Acute poisoning with pesticides.

Acute poisoning with inorganic acids and bases.

Pesticides are substances that are meant to control pests. The term pesticide includes all of the following: herbicide, insecticides (which may include insect growth regulators, termiticides, etc.) nematicide, molluscicide, piscicide, avicide, rodenticide, bactericide, insect repellent, animal repellent, antimicrobial, and fungicide. In general, a pesticide is a chemical (such as carbamate) or biological agent (such as a virus, bacterium, or fungus) that deters, incapacitates, kills, or otherwise discourages pests. Target pests can include insects, plant pathogens, weeds, molluscs, birds, mammals, fish, nematodes (roundworms), and microbes that destroy property, cause nuisance, or spread disease, or are disease vectors. Along with these benefits, pesticides also have drawbacks, such as potential toxicity to humans and other species.

Organochlorine Pesticide Toxicity

Chlorinated hydrocarbon (organochlorine) insecticides, solvents, and fumigants are widely used around the world. This class of chemicals comprises a variety of compounds containing carbon, hydrogen, and chlorine and are largely banned in North America and Europe, but are used extensively in many developing nations. In addition, these chemicals may still be found in storage in the United States; thus, exposure remains possible.

The toxicity of organochlorine (OC) pesticides varies according to their molecular size, volatility, and effects on the central nervous system (CNS). In general, they cause either CNS depression or stimulation, depending upon the agent and dose.

Chlorinated hydrocarbons can be highly toxic, and the overwhelming majority have been universally banned because of their unacceptably slow degradation and subsequent bioaccumulation and toxicity. [2] Among the more notable examples is dichlorodiphenyltrichloroethane (DDT).

Pathophysiology

Organochlorines can be separated into 5 groups, as follows:

- DDT and analogues (eg, dicofol, methoxychlor)

- Hexachlorocyclohexane (ie, benzene hexachloride) and isomers (eg, lindane, gamma-hexachlorocyclohexane)
- Cyclodienes (eg, endosulfan, chlordane, heptachlor, aldrin, dieldrin, endrin, isobenzan)
- Chlordecone, kelevan, and mirex
- Toxaphene

Organochlorines are well absorbed orally and by inhalation. Transdermal absorption is variable. For example, DDT is poorly absorbed transdermally, whereas cyclodienes have significant transdermal absorption rates. [5] Cyclodienes have high absorption levels when taken orally, as in the case of food contamination with these pesticides. [6] Lindane is known to be absorbed after topical application, but oral ingestions are not rare. [7] Young age, malnourishment, and frequent exposure increases the risk for toxicity. [8]

Organic chlorines are strongly lipid soluble and sequester in body tissues with high lipid content, such as the brain and liver. Consequently, blood levels tend to be much lower than fatty tissue levels. [5] The lipophilic tendency of organochlorines accounts for prolonged systemic effects in overdose. The half-life of DDT has been measured in months or years, whereas other organic chlorines are metabolized faster; for example, lindane has a half-life of 21 hours. [9]

Mechanism of toxicity

Toxicity in humans is largely due to stimulation of the CNS. Cyclodienes, hexachlorocyclohexanes, and toxaphene predominantly are gamma aminobenzoic acid (GABA) antagonists and inhibit calcium ion influx, but also may inhibit calcium and magnesium adenosine triphosphatase (ATPase). The resulting accumulation of calcium ions at neuronal endplates causes sustained release of excitatory neurotransmitters. [10, 11]

DDT affects potassium and voltage-dependent sodium channels. These changes can result in agitation, confusion, and seizures. Cardiac effects have been attributed to sensitization of the myocardium to circulating catecholamines.

Some of the more volatile organochlorines can be inhaled while in vapor form or swallowed while in liquid form. Inhalation of toxic vapors or aspiration of liquid after ingestion may lead to atelectasis, bronchospasm, hypoxia, and a chemical pneumonitis. In severe cases, this can lead to acute lung injury,

hemorrhage, and necrosis of lung tissue. In liquid form, they are easily absorbed through the skin and GI tract.

