop bronchospasm as the result of a exposure to lung damaging agents:

- Prior history of asthma or hay fever (even as a child).
- Prior history of eczema.
- Family history of asthma, hay fever, or eczema.
- History of chronic sinusitis or seasonal rhinitis.

Individuals with hyper-reactive airways will benefit from bronchodilator therapy and possibly from steroids after exposure to a lung damager. This statement, however, does not constitute an endorsement for routine steroid use in all toxic inhalational injuries.

Differential Diagnosis

Phosgene is distinguished by its odour, its generalised mucous membrane irritation in high concentrations, dyspnoea, and pulmonary oedema of delayed onset.

Riot-control agents produce tearing along with burning and pain sensation predominantly in the eyes, upper airways, mucous membranes and skin. This irritation is typically more intense than that caused by phosgene and is unaccompanied by the distinctive odour of phosgene.

Nerve agents induce the production of watery secretions as well as respiratory distress; however, their other characteristic effects (e.g. muscle twitching, miosis) distinguish nerve agent toxicity from organohalide inhalation injury.

Vesicants usually produce a delayed respiratory toxicity associated predominantly with the central, rather than the peripheral airways. Vesicant inhalation severe enough to cause dyspnoea typically causes signs of airway necrosis, often with pseudomembrane

formation and partial or complete upper airway obstruction. Finally, pulmonary parenchymal damage following vesicant exposure usually manifests itself as haemorrhage rather than pulmonary oedema.

Clinical Investigations

Sophisticated laboratory studies are of limited value in the immediate care of an exposed, injured individual. The following studies are of some predictive value in determining the severity of exposure and the likely outcome.

Chest Radiograph

The presence of hyperinflation suggests toxic injury of the smaller airways, which results in air being diffusely trapped in the alveoli. The presence of "batwing" infiltrates suggests pulmonary oedema secondary to toxic alveolar-capillary membrane damage. Atelectasis is often seen with more-central-toxic inhalant exposures. As radiological changes may lag behind clinical changes by hours to days, the chest radiograph may be of limited value, particularly if normal.

Arterial Blood Gases

Hypoxia often results from exposure to lung damaging materials such as chlorine. Measurement of the partial pressure of oxygen (PO_2) is a sensitive but non-specific tool in this setting; both the central and peripheral effects of pulmonary intoxicants may produce hypoxia. Arterial blood gases may show a low PaO_2 or $PaCO_2$, which are early, nonspecific warnings of increased interstitial fluid in the lung. At 4 to 6h, normal arterial blood gas values are a strong indication that a particular exposure has little likelihood of producing a lethal effect. Typically, carbon dioxide elevation is seen in individuals with underlying hyper-reactive airways; in this circumstance, it is thought that bronchospasm is triggered by exposure to the chemical.

Haematocrit

An increase in the hematocrit may reflect the hemoconcentration induced by transudation of fluid into the pulmonary parenchyma.

Pulmonary Function Tests

Peak expiratory flow rate may decrease soon after a massive exposure. This non-specific test helps to assess the degree of airway damage and the effect of bronchodilator therapy. Decreased lung compliance and carbon dioxide diffusing capacity are particularly sensitive indicators of interstitial fluid volume in the lung, but are complex tests for hospital use only. Ventilation/perfusion ratio (V/Q) scanning is very sensitive but is nonspecific and for hospital use only.

TREATMENT OF TOXIC INHALATIONAL INJURY

Medical Management

Terminate exposure as a vital first measure. This may be accomplished by physically removing the casualty from the hazard environment or by protecting with a properly fitting respirator. Decontamination of liquid agent on clothing or skin terminates exposure from that source.

Execute the ABCs of resuscitation as required. Establishing an airway is especially crucial in a patient exhibiting hoarseness or stridor; such individuals may face impending laryngeal spasm and require intubation. Establishing a clear airway also aids in interpretation of auscultatory findings. Steps to minimise the work of breathing must be taken. Because of the danger of hypotension induced by pulmonary oedema or positive airway pressure, accurate determination of the casualty's circulatory status is vital, not just initially, but also at regularly repeated intervals and whenever indicated by the clinical situation. Carefully replace intravascular volume as required to maintain hemodynamic stability.

Enforce rest. Even minimal physical exertion may shorten the clinical latent period and increase the severity of respiratory symptoms and signs in an organohalide casualty. Physical activity in a symptomatic patient may precipitate acute clinical deterioration and even death. Strict limitation of activity (i.e. forced bed rest) and litter evacuation are mandatory for patients suspected of having inhaled any agent that might cause pulmonary oedema. This is true whether or not the patient has respiratory symptoms and whether or not objective evidence of pulmonary oedema is present.

