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SHEEP DIPS : NATIONAL POISONS UNIT RESEARCH

Attached is the report of the work carried out by the National Poisons Unit during the Autumn 1991 dipping season. This was published by the VMD in October 1992 and was issued to Committee members as well as being widely distributed. Also attached is a copy of a letter which appeared in the British Medical Journal at the time of publication announcing the completion of the survey and the availability of the report.

Veterinary Medicines Directorate
March 1993

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LETTERS

Health effects of organophosphate sheep dips

EDITOR,—We wish to draw attention to the possible health effects of exposure to sheep dips containing organophosphates (diazinon, propetamphos, or chlorfenvinphos). Toxic exposure to organophosphate substances may cause acute cholinergic inhibition¹ that correlates poorly with clinical effects.² Acute clinical effects after exposure to organophosphate dips are uncommon, and because these effects are non-specific, resembling influenza, diagnosis may be difficult.

During the dipping season last year (22 September to 3 November) the National Poisons Unit, in collaboration with the Veterinary Medicines Directorate of the Ministry of Agriculture, Fisheries and Food, investigated cases of suspected exposure reported to the poisons unit by doctors requesting information on management. We obtained details of the cases by telephone and by sending follow up questionnaires to the doctors. If a case was reported within seven days of exposure the doctor was asked to take a blood sample (5 ml EDTA) straight away and another at least one month later. The National Poisons Unit Laboratory measured erythrocyte and plasma cholinesterase activities with an assay based on the method of Ellman *et al.*³

Thirty four reports were received. The age of the patients, recorded in 31 cases, ranged from 2 to 75 years. Twenty nine patients were exposed while working with sheep, but three were exposed accidentally, including a 2 year old child who fell into a dip. Circumstances were unknown in two cases.

Influenza-like symptoms, probably associated with organophosphate toxicity, were reported by 23 patients after occupational exposure. Fifteen of them reported that they had not worn protective clothing as recommended by the Health and Safety Executive⁴ and had probably been contaminated while putting sheep into a dip or handling recently dipped sheep.

Paired blood samples were obtained from nine of the occupationally exposed patients with influenza-like symptoms. In three patients a rise in the erythrocyte cholinesterase activity of at least 25% four to six weeks after exposure indicated that cholinesterase activity had been depressed, but in six patients measurements were either equivocal or did not show increased activity (copies of full report available from Mrs J Stear, Veterinary Medicines Directorate, New Haw, Addlestone KT15 3NB).

These findings are a matter of concern. To obtain more information about the scale and severity of the problem and formulate prevention strategies the National Poisons Unit is continuing surveillance between September and December this year in cooperation with the Veterinary Medicines Directorate, the Department of Health, and the Health and Safety Executive; we urge doctors to report suspected cases of exposure to the

unit. This surveillance is separate from the pesticide green card scheme operated by the West Midlands Poisons Information Centre for the Trent and West Midlands regions.

We are grateful to the Veterinary Medicines Directorate of the Ministry of Agriculture, Fisheries and Food, which contributed to the funding of the surveillance, and for information from the directorate's suspected adverse reaction surveillance scheme for veterinary medicines.

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- 1 Ballantyne B, Marrs TC, eds. *Clinical and experimental toxicology of organophosphates and carbamates*. Oxford: Butterworth and Heinemann, 1992.
- 2 Minton NA, Murray VSG. A review of organophosphate poisoning. *Medical Toxicology* 1988;3:350-75.
- 3 Ellman GL, Courtney D, Andres V, Featherstone RM. A new and rapid colorimetric determination of acetylcholinesterase activity. *Biochem Pharmacol* 1961;7:88-95.
- 4 Lewis PJ, Lowing RK, Gompertz D. Automated discrete kinetic method for erythrocyte acetylcholinesterase and plasma cholinesterase. *Clin Chem* 1981;27:926-9.
- 5 Health and Safety Executive. *Sheep dipping: protect your health*. Bootle: Health and Safety Executive, 1991. (Agricultural safety leaflet AS29.)

Surveillance of sheep dip exposures
23 September to 3 November 1991

FINAL REPORT

OCTOBER 1992

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SURVEILLANCE OF SHEEP DIP EXPOSURES
23 September to 3 November 1991

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SUMMARY

Inadequately protected workers exposed to organophosphate sheep dip have been reported to develop symptoms resembling an infectious disease, with nausea, vomiting, abdominal pain, diarrhoea, anorexia, sweating, salivation, pyrexia, weakness and constricted pupils. In some parts of the country these effects are known as "sheep flu".

Sheep dip exposures cause much anxiety in the public and medical communities. However, medical practitioners do not fully utilise the surveillance and reporting system developed by the Veterinary Medicines Directorate (VMD), possibly because of notification problems.

For the compulsory sheep dipping season, 23rd September to 3rd November 1991, the National Poisons Unit (NPU) set up a surveillance system as an adjunct to the VMD reporting system already in place. 34 cases of exposure to sheep dip were identified of which 29 were occupational exposures. Analytical data were available on 19 cases, 10 of which were considered by NPU to be confirmed cases of organophosphate exposure. No deaths were recorded.

The Pilot Study has identified more confirmed cases than expected. The immediate effects on human health from exposure to sheep dips have been recorded, but insufficient information has been gathered on the longer term or delayed effects. Further investigation of the problem by continuing surveillance and case assessment is needed and is continuing during 1992 and 1993.

SURVEILLANCE OF SHEEP DIP EXPOSURES

23 September to 3 November 1991

1. Project objectives

The aim of the project was to assess the effects on human health from exposure to sheep dips by surveillance and case review. The specific objectives were to:

- a. identify all emergency case enquiries to the National Poisons Information Service (London) relating to sheep dip exposures
- b. collect EDTA blood samples for rapid analyses by the Unit's laboratory for red blood cell and plasma cholinesterase activities and other analyses where appropriate
- c. provide 24 hour consultant medical cover to discuss all sheep dip related enquiries for the duration of the project
- d. follow up all cases using a specially designed questionnaire
- e. generate a report to cover the total number of enquiries received, the substances involved and the evaluation of patients' symptoms and analytical results where available.

