HSE
Health & Safety Executive

Symptom-reporting following occupational exposure to organophosphate pesticides in sheep dip

Prepared by the
Institute of Occupational Health
University of Birmingham
for the Health and Safety Executive

CONTRACT RESEARCH REPORT
371/2001

HSE
Health & Safety Executive

Symptom-reporting following occupational exposure to organophosphate pesticides in sheep dip

C A Jackson & A Spurgeon
Institute of Occupational Health
University of Birmingham
Edgbaston
B15 2TT

The aim of the study was to investigate whether the acute symptoms reported by farmers less than 24 hours after dipping with organophosphates (OPs) could be plausibly grouped into distinct symptom categories. Re-analysis of the symptom data obtained in the Health and Safety Executive's (HSE's) Contract Research Report 74/1995 was performed in order to identify any recognisable cluster of core symptoms in exposed subjects, and to evaluate if exposed and control subjects differed in their pattern of symptom reporting. The core symptom groups were also analysed alongside a surrogate of exposure data to assess if significant increases in reporting of any core symptoms were dose-related.

This report and the work it describes was funded by HSE. Its contents, including any opinions and/or conclusions expressed, are those of the authors alone and do not necessarily reflect HSE policy.

HSE BOOKS

First published 2001

ISBN 0 7176 2111 1

ACKNOWLEDGEMENTS

The authors acknowledge the support of the Health and Safety Executive in funding this work. Particular thanks are due to Dr Roger Rawbone for helpful comments and advice throughout, and also to the sheep farmers and quarry workers who participated in the original study used as the basis for this re-analysis.

CONTENTS

EXECUTIVE SUMMARY

The aim of the study was to investigate whether acute effects occurring in farmers who experience repeated exposure to organophosphates (OP's) through sheep dipping can be identified and classified as groups of core symptoms. The exposed group from the original study (HSE 74/1995) whose data formed the basis for the present re-analysis consisted of 146 male sheep farmers and farm workers (mean age 48 ± 9.8). The control group was comprised of 143 male quarry workers (mean age 43 ± 10.9) from the same geographical areas. Acute and delayed effects were assessed using a Symptoms Questionnaire, administered before exposure, 24 hours after exposure, and between 3-4 weeks after exposure. Information on exposure to OPs was obtained by biological monitoring (assessment of urinary metabolites) and by questionnaire. Controls completed the symptom questionnaire at comparable time intervals but without exposure to OPs. In the original study urinary diakylphosphate levels were significantly elevated in the exposed group following dipping, confirming recent exposure. Evidence of increased symptom reporting was however inconclusive. Controls were found to have significantly more reports of cardio-respiratory symptoms than exposed after dipping, while exposed subjects had significantly more reports of global symptoms after dipping than controls. There appeared to be little evidence of delayed symptoms consistent with delayed-effect syndromes previously reported in association with some forms of OP exposure.

Re-analysis of the original data showed that symptoms reported by dippers at 24 hours post dip were not on the whole representative of the anecdotal reports of "dippers' flu". Dippers and quarry workers differed in terms of the frequency of reporting of 25 individual symptoms, although only eleven of these were to the detriment of exposed workers. There was a moderate correlation (r=.34) between the symptoms reported by exposed and control subjects at 24 hours post-dip. Factor analysis showed that 38 symptoms distributed over 6 individual factors best represented the original symptom reports of exposed workers at 24 hours post-dip, but no significant association was found between symptom scores on these factors and the number of dipped sheep (exposure). It should be noted however that after removing missing cases, symptom data were available for only 100 cases and 96 controls, and the low number of cases relative to the number of symptom variables were not optimal conditions for factorial analysis and data reduction. Exposure was a better predictor of the sum of the 21 symptoms reported most frequently by dippers at 24 hours post-dip. However flock size still only accounted for thirteen percent of the variance in symptom reports. Subsequent cluster analysis of these 21 symptoms produced 5 symptom clusters. Data suggested that exposed individuals did report significantly more symptoms than controls after recent dipping, when measured on 3 of the 5

symptom clusters derived from k-means cluster analysis of the original data, as well as the total of those 5 clusters. This provides some tentative support for the view that future investigations of recently OP exposed workers could use smaller checklists of 21 symptoms spread across five clusters.

1. INTRODUCTION

There continue to be anecdotal reports amongst agricultural workers of acute symptoms following exposure to organophosphate pesticides (OPs). Although symptoms of acute intoxication, following high level exposure are well-defined[1,2] a range of non-specific symptoms have often been reported following lower level exposure, apparently in the absence of a significant cholinergic response as measured by changes in blood levels of cholinesterase. Because these symptoms often appear to mimick those present in a flu-like illness the term "dippers flu" has often been used to describe the condition. However the definition and severity of acute symptoms following exposure below levels normally associated with intoxication remains controversial.

In the UK, sheep farmers involved in sheep dipping have expressed considerable concern about this problem. However, only a few studies have collected data on symptoms before and shortly following exposure. A small-scale study of 24 Welsh sheep dippers [3] identified some symptoms consistent with cholinesterase inhibition despite only very small observed changes in erythrocyte and plasma cholinesterase levels before and after dipping.

The Institute of Occupational Health at Birmingham University investigated a larger sample of sheep dippers and matched controls as part of a wider investigation of the acute and chronic effects of exposure to organophosphates[4,5]. In this study, a symptom questionnaire was completed by sheep dippers the day before dipping, 24 hours post dip-completion and three weeks later. Controls completed the same questionnaire at similar time intervals but without exposure to OPs. Symptoms were selected for inclusion in the questionnaire on the basis of their having been reported at least once in a set of thirty eight papers, case histories and articles previously identified as reporting the acute, chronic or delayed effects of OP exposure. Some distractor items (symptoms which had never been associated with OP exposure) were also included as a correction for over-reporting. For the purpose of analysis, symptoms were grouped into eight categories as follows: cardio-respiratory; gastro-intestinal; localised; visual; cognitive; non-specific; global; distractor. (Table 1). These groupings were formed on an intuitive rather than a statistical basis. The list of individual symptoms and symptom groups is shown in Appendix 1.

Analysis was carried out to determine whether there was an increase in overall symptom reporting or reporting of any particular group of symptoms in sheep dippers during the dipping period relative to the level of symptom reporting in the control group.

Table 1: Table of symptom groups used in the original study Reproduced from HSE 74/1995

Grouping	Number of symptoms in group
Cardio-respiratory	10
Gastro-intestinal	13
Global symptoms	12
Localised symptoms	12
Visual symptoms	3
Psychiatric symptoms	4
Cognitive symptoms	6
Non-specific symptoms	7
All symptoms	67
Distracters symptoms	6
Total	**73**

The results of the study indicated that total symptom reporting, or reporting of symptom groups was not elevated in exposed subjects relative to that of controls. However, this was not consistent for all symptoms and it is possible that the particular (intuitive) grouping of symptoms adopted may have masked symptom patterns that could be revealed by a statistically - based approach. The current report therefore addresses this possibility by conducting further analysis on the original symptom data.

2. AIMS & OBJECTIVES

The rationale for the present report was that a more detailed statistical analysis of the symptoms reported by the sheep dippers might provide additional information on symptom patterns evident in sheep dippers following dipping, and that this in turn might provide the basis for comparison of symptom reporting between dippers and controls and for the investigation of dose-effect relationships in the OP exposed dippers group.

