

Medical aspects of work related exposures to Organo-phosphates

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This guidance is issued by the Health and Safety Executive. Following the guidance is not compulsory and you are Free to take other action. But if you follow the guidance you will normally be doing enough to comply with the law. Health and safety inspectors seek to secure compliance with the law and may refer to this guidance as illustrating good practice.

INTRODUCTION

1. The purpose of this Guidance Note is to inform doctors and other health professionals, particularly those concerned with occupational health, about the health effects which may arise from exposure to organophosphates and the role of biological monitoring and health surveillance of workers exposed to these compounds.
2. Organophosphates (OPs) are a broad group of chemicals which have a wide usage in agriculture, therapeutic (including veterinary) medicine and as insecticides in both domestic and public health applications. Within the group of OP compounds there is a wide variation in human toxicity and not all are cholinesterase inhibitors. Although organophosphates were initially developed for chemical warfare those intended for that purpose have significant structural differences, which markedly increased their toxicity to mammalian species, as compared to those in current general use.
3. OPs of interest all act by blocking the normal function of the enzyme acetyl cholinesterase at neuronal, parasympathetic effector organ or neuromuscular junctions and thus interfere with the normal function of nerve impulses.
4. Pesticides and veterinary medicines form the largest group of cholinergic organophosphates to which occupational health professionals are likely to be consulted.
5. Although OP pesticides are more short-lived in the environment and in biological systems than the organo-chlorine pesticides which they replaced by virtue of their toxic action, acute and repeated exposures can produce harmful effects in man, and it has been suggested that chronic exposure at lower doses may cause long term ill-health.
6. 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.

ROUTES OF ABSORPTION AND POTENTIAL OCCUPATIONAL SOURCES OF EXPOSURE.

7. Any job which involves contact with OP pesticides either directly or indirectly constitutes a potential source of exposure. Workers occupationally at risk include those involved with OP pesticides in:

- * (a) manufacture and packaging eg including research workers;
- * (b) transport, storage and distribution;
- * (c) application and use eg agricultural workers, pest control operatives, veterinary surgeons;
- * (d) handling used containers or contaminated clothing e.g. scrap recovery or ambulance workers.

8. Members of the public may also be accidentally exposed to OPs through work activity as for example in drift from the use of pesticides in orchard or crop spraying.

9. The most common routes of absorption of OP pesticides are via skin, respiratory tract and eyes. The low vapour pressure of the majority of commercial products (dichlorvos would be an exception) means that the major route of absorption is via the skin, with inhalation being less important. However the respiratory route of exposure may be important when formulations are used as sprays with the generation of finely divided aerosol. Under normal conditions of use ingestion is rare, although small amounts may be swallowed in contaminated saliva.

10. Where OPs are supplied as concentrates requiring dilution, as in sheep dip and agricultural pesticide formulations, then skin contamination with the concentrate may result in relatively high levels of absorption.

11. Good occupational hygiene practice is essential to minimise exposures. OP formulations including organic solvents may permeate protective clothing unless contamination is washed off promptly. This is more important with concentrate exposure. Poor occupational hygiene practices (eg trousers/leggings inside boots or too short a glove when dipping sheep) may also result in contamination with chemicals migrating around the PPE.

PHARMACOLOGY AND TOXICOLOGY

12. The chemistry of OP compounds is complex. The term is loosely applied to all compounds containing carbon which are derivatives of phosphorus containing acids. The structure is easily modified and there are many different OP compounds (at present some 200 OP insecticides are licenced somewhere in the world). Such wide ranging structure results in different steric, electronic and hydrophilic properties. In turn these lead to differing biological activity and species specificity.

13 OP anticholinesterases are esters of phosphoric, phosphonic, phosphorothioic or related acids. As an indicator the majority (over 75%) of OP anticholinesterases have one of the following elements in their approved names, *-pho-* or *-fos-* or *-vos-*, indicative of their phosphorus content (eg chlorfenvinfos.): *-thio-* or *-tho-*, indicative of their sulphur content (eg malathion). Important exceptions to this would include diazinon and demeton-S-methyl.

14. Cholinesterases, inhibition of which gives rise to the clinical symptoms, are of the B-esterase group of enzymes. A-esterase enzymes which also hydrolyse, and so detoxify, OPs are not themselves inhibited in the process. Clinical symptoms will be dependent on the relative amounts of the two groups of enzyme and on the affinity of the specific OP for each group.