2. Introduction

2.1 Definition

Sheep dip concentrates are preparations containing one or more medicaments (diazinon, propetamphos and chlorfenvinphos, organophosphates, or flumethrin, a pyrethroid), usually in the form of wettable powders, pastes or solutions which are used to prepare dilute suspensions or emulsions for the prevention and treatment of ectoparasitic infestations of animals (British Pharmacopoeia (Veterinary), 1985).

2.2 Licensing of Veterinary Medicines and Controls

Any pesticides applied to animals are classified as veterinary medicines under the provisions of the Medicines Act 1968. All veterinary medicines are required to be licensed under this legislation before they can be marketed in the UK. Licences are issued only after the Veterinary Products Committee (VPC) - an independent committee of scientists - is satisfied that the necessary standards of safety, quality and efficacy are met. In addition, a review of all licensed pharmaceutical veterinary medicines, including sheep dips, is currently under way in the UK, to ensure that such products meet up-to-date standards of safety, quality and efficacy. Under the Medicines Act (1968), sheep dips are classified as Pharmacy and Merchants List (PML) products, which means they can be sold to commercial keepers of animals by agricultural merchants registered with the Royal Pharmaceutical Society of Great Britain.

2.3 Use of sheep dips

Whilst there are certain regulations, enforced by the Ministry of Agriculture, Fisheries and Foods (MAFF), and the Health and Safety Executive (HSE), governing the conditions and timing of dipping procedures, the actual process is performed with little supervision.

The Agricultural Training Board produces a comprehensive leaflet on dipping and the HSE has published an advisory leaflet (Health and Safety Executive, 1991) for the dipping season which is intended for distribution with all dip sold. The VMD also produces a leaflet on safe handling and disposal of sheep dips. Nevertheless, according to HM Agricultural Inspectorate, several claims of illness as a result of dipping are made every year (Health and Safety Executive 1985-1990). The VMD have received over 240 reports of suspected adverse reactions to sheep dips, involving over 320 individuals, since 1985.

Contamination with sheep dips most often occurs when users and operators ignore recommendations about wearing personal protective equipment and are splashed when putting sheep into the bath or when handling dipped sheep. Poor operating practice, for instance dipping in a confined space or using incorrect dilutions or mixtures can increase the likelihood of contamination.

2.4 Public perception

Public concern over the use of pesticides, and the possible health effects on both consumer and agricultural worker, has increased dramatically over the last decade with the "greening" of society. As a result several media reports have appeared, some with possibly exaggerated claims about toxic hazard (Bartle 1991, McKenzie 1991).

Although the medical and scientific community have regarded such reports with some scepticism, it has not been possible to undertake adequate clinical evaluation, because of the lack of compliance with reporting systems by medical professionals. Since most medical professionals receive little or no training in medical toxicology, the toxicity of organophosphates and the variation in individual susceptibility are not widely understood and "sheep flu" is rarely included in a differential diagnosis of an influenza-type illness. Furthermore, the fragmented nature of the farming community makes it difficult to contact people who may have been affected.

2.5 Government and sponsored reporting schemes

There are several reporting schemes for incidents of suspected pesticide poisoning. These include:

- the Suspected Adverse Reaction Surveillance Scheme for VMD, (MAFF), 1981 onwards, for all reports of suspected adverse reactions to veterinary medicines including sheep dips.
- the Pesticide Incidents Appraisal Panel (PIAP) for all

pesticide incidents, including sheep dips, reported to HSE (health reporting and assessment scheme, 1980 onwards, results published since 1986 onwards by the HSE),. To increase awareness amongst the medical profession of the PIAP and VMD schemes, a letter was sent to them by the Chief Medical Officer in 1991.

- a "green card" reporting scheme developed by the West Midlands Poisons Unit for any suspected pesticide incident occurring in the area covered by West Midlands and Trent Area Health Authorities (Booth et al. 1991). This scheme is sponsored by HSE and will report in one years time.

These last two schemes both liaise with the VMD to ensure that the VMD is aware of suspected adverse reactions to sheep dips.

2.6 National Poisons Unit

The NPU provides a 24 hour information and advice service for doctors managing cases of confirmed or suspected poisoning. For many years it has been a matter of concern to improve the data available on the management of cases occurring as a result of exposure to pesticides. A retrospective review of cases of sheep dip exposure was undertaken recently.

2.6.1 Retrospective review of incidents

There are two sources of information available at the NIU for retrospective review.

Records of enquiries to the information service are reviewed weekly, and selected cases are followed up by writing to the doctor who made the enquiry. An archive of detailed case histories dating back to 1963, when the service was established, is a useful source of information on results of exposure to potentially toxic substances.

This file contained 18 case reports which implicated sheep dip exposure, including four received during or before 1982 (Table 1). Ten cases involved adults, of whom seven had been exposed while working with sheep, one had accidentally ingested sheep dip and two had deliberately ingested it. Eight cases involved children under the age of 12 years, most of whom were exposed by skin contamination, in some cases accompanied by ingestion. Three of the children had fallen into sheep dips.

The active ingredient most frequently implicated was diazinon (10 cases). Chlorfenvinphos (3 cases), propetamphos (4 cases) and carbophenothion (1 case) were also implicated.

Whilst the only death reported was after the purposeful ingestion of 2-4 pints of chlorfenvinphos (16/1986), moderate to severe symptoms were reported in 10 cases as a result of skin contamination occurring during the preparation of sheep dip or during the dipping process. None of the case histories included analytical data on cholinesterase activities.

Since 1983 all enquiries to the to the National Poisons

Information Service (London) about suspected poisoning have been logged on a computer database with a summary of data gathered at the time of the call, including information on active ingredients of products implicated in poisoning incidents. Analysis of the archive of all enquiries to the Information Service between 1983 and 1988, (approximately 500,000 enquiries), to determine whether the data from the follow-up file reflects overall trends in our total enquiries about sheep dips has not yet been carried out.

