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КАФЕДРА ОБЩЕСТВЕННОГО ЗДОРОВЬЯ И ЗДРАВООХРАНЕНИЯ

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ОТРАВЛЯЮЩИЕ И ВЫСОКОТОКСИЧНЫЕ ВЕЩЕСТВА ПУЛЬМОНОТОКСИЧЕСКОГО И РАЗДРАЖАЮЩЕГО ДЕЙСТВИЯ

POISONING AND HIGHLY TOXIC SUBSTANCES OF PULMONOTOXIC AND IRRITATING ACTION

Учебно-методическое пособие

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Приведена краткая токсикологическая характеристика боевых отравляющих веществ, аварийно-опасных химических веществ пульмонотоксического и раздражающего действия, их физико-химические свойства, механизмы токсического действия, клинические проявления острой экзогенной интоксикации, а также порядок оказания первой, скорой медицинской помощи на догоспитальном этапе и основные направления лечения в стационарных условиях.

Предназначено для студентов 3-го курса медицинского факультета иностранных учащихся, обучающихся на английском языке.

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MOTIVATIONAL CHARACTERISTICS OF THE TOPIC

Methodological recommendations are developed with the aim of the educational process optimization and are recommended for practical training of students on the topic "Poisoning and highly toxic substances with pulmonotoxic and irritating action". This topic is considered in the section "Military Toxicology and Toxicology of Emergency Situations" of the educational discipline "Disaster Medicine".

Teaching purpose: to consider the main specific features of the toxic process in acute poisoning with some extremely dangerous chemicals and chemical warfare agents that cause chemical respiratory distress syndrome in adults and upper and lower respiratory tract irritation syndrome, as well as clinical signs and symptoms that allow specialists to make a primary toxicological diagnosis.

Teaching objectives. The student should:

1. Know:

– brief toxicological characteristics and approaches to classification of the studied toxic substances;

– types of inhalation injuries, caused by the studied chemical agents;

– routes of exposure, mechanisms of toxic action;

– clinical signs and symptoms of acute severe poisoning;

– approaches to providing first aid and emergency medical care.

2. Be able to:

– make a primary toxicological diagnosis at the scene of chemical accident;

– provide first aid and emergency medical care at the prehospital stage.

3. Be familiar with:

– physical, chemical and organoleptic properties of warfare toxic agents and emergency hazardous chemicals of pulmonotoxic and irritating effect that can help identify contamination of the environment and decontamination of the affected persons.

Requirements to the initial level of knowledge. For better mastering of the topic student must revise the following notions from:

– first aid: personal safety at the scene of accident; the procedure of primary examination of the victims;

– anesthesiology and resuscitation: airways management; clinical manifestations and principles of acid-base and water-electrolyte balance disorders correction; signs and symptoms of hypovolemic shock; life-threatening syndromes of respiratory disorders.

Control issues of the related disciplines:

1. The main sources of threats to the rescuer at the scene.
2. The concept of "isolation of body tissues".
3. The algorithm of the primary examination of the affected persons at the scene.
4. Methods of providing airway patency.

5. Methods of the consciousness level evaluation.

6. Methods of the cardiovascular system functions evaluation.

7. Pathophysiology and principles of hypovolemic shock diagnosis and intensive therapy.

8. Principles of respiratory life-threatening syndromes diagnosis and intensive therapy

9. The basic forms of acid-base balance disorders, pathophysiology. Clinical manifestations, correction principles.

10. The main types of acid-base and water-electrolyte balance disorders, pathophysiology. Clinical signs, intensive therapy.

Issues for self-control:

1. Classification of poisoning substances of pulmonotoxic and irritating action.

2. Types of inhalation lesions.

3. Types of pulmonary edema.

4. Basic forms of the respiratory system pathology (chemical etiology).

5. Phosgene (CG): physical and chemical properties; toxicity; routes of exposure; mechanisms of toxic action; clinical signs and symptoms of acute poisoning; first and emergency medical care.

6. Diphosgene (DP): physical and chemical properties; toxicity; routes of exposure; mechanisms of toxic action; clinical signs and symptoms of acute poisoning; first and emergency medical care.

7. Nitrogen oxides: physical and chemical properties; toxicity; routes of exposure; mechanisms of toxic action; clinical signs and symptoms of acute poisoning; first and emergency medical care.

8. Paraquat: physical and chemical properties; toxicity; routes of exposure; mechanisms of toxic action; clinical signs and symptoms of acute poisoning; first and emergency medical care.

9. Chloroacetophenone (CN): physical and chemical properties; toxicity; routes of exposure; mechanisms of toxic action; clinical signs and symptoms of acute poisoning; first and emergency medical care.

10. Brombenzylcyanide (CA): physical and chemical properties; toxicity; routes of exposure; mechanisms of toxic action; clinical signs and symptoms of acute poisoning; first and emergency medical care.

11. Chlorobenzylidenemalonodinitrile (CS): physical and chemical properties; toxicity; routes of exposure; mechanisms of toxic action; clinical signs and symptoms of acute poisoning; first and emergency medical care.

12. Dibenzoxazepine (CR): physical and chemical properties; toxicity; routes of exposure; mechanisms of toxic action; clinical signs and symptoms of acute poisoning; first and emergency medical care.

13. Adamsite (DM): physical and chemical properties; toxicity; routes of exposure; mechanisms of toxic action; clinical signs and symptoms of acute poisoning; first and emergency medical care.

POISONING AND HIGHLY TOXIC SUBSTANCES WITH PULMONOTOXIC ACTION

Pulmonotoxicity is the property of chemicals affecting the human organism to cause structural and functional disorders to the part of the respiratory organs. Pulmonotoxicity can manifest itself both with local and resorptive action of toxic substances. A lot of chemicals have pulmonotoxic properties. Having a large surface area, the lungs are constantly exposed to xenobiotics contained in the inhaled air. In the vast majority of cases, when concentrations of substances are low, such effects do not manifest themselves in any way. If the level of exposure is high enough, a toxic process of varying severity occurs — from minor irritation (transient toxic reactions) to severe disruptions in the structure and function of many organs and systems (poisoning). Lung tissue is also extremely sensitive to certain compounds (e.g. paraquat) entering the body via non-inhalation routes (gastrointestinal tract).

Pulmonotoxic agents are substances to which the threshold of the respiratory organs sensitivity is significantly lower than that of other organs and systems, and the clinical picture of the damage is characterized primarily by structural and functional disorders of the respiratory organs. Many highly toxic substances that are the subject of military toxicology studies belong to this toxicological group (Table 1).

Table 1

Main pulmonotoxic agents used in chemical industry

Substance	Scope of application
Acrylonitrile	Production of synthetic fibers, synthetic rubber, rubbers, dyes
Ammonia	Production of nitric acid, hydrogen cyanide, acrylonitrile, synthetic fibers, fertilizers, explosives, as refrigerant
Nitric acid	In organic synthesis of coloring substances, nitration of cellulose, in metallurgy, in the production of nitrates, fertilizers
Carbon disulfide	Production of cellophane, fabrics, solvents, disinfectants, during vulcanization of rubber
Phosgene	Production of plastics, synthetic rubber, dyes, urea
Chlorine	Production of plastics, disinfectants, bleaching agents, glycerin, water purification, metallurgy
Chloropicrin	Pest control agent for agricultural plants, disinfectants

In order to develop effective toxic substances, the so-called “Warfare toxic agents of suffocating action” in military toxicology, the properties of such pulmonotoxicants as chlorine, phosgene and diphosgene, chloropicrin, sulfur pentafluoride, perfluorizobutylene, etc. have been studied in the past.

Currently, use of these substances as warfare toxic agents (WTA) is unlikely. At the same time, accidents and disasters at industrial chemical enterprises are dangerous first of all due to the release of pulmonotoxicants into the environment.

The properties of pulmonotoxicants are also manifested by irritating substances in high concentrations and toxic substances of cytotoxic action when inhaled in the form of vapor or aerosol.

Representatives of this group are very heterogeneous both in chemical structure and in the caused effects. It is advisable to divide all suffocating toxic substances according to their ability to cause irritating effect at the time of exposure into poisons for which the irritating effect is not expressed (phosgene, diphosgene), and toxic agents with a pronounced irritating effect. The poisons of the second group are mainly suffocating poisons (chlorine, sulfur chloride, sulfuric and hydrochloric acids) and compounds with a suffocating and pronounced resorption effect (Fig. 1).

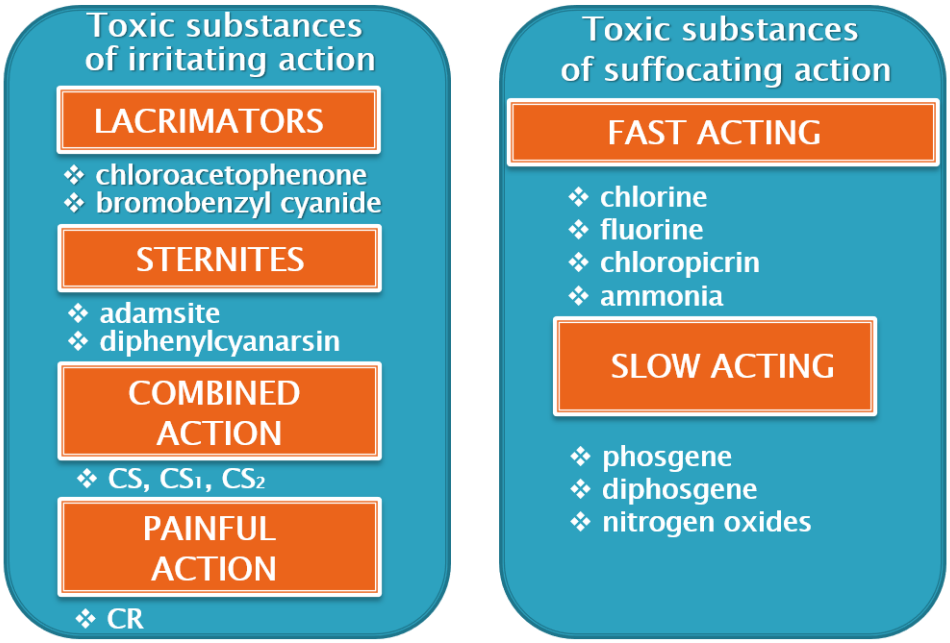


Fig. 1. Classification of poisoning substances with pulmonotoxic and irritating action

Basic variants of inhalation lesions can be divided into several types:

Type I: lesions to the mucous membranes of the upper airway and bronchial tree — conjunctivitis, rhinitis, pharyngitis, laryngitis, tracheitis, bronchitis. The main clinical manifestations: conjunctival irritation, nasal discharge, cough, chest pain, laryngeal edema, bronchospasm.

Type II: lesions to terminal bronchioles and lung parenchyma — bronchiolitis, pneumonia, non-cardiogenic pulmonary edema. The main clinical manifestations: shortness of breath, cyanosis, bronchospasm, crepitating wheezing, radiological changes.

Type III: primary pulmonary lesions are absent or minimal. The lungs serve as a surface for the absorption of toxic substances into the systemic bloodstream. In this case, lesions to the liver, blood, kidneys are observed and respiratory symptoms are secondary by nature (Table 2).

Table 2

Examples of toxic substances that cause inhalation lesions

Type I	Type II	Type III
chlorine ammonia formaldehyde sulfur dioxide hydrogen chloride hydrogen fluoride acetic acid irritating agents: CS, CR, DM	nitrogen dioxide nitrogen monoxide phosgene diphosgene	toluene carbon monoxide propane hydrogen cyanide

Pathological conditions associated with the acute effect of toxicants on the upper respiratory tract lead to two types of consequences:

a) arousal of reflexes (Table 3) due to irritation of the nerve endings of the olfactory, trigeminal, pharyngeal nerves (Kratschmar reflex), as well as the vagus nerve (Salem–Aviado reflex), accompanied by the development of apnea, bradycardia, bronchospasm, cough, opposite effects of blood pressure level;

b) development of inflammatory-necrotic changes in the respiratory tract, the severity of which is determined by the properties of toxicants and their concentration in the inhaled air. The consequence of inflammatory-necrotic changes is ulceration of the mucous membrane, hemorrhage, swelling of the larynx. Although the signs of the lesion appear quite quickly, the edematous reaction develops gradually, and stridor (obstruction of the larynx) may develop a few hours after exposure. In poisoned individuals, in addition to damage to the respiratory system, burns to the skin of the face, eyes and mouth may be observed.