The specific objectives were therefore as follows:

a) **to establish a plausible basis for grouping of symptoms contained in the symptom questionnaire, independent of that used in the original report**

b) **to identify any cluster of recognizable core -symptoms, consistently present in exposed subjects**

c) **to determine whether exposed subjects and controls differ significantly in terms of the pattern of symptom reporting as identified on the basis of (a) and (b)**

d) **to determine whether any identified significant increase in symptom reporting in exposed subjects is dose-related**

3. SUMMARY OF THE METHOD AND RESULTS OF HSE 74/1995

1.1 SUMMARY OF METHOD

Symptom reports were collected from exposed sheep dippers on three occasions – prior to dipping, 24 hours after dipping, and between 3 and 4 weeks after dipping. Information on the number of sheep dipped by each dipper was also recorded. Symptom reports were collected on three occasions from non-exposed controls (quarry workers) at the same period in time as the sheep farmers. Data were collected by field workers completing standardised interviews and questionnaires with subjects.

> *"…(the) questionnaire was constructed in order to quantify symptoms occurring following short term exposure at the time of sheep dipping. Symptom items were compiled from a review of both the scientific and general literature concerned with the effects of exposure to OPs. The review produced an index of reported acute, delayed and chronic effects of short and long term exposure to OPs. This index was compiled into the 67 items appearing in the questionnaire, to which were added a further six distracter items, to control for over responding."*

> *"The time frame of symptom occurrence was set to "within the last 24 hours". Items were arranged in random order on the questionnaire. Responses were "not at all", "some of the time", "most of the time" and "all of the time" for each item, and these were respectively scored 0, 1, 2 and 3."*

Urine samples, for analysis of metabolites of the OP diazinon, were collected from sheep dippers within 24 hours of dipping and from a sample of controls during a comparable time period.

1.2 SUMMARY OF RESULTS

Scores for the symptom groups were subjected to unpaired t-tests between exposed and control subjects, for both pre-dip, post-dip and delayed-effect stages, the results of which are shown in Tables 2a – 2c.

Table 2a: Mean scores (SD) for the Symptoms Questionnaire for exposed and control groups before dipping (n=215) in the original study. Reproduced from HSE 74/1995

Session	Pre-dip		
Group	**Exposed**	**Controls**	**P**
Total symptoms (219)	9.47 (11.1)	12.98 (12.8)	.035
Cardio-respiratory (30)	1.50 (2.2)	2.94 (2.9)	<.0001
Gastro-intestinal (39)	1.32 (2.6)	2.01 (2.7)	.061
Global (36)	2.37 (3.0)	2.38 (3.0)	.995
Localised (36)	1.62 (2.1)	2.19 (3.0)	.114
Visual (9)	0.40 (0.8)	0.58 (0.9)	.137
Cognitive (18)	1.17 (1.7)	1.26 (1.7)	.697
Psychiatric (12)	0.53 (.09)	0.68 (1.1)	.280
Flu (18)	1.32 (1.8)	1.49 (1.9)	.508
Non-specific (21)	1.00 (1.5)	1.36 (1.7)	.099
OP symptoms (42)	1.33 (2.3)	2.33 (3.1)	.008
Distracter items (18)	0.55 (0.8)	0.93 (1.2)	.007

Table 2b: Mean scores (SD) for the Symptoms Questionnaire for exposed and control groups 24 hours post dp (n=215) in the original study. Reproduced from HSE 74/1995

Session	24 hrs post-dip		
Group	**Exposed**	**Controls**	**P**
Total symptoms 219)	10.32 (11.8)	10.32 (11.4)	.997
Cardio-respiratory (30)	1.65 (2.3)	2.46 (2.5)	.014
Gastro-intestinal (39)	1.56 (2.5)	1.45 (2.5)	.758
Global (36)	2.92 (3.2)	1.93 (3.0)	.021
Localised (36)	1.76 (2.3)	1.83 (2.8)	.836
Visual (9)	0.56 (1.0)	0.42 (0.8)	.254
Cognitive (18)	0.86 (1.7)	0.92 (1.4)	.799
Psychiatric (12)	0.43 (0.9)	0.58 (0.9)	.244
Flu (18)	1.67 (1.9)	1.35 (1.9)	.216
Non-specific (21)	0.96 (1.3)	1.19 (1.6)	.271
OP symptoms (42)	1.26 (2.3)	1.69 (2.9)	.223
Distracter items (18)	0.58 (0.9)	0.73 (1.1)	.292

Table 2c: Mean scores (SD) for the Symptoms Questionnaire for exposed and control groups 3-4 weeks post dip (n=215) in the original study. Reproduced from HSE 74/1995

Session	3-4 wks post-dip		
Group	**Exposed**	**Controls**	**P**
Total symptoms 219)	10.04 (12.1)	11.98 (11.8)	.237
Cardio-respiratory (30)	1.41 (2.3)	2.49 (2.6)	.001
Gastro-intestinal (39)	1.42 (2.3)	1.67 (2.7)	.487
Global (36)	2.69 (3.4)	1.89 (2.8)	.063
Localised (36)	1.58 (2.4)	3.22 (3.3)	<.0001
Visual (9)	0.58 (1.2)	0.38 (0.8)	.134
Cognitive (18)	1.18 (1.9)	0.89 (1.5)	.214
Psychiatric (12)	0.50 (1.0)	0.65 (1.1)	.296
Flu (18)	1.45 (1.8)	1.38 (2.0)	.776
Non-specific (21)	0.97 (1.2)	1.32 (1.7)	.080
OP symptoms (42)	1.36 (2.4)	1.68 (2.7)	.369
Distracter items (18)	0.66 (1.1)	0.80 (1.3)	.402

In addition, changes in symptom reporting levels over the period of the three questionnaires were recorded in terms of difference scores for each symptom group i.e. the difference between questionnaire 2 (24 hours post dip) and the pre-dip questionnaire and the difference between questionnaire 3 and the pre-dip questionnaire. Difference scores for exposed and control groups were compared using unpaired 't' tests. The results are shown in Table 2d.

Table 2d: Difference between mean scores on the symptoms questionnaire, between sessions 24 hours post-dip and pre-dip, and 3-4 weeks post-dip and pre-dip for exposed and control groups. Reproduced from HSE 74/1995

Session	24 hours post-dip - baseline			3-4 wks post-dip - baseline		
Group	**Exposed**	**Controls**	**P**	**Exposed**	**Controls**	**P**
Total symptoms 219)	0.52	-2.55	.005	0.50	-1.28	.111
Cardio-respiratory (30)	0.16	-0.52	.020	-0.01	-0.58	.047
Gastro-intestinal (39)	0.08	-0.55	.037	0.01	-0.37	.269
Global (36)	0.52	-0.43	.007	0.41	-0.60	.002
Localised (36)	0.09	-0.33	.090	-0.05	1.02	.004
Visual (9)	0.06	-0.16	.066	0.14	-0.19	.004
Cognitive (18)	-0.34	-0.30	.808	-0.05	-0.39	.083
Psychiatric (12)	-0.12	-0.08	.690	-0.02	-0.03	.945
Flu (18)	0.25	-0.11	.101	0.17	-0.16	.151
Non-specific (21)	-0.02	-0.18	.296	-0.04	-0.04	.664
OP symptoms (42)	-0.16	-0.65	.101	-0.01	-0.67	.020
Distracter items (18)	0.07	-0.18	.047	0.07	-0.15	.150

Urinary dialkylphosphate levels of sheep dippers following dipping were significantly elevated relative to those of controls, confirming the dippers' recent exposure to OPs. Despite this, the symptom data did not suggest a marked increase in their symptom reporting following dipping. Perhaps surprisingly there appeared to be a general tendency for controls to report more symptoms at all points than exposed subjects, particularly cardio-respiratory symptoms which were reported significantly more frequently in the control group both pre-dip and subsequently. However, the exposed group did report significantly more global symptoms than controls at 24 hours post dip, a difference that resulted from an increase in the symptoms of the dippers and a decrease in the symptoms of the controls over a corresponding period. Therefore although this analysis did not provide strong evidence for acute symptoms associated with dipping, there were some indications of an increase in some particular symptoms which might merit further investigation.

