DEATH BY ORGANO-PHOSPHORUS POISONING IN SINGAPORE 1960 - 1969

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In 1959, there was an explosive outbreak in Singapore of mass poisoning from barley contaminated with an organo-phosphorus compound --parathion, involving 35 children and 3 adults, resulting in the death of 9 children.[3] Since then, legislation has been introduced to control the sale of parathion in the Poisons (Organo-phosphorus compounds) Rules 1960. However, there is a long list of preparations containing organo-phosphorus compounds which are not included in the control under the Poisons Rules, notably Malathion, Tolly, and Diazinon. These are known to be much less toxic then Parathion, and are poorly absorbed through the skin. If they are used carefully according to instructions, the danger of poisoning from exposure is minimal. But ingestion in sufficient quantities either by accident or in suicide will present classical symptoms and signs of organo-phosphorus poisoning. These compounds inactivate acetyl-cholinesterase by phosphorylation of the enzyme's active centre resulting in accumulation of acetyl-choline, producing alterations in the neural activity at three sites:

(*a*) Stimulation of post-ganglionic cholinergic nerves (Muscarinic action).
(*b*) Stimulation of pre-ganglionic cholinergic and somatic motor nerves (nicotinic action).
(*c*) Central Nervous System stimulation and depression.

Thus the clinical picture would show a combination of nausea, vomiting, sweating, excessive salivation, miosis, increased bronchial secretions and constriction, diarrhoea, muscular fasiculations, respiratory paralysis, anxiety, restlessness, confusion, drowsiness, coma and death.

PRESENT STUDY

In Singapore, all deaths by poisons are reported to the Coroner and are subjected to post-mortem. In the ten-year period from 1960-1969, there were a total of 337 documented deaths by poisons. The top three killers are caustic soda with 114 deaths, barbiturates 53 deaths and organo-phosphorus compounds 43-deaths or 12·8% of the total. In recent years, there is a slow decline in the usage of caustic soda as a suicidal poison, because of the strict control, but there is an upward trend of using organo-phosphorus compounds, which has moved up to the first place in deaths by poisons in 1969.

The yearly breakdown of deaths from organo-phosphorus compounds is shown in Fig. 1. In all the cases the route of poisoning was by ingestion. 37 cases or 86% of the total are due to Malathion, 2 cases due to parathion, 2 cases due to diazinon, 1 case due to not specified organo-phosphorus compounds, and the remaining case report was missing from file. The male to female ratio is 3:2, but further analysis shows that in the 15-25 year group female outnumbered male by 3:1 (Table I). 90% of these deaths were from suicidal acts and 10% from domestic accidents. The youngest suicide is a boy of 10 year old because of scolding from his mother, and the oldest suicide is a man of 84 years due to sickness. Majority of the female suicides in the 15-25 age group were from unhappy love affairs, only two died because of domestic troubles. There is a contrast in the males, only two succumbed to the treachery of love, the rest died from a variety of reasons including domestic troubles, loss of job and prolonged

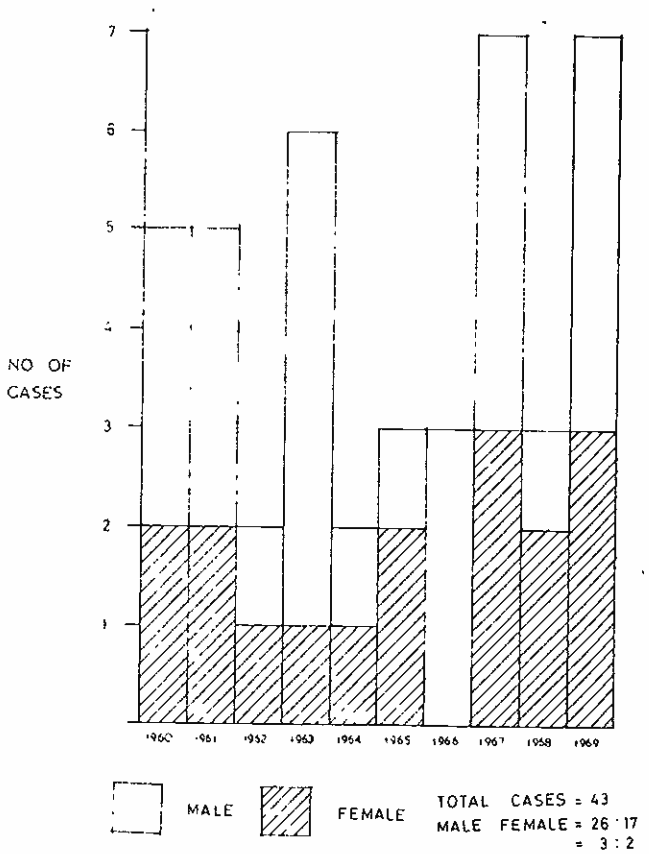


Fig. 1. Deaths from organo-phosphorus insecticide poisoning in Singapore 1960-1969.

illness. The accidental deaths are from the two extreme age groups of females. Racial distribution shows 41 Chinese and 2 Indians.

