

# Chronic Organophosphate Poisoning

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## SUMMARY

Prolonged exposure to organophosphates in low concentrations caused diarrhoea in 38 students, lecturers and other personnel at an agricultural college. The symptoms of those affected, plasma pseudocholinesterase levels, topography of the orchards and vegetable gardens, the various insecticides and quantities used, and the exposure due to prevailing winds have been studied. We conclude that safety and precautionary measures must be strictly enforced.

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Organophosphate compounds produce an anticholinesterase effect.<sup>1</sup> Symptoms of poisoning are associated with overstimulation of the muscarine and nicotine receptors. Acute organophosphate poisoning is well documented,<sup>2-4</sup> and several authors have referred to the chronic neurological manifestations.<sup>5-21</sup> However, organophosphate poisoning with intermittent symptoms due to long-term low concentration exposure has not been described. In the present study we have described the circumstances and symptoms of chronic organophosphate exposure.

## PATIENTS AND METHODS

### Patients

In November 1977 several staff members of an agricultural college as well as members of their families presented with a clinical picture of intermittent diarrhoea. When the agricultural college commenced the term of 1978, a number of students presented with similar symptoms. A total of 38 persons complained of intermittent diarrhoea. The diarrhoea was of a nonspecific type in all cases, with a stool frequency of 4-10 motions per 24 hours and a diurnal pattern. A watery or very soft stool was passed with no blood or mucus. Abdominal pain or discomfort was not a feature. Weight loss was evident in 55% of cases with a mean loss of 6,6 kg over a period of 8 months.

Clinical examination was negative. A detailed search for a suspected infective cause was carried out in the first 18 patients. Detailed haematological studies revealed sedimentation rates from 1 to 23 mm/h (Westergren) and normal red blood cell counts. White blood cell counts

ranged from  $3,3 \times 10^9/l$  to  $13,6 \times 10^9/l$  (normal  $4-11 \times 10^9/l$ ), and in 2 cases an eosinophilia of 10% was present.

Stools were examined microscopically and cultured for bacteria. In 3 cases pus cells were present, but no parasites or bacteria were seen or cultured. In 9 cases detailed viral investigations of blood, urine and stools were negative. The Department of Health carried out a detailed investigation for any sources of infection on the premises of the agricultural college, with no evidence of contamination of water or milk supplies.

At this stage the authors paid a personal visit to the agricultural college and a very strong aroma of organophosphate chemicals was noticed. The possibility of organophosphate poisoning was therefore considered.

### Methods

Blood samples were drawn from 14 White and 17 Black patients (some of the latter did the spraying) for pseudocholinesterase activity determination (plasma pseudocholinesterase activity was determined by the Merck-I cholinesterase kinetic test), and a questionnaire pertaining to muscarine and nicotine effects was completed by all patients (Table I). The body weight and any body weight loss were recorded.

TABLE I. QUESTIONNAIRE PERTAINING TO MUSCARINE AND NICOTINE EFFECTS IN 38 PATIENTS

Symptoms	Onset (%)	After 8 months (%)
Tightness in the chest	18,4	14,4
Dyspnoea	26,3	28,9
Productive cough	23,6	21,0
Nausea	31,5	13,1
Vomiting	18,4	13,1
Diarrhoea	94,7	89,5
Increased perspiration	23,7	26,3
Increased salivation	18,4	18,4
Increased lacrimation	5,2	7,9
Visual disturbances	29,0	31,5
Frequency or stranguria	21,0	29,0
Muscle fasciculation	50,0	50,0
Muscle cramps	31,5	34,2
Muscle weakness	31,5	23,7
Pallor	15,7	15,7
Dizziness	21,0	15,7
Anxiety	26,3	13,1
Restlessness	13,1	10,5
Nightmares	13,1	13,1
Depression	7,9	23,7
Confusional state	5,2	2,6

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## RESULTS

The activity of plasma pseudocholinesterase was below the lower limit of normal in 13 White patients. In only 1 patient was the activity within the normal range as defined in this laboratory (Fig. 1). The mean plasma activity (2,3 kU/l) was significantly reduced when compared with normal (3 - 8 kU/l). Eleven of the 17 Black patients also had a plasma pseudocholinesterase activity below the lower limit of normal. The mean plasma activity (2,72 kU/l) was below the lower limit of normal but significantly higher than that in the White patients (2,3 kU/l) (Fig. 1). The incidence of diarrhoea and other symptoms looked for is shown in Table I. None of these symptoms was detected in the Black patients, despite the high incidence of low plasma pseudocholinesterase activity. Weight loss was recorded in 55,5% of the White patients and the mean mass loss per person was 6,6 kg.

