Guidance Note MS 17
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# Biological monitoring of workers exposed to organo-phosphorus pesticides

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These Guidance Notes are published under five subject headings: Medical, Environmental Hygiene, Chemical Safety, Plant and Machinery, and General.

## INTRODUCTION

1 The term 'pesticide', as used in this Guidance Note, applies to preparations used to control or destroy living organisms that interfere with man's agricultural, environmental or amenity requirements.

2 Organo-phosphorus (OP) pesticides include phosphates, phosphites, phosphonates, phosphoramides, pyrophosphates and their sulphur analogues. Formulations are usually either liquids or powders which are mixed with water and applied as sprays, or are directly applied in granule form. A list of commonly used approved chemicals will be found in the booklet *Pesticides 198-. Pesticides approved under the Control of Pesticides Regulations 1986,* published annually by the Ministry of Agriculture, Fisheries and Food, reference 500.

3 There has been a rapid increase in the production and use of OP pesticides in recent years, because they are more short-lived in the environment and in biological systems than the organo-chlorine pesticides which they have replaced. However, acute and subacute exposure to OP pesticides can produce harmful effects in man, and repeated exposure at lower doses may cause insidious cumulative toxicity.

4 Another class of chemicals, the carbamates, are also used as agricultural pesticides and have similar pharmacological actions to the OP compounds. Exposure to both groups of chemicals produces similar symptoms of acute intoxication; the main difference lies in the speed of re-activation of the inhibited enzyme acetylcholinesterase. Recovery of the enzyme from carbamate inhibition is generally faster than recovery from OP inhibition, and there is no cumulative action.

5 Within the group of OP and carbamate compounds there is wide variation in toxicity and not all are cholinesterase inhibitors.

## POTENTIAL OCCUPATIONAL SOURCES OF EXPOSURE

6 Any job which involves contact with OP pesticides either directly or indirectly constitutes a potential source of absorption. Those at risk range from laboratory workers undertaking research on OP pesticides to ambulance workers who, during the course of their duties, may come into contact with injured operators or their contaminated clothing.

7 Workers occupationally at risk include those involved with OP pesticides in:

(a) manufacture and packaging;
(b) transport, storage and distribution;
(c) application and use;
(d) handling used containers eg scrap recovery.

## ROUTES OF ABSORPTION

8 The most common routes of absorption of OP pesticides are via skin, respiratory tract and eyes. Under normal conditions of use ingestion is rare, although small amounts may be swallowed in contaminated saliva. In agricultural practice, the major route of absorption is via the skin, with inhalation being less important. OP formulations based on organic solvents are liable to penetrate protective clothing unless contamination is washed off promptly. Contamination of the eyes may produce local effects and disturbance of vision.

## BIOLOGICAL EFFECTS

9 When poisoning with proprietary formulations of OP compounds occurs, the presence and influence of the solvent should not be forgotten. Local skin effects will almost certainly be due to the solvent; in exceptional and severe cases the presence of an organic solvent may encourage considerably the development of intoxication symptoms.

10 The toxic effects produced by OP compounds in man are generally considered to be due to inhibition of the nervous system acetyl cholinesterases.

## CLINICAL MANIFESTATIONS OF ORGANO-PHOSPHORUS POISONING

11 The diagnosis of OP poisoning is not easy. Some signs and symptoms can be clearly defined, whereas others, particularly those of central nervous system

origin may be variable and not easily detected. Some OPs require metabolic activation before they inhibit cholinesterase. Active metabolite may continue to be formed for some time after absorption.

12 Repeated absorption of small doses, as may occur from contaminated clothing, has cumulative effects resulting in progressive inhibition of nervous tissue cholinesterase. This happens when the repeat exposures occur within the cholinesterase recovery period. Further small exposure may then precipitate the classical condition of OP poisoning. Clinical effects do not generally appear until plasma cholinesterase activity has fallen to 30% of normal pre-exposure values.

13 Symptoms of poisoning include:

(a) non-specific symptoms: headache, giddiness, loss of appetite, nausea and diarrhoea;

(b) those related to over-reactivity of voluntary muscle: tremors, impaired co-ordination;

(c) those related to excessive activity of the autonomic nervous system: miosis (pin-point pupils), blurred vision, excessive salivation and sweating, increased bronchial gland secretion, bradycardia with decreased cardiac output and hypotension.

