

# OBSERVATIONS ON AGRICULTURAL WORKERS OCCUPATIONALLY EXPOSED TO ORGANOPHOSPHORUS INSECTICIDES OF LOW TOXICITY

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The level of cholinesterase activity of serum or blood has long been recognised as a reliable and sensitive means of detecting unsafe working conditions with the use of organophosphate esters in agriculture and industry, and for the detection of accidental poisoning (Edson, 1960). Gage (1955) proposed that in the case of individuals at risk, values of ChE that fall below 50 per cent of the average value of the general population, should be considered as an alerting signal, and appropriate measures should be actively taken. It was also recognised that this criterion is bound to fail to detect small, though significant, reduction in enzyme activity in subjects whose normal level is high. The determination of ChE activity of each individual prior to exposure provides a more definite base-line for subsequent comparisons, but this is feasible only in those cases where the risk of exposure is inherent in the nature of the individual's occupation.

The effects of acute intoxication by O.P. insecticides are well documented, but the results of toxicity in workers who have been at risk for years, are less well known. The literature on this aspect relates more to experimental rather than to actual practical observations in the field. This communication records the changes detected in a group of agricultural workers engaged in spraying campaigns since 1962. Some of the results presented here formed part of a previous publication (Grech, 1965).

## Material and Methods

The subjects studied belonged to one organisation, received the same precautionary instructions, had the same facilities, and shared the same duties. They were medically examined and declared fit for engagement only after the serum ChE activity was found to be within normal limits (130-310 units per ml.).

There were 12 operatives in the team in 1962, but by 1967 only 7 remained. The peak spraying period was generally between April and July, but for technical reasons, this period was extended to November in 1967. The O.P. insecticide used most extensively was malathion, and the slightly more toxic compounds Diptex, Diazinon, Dimethoate and Demeton-methyl, have also been used at times but only for relatively short periods.

Serum ChE estimations were carried out at variable intervals, and more frequently during the peak spraying periods. No estimations, however, were carried out in 1963, 1965 and 1966. Sera obtained from 30 healthy manual workers and 32 unselected blood donors provided the normal controls.

Serum pseudo-ChE activity was estimated by the colorimetric method of De la Hueriga, Yesinick and Popper (1952). Estimations by this method are in good agreement with those obtained by the Warburg technique, 1 Warburg unit being equivalent to 2 units by this method (Smith, Lowenthal, Lehmann and Ryan, 1959).

## Results

Figure 1 shows the levels of enzyme activity found in 152 determinations car-

ried out between 1962 and 1968; 126 of these were carried out on 7 of the operatives who have been continuously engaged since 1962 and who have been under observation ever since. The mean value at each interval has been plotted to show the overall trend of depression of pChE activity. This depression in enzyme activity coincides with the periods during which spraying is intensified. Spontaneous recovery of enzyme activity occurred even after repeated exposure, provided that a long enough interval elapsed between exposures.

This collective representation does not clearly reflect the degree of pChE depression suffered by each subject. Enzyme activity during exposure is expressed in Figure 2 as a percentage of the pre-exposure level for each individual. This illustrates the variations in two of the subjects that represent two extremes.

**Case 7** — This subject, like most of his mates, showed repeated depressions in enzyme activity coinciding with peak exposure. Moreover, he showed the lowest percentage depression observed in this series, i.e. to 61 per cent. It is also noted that he has at no time in 6 years recovered the full enzyme activity that he had before exposure.

**Case 3** — This subject also showed significant and at times marked depression in pChE levels, but he recovered with enzyme activities well above his initial value, and at times even above the upper limit of normal. This high activity was sustained for prolonged periods.

The other 5 subjects included in this series showed patterns that fell between these two extremes. In 3 subjects, though pre-exposure levels were exceeded at some time, the high values were not long sustained.