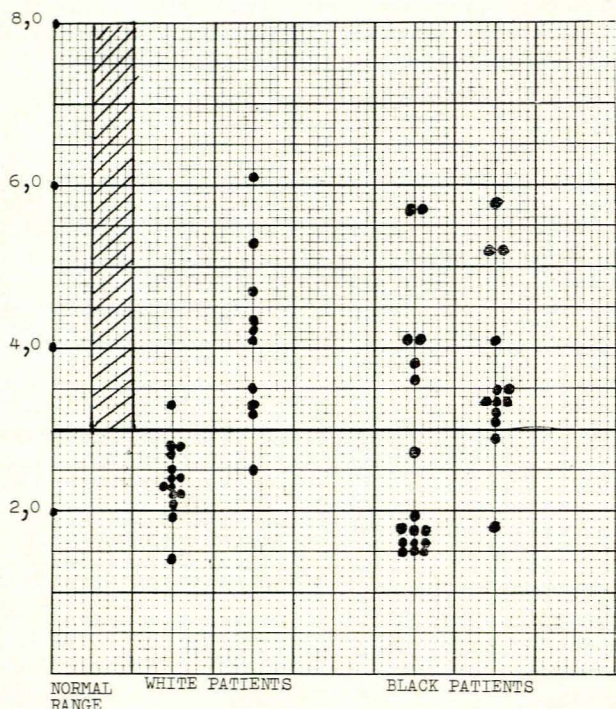


Fig. 1. Plasma pseudocholinesterase values before and after precautionary measures.

## Follow-up Studies

After the introduction of precautionary measures on 1 August 1978, follow-up studies during December revealed that no patients had developed further symptoms except for occasional episodes of frequent loose stools after severe exercise. Twelve of the White patients with periodic symptoms had normal plasma pseudocholinesterase levels, and only 2 of the 13 Black patients still had low values. With the exception of 4 Blacks all values were markedly increased in relation to the initial values (Fig. 1).

## DISCUSSION

The symptoms and signs of acute organophosphate poisoning are well documented<sup>2-4</sup> and the late neurological manifestations of acute poisoning have been discussed in a few articles.<sup>5-11</sup> This epidemiological study of organophosphate intoxication emphasizes the effects of prolonged exposure to low concentrations of the organophosphate compounds.

Of interest in this study is the difference between White and Black patients in relation to the incidence of toxic symptoms, for, although the latter group was actually in contact with the organophosphates and 11 out of 17 had low plasma pseudocholinesterase values, none showed symptoms of toxicity. It is possible that the Black patients may have had a higher threshold of symptoms, but genetic susceptibility to organophosphates has not been described to date.

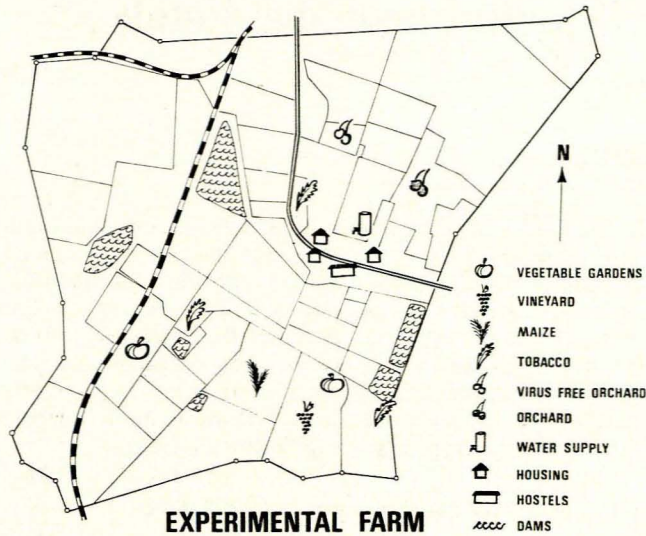
Several of the manifestations seen in these patients need to be emphasized. Diarrhoea was the prominent symptom in all cases but the cause is not known.<sup>12</sup> The symptoms may depend on the route of administration. Weight loss was evident in more than half the patients. Dyspnoea was present in 28,9% of patients; it occurred on effort and was often periodic in nature. A few patients had to stop all competitive sport.