4. METHOD

Given the focus on acute symptoms of OP exposure, the initial analysis involved only the data set comprising the symptom data collected 24 hours post-dip for sheep dippers. This data set also provided a simple exposure metric (number of sheep dipped) to allow for the investigation of dose-effect relationships.

4.1 DATA USED FOR RE-ANALYSIS

The original data consisted of completed symptom questionnaires (73 individual symptoms) for exposed dippers (n=119) and control quarry workers (n=118). Each symptom-response was coded with 0, 1, 2 or 3 representing "not at all", "some of the time", "most of the time" and "all of the time" respectively. Along with the 73 individual symptoms, each subject also had a score for each of the eight symptom groups, and a distractor symptom score i.e. symptoms with no reported associations with OP exposure, included as a check for over-reporting.

4.2 STRATEGY FOR RE-ANALYSIS

The strategy for the re-analysis of the original symptom data is shown below:

- Cluster analysis of symptom data using original symptom groups
- Rank individual symptoms by frequency
- Chi square analyses of individual symptoms
- Clean existing data and remove missing cases
- Factor analysis of 73 original symptoms
- Investigation of dose-effect relationships
- Cluster analysis of the symptom data

4.2.1 Rank Individual Symptoms by Frequency

Individual symptom responses were re-coded, with the original symptom reports of "some of the time (1)", "most of the time (2)" and "all of the time (3)" being re-coded as a value of "symptom confirmed (1)". The symptom report of "not at all (0)" remained un-altered. Cases of "symptom confirmed" for each individual symptom were summed, providing a rank table of the most frequently reported symptoms at 24 hours post-dip, for both exposed and control subjects.

4.2.2 Chi Square Analyses of Individual Symptom Reports

The frequency of confirmations of each symptom 24 hours post-dip were subjected to chi square analyses, with Yates' correction for continuity applied to any test when observed frequencies were less than 10.

4.2.3 Clean Existing Data and Remove Missing Cases

The symptom data collected 24 hrs post-dip included both exposed dippers (n=119) and control quarry workers (n=118). After casewise deletion of those individuals with missing data points, this was reduced to n=100 and n=96 respectively.

4.2.4 Factor Analysis of 73 Original Symptoms

Using the cleaned dataset containing 24 hours post-dip symptom reports for exposed subjects only, the 73 symptoms were subjected to factor analysis using principal components methods and varimax rotation.

4.2.5 Investigation of Dose-Response Relationships

Using different combinations of symptoms as outcome variables, the size of flock dipped 24 hours prior to symptom measurement was used as a predictor variable, being a surrogate measure of OP exposure. Linear regressions were performed to predict symptom outcomes from the exposure variable of number of recently dipped sheep.

4.2.6 Cluster Analyses of Symptom Data

Different cluster analyses were performed on the 24 hours post dip data obtained from exposed subjects only. Significance testing on such extracted clusters was performed between exposed and control subjects.

5. RESULTS

The exposed subjects' scores at 24 hour post-dip on the eight symptom groups used in the original study were subjected to cluster analysis using single linkage based on euclidian distance. The result was as shown in figure 1. The linkage between symptom groups appears to show little intuitive concordance in physiological terms of those groups that are clustered together. One possible explanation of the clusters offered by the analysis could be that of "belief in one's general malaise" – the two groups of globalised and non-specific symptoms would represent a general feeling of ill-health or fatigue of a diffuse nature. The next cluster of psychiatric symptoms could represent a symptomology of exposed individuals who possess a belief that they are unwell. This in turn would have much concordance with the next cluster of cognitive symptoms, which have the potential to be influenced by a belief of being generally unwell. It is noteworthy that symptom groups concerning specific target systems or organs (cardio-respiratory, gastro-intestinal, localised, distractor and visual) are located as the clusters become increasingly similar and vague, while symptom syndromes more susceptible to individuals' beliefs of non-specific or general illness are located as the most distinct symptom groups

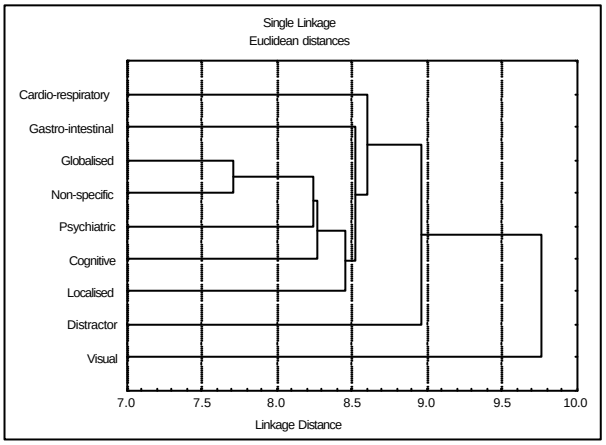


Figure 1
Cluster analysis of the eight original symptom groups and distractor symptoms, using data obtained 24 hours post-dip

5.1 SYMPTOM FREQUENCY

The frequency of confirmation of individual symptoms for both exposed and control subjects was established for the data collected 24 hours post-dip, and appears in Appendix 2. Symptoms are ordered by the most frequently occurring in the exposed group, and a comparative rank is given for the control group. Tables 3-5 also show the top-ten most frequently reported symptoms for both the exposed and control group, with symptoms common to both

occupational groups italicized. It is of interest to note that of the ten symptoms reported most frequently by the exposed group, only two (headache and weak muscles) are consistent with traditional reports of a flu-like illness. One of the ten symptoms reported most frequently by the control group (general ache) was also consistent with such an illness.

Table 3: Ten most frequently reported symptoms for both occupational groups at 24 hours-post dip

Exposed N=119					Controls N=118				
Symptom	**No**	**Yes**	**%**	**Rank**	**Symptom**	**No**	**Yes**	**%**	**Rank**
Gen. cramp	57	53	48.1	1	Gen. Ache	54	54	50	1
Lethargy	63	46	42.2	2	*Sneezing*	57	50	46.7	2
Headache	67	43	39	3	Cough	62	45	42.1	3
Shiver	69	41	37.2	4	*Lethargy*	66	41	38.3	4
Runny nose	70	40	36.3	5	*Runny nose*	67	41	38	5
Weak muscles	70	39	35.7	6	Cough phlegm	69	39	36.1	6
Stiff joints	74	34	31.4	7	Forgetfulness	74	34	31.5	7
Excess sleep	77	32	29.3	8	*Stiff joints*	74	33	30.8	8
Dry mouth	78	31	28.4	9	Aggression	78	30	27.8	9
Sneezing	80	29	26.6	10	*Excess sleep*	80	28	25.9	10

Table 4: Ten most frequently reported symptoms for recently exposed sheep dippers