Because adaptation to chronic poisoning may develop and symptoms may not be manifest even though a low ChE level is maintained (Barnes, 1954; Rider, Ellinwood and Coon, 1952), it has been our defined policy to withdraw from risk any subject whose pChE level drops to 70 per cent or below of his pre-exposure level. For this reason, 2 subjects were

suspended twice, and one subject only once. No workers were suspended because of any presenting symptom, but after a random medical check-up, one subject was withdrawn from work because of adverse physical signs. His pChE level at the time was reduced from the original level by 22 per cent, and on physical examination he was found to have bradycardia with a pulse rate of 50 per minute, and the E.C.G. showed sinus rhythm. Routine tests of liver function were within normal limits. Within three months, his pChE rose to the level he had showed before he was ever exposed to O.P. insecticides, and he has remained well and at his employment ever since.

## Discussion

The observations presented here provide evidence that in spite of the low level of toxicity of the compounds to which the subjects have been exposed, the amount being absorbed might have been enough to lead to serious intoxication. The routes by which these compounds are absorbed is difficult to establish with certainty in this type of worker who may fail to appreciate adequately the importance of personal protection. Climatic conditions may also increase the hazard of spraying with these compounds.

It is therefore essential that frequent checks be kept on ChE levels, and full use be made of this exceptional early indicator of poisoning. Ladell (1961) observed that there is no direct correlation between ChE depression in the blood and signs or symptoms of poisoning. In this series, the subjects have never presented with any complaint. This may be explained by the fact that the workers were withdrawn from risk before their ChE reached a dangerously low level. The observations of Holmes and Goan (1956) that with repeated minor exposures symptoms may occur at slightly higher ChE levels, are not corroborated by the present study. The results shown here lend support to Heath's (1961) view that a slow depression of enzyme activity from repeated spaced out doses, is not accompanied by symptoms of poisoning.

