

# ORGANOPHOSPHATE POISONING IN A FACTORY: RELATIONSHIP TO WORKLOAD AND PRODUCTION VOLUME

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## ABSTRACT

*In Singapore, all workers exposed to organophosphate compounds are required to undergo Statutory Medical Examinations. In this paper, the relationship between workload and worker exposure to these compounds is illustrated. In addition, the importance of performing detailed clinical examinations and baseline red blood cell acetylcholinesterase estimations for all organophosphate exposed workers is emphasised.*

*Keywords: organophosphates, Statutory Medical Examinations, red blood cell acetylcholinesterase*

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## INTRODUCTION

In Singapore, legislation requiring all organophosphate (OP) exposed workers to undergo Statutory Medical Examinations (SME's) was introduced in 1985<sup>(1)</sup>. Under these regulations, exposed workers are to have detailed medical examinations and baseline red blood cell acetylcholinesterase (rbc AChE) as well as plasma cholinesterase (ChE) estimations prior to work with OP's (pre-employment examinations). Thereafter, medical examinations with rbc AChE determinations are required 6-monthly (periodic examinations). Plasma ChE estimations need only be done in suspected cases of acute OP poisoning eg following accidental skin contact or acute high overexposures.

Suspension or removal from further exposure to OP's is also provided for in the legislation. Indications for suspension and notification of such workers include<sup>(2)</sup>:

- all cases of definite or suspected poisoning or excessive absorption,
- cases with rbc AChE of less than 50% of the pre-employment or laboratory's normal values, and
- cases with rbc AChE of between 50-70% of the pre-employment levels and showing a fall of more than 10% in their repeat results done one month later.

The last criterion is in line with American guidelines<sup>(3)</sup> where levels of rbc AChE equal to 70% of the individual's baseline is recommended as an indicator of a possible overexposure to organophosphorus chemicals.

Unfortunately, in Singapore, baseline rbc AChE levels are often not available for many workers exposed to OP's. The results of their periodic rbc AChE determinations then have to be compared to the laboratory's normal range. The

following incident serves to highlight the importance of the SME's and emphasises the usefulness of baseline AChE determinations. The relationship between workers' AChE levels and production volume of OP's is also illustrated.

## INCIDENT REPORT

Company A is engaged in blending various types of pesticides, including organophosphates, for the local and regional markets. Since 1987, they have been sending their workers who are involved in OP blending for 6-monthly SME's. In September 1991, our department was notified by the company's Designated Factory Doctor (DFD) that the five workers involved in pesticide blending were found to have low rbc AChE levels during their regular blood tests in July 1991 (Table I). Unfortunately, as no pre-employment levels were available for comparison, these levels were compared with the laboratory's lower limit of normality,  $8 \times 10^3$  u/l. Based on this, all workers had rbc AChE levels equal to, or in excess of 50% of the "normal" values and were therefore not immediately removed from exposure to OP's.

Table I - rbc AChE levels (in u/l) from Jul 91 to May 92

Worker No	26 Jul 91	8 Oct 91	21 May 92
1	4.4 (41.9%)	8.8 ( 83.8%)	*10.5 (100.0%)
2	6.2 (53.0%)	*11.7 (100.0%)	10.4 ( 88.9%)
3	4.0 (35.0%)	7.1 ( 62.3%)	*11.4 (100.0%)
4	7.0 (69.3%)	6.2 ( 61.4%)	*10.1 (100.0%)
5	5.3 (40.8%)	6.5 ( 50.0%)	*13.0 (100.0%)

figures in parentheses indicate percentages compared to the highest levels attained indicated by\*

However, a symptom questionnaire performed later of four of the workers showed that all had complaints of lethargy, giddiness, nausea and other gastrointestinal symptoms during that period, suggestive of OP poisoning.