Table 3

Brief description of the reflexes underlying the reactions of external respiration and possible toxic effects (D. M. Aviado, H. Salem, 1987)

Brief description of the reflexes underlying the localization of receptors (cranial nerves)	Physiological and chemical stimuli	Respiratory and Cardiovascular system reactions
Upper airway (I, V, X)	Gases, vapors, aerosols of irritants	Apnea, bradycardia, vascular spasm
Lower airway	Gases, vapors, aerosols of irritants	Cough
Bronchoalveolar Receptors: (X) slow-adapting (X) quickly adaptable	 Moderate inflammatory reaction. Atelectasis; Pronounced inflammatory reaction	Tachypnea, apnea
Cardiopulmonary Receptors: (X) pulmonary veins (X) left ventricle	Lowering blood pressure. Increase in blood pressure. Alkaloids of the veratrin group	Bradycardia, vasodilation, apnea
Baroreceptors: (X) aortic arch (IX) carotid glomerulus	Lowering blood pressure	Bradycardia, vasodilation, apnea

End of the Table 3

Brief description of the reflexes underlying the localization of receptors (cranial nerves)	**Physiological and chemical stimuli**	**Respiratory and Cardiovascular system reactions**
Chemoreceptors: (X) aortic arch (IX) carotid glomerulus	Hypoxia; cyanides	Tachypnea, tachycardia, vasodilation
Somatic receptors: Pain receptors Muscle receptors Visceral receptors	Inflammation. Pain stimulating agents. Irritating agents. Physical work. Compression	Tachypnea

A characteristic form of lung damage with pulmonotoxicants is pulmonary edema. The essence of the pathological condition is the release of blood plasma first into the wall of the alveoli, and then into the lumen of the alveoli and the respiratory tract. Edematous fluid fills the lungs — a condition, previously referred to as "drowning on the land", develops. There are three types of pulmonary edema:

– **hemodynamic pulmonary edema**, is based on the BP increase in the small circle of blood circulation, with the absence of damage to the alveolar capillary membrane;

– **toxic pulmonary edema**, develops as a result of primary damage to the alveolar capillary membrane against the background of normal intra-pulmonary blood pressure during the initial period;

– **pulmonary edema of a mixed type**, develops when the victims have both a damage of the properties of the alveolar-capillary barrier and the contractile properties of the myocardium (Table 4).

Table 4

Substances which cause different types of pulmonary edema

Hemodynamic pulmonary edema	**Toxic pulmonary edema**	**Pulmonary edema of a mixed type**
ethylene glycol cyanidescarbon monoxide arsin thallium cadmium phosphorus organophosphates, etc.	ammonia cadmium oxide chlorine chloropicrin tetrachlorodinitroethane methyl sulfate oxygen (with prolonged inhalation under high pressure, ozone) phosgene diphosgene sulfur dioxide nitrogen oxides sulfur pentafluoride paraquat chlorine trifluoride, etc.	dichloroethane trichloroethylene lewisite, etc.

Basic forms of the respiratory system pathology of chemical etiology. Acute lesions with pulmonotoxic agents are accompanied by the formation of a number of pathological processes, including the main (in addition to the phenomenon of irritation) inflammatory processes in the respiratory tract (acute laryngitis and tracheobronchitis) and pulmonary parenchyma (pneumonia), as well as toxic pulmonary edema.

LOCALIZATION OF THE LESIONS

The effect of inhaled gases and vapors is determined by the degree of their solubility in bronchial secretions, covering the mucous membrane of the respiratory tract and alveolar epithelium. Substances that are highly soluble in water, for example, ammonia, sulfur dioxide, are mainly fixed by the upper respiratory tract.

For this reason, the main toxic effect of these xenobiotics is realized in the upper respiratory tract, and the underlying parts are damaged only at very high concentrations. On the contrary, poorly water soluble substances, such as phosgene, diphosgene, nitrogen oxides, perfluorizobutylene, mainly affect the deep parts of the lungs. That is why, the less soluble gas is in the water, the higher its potential in terms of damage to the lung parenchyma. Water-soluble substances reach the deep parts of the lungs when breathing through the mouth, which is observed during physical exertion, or when a person is unconscious. In both cases, the degree of damage to the lung parenchyma by toxicants, in cases when all other conditions are being equal, increases.

The important factor determining the lesion nature of the respiratory organs is the type of cells prevailing in the area of the primary effect of the toxic substance. There are more than 40 types of cells in the tissues of the lungs and bronchi, each of them has significant morphological & functional features and special sensitivity to the action of toxicants (Table 5).

Table 5

Sensitivity of the main types of lung cells to certain pulmonotoxicants

Pulmonotoxic agent	Cell elements		
	Pneumatocytes	Endotheliocytes	Clara cells
Paraquat	+++	+	–
Nitrogen oxide	+++	++	–
Chlorine (halogens)	+++	+	–
Nickel tetracarbonyl	+++	+	–
Chloropicrin	+++	++	–
Monocrotalin	+	+++	–
Oxygen (98–100 %)	+	+++	+
Phosgene	+	+++	+
Carbon tetrachloride	+	–	+++
Brombenzene	++	+	+++

Damage to the Respiratory Tract

The airways are covered with ciliated epithelium. Secretory cells, goblet cells, brush cells, Clara cells and a number of other cells produce a secret that lines the mucous membrane of the respiratory tract with a thin layer.

The cilia of the epithelium make rhythmic movements, maintaining the flow of mucus from the lungs. With this flow, particles of substances adsorbed on the surface of the epithelium that do not dissolve in the secret of the tracheobronchial glands are removed from the lungs and the respiratory tract.

The speed of particles movement on the surface of the trachea and bronchi epithelium is 1–4 microns/min.

As it was mentioned above, negative effects of toxic substances on the upper respiratory tract is accompanied by both functional disorders due to irritation of the nerve endings of the olfactory, trigeminal, pharyngeal and vagal nerves and the development of inflammatory-necrotic changes in the respiratory tract, determined by the properties of toxic agents.

Functional disorders are manifested by cough, mucus secretion, bronchospasms and moderate edema of the respiratory tract (protective reactions to harmful effects). With intense exposure, such transient toxic reactions develop into severe pathological conditions. So, excessive in severity or duration cough can cause serious dysfunctions, especially in persons, sensitive to toxicants. Stimulation of mucus secretion by the submucosal glands of the respiratory tract and goblet cells (protective reaction) can also cause pathology.

Manifestation of inflammatory-necrotic changes is ulceration of the mucous membrane, hemorrhage and swelling of the larynx. Although signs of damage appear quickly, laryngeal edema may develop only after a few hours of exposure. In patients, along with damage to the respiratory system, there may be a burn to the face skin, eyes, oral cavity mucosa, which makes it difficult to provide assistance. Usually, the more pronounced the lesion to the upper respiratory tract, the higher the probability of damage to the deep one.

In the most cases mild lesions of the lower respiratory tract of chemical etiology are resolved practically without consequences (in case of exposure with irritating agents — within a few minutes after leaving the contamination zone). However, pronounced exudation, accompanied by spasm of the respiratory tract, reflex depression of the respiratory and vasomotor centers, can lead to asphyxia syndrome (cyanosis, dyspnea, loss of consciousness).

Moderate edema of the airways tissue is a consequence of damage to the epithelium with inhaled substances. However, this effect is also caused by stimulation of the axonal reflex through the afferent nerves of the respiratory tract, including the effect of xenobiotics in very low concentrations. At the same time, the nerve endings release low-molecular biologically active substances — tachykinins. These substances cause vasodilation and increased vascular permeability of the submucosal layer of the airways. As shown in the experiment, acrolein, formaldehyde, isocyanates may act in the similar way.

Transient bronchospasm is a normal reaction to the action of irritants, which protects the lung parenchyma from damage. However, persistent and pronounced bronchospasm significantly deteriorates the affected person's condition. Some pulmonotoxic substances cause bronchospasm even in concentrations that do not cause damage to the lung tissue (sulfur dioxide). Others (ammonia) cause bronchospasm only in concentrations that damage lung tissue at the same time. Some more (phosgene) affect the parenchyma of the lungs practically without provoking bronchospasm.

Damage to the cells of the mucous membrane of the respiratory tract (up to their death) develops with inhalation of toxicants in rather high concentrations. At the same time, a number of processes are launched that adversely affect the respiratory status of the victims. Usually, close contact between epithelial cells is disrupted, the epithelial layer becomes porous (which allows bacteria to penetrate into the tissues), peeling and detachment of dead epithelium can cause airway obstruction. Finally, activation of synthesis and release of various cytokines and other biologically active substances by damaged cells leads to inflammation, edema and spasm of the bronchi smooth muscles. Thus, direct damage to the epithelium with inhaled toxicants in high concentrations significantly enhances the reactions provoked by these agents in low concentrations.

When carrying out medical assistance to victims, it is necessary to take into account that the manifestations of acute tracheobronchitis can develop both immediately and long term after the exposure to toxicants. Thereby, progressive edema of the respiratory tract reaches its maximum, as a rule, 8–24 hours after exposure with pulmonotoxic poisons. After 48–72 hours, with severe lesions, detachment of the mucous membrane is observed (the so-called pseudomembranous tracheobronchitis).

The condition of the majority of the affected persons with adequate therapy normalizes within a few days or weeks (depending on the severity of the pathological process) due to the complete regeneration of the damaged tissue.

However, some individuals may develop hypersensitivity to toxicants, manifested by the syndrome of reactive airway dysfunction. Substances, which cause a condition, similar to bronchial asthma attack after a single exposure, are called isocyanates. Some people who have been acutely exposed to chemicals develop a progressive inflammatory process, which can result in tracheal stenosis, bronchiectatic disease, obliteration of lower airways.

Lesions to the Lung Parenchyma

Gas exchange in the lungs is inhibited in case of damage to any element of the alveolar-capillary barrier (epithelium (pneumatocytes), endothelium, interstitium). Epithelial disruption leads to the synthesis damage, storage and deposition of surfactants, increase in the permeability of the alveolar-capillary barrier and edematous fluid exudation growth into the lumen of the alveoli. It also increases the permeability of the alveolar-capillary barrier, causes hemodynamic disturbances in the lungs, changes the normal ratio of ventilation volume and

hemoperfusion of the lungs, etc. As a result of gas exchange pathology, oxygen insufficiency develops, which manifests itself first during physical exertion, and then at rest. In lung pathology, gas exchange obstruction is the main cause of conditions that threaten the life of the victim, and sometimes leads to death.

Toxic Pneumonia

The group of acute pneumonia of chemical etiology includes various, often combined, lesions, the morphological features of which are determined by the characteristics of the xenobiotics toxic effect. Examples of some highly toxic substances that cause chemical pneumonia include acrolein, vapors of mineral acids, ammonia, mustard gas, sulfur dioxide, arsenic organic compounds.

Toxicants damage the parenchyma of the lungs, involving both the alveolar wall (acute, sometimes hemorrhagic, exudative alveolitis) and pulmonary interstitial tissue (diffuse interstitial pneumonia). In severe cases, necrosis of the lung tissue and superinfection occur with the formation of abscesses (acrolein), obstructive airway damage (carbon dioxide). Often acute exposure leads to the development of long-term and sluggish toxic processes in the lungs. Delay in the development of the pathological process in the lungs may be a consequence not of direct damage to the lung tissue by the toxicant, but of damage to its polymorphonuclear leukocytes and macrophages, which, when exposed to toxic gases, accumulate in the parenchyma of the lungs and respiratory tract.

The death of these cells leads to the release of lysosomal enzymes, prostaglandins, collagenase, elastase, plasmin activating factors and other biologically active substances into the lung tissue, which stimulates the inflammatory process, fibrosis, emphysema, granulomatosis, etc.

Toxic Pulmonary Edema

Pulmonary edema is a manifestation of water disbalance in the lung tissue (the ratio of the fluid content inside the vessels, in the interstitial space and inside the alveoli). Normally, blood flow of the lungs is balanced by its outflow through the venous and lymphatic vessels (the rate of lymph outflow is about 7 ml/h).

The water balance of the fluid in the lungs is maintained by:

– regulation of pressure in the small circle of blood circulation (in the normal conditions of 7–9 mm Hg, critical pressure — more than 30 mm Hg, blood flow rate — 2.1 l/min);

– barrier functions of the alveolar-capillary membrane separating the air in the alveoli from the blood flowing through the capillaries.

As it was mentioned above, pulmonary edema can occur as a result of both regulatory mechanisms (mixed variant), and each mechanism separately pathology (hemodynamic and toxic pulmonary edema).

Actually, toxic pulmonary edema is associated with damage by toxic substances to cells involved in the formation of the alveolar-capillary barrier. Military-grade toxicants capable of causing toxic pulmonary edema, are called WTA of suffocating action or suffocating agents.

The mechanism of damage to lung tissue cells with suffocating WTA is not the same, but the processes developing after that are quite similar (Fig. 2).