			Exposed N=119		
Symptom	**No**	**Yes**	**%**	**Rank**	**Associated with**
Gen. cramp	57	53	48.1	1	
Lethargy	63	46	42.2	2	
Headache	67	43	39	3	"Dippers' flu"
Shiver	69	41	37.2	4	
Runny nose	70	40	36.3	5	
Weak muscles	70	39	35.7	6	"Dippers' flu"
Stiff joints	74	34	31.4	7	
Excess sleep	77	32	29.3	8	
Dry mouth	78	31	28.4	9	
Sneezing	80	29	26.6	10	

Table 5: Ten most frequently reported symptoms for non-exposed quarry workers

			Control N=118		
Symptom	**No**	**Yes**	**%**	**Rank**	**Associated with**
Gen. Ache	54	54	50	1	"Dippers' flu"
Sneezing	57	50	46.7	2	
Cough	62	45	42.1	3	
Lethargy	66	41	38.3	4	
Runny nose	67	41	38	5	
Cough phlegm	69	39	36.1	6	
Forgetfulness	74	34	31.5	7	
Stiff joints	74	33	30.8	8	
Aggression	78	30	27.8	9	
Excess sleep	80	28	25.9	10	

The frequency of symptoms at 24 hour post-dip being reported by each group were subjected to chi square analysis. With a typical significance level of 5%, it would be expected that out of 73

individual chi square analyses, there would be significant differences in symptom reporting between the exposure groups by chance alone for at least 3 – 4 symptoms. Table 6 presents the results of chi square analyses for symptom reports between the two occupational groups.

Table 6: Frequency of symptoms reported by sheep dippers after recent exposure and control subjects, ranked by greatest frequency in the exposed group

Symptom	Yes in exposed N=119	Yes in controls N=118	X^2	P	> frequency in….	Rank (exposed)
Gen. cramp	53	10	39.23	0.000	Exposed	1
Lethargy	46	41	0.34	0.560		2
Headache	43	24	7.05	0.007	Exposed	3
Shiver	41	8	25.87 [y]	0.000	Exposed	4
Runny nose	40	41	0.06	0.800		5
Weak muscles	39	18	10.23	0.001	Exposed	6
Stiff joints	34	33	0.01	0.910		7
Excess sleep	32	28	0.32	0.570		8
Dry mouth	31	25	0.72	0.390		9
Sneezing	29	50	9.43	0.002	Controls	10
Sleep walking	28	1	26.3 [y]	0.000	Exposed	11
Thinking problems	28	13	6.42	0.011	Exposed	12
Productive cough	27	45	3.14	0.070		13
Judging distance	27	4	17.98 [y]	0.000	Exposed	14
Numb toes	26	8	9.71 [y]	0.001	Exposed	15
Sore throat	25	24	0.03	0.870		16
Cough	25	45	9.01	0.002	Controls	17
Nose bleeds	23	5	11.32 [y]	0.000	Exposed	18
Feeling down	22	25	0.36	0.540		19
Excess sweating	19	17	0.11	0.730		20.5
Judging time	19	17	0.09	0.760		20.5
Skin eruptions	16	8	2.15 [y]	0.140		22
Cough blood	18	45	16.07	0.001	Controls	24
Dizziness	18	9	2.46 [y]	0.110		24
Ear ache	18	4	8.28 [y]	0.004	Exposed	24
Blurred vision	16	10	0.99 [y]	0.310		26
Problems seeing	16	10	1.09 [y]	0.290		27
Forgetfulness	16	34	8.64	0.003		28
Poor libido	15	13	0.14	0.700		29
Stomach pain	15	8	1.63 [y]	0.200		30
Sore feet	14	11	0.14 [y]	0.700		31
Heartburn	13	19	1.32	0.250		32
Upset stomach	13	13	0	0.960		33
Breathlessness	11	17	1.08 [y]	0.290		36
Watery eyes	11	21	3.88	0.048	Controls	36
Stiff muscles	11	27	8.52	0.003	Controls	36
Twitching muscles	11	13	0.25	0.610		36
Speech difficulty	11	9	0.05 [y]	0.830		36
Fever	10	2	4.25 [y]	0.039	Exposed	39
Generally unwell	10	16	1.26 [y]	0.260		40
Tight upper stomach	9	10	0 [y]	0.980		41
Discoloured urine	9	7	0.06 [y]	0.800		43
General ache	9	54	3.88 [y]	0.000	Controls	43
Light headedness	9	11	0.07 [y]	0.790		43
Increased Saliva	9	8	0 [y]	0.960		45
Chest pain	8	9	0 [y]	0.980		47
Irregular heartbeat	8	14	1.32 [y]	0.250		47
Weeping	8	1	4.12 [y]	0.042		47

continued

continued

Symptom	Yes in exposed N=119	Yes in controls N=118	X^2	P	> frequency in….	Rank (exposed)
Feelings of nausea	8	8	0.05 [y]	0.820		49.5
Feeling shaky	8	9	0.05 [y]	0.820		49.5
Loss of appetite	7	11	0.58 [y]	0.440		51.5
Diarrhoea	7	6	0 [y]	0.980		51.5
Impotence	6	4	0.09 [y]	0.760		53.5
Pins and needles	6	18	5.89 [y]	0.015	Controls	53.5
OP smell sensitivity	5	2	0.53 [y]	0.460		55
Tingling toes	4	8	0.79 [y]	0.370		56
Bowel problems	4	1	0.78 [y]	0.370		59
Buzzing ears	4	19	9.82 [y]	0.001	Controls	59
Itchy skin	4	25	17.05 [y]	0.000	Controls	59
Stomach cramps	4	6	0.12 [y]	0.720		59
Sore hands	4	9	1.39 [y]	0.280		59
Flaking skin	3	13	5.64 [y]	0.017	Controls	62
Trouble reading	3	10	3.07v	0.070		62
Trouble sleeping	3	20	12.77 [y]	0.000	Controls	62
Swollen ankles	2	4	0.19 [y]	0.660		66.5
Flushes	2	14	8.38 [y]	0.003	Controls	66.5
Hallucinations	2	1	0 [y]	0.990		66.5
Vomiting	2	5	0.61 [y]	0.430		66.5
Feeling aggressive	1	30	30.09 [y]	0.000	Controls	70.5
Bluish skin	1	4	0.84 [y]	0.360		70.5
Mouth ulcer	1	7	3.34 [y]	0.060		70.5
Pale skin	1	6	2.4 [y]	0.120		70.5
General weakness	0	15	14.04 [y]	0.000	Controls	73

[y] Denotes use of Yates' correction for continuity due to small frequencies

The chi square analyses revealed significant differences between exposed and controls on twenty-five separate symptoms at 24 hours post-dip. The twenty-five symptoms accounted for 34% of the number of symptoms that were recorded, which was considerably higher than the 5% (3 – 4 symptoms) that would have been expected by chance alone. Table 7 shows the symptoms that were reported significantly more by each exposure group.

Table 7: Symptoms reported significantly more by each sheep dippers after recent exposure and quarry workers

Reported more by Exposed N=100	Reported more by Controls N=96
Gen. Cramp	Sneezing
Headache	Cough
Shiver	Watery eyes
Weak muscles	Stiff muscles
Sleep walking	General ache
Thinking problems	Pins and needles
Judging distance	Buzzing ears
Numb toes	Itchy skin
Nose bleeds	Flaking skin
Ear ache	Trouble sleeping
Fever	Flushes
	Feeling aggressive
	General weakness
	Cough blood

Correlational analysis (Spearman's rank) was applied to the ranking of symptom frequencies reported by both exposed and control subjects. A highly significant (P=.01) but moderate correlation of R=.34 was found to exist between the symptoms reported by both groups.