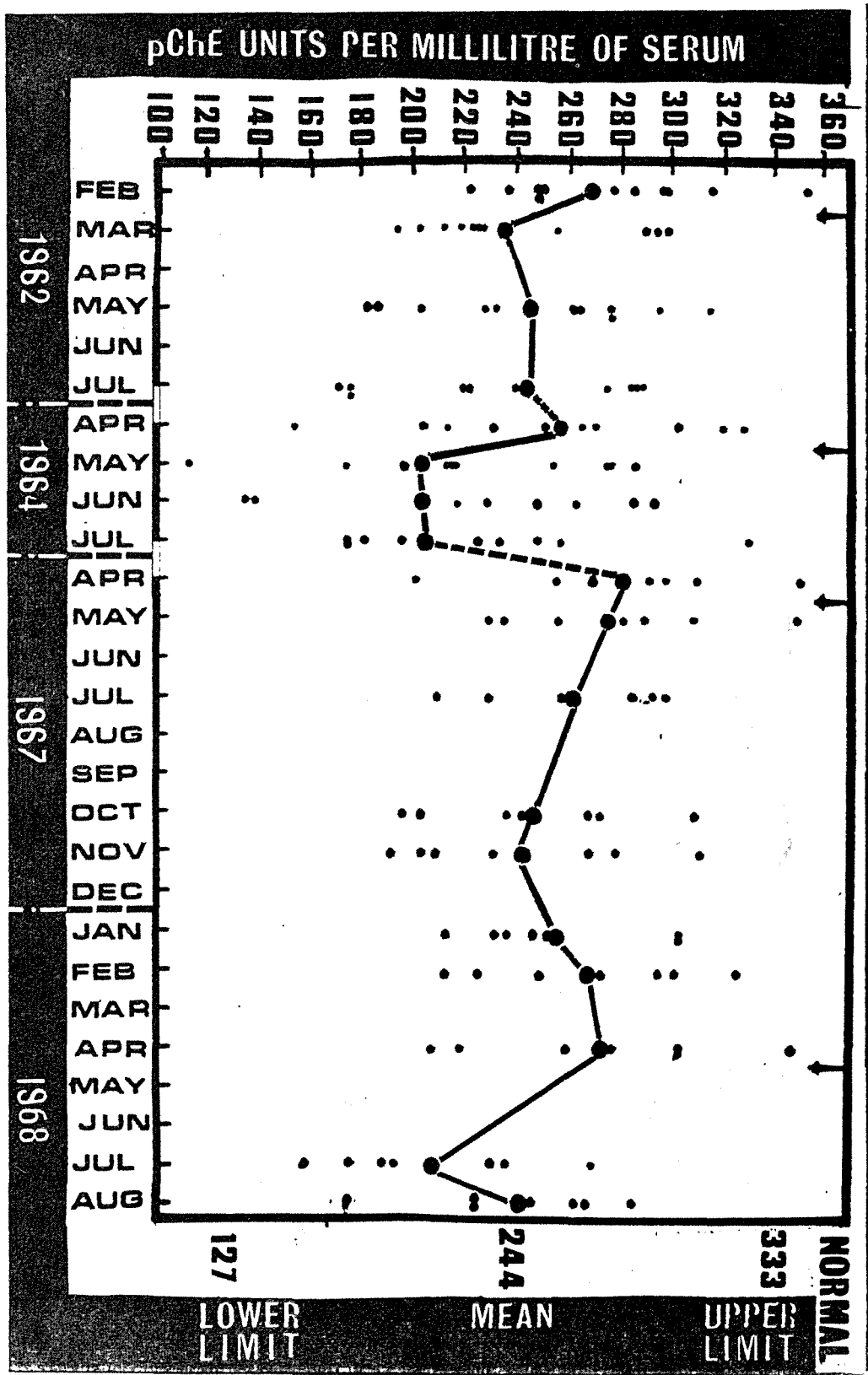
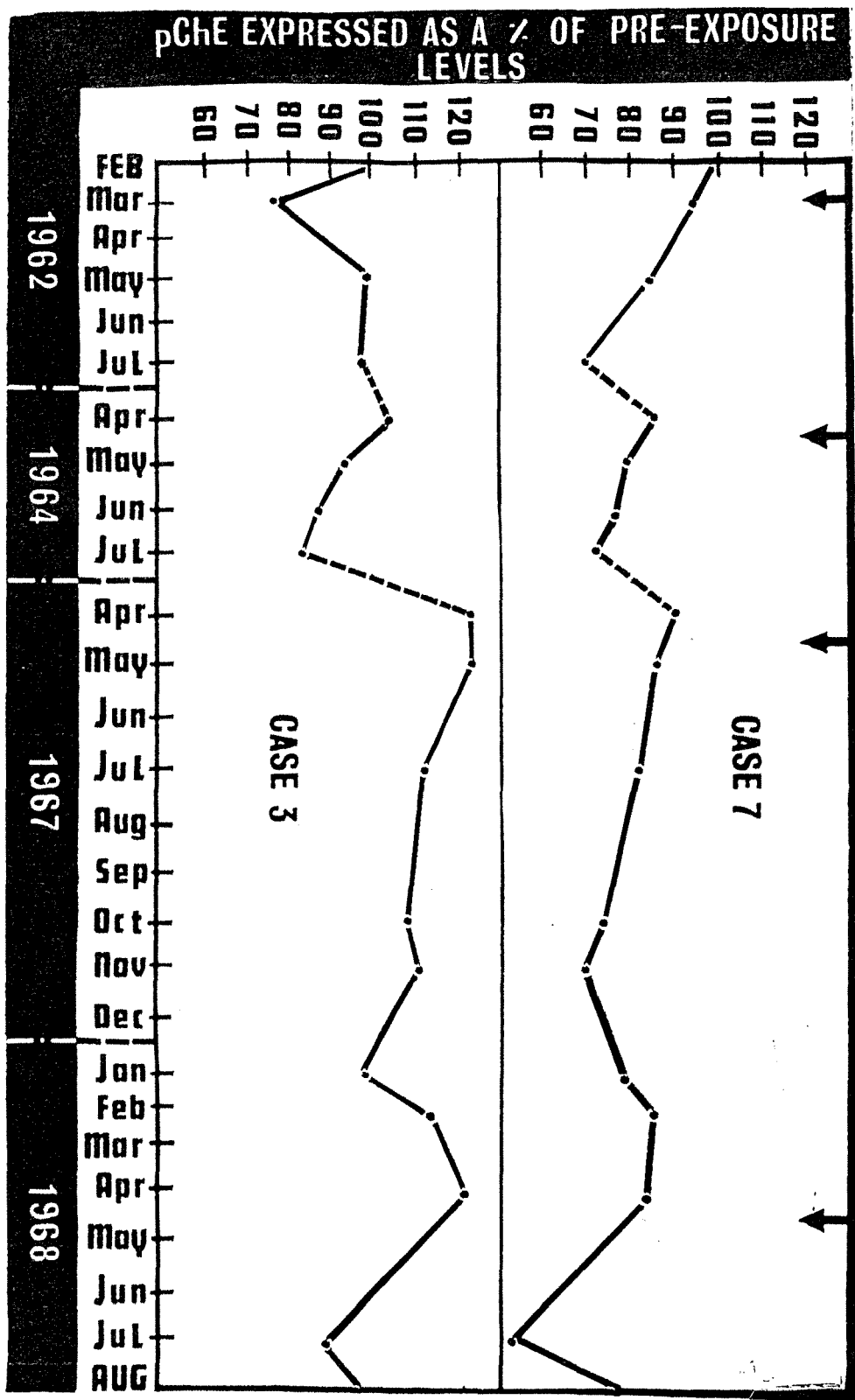