Highly toxic organochlorines include:

- Aldrin
- Dieldrin [12]
- Endrin [13]
- Endosulfan [14, 15]

Moderately toxic organochlorines include:

- Chlordane
- DDT
- Heptachlor
- Kepone
- Lindane
- Mirex
- Toxaphene

Onset of symptoms is characteristically abrupt. Central nervous system (CNS) excitation and depression are the primary effects observed in acute organochlorine toxicity; therefore, the patient may appear agitated, lethargic, intoxicated, or may even be unconscious. Initial euphoria with auditory or visual hallucinations and perceptual disturbances are common in the setting of acute toxicity.

Organochlorines lower the seizure threshold, which may precipitate seizure activity. Strong external stimuli and reflex hyperexcitability may precipitate muscle fasciculations and tonic spasms, which may evolve into seizures.

Patients may have pulmonary complaints or may be in severe respiratory distress. Cardiac dysrhythmias may complicate the initial clinical presentation.

Other symptoms include the following:

Pulmonary - Cough, shortness of breath

Dermatologic - Rash

Gastrointestinal - Nausea, vomiting, diarrhea, and abdominal pain

Nervous system - Headache, dizziness, or paresthesias of the face, tongue, and extremities

Because of the high lipid solubility, duration of toxicity can be prolonged. Life-threatening complications are seizures secondary to prolonged CNS stimulation and consequent hypoxia.

Physical examination findings vary by type of exposure, as follows:

- Ingestion
- Skin absorption or inhalation
- Chronic exposure

Ingestion produces the following manifestations:

- Nausea and vomiting
- Confusion, tremor, myoclonus, coma, and seizures
- Respiratory depression or failure
- Unusual odor - Toxaphene may have a turpentine-like odor; endosulfan may have a sulfurous odor

Skin absorption or inhalation produces the following manifestations:

- Ear, nose, and throat irritation
- Blurred vision
- Cough
- Acute lung injury (ALI)
- Dermatitis

Long-term occupational exposure to organochlorine pesticides may result in various nonspecific symptoms, including headaches, nausea, fatigue, muscle

twitching, and visual disturbances. In addition, chronic exposure to these agents may be associated with the development of blood dyscrasias, including aplastic anemia and leukemia in humans (inconclusive).

Other manifestations of chronic exposure are as follows:

- Anorexia
- Hepatotoxicity
- Renal toxicity
- CNS disturbances

Approach Considerations

Supportive care and observation for signs of end-organ damage (eg, central nervous system [CNS], heart, lung, liver) are the mainstays of therapy. No specific antidotes are available for organochlorine poisoning. Decontamination may be indicated to prevent continued absorption, as well as exposure of health care personnel. For dermal decontamination, remove clothing and wash skin with soap and water. This is best performed in the field.

Observe patients with an apparent nonsignificant and nontoxic exposure in the emergency department (ED) for 6-8 hours. If any signs or symptoms of toxicity develop during that time, admit the patient to the hospital. Intensive care unit admission is indicated for patients with significant exposure or with signs and symptoms of intoxication.

Attend to the ABCs (airway, breathing, circulation). Protect the airway at all times.

Remove the patient from source of exposure and prevent contamination of others. Consider skin decontamination by washing with soap and water and removing clothing (place in plastic bags) as early as possible. Skin decontamination is performed best in the field.

Do not induce emesis, because the patient may have a sudden change in mental status and could aspirate gastric contents. Avoid strong external stimuli

to the patient, which may precipitate convulsions. Initiate cooling measures if the patient is hyperthermic.

Do not forget that other persons still may be at risk of intoxication. Medically evaluate all of these persons as soon as possible. With massive exposure or multiple victims, contact a hazardous materials (HAZMAT) team for assistance.

Emergency Department Treatment

Repeated assessments of the patient's airway, breathing, and circulation (ABCs) and vital signs are of extreme importance in cases of acute poisoning. In particular, airway protection must be assured. Consider early rapid-sequence intubation to facilitate aggressive benzodiazepine use.

Seizures may begin without any prodromal signs or symptoms. If the patient is paralyzed after intubation, electroencephalographic monitoring is warranted. Termination of seizure activity should be attempted using traditional treatment algorithms, starting with benzodiazepines and progressing if necessary to phenytoin or fosphenytoin, propofol, and barbiturates. Rhabdomyolysis should be considered in patients with prolonged convulsions or those who have acute renal failure with or without hyperkalemia.