This initial review indicated that the National Poisons Unit had limited information on accidental and deliberate exposures to sheep dip.

2.6.2 Laboratory facilities

The NPU Laboratory has established various methods for the measurement of pesticides by Gas Liquid Chromatography (GLC) and other analytical techniques. These methods can, in most cases, provide quantitative measurements, but there are some pesticides, including chlorophenoxy herbicides, triazines, organochlorines and glyphosate, for which only qualitative assays can be undertaken. Methods are being established to measure plasma levels of certain organophosphate insecticides, subject to their stability in samples.

The NPU, during its routine dealings with doctors managing cases of suspected pesticide poisoning, has found that red cell cholinesterase estimation is rarely available to either hospital doctors or general practitioners. When such services are available, the results of analyses usually fail to correlate with the clinical effects reported. Work done by the NPU Laboratory suggests two possible reasons for this. Firstly, the methods used are rarely specific enough, and secondly, although the cholinesterase activity in a stored blood sample changes with time, the potential confounding effect of delays in delivery of blood samples is not generally taken into account.

The Unit Laboratory has developed a reliable method for estimating red cell cholinesterase, but little work has been done to identify the optimum storage conditions for blood samples.

2.7 Summary

- a. A retrospective review of cases reported to the Unit found some serious incidents had occurred during the period 1980 - 1988, including one fatality as a result of deliberate ingestion.
- b. The VMD (MAFF) has a comprehensive database system for recording cases of suspected exposure to sheep dips, and other veterinary medicines. However, at present, it is acknowledged that suspected adverse reactions are under-reported.
- c. No single system exists in the UK for assessing hazards from this group of products.

As a result of these findings the NPU, with support from the VMD,

undertook a period of increased surveillance in order to identify cases quickly so that action could be taken to minimise harm if necessary, and to ensure that these incidents would be adequately recorded and evaluated.

3. Methods

3.1 National Poisons Unit toxicovigilance methods

The methods and procedures used in this study to monitor, record and follow up case enquiries, have been used for routine toxicovigilance in the NPU for many years. Each enquiry is recorded in a standard format (annex 1) and summary information is entered to a computer database. Routine surveillance of this body of data is carried out to identify potential problems rapidly and initiate alerts if needed. Toxicovigilance surveys are undertaken to determine the size of the problem and this information is reported to those agencies and authorities responsible for prevention.

3.2 Sheep dip surveillance methods

After obtaining support from the VMD the NPU developed a protocol to:

- a. identify all emergency case enquiries to the National Poisons Information Service (London) relating to sheep dip exposures, and record information on the enquirer's name, address and telephone number, the name, age, sex and symptoms of the patient or patients, the product or substance name, the time since exposure, the route of exposure, and whether the patient was wearing any protective clothing recommended by HSE (Health and Safety Executive, 1991);
- b. request the collection of two 5 ml. EDTA blood samples from every patient, and their urgent dispatch to the NPU laboratory for measurement of red blood cell and plasma cholinesterase activities and other analyses where appropriate; At least two measurements are needed, the first taken soon after exposure and the second after 4-6 weeks.
- c. provide 24 hour consultant medical cover for the duration of the project to discuss all enquiries related to sheep dip, and thereby to improve recording of information at the time of the initial enquiry, improve sample collection and promote compliance with follow-up requests;
- d. follow up all suspected incidents using a specially designed questionnaire; a previous study carried out at the NPU has shown a return rate of approximately 70% of follow-up questionnaires from selected cases of suspected pesticide exposure.
- e. send out, on behalf of the VMD, yellow suspected adverse reaction reporting forms and guidance letters with the NPU follow-up questionnaires.

The project team included a consultant medical toxicologist (VM), two information scientists (IM and HW) and two biochemists (SD and IH).

3.3 Laboratory Analysis

Analyses for red cell cholinesterase and plasma cholinesterase were carried out by the NPU Laboratory. The interval between collection and analysis was kept as short as possible to avoid inaccuracies caused by deterioration during storage.

3.4 Publicity

Although most doctors are aware of the NPU, it was considered appropriate to publicise the survey in the medical and trade journals in order to obtain as comprehensive reporting as possible.

4. Results (Tables 2 and 3)

4.1 Total number of enquiries

The enhanced surveillance was undertaken for the six weeks of the compulsory dipping season, from 22 September to 3 November 1991. During this period, 34 emergency case enquiries related to sheep dip exposure were received by the National Poisons Information Service (London). These represented less than 1% of the total 8,500 emergency case enquiries received by the information service during that period.

4.2 Patient data

Reports were received on 33 adults and one two year old child. The age of the adults, recorded in 30 cases, ranged from 17 - 75 years, with 53% aged over 40 years, and 20% aged over 60 years. They included 29 men and four women.

4.3 Substance data

Information on sheep dip substances was available for 27 (79%) of these cases: diazinon was implicated in 15 cases, propetamphos in 11, and chlorfenvinphos in two (one patient was exposed to a product containing both diazinon and chlorfenvinphos). In one case (7) the history suggested that clinical effects were due to exposure to the phenolic component of a dip.

4.4 Circumstances of exposure and protective clothing

The circumstances of exposure were recorded for 32 emergency case enquiries (94%). Twenty-nine cases were occupational exposures involving farm workers or members of the farmer's family, who were exposed while dipping sheep or handling dip, and in one case while working for several hours in a Portakabin in close proximity to a spill. Three exposures happened accidentally including a child who fell into a dip and her father who gave mouth to mouth resuscitation.

Duration of exposure was specified in 23 occupational cases. Twelve patients had been exposed for one day or less, six had been exposed for between two and four days, one had been exposed for six days and four had been exposed for at least a month.

Information on use of protective clothing was available in 15 of the 29 occupational exposures. According to these reports, two people did not wear any protective clothing and the others used one or more of the recommended items but only two people wore gloves, rubber boots and a bib apron.

It was explicitly stated, or could be inferred from the case history, that 21 patients had used sheep dips before, some for many years, and it is probable that some other patients had previously used dips even though they did not report it.