Figure 1. Showing the individual levels of pChE values during the period of observation and the mean values at each interval. The arrows indicate the times of intensification of the spraying with O.P. insecticides.



Figuro 2. Showing the individual levels of pChE values expressed as a percentage of the pre-exposure levels in Case 7 and in Case 3. The arrows indicate the times of intensification of the spraying with O.P. insecticides.

There is some indication that the mean rate of recovery of pChE of these workers is less than 2.5 per cent per day, as reported by Callaway, Davies and Risley (1952). It is interesting to note, however, that in 4 of the 7 subjects, values considerably higher than their respective pre-exposures levels have been recorded. This appears to be an individual characteristic as it occurred in more than one recovery phase of the same subject. Poisoned animals have been observed by Koelle and Gilman (1946) and by Austin and Davies (1954) to behave in a similar way. Locker and Siedek (1952) suggested that low levels of inhibitors stimulate the synthesis of ChE; but Vandekar and Heath (1957) produced evidence to the contrary and showed that reversibility of ChE in poisoned animals depended on whether the O.P. esters in the body have been degraded. It is therefore possible that the role of the enzymes that degrade the poison in the body may be a factor of primary importance in re-establishing normal ChE levels in man, and that the rate of regeneration of ChE may, as a result, be more closely related to the degree of activity of these detoxifying enzymes. Moreover, it is not unlikely that the constitutional pattern of these degrading enzymes differs substantially in the population, and that it is this that determines the different response of individuals to the same toxic dose. Kreuger and O'Brien (1959) have shown that the susceptibility of species to malathion is related to the carboxyesterase activity of the species, and O'Brien (1960) suggested that phosphatase activity may also be an important factor in determining the degree of resistance.

Investigations along these lines in man are worthy of consideration, and may help in the selection of workers and in reducing the risk of fatalities in agriculture and industry.

### Summary

The results of pChE estimations on the sera of agricultural workers employed in

spraying with organophosphorus insecticides of low toxicity are reported. The findings on 7 workers observed over the period 1962 to 1968 show that periodic intoxication coincided with the times at which spraying was intensified, and the spontaneous recoveries of pChE occurred in the intervals. Depression of pChE activity was not associated with clinical manifestations of poisoning.

Reliance on the use of O.P. compounds of low toxicity only as the sole measure of safety is insufficient. ChE estimations should be regularly carried out on the workers as this provides the earliest indication of poisoning.

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