15. Many OP pesticides and veterinary medicines are phosphorothioates which contain P=S groups and as such require activation by the liver with conversion of the P=S moiety to the P=O form in order to manifest their toxicity. Thus, for example, parathion is converted to paraoxon and malathion to maloxon. This need for activation may affect the clinical symptoms in that local effects at the site of exposure would not be expected and systemic toxicity may be more prominent.

16. These features of activation metabolism and detoxification metabolism and the balance between them for any specific OP, together with inter-individual differences in respect of enzyme polymorphisms, will affect the relationship between exposure and toxicity.

17. The main enzymes inhibited by OPs are cholinesterases. They can be divided into acetylcholinesterase and butyrylcholinesterase on the basis of their preferred substrate. The enzyme found in plasma is butyrylcholinesterase, which is sometimes known as pseudocholinesterase; the enzyme found in the nervous system and in muscle, and also in the erythrocyte is acetylcholinesterase. Whilst acetylcholinesterase, as an enzyme, has a clear functional role, the role of butyrylcholinesterase is unclear.

18. Whilst inhibition of cholinesterase enzymes form a major action of these OPs other enzyme systems may be affected. However, the potential clinical consequences of their inhibition, with the exception of neurotoxic or neuropathy target esterase (NTE), remains undefined.

19. The toxic effects produced by OP compounds in humans are generally considered to be due to inhibition of the nervous system acetylcholinesterase. In normal conditions following hydrolysis of acetylcholinesterase, there is a reactivation of the enzyme in less than a second. In the presence of an OP this reactivation is much slower (or non existent) leading to effective enzyme inhibition and, in turn, a prolonged build up of acetylcholine.

20. Acetylcholine acts as a neurotransmitter in many parts of the nervous system

- * preganglionic to postganglionic neurones (nicotinic)
- parasympathetic
- sympathetic
- * postganglionic (muscarinic)
- parasympathetic fibres to effector organs

sympathetic fibres to sweat glands
* motor nerves to skeletal muscle (nicotinic)
* some nerve synapses in the CNS

21. The level of inhibition of erythrocyte acetylcholinesterase ('true' cholinesterase) is reasonably well correlated with severity of OP poisoning symptoms, and by inference therefore with nervous system acetylcholinesterases, although the influence of toxicodynamics in the distribution of OP between blood, storage depots in fatty tissue and target nervous tissue is important in limiting the strength of this relationship.

22. Inhibition of cholinesterase is caused by phosphorylation of the active site of the enzyme by the OP. In causing this phosphorylation of enzyme the OP structure is split with a 'leaving' group being displaced from the enzyme and the alkyl phosphate moiety of the OP attaching to serine amino acid within the enzyme active site.

23. After inhibition by an OP acetylcholinesterase can undergo two fates. One leads to an 'aged enzyme' where, after a molecular rearrangement of the alkyl phosphate group attached to the serine residue, the enzyme is irreversibly inhibited and enzyme activity can only return by replacement of 'aged enzyme' by newly synthesised enzyme. On the other hand the inactivated enzyme can spontaneously reactivate back to the normal active enzyme. These two reactions have different rates of reaction which are said to depend on the nature of the alkyl phosphate group of the OP.

24. For the erythrocyte enzyme, the replacement of any 'aged enzyme' is dependent on the lifetime of the erythrocyte in circulation (approx. 120 days) whilst the replacement rate of plasma butyrylcholinesterase is considerably faster, the reported half-life being in the order of 12 days.

CLINICAL MANIFESTATIONS OF ORGANO-PHOSPHORUS POISONING

Acute

25. 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. The pattern of signs and symptoms that develop will depend not only on the particular OP compound but also, to some extent, upon the route of absorption.

26. Some OPs require metabolic activation before they inhibit cholinesterase and active metabolite may continue to be formed for some time after absorption. Similarly redistribution from lipid or fat storage depots may affect the development of symptoms. The picture will also be confounded by OP affinity towards acetylcholinesterase and butyrylcholinesterase and subsequent ageing and reactivation.

27. Repeated absorption of small doses, as may occur from wearing contaminated clothing, may result in progressive, cumulative inhibition of nervous tissue cholinesterase. This happens when the repeat exposures occur within the cholinesterase recovery period. Further small exposure may then precipitate the symptoms of acute OP poisoning. This is distinct from chronic toxicity as described below.