Continuous cardiac monitoring is indicated. Use epinephrine and sympathomimetic amines with caution because dysrhythmias can be induced, as a result of increased myocardial sensitization to catecholamines. Use of beta-blockers is reported to control ventricular dysrhythmias because of sensitized myocardium. If the patient is hypotensive and unresponsive to fluids, intravenous administration of a pure alpha-adrenergic agonist agent (eg, phenylephrine) is the therapy of choice.

In cases of ingestion, do not induce emesis. Insertion of a nasogastric tube for stomach evacuation is controversial; it may induce vomiting with subsequent aspiration. Carefully perform orogastric lavage with suction, especially for recent liquid ingestion. Always secure the airway well before executing lavage. If nasogastric suction is used, a small-bore tube should be used.

Regardless of the route of exposure, consider multiple-dose activated charcoal (MDAC) because it may enhance fecal elimination by interrupting the biliary-enterohepatic and enteroenteric recirculation of the toxin. MDAC should be used with caution because patients are at increased risk for seizures [28] and consequent aspiration. Aqueous-based activated charcoal should be used, as sorbitol-based activated charcoal may induce vomiting.

Cholestyramine may be used to bind these highly lipophilic agents. Cholestyramine reduces reabsorption and retains bound agent in the GI tract for fecal elimination. [29] In patients who have ingested chlordecone, multiple repeated doses of cholestyramine can be administered to interrupt enteroenteric and enterohepatic recirculation. [30]

Sucrose polyester (Olestra) has also been shown to increase excretion of fat-soluble organic chlorine chemicals. [31] Whole-bowel irrigation may be indicated, but it is not without risk and so should be performed only at the discretion of a medical toxicologist or a poison control center. Induced diuresis, hemodialysis, and hemoperfusion have not been shown to be effective enhanced elimination techniques.

If liver abnormality or necrosis is suspected (eg, because of elevated serum levels of liver enzymes), administration of N-acetylcysteine (NAC) may in theory prevent irreversible hepatic injury. Generally, the only significant adverse event associated with oral use of NAC is pulmonary aspiration; therefore, ensure proper protection of the airway.

In contrast to organophosphate poisoning, atropine and oximes are not established antidotes for organochlorine toxicity. [32] The use of steroids or prophylactic antibiotics for aspiration is controversial and cannot be recommended because of a lack of evidence for their efficacy. External cooling may be used for hyperthermia.

Arrange follow-up care before discharge so that the patient may be monitored for possible long-term sequelae. Arrange for patient education on proper storage and use of pesticides. Survey for ongoing exposure in the home and work environment is important.

Obtain a psychiatric evaluation, if warranted, before discharge. Explore the possibility of child, elder, or vulnerable adult abuse or neglect.

Most patients exposed to organophosphates come into contact with insecticides.

Organophosphate pesticide exposure may occur through inhalation, ingestion, or dermal contact. Crops that farmworkers come into contact with that also may include organophosphates such as apples, celery, bell peppers, peaches, strawberries, nectarines, grapes, spinach, lettuce, cucumbers, domestic blueberries, and potatoes.

The severity of the symptoms depends on the amount ingested, route of absorption and rate of metabolic breakdown of the insecticide.

The key feature of organophosphate insecticides is the inhibition of carboxyl ester hydrolases, chiefly inhibition of acetylcholinesterase (AChE). This enzyme plays a vital role in the breakdown of the neurotransmitter acetylcholine, which is found in both the peripheral and central nervous systems.

The organophosphate insecticide inactivates AChE by phosphorylating the serine hydroxyl group on the enzyme. This is followed by the accumulation of acetylcholine which then overstimulates the nicotinic and muscarinic receptors.

Organophosphate molecules can be absorbed via the skin, inhalation, or in the gastrointestinal tract. Once absorbed, the molecule binds to an acetylcholinesterase molecule in red blood cells thus making the enzyme inactive. This leads to an overabundance of acetylcholine within synapses and neuromuscular junctions. Overstimulation of nicotinic receptors found at

neuromuscular junctions can lead to fasciculations and myoclonic jerks. This eventually leads to flaccid paralysis because of the depolarizing block. Nicotinic receptors also are found in the adrenal glands which may cause hypertension, sweating, tachycardia, and leukocytosis with left shift. [6][7][8][9]

Organophosphate poisoning also produces symptoms based on its action at muscarinic receptors. These effects are usually slower than the nicotinic receptors because the effects occur via a G-protein-coupled receptor mechanism. Muscarinic receptors are found in the parasympathetic and sympathetic nervous systems. Sweat glands within the sympathetic nervous system get overstimulated and cause large amounts of sweating. The parasympathetic effects of organophosphate poisoning can be seen in multiple systems including the heart, exocrine glands, and smooth muscles. At some point, which is different for each specific compound, the acetylcholinesterase-organophosphate compound undergoes a process called aging. This is a conformational change that renders the enzyme resistant to reactivation, making some treatment options useless.

