PARATHION POISONING

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The increasing use of the alkyl phosphates (organophosphates) as insecticides, both agriculturally and in the home garden, has produced an ever-increasing number of cases of poisoning, many of them fatal.

A warning about the danger of parathion appeared in this *Journal* in 1952.[1] In July 1956 warnings were published in the South African lay press[2,3] against the use of parathion preparations to combat domestic flies and other household insects, and the most stringent precautions were recommended for its storage and use and even the disposal of empty containers.

From February 1953 to June 1956 74 people lost their lives through parathion poisoning. Although only one case report has appeared in the South African medical literature,[4] many more such cases are known to the analysts engaged in the forensic and toxicological sections of the Government Chemical Laboratories, Johannesburg.[5] The majority of these were cases of accidental poisoning, but a number were suicidal and homicidal. Four further cases of accidental poisoning, one of them fatal, are reported here.

CASE REPORTS

On 6 February 1959 4 members of a family who had eaten a meal at about 7 p.m. were admitted to the South Rand Hospital. The meal had consisted of stew, tinned tomato soup, and home-preserved peaches. Shortly after supper these 4 people started feeling ill. The father, who had not partaken of that meal because he was still at work, made the suggestion to the casualty officer on duty that the noxious agent might have been 'foliodol', a parathion-containing liquid.

Case 1

A boy, aged 7 years, was admitted at 10.20 p.m. in coma. His pupils were widely dilated, he was sweating profusely, and his pulse rate was 80 per minute. Atropine, 1/50 gr., was given by intravenous injection. At 11 p.m. convulsive twitching of arms and eyelids occurred, together with incontinence; the pulse rate increased rapidly, the chest became very moist, breathing stopped and the pupils became 'pinpoint'; 1/100 gr. more of atropine was given intravenously, and further efforts at resuscitation were unsuccessful. On post-mortem examination parathion was found to be present in the stomach contents.

Case 2

A girl of 10 years, sister of case 1, was in a better condition than her brother when she was admitted at 11 p.m. She complained of nausea and vague epigastric pain. The blood pressure was 130/80 mm. Hg, and the pulse rate 100 per minute. Her pupils were widely dilated.

At 12 p.m. her condition deteriorated and an intravenous drip containing solucortef and levophed was set up and 1/100 gr. of atropine given 2-hourly by intramuscular injection.

At 4 a.m. the pupils became constricted, convulsions appeared, and respirations became irregular. Cyanosis and bronchospasm appeared and, as bronchial obstruction from inhalation was feared, bronchoscopy was performed, the findings being normal. Treatment with atropine, 1/100 gr. at intervals of 1½-2 hours, was continued, together with paraldehyde administration for control of fasciculation.

The child regained consciousness at about 4 p.m. and the further course was uneventful.

A serum-cholinesterase estimation performed shortly after admission showed 20% of average normal activity, but no follow-up estimations were done. Analysis of a specimen of the gastric lavage did not reveal the presence of parathion.

Case 3

The mother of cases 1 and 2, aged 29, was admitted at 11 p.m. in a state of collapse. Her main complaint was a feeling of intense coldness, nausea and weakness. The pulse rate was 90 per minute and the blood pressure 90/60 mm. Hg. Her pupils were normal in size and reaction. Her general condition necessitated the use of an intravenous drip containing levophed and solucortef; 1/100 gr. of atropine was given at 2-hourly intervals. The course of her illness was uneventful.

A series of serum-cholinesterase estimations were performed, with the following results: On admission 15% of average normal

activity, on 9 February 22%, on 18 February 53%, and on 20 March 100%.

Case 4

The grandmother of cases 1 and 2, aged 64 years, was admitted at 6 a.m. on 7 February. She complained only of generalized weakness. Her general condition was good. She was treated with atropine only.

The results of serum cholinesterase studies were as follows: On admission 57%, on 7 February 75%, and on 18 February 100%.

Toxicological analysis of the meal that had been eaten showed the presence of parathion in the stew.

