

Organization and structure of toxicological care in Bulgaria. Etiology, epidemiology, classification of poisonings. Basic terms and concepts in clinical toxicology. Toxo-allergic (anaphylactic) shock.

Toxicology is a discipline overlapping with biology, chemistry, pharmacology, medicine and nursing, that involves the study of the adverse effects of chemical substances on living organisms and the practice of diagnosing and treating exposure to toxins.

Clinical /Medical Toxicology is a separate specialty in Bulgaria, as in many former Soviet Union or eastern European countries, whereas its part of the Emergency medicine in the western countries.

Unlike the latter, where intoxicated patients are triaged in A&Es and the severe ones admitted in ICUs, in Bulgaria there are several specialized poison centers- toxicology departments at the bigger university hospitals

- Clinical Toxicology department of the National Institute of emergency medicine "Pirogov" Sofia

-Clinical Toxicology department- Military Academy Hospital Sofia

-Clinical Toxicology departments of University Hospitals in Plovdiv, Varna, Pleven

Etiology

Acute poisoning is ubiquitous and is one of the leading causes of emergency hospitalization. Chronic poisonings of varying severity affect significant human populations when concentrations of toxic gases and aerosols from industry and the household rise above environmentally safe standards. With the widespread use of preparations for control of biological species unfavorable for economic production (insects, parasites, weeds), toxic substances enter the food chain of humans and animals and pose a cumulative danger to health. The toxicological threat is also exacerbated by the numerous home remedies, household hygiene products and the growing prevalence of drugs.

Epidemiology

The annual number of intoxicated patients treated in the Toxicology clinic Plovdiv is on steady decline after it peaked in mid 80s and the scope of the intoxications has changed drastically. Due to the expansion of industrial /chemical plants back then industrial poisonings and chronic professional intoxications prevailed, plus the population was at its highest hence proportionally the number of patients was bigger.

After the economic collapse in the early 90s we see an increasing number of intentional self harming poisonings and accidental drug overdoses or substance misuse due to many factors as easy, uncontrolled access to prescription medications, popularity of less toxic new brands of drugs. Most common intoxications nowadays include the misuse of psychoactive drugs such as benzodiazepines, antipsychotics, anticonvulsants, NSAIDs incl aspirin/paracetamol, antihypertensives and oral hypoglycaemic drugs, followed by acute poisonings with alcohols- ethanol/methanol/ethylenglycol, pesticides, domestic products- corrosives, as well as toxic gases after fires, falloid mushroom poisoning, and envenomations- insect stings, snake bites. We treat more than 600 or 100-150/100 000 patients annually with a mortality rate of around 1%

Classification

1. According to the entry route

- oral
- inhalatory
- percutaneous
- parenteral

2. According to the severity of poisoning

- mild
- moderate
- severe
- extreme/lethal

3. According to the onset/symptom progression

- acute - sudden toxic effects resulting from a single contact of the body with higher doses / concentrations of a toxic substance; it is characterized by a severe clinical picture, often ending in death
- subacute - occur with single or multiple entry into the body of lower doses of the toxic substance; without particularly severe symptoms; the pathological process is milder, develops more slowly
- chronic - with prolonged systemic intake of small amounts of xenobiotics, which in a single action do not cause symptoms of poisoning; the manifestations of poisoning occur slowly and appear after a differently long latency period

4. According to the site of the incident

- domestic
- professional

5. According to the situation leading to the poisoning

- accidental
- * self-medication
- * drug overdose
- * alcohol or drug intoxication - debut
- * medical error/yatrogenic
- * workplace/industrial accident
- intentional poisoning
- * poisoning - for the purpose of murder or helplessness
- * self-poisoning - first attempt or relapse
- alcoholism

-drug addiction

6. According to the selective toxicity of xenobiotics

-neurotropic -drugs, glutamate, aspartate, tranquilizers, hypnotics, antidepressants, ethanol