Organophosphates stimulate both the sympathetic and parasympathetic nervous systems. A typical clinical scenario will involve symptoms of overstimulation of the parasympathetic system. An exception is in children, as they typically have a predominance of symptoms mediated by nicotinic receptors.

There are a couple of mnemonics that are helpful to remember the symptoms of organophosphate poisonings and the receptor that is responsible.

For nicotinic signs of acetylcholinesterase inhibitor toxicity, think of the days of the week:

- Monday = Mydriasis
- Tuesday = Tachycardia
- Wednesday = Weakness
- Thursday = Hypertension
- Friday = Fasciculations.

The more common mnemonic that captures the muscarinic effects of organophosphate poisonings is DUMBELS:

- D = Defecation/diaphoresis

- U = Urination
- M = Miosis
- B = Bronchospasm/bronchorrhea
- E = Emesis
- L = Lacrimation
- S = Salivation.

Additional symptoms can include anxiety, confusion, drowsiness, emotional lability, seizures, hallucinations, headaches, insomnia, memory loss, and circulatory or respiratory depression. When death occurs, the most common reason is respiratory failure stemming from bronchoconstriction, bronchorrhea, central respiratory depression or weakness/paralysis of the respiratory muscles. If the patient survives the acute poisoning, there are other long-term complications.

Intermediate neurologic symptoms typically occur 24 to 96 hours after exposure. Symptoms include neck flexions, weakness, decreased deep tendon reflexes, cranial nerve abnormalities, proximal muscle weakness, and respiratory insufficiency. With supportive care, these patients can have a complete return to normal neurologic function within 2 to 3 weeks. Another later complication is neuropathy. This is linked to very specific organophosphate compounds that contain chlorpyrifos. Most commonly this starts as stocking-glove paresthesia and progresses to symmetric polyneuropathy with flaccid weakness that starts in the lower extremities and progresses to include the upper extremities.

Those who survive may also develop the following neuropsychiatric deficits:

- Confusion
- Impairment in memory
- Lethargy
- Psychosis
- Irritability
- Parkinson like symptoms

The first step in the management of patients with organophosphate poisoning is putting on personal protective equipment. These patients may still have the compound on them, and you must protect yourself from exposure. Secondly, you must decontaminate the patient. This means removing and destroying all clothing because it may be contaminated even after washing. The patient's skin needs to be flushed with water. Dry agents such as flour, sand, or bentonite also can be used to decontaminate the skin. In the case of ingestion, vomiting and diarrhea may limit the amount of substance absorbed but should never be induced. Activated charcoal can be given if the patient presents within 1 hour of ingestion, but studies have not shown a benefit.

Airway control is vital. In some patients, intubation may be required due to bronchospasm, seizures or bronchorrhea. During intubation, succinylcholine must be avoided as it may prolong the paralysis. The reason is that succinylcholine is also degraded by acetylcholine esterase.

Good intravenous access, cardiac monitoring, and pulse oximetry are the standard of care.

The definitive treatment for organophosphate poisoning is atropine, which competes with acetylcholine at the muscarinic receptors. The initial dose for adults is 2 to 5 mg IV or 0.05 mg/kg IV for children until reaching the adult dose. If the patient does not respond to the treatment, double the dose every 3 to 5 minutes until respiratory secretions have cleared and there is no bronchoconstriction. In patients with severe poisoning, it may take hundreds of milligrams of atropine given in bolus or continuous infusion over several days before the patient improves.

Pralidoxime (2-PAM) also should be given to affect the nicotinic receptors since atropine only works on muscarinic receptors. Pralidoxime works by reactivating the phosphorylated AChE by binding to the organophosphate. However, to work it has to be given within 48 hours of the poisoning. The agent does not depress the respiratory center and can be combined with atropine.

