

US EPA ARCHIVE DOCUMENT

DATA EVALUATION RECORD

- (1) CHEMICAL: Trichlorfon
- (2) TYPE OF FORMULATION: Unspecified
- (3) CITATION: Akimov, G.A., Buchko, V.M., and Kremleva, R.V.
1975. [Neurological disorders in chlorophos poisoning.]
Klin. Med. 53:65-69 (Translated from Russian)

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- (6) TOPIC: This study has information pertinent to discipline toxicology, topic human neurotoxicity. It relates to none of the Proposed Guidelines data requirements.

(7) CONCLUSION: A clinical study of 160 patients with acute and subchronic poisoning with chlorophos was made. It included 27 patients with mild poisoning, 65 with medium severity, and 67 with severe poisoning. All patients had symptoms caused by an anticholinesterase effect of chlorophos. The most marked changes of the nervous system were observed in the patients with severe poisoning. They were characterized by consciousness disorders, spasms, and disturbances in respiration and cardiovascular activity and in the motor and reflex spheres. Low amplitude quick activity persisting for a period of 6-7 and 7-9 days was recorded on the electroencephalograph during the first day of poisoning in patients with poisoning of mild and moderate severity. Low-amplitude slow activity persisting for a period of 9-12 days was recorded in the patients with severe poisoning accompanied by consciousness disorders. Severe polyneuritis affecting the upper and lower extremities developed in 38 patients after severe poisoning.

(8) MATERIALS AND METHODS:

Subjects: A total of 160 patients were studied. The severity of poisoning was classified as mild for 28, moderate for 65, and severe for 67. Some patients were chronic alcoholics. The age, sex, and occupation of the patients were not reported.

Chemical: Exposure was to "chlorophos." No other details were given.

Route of exposure: According to the summary, exposure was peroral, but this was not specified in the text.

Symptoms: The symptoms used in classifying the severity of poisoning were:

Mild poisoning - Constriction of the pupils, hyperhidrosis, bradycardia, and fascicular and fibrillar twitching of the muscles were observed. In some cases, a gastrointestinal syndrome predominated: vomiting, abdominal pains, liquid stool.

Moderate poisoning - The symptoms were more pronounced, respiration was accelerated, bronchorrhea appeared, and salivation increased. The abdominal pains often resembled labor pains.

Severe poisoning - Respiratory disorders up to total arrest, clonic-tonic convulsions, disorders in consciousness, and hemodynamic disorders predominated.

Treatment: In the acute period of poisoning, measures were included to rapidly eliminate the toxin from the body and halt its absorption (gastric lavage, increasing diuresis by a preliminary water load and subsequent use of diuretics, siphonage).

Mild poisoning - The patients were given an initial 2-ml dose of a 0.1% solution of atropine sulfate subcutaneously, in case of relapse, atropine was administered again.

Moderate poisoning - A solution of 0.1% atropine was given intravenously in an initial dose of 4-6 ml followed by 2 ml subcutaneously, which was repeated as a function of the clinical course.

Severe poisoning - A solution of 0.1% atropine in a dose of 10-15 ml was given intravenously, followed by repeated subcutaneous injections of 2-3 ml. Some patients received 50-80 ml of 0.1% atropine sulfate solution during treatment.

Dipyroxime, a cholinesterase activator, was given intramuscularly at a dosage of 150-300 mg four times a day for the first 2-3 days.

The bronchial tree was drained for preventive purposes, and antibiotics and, if necessary, cardiac agents were administered to treat pneumonia. The patients with respiratory insufficiency, especially those with severe poisoning, were placed on artificial ventilation with a RO device.

Treatment of motor disorders was based on the general principals for treating postintoxication polyneuritis, excluding administration of drugs with an anticholinesterase action.

(9) REPORTED RESULTS:

Clinical laboratory tests: "A decrease in plasma cholinesterase and erythrocytes was observed in all patients."

(Methods and data are not reported. Presumably this means

that erythrocyte cholinesterase rather than erythrocyte count was decreased. There is no data to indicate whether or not the patients were anemic.)

Neurologic examinations: The incidence and degree of individual neurological disorders were a function of the severity of poisoning as follows. These syndromes were absent in mild poisoning.

