

US EPA ARCHIVE DOCUMENT

UNDATED

TR. 1715  
Carbayl

IMPORTANCE OF NONSPECIFIC MANIFESTATIONS OF PESTICIDE POISONING  
IN SETTING NORMS FOR THEIR RESIDUAL QUANTITIES  
[Znachenije respetsificheskikh proyavleniy intoksikatsii  
pestitsidami v normirovani i kh ostatochnykh kolichestv]

by

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Published in Vop. Gig. Toksikol. Pestits.,  
Tr. Nauch. Sess. Akad. Md. Nauk SSR (1967)  
[Questions of Toxicology and Pesticide Hygiene,  
Transactions of the Scientific Session of the  
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The authors examine nonspecific symptoms of poisoning with low doses of some organophosphorus compounds, studying in particular these compounds' effects on cholinesterase activity, serotonin content in the blood and basal metabolism of test animals.

Sanitary supervisory organs' practical work on control over the proper

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Translated for Perrine Primate Laboratory from the Russian by LEO  
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(415) 338-2011, April 1972.

use of toxic chemicals is hampered by the absence of norms for the permissible content of many pesticides in the air of work zones and in food products. The number of toxic chemicals for which such norms have been established amounts to only half of the list of chemical substances authorized for employment in the battle against pests, plant diseases and weeds.

Setting norms for maximum permissible concentrations of poisons in the atmosphere and of residual quantities of them in food products is one of the most important, responsible and at the same time complex tasks of toxicology. Setting norms for those toxic chemicals that do not have a pronounced specific effect on animals' organisms is especially complex. In these cases experimenters use integral tests, i.e. study of conditioned reflex activity, work capacity etc. When setting norms for toxins that possess a specific effect, study of changes in animal organisms that are not connected with characteristic manifestations of poisoning are usually limited to the most general research (body weight, relative weight of internal organs, morphological composition of the blood). However as study of various pesticides in the toxicology division of the Byelorussian Scientific Research Sanitary Hygiene Institute and in the department of hygiene of the Minsk State Medical Institute have shown, even in cases in which toxins possess pronounced specific effects, the earliest symptoms of poisoning are often manifestations that are not connected with selective lesions to given systems.

Organophosphorus compounds that are derivatives of carbamic acid and chlorine derivatives of phenoxy acid were used to compare the sensitivity of some tests at minimum degrees of poisoning.

When studying organophosphorus insecticides and carbamic acid derivatives, especially for purposes of setting norms for them, it was right that fundamental attention be paid to detecting the activity of cholinesterase, which in many cases is considered a factor that limits injury. In the experiments that were conducted changes in cholinesterase activity (determined according to Khestrin's method) were compared with some nonspecific manifestations of poisoning when administering low doses of organophosphorus compounds: octamethyl pyrophosphoramidate, dithiophos [a tetraethyl dithiopyrophosphate insecticide], cynophos, and preparation OVS-13 [oxidation reduction medium]. As the research carried out above has shown, when albino rats are poisoned by octomethyl pyrophosphoramidate and dithiophos, basic changes are noted in the serotonin content of the blood, central nervous system and enterochromaffin system. These data determined the choice of a biological method, determination of serotonin in the blood - and a histochemical method, ascertainment of the amount and saturation of enterochromaffin Kul'chitskiy cells in the duodinal intestine, in the capacity of sensitive tests.

The research that was conducted showed that organophosphorus insecticides administered in doses of  $1/5$   $LD_{50}$  causes a significant drop in cholinesterase activity in the blood and internal organs, a statistically reliable increase in serotonin content in the blood, and an increase in the number and saturation of enterochromaffin Kul'chitskiy cells in the duodinal intestine. Activation of the hypophysis-adrenal system is noted simultaneously. It is manifested by an increase in the relative weight of the adrenal glands, decrease in the ascorbic acid content in them, eosinopenia and involution of the thymo-lymphatic system.

In single administration of organophosphorus compounds in a  $1/10$   $LD_{50}$

dose, a tendency toward a decrease in cholinesterase activity and statistically reliable increase in the serotonin content in the blood were observed. Increase in the number of Kul'chitskiy cells in the duodinal intestine was also distinctly observable.

The high sensitivity of the serotonin test was manifested in an especially graphic way during long-term poisoning of albino rats with cynophos. Administration of this preparation for a 9-month period in a  $1/20$  LD<sub>50</sub> dose practically did not change cholinesterase activity in the blood plasma and erythrocytes whereas increase in serotonin content was sufficiently clearly pronounced. Use of cynophos in a  $1/5$  LD<sub>50</sub> dose in a long-term experiment led to an 8-9% depression of blood cholinesterase while the serotonin content increased more than 2 times.

Sevin, the most promising preparation having pronounced anticholinesterase properties, was chosen as a representative of the carbamic acid derivatives. It was administered once into the stomachs of albino rats. Experiments showed that it was necessary to administer no less than 60 mg of Sevin per 1 kg of the animal's body weight for a statistically reliable decrease in cholinesterase activity in the blood plasma and erythrocytes. When such a dose is administered serotonin content increases almost 3 times. When albino rats are inoculated with Sevin in a 10 mg/kg dose, the serotonin content in the blood increases by 21%; in a 15 mg/kg dose, it increases by 34%. Moreover there is a sharp increase in the histochemically ascertainable amount of serotonin in enterochromaffin cells of the duodinal intestine.

A drop in basal metabolism plays an important role in poisoning with phenoxy acid-chlorine derivative herbicides. It is observed in poisoning with various compounds of this group (2, 4 dichlorophenoxyacetic acid, its

sodium and amino salts, the butyl ester of 2, 4-D etc.). Minimum herbicide doses that produce a statistically reliable drop in basal metabolism in albino mice with single administration into the stomach are many times lower than minimum tolerance doses for acids of 2, 4-D, 10 times lower than tolerance doses for its amino salts and butyl esters and 5 times lower than tolerance doses for the sodium salt of 2, 4-D. However when choosing the most sensitive tests for conduct of long-term experiments it was revealed that the most indicative one is change in the activity of the carbohydrate metabolism enzymes aldolase and phosphohexose isomerase. It was established in experiments on albino rats that reliable disruption of these enzymes' activity is recorded during administration of phenoxy acid-chlorine derivative herbicides to the animals in doses 20-30 times lower than maximum tolerance doses.

These enzymes' high sensitivity was also noted in poisoning with low doses of Eptam and Tillam.

The research that was conducted indicates the necessity of studying nonspecific symptoms of poisoning even in cases in which the pesticide's selective capacity to injure various of the organism's systems is known. Special research to find the most sensitive symptoms of low-dose poisoning are necessary in order to set norms for each toxic chemical.