In the course of our investigations, it was also found that the production volume of OP's in this company increased sharply in July 1991 to 71,400 l (Table II) from a volume of less than 40,000 l in June 1991. Correspondingly, the five workers involved in pesticide blending had to perform up to 12-hour shifts daily, six days a week. This production volume decreased somewhat in the subsequent

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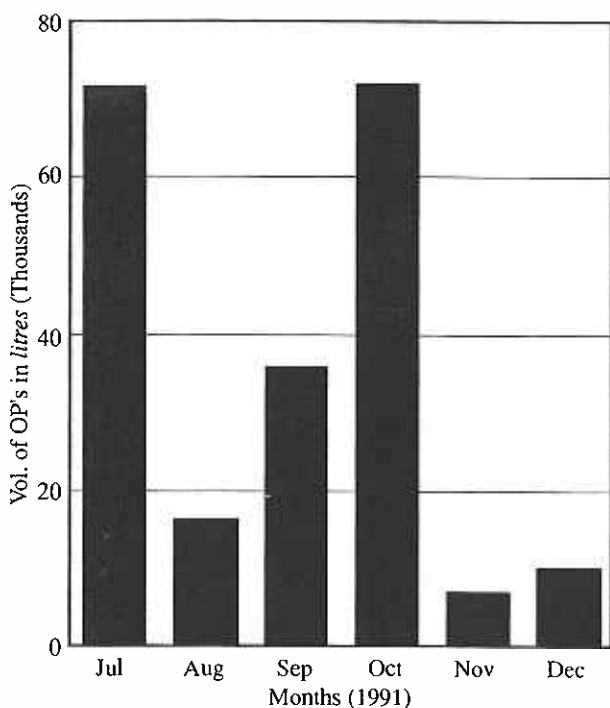
2 months but rose again to 71800 l of OP's in October 1991, before tailing-off again towards the end of the year (Fig 1).

**Table II – Production volume of OP's (in 10<sup>3</sup> litres) by month in 1991**

Month	July	Aug	Sep	Oct	Nov	Dec
OP's	71.4	16.4	35.5	71.8*	0.7	10.0

\*71,800 l is the total production volume of OP's in Oct 91. By 8 Oct 91, only 1800 l of OP's had been blended.

**Fig 1 – Production volume of OP's**



It was also found that workers were provided with long-sleeved overalls, safety shoes and elbow-length rubber gloves by the company. Cannister-type respirators were also available but were seldom used, the workers preferring to use paper masks instead. In addition, it was discovered that the type of cartridge supplied in the respirators was inappropriate as they did not have pesticide prefilters.

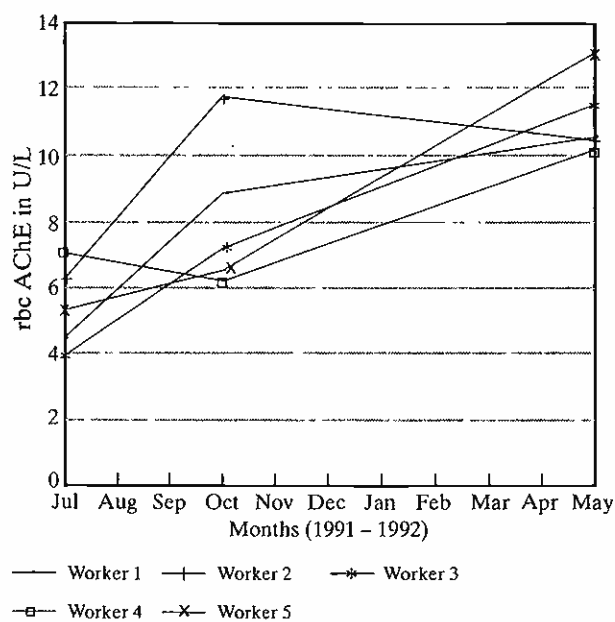
With subsequent decrease in production of OP's due, in part, to rescheduling, together with worker education and usage of proper personal protective equipment, the levels of rbc AChE had returned to normal by May 1992 (Fig 2).

## DISCUSSION

Most physicians are aware of the usefulness of plasma cholinesterase (ChE) measurements in cases of acute OP poisoning. However, because plasma ChE is synthesised in the liver, its activity reflects hepatic function and is decreased in hepatitis, alcoholic cirrhosis and other liver diseases<sup>(4)</sup>.