TABLE I

AGE AND SEX DISTRIBUTION

Age	Male	Female	Total
5 - 15	1	2	3
15 - 25	3	11	14
25 - 35	4	—	4
35 - 45	4	2	6
45 - 55	4	—	4
55 - 65	6	—	6
Above 65	4	2	6
	26	17	43

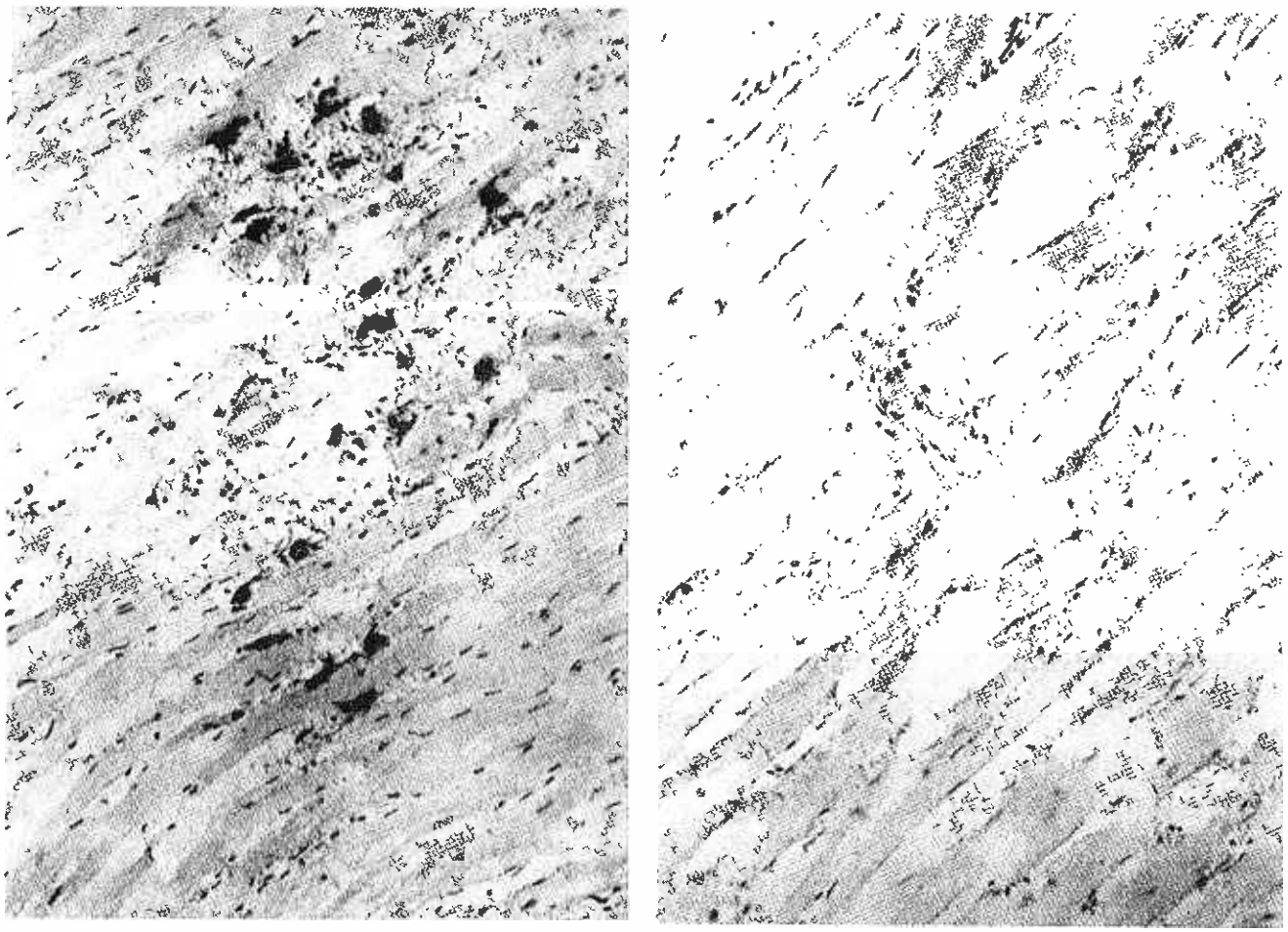
POST-MORTEM

At post-mortem, almost all the cases show pulmonary oedema and excessive bronchial secretions. Some of them show frothing at mouth. In those cases where the poison remains stomach would contain milky white fluid emiting a kerosene or fruity smell. There is no erosion or ulceration in the stomach mucosa. Stomach contents are sent routinely for analysis, and poisons were recovered even from two decomposed corpses. Amount of organo-phosphorus compound present in the stomach of those cases that are found dead or admitted and died prior to a stomach washout varies from 33 mg. to 54 gm. When the poison is absent from the stomach due to a previous washout, then two laboratory confirmatory tests are of value. They are:

(*a*) Estimation of serum acetyl-cholinesterase levels; and

(*b*) Histochemical staining of acetyl-cholinesterase activity at the neuro-muscular junctions in the intercostal muscles.

The normal acetyl-cholinesterase levels estimated by published methods[1, 2] is established in our laboratories to be 95-177 Biggs' units, which is based on one micromole of acetic acid liberated from acetyl-choline in one millilitre serum in 30 minutes at 37°C. In cases of acute poisoning



(a) (b)

Fig. 2.

Fig. 2. Intercostal muscles ×500 Koelle technique for demonstration of acetyl-cholinesterase activities in neuromuscular junctions. (a) Normal muscle showing activity. (b) Absent activity in organo-phosphorus insecticides poisoning.

it will go down to between 5 to 15 units. This is a good confirmatory test in the diagnosis of organo-phosphorus poisoning in both clinical as well as post-mortem cases. Acetyl-cholinesterase does not deteriorate with time and determinations may be performed on blood samples which have been kept at room temperature for one month.[4]

Acetyl-cholinesterase activity in the neuro-muscular junction can be demonstrated by histo-chemical staining of the intercostal muscles at post-mortem by the Koelle Technique (Fig. 2).