4.5 Clinical effects

No enquiries were known to have been prompted by asymptomatic exposures, but in two cases information on clinical effects was not available.

Twenty-nine patients reported acute effects after occupational exposure to sheep dips. Clinical effects were judged by VM to be definitely related to the exposure in 10 cases (Tables 2 and 3, case numbers 2, 4, 6, 9, 10, 13, 16, 19, 30, 33). In the remaining 19 cases it was not possible to make a definite link between clinical effects and exposure to sheep dip.

Six patients, four of whom were aged between 59-72 years, reported one or more previous acute symptomatic episodes in addition to the exposure which prompted the enquiry to the information service. However, in only three cases were the acute episodes which prompted the enquiry to the information service judged to be definitely related to sheep dip exposure.

Nine patients (6 of whom were confirmed cases) reported chronic effects.

4.6 Analytical data

Blood samples were sent to the NPU from 17 patients for estimations of red blood cell cholinesterase and plasma cholinesterase activity, in 10 cases an additional one or more samples were sent after an interval of more than four weeks. In two cases blood samples were sent to other laboratories.

In three cases, (6, 9, 10), comparison of two or more measurements showed an increase in red blood cell cholinesterase and plasma cholinesterase activity of more than 25%, more than a month after exposure, indicating the probability that exposure to sheep dip had resulted in depression of cholinesterase activity and acute clinical effects.

For five patients who reported influenza-like symptoms after occupational exposure, (1,5,7,12,14), there was less than 25% increase in red blood cell cholinesterase and plasma cholinesterase activity between the two blood samples. They were

judged to be unconfirmed cases.

Apart from case 7, the patient thought to have been affected by the phenol component of a dip, after a spill outside the Portakabin where he had been working, there does not seem to be any obvious difference between these two sets of cases either in the nature of the clinical effects reported, the wearing of protective clothing, a history of previous exposures, the duration of the latest exposure or the active agent involved.

The analytical results for case 16, judged to be a confirmed exposure, were difficult to interpret, because the cholinesterase activity of the 8 week sample was higher than concentration of the 13 week sample.

Of the cases where only one sample was provided, four (2,4,13,19) were judged on the basis of the case history to be confirmed cases and five were judged to be unconfirmed cases (3,8,11,15,18), although activity was below normal in cases 3, 15, and 18.

Results of analyses performed by HSE for one confirmed case (2) were unavailable at the time of writing this report.

4.7 Clinical assessment

Three patients were referred to the NPU Medical Toxicology Outpatients Clinic and were seen by VM. Another patient, not included in the tables, was referred to the Outpatient Clinic because he had been exposed to sheep dip approximately four years before this compulsory dipping period. Information on clinical assessment for these patients was not available at the time of writing this report.

4.8 Publicity

Considerable publicity for the project was achieved in the medical press (Communicable Disease Report 1991, Hospital Doctor 1991), the trade press (Farmer's Weekly 1991) and the media (Prestige 1991). Unfortunately much of the publicity occurred after the start of the compulsory dipping period rather than before it.

Responding to requests for information from the media was time-consuming, but the publicity was of considerable benefit in raising awareness and increasing the number of reports of adverse effects from sheep dip.

5. Discussion

Many factors influence the risk from contact with sheep dip: the chemical composition of the sheep dip; the amount of pesticide absorbed, which depends on the duration and type of exposure and the use of protective clothing; the age, health and susceptibility of the individual and a history of previous exposure.

There were too few cases in the survey to be able to assess the contribution of different factors or recognise trends. The attributes of the individuals included in the survey varied

widely, even the age range of affected individuals was wider than would normally be expected in a study of occupational health, due to the fact that some farmers were working long after normal retirement age.

In many cases there was insufficient information about the circumstances and duration of the exposure to be able to compare the extent of exposure in different individuals or to assess the contribution of previous exposures to sheep dip. Some patients reporting clinical effects after only a few hours exposure had a history of previous exposure; some having used sheep dips for many years. Some workers may also have been exposed to other organophosphate pesticides used for other purposes, before, during or after sheep dipping, but information about such exposures was obtained for only a few cases and their effect was not considered in this survey as a whole.

Thus there is insufficient information to assess the possibility that clinical effects might, in some cases, have been the result of a number of small repeated doses over several days or weeks rather than the result of a single exposure of only a few hours. Some organophosphates produce inhibition of cholinesterase which is only slowly reversible and repeated doses result in an accumulated inhibition of cholinesterase, producing signs and symptoms only when reaching a critical level.

The clinical effects resulting from exposure to organophosphate sheep dip are nonspecific. Confirmation that clinical effects are related to exposure to organophosphates is best shown by demonstrating that red blood cell cholinesterase and plasma cholinesterase activity were depressed by 20% after exposure. Activity measured 4-6 weeks after exposure should be 25% higher than activity measured within days of exposure.

It is thus important for diagnosis that blood samples are taken as quickly as possible after exposure. This depends on both workers and general practitioners being aware of the significance of influenza-like illnesses developing after use of sheep dip. Workers should consult their general practitioners as soon as possible if they develop such symptoms after using sheep dip, and general practitioners should be aware of the importance of taking blood samples, if the patient is seen soon after the exposure.

There were no individuals in this survey with depressed cholinesterase activity in the absence of clinical effects. Although there had been extensive publicity no doctor requested cholinesterase analyses to check the health of a patient who had been using sheep dip without experiencing clinical effects. However, it is possible for minimal exposure to organophosphates to alter red cell or plasma cholinesterase activity without causing symptoms. There is also evidence that repeated exposure to organophosphates can lead to tolerance to reduced cholinesterase activity, with less physiological response (Murphy, 1986).

Chronic exposure to a toxin is more difficult to identify than acute exposure to a toxin which leads to a time related effect. Incidents of chronic exposure were sought and recorded, but were

less likely to be reported to the Unit. However, investigation of chronic cases was not a priority in the first phase of the surveillance project.