Some researchers have also found a statistically significant increase in plasma ChE levels in normal subjects with advancing age<sup>(5)</sup>. In addition, because rbc AChE reflects AChE activity in nerve synapses, it is a better indicator of biological effect<sup>(6)</sup>. Rbc AChE estimations have therefore been widely used in medical surveillance of workers exposed to OP's.

**Fig 2 – rbc AChE Levels**



Studies have shown that there is a wide range of rbc AChE activity in normal subjects<sup>(6)</sup> and a correspondingly wide range in laboratories' normal values<sup>(7)</sup>. This is seen in the laboratory used by Company A where the lower limit of normality for rbc AChE levels ( $8 \times 10^3$  u/l) is only about 62% that of the upper limit of  $13 \times 10^3$  u/l.

In Table I, the figures in parentheses show the percentage decrease in rbc AChE levels of each worker in comparison to the highest levels found in subsequent tests (assuming that these levels were more representative of their true normal values). Thus compared, three of the workers had levels below 50% of normal in July 1991 and would have been immediately suspended from further exposure to OP's<sup>(2)</sup>. Indeed, these three workers were later found to have complaints suggestive of OP poisoning during that period. It is thus seen that comparison to laboratory's normal values often give rise to inaccurate interpretations. Baseline rbc AChE estimations are therefore an important facet in the surveillance of all workers exposed to OP's. The importance of a clinical examination to look for signs and symptoms suggestive of OP poisoning is also seen.

The rbc AChE levels of all five workers involved in pesticide blending are also seen to be related to production volume, dropping to below normal values in July 1991. In October 1991, all but one worker showed an increasing trend in rbc AChE levels (Fig 2). Although this is not in-keeping with the large production volume of OP's during that month, it must be kept in mind, however, that of the total production volume of 71,800 l of OP's for the month of October 1991, when the blood tests were done on 8 October, only 1,800 l of OP's had been blended (Table II). In addition, the rbc AChE levels probably better reflected the exposures of the previous month as the time taken for recovery of rbc AChE activity is reported in the literature to range from 2 weeks<sup>(4)</sup> to 66 days<sup>(8)</sup>.

## CONCLUSION

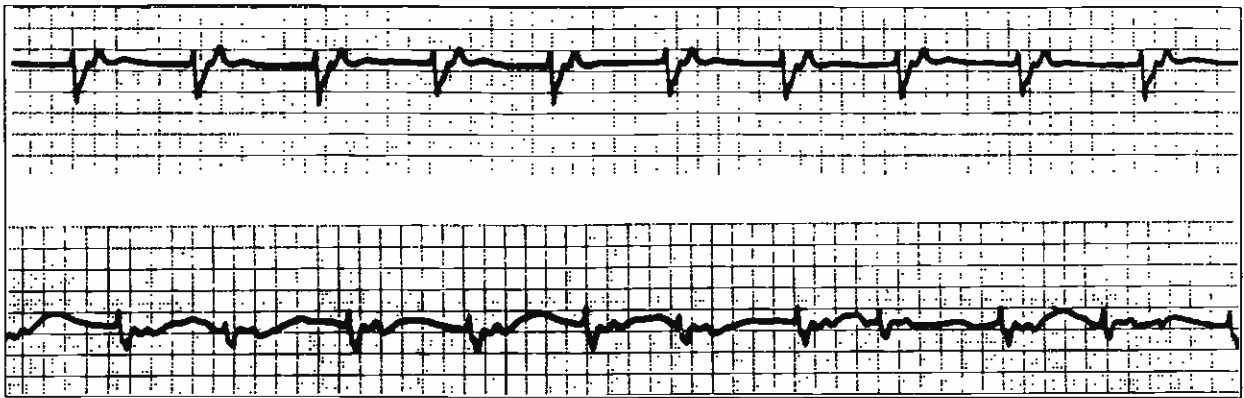
This interesting case study in occupational medical practice shows the obvious but often overlooked relationship between work schedule, production volume and worker exposure. It also highlights the importance of a detailed

history and clinical examination and the usefulness of determining baseline rbc AChE levels for each worker exposed to OP's. The need for proper and adequate personal protection of all such workers is also emphasised.