From early 1969, these two laboratory tests are employed routinely in cases of organo-phosphorus insecticide deaths, and in the five cases done, four showed a serum acetyl-cholinesterase level of 8 units and one 16 units, all had absent activity at the neuro-muscular junction.

DISCUSSION

In recent years, because of the unrestricted sale and availability of the organo-phosphorus insecticides, they have become the poison of choice in suicidal bids. The clinical picture is characteristic and the best confirmatory test is estimation of serum acetyl-cholinesterase level. Treatment is by large doses of atrophine. The danger of over atropinisation is slight compared to inadequate therapy. Recently cholinesterase reactivator oximes have been used, such as P.A.M. (Pyridine-2-aldoxime methiodide) and Protopam (Pralidoxime chloride). But these are used as adjuncts to atropine and not replacing it. One observation is that the patient should be kept atropinised until cholinesterase regenerates, which is a slow process. Plasma cholinesterase regenerates first but it takes about three weeks to return to normal. Serial serum acetyl-cholinesterase levels must be done, and not until a satisfactory level is reached, the patient should be atropinised, as during therapy, clinical observation may reveal well-being while serum acetyl-cholinesterase is still low. If atropine is withdrawn at this stage, signs of poisoning will recur and death may result.

SUMMARY

43 deaths from organo-phosphorus poisoning in 1960-1969 are analysed. The male to female ratio is 3:2 and 90% are results of suicidal acts and 10% from domestic accidents. Serum acetyl-cholinesterase are lowered in these cases.

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REFERENCES

1. Biggs, H. G., Carey, S. and Morrison, D. B. (1958): "A Simple Colorimetric Method for Measuring Activities of Cellular and Plasma Cholinesterase." Amer. J. Clin. Path., 30, 181.
2. Johnson, J. K. and Whitehead, T. P. (1965): "Rapid estimation of Serum Cholinesterase Activity Using the Astrup Micro Equipment." J. Clin. Path., 18, 435.
3. Kanagaratnam, K., Wong, H. B. and Tan, K. H. (1960): "Parathion Poisoning from Contaminated Barley." Lancet I, 538.
4. Petty, C. S., Lovell, M. P. and Moore, E. J.: "Organic Phosphorus Insecticides and Postmortem Blood Cholinesterase Levels." J. Forens. Sc., 3, 226.