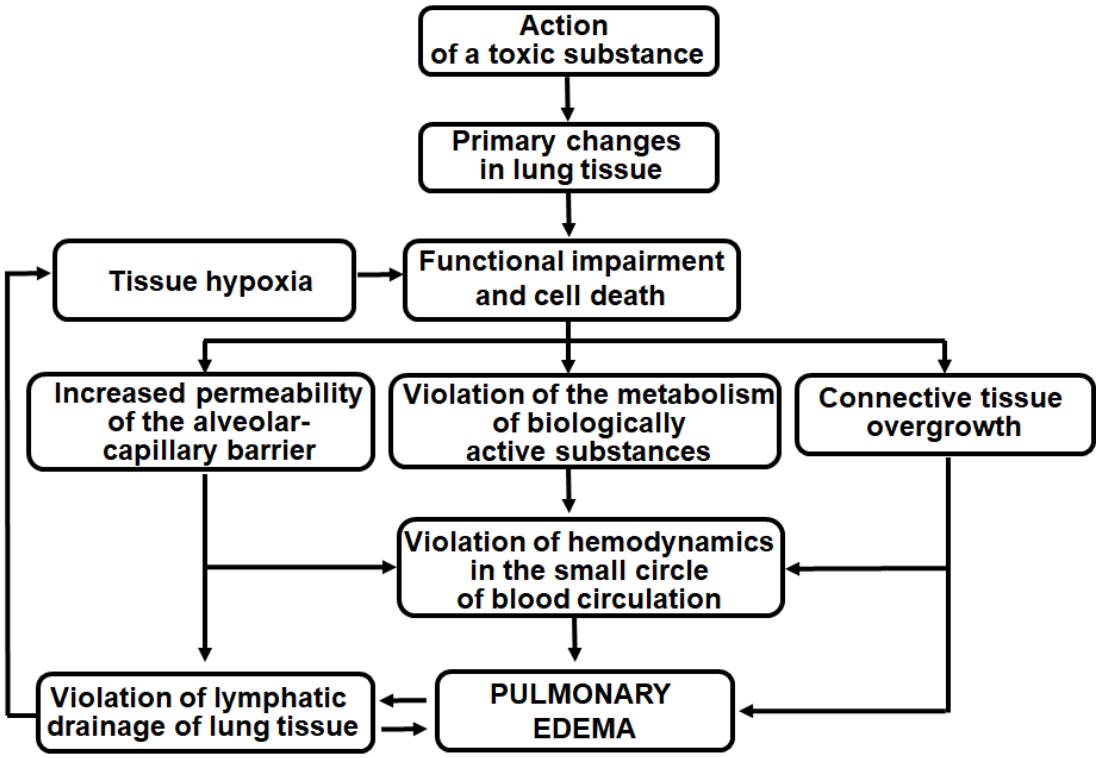


Fig. 2. Scheme of pathogenesis of toxic pulmonary edema

Damage to cells and their death lead to increased permeability of the barrier and disruption of the metabolism of biologically active substances in the lungs. Permeability of the capillary and alveolar parts of the barrier varies. Initially, the permeability of the endothelial layer increases, and the vascular fluid transfers into the interstitial space, where it temporarily accumulates. This phase of the pulmonary edema development is called interstitial. During the interstitial phase, the lymph outflow accelerates compensatory, approximately by 10 times.

However, this adaptive reaction turns out to be insufficient, and the edematous fluid gradually penetrates through the layer of destructively altered alveolar cells into the cavity of the alveoli and fills them. This phase of the pulmonary edema development is called alveolar and is characterized by the appearance of distinct clinical signs.

Excluding ("switching off") part of the alveoli from the gas exchange process is compensated by stretching of the intact alveoli (emphysema), which leads to mechanical compression of the capillaries of the lungs and lymphatic vessels.

Cell damage is accompanied by the accumulation of biologically active substances in the lung tissue, such as norepinephrine, acetylcholine, serotonin, histamine, angiotensin I, prostaglandins E_1, E_2, F_2, bradykinins. It leads to the additional increase in the permeability of the alveolar-capillary barrier and hemodynamics pathology in the lungs. The speed of blood flow decreases while the pressure in the small circle of blood circulation increases.

Edema continues to progress, the fluid fills the respiratory and terminal bronchioles, while due to the turbulent movement of air in the respiratory tract, foam, stabilized by the washed alveolar surfactant, emerges.

The surfactant content in the lung tissue decreases immediately after exposure to toxicants. This explains the early development of peripheral atelectasis in the affected persons. In addition to these changes, systemic disorders that are included in the pathological process and increase as pulmonary edema develops, are of great importance). The most important of them are the following: violations of the gas composition of blood (hypoxia, hyper-, and then hypocapnia), changes in the cellular composition and rheological properties (viscosity, clotting ability) of blood, disorders of hemodynamics in a large circle of blood circulation, impaired kidney and central nervous system functions.

CHARACTERISTICS OF CERTAIN REPRESENTATIVES OF SUFFOCATING AGENTS

PHOSGENE, DIPHOSGENE

Phosgene belongs to the group of halogen derivatives of carbonic acid. The condition for the physiological activity of such compounds is presence of a halogen — carbonyl group bond. Substitution of one of the halogens in the compound molecule with hydrogen or an alkyl radical leads to a sharp decrease in pulmonotoxicity.

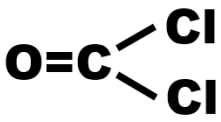
Chloro-, bromine- and fluorine derivatives of carbonic acid have been synthesized; their toxicity is close to phosgene. To a greater extent, the chlorine derivatives met the requirements for WTA.

In addition to phosgene, carbonic acid trichloromethyl ether (diphosgene) is considered as potential WTA. These substances have the same biological activity. It is generally believed that the effect of diphosgene is due to the splitting of its molecule into two phosgene molecules in contact with lung tissues.

Phosgene was obtained in 1912 by the English chemist Devi, who observed the interaction of chlorine with carbon monoxide in sunlight, hence the name of the substance (from Greek. Phosgene — “light-born”). It was used for the first time as WTA in 1915 by German Armed Forces. The total amount of WTA synthesized during the period 1915–1918 is estimated at 150 000 tons. About 80 % of those who died during the World War I from chemical agents accounted for those poisoned with phosgene. Currently, stocks of phosgene and diphosgene stored in army warehouses are subject to destruction. However, phosgene and its derivatives is an important starting product of the synthesis of plastics, synthetic fibers, dyes, and pesticides. Therefore, production of this substance in all countries with a developed chemical industry is steadily increasing. Phosgene is one of the toxic products of the thermal destruction of organochlorine compounds (freons, polyvinyl chloride plastic, teflon, carbon tetrachloride), which also needs to be taken into account in medical care providing during accidents and catastrophes.

Physical and Chemical Properties. Routes of Exposure. Toxicity

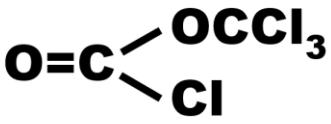
Phosgene (CG) is a carbonic acid dichloranhydride; under normal conditions a colorless gas with the smell of rotten apples or musty hay, in small concentrations has a pleasant fruity odor. Gaseous phosgene is 2.48 times heavier than air. At a temperature of 0 °C, the substance is a liquid with a density of 1.432, boiling at +8.2 °C, freezing at –118 °C. It dissolves poorly in water: in one volume of water — two volumes of gaseous phosgene (at a measured 0.8 %).



It is well soluble in organic solvents and some other compounds — in glacial acetic acid, arsenic chloride, chloroform, etc. When interacting with water, phosgene is hydrolyzed to hydrochloric and carbonic acids. In an alkaline environment and when heated, hydrolysis accelerates. With tertiary amines (e.g. with urotropin), it forms attachment products. This property formed the basis of the protective effect of a wet gas mask. It is neutralized with ammonia. It has a cumulative effect. Resistance in summer is up to 1–1.5 hours.

Diphosgene (DP) is trichloromethyl ether of chlorogenic acid, colorless liquid with the smell of rotten apples; specific gravity at 15 °C is 1.64, boiling point is 128 °C, freezing point is –57 °C, volatility at 20 °C is 120 mg/l, air density is 6.9. The toxicity of phosgene and diphosgene is approximately the same and it is rather high when they are used in the form of vapors.

The smell of phosgene is felt at a concentration of 0.004 g/m^3. Staying in an atmosphere containing up to 0.01 g/m^3 without consequences is possible for no more than an hour. Concentration of 1 g/m^3 reaches in 5 min. exposure leads to death in more than 50 % of cases. Lethal toxodose: LCt_{100} is 5 g × min/m^3, LCt_{50} — 3.2 g × min/m^3, the average incapacitating dose ICt_{50} — 1.6 g × min/m^3.



Resistance of phosgene and diphosgene in open areas in case of their combat use is insignificant and at positive temperatures does not exceed one hour. In case of accidental or deliberate release into the surrounding environment, it forms unstable slow-acting foci of chemical contamination. In the forest, ravines, basements, resistance increases up to 2–3 hours, forms the so-called “gas swamps”.

In cold seasons resistance of phosgene increases many times.

In case of accidents on industrial enterprises, stability of WTA due to constant desorption from the spill site increases up to several days.

Phosgene acts only by inhalation, has a specific effect on the respiratory organs, and at the time of contact — a weak irritating (sometimes imperceptible) effect on the eyes and mucous membranes. It does not penetrate into internal environments, decomposing upon contact with the lung tissue.

Mechanisms of Toxic Action

Getting into the respiratory system, the substance is slightly reained in the respiratory tract due to low hydrophilicity. Lung damage is a consequence of toxic agent direct action to the cellular structures of the air-blood barrier.

According to the mechanism of toxic action, phosgene refers to alkylating agents capable of binding to SH-, NH_2- and CO-groups of biological molecules.

Interacting with type II alveolocytes, the toxicant damages them, inhibiting the activity of phospholipid and surfactant synthesis enzymes. Since the period of semi-exchange of surfactant in humans is rather long (12–24 hours), an increase in the surface tension in the alveoli and their "subsidence" is detected only a few hours after inhalation of the substance. Penetrating further along the concentration gradient into the depth of the alveolar-capillary barrier, phosgene reduces the viability and metabolic activity of the endothelial cells of the lung capillaries. The important role in the pathology development belongs to the action of the substance on the endings of the afferent fibers of the vagus nerve, innervating the deep parts of the respiratory system (Fig. 3).

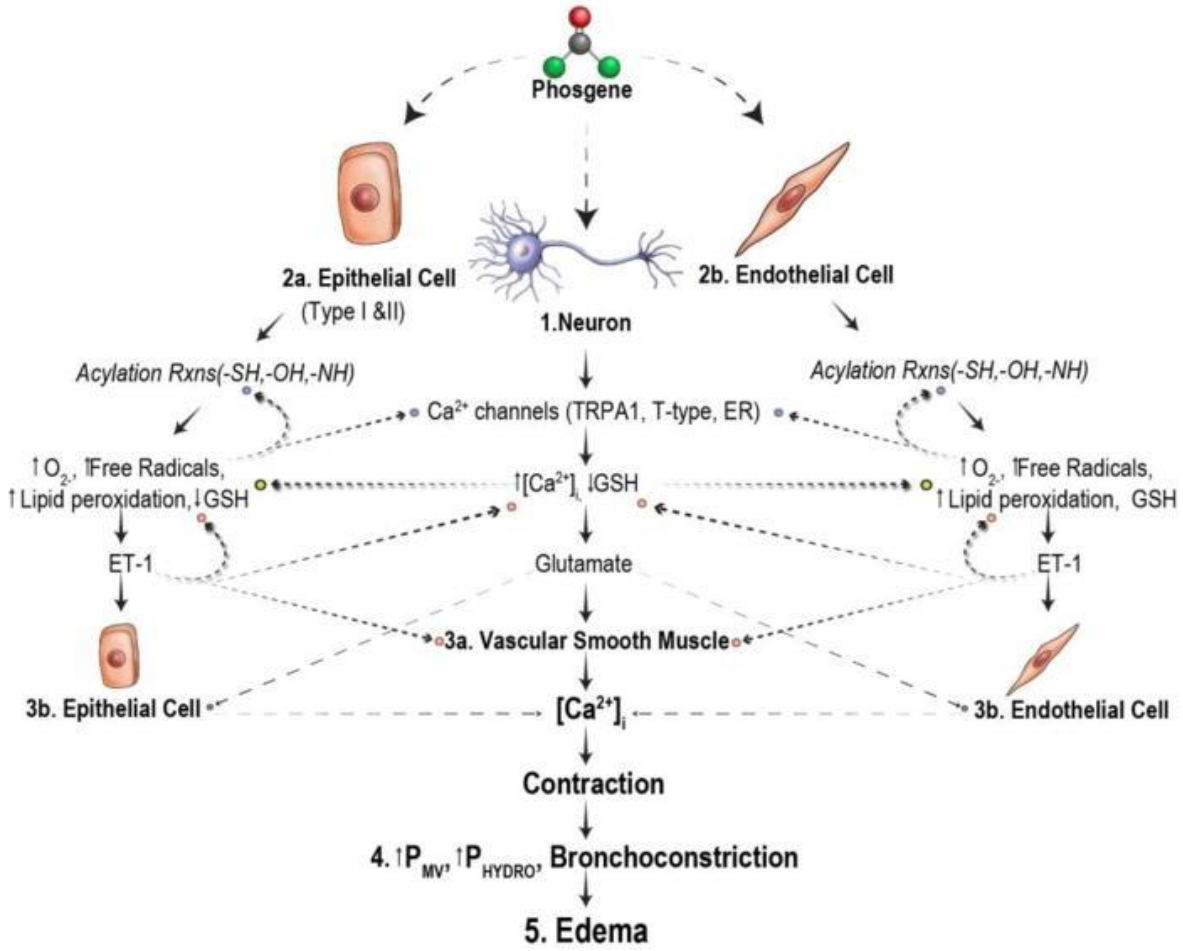


Fig 3. Putative mechanism of phosgene-induced lung injury:
GSH — glutathione; TRPA1 — transient receptor potential cation channel, member A1; NMDA — N-Methyl-D-aspartic acid; Met, metabotropic; ET-1 — endothelin 1; ETA — endothelin receptor A; ETB — endothelin receptor B; Pmv — pulmonary microvascular pressure; SOCE — store-operated calcium entry; Rxns — reactions