28. The signs and symptoms of acute poisoning include

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

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

* non-specific symptoms: headache, giddiness, loss of appetite, nausea and diarrhoea;

29. Other signs and symptoms may include:

* urinary incontinence, abdominal cramps, pain, vomiting and broncho-constriction caused by over-activity of smooth muscle;

* glycosuria and hyperglycaemia and a leucocytosis and low grade fever may be recorded.

* central nervous system effects:

- depression of the respiratory centre accompanied by low arterial oxygen saturation and metabolic acidosis;

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

30. In as much as the pattern of signs and symptoms depend upon the route of absorption of the OP compound then, following inhalation, the earliest effects may be rhinitis and chest tightness (this has been described particularly following exposure to dichlorvos); and following ingestion the early features may include intestinal colic, nausea, vomiting and diarrhoea. Miosis, rhinitis and chest tightness are unlikely to develop after skin absorption.

31. Death following an acute exposure to OP may be caused by respiratory failure due to paralysis of respiratory muscles aggravated by central depression of the respiratory centre, broncho-constriction and decreased bronchial secretion.

32. When poisoning with a proprietary formulation of OP pesticide or veterinary medicine, the presence and influence of the solvent should not be forgotten. Local skin effects will almost certainly be due to the solvent and in exceptional and

severe cases the presence of an organic solvent may encourage considerably the development of intoxication symptoms.

Post acute

33. A number of well recognised conditions may follow acute OP poisoning although, because of the complex pharmacology and toxicology of this group of compounds, not all OPs will give rise to these complications.

34. Intermediate syndrome – this syndrome which occurs typically 1 to 4 days following an acute poisoning was first described in 1987. It is considered to be a dose related phenomenon. The individual develops a proximal muscle weakness which may affect the head, neck and respiratory muscles, leading to respiratory failure. The effects are self limiting, generally lasting between one and three weeks. The underlying basis of the condition is unknown but muscle end plate necrosis may be implicated.

35. OP Induced delayed Polyneuropathy (OPIDP) is associated with inhibition of the enzyme neurotoxic or neuropathy target esterase (NTE). This may be accompanied, 10 to 14 days after the acute toxic poisoning, by a selective degeneration of long and large fibre tracts of the spinal cord and peripheral nervous system in a 'dying back' pattern of degeneration. This neuropathy affects the motor and sensory nerves particularly to the lower limbs with resultant weakness, clumsiness, tingling and ultimately paralysis. Although there may be some recovery, initially in the sensory system, residual signs and symptoms are not uncommon. OPIDN has been described in species other than human and the current standard neurotoxicity screening test for OP compounds, prior to marketing, is whether or not the substance inhibits NTE in hens with associated clinical and histopathological endpoints. If this test is positive the product is not authorised/approved.

36 Other less clearly defined neurobehavioural effects subsequent to acute OP poisoning have been ascribed to cerebral hypoxia during the toxic episode.

Chronic

37. A number of reports have suggested that exposure to OPs at levels which have not resulted in acute toxic symptoms with cholinesterase depression, may give rise to chronic, and in some cases disabling, health effects. These effects have been described as neurobehavioural, neurological, neurophysiological and autonomic.

38. Published reports in the literature are, however, inconsistent and the magnitude of the objective changes found are, in the majority of studies, subtle and below the threshold of clinical manifestation.

39. Many of the symptoms attributed to chronic ill health from OP exposure are indeterminate (headache, fatigue, tiredness, irritability, loss of concentration) and there are no clearly defined patterns which are sufficiently robust as to enable a case definition. Furthermore there is no identified mechanism which can currently account for the occurrence of chronic effects. However, the possibility that effects other than those related to the inhibition of cholinesterase enzyme systems can exist need to be considered.

40. Depression with suicidal intent, chronic fatigue and multiple chemical sensitivity are specific conditions which have been associated with exposure to pesticides and veterinary medicines, including OPs. A number of other conditions have also received attention including cardiomyopathy, osteoporosis, malignancy and developmental abnormalities.