Atropine must be given before 2-PAM to avoid worsening of muscarinic-mediated symptoms. A bolus of at least 30 mg/kg in adults or 20 to 50 mg/kg for children should be given over 30 minutes. Rapid administration can cause cardiac arrest. After the bolus, a continuous infusion of at least 8 mg/kg/hr for adults and 10 to 20 mg/kg/hr for children should be started and may be needed for several days.

Patients with seizures may benefit from benzodiazepines.

Carbamates

Carbamates are a class of insecticides structurally and mechanistically similar to organophosphate (OP) insecticides. Carbamates are N-methyl Carbamates derived from a carbamic acid and cause carbamylation of acetylcholinesterase at neuronal synapses and neuromuscular junctions. While they possess a similar mechanism of action to the irreversible phosphorylation of acetylcholinesterase by organophosphates, carbamates bind to acetylcholinesterase reversibly. Subsequently, carbamates have a similar toxicological presentation to OP poisonings with a duration of toxicity that is typically less than 24 hours.

Toxic exposures to carbamates can occur via dermal, inhalational, and gastrointestinal (GI) exposures.

Acetylcholinesterase (AChE) normally hydrolyzes acetylcholine to acetic acid and choline, leading to the cessation of neurotransmitter signaling. Carbamates cause reversible inhibition of the acetylcholinesterase enzyme. Persistently elevated acetylcholine levels due to AChE inhibition leads to increased neurotransmitter signaling. Central nervous system symptoms from increased acetylcholine include confusion, delirium, hallucinations, tremor, and seizures. Increased acetylcholine levels in the autonomic nervous system increase sympathetic and parasympathetic activity. Classic mnemonics emphasize the parasympathetic symptoms from carbamate and OP toxicity. For example, "DUMBBELS" stands for defecation, urination, miosis, bronchospasm or bronchorrhea, emesis, lacrimation, salivation.

It is important to remember that the adrenergic symptoms of tachycardia, hypertension, and mydriasis also may be present due to acetylcholine-dependent activation of nicotinic receptors in sympathetic ganglia. Nicotinic receptors at the neuromuscular junction lead to muscle fasciculations similar to the effects of depolarizing neuromuscular blocker medications (i.e., succinylcholine), and severe poisonings result in flaccid paralysis. Exposure may be chronic or acute and absorbed from the skin, lungs, conjunctiva, mucous membranes, lungs, and GI tract. Dermal absorption appears to be low with increasing absorption in cases of disruption in the skin and exposure to highly toxic carbamates.

After massive exposures, patients may become symptomatic within 5 minutes. The time to symptom onset is dependent on the exposure dose and the toxicity of the given carbamate. Highly lipophilic carbamates will redistribute into fat stores from the extracellular fluid quickly and have decreased clinical effects initially.

Carbamates are hepatically metabolized via hydrolysis, hydroxylation, and conjugation, and 90% are renally excreted in a matter of days. Carbamates do not undergo the “aging” that occurs during the phosphorylation of organophosphates to acetylcholinesterase, and the carbamate-cholinesterase bond hydrolyzes spontaneously within hours.

Treatment for carbamate and OP toxicity is going to be the same, as the manifestations of acute poisoning are similar.

Evidence of hypersalivation, lacrimation, GI distress, bronchorrhea, and diaphoresis on examination support the diagnosis. Patients may be bradycardic or tachycardic**,** and their pupil exam may show miosis or mydriasis due to the mixed stimulation of the parasympathetic and sympathetic nervous systems. OP and carbamate toxicity should be considered for the differential diagnosis in patients presenting with pinpoint pupils, excessive sweating, and difficulty breathing. Chronic neuropathy may develop.

Decontamination

Due to the continued cutaneous absorption of carbamate pesticides, decontamination should take place as soon as possible. All clothing should be removed from the patients, and the skin should be triple-washed with water, then soap and water, and then rinsed again with water. Vomitus and diarrhea may cause cutaneous absorption in providers in cases of GI ingestions.

In massive, life-threatening ingestions, GI decontamination may be considered if (1) the patient has not had bouts of emesis, (2) the ingestion occurred within 1 hour, and (3) if the patient is protecting their airway. In this instance, nasogastric lavage can be instituted. In severe toxicity, patients may have seizures, respiratory paralysis, and coma. Airway protection should take place before GI decontamination if any of these features are present.