14 Other symptoms include:

(a) urinary incontinence, abdominal pain, vomiting and broncho-constriction caused by over-activity of smooth muscle;

(b) central nervous system effects:

(i) depression of the respiratory centre;

(ii) various non-specific psycho-motor effects eg apprehension, anxiety, restlessness, irritability, depression, sleep problems such as insomnia and dreaming, hallucinations, expressive language defects, changes of mood, lack of concentration, memory impairment, slowed reaction time.

15 The pattern of signs and symptoms as they develop will to some extent depend upon the route of absorption of the OP compound. Thus, following inhalation, the earliest effects may be miosis, rhinitis and chest tightness. Following ingestion, intestinal colic, nausea, vomiting and diarrhoea are early features. Miosis, rhinitis and chest tightness may not develop after skin absorption.

16 Death may be caused by respiratory failure due to paralysis of respiratory muscles aggravated by central depression of the respiratory centre, broncho-constriction and increased bronchial secretion.

## MEASUREMENT OF CHOLINESTERASE ACTIVITY AS AN INDEX OF ORGANO-PHOSPHORUS UPTAKE AND EFFECT

17 Although different OP compounds inhibit neural, erythrocyte and plasma cholinesterases to varying extents, and with differing time courses, the measurement of erythrocyte and plasma cholinesterase activity provides an indication of the uptake of these compounds. Such measurements have therefore found a place in monitoring workers exposed to OP compounds, especially in the case of repeated exposures.

18 Erythrocyte and plasma cholinesterases have different substrate specificities. The erythrocyte acetyl cholinesterase has its major activity towards acetylcholine and acetyl thiocholine, whereas the plasma enzyme has a broader range with increased activity towards propionyl and butyryl cholines using acetyl choline as substrate, over 80% of enzyme activity of whole blood is then provided by the erythrocyte enzyme.

19 There is a series of genetically determined variants of plasma cholinesterase and these may be associated with increased sensitivity to the muscle relaxant succinyl choline, used by anaesthetists. Anyone who has such an abnormal variant may show a low level of plasma cholinesterase activity even though unexposed to OPs. Although this may make routine monitoring more difficult, it does not increase sensitivity to OP compounds.

20 Several methods of measuring plasma and erythrocyte cholinesterases are available, including electrometric and spectrophotometric methods. The units in which activity is expressed (and the normal range) depend on the method used.

21 A convenient spectrophotometric way of measuring plasma and erythrocyte cholinesterase activity is Ellman's method which uses acetyl thiocholine as the substrate. One version of this method which has proved useful for routine screening is the 'Automated discrete kinetic method for erythrocyte acetyl cholinesterase and plasma cholinesterase' described by P J Lewis, R K Lowing and D Gompertz in *Clinical Chemistry* 1981 **27** 926.

22 Both erythrocyte and plasma cholinesterases have a wide range of values in normal unexposed individuals, although in any one individual activity varies little with time. Interpretation of measurements in exposed subjects is greatly assisted if pre-exposure levels are available for both enzyme activities. In the absence of such base-line measurements true falls in enzyme activity may remain undetected.

23 In spite of its limitations as an index of functional disorder, the technique has found considerable practical value as a monitor for exposure to OP compounds.

## BIOLOGICAL MONITORING

24 The success of any system of monitoring designed to detect early toxic effects depends on:

(a) the availability of adequate pre-exposure information;

(b) whether the procedure is carried out on a regular

basis using appropriate technology, suitably trained staff and with the full co-operation of employees and management.

25 Regular monitoring should be considered for anything more than occasional exposure to OP compounds eg garden use. An effective programme for screening workers regularly exposed to OP compounds would include:

(a) pre-exposure measurement of both plasma and erythrocyte enzymes. There should be a minimum of 60 days without exposure, including maintenance operations on contaminated plant, before these measurements are made. At the same time advice can be given on safe methods of use and the recognition of early signs of poisoning;

(b) regular monitoring of plasma cholinesterase levels in repeatedly exposed subjects. Every four weeks would be reasonable for most workers. A shorter interval should be considered for workers potentially heavily exposed, eg contract sprayers, and for those in occupations, eg pilots involved in aerial spraying, where early symptoms such as blurred vision and impaired co-ordination could present a special hazard to the person affected, other workers or the general public;

(c) measurement of both enzymes in cases of acute heavy exposure and investigations of possible incidents. The measurement of erythrocyte as well as plasma cholinesterases in workers under regular health surveillance offers little advantage. However, in cases of over-exposure when the base line measurements are not available, measurements of both enzymes are desirable.