-hepatotropic - phalloid fungi, paracetamol, ethanol, phosphorus

-cardiotropic - cardiac glycosides, verapamil

-pulmotropic - toxic gases, asbestos, silicon

-haematotropic - chloramphenicol, cytostatics, methemoglobin

-nephrotoxic - ethylene glycol, aminoglycosides, traces of heavy metals

. Mixed classification

-poisonings with inorganic compounds

-poisonings with organic compounds

-poisoning with drugs

-poisoning with war poisons

-poisonings with plant poisons

-poisonings with animal poisons

-food poisoning

Frequently used terms:

xenobiotics- chemical substance not familiar /deriving out of a living organism

Toxin-xenobiotic with potentially harmful effect on an organism

toxicants – synthetic poisons created by artificial processes

venoms- form of toxin secreted by an animal for the purpose of causing harm to another and delivered by a certain means like bites or stings

poison- a generalized term for any substance that could have adverse effects on an organism

toxicity- the degree to which a poison can damage the organism, including the effect on the whole organism or on a substructure- hepatotoxicity, cytotoxicity, nephrotoxicity

Paracelsus- everything could be poison or the dose makes the poison

types of toxins

chemical toxicants – inorganic/organic, most of the known poisons in practice, excluding radioactive substances

nonliving biological toxicants are called **toxins** if produced by bacteria, plant or fungus and **venoms** if produced by animals

physical toxicants – substances that interfere with biological processes – coal dust, asbestos, inert gases, water

acute poisoning – exposure to a poison on one occasion or during short period of time

chronic poisoning – long term repeated or continuous exposure to a poison where symptoms do not occur immediately or after the exposure

acute toxicity lethal or harmful effects after oral dermatological or inhalation exposure to environmental and occupation hazards

median toxic dose – TD50- the dose at which toxicity occurs in 50% of the cases. It should be greater than the half maximum effective concentration and less than LD50

median lethal dose LD50- the dose required to kill half of the members of the tested population, lower Ld50 greater toxicity

therapeutic index TI the ratio between the efficacious and the lethal dose of drug that causes adverse effects

TI= Ld50/ED50 morphine 70/1 diazepam 100/1 cocaine 15/1 ethanol 10/1 digoxin 2/1 (paracetamol warfarin lithium, gentamicin vancomycin, amphotericin B)

lowest published toxic concentration and lethal dose TCLo and LDLo

Anaphylaxis/Shock

DEFINITION- an acute allergic, potentially fatal multiorgan system reaction caused by release of chemical mediators from mast cells and basophils

Anaphylactoid reaction - a condition clinically similar to anaphylactic shock, but the release of mediators in it is a consequence of direct exposure to substances called histamine liberators on basophils and mast cells, or by activating the complement system.

Definition of anaphylactic shock - an acute systemic allergic p-ya, most often mediated by Ig E in a previously sensitized individual, clinically manifesting symptoms:

- acute hypotension with or without loss of consciousness
- inspiratory or expiratory dyspnoea due to laryngeal edema or obstruction of the small and medium bronchi
- skin-mucous manifestations - itching, urticaria and / or angioedema
- symptoms from the gastrointestinal tract - nausea, vomiting, abdominal pain, diarrhea

Etiology

1. Medications

- antibiotics - most often from the group of penicillin, cephalosporins, beta-lactam antibiotics, quinolones, etc.
- muscle relaxants
- anesthetics - intravenous and local
- opioid analgesics
- aspirin and NSAIDs
- ACE inhibitors

2. Bioproducts and allergens for immunotherapy

- serums and vaccines
- preparations for biological treatment
- blood products

3. Food allergens and products

-nuts - peanuts, walnuts, almonds

-milk and milk products

-fish and seafood

-eggs and egg products

-meat and meat products

4. Insects

5. Massive exposure to allergens (pollens)

6. Latex and latex products

7. Idiopathic forms - the cause remains unknown

Pathogenesis of anaphylactic reactions and anaphylactic shock

IgE mediated-classic form- sensitizing antigen elicits IgE response, that bind to the mast cells and basophils Fc-receptors. Subsequent exposure to the allergen causes cross linking of the cell bound IgE and degranulation.