Respiratory

Respiratory failure and hypoxemia is the primary cause of death after toxic exposure to AChE inhibitors. This is multifactorial secondary to bronchorrhea, muscular weakness with potential flaccid paralysis, and depression of CNS respiratory drive.

Atropine

Atropine competitively antagonizes the increased acetylcholine levels at muscarinic receptors and decreases symptoms of lacrimation, salivation, miosis, emesis, diarrhea, diaphoresis, urinary incontinence, bronchospasm, and excessive respiratory secretions. Atropine, starting at doses of 1 to 3 milligrams intravenously (IV) in adults or 0.05mg/kg IV in pediatric patients with a minimum dose of 0.1mg, should be administered. The dose should be doubled every five minutes if the previous dose provides an inadequate response.

Pralidoxime (2-PAM) is commonly given to patients with OP toxicity early in the presentation to prevent the “aging” process as OPs irreversibly bind to AChE. Carbamates will spontaneously disassociate from AChE and recover function within 24 to 48 hours.

Benzodiazepines

Benzodiazepines are used for the treatment of seizures and agitation for intubated patients after carbamate toxicity.

Pyrethroid

Pyrethroid compounds are widely used as insecticides. These compounds not only have a versatile application, but also have favourable toxicological profiles with high selectivity and toxicity to insects and low toxicity to humans.

The mechanism of pyrethroid toxicity is complex due to its—action on several channels and proteins. Pyrethroids act mainly on sodium and chloride channels. Excitable (nerve and muscle) cells are hence the key targets of pyrethroid toxicity.

Pyrethroids have been found to modify the gating characteristics of voltage-sensitive sodium channels, thereby delaying their closure. This results in a protracted sodium influx (referred to as a sodium “tail current”), which if sufficiently large and/or long, lowers the action potential threshold, and causes repetitive firing. The amplitude of the current depends on the pyrethroid concentration and the number of affected sodium channels. The duration of the current however mainly depends on the type of compound; type II pyrethroids have been found to have a longer duration. At high pyrethroid concentrations, the sodium tail current may increase to the extent that it blocks further action potential generation and a “conduction block” can result.

This action on the sodium channels may be the mechanism responsible for the clinical features of paraesthesia and proarrhythmogenic potential.[8]

Pyrethroids have also decreased chloride channel currents in the brain, nerves, muscles, and salivary glands. It is possible that these results in salivation and myotonia. Type II pyrethroids act on the voltage-dependent chloride channels and this action probably contributes significantly to the features of poisoning with type II compounds. At relatively high concentrations, pyrethroids can also act on gamma amino butyric acid (GABA)-gated chloride channels, which may be responsible for the seizures seen with severe type II poisoning.

Pyrethroids are lipophilic compounds and are distributed extensively in the body in the liver, stomach, intestine, adipose tissues, nervous system, and kidneys. They are generally poorly absorbed through the skin in humans and are rapidly metabolized in the liver. Various hydrophilic metabolites are excreted in the urine.

Acute Toxicity

Pyrethroid toxicity in humans can be due to occupational exposure through skin contact or inhalation of sprays or ingestion of pyrethroid compounds. Common reported symptoms included facial paraesthesia, skin itching, skin burning, dizziness, nausea, vomiting, and more severe cases of muscle fasciculations.

Two distinct toxidromes have been identified. Exposure to type I pyrethroids results in reflex hyperexcitability and fine tremors or the T syndrome or type I syndrome.
Incoordination, choreoathetosis, seizures, direct effects on the skeletal and cardiac muscle, and salivary gland, also known as choreoathetosis–salivation or type II syndrome is caused by type II pyrethroids.

Acute poisoning rarely poses a life-threatening risk but severe poisoning with mortality risk can occur if large quantities of pyrethroid compounds are ingested. Life-threatening manifestations mentioned in the literature are seizures, coma, pulmonary edema, and hemorrhage.

Atypical manifestations are usual in pyrethroid poisoning- low sensorium, respiratory failure requiring ventilator support , acute kidney injury, hypotension, pneumonia and seizures.

Hyperglycemia has been reported to be associated with adverse outcomes in pyrethroid poisoning.

The diagnosis of pyrethroid poisoning is based mainly on the clinical presentation and compound identification on the container brought by the patient or relatives.