DISCUSSION

Of the organic phosphates in common use as insecticides, hexa-ethyl tetraphosphate, tetra-ethyl pyrophosphate (TEPP) and parathion, the last-mentioned is the most versatile poison because of its greater stability in the presence of water and its greater solubility in lipid media, including the waxy outer layer of fruit and leaves; unfortunately the same factors are responsible for the greater danger presented by parathion when used in the environment of man and domestic animals. In some cases the chemical is absorbed by plants and may remain toxic for several days, and it is thus recommended that sprayed food crops should not be *harvested* for 3-6 weeks.

Since the insecticide may be absorbed through the skin,[4] respiratory tract,[6] conjunctivae or gastro-intestinal tract, or by injection (suicide or homicide), exposure may occur at any stage in the production, packaging, handling or spraying of insecticide preparations, or in the harvesting of sprayed fruit or vegetables which have been insufficiently weathered, or by the ingestion of such products.

Despite these numerous potential risks, the majority of cases of poisoning have occurred through carelessness on the part of workmen, either unwittingly or in some instances as the result of gross disregard of the safety precautions recommended.[7] Accidental ingestion is not common, but it does sometimes occur, as in the case of a number of people in Johannesburg who ate a cake in which parathion had been used instead of vanilla essence;[8] and a 10-year-old boy who drank from a 'whisky bottle' which he found in the fork of a tree.[7]

In a report to the American Council on Pharmacy and Chemistry[7] it is stated that, if the recommendations of the Bureau of Entomology and Plant Quarantine of the US Department of Agriculture are carried out with particular reference to the time between the last spraying and harvesting of fruit, then normal weathering should reduce the parathion to residues which are of no practical significance.

Barnes and Davies[9] undertook a survey of blood-cholinesterase levels in a group of workers exposed to organo-phosphorus insecticides. Many thousands of square miles had been sprayed with parathion without any accidental poisoning. Of 50 sprayers examined during the height of the spraying season, only 3 showed the slightest evidence of absorption as reflected by cholinesterase levels. In only 9 out of 30 factory or laboratory workers could any abnormality be recognized, and that only by the most stringent of criteria. These facts tend to demonstrate quite clearly that these insecticides may be manufactured and applied without risk, provided manufacturers, consumers and their employees adhere rigidly to all the safety devices and procedures that have been developed to this end.

It has been found that although extensive day to day exposure is regularly associated with reduced blood-cholinesterase activity, the only fatal or near-fatal cases of poisoning are associated with brief massive exposures and gross carelessness.[13] It is, however, an important fact that an increased susceptibility to an anticholinesterase may be developed by previous poisoning with doses which have shown no clinical signs or symptoms, and the level of blood cholinesterase is an index of this susceptibility. Crashes of dusting aeroplanes have been attributed to the effects of subclinical poisoning of the pilots.[10] Regular checking of blood-cholinesterase levels in workers is thus of the greatest importance in the establishment of an objective index of inadequate safety precautions or faulty handling of these poisons.

SYMPTOMATOLOGY OF POISONING

The toxic manifestations in anticholinesterase poisoning are directly related to the inhibition of the enzyme cholinesterase (ChE) in the central nervous system, the parasympathetic nervous system, and at the neuromuscular junctions, resulting in a local accumulation of acetyl-choline, which produces increased activity of smooth muscle and glands and also some involuntary muscular fasciculation.

The signs and symptoms are as follows: Dizziness, nausea, vomiting, diarrhoea, salivation, bronchorrhoea, pulmonary oedema, asthma-like constriction of the chest, myosis with blurring of vision (although mydriasis may occur, possibly owing to central hypoxia or the presence of extreme anxiety), sweating, bradycardia, convulsions, coma and death. In severe anticholinesterase intoxication death occurs as the result of paralysis of the muscles of respiration and of the pharynx and tongue, unless artificial respiration and an open air-way are maintained until recovery.

The anticholinesterase activity of these organo-phosphate compounds is reflected by a fall in the red-cell and serum ChE activity. Although it is the red-cell ChE which is of importance in hydrolysis of acetyl-choline, its level is reflected by the serum ChE, which, as a matter of convenience, is what is actually measured by the laboratory.