5.2 FACTOR ANALYSIS OF SYMPTOMS REPORTED AT 24 HOURS POST DIP

Using the dataset containing symptom reports for recently exposed workers, the 73 symptoms were subjected to factor analysis using principal components methods. No limitations were specified for the number of potential factors to be extracted, but a limit of a minimum eigenvalue of 1 for each extracted factor was specified. The results of the factor analysis are shown in table 8, which produced 21 factors with eigenvalues of 1 or above, as recommended by the Kaiser criterion [6]. Tables 9-29 show symptom groupings for each extracted factor after a varimax rotation.

Table 8: Results of principle components factor analysis performed on the 73 symptoms reported by sheep dippers after recent exposure

Factor	Eigenvalue	% total variance	Cumulative eigenvalue	Cumulative %
1	14.97	20.51	14.97	20.51
2	5.71	7.83	20.69	28.34
3	4.12	5.64	24.81	33.99
4	3.47	4.75	28.28	38.74
5	3.18	4.36	31.47	43.11
6	2.66	3.65	34.13	46.76
7	2.56	3.50	36.69	50.27
8	2.34	3.20	39.04	53.48
9	2.23	3.06	41.28	56.54
10	2.05	2.80	43.33	59.35
11	1.94	2.65	45.27	62.01
12	1.73	2.37	47.00	64.39
13	1.69	2.32	48.70	66.71
14	1.51	2.07	50.22	68.79
15	1.49	2.05	51.71	70.84
16	1.45	1.98	53.16	72.83
17	1.25	1.72	54.42	74.55
18	1.20	1.64	55.62	76.20
19	1.15	1.57	56.77	77.77
20	1.10	1.51	57.88	79.29
21	1.01	1.38	58.89	80.68

Table 9: First factor extracted from symptom data at 24 hours post dip.

Factor	Symptom	Factor loading
1	Pale skin	.95
	Diarrhoea	.76
	Dry mouth	.41
	Shaky	.66
	Excess sleep	.50
	Lethargy	.36
	Numb toes	.58
	Trouble reading	.67
	Weeping	.61
	Hallucinations	.92
	Feeling aggressive	.95
	Excess sweating	.53
	Nose bleeds	.47
	General ache	.44

Table 10: Second factor extracted from symptom data at 24 hours post dip.

Factor	Symptom	Factor loading
2	Stomach pain	.54
	Vomiting	.95
	Light headedness	.66
	Sore hands	.67
	Feeling down	.58
	Swollen ankles	.93

Table 11: Third factor extracted from symptom data at 24 hours post dip

Factor	Symptom	Factor loading
3	Upset stomach	.70
	Tight upper stomach	.79
	Nausea	.85
	Loss of appetite	.58
	Dizziness	.51
	Poor Libido	.65
	Cough blood	.49

Table 12: Fourth factor extracted from symptom data at 24 hours post dip

Factor	Symptom	Factor loading
4	Sleep walking	.26
	Ear ache	.50
	Trouble speaking	.66
	Discoloured urine	.54

Table 13: Fifth factor extracted from symptom data at 24 hours post dip

Factor	Symptom	Factor loading
5	Cough	.50
	Runny nose	.56
	OP smell sensitivity	.87
	Trouble sleeping	.94
	Fever	.59

Table 14: Sixth factor extracted from symptom data at 24 hours post dip

Factor	Symptom	Factor loading
6	Tingling toes	.73
	Pins and needles	.83

Table 15: Seventh factor extracted from symptom data at 24 hours post dip

Factor	Symptom	Factor loading
7	Headache	.46
	Stiff muscles	.79
	Skin eruptions	.68

Table 16: Eighth factor extracted from symptom data at 24 hours post dip

Factor	Symptom	Factor loading
8	Bluish skin	.92
	Bowel problems	.70
	Stomach cramps	.55

Table 17: Ninth factor extracted from symptom data at 24 hours post dip

Factor	Symptom	Factor loading
9	Impotence	.85
	Gen. unwell	.77
	Shiver	.39

Table 18: Tenth factor extracted from symptom data at 24 hours post dip

Factor	Symptom	Factor loading
10	Gen. Cramp	.48
	Weak muscles	.70
	Stiff joints	.84

Table 19: Eleventh factor extracted from symptom data at 24 hours post dip

Factor	Symptom	Factor loading
11	Buzzing ears	.65
	Problems seeing	.84

Table 20: Twelfth factor extracted from symptom data at 24 hours post dip

Factor	Symptom	Factor loading
12	Itchy skin	.67
	Flaking skin	.83

Table 21: Thirteenth factor extracted from symptom data at 24 hours post dip

Factor	Symptom	Factor loading
13	Irregular heartbeat	.42
	Twitching muscles	.70

Table 22: Fourteenth factor extracted from symptom data at 24 hours post dip

Factor	Symptom	Factor loading
14	Judging time	.69
	Forgetfulness	.66
	Judging distance	.59

Table 23: Fifteenth factor extracted from symptom data at 24 hours post dip

Factor	Symptom	Factor loading
15	Blurred vision	.70
	Watery eyes	.82

Table 24: Sixteenth factor extracted from symptom data at 24 hours post dip

Factor	Symptom	Factor loading
16	Breathlessness	.40
	Chest pain	.77

Table 25: Seventeenth factor extracted from symptom data at 24 hours post dip

Factor	Symptom	Factor loading
17	Mouth ulcer	.88

Table 26: Eighteenth factor extracted from symptom data at 24 hours post dip

Factor	Symptom	Factor loading
18	Sore throat	.62
	General weakness	.89
	Thinking problems	.32

Table 27: Nineteenth factor extracted from symptom data at 24 hours post dip

Factor	Symptom	Factor loading
19	Sneezing	.36
	Flushing	.86
	Heart burn	.27

Table 28: Twentieth factor extracted from symptom data at 24 hours post dip

Factor	Symptom	Factor loading
20	Productive cough	.60

Table 29: Twenty-first factor extracted from symptom data at 24 hours post dip

Factor	Symptom	Factor loading
21	Increased Saliva	.78

Twenty-one factors with eigenvalues >1 were extracted, which necessitated another method of choosing a cut-off point to decide which factors best represented the symptoms reported by the recently exposed dippers. Fig 2 shows a scree plot of the eigenvalues for each extracted factor in accordance with this graphical method proposed by Cattell[7]. The point on the graph where the smooth decrease of eigenvalues appears to level off occurs after factor number 6, and for this reason, factors 1 – 6 were retained, and factors 7 – 21 discarded.