Many studies have been carried out to investigate the late effects of acute exposure to organophosphates, but unfortunately none is above criticism. It is difficult to draw any conclusion as to whether organophosphates, at doses below those causing convulsions, cause long term CNS changes (Levin et al., 1976, Rodnitzky et al 1975, Maizlish et al., 1987, Savage et al., 1988) and this remains one of a number of areas of controversy.

6. Conclusions and recommendations

The results of this first phase have demonstrated a medical problem from occupational exposure to sheep dip. It has also gathered evidence from media reports and from case histories, that not all cases are notified to relevant agencies.

The Unit is in a unique position to obtain detailed information on both circumstances and clinical effects of exposure and to undertake reliable analyses to confirm the diagnosis. This information is very valuable for the assessment of risk and for indicating the need for measures to prevent poisoning, even in some instances, indicating the kind of measures which should be taken. However, it is clear that even with an intensive surveillance programme such as that undertaken for this study, it will be difficult to obtain sufficiently detailed case histories with adequate analytical data to make an assessment of risk.

Further investigation of this problem is needed. The National Poisons Unit will be continuing surveillance between September 1992 to December 1992 with information, medical and analytical toxicology service follow-up continuing for six months after the end of the season. Follow up procedure will be improved by rewriting the original questionnaire and letter and sending a second questionnaire after an interval of at least 4-6 weeks with the request for a second blood sample.

We recommend further cooperation and consultation between all appropriate agencies to discuss ways of increasing the awareness of the medical profession to the possible health hazards for exposure to sheep dips to achieve comprehensive reporting of cases, and to consider ways to improve data collection.

A possible development would be to continue the study for a longer period of time, to follow up and investigate chronic effects and include neurological assessment. More detailed information could be collected on the history of exposure for each individual. The analytical part of any future survey could also include the analysis for active ingredients of sheep dips and their metabolites in the urine. Until now this approach to diagnosis has been mainly a research tool but it could be developed for use in biological monitoring (Minton and Murray, 1988).

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Table 1: Analysis of sheep dip emergency case enquiries with follow up data by year

Case number and year	Age	Sex	Sheep dip	Route of exposure	Type of exposure	Symptoms, time of onset and duration	Treatment	Outcome
1 / 1982	4	M	Carbophenothion 5 mls	Ingestion	Accidental	Increased salivation, muscular weakness and convulsions, all 6 hours post exposure, lasting up to 72 hours; raised liver enzymes	Atropine 0.3 mg Pralidoxime 1.2 g i.v. fluids	Admitted for 12 days
2 / 1980	2.5	M	Chlorfenvinphos	Skin contamination	Accidental: fell into dip for ~10 seconds	None	Decontamination by washing	Admitted overnight
3 / 1980	NK	M	Diazinon	Skin contamination	Occupational; a few splashes over 3 hours	Vomiting, epigastric pain, diarrhoea, headache, all 10 hours post exposure and lasting for 2 - 4 days	Oral fluids	Recovered
4 / 1980	NK	M	Diazinon	Skin contamination	Occupational; a few splashes over 3 hours	Vomiting, epigastric pain, diarrhoea, headache, all 10 hours post exposure and lasting for 2 - 4 days	Oral fluids	Recovered
5 / 1984	1.5	M	Chlorfenvinphos	Skin contamination	Accidental: fell into dip	Pyrexial	Decontamination by washing, chest X-ray, paracetamol	Recovered
6 / 1984	2.5	M	Diazinon	Ingestion and skin contamination	Accidental: totally immersed in dip for a few seconds	None recorded	Ipecac and oral fluids	Admitted for 24 hours
7 / 1984	Adult	M	Diazinon	Ingestion	Accidental: ingestion of approx 5 mls	Vomiting, nausea, epigastric pain, rapid atrial fibrillation and multiple ectopics	Atropine 2 mg, Pralidoxime 1 g, SWO with respiratory protection	Admitted for 2 days

Case number and year	Age	Sex	Sheep dip	Route of exposure	Type of exposure	Symptoms, time of onset and duration	Treatment	Outcome
8 / 1984	Adult	M	Diazinon	Skin contamination and 7 ingestion	Occupational: fell into sheep dip, stayed in wet clothes for 5 mins	None recorded	Decontamination	Refused admission
9 / 1985	Adult	M	Phosmet	Skin contamination	Occupational: wearing clothing contaminated by dip	Nausea, vomiting, epigastric pain, started following day and lasted for 5 days	None	Admitted for 2 days
10 / 1985	21	F	Phosmet	Skin contamination	Occupational: wearing thin gloves for 1.5 hours	Nausea, epigastric pain, diarrhoea, starting day after exposure and lasting 12 hours	None	Recovered
11 / 1985	21	M	Phosmet	Skin contamination	Deliberate: poured over scalp	None recorded	None	Recovered
12 / 1985	Adult	M	Propetamphos	Inhalation	Occupational	Nausea, epigastric pain, sweating, chest pain, dizziness, starting day after exposure and lasting several days	Oral fluids	Recovered
13 / 1985	4	M	Diazinon	Skin contamination and 7 ingestion	Accidental	None recorded	Ipecac and oral fluids	Recovered
14 / 1986	Adult	M	Propetamphos	Skin contamination	Occupational: cut hand whilst putting sheep through dip	Nausea, epigastric pain, sweating, increased salivation, dizziness, muscular weakness and twitching, starting 12 hours post exposure and lasting 36 hours	Atropine 0.5 mg Oral fluids	Admitted 24 hours
15 / 1986	Adult	M	Propetamphos	Skin contamination and inhalation	Occupational: exposed whilst mixing dip	Coughing, chest tightness	None	Recovered