The Main Clinical Manifestations of Intoxication

In severe cases, the course of poisoning can be divided into four periods: ***primary exposure***, ***latent period***, ***toxic pulmonary edema***, ***resolution of edema***.

During the exposure period, the severity of intoxication manifestations depends on the concentration of phosgene. WTA in a small concentration at the time of contact usually does not cause irritation phenomena. With an increase in concentration, unpleasant sensations appear in the nasopharynx and behind the sternum, difficulty breathing, salivation and cough. These phenomena disappear when contact with the WTA is finished.

The latent period is characterized by a subjective feeling of imaginary well-being. Its duration averages 4–6 hours and is determined by the severity of intoxication, depends on the general state of the body at the time of poisoning; so deviations in both directions are possible (1–24 hours).

The main manifestations of intoxication are observed in the third period when ***toxic pulmonary edema appears*** and edematous fluid fills in the alveoli. Inspiratory shortness of breath increases (up to 50–60 respirations per minute). Gradually increasing cough appears, accompanied by discharge from the mouth and the nose of a large amount of foamy sputum. Percussion reveals a lowering of the lower borders of the lungs and the heterogeneous percussion sound is determined. Wet wheezes of different calibers are heard. As the edema increases, the fluid fills in not only the alveoli, but also the bronchioles and bronchi. Edema reaches its maximum development by the end of the first day.

With a favorable course of intoxication, ***the period of edema resolution*** begins from the 3^{rd}–4^{th} day. However, against this background, pneumonia may develop as a secondary infection, and can later cause death (in 8–15 days).

When inhaling a poisonous substance in low concentrations, pulmonary edema does not develop. Initial manifestations of intoxication include dizziness, weakness, cough, chest tightness and dyspnea. Possible development of lacrimation, nausea, headache. These phenomena disappear within a short period of time after cessation of exposure to WTA.

NITROGEN OXIDES

Physical and Chemical Properties. Toxicity. Routes of Exposure

Nitrogen oxides (nitrous oxide — N_2O; NO; trioxide — N_2O_3; dioxide — NO_2; tetraoxide — N_2O_4; pentoxide — N_2O_5) are part of the so-called explosive and powder gases formed during firing, explosions, launching rockets equipped with engines running on solid rocket fuel. At the same time, the content of nitrogen oxides in the air can increase to 20–40 %, which leads to intoxication; its nature is determined by explosive gases composition.

Nitrogen dioxide (NO_2) and nitrogen monoxide (NO) are of the greatest importance from the point of view of the danger of exposure to humans.

When inhaled, nitrogen oxides are dangerous even at a concentration of 0.1 g/m^3; at a concentration of 0.5–0.7 g/m^3, pulmonary edema may develop.

The threshold of irritant effect at 4-minute exposure is 0.15 g/m^3, at 15-minute exposure 0.09 g/m^3.

Mechanisms of Toxic Action

For nitrogen oxides the most typical is a suffocating effect, leading to the development of pulmonary edema. The action is based on the ability of substances to activate free radical processes in cells forming the alveolar-capillary barrier.

Thus, NO_2, interacting with oxygen in an aqueous space, initiates the formation of superoxide and hydroxyl radicals, hydrogen peroxide. Acting on glutathione, ascorbic acid, tocopherol, etc., the toxicant damages the low molecular weight elements of the antiradical protection of cells. As a result, lipid peroxidation is activated and the biological membranes of cells forming the alveolar-capillary barrier are damaged. Other macromolecules are also attacked and the processes underlying cytotoxicity are initiated.

Clinical Manifestations

Inhalation of nitrogen dioxide in very high concentrations leads to the rapid development of nitrite shock, often resulting in the death of victims. Nitrite shock is based on the massive formation of methemoglobin in the blood and chemical burn to the lungs. When nitrogen monoxide is inhaled, nitrosyl hemoglobin is formed, followed by its transformation into methemoglobin. The amount of methemoglobin formed during inhalation of nitric oxide in concentrations up to 0.15 g/m^3 is small and does not play a significant role in the manifestation of toxic effects. At higher concentrations, the role of methemoglobin formation in the mechanism of pathology development increases.

Finally, in case of the predominance of nitrogen monoxide in the gas mixture, the so-called reversible form of intoxication develops. The lesion is accompanied by shortness of breath, vomiting, and falling down in arterial pressure due to the vasodilating effect of NO. These phenomena disappear quickly after removal of the affected person from the contaminated atmosphere.

Thereby, depending on the conditions (concentration and ratio of substances in the inhaled air) intoxication with nitrogen oxides, either suffocating (toxic pulmonary edema) or shock-like (methemoglobin formation, burn of lungs), or by a reversible (falling down of blood pressure) may develop

PARAQUAT

Paraquat — 1,1-dimethyl,4,4-dipyridyl chloride, is a contact nonselective herbicide. In 1955, it was widely used in agriculture.

The main suppliers of the pesticide are China, Taiwan, Italy, Japan, the UK and the USA. Use of the chemical has been allowed in more than 130 countries.

Physical and Chemical Properties. Toxicity

Paraquat is a crystalline substance of white color, odorless. It dissolves well in water and alcohol; the boiling point is 300 °C (while the toxic agent decomposes). Paraquat is used in the form of a coarse aerosol (300–600 microns). After aerosol particles settle on the soil, the agent rapidly destroys with the formation of low-toxic products. Therefore, even with intensive use of the toxic chemical, its accumulation in the environment was not noted. The lethal dose for humans is approximately 3–5 g.

Routes of Exposure

The most common cause of poisoning is the intake of paraquat orally. After ingestion, the substance is absorbed in the small intestine (no more than 20 % of the administrated amount). The lungs actively capture paraquat through the mechanism of biogenic amines accumulation, the metabolism of which mainly takes place in the lung tissue.

Mechanisms of Toxic Action. Main Clinical Manifestations of Intoxica

Acting in doses above the average level, the substance affects all vital organs (the liver, kidneys, lungs). Burn to the mucous membrane of the gastrointestinal tract, diarrhea, damage to parenchymal organs and acute toxic alveolitis may develop. The characteristic feature is delayed death (in a few days or weeks) of the poisoned persons from the increasing fibrosis of the lungs.

Lung damage caused by paraquat intoxication occurs in two phases. In the first — destructive (1^{st}–3^{rd} day) — death and desquamation of alveolocytes of the 1^{st} and 2^{nd} types is observed, causing acute alveolitis, toxic pulmonary edema. In the second (proliferative) phase there is a replacement of alveolocytes with cuboid cells, and gradual proliferation of fibrous tissue. In the mechanism of the toxic effect of paraquat the leading role plays the active intermediate product, formed in cells during its accumulation and initiating the free radical process. Damage to membranes due to activation of lipid peroxidation (LP) is accompanied by the death of cells forming the alveolar-capillary barrier.

Type I alveolocytes are the most sensitive to paraquat. It is possible that the alveolocyte damage is based not only on the activation of LP, but also on other mechanisms.

Alveolar macrophages and blood neutrophils are important in the process of connective tissue proliferation in the lungs. These paraquat-activated cells produce specific glycoproteins that enhance proliferation of fibroblasts and their fixation on the basement membrane of the alveoli. In practice, it is not possible to prevent the accumulation of paraquat in the lungs after taking it.

The competing substrates of the poison (cystamine, putrescine, etc.) can have an effect only at the early stages from the onset of intoxication (the first 8–12 hours).

In case of poisoning with paraquat, oxygen therapy is absolutely contraindicated. This event significantly accelerates the death of poisoned patients. Oxygen inhalation is possible only in cases of life-threatening hypoxemia (pO_2 in arterial blood is less than 40 mm Hg).

DIAGNOSIS OF POISONING WITH SUFFOCATING AGENTS

The first step towards identifying persons who have been exposed to acute toxicants is to state the fact of exposure itself. Since transient toxic reactions quickly disappear, and persistent signs of acute inhalation damage are formed gradually, to make a diagnosis of the developing pathology at the early stages difficult.

There are no radiographic changes in the lungs during the first hours after exposure to suffocating agents; the gas content in the blood is within normal limits. There are indirect signs suggesting the possibility of damage with pulmonotoxicants. These include burn to the skin of the face, salivation, difficulty breathing, cough, etc.

Persons delivered from the fire zone (especially in case of ignition of synthetic materials) or explosion in an enclosed space should always be considered as potentially poisoned. Particular attention should be paid to victims who are unconscious, since they are more likely to be severely poisoned.

MEDICAL PROTECTION AND EMERGENCY MEDICAL CARE

Prehospital Management

Hot Zone. Rescuers should be trained and appropriately attired before entering the Hot Zone. Pulmonary toxic substances cause severe irritation of the respiratory tract and skin; contact with liquid causes frostbite. In response situations involving exposure to potentially hazardous concentrations of substances that cause pulmonary toxicity, the use of a positive-pressure self-contained breathing apparatus (SCBA) is recommended. Chemical-protective clothing is recommended because substances of pulmonotoxic action can cause skin irritation and burns. Get access to an open airway quickly and ensure adequate breathing and pulse. If injury is suspected, maintain cervical immobilization manually and apply a cervical collar and backboard whenever possible. If casualties can walk, move them from the hot zone to the decontamination area. Casualties who cannot walk may be carried on backboards or stretchers; if these are not available, carefully carry or drag casualties to safety. Casualties should be kept warm and quiet; any activity after exposure may increase the likelihood of death. Consider appropriate management of chemically contaminated children, such as measures to reduce separation anxiety if a child has been separated from a parent or other adult.

Decontamination Zone. Victims exposed only to substances of pulmonotoxic action without the evidence of skin or eye irritation may be transferred immediately to the Support Zone. Other patients will require decontamination as described below.

If exposure levels are determined to be safe, decontamination may be conducted by personnel wearing a lower level of protection than that worn in the Hot Zone (described above).

Quickly get access to the patent's airway, ensure adequate respiration and pulse. Stabilize the cervical spine with a collar and a backboard if trauma is suspected. Administer supplemental oxygen as required. Assist ventilation with a bag-valve-mask device if necessary.

Victims should be kept warm and quiet; any activity subsequent to exposure may increase the likelihood of death. Victims who are able may assist with their own decontamination. If the exposure involved liquid substances of pulmonotoxic action (ambient temperature below 8 °C) and if clothing is contaminated, remove and doublebag the clothing.

Flush exposed skin and hair with plain water for 3 to 5 minutes. Wash thoroughly with soap and water. Use caution to avoid hypothermia when decontaminating children or the elderly. Use blankets or warmers when appropriate.

Flush exposed or irritated eyes with plain water or saline for at least 15 minutes. Remove contact lenses if easily removable without additional trauma to the eye. If a caustic material is suspected or if pain or injury is evident, continue irrigation while transferring the victim to the Support Zone.

Consider appropriate management of chemically contaminated children at the exposure site. Provide reassurance to the child during decontamination, especially if separation from a parent occurs. As soon as basic decontamination is complete, move the victim to the Support Zone.