Manage airway secretions and prevent/treat bronchospasm. Unless super-infection is present, secretions present in the airways of phosgene casualties are usually copious and watery. They may serve as an index to the degree of pulmonary oedema and do not require specific therapy apart from suction and drainage. Antibiotics should be reserved for those patients with an infectious process documented by sputum gram-staining and culture. An elevation of the partial pressure of carbon dioxide (PCO_2) greater than 45 mm Hg suggests that bronchospasm is the most likely cause of hypercarbia, therefore bronchodilators should be used aggressively. Bronchospasm may occur in individuals with reactive airways, and these patients should receive beta-adrenergic bronchodilators. Steroid therapy is also indicated for bronchospasm. Parenteral administration is the preferred route of steroid administration as inhaled routes may result in inadequate distribution to damaged airways. Methylprednisolone, 700-1000 mg or its equivalent, may be given intravenously in divided doses

during the first day and then tapered during the duration of the clinical illness. The increased susceptibility to bacterial infection during steroid therapy mandates careful surveillance of the patient. No human studies have shown any benefit from steroids, thus steroids are not recommended in individuals without evidence of overt or latent reactive airway disease.

Prevent/treat pulmonary oedema. Positive airway pressure provides some control over the clinical complications of pulmonary oedema. Early use of a positive pressure mask may be beneficial. Positive airway pressure may exacerbate hypotension by decreasing thoracic venous return, necessitating intravenous fluid administration and perhaps judicious use of the pneumatic anti-shock garment. Pulmonary oedema noted after a toxic inhalant exposure should be treated similarly to adult respiratory distress syndrome (ARDS) or "noncardiac" pulmonary oedema. The early application of PEEP is desirable, possibly delaying or reducing the severity of pulmonary oedema. Diuretics are of limited value; however, if diuretics are used, it is useful to monitor their effect by means of the pulmonary artery wedge pressure measurement because excessive diuretics may predispose the patient to hypotension if PEEP or positive-pressure ventilation is applied.

Prevent/treat hypoxia. Oxygen therapy is definitely indicated and may require supplemental positive airway pressure administered via one of several available devices for generating intermittent or continuous positive pressure. Intubation with or without ventilatory assistance may be required, and positive pressure may need to be applied during at least the end-expiratory phase of the ventilator cycle.

Prevent/treat hypotension. Sequestration of plasma-derived fluid in the lungs may cause hypotension that may be exacerbated by positive airway pressure. Urgent intravenous administration of either crystalloid or colloid (which in this situation appear equally effective) may need to be supplemented by the judicious application of the pneumatic anti-shock garment. The use of vasopressors is a temporary measure until fluids can be replaced.

Steroid Therapy

Systemic steroid therapy has been considered for use in certain toxic inhalational exposures. Human evidence of benefit from steroids in phosgene exposure is scanty. There is some support in the literature for steroid use in exposure to zinc/zinc oxide and oxides of nitrogen. However, there is no other strong support in the literature for the treatment of other specific toxic inhalations with systemic steroids.

A significant percentage of the population

has a degree of airway irritability or hypersensitivity, as exemplified by persons with asthma. These individuals are likely to display heightened sensitivity or even bronchospasm, non-specifically after an inhalational exposure. The use of systemic steroids would be indicated in this population if their bronchospasm was not readily controlled with more routine bronchodilators. If used in this setting, systemic steroids may be required for prolonged periods, particularly if superinfection should supervene. Inhaled steroids may be less effective than systemic steroids in circumstances of acute exposure, especially if later infected. Inhaled steroids appear most useful as an adjunct to the gradual reduction or weaning or both from a systemic steroid use.

Combined Injuries

Acute lung injury may complicate resuscitation and aggravate hypovolaemic shock associated with traumatic injury. In such cases the latent period between exposure and the development of pulmonary oedema may also be shortened

Triage

Patients seen within 12 h of exposure. A patient with pulmonary oedema only is classified **immediate** if intensive pulmonary care is immediately available. In general, a shorter latent period portends a more serious illness. A **delayed** patient is dyspnoeic without objective signs and should be observed closely and re-triaged hourly. An asymptomatic patient with known exposure should be classified **minimal** and observed and re-triaged every two hours. If the patient remains asymptomatic 24 h after exposure, discharge the patient. If exposure is doubtful and the patient remains asymptomatic 12 h following putative exposure, consider discharge. An **expectant** patient presents with pulmonary oedema, cyanosis and hypotension. A casualty who presents with these signs within 6 h of exposure generally will not survive; a casualty with the onset of these signs 4 h or longer after exposure may survive with immediate, intensive medical care.

Patients seen more than 12 h after exposure. A patient with pulmonary oedema is classified **immediate** provided he will receive intensive care within several hours. If cyanosis and hypotension are also present, triage the patient as **expectant**. A **delayed** patient is dyspnoeic and should be observed closely and re-triaged every 2 h. If the patient is recovering, discharge 24 h after exposure. An asymptomatic patient or patient with resolving dyspnoea is classified **minimal**. If the patient is asymptomatic 24 h after exposure, he is fit for discharge. A patient with persistent hypotension despite intensive medical care is **expectant**.

Further Reading

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