BASF Chemical Emergency Medical Guidelines

Cholinesterase-inhibiting Chemicals C 1

Information and recommendations for doctors at hospitals/emergency departments

- **Patients whose vomitus, skin or clothing is contaminated with cholinesterase-inhibiting chemical may secondarily contaminate rescue and medical personnel.**
- **Severe cholinesterase-inhibiting chemical poisoning may lead to death within minutes. Given reason to believe that cholinesterase-inhibiting chemical is present, there are many symptoms and signs with a large range of severity such as vomiting, diarrhea, excessive secretions, sweating, shortness of breath, tremor, weakness, headache, confusion, or coma to suggest the diagnosis.**
- **Administer the antidote atropine. Doses should be based on the severity of the poisoning. In case of organophosphate poisoning an enzyme reactivator such as pralidoxime or obidoxime may be an effective adjunct to atropine.**

1. Substance information

Cholinesterase-inhibiting chemicals, such as terbufos (COUNTER), phorate (THIMET), dimethoate (CYGON), temephos (ABATE), carbaryl. Synonyms: Anti-cholinesterase pesticides; **organophosphate** and N-methyl carbamate insecticides.
These chemicals are the most widely used insecticides available today. All apparently share a common mechanism of cholinesterase inhibition and can cause similar acute symptoms. However, there is a wide range of potency among these agents and there may be some differences in toxicity and management. Thus, identification of the specific agent or of the general class of agent is quite important.

2. Routes of exposure

Inhalation

Cholinesterase-inhibiting chemicals are efficiently absorbed via the lung.

Skin/eye contact

Cholinesterase-inhibiting chemicals are absorbed through skin or mucous membranes.

Ingestion

Cholinesterase-inhibiting chemicals are absorbed from the gastrointestinal tract.

3. Acute health effects

Onset of symptoms may occur in minutes or be delayed up to 12 hours. While low-level exposures may cause biochemical effects without producing symptoms, mild poisoning typically results in a normal level of consciousness and a small increase in secretions such as saliva, tears, nasal discharge, and phlegm. Classic first-onset symptoms can be remembered by the acronym ”SLUDGE”: salivation, lacrimation, urination, diarrhea, gastrointestinal distress, and emesis. Some other presenting symptoms include nausea, sweating, and a tight chest. Pupillary constriction is a characteristic sign, but its absence does not exclude the diagnosis, and enlargement may be seen early on. Severe poisoning includes an altered state of consciousness, heavy secretions and sweating, abnormal pupillary size, weakness and muscle twitching, chest pain, and shortness of breath. Life-threatening poisoning includes coma, seizures, massive secretions, cyanosis, pulmonary edema, and respiratory failure. Death can result if treatment is not begun rapidly.

	Cholinesterase inhibition alters neurotransmission at all cholinergic synapses and can produce symptoms in four functional receptor divisions: muscarinic, nicotinic-ganglionic, nicotinic-skeletal muscle and CNS. In general, muscarinic symptoms occur first (recall SLUDGE acronym). Stimulation of ganglia can activate sympathetic responses, which can confuse the expected clinical picture of muscarinic stimulation.
	Signs, symptoms, and onset of poisoning vary according to patient age, the specific agent, and amount of exposure. Cholinesterase activity is highly variable between individuals. Comparison of laboratory results with a normal range reported by the lab is of limited use in confirming diagnosis in a minimally symptomatic patient. Assessment and treatment must be directed by clinical signs and symptoms, especially when a baseline value is not available for the individual.
Muscarinic	Salivation**,** lacrimation, rhinorrhea, urinary urgency, incontinence, cramping, diarrhea, emesis, miosis, blurred vision, bradycardia, hypotension, bronchospasm, bronchorrhea, diaphoresis
Nicotinic-ganglionic	Tachycardia, hypertension, mydriasis
Nicotinic-skeletal muscle	Tremor, fasciculation, spasm, weakness, atonia, poor respiratory effort
CNS	Giddiness, agitation, anxiety, headache, stupor, seizures, coma
Respiratory	Narrowing of the bronchi and markedly increased bronchial secretions can occur. Respiratory failure results from central respiratory depression coupled with paralysis of the respiratory muscles and progressive airway obstruction from bronchorrhea.
Cardiovascular	Initially there is bradycardia, a result of muscarinic effects, but as exposure increases the recruitment of nicotinic effects can result in paralysis of peripheral ganglia resulting in tachycardia. (It is critical to distinguish this effect from the one due to atropine treatment.) Irregular heartbeat may occur.
CNS	Acute CNS effects are a common feature of significant poisoning in adults and may dominate the clinical picture in children. CNS effects include irritability, nervousness, giddiness, fatigue, lethargy, confusion, slurred speech, convulsions, coma, and respiratory depression.
Gastrointestinal	Nausea, vomiting, abdominal cramps, diarrhea, and fecal incontinence are common manifestations, regardless of the exposure route.
Metabolic	Profuse sweating is likely to occur and may lead to profound dehydration.
Dermal	Cholinesterase-inhibiting chemicals are readily absorbed through the skin. Systemic effects can result from dermal contact.
Ocular	Local contamination of the eye invariably produces miosis. Systemic poisoning may cause either mydriasis or miosis. Spasm of the muscle of visual accommodation (i.e., ciliary muscle) leads to blurred vision and aching pain in the eye. The hydrocarbon solvents used in commercial pesticide preparations may cause eye irritation.
Potential sequelae	In uncomplicated cases, clinical recovery should occur within 1 –2 weeks. Cases may be complicated by intermediate and delayed neurologic syndromes, aspiration pneumonia, respiratory failure due to pneumonia or sepsis, or to other events inherent to prolonged ICU management. Patients who suffered prolonged hypoxia from acute respiratory failure may sustain damage to brain or other organs.