REQUIREMENTS OF COSHH

41. Under the Control of Substances Hazardous to Health Regulations 1994 (COSHH) an employer or self employed person must assess the risks to health from work involving hazardous substances. The prime purpose of the risk assessment is to determine the measures required to prevent ill health. If there is a risk, employers are required to decide on the action needed to prevent or minimise that risk and protect employees' health.

42. The prime purpose of the risk assessment is to determine the measures required to prevent ill health. If there is a risk, employers are required to decide on the action needed to prevent or minimise that risk and protect the health of employees and others who may be affected by the work activity.

43. Wherever it is reasonably practicable to do so, COSHH requires that exposure to substances known to cause ill health should be prevented by the use of alternative substances or processes and by minimising the numbers exposed. Where it is not reasonably practicable to prevent exposures, employers have a duty to ensure that any exposure is adequately controlled and the health of employees is protected.

44. Detailed advice on the control measures, other than health surveillance, required under COSHH are beyond the scope of this Guidance Note. Practical guidance on the Regulations themselves is given in the COSHH general Approved Code of Practice. HSE has also published a general guide on Health Surveillance under COSHH Guidance for Employers.

45. Specific recommendations about control will be set out as approved conditions under specific pesticide and medicines legislation and will appear on product labels or pack inserts.

46. Where valid and suitable occupational hygiene methods are available and any deterioration in control might otherwise not be detected sufficiently quickly, exposure should be monitored to detect failure or deterioration of adopted control measures.

47. Where the employer's assessment has revealed a risk to health which cannot be eliminated then health surveillance of exposed employees may be required under COSHH in order to identify possible causes.

MEASUREMENT OF METABOLITES AS AN INDEX OF EXPOSURE

48. HSE has produced general guidance on the practical application of biological monitoring in the workplace for the assessment of chemical exposure. Biological monitoring by the measurement of the alkyl phosphate / phosphorothioate metabolites of OPs in the urine provides a relatively non invasive means of investigating exposure although at the current time there are few laboratories which can offer this as a routine service.

49. There are a relatively small number of the alkyl phosphate / phosphorothioate metabolites compared to the potential number of different OPs. A measure of six of these 'alkyl phosphates' will cover about 85% of likely encountered OPs and can be quantified in a single GC analysis run after derivatisation with pentafluorobenzylbromide using a flame photometric detector.

50. The method is very sensitive being able to detect increased levels of 'alkyl phosphates' well below OP exposures that cause cholinesterase inhibition. Low levels of some urinary metabolites can be found in seemingly unexposed subjects however the origin of such background levels has yet to be determined.

51. Urinary 'alkyl phosphates' have a relatively short half life of around 10-14 hours in urine after a single exposure and therefore any urine sample has to be taken close to the time of OP exposure.

52. Urinary metabolites have a potential role in the practical investigation of isolated subacute accidental exposures and as a research tool as, for example, in the investigation of the effectiveness of personal protective equipment such as gloves and clothing, in preventing exposure.

53. Urinary metabolite measurements may also prove useful in monitoring workers with a high potential risk of exposure (eg sheep dip contractors) or to establish that control measures are adequate where there are changes in working practices. In effect a local baseline can be established, from measurements made at a time when controls are known by independent observation to be good, against which change can be assessed.

54. The relationship between urinary metabolites and cholinesterase inhibition (and hence acute toxicity) has not been defined but because of the wide range of OP potencies (ie enzyme affinity) this relationship is likely to be specific to each OP. At the present time urinary metabolites remain an indicator of exposure and cannot be interpreted in health terms.

MEASUREMENT OF CHOLINESTERASE ACTIVITY AS AN INDEX OF OP UPTAKE AND EFFECT

55. Although different OP compounds inhibit neural, erythrocyte and butyrylcholinesterases to varying extents, and with differing time courses, the measurement of erythrocyte ('true') acetylcholinesterase and plasma ('pseudo') butyrylcholinesterase activity provides an indication of the uptake of these compounds. Such measurements have therefore found a place in monitoring workers exposed to OP compounds.

56. In their active oxo form OPs are widely different in their affinities for the erythrocyte acetylcholinesterase and the plasma butyrylcholinesterase which, in vitro, may be as great as a thousandfold at the concentrations which cause a significant depression. This will effect the dose effect relationship which, as with the measurement of urinary alkylphosphates, will be specific to each OP.