26 If, during routine monitoring, plasma cholinesterase activity has been shown to have fallen by more than 30% of pre-exposure levels, the workers should be medically examined. The medical officer may then, at his own discretion, taking into account the nature of the work involved and the clinical symptoms, recommend that the worker be suspended from further exposure to OP compounds until considered fit to resume normal work. The rate of recovery of enzyme activity varies with the chemical structure of the OP compound to which the individual has been exposed. The return of enzyme activity to pre-exposure level may occasionally take as long as 60 days. It is not necessary for pre-exposure cholinesterase levels to be reached before resumption of normal work. The medical officer should base his decision on both clinical evidence and the results of biological monitoring.

## ELECTRO PHYSIOLOGICAL MONITORING

27 Electromyograph (EMG) measurements have been used to screen workers for occupational over-exposure to OP compounds. Doubts have been expressed as to the value of EMG measurements as part of routine monitoring. Such measurements are more likely to be of use in the clinical evaluation of special cases of suspected OP toxicity rather than in routine monitoring.

## EMERGENCY TREATMENT

28 If a worker is suspected of having OP poisoning, medical attention should be sought as soon as possible.

29 Recommended first-aid treatment:

(a) stop the patient working, remove him from the exposure area into protective cover and keep him at rest;

(b) remove contaminated clothing, taking care to avoid contaminating your own skin. Wash contaminated skin with plenty of water. Cover the patient with a clean blanket, rug or coat;

(c) if breathing weakens or ceases, make sure the breathing passages are clear, remove false teeth or other obstructions from the mouth and apply mouth to mouth artificial respiration, unless the mouth is contaminated, when a manual method should be used. If the patient's eyes are affected, wash them out with clean running water for several minutes. When transporting the patient to hospital, see that he is in the recovery position to prevent inhalation of vomit;

(d) remember to tell the hospital and the doctor which chemical the patient has been using and show them any available leaflet or label regarding the chemical; or give them a note showing the name copied from the container. The free leaflet MS(B)7 *Poisoning by pesticides* published by the Health and Safety Executive gives details of treatment.

30 A sample of the patient's blood should be taken as soon as possible after exposure and separated (if possible). The sample should then be stored at 4°C until the cholinesterase activities can be measured. Plasma cholinesterase can be measured at most hospitals, but erythrocyte acetyl cholinesterase analysis requires a specialist laboratory.

31 A medical officer should treat a patient presenting signs of OP poisoning with Atropine (2 mg intramuscularly or subcutaneously). If the condition is severe, Atropine may be given intravenously. When symptoms are not promptly relieved, the dose may be repeated every 5 to 10 minutes until the patient is fully atropinised. Victims of OP poisoning can tolerate doses of Atropine which are very large by conventional standards. Pralidoxime mesylate (P2S), available from Poisons Centres, is a specific antidote but should not be used alone as first-aid treatment. A list of hospitals which have facilities for this antidote and treatment can be found in the DHSS booklet *Pesticide poisoning — notes for the guidance of medical practioners*. Both Atropine and Pralidoxime are most effective during the first 24 hours post exposure and an assessment of the need to continue with Atropine should certainly be made after 24 hours. The heart rate is a useful guide and a rate between 70 and 80 beats per minute should

be the target. When muscular activity and convulsions are a feature, Diazepam by injection will be of considerable value.

## NOTIFICATION

32 OP poisoning is a reportable disease under the Reporting of Injuries, Disease and Dangerous Occurrences Regulations 1985 and is also a prescribed disease under the Industrial Injuries Provisions of the Social Security Act 1975. An HSE agricultural inspector must be informed when an agricultural worker or a self-employed person is suspected of suffering from OP poisoning caused by a substance specified in the Poisonous Substances in Agriculture Regulations 1984.

## REFERENCES


1 Ministry of Agriculture, Fisheries and Food, Ref 500 *Pesticides 198-, Pesticides approved under the Control of Pesticides Regulations 1986.* HMSO published annually.

2 Ministry of Agriculture, Fisheries and Food, *Pesticides Safety Precautions Scheme 1984. Products cleared for agricultural, food storage, public hygiene, domestic and related uses in the United Kingdom.* HMSO published annually.

3 Lewis P J, Lowing R K and Gompertz D, Automated discrete kinetic method for erythrocyte acetyl cholinesterase and plasma cholinesterase. *Clinical Chemistry* 1981 **27** 926.

4 Health and Safety Executive, *Poisoning by pesticides.* MS(B)7

5 Department of Health and Social Security. *Pesticide poisoning — notes for the guidance of medical practioners.* 1984 HMSO.


## FURTHER INFORMATION

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