Support Zone. Ensure that casualties have been adequately decontaminated (see Decontamination Zone above). Casualties who have been decontaminated or exposed to phosgene alone do not usually pose a significant risk of secondary contamination. In such cases, Support Zone personnel do not require special protective equipment. Quickly obtain an open airway for a patient. If injury is suspected, manually maintain cervical immobilization and, if possible, apply a cervical collar and backboard. Ensure adequate breathing and pulse. Give supplemental oxygen and establish intravenous access as needed. Install a cardiac monitor. Observe for signs of edema and airway obstruction such as progressive hoarseness, stridor, or cyanosis.

Advanced Treatment. In cases of respiratory failure, establish a patent airway and breathing with endotracheal intubation. Avoid blind nasotracheal intubation or use of an esophageal obturator. Use direct visualization for intubation. If the patient's condition precludes endotracheal intubation, perform cricothyroidectomy if you are equipped and trained to do so. Treat patients with bronchospasm with aerosolized bronchodilators. Use of bronchial sensitizing agents in situations of multiple chemical exposure may pose additional risks. Assess myocardial status before choosing which type of bronchodilator to administer. Cardiac sensitizing agents may be appropriate; however, use of cardiac sensitizing agents after exposure to certain chemicals may pose an increased risk

of cardiac arrhythmias (especially in the elderly). Consider use of racemic epinephrine aerosol for children who develop stridor. Dose 0.25–0.7 m 2.25 % racemic epinephrine in 2.5 cc water, repeated every 20 minutes as needed, with caution about myocardial variability. Patients who are comatose, hypotensive, or with seizures or cardiac arrhythmia should be treated according to advanced life support (ALS) protocols. Only decontaminated patients or patients not requiring decontamination should be transported to a medical facility.

Patients with signs of significant exposure (e.g., severe or persistent cough, shortness of breath, or chemical burns) should be transported to a medical facility for examination. Because serious complications may not occur for up to 48 hours after exposure, all patients suspected of having been exposed to phosgene should be transported to a medical facility for examination. Patients with minor or temporary eye or throat irritation may be discharged from the scene after their names, addresses, and telephone numbers are recorded. They should be advised to seek immediate medical attention if symptoms develop or recur.

Emergency Department Management. Unless previously decontaminated, all patients require decontamination as described below. Because contact with liquid phosgene may cause burns, put on butyl rubber gloves, apron and eye protection before treating patients. All other patients may be transferred immediately to the Critical Care Area. Be aware that use of protective equipment by the provider may cause fear in children, resulting in decreased compliance with further management efforts. Because of their relatively larger surface area to weight ratio, children are more vulnerable to toxicants affecting the skin. In addition, emergency department personnel should examine the oral cavity of children because of their frequent use of hands to mouth. Assess and maintain airway, breathing, and circulation. Children may be more vulnerable to caustic agents than adults because of their smaller airway diameter. If breathing is compromised, establish a patent airway and breathing by means of endotracheal intubation. If this is not possible, establish a patent airway surgically.

Treat patients who have bronchospasm with aerosolized bronchodilators. The use of bronchial sensitizing agents in situations of multiple chemical exposures may pose additional risks. Consider the health of the myocardium before choosing which type of bronchodilator should be administered. Cardiac sensitizing agents may be appropriate; however, the use of cardiac sensitizing agents after exposure to certain chemicals may pose enhanced risk of cardiac arrhythmias (especially in the elderly). Chlorine poisoning is not known to pose additional risk during the use of bronchial or cardiac sensitizing agents.

Consider racemic epinephrine aerosol for children who develop stridor. The dosage is 0.25–0.75 mL of 2.25 % racemic epinephrine solution in 2.5 cc water; repeat every 20 minutes as needed cautioning for myocardial variability.

Patients who are comatose, hypotensive, or have seizures or cardiac arrhythmias should be treated routinely.Victims who are able may assist with their own decontamination. If the exposure involved liquid phosgene (ambient temperature below 8 °C) and if clothing is contaminated, remove it and doublebag.

Flush exposed skin and hair with plain water for 3 to 5 minutes. Wash thoroughly with soap and water. Be cautious to avoid hypothermia when decontaminating children or the elderly. Use blankets or warmers when appropriate.

Flush exposed or irritated eyes with plain water or saline for at least 15 minutes. Remove contact lenses if easily removable without additional trauma to the eye. If a caustic material is suspected or if pain or injury is evident, continue eye irrigation while transferring the patient to the Critical Care Area(Unit).

Ophthalmic anesthesia, such as 0.5 % tetracaine, may be required to relieve blepharospasm, and eyelid retractors may be needed to ensure adequate sublid irrigation.

Critical Care Area (Unit). Be certain that appropriate decontamination has been provided. Evaluate and support airway, breathing, and circulation as in ABC Reminders above. Establish intravenous access in seriously ill patients if this has not been done previously. Continuously monitor cardiac rhythm. Patients who are comatose, hypotensive, or have seizures or cardiac arrhythmias should be treated in the routinely. Administer supplemental oxygen by mask application to patients who have respiratory complaints. Treat patients with bronchospasms with aerosolized bronchodilators. Use of bronchial sensitizing agents in situations of multiple chemical exposures may pose additional risks. Consider the health of the myocardium before choosing which type of bronchodilator should be administered. Cardiac sensitizing agents may be appropriate; however, the use of cardiac sensitizing agents after exposure to certain chemicals may pose enhanced risk of cardiac arrhythmias (especially in the elderly). Phosgene poisoning is not known to pose additional risk during application of bronchial or cardiac sensitizing agents.

Consider racemic epinephrine aerosol for children who develop stridor. Dose 0.25–0.75 mL of 2.25 % racemic epinephrine solution in 2.5 cc water, repeat every 20 minutes as needed, cautioning for myocardial variability.

Follow up patients who are in respiratory distress for up to 48 hours and periodically reexamine their chests and perform other appropriate studies. Follow up as clinically indicated.

Corticosteroids are suggested for intense inflammation, especially inflammation of the respiratory epithelium. If the patient has been severely exposured, consider intravenous steroid therapy while the patient is asymptomatic.

Prophylactic antibiotics are not routinely recommended but may be used based on the obtained data of sputum cultures. Pneumonia can complicate severe pulmonary edema and may cause death up to 48 hours after onset of pulmonary edema.

Diuretics are contraindicated. Pulmonary edema due to phosgene inhalation is not hypervolemic in origin; patients tend to be hypovolemic and hypotensive. Dopamine may be required for treatment of hypotension, bradycardia, or renal failure. Initiate fluid resuscitation as needed.

If concentrated chlorine gas or chlorine-generating solutions contact the skin, chemical burns may occur; treat them as thermal burns. If the liquefied

compressed gas is released and contacts the skin, frostbite may result. In such cases treat them by rewarming the affected areas in a water bath at a temperature of 40 to 42 °C) for 20 to 30 minutes and continue until a flush has returned to the affected area.

Because of their larger surface area to body weight ratio children are more vulnerable to toxicants absorbed through the skin.

Eyes exposed to pulmonary toxicants should be flushed for at least 15 minutes. Check visual acuity and examine the eyes for corneal damage and treat accordingly. Patients with corneal injuries should immediately consult an ophthalmologist.

There is no specific antidote for substances of pulmonotoxic action. Treatment should be supportive (Table 6).

Table 6

Protective medications used in case of exposure to suffocating agents

Signs and symptoms	Treatment
Pain syndrome	Fentanyl: 50 mcg/ml intramuscularly Morphine: 1 % — 1 ml intramuscularly Promedol: 2 % — 1 ml intramuscularly
Cough	Codeine: 0.015 — 1 tablet 3 times a day
Psychomotor agitation	Phenazepam: 0.0005; seduxen: 0.005 1 tablet 3 times a day Haloperidol: 0.0015 1 tablet 3 times a day Droperidol: 0.25 % — 1–10 ml intramuscularly
Difficulty breathing	Menthol: 10 % solution in chloroform (inhalation) Theophylline retard: 0.2–0.3 1 tablet 1–2 times a day Aminophylline: 0.15 1 tablet 2–3 times a day Salbutamol (inhalation): 2–3 times a day
Laryngospasm	Atropine: 0.1 % — 1 ml subcutaneously
Bronchospasm	Aminophylline: 2.4 % — 5–10 ml intravenously slowly Salbutamol (inhalation): 2–3 times a day
Hypoxia	Inhalation of O_2 and oxygen-air mixtures
Pulmonary edema	Prednisolone: up to 3000 mg intravenously Dexamethasone: 160 mg per os Dexamethasone-21-isonicotinate: inhalation Beclomethasone-dipropionate: inhalation Ascorbic acid: 5 % — 5 ml 2 times a day intramuscularly Sodium hyposulfite 2 % (aerosol) — inhalation D-penicylamine: 0.3 2 tablets 4 times a day Cordiamine: 2 ml subcutaneously Caffeine-sodium benzoate: 20 % sol. — 1 ml subcutaneously Furosemide: 40 mg intravenously 2 times a day Oxygen therapy with antifoam agents (inhalation of alcohol)

POISONOUS AND HIGHLY TOXIC SUBSTANCES WITH IRRITATING ACTION

Irritation is the effect of chemicals on the endings of sensitive nerve fibers branching in the cover tissues, accompanied by a number of local and general reflex reactions and subjectively perceived as an unpleasant feeling of tingling, burning, cutting, pain, etc.

Irritant effect is observed in a large number of chemical compounds, including those widely used in economic activities. Among them are: halogens (chlorine, bromine), aldehydes (acrolein), ketones (acetone), acid vapors, acid anhydrides, etc.

The severity of the irritant effect in each case is determined by the structure of the toxic substance, its amount in the ambient air and the place of application. Most substances, acting in concentrations that cause irritation of the mucous membranes (eyes, respiratory tract), initiate other forms of the toxic process. Substances that have a high selectivity in their action on sensitive nerve endings branching in the integumentary (skin) tissues are called irritants. Their damage in real conditions is usually limited to manifestations of an exclusively irritating effect. Such substances as toxic agents or self-defense means can be used.

GENERAL CHARACTERISTICS. CLASSIFICATION OF POISONING SUBSTANCES WITH IRRITATING ACTION

Only those chemical compounds for which the average effective concentration of local (irritating) action is thousands of times less than the average lethal one can be considered as irritating toxic substances. Therefore, they are considered as temporarily disabling the enemy's manpower.

In order to create new samples of irritating agents, the following classes of chemicals were studied at different times:

1. Aliphatic and aromatic halogenated ketones.
2. Nitrile derivatives.
3. Aromatic organic arsenic compounds.
4. Other aromatic and heterocyclic compounds.

According to the ability to transfer the properties of an irritant to a halogenated ketone molecule, the halogen atoms are arranged in the sequence: F < C1 < Br < I. Among the aliphatic ketones, bromopropanone and brombutanone are the most active (both substances are liquids), among the halogen derivatives of aromatic ketones — chloroacetophenone (according to the nomenclature of some armies — CN).

The overall toxicity of nitriles decreases when introduced into the halogen molecule. The irritating effect, on the contrary, increases. Among the substances of this group, the most well-known are brombenzyl cyanide (CA) and orthochlorobenzalmalonodinitrile (CS).

Some derivatives of trivalent arsenic have a pronounced irritant effect. In these compounds, due to two valences, arsenic is bound to an organic radical. The third one, as a rule, is occupied by a halogen or CN-group. The effect of halogen atoms on the physiological activity of organic arsenic substances is the opposite of that they have on the toxic substance of the first two groups. The activity of poisoning agents varies in a series of derivatives I < Br < Cl. CN-group enhances the biological effect to the greatest extent. The most famous representative of the group is phenarsazine chloride (adamsite — DM). But other aromatic organic arsenic compounds have a high irritating activity. Among them: diphenylcyanarsin (DC), diphenylchlorarsin (DA), etc.

Compounds of complex structure, such as dibenzoxazepine (CR), capsaicin extract of red pepper, pelargonic acid morpholide, methoxy cycloheptatriene (CH), etc., have high irritating activity.

Irritating agents are used by law enforcement agencies as a means of combating offenders of public order, to neutralize terrorists and criminal elements. In some countries, devices containing irritating substances are sold for individual use (self-defense).

The prevailing opinion is that the correct use of irritating substances ensures the formation of a transient toxic effect without serious consequences for the victim, nevertheless, the results of the use of this weapon are sometimes difficult to control, and the resulting effects are poorly defined. An irresistible desire to get out of the infected atmosphere almost always provokes panic.

The widespread use of irritants can lead to a large number of casualties, and it is possible that medical personnel involved in providing medical care may be affected by substances remaining on the clothing and skin of the affected individuals.