Muscle fasciculation, muscle cramps and muscle weakness were present. Psychiatric symptoms, especially anxiety and depression, were common, as has been reported in several publications.<sup>4</sup> Patients with previous psychiatric symptoms may have acute exacerbations of anxiety, schizophrenia or depression.<sup>13</sup> These symptoms may persist up to 1 year after exposure to the poison has been terminated.<sup>14</sup>

The distribution of the symptoms among personnel and students in relation to the location of their work and residence raised the possibility that contamination might have occurred through the skin, the wind being responsible for the spreading of organophosphates, since not one of the affected persons had direct contact with organophosphate insecticides, and no contamination of water supplies, milk or food was evident from the tests conducted.

The boarding house for students, the annexe and houses of personnel are surrounded by vegetable gardens, vineyards and fruit orchards (Fig. 2). From January to July 1978 a total amount of 6 500 litres of Lebaycid (fenithion) and 30 litres of Malathion was sprayed by pressure from sprays on the orchards. In the virus-free orchard, 10 different spray poisons were used from February to March 1978, of which at least 3 were organophosphates. The total amount was not charted for this particular orchard. In the vegetable gardens, Lebaycid was the primary choice of insecticide, but quantities are not documented. From January to March 1978 (68 days) it was windless at 08h00 on 36 days, but at 14h00 only 7 days were windless according to the weather bureau charts at the college. The prevailing winds were from the south and south-east, and to a lesser degree from the north-west (Figs 3 and 4).





EXPERIMENTAL FARM

Fig. 2. Topography of farm.

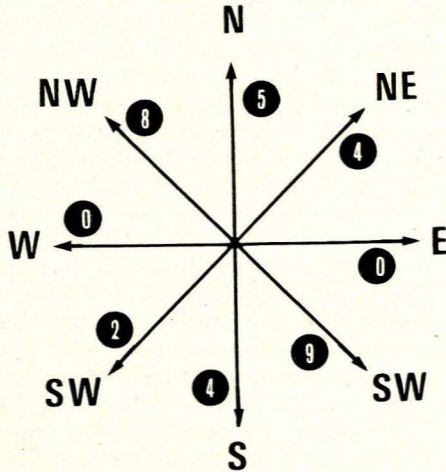


Fig. 3. Prevailing wind studies at 08h00 during 68 consecutive days.

From the above findings it was possible to postulate that long-term poisoning probably occurred through the skin and that poisoning via this route is more likely to cause the nicotine-like symptoms than that via other routes of entry.<sup>12</sup>

It is evident that prolonged low-grade exposure to organophosphates may cause diverse symptoms of a nonspecific nature. In cases where indirect exposure is present, the necessary investigations should be done to confirm the possible diagnosis. The occurrence of this epidemic of poisoning at an agricultural college would only emphasize the importance of punctilious execution of the safety measures prescribed by the various manu-

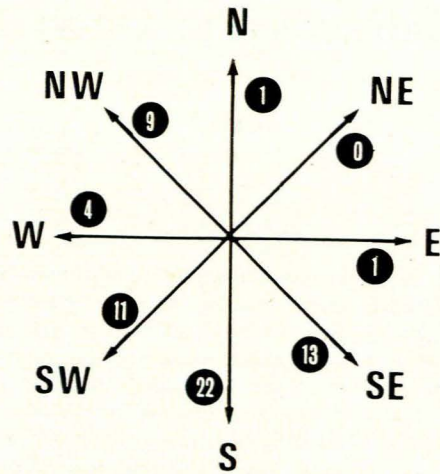


Fig. 4. Prevailing wind studies at 14h00 during 68 consecutive days.

facturers of organophosphate-containing insecticides.

We recommend that the following precautionary measures be adopted by personnel using organophosphate poisons: (i) personnel handling the pesticides should be fully informed as to their proper usage as well as the inherent dangers; (ii) dilutions should be strictly in accordance with the manufacturers' recommendations; (iii) spraying must only be carried out on wind-free days; (iv) the user must wear gloves and protective overalls; (v) any skin contamination must immediately be washed off; (vi) all containers must be effectively destroyed; (vii) while the poison is being used, no food or fluids must be taken and smoking must be forbidden.

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