<u>Syndrome</u>	<u>Degree of Severity</u>	
	<u>Moderate (65 patients)</u>	<u>Severe (67 patients)</u>
Disorders in consciousness	2	33
Convulsions	-	7
Hyperkinesia	-	2
Mental disturbances	4	13
Disorders in craniocerebral innervation	4	13
Diffuse paresis	12	38
Paresis of the proximal muscles	57	67

The disorders in consciousness were sopor or coma (grade I-II) and lasted 3 hours to several days. Convulsions and choreic hyperkinesia occurred in patients with severe respiratory disorders. Mental disturbances in the form of an acute psychosis were observed in 3-4 or 7-10 days and continued for 2-7 days. Disorders in craniocerebral

innervation were observed in the form of nystagmus and difficulty in swallowing in the first 24-36 hours. Diffuse paresis, that is paresis of all groups of muscles, was observed in the first 1-3 days. This diffuse paresis subsequently turned into paresis of the proximal groups of muscles. Many patients developed paresis of the proximal muscles initially without having diffuse paresis. Some of these patients were unable to sit up in bed or assume a seated position using their hands; sometimes they were unable to hold up their heads or keep their limbs lifted.

The presence of respiratory insufficiency was correlated with diffuse and proximal muscle paresis. Respiratory insufficiency developed in the first 3 days in 24 of 46 patients with a history of diffuse paresis, and in 22 patients in 4-9 days with a history of paresis of the proximal muscles.

Motor disorders developed 15-35 days after poisoning and had a direct relationship to the severity of poisoning:

<u>Motor Disorder</u>	<u>Degree of Severity</u>		
	<u>Mild</u>	<u>Moderate</u>	<u>Severe</u>
Paresis and paralysis of the dorsal flexors:			
Foot	1	4	9
Foot and knee muscles	-	2	3
Paresis of muscles in the lower extremities and hands	-	2	13
Diffuse paresis of muscles in the extremities and trunk	-	-	4
TOTAL	1	8	29

Four of the 29 patients with motor complications also exhibited disorders in consciousness and severe respiratory insufficiency that required artificial ventilation of the lungs. Paresis and paralysis of the upper extremities and torso developed 10-16 days after the onset of paresis in the lower extremities. Pain in the lower extremities preceded the paresis by 4-7 days. Paresis and paralysis of the dorsal flexors in the feet was always associated with a decrease in or total absence of Achilles reflexes; the patellar reflexes and reflexes in the upper extremities were often increased. Deep reflexes could not be produced in diffuse paresis that affected the extremities and torso.

Motor disorders predominated in all cases. Hypesthesia of the superficial sensitivity of the feet was observed in only 10 patients.

A severe painful syndrome resulting in strong, burning pains in the feet developed in 11 patients with severe chlorophos poisoning 30-36 days after the onset of paresis.

Muscular atrophy developed 2-3 weeks after the onset of paresis and became more pronounced in 1.5-2 months.

Patients with severe motor disorders began to improve in 6-8 months, and in some cases after 1 or more years.

Electroencephalographic (EEG) examinations: Moderate changes were found in patients with mild poisoning; they were manifested by predominance of rapid oscillations in the absence of regional differences. The EEG became totally normal in 6-7 days. In patients with moderate poisoning, low-amplitude rapid activity with no regional differences was observed in 1-2 days. Rapid oscillations predominated in 4-5 days only in the anterior sections with leveled regional differences. In 7-9 days, the EEG was normal. Rapid spike rhythm without regional differences was observed in patients with severe poisoning in 5-7 days; the EEG normalized in 9-12 days.

Low amplitude theta and delta rhythm was recorded in 3-4 days in four comatose patients with respiratory insufficiency on artificial ventilation.

Outcome: Of the 67 patients with severe chlorophos poisoning, 27 died. The direct cause of death was cardiovascular and respiratory disorders. Death occurred in the first 5-6 days. Postmortem examinations revealed pulmonary and cerebral edema, and multiple punctate hemorrhages in the brain. Diffuse degenerative changes in nerve cells and demyelination of nerve fibers were constantly found when patients survived for long periods after poisoning.

- (10) DISCUSSION: The authors have compiled neurological data from 160 patients, reported as chlorophos poisoning. The report has merit in assessing the clinical course and treatment measures used in cases of organic phosphate as well as chlorophos poisoning. It is unfortunate that more information on the chemical, patients, exposure, and clinical laboratory studies were not reported. The statement in the summary that exposure was peroral was not supported in the text. The statement that "a decrease in...erythrocytes was observed in all patients" may have not been translated accurately. The decrease was probably in erythrocyte cholinesterase rather than in erythrocytes themselves.

- (11) TECHNICAL REVIEW TIME: 6.0 hours