Determination of the Exposure to Fenitrothion
(0,0-dimethyl-0/3-methyl-4-nitrophenyl/thiophosphate)
on the Basis of the Excretion of p-nitro-m-cresol
by the Urine of the Persons Tested

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Summary. The excretion of p-nitro-m-cresol and changes in the activity of
cholinesterase in volunteers were studied after single and repeated doses of fenitrothion.

Fenitrothion in single doses was given in quantities of 2.5, 5, 10, 15 and 20 mg. Practically the whole quantity of p-nitro-m-cresol was discharged within the first twenty-four hours after administration, the maximum excretion being within the first 12 hours. The quantity of p-nitro-m-cresol was proportional to the dose of fenitrothion, but expressed as a percentage of theoretical quantity depends, to a certain extent, on the size of the dose administered. After receiving doses of 2.5 mg of fenitrothion the people tested discharged on an average 70.4 ± 3.4% of p-nitro-m-cresol; after doses of 5 mg 58.7 ± 8.7%; after 10 mg 51.9 ± 5.6%; after 15 mg 49.5 ± 1.9%; after 20 mg 48.1 ± 7.6%. A statistically significant difference in the discharge of p-nitro-m-cresol is to be found only between the dose 2.5 mg and the doses 10, 15 and 20 mg of fenitrothion.

The plasma and red cell cholinesterase activity, with one exception, did not drop below the limit of normal variations among individuals.

Repeated doses of fenitrothion were given in 24 hours' intervals, in doses of 4 × 2.5 mg and 4 × 5 mg. The p-nitro-m-cresol was determined in urine collected 0 to 12 and 12 to 24 hours after administration. Almost the entire quantity of p-nitro-m-cresol was excreted in the intervals from 0 to 12 hours. No signs of cumulation of fenitrothion appeared. The activity of red cell cholinesterase, after the 3rd and 4th dose of fenitrothion showed a moderately rising tendency.

From the results obtained with single and repeated doses of fenitrothion administered to persons experimented on it follows that exposure to fenitrothion which does not yet cause a drop in the activity of cholinesterase can reliably be proved on the basis of the discharge of p-nitro-m-cresol in the urine.

Fenitrothion (0.0-dimethyl-0/3-methyl-4-nitrophenyl/thiophosphate) is an organophosphorus insecticide of low toxicity developed by the staff of the Research Institute of agrochemical technology in Bratislava (DRAŽEK, PELIKÁN). It is to be found on the market under the names of Metation (Czechoslovakia), Folithion (West Germany) and Sumithion (Japan).
Determination of the Exposure to Fenitrothion

The most common and one of the first exposure tests for organophosphorus insecticides (OPI) is the determination of cholinesterase. The activity of cholinesterase is inhibited in various degrees by all organophosphorus insecticides as well as by some carbamides and is liable to be influenced by a number of various factors (Kolle). That is why, from the very beginning of the spread and use of OPI attempts were made at finding specific exposure tests. As early as 1951 Mountain et al. drew attention to the possibility of using the discharge of p-nitrophenol (NP) as exposure test for parathion. In the case of people professionally exposed as well as in the case of persons tested, several authors studied the relationship between exposure to parathion, the discharge of NP and changes in the activity of cholinesterase (Chichester, Durham, Rossi and Argento). They have found that the NP test is reliable in showing exposure to parathion and that it is more suitable in some cases than the determination of the activity of cholinesterase.

In our previous experiments we have identified and isolated a metabolite of fenitrothion p-nitr-m-cresol (NC) in the urine of experimental animals and studied its discharge in urine after application of fenitrothion to white rats (Hladká, 1966; Hladká and Nosál').

**Experimental Part**

*Analytic Methods Used*

For the determination of NC in the urine of people experimented on we have used a method developed in our own laboratory (Hladká, 1968).

The activity of the plasma and red cell cholinesterase was determined by Michel’s method. Blood was taken from the vein with a syringe rinsed with heparin. The blood samples were taken 24 hours before and immediately before administration of fenitrothion, and then 6 and 24 hours after administration of fenitrothion. Three parallel determinations were made from each sample of plasma and erythrocytes. The people experimented on were kept, during the testing period, at the clinic for occupational diseases. Together with NC discharge, changes in the activity of plasma and red cell cholinesterase were studied in the persons tested.

Fenitrothion was administered in a solution of olive oil in gelatine capsules, orally, in the morning. The standard contained 98 and 100% of fenitrothion. No elements were present that could have disturbed the course of the experiments.

1. Following the Discharge of NC and of the Activity of the Cholinesterase after the Administration of one Dose of Fenitrothion

The people tested were given fenitrothion in doses of 2.5, 5, 10, 15 and 20 mg. The NC in urine was determined in the entire lot of urine produced in 24 hours (first day) and in the urine produced from 24 to 48 hours (second day). The discharge dynamics of NC was observed in the individual portions of urine.

The values shown in Table 1 we see that the discharge of NC practically ends within 24 hours after administration of fenitrothion, independently of the magnitude of the dose.