57. Large inhibitions in butyrylcholinesterase have been noted in the absence of any significant symptoms of toxicity to the cholinergic nervous system and is considered to be a more sensitive indicator of OP exposure than of toxicity. Erythrocyte acetylcholinesterase, on the other hand, appears to correlate reasonably well with the severity of acute OP poisoning symptoms. This difference may, however, be a function of a higher affinity for butyrylcholinesterase than for acetylcholinesterase.

58. Several spectrophotometric assays for the measurement of butyryl- and acetylcholinesterases are available. The units in which activity is expressed and the normal range will depend on the substrate used but the differing methods will not affect the sensitivity to detect OP induced depressions.

59. Both erythrocyte acetylcholinesterase and plasma butyrylcholinesterase 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, although where serial measurements are taken a change outside the normal expected variation (an 18% fall) may be indicative of a likely OP effect.

60. Depression in butyrylcholinesterase activity may, in particular, be associated with

- * physiological variation (eg pregnancy)
- * disease (eg cancer, liver disease)
- * iatrogenic (eg plasma inhibition or reduced synthesis by drugs)
- * genetic in 3% of the population

61. There is a series of genetically determined variants of butyrylcholinesterase 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 butyrylcholinesterase activity even though unexposed to OPs. Although this may make routine monitoring more difficult, it does not increase the individuals sensitivity to OPs or other anticholinesterase compounds.

HEALTH SURVEILLANCE

62. The employer's COSHH assessment should identify the presence of hazardous substances in the workplace, the risks to health, and the measures to prevent or control exposure. Relevant information on these matters should be given to employees.

63. Employers should also determine as part of the assessment whether health surveillance is required. Health surveillance is for the protection of individuals, to identify at as early a stage as possible any indications of disease or adverse changes related to exposure, so that steps can be taken to treat their condition and to advise them for the future. It may also provide early warning of lapses in control and indicate the need for a reassessment of the risk.

64. Health surveillance is considered appropriate (COSHH Regulation 11, paragraph (2)(b)) where – “the exposure of the employee to a substance hazardous to health is such that an identifiable disease or adverse health effect may be related to the exposure, there is a reasonable likelihood that the disease or effect may occur under the particular conditions of his work, and there are valid techniques for detecting indications of the disease or effect.”

65. The success of any programme of health surveillance depends on:

- * the provision of information about relevant symptoms and advice to report such symptoms to an identified health professional or responsible person;
- * the availability of adequate pre-exposure information (clinical and/or biochemical) to act as a baseline;
- * whether the appropriate procedures are performed on a regular basis by suitably trained staff and with the full co-operation of employees and management.

66. The two planks of health surveillance for workers regularly exposed to OPs are the clinical assessment and, where appropriate, biological effect monitoring by measurement of cholinesterase.

67. The basis for health surveillance is the employers risk assessment but it is likely that regular health surveillance would be considered for any employee repeatedly handling OP concentrate within any one month or for anyone substantially exposed to diluted OP formulations. As a guideline this latter may be taken as being 30 hours exposure in any one month or as exposure on 3 consecutive days or on 6 days in any 21 day period.

68. The frequency of health surveillance and the necessity for biological effect monitoring will depend upon the pattern and level of exposure. Health surveillance is not, however, a substitute for exposure control. The primary aim of any programme of health surveillance is to detect an impending acute toxic episode arising from repeated absorption of small doses of OP, where exposures may occur within the cholinesterase recovery period.

69. A programme of health surveillance might include:

- * a pre-exposure clinical assessment with full medical and occupational history and physical examination. At the same time advice can be given on safe methods of use and the recognition of early signs of poisoning.
- * 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, in an ideal situation two measurements would be made with a minimum interval of 7 days and a repeat measurement taken if the results gave a >20% difference.
- * regular symptom enquiry and physical examination. This may be particularly relevant where OPs are in the active (oxon) form and the route of exposure clearly defined thus enabling examination for specific local signs of toxicity. In any event workers should be aware of the symptoms of OP poisoning and the route by which these can be reported to a responsible person.
- * monitoring of plasma and erythrocyte cholinesterase levels in repeatedly exposed subjects.

70. Health surveillance may be conducted in parallel with biological monitoring to assess exposure in which situation the frequency of (blood) sampling will be governed by working practices and particularly by any variation or change to those practices.