The most sensitive to irritation are the cover tissues, in which the density of nerve endings is higher, where they are more accessible to the action of chemicals. This is, first of all, the conjunctiva of the eyes, the mucous membrane of the respiratory tract. The cover tissues in these areas have structural features, innervation and therefore are not equally sensitive to various substances. Some substances cause predominant irritation of eyes (tear agents — lacrimators), others — nasopharynx and respiratory organs (sneezing agents — sternites).

Halogenated ketones and nitriles exhibit the properties of lacrimators, organic arsenic compounds — sternites, the rest are equally irritating to the eyes and respiratory tract (and even the skin).

The comparative characteristics of some toxic substances of irritating action are presented in the Table 7.

Earlier, when developing samples of chemical weapons, it was planned to use not only “pure” agents for military purposes, but also their mixtures. For example, the CNS formulation was a mixture of chloroacetophenone, chloroform and chloropicrin. The effect of such formulations is accompanied by the development of not only irritating, but also more severe processes, such as pulmonary edema.

Table 7

Physical and chemical properties of DM, CS, CR, CN

Parameter	WTA			
	DM	**CS**	**CR**	**CN**
Aggregate state	Bright yellow crystals, technical product — of dark green color	Colorless solid substance	Yellow powder	Colorless crystalline substance, technical product is of yellow or brown color
Odor	absent	absent	absent	cherry blossoms, violets
Melting T°	195	95	72	59
Boiling T°	410 (with decomposition)	310–315 (with partial decomposition)	About 400	244–245
Solubility in water	No soluble	Poorly soluble	Highly soluble, solutions are stable	Poorly soluble (1 g/1 l)
Solubility in organic solvents	Highly soluble			
Method of application	aerosol	aerosol	Liquid aerosol, fumes	Aerosols, solutions, mixtures with another WTA
Routes of exposure	Inhalation Eye lesions	Inhalation Ingestion Skin lesions Eye lesions	Inhalation Ingestion Skin lesions Eye contact	Eye lesions Inhalation Skin lesions
Affecting concentration, mg/m^3	5	5	0,8	15
Intolerable toxodoze, $g \times min/m^3$	0,015	0,02	0,001	0,08
Lethal toxodoze, $g \times min/m^3$	30	25	–	85

Industrial toxicants with a pronounced irritant effect can be solid, liquid and gaseous. The difference in doses that cause the phenomenon of intolerable irritation of the mucous membranes and lethal effects in such compounds may not be as large as in “pure” WTA, therefore, life-threatening forms of pathology can often be observed in the chemical foci formed by these toxicants during accidents on chemically hazardous facilities.

Most of the irritant agents are insoluble in water, non-volatile at normal ambient temperature. All of them are crystalline substances of various colors, so the main form of their use is burning in order to produce toxic irritating smoke, or their use for military purposes involves the need to use special devices to create aerosols. At the same time, conditions are formed that ensure the formation of an aerosol cloud with a particle diameter of 0.5–2 microns. In windless weather,

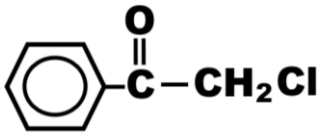
the radius of such a cloud, which persists for 6–10 minutes, is 5–7 m. In the epicenter, the concentration of the substance can reach 2–5 g/m^3.

To create extensive zones (with a depth of contamination up to 10 km), toxic smoke bombs are used. In the epicenter of the contamination zone, the concentration of substances can reach 2–5 g/m^3. To increase the resistance of WTA on the ground, special formulations are used. So, in Vietnam, the US Army (the 70s of the XX century) used two formulations: CS-1 and CS-2. CS-1 — almost a pure substance — contaminated the territory for about 2 weeks, and CS-2 — a more resistant formulation in which every particle of crystalline CS is covered with water-repellent silicone film, which caused contamination of the area for up to a month.

PHYSICAL AND CHEMICAL PROPERTIES. TOXICITY

Toxic substances of irritating and tear action include chloracetophenone (affects the eyes), adamsite (irritates the respiratory tract), CS (irritates the eyes, respiratory tract, the skin), CR (irritates eyes, respiratory tract and skin).

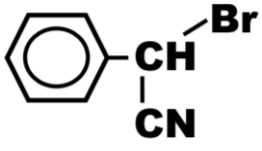
Chloroacetophenone (CN) is a phenyl chloromethyl ketone, a crystalline substance with a melting point of about 59 °C and a boiling point of 244–245 °C.



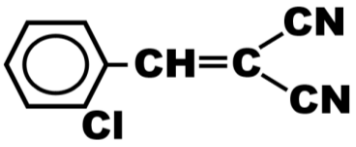
Vapors are 5.3 times heavier than air. The volatility at 20 °C is 0.105 mg/l. It has a fragrant smell. Poorly soluble in water (1 × 10–1 g/m^3), but well soluble in organic solvents. Chemically resistant, slowly hydrolyzed with water. It is degassed by alcoholic solutions of alkalis or sodium sulfide when heated. It is used in the form of aerosols. The affecting concentration is 15 mg/m^3. The intolerable toxic dose is 0.08 g × min/m^3. The average lethal (LCt_{50}) is 85 g × min/m^3, death occurs from the development of toxic pulmonary edema. In concentration of 0.01 mg/m^3 it leads to the development of erythematous bullous dermatitis. The predominant action: shows properties of typical lacrimator.

Brombenzylcyanide (CA) is a crystalline substance with a melting point of 25 °C and a boiling point of about 132–134 °C. The vapor density in the air is 6.6. The volatility at 20 °C is 0.13 mg/l.

Chemically rather resistant. It is degassed by alcoholic solutions of alkalis and aqueous-alcoholic solutions of sodium sulfide. It is used as an aerosol. Irritating concentration is 0.00015 mg/l (1.5×10^{-4} g/m^3), the intolerable concentration is 0.0008 mg/l (8 mg/m^3), the average lethal toxic dose (LD_{50}) is 35 g × min/m^3, death occurs from the development of toxic pulmonary edema. The predominant action is lacrimator.

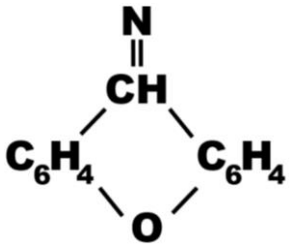


Chlorobenzylidenemalonodinitrile (CS) is a crystalline substance with a melting point of 95 °C and a boiling point of 310–315 °C (with partial decomposition), insoluble in water, but well soluble in organic solvents.



It has a peppery smell. The damaging concentration is 5 mg/m^3. The intolerable toxic dose is 0.02 g × min/m^3. The average lethal toxic dose (LCt_{50}) is 25 g × min/m^3. It is used as an aerosol. Mainly shows properties of a lacrimator (the damaging effect on the skin is twice as strong as that of chloroacetophenone and brombenzylcyanide).

Dibenzoxazepine (CR) is a crystalline substance, almost insoluble in water, well soluble in organic solvents. It has no smell. It is used as an aerosol. The predominant effect is that of lacrimator (however, as well as CS has a pronounced skin-damaging effect). The damaging concentration is 0.8 mg/m^3. The intolerable toxic dose is 0.001 g × min/m^3.



Adamsite (DM) is phenarsazine chloride, a solid with a melting point of 195 °C, a boiling point of 410 °C (with partial decomposition) and a volatility at 20 °C of 0.00002 mg/l.

It doesn't have any smell, almost insoluble in water (2×10^{-5} g/m^3); but soluble in organic solvents. It is degassed with water-alcohol solutions of alkalis, hydrogen peroxide, bleach and other oxidizing agents. The damaging concentration is 5 mg/m^3. The intolerable toxic dose is 0.015 g × min/m^3. The average lethal toxic dose (LCt_{50}) is 30 g × min/m^3. The predominant effect is sternite. It does not affect the skin.

The basic WTA of the US Army are CS and CR, reserve — chloroacetophenone and adamsite.

According to foreign experts, the use of irritating agents in combat conditions does not have much tactical significance, since the irritating effect quickly reveals itself and regular troops will be able to use gas masks promptly.

However, long stay in a gas mask negatively affects the combat capability of military personnel.

Typical means of delivering irritating agents can be cluster bombs, containers with generators that are dropped from helicopters, artillery mines with a special heating device. Generators for burning explosives can be installed in trenches, checkers, grenades with irritating agents are also used.

As a rule, poisonous fumes form unstable foci of contamination. However, the addition of silica gel powder to ammunition increases their durability to a large extent. For example, CS in a mixture with silica gel is stored on the ground for up to 30 days, which necessitates special processing and organization of examination of water and food.

ROUTES OF EXPOSURE. MECHANISMS OF TOXIC ACTION

Toxic fumes irritate the sensitive nerve endings of the mucous membranes of the nasopharynx and respiratory tract. The irritating effect is associated with the presence of active radicals of chlorine, arsenic, cyanide groups in the molecular structure, which are able to interact with thiol groups of mucosal receptors.

Solid smoke particles settle on the mucous membranes and dissolve in their contents. The endings of sensitive nerves are irritated — oculomotor, facial, pharyngeal, as well as parts of sympathetic nerves branches going to the eyeball, lacrimal and salivary glands, to the lungs. Reflex reactions appear in the form of pain in the nasopharynx, larynx, jaws, teeth and chest, coughing, slowing down or temporary stopping of breathing, hypersecretion of the nasal mucosa, salivary, lacrimal glands, as well as slowing of heart contractions, increased blood pressure due to vascular spasm (Fig. 4).

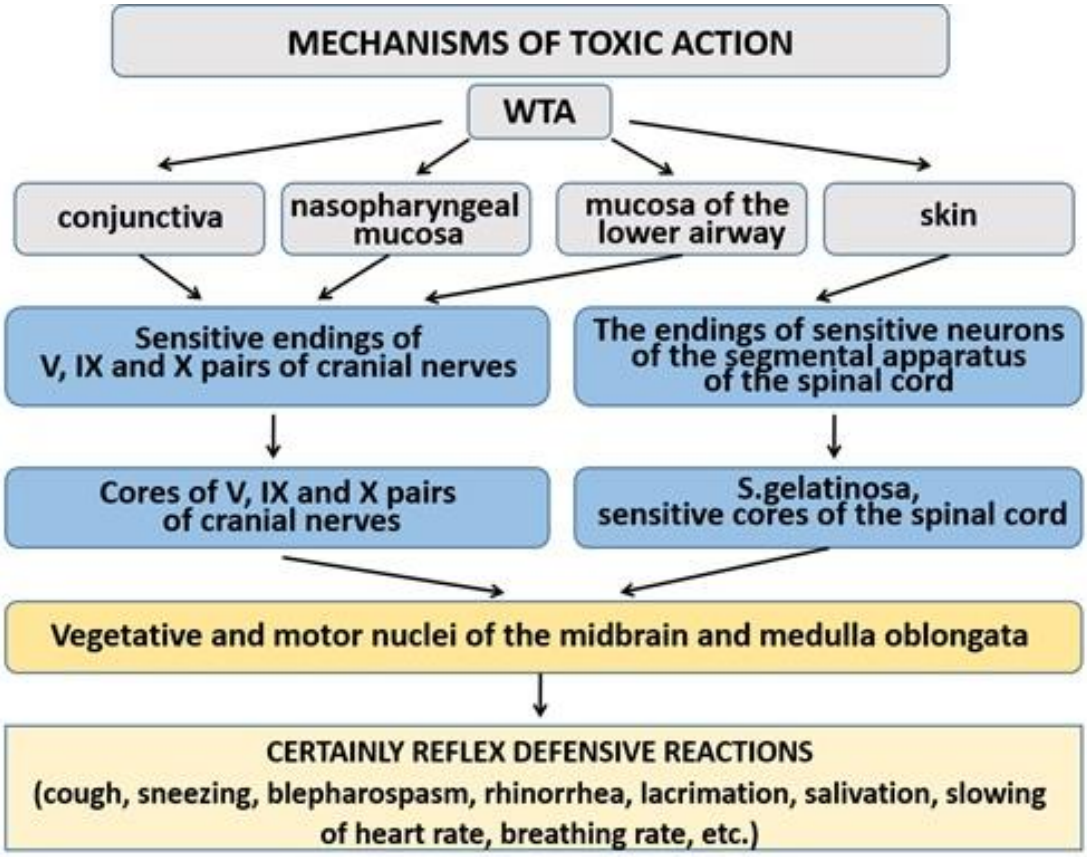


Fig. 4. Pathogenesis of toxic action of irritating and tear agents

When poisonous smoke penetrates into the lower respiratory tract, shortness of breath, bronchial spasm and bronchorrhea are observed. Reflexes from the upper respiratory tract are antagonistic in action:

1. Slowing of breathing → stopping → shortness of breath, breathing becomes irregular, spasmodic, convulsive, painful subjective feelings of suffocation appear.