Case number and year	Age	Sex	Sheep dip	Route of exposure	Type of exposure	Symptoms, time of onset and duration	Treatment	Outcome
16 / 1986	Adult	F	Chlorfenvinphos	Ingested	Deliberate; ingested 2 - 4 pints	Vomiting, hypotensive, sweating, increased salivation, muscular twitching, coma	Atropine Pralidoxime 1g BD for 8 days Ventilated	Died
17 / 1986	Adult	M	Diazinon	Skin contamination	Occupational	Nausea, dizziness, sweating, vertigo, all starting within 2 hours of exposure	None	Recovered
18 / 1987	2	F	Propetamphos	Ingestion and skin contamination	Accidental	None recorded	Ipecac	Recovered
19 / 1987	2	F	Diazinon	Skin contamination and inhalation	Accidental	None recorded	Ipecac	Recovered
20 / 1987	11	M	Diazinon	Skin contamination	Accidental exposure lasting 1 hour	Nausea, headache	None	Recovered
21 / 1987	22	F	Diazinon	Skin contamination and inhaled	Occupational exposure lasting 24 hours	Nausea, abdominal pain, sweating, dizziness, muscle twitching	Observation only	Recovered

Table 2: All sheep dip exposures with analytical data

Case Number c=confirmed case	Date of contact	Age	Sex	Substance	Exposure Details	Clinical Effects	Cholinesterase Activity (n.r. RBC >12 Serum >1.6)	Comments
1	24.9.91	56	M	Diazinon	24.9.91: occupational exposure with 3-4 hours dipping. Wore wellingtons only	1-2 days post-exposure: nausea, flushing, ataxia, weakness, twitching, slight sweating, light headed (lasting 1-2 days).	25.9.91: RBC: 14.4 Plasma: 2.1 4.11.91: RBC: 13.15 Plasma: 2.22	Farmer with a history of organophosphate exposure in 1985.
2	early Oct. 91	55	M		Occupational exposure whilst assisting contractor organised dipping, overalls and wellingtons only; continued exposure for 1 month during lambing	2 days post exposure: blurred vision (felt unsafe to drive), fatigue, muscle weakness, headaches, memory impairment and reduction in ability to concentrate; lasting approximately 4 - 5 months, gradual improvement	HSE results Jan 1992	Sheep farmer for more than 20 years, has used same dip for several years, sheep dipped by contractor to reduce exposure
3	7.10.91	40	M	Organophosphate sheep dip, type not specified	6.10.91: occupational exposure whilst washing sheep, ingested 2 mouthfuls	18hrs post exposure: nausea, pyrexia, epigastric pain, weakness, sore throat, insomnia.	7.10.91: RBC: 10.9 Plasma: 4.2	Farmer, exposed whilst washing sheep. Follow up not returned
4	7.10.91	39	M	Propetamphos	7.10.91: occupational exposure to dip	Same evening: vomiting, blurred vision and muscle weakness, admitted to hospital. Long term effect: muscle weakness	(18.10.91 RBC: 303 Plasma: 208) ¹	Works as a shepherd and has several similar exposures. This case was also reported on the Green Card Scheme.
5	11.10.91	67	M	Diazinon	27.9.91-1.10.91: occupational exposure to sheep dip, wore bib apron only.	2.10.91: nausea, vomiting, malaise, sore throat.	2.10.91: RBC: 14.5 Plasma: 2.0 9.12.91 RBC: 16.73 Plasma: 2.35	Farmer, had been wearing contaminated trousers for six days before seeing G.P.

¹ analysis not undertaken at National Poisons Unit laboratory

Case Number C=confirmed case	Date of contact	Age	Sex	Substance	Exposure Details	Clinical Effects	Cholinesterase Activity (n.r. RBC >12 Serum >1.6)	Comments
6 c	11.10.91	46	F	Diazinon	20.9.91: occupational exposure, dipping for 5 hours, wearing gloves, bib apron and wellingtons.	Acute: 20.9.91: headaches for 48 hours, muscular aches and twitching for 7 days 27.9.91: nausea, vomiting, diarrhoea, anxiety, sweating, pyrexia, muscle weakness (lasting 2 weeks)	<u>11.10.91:</u> RBC: 10.0 Plasma: 2.19 <u>9.12.91</u> RBC: 16.7 Plasma: 2.97	Farmer's wife, helps with sheep dipping
7	11.10.91	53	M	diazinon in phenolic base	10.10.91: occupational exposure for 6 hours, after a spill outside the Portakabin where he was working.	Acute: 10.10.91: nausea, sweating, dizziness, ataxia, worst 1 day post exposure 11.10.91: sore throat Chronic: symptoms recurred intermittently for 3-4 months	<u>11.10.91:</u> RBC: 11.0 Plasma: 2.3 <u>28.2.92</u> RBC: 12.33 Plasma: 2.56	Part-time farmer and part time office worker. Uses pyrethroid dip. Clinical effects probably due to phenol after spill.
8	12.10.91	48	F	Not known	Accidental exposure to sheep dip	Flu like symptoms, patient concerned that they were due to sheep dip	<u>16.10.91</u> Plasma: 1.94	Admitted to hospital, consultant concerned to exclude organophosphate exposure
9 c	22.10.91	22	M	Organophosphate exposure, data on which type not available	October 1991: Occupational exposure to dip	Acute: flu like symptoms, follow up data not returned Chronic: fatigue	<u>22.10.91</u> RBC: 7.93 Plasma: 2.82 <u>9.12.91</u> RBC: 14.95 Plasma: 2.69	Referred for consultant medical opinion for fatigue and other symptoms
10 c	24.10.91	30	M	70 Diazinon - follow up not received	14.10.91: occupational exposure to dip, wore overalls and coat, no mask or gloves.	24.10.91: lethargy and shivering	<u>24.10.91:</u> RBC: 5.38 Serum: 3.52 <u>9.12.91</u> RBC: 14.95 Plasma: 2.69 <u>30.3.92</u> RBC: 16.03	Not admitted to hospital, managed by G.P. only
11	26.10.91	49	M	Propetamphos	19.10.91: occupational exposure during dipping	26.10.91: 'flu-like symptoms', nausea, vomiting, sore throat, earache	<u>26.10.91:</u> RBC: 15.5 Plasma: 2.52	Follow up sent but not returned
12	29.10.91	67	M	Chlorfenvinphos	Occupational exposure whilst dipping for 2 days, wore gloves, wellingtons and over-trousers.	1 day post exposure: flu-like symptoms including sweating, muscle weakness, twitching, aches, sore throat.	<u>30.10.91:</u> RBC: 17.1 Plasma: 2.7 <u>18.12.91</u> RBC: 18.3 Plasma: 3.27	Farmer, went to G.P. because he had read about the problem in the papers