71. If, during a biological effect monitoring programme, the plasma butyrylcholinesterase activity is shown to have fallen by more than 30% of pre-exposure levels, the worker should be given a complete medical examination. A measurement of acetylcholinesterase should be obtained to further assess the situation if this has not been routinely measured. 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. Such a change would also indicate a need to investigate why control measures had failed and allowed excessive exposure.

72. The rate of recovery of enzyme activity varies with the chemical structure of the OP compound to which the individual has been exposed. 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 further biological effect monitoring.

73. Where health surveillance is undertaken there is a legal requirement under COSHH for a health record to be kept and maintained for at least 40 years from the date of the last entry. This record should contain the identifying details of the employee, the history of jobs involving work with hazardous substances and the conclusions of health surveillance

procedures. The conclusions should be phrased in terms of fitness for work and, where applicable, decisions made by the person responsible for the surveillance. Clinical details of a confidential nature should not be entered in the COSHH record.

74. HSE Medical Inspectors will provide advice on all aspects of health surveillance. Where blood or urine testing is considered appropriate analytical facilities may be found in commercial laboratories or local hospital departments of clinical chemistry (biochemistry / chemical pathology).

EMERGENCY TREATMENT

75. If a worker is suspected of having a severe acute OP poisoning, this should be considered a medical emergency and the individual admitted to hospital.

76. Recommended first-aid treatment:

- * stop the individual working, remove from the exposure area and keep at rest. Cover the patient with a blanket or similar to keep them warm. Do not delay transfer to hospital.
- * maintain vital signs by artificial; respiration, cardiac resuscitation and control of convulsions.
- * if circumstances and time permit remove contaminated clothing, taking care to avoid contaminating your own skin.

Wash contaminated skin with plenty of water.

- * if the OP has been swallowed oral activated charcoal (50-100 g for an adult) may be given if available and impaired consciousness and convulsions are not present. Its value is, however, unproven.

77. 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. (preferably within 48 hours). A low plasma butyrylcholinesterase should always be followed by a measurement of erythrocyte acetylcholinesterase.

78. The direct measurement of OPs or their metabolites in body fluids, whilst they may provide subsequent confirmatory evidence, has no place in the immediate diagnosis or management of poisoning which should be based on a history of exposure and the clinical signs.

79. Hospital management may include

- * supportive treatment including maintenance of the airway and supplemental oxygen. Intubation and mechanical ventilation may be required.
- * administration of antidotes
 - atropine antagonises the effect of accumulated acetylcholine at muscarinic receptors. The dose (2mg for an adult) may be repeated until the patient is fully atropinised. In severe cases, adults may require a total dose of atropine (100mg) which would be considered very large by conventional standards.
 - oximes such as pralidoxime are able to reverse enzyme inhibition as long as the acetylcholine remains in the 'unaged' form. Pralidoxime mesylate can, in the UK, only be obtained from designated centres and details should be obtained from the local National Poisons Information Centre.
- * the administration of diazepam which appears to have a beneficial, non specific effect in addition to controlling tremors and convulsions.

NOTIFICATION

80. It is important that cases of ill health associated with exposure to OPs (particularly pesticides and veterinary medicines) are reported to enforcing authorities. Reporting cases of ill health will help those authorities to be aware of any unanticipated harmful effects, take enforcement action where appropriate and prevent further incidents. Further assessment of ill health is made by the authorisation/approval authority so that, if necessary the product information can be amended, or the product can be withdrawn from the market.

81. Incidents of pesticide poisoning may be investigated by HSE or local authorities as appropriate. Once an investigation is complete details are passed to HSE's Pesticide Incidents Appraisal Panel (PIAP), which takes an overview of alleged ill health attributed to pesticide exposure. This allows new issues and trends to be identified and used to inform the approval process.

82. In the case of veterinary medicines, the Veterinary Medicines Directorate operate the Suspected Adverse Reactions Surveillance Scheme (SARSS) to which cases of suspected ill health should be reported.

83. OP poisoning is a reportable disease under the Reporting of Injuries Disease and Dangerous Occurrences Regulations (RIDDOR), 1995. Where there is medical opinion of OP poisoning, an employer or self employed person must report the disease to their enforcing authority – HSE or the local authority. It is also a prescribed disease under the Industrial Injuries Provisions of the Social Security Act 1975.

REFERENCES

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APPENDIX

The reporting and investigation of incidents involving people's health.