Management is largely supportive and symptomatic because there is no available antidote. Optimization of the airway, breathing, and circulation is vital. Immediate decontamination of skin with soap and water can be considered. Gastric lavage is best avoided in the case of pyrethroid ingestion as the risk of aspiration pneumonia with the solvent is high. Evidence for the use of activated charcoal is limited; however, this can be considered if the patient presents within 1 hour of ingestion.

Seizures should be adequately controlled with antiepileptic therapy.

Corrosives

Oral intoxication with corrosive agents occurs by ingestion of: acids, alkalis, heavy metal salts (sublimate), formalin, iodine tincture and many other chemical substances.

Acids

In our environment the most common abused acid is hydrochloric acid which is easily accessible as a sanitary cleansing agent. It usually causes gastric stenosis although cases of esophageal stenosis have also been described.

Alkalis

Beside acids, corrosive alkalis are also being abused, such as sodium hydroxide (NaOH) and potassium hydroxide (KOH). They have a high Ph value and are found as components in the detergents, soaps, cleansing tablets and cosmetics. They are used in everyday life for cleaning sanitary surfaces and as drain openers. These substances may cause severe post-corrosive injuries of the upper gastrointestinal tract, including perforation that often results in death. The most common complications are esophageal and gastric stenosis, which are found in greater percentage than in poisonings with acid substances.

Pathophysiology and pathology

In contact with acids, tissue proteins are transformed into acid proteins and hemoglobin is transformed into hematine. The final outcome is the so-called coagulation necrosis.

In contact with alkalis, tissue proteins are transformed into proteinates and fats into soaps, resulting in penetrating, that is liquefaction necrosis

Corrosive substances with a Ph of less than 2 or greater than 12 are highly corrosive and can cause tissue necrosis. A concentrated solution of sodium hydroxide in contact with the esophagus can produce perforation of the esophageal wall, mediastinitis and fatal outcome. The severity of the chemical burns that affect the entire gastrointestinal tract depends on several factors: nature of the corrosive substance, Ph value, the quantity and concentration ingested, duration of exposure and the act of swallowing. The physical characteristics of the corrosive substances (fluid or solid form, gel or granules) might influence on the localization of the post-corrosive injury. Ingestion of corrosive substance in a solid or gel form causes injuries at the level of the oropharynx and proximal segment of the esophagus, while corrosive liquid substances cause injuries on the middle and distal segments of the esophagus and stomach.

Few hours after corrosive ingestion, thrombosis of small vessels appears, producing heat that exacerbates the injury. These processes in the esophageal wall and stomach continue in the next several days when bacterial invasion occurs as well as the so-called inflammatory response and development of

granulation tissue. Consequently, collagen deposition is minor until the second week after ingestion, and the healing process begins three weeks after ingestion. Three weeks after ingestion, tissue fibrosis occurs, resulting in narrowing of esophageal and/or stomach lumen and stricture formation.

The pathologic classification of corrosive injuries of the upper gastrointestinal tract is similar to the classification of thermal skin burns. First degree: is characterized by superficial damage followed by onset of mucous edema and erythema. The affected mucous layer regenerates in a few days and usually does not manifest complications such as scars or stricture formation.

Second degree: is characterized by caustic penetration through the submucosa into the muscular layer of the organ. After one to two weeks, deep ulcerations and granulation tissue develop on the esophageal or gastric wall. Additionally fibroblast reaction follows, production of collagen tissue that loses its humidity and is subjected to contraction over a period of several weeks or months. These processes along with the neighboring injuries may cause narrowing of the esophageal or stomach lumen within the next 8 weeks to 8 months and stricture or stenosis may appear.

The third degree is characterized with perforation of the wall of the esophagus or stomach

CLINICAL CHARACTERISTICS

Clinical presentation of corrosive injuries in the upper gastrointestinal tract depends on the physical state, type and quantity of the corrosive substance. After caustic ingestion patients complain on painful and burning mouth and throat, retrosternal chest and stomach pains, nausea, vomiting, often with bloody content. These symptoms may develop immediately after caustic ingestion, or be delayed for few hours after ingestion and they may last days and weeks. Hypersalivation, difficulty in swallowing with edema, ulceration or whitish plaques in the oral cavity, palatal mucosa and pharynx are common phenomena.