Case Number confirmed case	Date of contact	Age	Sex	Substance	Exposure Details	Clinical Effects	Cholinesterase Activity (n.r. RBC >12 Serum >1.6)	Comments
13 c	29.10.91	19	F	Various sheep dips	Last occupational exposure more than 1 month before.	Chronic: nausea, sweating, blurred vision, coughing, dizziness, headache. Patient says she usually gets flu like symptoms day after dipping	29.10.91: RBC: 17.2 Plasma: 2.66	Farmer's daughter, concerned about cumulative effects, has been helping with dipping for 6 years.
14	29.10.91	69	M	Propetamphos	1.10.91: occupational exposure for 2 days whilst loading sheep from dip back into lorry, wore gloves, bib apron and wellingtons	5 - 7 days post exposure has flu like symptoms of nausea, vomiting, epigastric pain, sweating, pyrexia, nosebleeds. These symptoms keep recurring after exposure to sheep dip.	29.10.91 RBC: 18.8 Plasma: 3.03 9.12.91 RBC: 19.85 Plasma: 3.22	24.10.91: Hb, WBC and platelets normal
15		31	M				29.10.91 RBC: 14.6 Plasma: 1.56	
16 c	8.11.91	30	M	Diazinon and chlorfenvinphos	4.10.91: occupational exposure to dip without using protective clothing	Flu like symptoms of pyrexia, shortness of breath and muscle aching for 3 weeks after re-exposure.	2.12.91 RBC: 12.3 Plasma: 4.51 13.1.92 RBC: 8.65 Plasma: 4.6	Shepherd, has worked with sheep for 12 years and has done contract sheep dipping. Also uses organophosphates for cereal and pest control.
17	27.11.91	2	F	Propetamphos	27.10.91: accidental: fell into dip	Respiratory Arrest,	27.11.91 RBC: 15.38 Plasma: 2.08 2.12.91 RBC: 14.35 Plasma: 2.66	
18		29	M				14.1.92 RBC: 9.5 Plasma: 5.6	
19 c	30.3.92	53	M	Diazinon	September 1991: 1 hour and 5 hours occupational exposure to sheep dip	Acute: sweating, paraesthesia, blurred vision, dizziness, anxiety, chest tightness, muscular weakness and twitching Chronic intermittent: sweating, dizziness, muscular twitching, mildly abnormal liver function	31.3.92 RBC: 21.03 Plasma: 2.47	Small farm farmer. Has been referred to local medical consultant.

Table 3: All sheep dip emergency case enquiries without analytical data

Case Number confirmed case	Date of contact	Age	Sex	Substance	Exposure Details	Clinical Effects	Cholinesterase Activity (n.r. RBC >12 Serum >1.6)	Comments
20	19.9.91	65	M	Diazinon	15.9.91: occupational exposure for 4 days, wore mask only	Within 12 hours: nausea, sweating, vomiting, weakness, tremor, pain in legs.	Sample sent but not received	Has used dip for last 3-4 years.
21	3.10.91	17	M	Diazinon	3.10.91: occupational exposure to dip for six hours, no protective clothing, but did shower after exposure	Went to hospital as 2 - 3 hours after exposure developed nausea, flushed, tachycardia	Sample requested but not received	Farm labourer, sheep was drowning in dip, patient went in and pulled sheep out
22	11.10.91	65	M	Propetamphos	9 - 11.10.91: occupational exposure to dip	Within 24 hours: epigastric pain (lasting 2 days), hypersalivation (lasting few hours), muscle weakness, tight chest, s.o.b. depressed peak flow (lasting 1-2 days).	Sample requested but not received	Farmer, experienced a similar incident 12 years ago, that dip since withdrawn. Admitted to hospital 11.10.91. for 3 days for observation
23	24.10.91	75	M	Diazinon	Occupational exposure for approx 4 hours for 3 days.	After last dipping: flu like symptoms, tight chest, sweating, weakness, muscle aches; in bed for 2 days, unfit to work for 1 week	Time since exposure more than two weeks, sample not requested	Farmer, occupational exposure to dip in June and October for the last "several" years.
24	30.10.91 (Letter)	59	M	Diazinon	10.7.91 & 9.10.91: occupational exposure to dip, wore wellingtons only.	After last dipping, developed nausea, epigastric pain, anorexia, sweating, dizziness, tight chest, muscle weakness and stiffness, and fatigue.	Sample not requested	Farmer, also developed flu like symptoms after spring dipping
25	5.11.91	Adult	M	Diazinon	Occupational exposure to dip	Flu like symptoms and fatigue for up to 1 month post-exposure	Sample not requested as interval between dipping and enquiry over 1 month	Small holders dipping 25 sheep; same dip used every year, see case number 26. Patient is also a G.P.