Non IgE mediated anaphylaxis- involves complement cascade activation of C3a C4a C5a-anaphylatoxins that cause degranulation

Histamine and leucotriens/Pg and PAF are released

As a result of mast cell degranulation and histaminoliberation, generalized vasodilation occurs, to the extent of distributive shock, increased capillary permeability with soft tissue edema, especially in the pharynx / larynx, and bronchospasm leading to severe respiratory insufficiency.

Anaphylactic shock is hypovolemic shock with hemoconcentration. Hypotension affects the functions of the heart, brain, kidneys and liver

Anamnesis and clinical manifestation -most commonly involves the cutaneous respiratory cardiovascular and GI systems

onset- within seconds to minutes, but 1-8-10hours if delayed, less than 1 to max of 23% recurrence in different reports

risk factors- atopy as rhinitis, dermatitis, asthma,
route of administration food<parenteral,
shorter intervals between exposures,
concomitant use of medication especially ACE (2x greater risk)

skin/mucoses 80-90% some combination of urticaria, pruritus ,erythema,flushing or angioedema, SOME OF THE MORE SEVERE CASES CAN PRESENT WITHOUT CUTANEOUS SYMPTOMS

-rhinorrhea, sneezing throat tightness, wheezing, SOB, cough, hoarsenes, severe angioedema of lips and tongue, tachypnea, stridor, dysphonia

-dizziness, weakness, chest pain, [palpitations, syncope,tachycardia,hypotension, shock-occurring immediately without any other findings sometimes

-nausea, vomiting, diarrhea

-altered mental state, depressed LOC (level of consciousness) or agitated/combatative, feeling of impending doom

Testing – not usually required as an emergency but if syndrome recurring-

-serum triptase, urinary 24-histamine, skin testing for food, drug or other IgE-independent reactions

Treatment

-call for help, lie patient flat, raise legs

-ABCDE in case of established cardiac arrest

-in case of refractory or very severe anaphylaxis –CVS and resp symptoms ,patients should be admitted and treated/observed for a longer period in A&E or ICU for

*airway management,high flow oxygen

*cardiac monitoring,pulse oxymetry,fluid resuscitation and medication

Medication

1.OXYGEN-HIGH FLOW

2.Adrenergic agonists- adrenaline(epinephrine)

adult and child >12y/o 500mcg per dose of the 1:1000 ampules im

child 6-12 y 300mcg of 1:1000 amp im

child less than 6y 150mcg of 1:1000 amp im

REPEAT DOSES EVERY 5-10MINS

IV ADRENALINE ONLY BY EXPERIENCED SPECIALISTS 50MCG PER DOSE – ADULTS, 1MCG/KG PAED

EPIPEN AUTOINJECTORS 300MCG PER DOSE- APPLY TO OUTER MID THIGH , REPEAT DOSE IN 5-10MINS

3. Fluid resuscitation 500-1000ml/boluses 20ml/kg in paed

4.Antihistamines diphenhydramine- Benadryl, chlorphenamine- piriton, hydroxyzine

Chlorphenamin adults/children >12 y 10mg iv stat or im followed by 4mg po q4-6h

child 6-12y 5mg iv/im

child <6y 2,5 mg iv/im

5.Corticosteroids

HYDROCORTISONE ADULTS /children >12y 200mg iv/im stat followed by 100mg q6h

child 6-12 100mg iv/im stat

child 6m to 6y 50mg iv/im stat

METHYLPREDNISOLON 1MG/KG

6.Bronchodilators-salbutamol nebulized 0,5 mg/2,5mls NS

7.Vasopressors dopamine 5-20mcg/kg/min, noradrenaline 0,01-2mcg/kg/min

monitor- pulsoxymetry, ECG,blood gases, BP

*in extreme situations- cryothyrotomy

Follow up

mortality rate 0,65-2%, in the UK half of the fatalities are iatrogenic in origin, most common cause of death is airway obstruction, cardiac arrest averages 20-30min in onset, 5mins

inhospital, 10mins in prehospital, 10-20mins prehospital

prevention patient education, identification tags, epinephrine autoinjectors- not stored in fridge and avoid exp to heat