2. Early interruption of inhalation → frequent shallow breathing.

There are 2 possible mechanisms for the effect of chemicals on nerve endings:

– *direct* (inhibition by arsines of SH-groups of structural proteins and enzymes, the action of capsaicin on the ion channels of the excitable membrane, etc.), leading to the damage of metabolism in nerve fibers and their excitation;

– *mediated* (via activation of the formation of bradykinin, prostaglandins, serotonin, etc., in the cover tissues, which excite the endings of nociceptive fibers.

At high concentrations of arsenic-containing fumes, inflammatory and necrotic changes in the respiratory tract may occur with the formation of pseudodiphtheric films and the development of acute serous hemorrhagic pneumonia. The irritating effect of CS and CR also depends on the ability of the substance to affect thiol disulfide metabolism. It causes a painful reaction by increasing bradykinin activity in the affected tissues. The toxic effect on tissue respiration is probably due to the presence of cyanide in the molecule: in the experiment, clonic-tonic convulsions occurred in animals, cyanide was detected in the blood. At inhaled lethal concentrations toxic pulmonary edema develops.

CLINICAL MANIFESTATIONS

The main manifestations of human lesions with various tear agents are largely the same. Chloracetophenone, CS, CR act on the external mucous membranes almost instantly, after a few seconds, the defeat with adamsite manifests itself in 5–10 minutes. The total duration of the lesion is almost equal to the time spent in an contaminated atmosphere. When leaving the focus of chemical contamination, most of the affected people recover their working capacity after 5–10 minutes, however, photophobia persists for 25–30 minutes.

In the focus, when exposed to the eyes, there is a feeling of “sand” in the eyes, copious lacrimation, convulsive spasm of the eyelids with the closure of the eye slit, i.e. a picture of acute conjunctivitis. CR in negligible amounts causes the development of blepharospasm, profuse salivation, severe pain syndrome. Victims lose the ability to coordinate actions for 15–20 minutes. The injection of conjunctival vessels, edema of the eyelids are objectively determined. Manifestations of intoxication can be observed within 2–6 hours after leaving the focus of chemical contamination.

Administration of irritating agents into the respiratory tract causes a feeling of tickling, soreness, burning in the nose and throat. Then there is a scratching pain behind the sternum and a feeling of tightness in the chest. The victims complain of headache, pain in the teeth, gums, jaws, in the ears. At the same time, rhinorrhea, dry cough, sneezing, salivation, nausea, vomiting, abdominal pain are

noted. Objectively, there is only hyperemia of the mucous membranes, their puffiness. Bradycardia, hypertension, respiratory retardation, apnea occur reflexively.

The duration of symptoms is within a few hours – days. CS and CR act on the skin. In mild cases, the effect is manifested by the formation of transient erythema on the face and neck. Increased humidity and high ambient temperature improve the permeability of the epidermis to these substances, which increases the lesion of the skin. CS, acting in a toxic dose of more than 14 g × min/m^3, can cause persistent erythema, bullous lesion of the skin of the forearms. In case of repeated contacts with irritating agents, an allergic eczematous reaction may develop.

CR causes skin damage in concentrations 20 times less than CS. When the substance comes into contact with the skin, the victim feels burning pain, erythema develops. Shortly after the removal of the victim from the focus, erythema disappears, but the increased sensitivity of the affected area to the effects of adverse factors persists. Contact with cold water provokes a pronounced pain syndrome.

When inhaling high concentrations, the affected person experiences mortal fear. He has convulsive-spastic breathing, nose bleeding. If it is impossible to get out promptly of the polluted atmosphere in the absence of a gas mask, toxic pulmonary edema develops. With prolonged exposure to tear agents in high concentrations, lethal outcomes are possible. The cause of death is usually toxic pulmonary edema.

With the action of agents irritating the nasopharynx (sternites), the symptoms of the lesion occur later than in the case of tear-action agents. The duration of the latent period depends on the concentration of toxic substances and ranges from 4 to 30 minutes. With a very high content of organoarsenic compounds in the ambient air, symptoms may appear after 30 seconds. After removing the victim from the contaminated zone, the manifestations of intoxication continue to increase, reaching maximum severity after 30–60 minutes, and in the next 2–3 hours gradually subside. By the end of the second day, a full recovery occurs.

With mild inhalation lesions, one of the earliest manifestations of the irritating effect of these agents is a change in the respiratory rate and sensitivity of the olfactory analyzer. Subjectively, burning sensation, pain in the nose, throat, in the frontal sinuses, upper jaw bones, headache, stomachache, nausea are felt. These sensations are accompanied by an uncontrollable attack of sneezing, coughing, copious discharge of mucus from the nose, salivation. At the same time, the effect of irritating agents on the organ of vision is manifested, which is expressed in lacrimation, photophobia.

In severe poisoning with adamsite, the phenomena of irritation of the mucous membranes are accompanied by painful sensations and vomiting. Lower respiratory tract is affected too. Subjectively, this is manifested by a feeling of suffocation. The pain syndrome is very pronounced. The pain irradiates and is felt in the ears, back, joints and muscles of the extremities. There is a scratching chest pain, which can be compared by severity with the sensations caused by a burn.

The pain can be so excruciating that the affected persons are barely able to tolerate it. Against this background, psychomotor agitation is observed, sometimes the central nervous system functions pathology — motor, mental sphere (twitching of individual muscle groups, shaky gait, weakness in the legs, depression, sopor state) may be noted. Expressed irritation of the respiratory tract can lead to severe bronchospasm, respiratory arrest at the exhalation phase, slowing of cardiac activity, complete cardiac arrest. The defeat of the deep parts of the respiratory tract leads to a sharp increase in breathing with a simultaneous decrease in its amplitude.

Painful, sometimes unbearable, subjective sensations associated with the effect of irritating substances on the respiratory tract are objectively expressed only in a small injection of the vessels of the mucous membrane of the pharynx, unexpressed hyperemia of the larynx and nasal cavity.

In extremely severe cases, toxic pulmonary edema can develop. A prognostic sign of the onset of this life-threatening complication is the chest pain that does not subside for 2 hours.

A characteristic feature of irritating substances is their ability to sensitize the body. Repeated exposures are accompanied by a sharp increase in sensitivity to these seemingly low-risk poisons: a pronounced reaction is formed to insignificant amounts of the substance in the surrounding air. Allergic dermatitis often develops.

Thus, most of the affected persons with irritating agents have a mild lesion in the form of toxic ceratoconjunctivitis and acute inflammation of the upper respiratory tract.

FIRST AID AND EMERGENCY MEDICAL CARE

There is no antidote for individuals affected with CR, CS or CN; treatment mainly consistis of thorough decontamination and symptom-directed supportive care. Removal of those exposed from the contaminated area and to fresh air is the most important initial undertaking. Aerosolised tear gases are heavier than air, and any exposed patient who has lost consciousness or is lying should be lifted off the ground; emergency response vehicles should also try and park in higher areas. Transport to a medical facility is recommended for symptomatic exposures. A concern with the medical management of those affected by CN or CS is secondary contamination of first responders such as police or ambulance, or the medical staff at the hospital. Although cases of severe contamination of people following exposure to these products are rare, there is a risk of secondary exposure. For example, among attending physicians treating exposed patients, minor effects, such as facial pruritis and respiratory and eye irritation, may develop. Removal of contaminated clothing, prompt decontamination, use of gloves, goggles, gowns and surgical masks by medical personnel, and, if possible, treatment in a well-ventilated room are recommended to minimize secondary contamination. Removed contaminated clothing should be sealed in a double plastic bag.

Treatment for ocular exposures initially requires thorough eye decontamination. Flushing the eyes with water or saline for 10–20 min is the most often recommended initial treatment for decontamination of the eyes. Patents may require a topical anaesthetic to enable them to open their eyelids sufficiently for effective irrigation. Contact lenses should be removed before flushing. If more than mild, resolving symptoms are observed after irrigation, a full ophthalmological examination should be undertaken, including fluorescein staining and slit-lamp examination. For persistent symptoms or in case of injury special ophthalmological assessment is recommended. Further treatment may include oral analgesics, topical antibiotics and a cycloplegic or mydriatic. In some situations, for example, when a tear gas grenade explodes in close proximity to the face, there may be particles embedded in the cornea or conjuctiva. Following flushing, removal of these particles is necessary; use of a cotton wool swab or a needle tip at a slit lamp is recommended.

Areas of skin damage should be thoroughly decontaminated and washed with plenty of running water and soap to remove dirt and eliminate burning sensation. The face should be wiped to remove any particles before being washed. Saline irrigation should be used for vesiculated skin. It is rare that severe contact dermatitis occurs, in such cases it is generally treated with topical corticosteroids and/or antihistamines including diphenhydramine; systemic steroids may be required if symptoms are severe. Significant chemical burns should be treated in the same way as thermal burns.

While the majority of respiratory symptoms are mild and should improve with cessation of exposure and removal to fresh air, high concentrations (such as exposure in a confined space) or prolonged exposure periods may cause significant respiratory symptoms. Monitoring and support of respiratory function is important in any symptomatic patient. Pulse oximetry and arterial blood gases should be monitored. If significant respiratory distress develops, initial supportive treatment includes oxygen administration. Chest radiographs can assist in identifying any pulmonary complications. Suctioning may be required for those with copious respiratory secretions. Along with continued oxygen therapy, inhaled bronchodilators such as β_2-agonists (i.e., salbutamol) may assist those with bronchospasm and/or obstructive changes on lung function tests. Inhaled steroids may also assist in patients with bronchospasm (or non-productive cough). Respiratory failure may rarely occur secondary to laryngospasm; airway protection and assisted ventilation may be required. Exacerbation of asthma, emphysema or bronchitis may occur in those with a pre-existing respiratory condition, or uncommonly, asthma may develop due to an allergic respiratory response to the agent.

Standard asthma treatment protocols should be followed. Reactive airways dysfunction or pulmonary edema has only rarely been reported and may be delayed or exercise induced. Pulmonary edema is managed primarily by non-pharmacological treatments, including resting from activity and oxygen therapy. Standard face mask supply of 50–60 % oxygen may maintain adequate

oxygenation. However, mechanical ventilation with continuous positive airway pressure or positive-end-expiratory pressure ventilation may be required if PaO_2 cannot be maintained above 50–55 mm Hg.

While gastrointestinal symptoms are not common, retching, nausea and vomiting can occur due to the irritant effects. Some people appear to be especially sensitive to the effects and may vomit more readily, while vomiting also appears more common when high concentrations are attained, as in cases when exposure occurs in a confined space or exposure lasts for a long time. Ingestion of contaminated saliva may also contribute to vomiting and diarrhoea. Very rarely actual ingestion occurs leading to gastrointestinal disturbances. Overall gastrointestinal symptoms typically resolve spontaneously, and further specific treatment is not required. However, if vomiting or diarrhoea is persistent or severe, it may contribute to fluid and electrolyte imbalances, acidosis, shock, seizures, obtundation and hypokalaemia. In such cases, patients may require symptomatic care with intravenous rehydration, antiemetic agents and adequate electrolyte replacement.

CLINICAL CASES

When solving clinical cases:
1. Make a preliminary toxicological diagnosis.
2. Specify the mechanisms of the toxic effect of the assumed toxic substance.
3. Make the plan of the first and emergency medical care measures.
4. Specify the need for evacuation and its conditions.

TOXIC AGENTS OF IRRITATING ACTION

Case 1

To stop the riots, law enforcement agencies used cassettes with irritating substances, as a result of which a group of people who were in the area of use developed symptoms of damage.

The affected M. complains of burning in the eyes, pain in the forehead and behind the sternum, a feeling of heat on the neck skin in the area of the collar of clothing. On examination: lacrimation, rhinorrhea, hyperemia of the conjunctiva of the eyes are noted.

Case 2

For the purpose of self-defense, a gas canister containing an irritating substance was used. After 2–3 seconds, the attacker showed signs of defeat: profuse lacrimation, sharp pain in the upper respiratory tract, coughing attacks, accompanied by vomiting.

Case 3

During the terrorist attack, terrorists sprayed a gaseous substance in a residential building. In persons trapped in the smoke zone, the gaseous substance caused: painful cough; tearing and scratching chest pain radiating to the back; nausea and vomiting; difficulty, frequent (up to 32–35 respiratory movements per minute) and shallow breathing with a feeling of sharp lack of air; loss of speech; severe burning in the nose and mucus secretion; lacrimation; loss of voice. The pain is so excruciating that the affected people are barely able to catch their breath. Clinical examination revealed psychomotor agitation with impaired central nervous system function (twitching of individual muscle groups, shaky gait, weakness in the legs), a decrease in heart rate to 40–50 beats per minute.