Corrosive substance ingestion in the acute phase may result in injuries of the larynx and may cause laryngospasm associated with dyspnea, tachypnea, dysphonia and aphonia. Aspiration of the corrosive substance may cause endotracheal or bronchial necrosis with mediastinitis, often leading to fatal outcome.

Local obvious lesions are painful and contact bleeding. Presence of hoarseness induces laryngeal, epiglottal or hypopharyngeal complications. High temperature accompanied with fever induces perforation and suggests consultation with a surgeon. The absence of oropharyngeal changes does not preclude severe injuries of other segments of the gastrointestinal tract.

Loss of large quantity of liquids and metabolic complications (acidosis) along with renal failure even more complicate the general condition of the patient. Severe caustic injuries of the stomach may result in perforation of its wall and development of acute abdomen, which requires emergency surgery. These injuries may appear in the first 48 hours or they may be delayed until the 14^{th} day after corrosive ingestion.

POST-CORROSIVE LATE COMPLICATIONS

The most common late complications are esophageal strictures and stenosis, gastric stenosis of the antrum and pyloris, esophageal and stomach cancer

MANAGEMENT

Prehospital procedures – gastric lavage, induced vomiting and activated charcoal are contraindicated because re-exposure of the esophagus to the corrosive agent might happen and produce additional injuries. Milk and water are suggested to be useful in the acute phase (the first 1-3 hours) but their eff ectiveness has not been proven in controlled studies. Milk may compromise urgent esophagogastroduodenoscopy and the heat produced during the chemical reaction might cause additional post-corrosive injuries .

Radiologic studies – in the acute phase, a plain radiography of the chest and abdomen may give useful data about the dimensions of the mediastinum and may reveal air in the mediastinum or under the diaphragm suggesting esophageal or gastric perforation.

TREATMENT

The aim of the therapy is to prevent perforation and to avoid progressive fibrosis and stenosis of the esophagus and stomach. Possible perforation of the esophagus or stomach can be treated only surgically.

Emergency surgery – Emergency surgical intervention is indicated in cases of esophageal or gastric perforation. Patients with shock, coagulation disorders or acidosis and those who have ingested a large quantity of corrosive substances

tend to develop severe post-corrosive injuries and laparotomy and resection of damaged segments may be beneficial in the treatment of these patients.

Neutralization of corrosive substances –Alkalis can be neutralized with mild vinegar, lemon or orange juice. Acids can be neutralized with milk, eggs or antacids. Sodium bicarbonate is not recommended because it produces carbon dioxide, which increases the risk of perforation. Some authors think that the heat produced in the neutralization reaction increases the possibility of additional injuries of upper gastrointestinal tract. Emetics are contraindicated because of re-exposition to the corrosive substance leading to injury exacerbation. Activated charcoal is also contraindicated.

Antibiotics –bacterial invasion of post-corrosively damaged mucosa and severe inflammation induce tissue granulation with a resultant formation of tissue fibrosis. administration of broad spectrum of antibiotics, most commonly of the penicillin group.

Nutrition – Extensive damage of the gastrointestinal tract hinder physiological nutrition in these patients. Within a short period of time, these patients fell into a severe general condition due to hypercatabolic state and negative alkali balance (5). The type of the artificial nutrition depends on the degree of esophageal or gastric damage seen by endoscopy.

In patients with I and II A grade of damage, total parenteral nutrition in the first 24-48 hours is followed by liquid diet until the 10^{th} day. Afterwards, food intake can be in a more liberal regimen.

In patients with II B and III grade of damage the socalled “esophageal rest” is recommended, that is, the patient must not take food per os (NPO). During the “rest”, the patient is fed by nasogastric or nasoenteral tube, gastrostoma or jejunostoma and parenterally by peripheral or central vein. Esophageal rest is explained with the fact that food particles enter the granulocytes of the esophageal wall and exacerbate the inflammation. Esophageal rest may last until the 10^{th} day after corrosive ingestion.

Esophageal dilation – Retrograde intraluminal esophageal dilation is performed for prevention or dilation of the already created esophageal narrowing. According to some authors, it can be done immediately after injury or 15 days after ingestion.

Surgery – Surgical intervention is indicated when there is a:

- complete stenosis that cannot be treated with usual conservative methods;
- defect of the esophagus or stomach detected with x-ray examination;
- fistula formation.