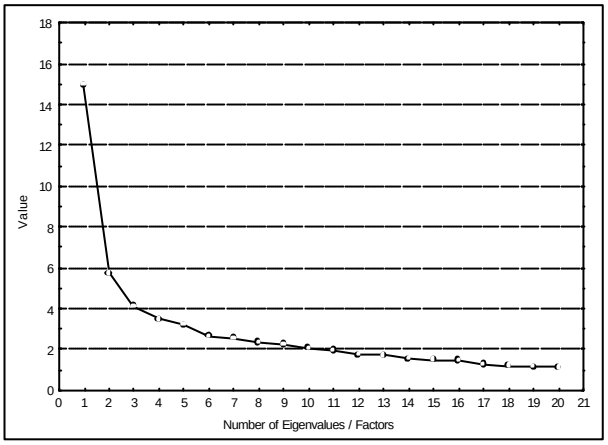


Figure 2
Scree plot of factors extracted from symptom data at 24 hours post dip

5.2.1 Statistical Caveat.

Both the Kaiser criteria and the scree test have been used as methods for factor retention[8], with the Kaiser method often retaining too many factors, and the scree method often retaining too few. Both have been shown to operate well under normal conditions (few factors and many cases). However, this present study could be described as the opposite of optimal conditions for factor analysis, in that there are many factors (73) and relatively few cases (100). An additional consideration is that of interpretability, where the number of factors that are retained make the best sense of the data, and on this basis, retention of fewer factors is usually preferable to too many.

The six remaining factors, the product of 38 individual symptoms accounted for 46% of the variance in symptom scores from the recently exposed dippers, and are reviewed in table 30.

Table 30: Six best factors extracted from symptom data at 24 hours post dip

	Factor 1	Factor 2	Factor 3	Factor 4	Factor 5	Factor 6	Total
Eigenvalue	14.97	5.71	4.12	3.47	3.18	2.66	34.11
% total variance	20.51	7.83	5.64	4.75	4.36	3.65	46.74
Cum. Eigenvalue	14.97	20.68	24.80	28.27	31.45	34.11	34.11
Cum. %	20.51	28.34	33.98	38.73	43.09	46.74	46.74
Symptoms	14	6	7	4	5	2	38

5.3 DOSE-EFFECT RELATIONSHIPS AT 24 HOURS POST DIP

5.3.1 Use of 6 Extracted Factors as an Outcome Variable.

The size of flock that was dipped 24 hours prior to symptom measurement was used as a predictor variable, being a surrogate measure of OP exposure. The six factors extracted from the principal components analysis were summed to provide a global outcome factor. The mean "global outcome score" among the 100 recently exposed dippers was 4.93 (± 6.99) with a minimum of 0 and a maximum score of 46. The flock size was established for 83 dippers, the mean of which being 877 sheep (± 766) with a minimum flock of 30 and a maximum size of 5000.

The correlation between flock size and the summed scores of factors 1-6 reported 24 hours after dipping was r = .06. Figure 3 shows the regression of flock size and the summed scores of factors 1-6 reported 24 hours after dipping, with two distinct outliers marked by arrows. A linear regression model was applied to investigate any (predictive) relationship between the surrogate measure of exposure (flock size) and the global outcome factor score from the factor analysis. Table 31 shows the results of the regression.

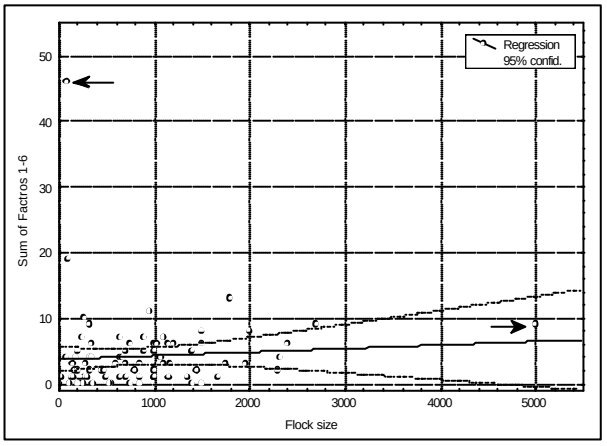


Figure 3
Plot of the regression of flock size as a predictor of the "global outcome symptoms" (factors 1-6)

Table 31: Summary of the regression of flock size as a predictor of the "global outcome symptom" (factors 1-6)

	Beta	St. err of beta	B	St. err of B	t (81)	P
Intercept			3.84	.96	3.97	.0001
Flock size	.06	.11	.0004	.0008	.57	.57
R= .06	R^2= .003	Adjusted R^2= -.008		Std.Error of estimate: 5.78		

The two outliers were removed (individual *x* with flock size of 84 & global outcome score of 46 and individual *y* with flock size of 5000 & global outcome score of 9) and the correlation between flock size and global outcome score was r =.20. The regression was repeated without the outliers, with the results shown in figure 4 and table 32, and can be expressed thus:

Sum of factors 1 to 6 = (Flock size x 0.001) + 2.74

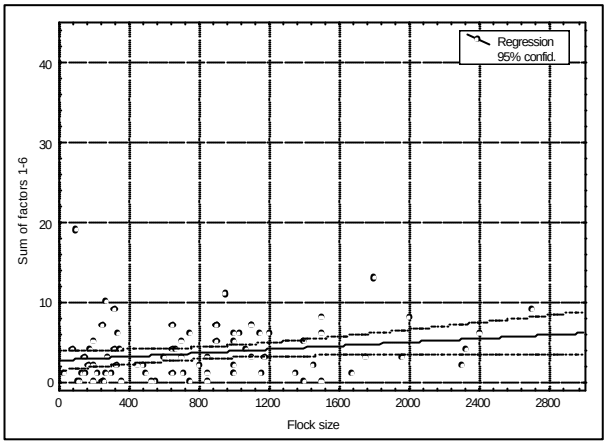


Figure 4
Plot of the regression of flock size as a predictor of the "global outcome symptom" (factors 1-6) with 2 outliers removed

Table 32: Summary of the regression of flock size as a predictor of the "global outcome symptom" (factors 1-6) with 2 outliers removed

	Beta	St. err of beta	B	St. err of B	t (79)	P
Intercept			2.74	.630	4.34	.00004
Flock size	.20	.11	.001	.0006	1.86	..065
R= .20	R^2= .042	Adjusted R^2= .030		Std.Error of estimate: 3.35		

5.3.2 Use of 21 Most Frequently Reported Symptoms as an Outcome Variable

The twenty-one symptoms reported most frequently by exposed dippers at 24 hours post dip were summed as an alternative global outcome variable. The size of flock that was dipped 24 hours prior to symptom measurement was used as a predictor variable, being a surrogate measure of OP exposure. The mean global score among the 100 recently exposed dippers was 6.7 (± 6.26) with a minimum of 0 and a maximum score of 36. The flock size was established for 83 dippers, the mean of which was 877 sheep (± 766) with a minimum flock of 30 and a maximum size of 5000. The correlation between flock size and the alternative global symptom score (derived from the sum of the top 21 symptoms) for recently exposed dippers was r = .17.