Case Number c=confirmed case	Date of contact	Age	Sex	Substance	Exposure Details	Clinical Effects	Cholinesterase Activity (n.r. RBC >12 Serum >1.6)	Comments
26	5.11.91	Adult	F	Diazinon	Occupational exposure to dip	Flu like symptoms 1 day post exposure, fatigue/malaise for 1 week after dipping	Sample not requested as interval between dipping and enquiry over 1 month	Small holders dipping 25 sheep; same dip used every year, see case number 25.
27	5.11.91	Adult	M	Diazinon	Occupational exposure to dip	Non-specific neuralgia for the last 2 years.	Sample not requested as interval between dipping and enquiry over 1 month	Farmer
28	12.11.91 (Letter)	59	M	Propetamphos	Occupational exposure to dipped sheep: knees got wet from sheep.	Furunculosis	Sample not requested	.Dipped sheep using full protective clothing, exposed in ordinary clothing 1 week later
29	12.11.91 (Letter)	23	M	Propetamphos	Occupational exposure to dipped sheep: knees got wet from sheep	Furunculosis	Sample not requested	Dipped sheep using full protective clothing, exposed in ordinary clothing 1 week later
30 c	15.11.91 (Letter)	72	M	Diazinon	12.10.91 for 1.5 hr: occupational exposure to dip, wore bib apron and wellingtons	19.10.91: blurred vision, ataxia, dizziness, tight chest, shortness of breath, poor memory and irritability; reported exposure and symptoms to G.P. on 28.10.91	Sample not requested as interval between dipping and enquiry over 1 month	Farmer, previous recorded occupational exposure to dip on 16.6.91 for 1.5 hr when he experienced similar symptoms
31	27.11.91	Adult	M	Propetamphos	27.10.91:accidental	shock and anxiety	Sample requested, not received	Gave daughter mouth to mouth resuscitation
32	28.11.91	44	M	Propetamphos	Continual and intermittent occupational exposure to dip for one month (October), wore wellingtons only.	Acute: dizziness, flu like symptoms of hypersalivation, coughing, tight chest, anxiety, coughing; symptoms present for 2 - 3 days after each dipping, then improving.	Sample not requested as interval between dipping and enquiry over 1 month	Farmer; chronic chest problems after routine use

Case Number C=confirmed case	Date of contact	Age	Sex	Substance	Exposure Details	Clinical Effects	Cholinesterase Activity (n.r. RBC >12 Serum >1.6)	Comments
33 c	28.11.91	27	M	Propetamphos	Multiple occupational exposures; wore wellingtons and bib apron only; skin contamination, inhalation and eye contact.	Acute: flu like symptoms and fatigue for 2 days following exposure Chronic: nausea, epigastric pain, anorexia, sweating, blurred vision, dizziness, flushing, anxiety, sore throat, headache, memory loss, difficulty in concentration; severity of symptoms vary and improve between dipping and handling wet or warm sheep.	Sample not requested as interval between dipping and enquiry over 1 month	Farmer and contractor; sheep dip used approximately every 3 weeks from July to November.
34	28.11.91	24	M	Propetamphos	27.10.91: occupational exposure to dip, wore wellingtons only; skin contamination of face from splash.	Acute: dizziness, local skin rash on face with burn type reaction with vesicles around mouth and nose. On follow up, area affected has become hyperpigmented	Sample not requested as Interval between dipping and enquiry over 1 month	Farmer / forestry

Table 3: All sheep dip emergency case enquiries without analytical data

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20	19.9.91	65	M	Diazinon	15.9.91: occupational exposure for 4 days, wore mask only	Within 12 hours: nausea, sweating, vomiting, weakness, tremor, pain in legs.	Sample sent but not received	Has used dip for last 3-4 years.
21	3.10.91	17	M	Diazinon	3.10.91: occupational exposure to dip for six hours, no protective clothing, but did shower after exposure	Went to hospital as 2 - 3 hours after exposure developed nausea, flushed, tachycardia	Sample requested but not received	Farm labourer, sheep was drowning in dip, patient went in and pulled sheep out
22	11.10.91	65	M	Propetamphos	9 - 11.10.91: occupational exposure to dip	Within 24 hours: epigastric pain (lasting 2 days), hypersalivation (lasting few hours), muscle weakness, tight chest, s.o.b. depressed peak flow (lasting 1-2 days).	Sample requested but not received	Farmer, experienced a similar incident 12 years ago, that dip since withdrawn. Admitted to hospital 11.10.91. for 3 days for observation
23	24.10.91	75	M	Diazinon	Occupational exposure for approx 4 hours for 3 days.	After last dipping: flu like symptoms, tight chest, sweating, weakness, muscle aches; in bed for 2 days, unfit to work for 1 week	Time since exposure more than two weeks, sample not requested	Farmer, occupational exposure to dip in June and October for the last "several" years.
24	30.10.91 (Letter)	59	M	Diazinon	10.7.91 & 9.10.91: occupational exposure to dip, wore wellingtons only.	After last dipping, developed nausea, epigastric pain, anorexia, sweating, dizziness, tight chest, muscle weakness and stiffness, and fatigue.	Sample not requested	Farmer, also developed flu like symptoms after spring dipping
25	5.11.91	Adult	M	Diazinon	Occupational exposure to dip	Flu like symptoms and fatigue for up to 1 month post-exposure	Sample not requested as interval between dipping and enquiry over 1 month	Small holders dipping 25 sheep; same dip used every year, see case number 26. Patient is also a G.P.

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22	11.10.91	65	M	Propetamphos	9 - 11.10.91: occupational exposure to dip	Within 24 hours: epigastric pain (lasting 2 days), hypersalivation (lasting few hours), muscle weakness, tight chest, a.o.b. depressed peak flow (lasting 1-2 days).	Sample requested but not received	Farmer, experienced a similar incident 12 years ago, that dip since withdrawn. Admitted to hospital 11.10.91. for 3 days for observation
23	24.10.91	75	M	Diazinon	Occupational exposure for approx 4 hours for 3 days.	After last dipping: flu like symptoms, tight chest, sweating, weakness, muscle aches; in bed for 2 days, unfit to work for 1 week	Time since exposure more than two weeks, sample not requested	Farmer, occupational exposure to dip in June and October for the last "several" years.
24	30.10.91 (letter)	59	M	Diazinon	10.7.91 & 9.10.91: occupational exposure to dip, wore wellingtons only.	After last dipping, developed nausea, epigastric pain, anorexia, sweating, dizziness, tight chest, muscle weakness and stiffness, and fatigue.	Sample not requested	Farmer, also developed flu like symptoms after spring dipping
25	5.11.91	Adult	M	Diazinon	Occupational exposure to dip	Flu like symptoms and fatigue for up to 1 month post-exposure	Sample not requested as interval between dipping and enquiry over 1 month	Small holders dipping 25 sheep; same dip used every year, see case number 26. Patient is also a G.P.