It is of significance that although ChE levels are vitally important for confirmation of the diagnosis of poisoning or over-exposure, low activity results may bear no obvious relationship to the clinical severity of effects and some workers have been found with ChE levels of 20% without clinical manifestations of toxicity.

TREATMENT

The mainstay of treatment is still the exhibition of atropine, but it has recently been demonstrated that ChE inhibition, neuromuscular block, and lethal effects produced by organo-phosphorus anticholinesterase compounds, may be reversed by a number of oximes, the most effective known at present being 2PAM (pyridine-2-aldoxime methiodide),[11] which, when administered in therapeutic dosage, has not produced any side-effects besides very transient local discomfort.

Atropine relieves only some of the symptoms of poisoning and does not affect others such as muscular fasciculation, while 2PAM has little effect on gastro-intestinal symptoms, sweating, salivation, and some of the central nervous system symptoms, so that it is essential to use a combination of both drugs in treatment.

The following scheme of treatment is recommended by Grob and Johns:[12]

1. Terminate exposure by removal from site of poisoning, removal of contaminated clothing, copious washing of skin and eyes, and gastric lavage.

2. Maintain a patent air-way by endotracheal intubation or tracheotomy if necessary.

3. Apply artificial respiration manually or by the use of the poliomat, artificial lung, or bellows on closed-circuit anaesthetic machine.

4. Administer atropine, 2 - 4 mg. (1/30—1/15 gr.) intravenously, followed by 2 mg. every 3-8 minutes until muscarine-like symptoms disappear, and whenever they reappear; a total of 24-48 mg. may be required the first day.

In less severe intoxication give 2 mg. intravenously or intramuscularly, and repeat at 20-minute intervals until muscarine-like symptoms are relieved; maintain a mild degree of atropinization for 24 - 48 hours.

5. In severe intoxication give 2,000 mg. of 2PAM (500 mg. per minute) intravenously, and repeat the dose if weakness is not relieved, or recurs. In moderate intoxication give 1,000 mg. intravenously and repeat if necessary.

6. Alleviate convulsions by anaethesia if necessary.

COMMENTS

It is difficult to explain the presence of parathion in the stew consumed by the family. It is possible that sprayed vegetables may have been included in the stew or that there was contamination during its preparation. The patients lived on a fruit and vegetable farm where 'foliodol' had been extensively used. It may perhaps be argued that any parathion present would have been hydrolysed by boiling, but this is not really so, for such breakdown only occurs to a very small extent.

It is almost certain that the amounts of poison ingested were not similar in all cases, and this might explain the difference in the symptoms. It is also suggested that children may be more susceptible to poisoning with this substance.

On theoretical grounds it has been stated that intravenous fluids are contra-indicated because of the possibility of overloading an already poor circulation;[12] but post-mortem examination on a number of cases of this type of poisoning has shown very little evidence of pulmonary oedema, and it has been suggested that the respiratory obstructive symptomatology is due to intense salivation with leaking down of secretions.

In the cases reported here it is felt that the use of intravenous solucortef and levophed may have been life-saving; these measures are not mentioned in Grob and John's recommendations.[12]

It is obvious that these recommendations on treatment were not all carried out; I feel that this is mainly because at the time of the occurence of the poisonings these methods were too little known to the staff of this hospital. In view of the intense salivation, sweating and, in some cases, purging I feel that intravenous fluid therapy and replacement of lost electrolytes is of importance in these cases.

It is hoped that this article will draw attention once again to a fairly easily available noxious agent in our midst, and it is also hoped that practitioners may become aware of the methods of treatment. Stocks of 2PAM should be readily available in all hospitals at least, and in the doctor's bag if possible.

In poisoning cases it may be extremely difficult to assess rapidly and accurately the noxious agent responsible in order that the specific methods of treatment available for some types of poisoning (e.g. barbiturates and organic phosphates) may be used. Unfortunately a history of the actual substance ingested is often absent, in which case the diagnosis of the syndrome of parathion poisoning usually depends mainly on awareness of the syndrome and the high index of suspicion which should exist in areas where the organic phosphorus insecticides are being used.

SUMMARY

Four cases of poisoning with parathion are reported. In organic phosphate poisoning the mode of poisoning, the effects and the treatment are described.

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