When two outliers were removed (individual x with flock size of 84 & top 21 symptom score of 36, and individual y with flock size of 100 & top 21 symptom score of 23) the correlation was

elevated to r = .35. A linear regression model was applied to investigate any (predictive) relationship between the surrogate measure of exposure (flock size) and the sum of the top 21 symptoms at 24 hours post dip. Figure 5 and table 33 show the regression of flock size and the summed scores of the top 21 symptoms, 24 hours post dip, after removal of the two outliers. The regression can be expressed thus:

Sum of top 21 symptoms = (Flock size x 0.002) + 3.88

Table 33: Summary of the regression of flock size as a predictor of the sum of the top 21 symptoms with 2 outliers removed

	Beta	St. err of beta	B	St. err of B	t (79)	P
Intercept			3.88	.709	5.47	.0000
Flock size	.35	.10	.002	.0006	3.38	.001

R= .35 R^2= .12 Adjusted R^2=.11 Std.Error of estimate: 4.13

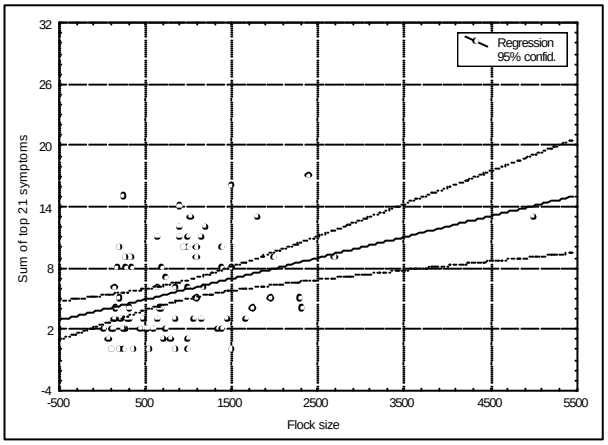


Figure 5
Plot of the regression of flock size as a predictor of the top 21 symptoms at 24 hours post-dip, with 3 outliers removed

5.4 CLUSTER ANALYSIS OF SYMPTOMS REPORTED AT 24 HOURS POST DIP

No standardization of the symptom scores were needed prior to any cluster analyses as all variables (symptoms) were scored in an identical manner. Clustering methods were attempted on all 73 symptoms (5.4.1) on those 12 symptoms reported significantly more by exposed subjects 24 hours post dip (5.4.2) and on the 21 symptoms reported most frequently by exposed subjects 24 hours post dip (5.4.3).

5.4.1 Cluster Analysis of All Symptoms

All symptoms reported by dippers 24 hour post-dip were subjected to cluster analysis using single linkage, based on euclidian distances, the result of which is shown in Appendix 3. No discernable clustering was detected, almost certainly due to the number of factors (73 symptoms) nearly equaling the number of cases (n=100).

5.4.2 Cluster Analysis of 12 Symptoms Reported Significantly More by Dippers

A method was chosen whereby the number of symptoms used in the analysis were greatly reduced. The twelve symptoms reported more by dippers at 24 hours post-dip than by controls (table 7) were subjected to cluster analysis using single linkage, based on euclidian distances. Figure 6 shows the relative distances between symptoms after clustering.

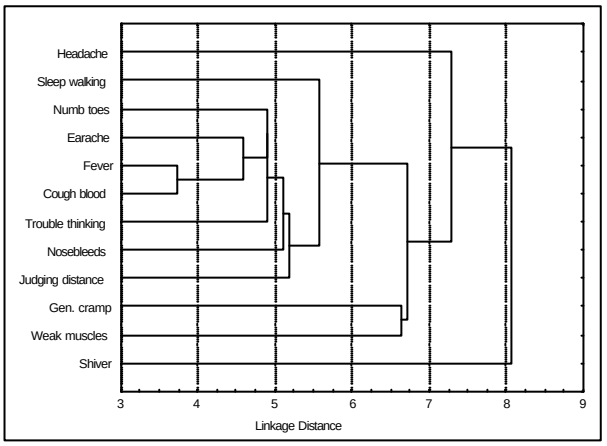


Figure 6
Horizontal hierarchical tree plot of euclidian distances between the 12 symptoms reported more by exposed than controls by 24 hours post dip

5.4.2.1 K-means Analysis of Symptoms Reported Significantly More by Dippers

The twelve symptoms reported more by dippers at 24 hours post-dip than by controls were subjected to cluster analysis using single linkage, based on k-means clustering. This allowed clusters to be developed on the basis of being most distinct from each other. The number of desired clusters to be produced was specified as three, and tables 34 & 35 show the grouping of those symptoms into the three most disparate clusters.

Table 34: Symptoms grouped into three most distinct clusters on the basis of k-means clustering

Cluster 1	D	Cluster 2	D	Cluster 3	D
Sleep walking	.44	Headache	.00	Gen. cramp	.41
Numb toes	.39			Weak muscles	.43
Ear ache	.38			Shiver	.57
Thinking problems	.37				
Judging distance	.38				
Fever	.26				
Nose bleeds	.41				
Cough blood	.31				

D represents the distance from the center of the respective cluster

Table 35: Euclidian distances between the three clusters (below diagonal) and squared euclidian distances (above diagonal)

	Cluster 1	Cluster 2	Cluster 3
Cluster 1	.00	.50	.22
Cluster 2	.71	.00	.65
Cluster 3	.47	.81	.00

5.4.3 Cluster Analysis of 21 Symptoms Reported Most Frequently by Dippers

The twenty-one symptoms (two symptoms tied and were ranked 20.5 each) reported most frequently by dippers at 24 hours post-dip were subjected to cluster analysis using single linkage, based on euclidian distances. Figure 7 shows the relative distances between symptoms after clustering.

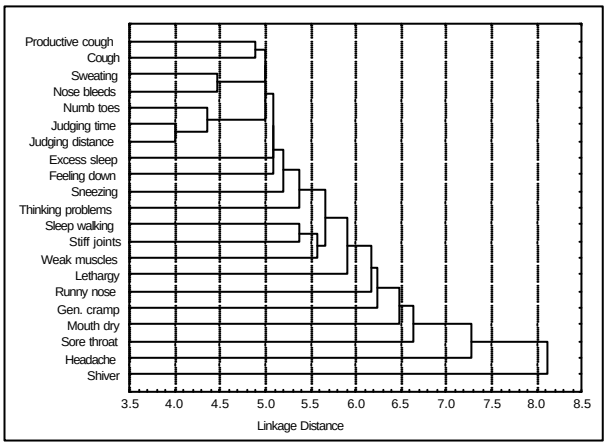


Figure 7
Horizontal hierarchical tree plot of euclidian distances between the 21 symptoms reported most by dippers at 24 hours post dip

5.4.3.1 K-means Analysis of 21 Symptoms Reported Most Frequently by Dippers

The twenty-one symptoms reported most frequently by dippers at 24 hours post-dip were subjected to cluster analysis using single linkage, based on k-means clustering. This allowed clusters to be developed on the basis of being most distinct from each other. The number of desired clusters to be produced was specified as five, and tables 36 & 37 show the grouping of those symptoms into the five most distinct clusters.

Table 36: Symptoms grouped into five most distinct clusters on the basis of k-means clustering

Cluster 1	D	Cluster 2	D	Cluster 3	D	Cluster 4	D	Cluster 5	D
Excess sleep	.35	Shiver	.00	Phlegm	.35	Gen. Cramp	.39	Mouth dry	.47
Lethargy	.48			Cough	.33	Weak muscles	.34	Sore throat	.48
Numb toes	.33			Runny nose	.45	Stiff joints	.33	Headache	.56
Judging time	.31			Sneezing	.32			Sleep walking	.37
Judging distance	.39							Trouble thinking	.39
Feeling down	.41								
Excess sweating	.33								
Nose bleeds	.33								

D represents the distance from the center of the respective cluster

Table 37: Euclidian distances between the five clusters (below diagonal) and squared euclidian distances (above diagonal)

	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Cluster 5
Cluster 1	.00	.60	.55	.19	.13
Cluster 2	.77	.00	1.13	.61	.57
Cluster 3	.74	1.06	.00	.60	.50
Cluster 4	.44	.78	.77	.00	.19
Cluster 5	.37	.76	.71	.44	.00

5.4.3.2 Testing of the Five Clusters Between Exposed and Control Workers

Scores on the five clusters derived from K-means analysis of the twenty-one symptoms reported most frequently by exposed dippers at 24 hours post-dip were subjected to analysis of variance between exposed and control workers, with the results shown in table 38.