Residual neuropsychiatric symptoms such as confusion, fatigue, irritability, nervousness, and impaired memory can occasionally last for several weeks. Six to twenty-one days after acute exposure to some organophosphate compounds, onset of delayed neuropathy of mixed sensory-motor type may occur.

4. Actions

Rescuer self-protection

Patients whose skin or clothing is contaminated with materials containing cholinesterase-inhibiting chemical may secondarily contaminate rescue and medical personnel by direct contact. **Avoid direct contact with contaminated clothing, skin and vomitus of victims as well as surfaces that may be contaminated themselves. Wear neoprene or nitrile gloves. Vinyl or leather gloves provide no protection.** Note: inside surfaces of gloves, boots, and headgear can become contaminated. Equipment can become contaminated.

Initial Treatment

Speed is critical. For symptomatic patients, secure an airway and provide 100% oxygen. Prepare the specific antidote, atropine, if within professional scope of practice. Tissue oxygenation should be improved as much as possible before administering atropine, so as to minimize the risk of arrhythmia. Treatment should be given simultaneously with decontamination procedures in severe cases.
In case of ingestion **do not induce emesis.**

Remove oral secretions and vomitus by suctioning to avoid aspiration but protect against direct contact with contaminated fluids. Be aware that intubation, suctioning, and other manipulations of the head and neck can induce profound bradycardia in these patients prior to atropinization. Gastric emptying by gastric lavage may be considered after ingestion of a potentially life-threatening amount if it can be performed soon after ingestion (within an hour). If the patient is not vomiting, a slurry of activated charcoal may be medically warranted at an oral dose appropriate for adult, child, or infant.

However, in significant ingestions, diarrhea and/or vomiting are so likely that charcoal absorption and catharsis are not indicated. Isolate gastric washings and vomitus.

Decontamination

All patients with suspected exposure to material containing cholinesterase-inhibiting chemical require decontamination. Patients who are able and cooperative may assist with their own decontamination. **Rapidly remove and double-bag (in plastic bags) contaminated clothing while flushing exposed skin and hair with water for 2-3 minutes.** Gently wash skin and hair with soap or mild dishwashing liquid and water.
Contaminated clothing is to be laundered separately before reusing. Contaminated leather such as shoes, belts, or wallets should be discarded.

Irrigate exposed or irritated eyes with plain water or saline for 5 minutes. Continue eye irrigation during other basic care or transport. Remove contact lenses if present and easily removable without additional trauma to the eye. Protect eyes during flushing of skin and hair.

Antidotal treatment

The following treatment with antidotes should be given as appropriate under medical supervision for those with known or suspected cholinesterase-inhibiting chemical poisoning. The availability of antidotes may vary due to statutory and regulatory differences among different countries.

Give atropine intravenously (IV) or, if not immediately possible IV, through an alternative route such as an endotracheal tube or subcutaneously. Depending on severity of poisoning, use 1 to 2 mg initially IV in adults (or 0.05 mg/kg in children under 12 years), then give appropriate doses every 15 minutes until excessive secretions and sweating have been controlled. If the diagnosis is certain but no clinical response to treatment occurs, administration of higher doses should be considered. Atropine is ineffective against nicotinic actions, specifically muscle weakness and twitching, and respiratory depression. Proceed concurrently with decontamination using proper protective gear. Maintain atropinization by repeated doses based on recurrence of symptoms. For severe **organophosphate** poisoning, 50 mg may be required as a bolus at the beginning, followed by a continuous infusion of 0.5 – 2.0 mg/h for several days. Preservative-free atropine preparation should be used if large doses are required. **Carbamate** poisonings usually require much smaller dosages of atropine for a shorter period of time. **Avoid opiates, parasympathomimetic agents, theophylline, reserpine, and phenothiazines.** Adrenergic amines should be given only if there is a specific indication, such as marked hypotension.

In patients with significant impairment in CNS and/or skeletal muscle function from organophosphate poisoning (NOT carbamates), an enzyme reactivator such as pralidoxime or obidoxime may be an effective adjunct to atropine. It is most effective when used as soon as possible.