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Fig 3 – Rhythm strip still showing features of hyperkalaemia during correction phase.



## ANSWER TO ELECTROCARDIOGRAPHIC CASE

Serum potassium. Patient had hyperkalaemia.

### DISCUSSION

The ECG at the emergency department two days prior to admission (Fig 2) showed tall, narrow, symmetric, peaked T waves consistent with early hyperkalaemic change. The patient had been taking potassium citrate prescribed as part of the general practitioner's treatment for her urinary tract infection. At the hospital emergency department, after diagnosing 'mild heart failure' the resident had sent the patient home on frusemide and potassium supplements. The cumulative potassium load resulted in ECG changes of sinus arrest with bizarre ventricular arrhythmia shown in Fig 1. The serum potassium on admission was 7.4 mmol/L.

It is still not established whether the ECG changes in hyperpotassaemia reflect (1) intracellular potassium changes, (2) changes in the potassium gradient of the cell membrane, or (3) potassium level solely in the serum. Serum potassium levels outside the normal range are not always associated with ECG alterations. At times, the serum potassium may be severely elevated or depressed without significant ECG findings<sup>(1)</sup>. Conversely, the ECG may show characteristic changes of hyperkalaemia or hypokalaemia with normal serum potassium levels. This is due probably to the influence of other electrolytes (notably sodium) as well. Because of such variability in manifestation, no two individuals will display a similar degree of ECG alteration on the same serum potassium value<sup>(2)</sup>.

An evolutionary sequence of ECG changes with rising serum potassium concentration is well recognised<sup>(3,5)</sup>. At between 5.5 and 7.8 mmol/L, the T waves become tall, narrow and symmetric with a "scooped" appearance. As the level rises, ST segment depression occurs, first degree AV block appears, lowering and widening of the P wave with subsequent atrial arrest (plasma K concentration 8 mmol/L or greater) or atrial fibrillation ensues and the QRS complex begins to widen due to depression of conduction in all regions of the myocardium. The U wave is absent. The R wave amplitude diminishes as the S wave becomes wider and deeper. Eventually the T wave surpasses the R wave in height. With potassium levels in the region of 10 mmol/L, the QRS becomes so prolonged that it blends with the ST segment and tall T wave to produce a diphasic curve, the ST segment forming a straight line from the nadir of the S wave to the peak of the T wave (terminal stage). Ectopic ventricular arrhythmia characterised by irregular, bizarre undulations may be encountered in the advanced stages and often appear prior to terminal ventricular standstill. In

patients with atrial fibrillation, hyperkalaemia may result in atrial arrest. Sinoventricular rhythm may also occur<sup>(6)</sup>; this is recognised by a regular ventricular rate and absence of P waves and is presumed to be due to conduction of the sinus impulses through the specialised atrial pathways to the AV node without activating the atrial muscle. Attempts to pace such patients for "sinus arrest" or "ventricular standstill" may result in failure as hyperkalaemia has been shown to render the myocardium unresponsive to pacemaker stimuli<sup>(7)</sup>.

The most rapid means of countering the toxic cardiac effects of hyperkalaemia is intravenous calcium administration. However this does not lower the elevated serum potassium concentration. The latter can be achieved by insulin injection which redistributes the serum potassium from the extracellular to the intracellular space. Glucose has to be given immediately following insulin administration to prevent hypoglycaemia. In patients with hyperkalaemia and acidosis, sodium bicarbonate may be considered. Explanations for its potassium lowering effect include exchange of hydrogen and potassium ions across cell membranes, enhanced distal tubular potassium secretion and a specific effect of the bicarbonate anion itself<sup>(8)</sup>. Further means of treating hyperkalaemia involve removal of potassium from the body, which can be accomplished by use of cation exchange resins and dialysis.

The ECG rhythm strip in Fig 3 shows the apparent loss of P waves, QRS widening with stunted R waves, prominent and wide S waves and ST depression still evident of hyperkalaemia during the correction phase of the electrolyte abnormality. Following biochemical correction with resultant ECG normalisation, the patient was eventually referred to the renal physician for scrutiny of her renal function.

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