ANSWERS

Case 1

1. Acute damage with a vaporous irritating agent of mild degree; reactive conjunctivitis, reactive rhinitis, reactive tracheobronchitis.

2. Activation of pain receptors of the skin and mucous membranes.

3. First aid. In the focus of chemical contamination: putting on a gas mask, inhaling ficilin or an anti-smoke mixture (place the crushed ampoule in the undermask space of the gas mask). Outside the focus of chemical contamination: copious rinsing of the eyes with water, rinsing of the mouth and nasopharynx with 2 % sodium bicarbonate solution.

Emergency medical care (provided only in case of severe and prolonged irritation): not recommended.

4. Evacuation is not recommended.

Case 2

1. Acute lesion with a vaporous irritating agent of moderate degree of severity; reactive conjunctivitis, reactive tracheobronchitis.

2. Activation of pain receptors of the skin and mucous membranes.

3. First aid. In the focus of chemical contamination: putting on a gas mask, inhaling ficilin or an anti-smoke mixture (place the crushed ampoule in the undermask space of the gas mask). Outside the focus of chemical contamination: copious rinsing of the eyes with water, rinsing of the mouth and nasopharynx with 2 % sodium bicarbonate solution; inhalation of ficilin.

Emergency medical care: repeated inhalation of ficilin or an anti-smoke mixture; copious rinsing of the eyes, mouth and nasopharynx, washing the face of the face and hands with 2 % sodium bicarbonate solution; administration of an eye medicinal film with dicaine behind the eyelid. Application of analgesics (topical eye drops with 0.5 % dicaine solution, inside 0.5 g of analgin); 1 ml of 2 % promedol solution subcutaneously; repeated lavage of the cavity, mouth, eyes, face and hands with 2 % sodium bicarbonate solution.

4. Evacuation to a medical facility by general purpose transport.

Case 3

1. Acute severe adamsite lesion; reactive rhinolaryngotracheobronchitis, reactive conjunctivitis, acute respiratory failure of the III degree.

2. Chemical burn of the mucous membranes of the nasopharynx, vocal folds, bronchi, conjunctiva, reflex dysfunction of the cardiovascular and respiratory systems.

3. First aid. In the focus of chemical contamination: putting on a gas mask, inhaling ficilin or an anti-smoke mixture (place the crushed ampoule in the undermask space of the gas mask). Outside the lesion: copious rinsing of the eyes with water, rinsing of the mouth and nasopharynx with 2 % sodium bicarbonate solution; inhalation of ficilin.

Emergency medical care: injection of 1 ml of cordiamine subcutaneously, inhalation of oxygen for 5–10 minutes. Use of analgesics (inhalation of ficilin, topical eye drops with 0.5 % dicaine solution, inside 0.5 g of analgin); 1 ml of 2 % promedol solution subcutaneously; repeated lavage of the cavity, mouth, eyes, face and hands with 2 % sodium bicarbonate solution; cardiac glycosides (1 ml of 0.06 % corglycone solution or 0.5 ml of 0.05 % strophanthin solution into a vein); vasopressors (1 ml of 1 % mezaton solution or 1–2 ml of 0.02 % norepinephrine hydrothartrate solution into a vein slowly); inhalation of oxygen, oxygen-air mixture; administration of sedatives and tranquilizers.

4. Evacuation to a nearest hospital, first term, by specialized medical transport in a semi sitting position, accompanied by medical stuff.

HIGHLY TOXIC SUBSTANCES OF SUFFOCATING ACTION

Case 1

Victim A. belatedly put on a gas mask during an accident at a chemically dangerous facility. He felt an unpleasant smell of rotten fruits, general weakness, dizziness, sore throat and chest, suffocation. After leaving the focus of chemical contamination after 20 minutes, his condition became better. He was taken to the emergency department of the regional hospital on stretchers 2 hours after the accident. Complains of general weakness, headache, bruising, slight shortness of breath, tightness and heaviness in the chest. The frequency of respiratory movements is 26 per minute. During auscultation, weakened breathing, isolated small-bubbly wheezes are heard. The accent of the second tone is over the pulmonary artery. A percussion sound with a tympanic tinge above the lungs is revealed, the lower border of the lungs is lowered. Pulse is 90 beats per minute, blood pressure is 90/60 mm Hg.

Case 2

The patient B. was taken from the chemical accident site at the water station as a result of a chlorine gas leak. Complaints of a runny nose, a feeling of dryness and burning in the throat, hoarseness of voice, sour taste in the mouth, headache,

sore eyes, watery eyes, chest pain, dry painful cough, sometimes vomiting. The mucous membrane of the nasal cavity is sharply hyperemic, abundant serous discharge from the nose is observed, breathing through the nose is very difficult. The uvula is enlarged and hyperemic, the arches of the tonsils, the true and false vocal folds are swollen (the latter do not fully close). The mucous membrane of the trachea is covered with foamy whitish sputum, sometimes with streaks of blood, sometimes there is loss of voice. Breathing is accelerated to 30 breaths per minute, pronounced cyanosis. The auxiliary respiratory muscles are tense. There are abundant dry whistling wheezes, wet wheezes of various calibers.

Case 3

At the enterprise for the production of nitrogen fertilizers, a container with nitric acid was destroyed in one of the rooms. At the same time, the workers who were in the accident site had no direct contact with nitric acid. However, 5 minutes after the beginning of the liquidation of the accident, two participants in emergency rescue operations with damaged respiratory protection equipment developed a severe cough, headache, and vomiting. After leaving the focus of chemical contamination, the described manifestations quickly disapeared, and the workers, having replaced the protective equipment, continued their work. But after 8 hours, a feeling of fear and severe weakness developed, an increasing cough with lemon yellow, and then with bloody sputum, chills, an increase in body temperature to 40 °C, palpitations up to 110 beats per minute, nausea, excruciating pain in the diaphragm, vomiting, diarrhea, severe thirst joined. An ambulance team was called; the patient was taken to the hospital. Clinical examination: increasing shortness of breath up to 30 respiratory movements, a dull percussion sound over all lobes of the lungs, a decrease in blood pressure to 90/50 mm Hg, heart rate — 100–110 beats per minute, erythrocytes and protein in the urine.

ANSWERS

Case 1

1. Acute inhalation injury with phosgene of severe degree; toxic pulmonary edema; latent period, respiratory failure of the II degree.

2. Toxic damage to alveolocytes and vascular endothelium of the pulmonary parenchyma.

3. *First aid*. In the focus of chemical contamination: putting on a gas mask, inhaling ficilin or an anti-smoke mixture (place the crushed ampoule into the undermask space of the gas mask). Outside the focus of chemical contamination: copious rinsing of the eyes with water, rinsingof the mouth and nasopharynx with 2 % sodium bicarbonate solution; inhalation of ficilin.

Emergency medical care: injection of 1 ml of cordiamine under the skin, inhalation of oxygen for 5–10 minutes. 100–200 mg of prednisolone intravenously (every 4 hours), 50 ml of 5 % ascorbic acid solution intravenously (or 2 g inside),

10 ml of 10 % calcium chloride solution into a vein, bloodletting 250–300 ml, oxygen therapy with inhalation of alcohol vapor, 2–4 ml of 2 % furosemide (lasix) solution into a vein, 1000–1500 units of heparin intravenously (every 1–1.5 hours); 2 ml of cordiamine intramuscularly. Delayed measures: preventive administration of antibiotics, sedatives and antihistamines (diphenhydramine 1 ml of 1 % solution).

4. Evacuation to the nearest hospital under the control of the state of cardiovascular and respiratory activity, primarily by specialized medical transport in a semi sitting position, accompanied by medical stuff.

Case 2

1. Acute inhalation injury with chlorine of severe degree; toxic pulmonary edema, acute respiratory failure of the III degree.

2. Toxic damage to alveolocytes and vascular endothelium of the pulmonary parenchyma.

3. First aid. In the focus of chemical contamination: putting on a gas mask, inhaling of ficilin or an anti-smoke mixture (place the crushed ampoule into the undermask space of the gas mask). Outside the focus of chemical contamination: copious rinsing of the eyes with water, rinsing of the mouth and nasopharynx with 2 % sodium bicarbonate solution; inhalation of ficilin.

Emergency medical care: injection of 1 ml of cordiamine under the skin, inhalation of oxygen for 5–10 minutes. 100–200 mg of prednisolone into a vein (every 4 hours), 50 ml of 5 % ascorbic acid solution into a vein (or 2 g inside), 10 ml of 10 % calcium chloride solution into a vein, bloodletting 250–300 ml, oxygen therapy with inhalation of alcohol vapor, 2–4 ml of 2 % furosemide (lasix) solution into a vein, 1000–1500 units of heparin into a vein (every 1–1.5 hours); 2 ml of cordiamine into a muscle. Delayed measures: preventive administration of antibiotics, sedatives and antihistamines (diphenhydramine 1 ml of 1 % solution).

4. Evacuation to a hospital in a stable state of cardiovascular and respiratory activity, primarily on specialized medical transport in a reclining position, accompanied by a paramedic.

Case 3

1. Acute severe inhalation injury with nitric acid vapor; toxic pulmonary edema, respiratory failure of the III degree, toxic nephropathy.

2. Toxic damage to alveolocytes and vascular endothelium of the pulmonary parenchyma. Reflex dysfunction of the respiratory and cardiovascular systems, violation of the acid-base balance of the body.

3. *First aid*. Removal of the victim from the contaminated area in a semi-sitting position, insure absolute physical rest, at least for 24 hours (even in seemingly “mild cases”), protect from hypothermia.

Abundant rinsing of the eyes with water, rinsing of the mouth and nasopharynx with 2 % sodium bicarbonate solution. Transport only in the supine position.

First aid: injection of 1 ml of cordiamine under the skin, inhalation of oxygen for 5–10 minutes, with the threat of pulmonary edema: injection of 10–20 ml of 20 % calcium gluconate solution into a vein (slowly). To relieve reflex bronchospasm administer atropine sulfate or ephedrine hydrochloride under the skin 1 ml.

TEST TASKS

1. Specify the effects of ammonia on the human body:

a) irritating effect;
b) suffocating effect;
c) narcotic effect;
d) psychodisleptic effect.

2. Indicate the most likely causes of adverse outcomes in case of chlorine poisoning:

a) reflex respiratory and circulatory arrest at high concentration of chlorine in the inhaled air;
b) paralysis of the respiratory muscles due to a damage of the nerve impulse;
c) acute hepatic-renal insufficiency;
d) progressive acute respiratory failure in the alveolar phase of toxic pulmonary edema.

3. Specify the statements valid for hydrogen sulfide:

a) has a long half-life from the human body;
b) in the atmosphere with a high concentration, the smell is practically not felt;
c) in small amounts, hydrogen sulfide depresses the central nervous system, in moderate amounts it excites;
d) the main route of exposure is inhalation; ingestion and administration through the intact skin are also possible.

4. Specify mechanisms of toxic action of hydrogen peroxide:

a) chemical burns of the skin and mucous membranes;
b) hemolysis of erythrocytes;
c) paralysis of the respiratory muscles;
d) formation of methemoglobin.

5. Specify the statements that are valid for carbon disulfide:

a) it is a yellowish gas with characteristic garlic smell;
b) the only route of administration is inhalation;
c) in the process of metabolism, about 50 % is released unchanged with the exhaled air;
d) almost insoluble in water, soluble in alcohol and ether.

6. Specify the intermediate metabolites that determine the clinical manifestations of severe methanol intoxication:

a) Acetaldehyde;
b) Formaldehyde;
c) Formic acid;
d) Oxalic acid.

7. Antidote used for methanol intoxication:

a) Ethylene Glycol;
b) Ethyl alcohol;
c) Methylene Blue;
d) Atropine.

8. What syndromes are the most characteristic for ethylene glycol intoxication:

a) toxic coma;
b) acute renal failure;
c) hemolytic anemia;
d) convulsive syndrome?

9. Specify the antidotes used for ethylene glycol intoxication:

a) Ethyl alcohol;
b) 4-methylpyrazole;
c) Calcium Gluconate;
d) Ficilin.

10. What detoxification methods are used in case of poisoning with chlorinated hydrocarbons:

a) probe gastric lavage followed by the enterosorbent given through the probe;
b) probe gastric lavage without the enterosorbent due to poor sorption of chlorinated hydrocarbons;
c) hemosorption;
d) peritoneal dialysis?

Keys for test tasks: 1 — a, b; **2** — a, d; **3** — b, c, d; **4** — a, b, d; **5** — c, d; **6** — b, c; **7** — b; **8** — a, b; **9** — a, b, c; **10** — a, c d.

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CONTENT

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