Before its administration, obtain appropriate blood samples for serum and RBC cholinesterase analysis adhering to the techniques required for accuracy. Adjusting for age and weight, obidoxime/pralidoxime may be administered as a continuous infusion after a loading dose or using a slow bolus method. One recommended regimen for obidoxime is 250 mg intravenously followed by 750 mg/d as continuous infusion (pralidoxime: 1.0 to 2.0 grams by intravenous infusion for patients older than twelve years of age at a rate of no more than 0.2 grams per minute.)

Note: Diethyl organophosphates (e.g. parathion, phoxin, pyrazophos) exhibit a slow aging whereas dimethyl organophosphates (e.g. dimethoate, omethoate, phosphamidone) exhibit a fast aging. In the first group of compounds the administration of oximes is generally useful, whereas in the second group oximes can reactivate the enzyme or prolong the aging process only if given very early.

Further evaluation and treatment

To the standard intake history, physical examination, and vital signs, add pulse oximetry monitoring and a PA chest x-ray. Continuous ECG monitoring and control of electrolytes, in particular potassium levels, are strongly recommended in all cases treated with atropine.

For seizures after atropine/oxime therapy, consider giving a benzodiazepine such as diazepam intravenously. If seizures persist or recur, administer phenobarbital followed by phenytoin if necessary. Furosemide may be considered for relief of pulmonary edema if crackles persist in the lungs even after full atropinization.

Hemoperfusion, hemodialysis, and exchange transfusion have not been shown to affect outcome or duration of toxicity in controlled trials of

organophosphate poisoning. Observe the patient continuously after the atropine is stopped for at least 72 hours for organophosphate and 24 hours for carbamate poisoning to ensure that symptoms do not recur and that pulmonary ventilation is maintained.

Allow no further exposure to cholinesterase-inhibiting chemicals until sufficient cholinesterase regeneration has taken place as determined by blood tests.

Laboratory tests

The diagnosis of acute cholinesterase-inhibiting chemical toxicity is primarily a clinical one, based on the rapid onset of characteristic symptoms of increased secretions, muscle fasciculations and weakness, and alteration in mental status together with known or strongly suspected exposure to cholinesterase-inhibiting chemical. **If there are strong clinical indications of acute poisoning by anti-cholinesterase chemical, with or without a history of exposure, treat the patient immediately. Do not wait for laboratory confirmation.** If the condition is not due to cholinesterase inhibition, the patient will develop anticholinergic signs with the initial dose of atropine and other causes for the condition can then be sought. Laboratory testing for plasma pseudocholinesterase and erythrocyte acetyl cholinesterase is useful for monitoring the patient who is toxic from organophosphate cholinesterase-inhibiting chemical. Be advised that unless a substantial amount of N-methyl carbamate has been absorbed and a blood sample is taken within an hour or two, it is unlikely that the blood cholinesterase activities will be found depressed. Routine laboratory studies include complete blood count, glucose, amylase, and electrolyte determinations. Save samples of urine (or vomitus if the agent was ingested) for metabolite analysis if there is a need to identify the agent responsible for the poisoning. Arterial blood gases should be performed to assess oxygenation and acid-base balance in significant poisonings. Correct metabolic acidosis with bicarbonate when blood pH falls below 7.15. Also evaluate and treat electrolyte imbalance (e.g. hyperkalemia).

Patient release/ follow-up instructions

Patients who remain **asymptomatic for 12 hours after exposure and have not received antidotes** and patients who have **received antidote and no longer have any symptoms after observation for 72 hours for organophosphate poisoning or 24 hours for carbamate poisoning** may be discharged in the following circumstances:

a) The evaluating physician is experienced in the evaluation of individuals with cholinesterase-inhibiting chemical exposure.

b) Information and recommendations for patients with follow-up instructions are provided verbally and in writing. Patients are advised to seek medical care promptly if symptoms develop or recur. Individuals who have been clinically poisoned should not be re-exposed to cholinesterase-inhibiting chemicals until signs and symptoms have completely resolved and the blood cholinesterase levels are at least 80 percent of pre-poisoning levels (or above minimum normal level if pre-poisoning baseline value is not known).

c) The physician is comfortable that the patient understands the health effects of cholinesterase-inhibiting chemicals and the provided follow-up instructions.

d) Arrangements should be made to contact the patient at regular intervals in the 24-hour period following release.

e) Heavy physical work should be precluded for 24 hours.

f) Exposure to cigarette smoke should be avoided for 72 hours; smoke may worsen the condition of the lungs.

In this document BASF has made a diligent effort to ensure the accuracy and currency of the information presented but makes no claim that the document comprehensively addresses all possible situations related to this topic. This document is intended as an additional resource for doctors in assessing the condition and managing the treatment of patients exposed to cholinesterase-inhibiting chemicals. It is not, however, a substitute for the professional judgement of a doctor and must be interpreted in the light of specific information regarding the patient available to such a doctor and in conjunction with other sources of authority.

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