Table 38: Mean scores (SD) of exposed and controls on each of the five clusters derived from k-means cluster analysis

	Exposed n=100	Controls N=96	F	P
Cluster 1	2.11 (3.07)	1.43 (1.92)	3.34	.069
Cluster 2	0.46 (0.74)	0.05 (0.26)	25.68	<.0000
Cluster 3	1.24 (1.68)	1.65 (1.70)	2.95	.087
Cluster 4	1.23 (1.38)	0.60 (1.14)	11.83	.0007
Cluster 5	1.66 (1.78)	0.86 (1.21)	13.19	.0003
Total	6.70 (6.26)	4.61 (4.98)	6.61	.010

6. SUMMARY OF RESULTS

When symptoms were ranked for exposed and control subjects, both occupational groups showed a large degree of commonality in terms of the most frequent symptoms that were reported. Five out of the ten most frequent symptoms for both dippers and quarry workers were shared: Lethargy, Runny nose, Stiff joints, Excessive sleeping, and Sneezing. For the exposed group, only two of their ten most frequently reported symptoms have been anecdotally associated with OP exposure (Headaches and Weak muscles). The next symptom anecdotally associated with OP exposure that was reported by the exposed subjects was the 39th most frequent symptom, that of "fever". Other symptoms consistent with a flu-like illness did not feature prominently in the reports of dippers: "general aches and pain" (ranked 43rd), "loss of appetite" (51.5) and "general weakness" (73rd). This suggests that the exposed group as a whole were not reporting symptoms which have been anecdotally associated with OP exposure. Quarry workers had 1 symptom in their respective top ten that has been associated with OP exposure (general weakness) but which could also be reasonably attributed to the physical labor of quarry-working.

Significance testing between the two occupational groups showed significant differences on 25 (34%) of the symptoms that were reported, which was much higher than would be expected due to chance. Of the twelve symptoms reported significantly more often by sheep dippers, only three were of the type anecdotally associated with OP exposure, (headaches, weak muscles, and fever). The other eight symptoms reported significantly more by dippers were very varied and could only be described collectively as "non-specific" due to their variety (general cramps, shivers, sleep walking, thinking problems, trouble judging distances, numb toes, nose bleeds, and ear ache). The two symptoms concerning "trouble with thinking" and "trouble judging distances" would appear to be neuropsychological or cognitive in nature. Of the fourteen symptoms reported more often by non-exposed controls, two have been anecdotally associated with OP exposure (general aches and general weakness), but again could reasonably be attributed to the physical nature of the work.

Factor analyses of the original 73 symptoms reported by dippers 24 hours after exposure resulted in 21 factors with eigenvalues greater than 1. Scree analysis reduced the factors to just six in number, composed of 38 individual symptoms that accounted for only 47% of the variance in symptom reports. The six factors were composed of various individual symptoms with seemingly little physiological connection between them. Only factor six (composed of the symptoms of tingling toes and pins and needles) had a consistent theme that could best be

described as “sensory discomfort”. Factors 1–5 appeared too varied in terms of their constituent symptoms to have any plausible physiological basis.

Other factors identified by factor analysis that appeared to have a consistent theme in terms of their constituent symptoms could be described in the following way: Factor 10, (results of) physical exertion; Factor 11, Sensory disturbance; Factor 12, Dermal discomfort; Factor 14, Cognitive problems; Factor 15, Visual problems. All other factors appeared to be comprised of symptoms too varied to be labeled on a physiological basis.

Linear regressions were performed, using the size of flock dipped by farmers as a surrogate measure of OP exposure. Two alternative global outcome measures were explored: the sum of the six best factors resulting from the factor analysis, and the sum of the twenty-one symptoms reported most frequently by dippers. Using flock size to predict symptom outcome on the basis of the six summed factors accounted for only 4% of the variance present in those six symptom factors. Using flock size to predict symptom outcome on the basis of the sum of the top twenty-one symptoms accounted for only 12% of the variance in the top twenty-one symptoms. In this respect, flock size (as a surrogate of OP exposure when dipping) proved unsatisfactory in accounting for reports of symptoms among dippers at 24 hours post dip, even after adjustments were made for two individual cases with outlying values. A moderate correlation was demonstrated between flock size and the sum of the 21 most frequently occurring symptoms, but the lack of anecdotally reported OP exposure-related symptoms in this group of 2I point to physical exertion as a plausible explanation for this relationship.

When reports of the 73 original symptoms were subjected to cluster analysis, little meaningful or interpretable information was evident. K-means clustering of the 12 symptoms reported significantly more by exposed subjects than controls resulted in three distinct clusters of symptoms (table 34), comprised of eight, one, and three symptoms respectively. However, K-means clustering of the top 21 symptoms reported by exposed workers produced 5 distinct symptom clusters (table 36), comprised of eight, one, four, three and five symptoms respectively. The symptoms in these five clusters did appear to have some interpretable qualities in physiological terms. Cluster 1 was comprised of global, local, and neurobehavioural symptoms, and could perhaps be described as the “gross” cluster. Cluster 2 was one single symptom (shiver) in isolation. Cluster 3 possessed symptoms that might be associated with a flu-like condition, while cluster 4 contained symptoms that were muscular or muscular related. Cluster 5 seemed to be less well-defined than the other clusters, and contained symptoms that were seemingly mostly global in nature, with the presence of one cognitive symptom (trouble thinking clearly).

Analysis of variance to compare scores on the five clusters reported by exposed and controls revealed some significant differences between the two exposure groups, consistently to the detriment of exposed individuals. Clusters 2, 4, 5 and the total of all of the five clusters were significantly different at the $P<.01$ level. This suggests that the symptoms involved in the five clusters developed in section 5.4.3.1, especially clusters 2, 4 and 5, may provide a useful and more manageable set of symptoms on which to focus in future investigations, although these initial findings require further verification.

7. CONCLUSIONS

The results show that there was a high frequency of symptom reporting in both of the occupational groups involved in the original study, amounting to an approximate 50-50 split in the proportion of symptoms reported significantly more by one group than the other. The symptoms reported significantly more frequently by the exposed than by the controls were not of the type traditionally linked with exposure to OP's and sheep dip. No plausible pattern was apparent in the type of symptoms reported more frequently by dippers than controls, and thus the data produced a rather confusing picture. Further, when 24 hours post-dip symptoms were ranked according to frequency of reports, a significant and moderate correlation existed in the frequency rankings of symptoms between the two occupational groups.

The earlier report of HSE 74/1995 made use of symptoms grouped together on the basis of other cases and epidemiological studies, and not on any analyses of the current data collected from exposed and control participants. However, subjecting the original nine symptom groups (reported by exposed workers at 24 hours post-dip) to cluster analysis did suggest that globalized, non-specific and psychological symptoms were distinct from more specific and localized symptoms. This would suggest that exposed workers were primarily reporting a general feeling of malaise rather than symptoms related to specific target organs or organ systems.

When symptom data collected from the exposed workers at 24 hours post-dip were subjected to factor analysis, twenty-one unwieldy factors emerged, and were reduced to six factors (38 symptoms) as the best representation of the symptom data set. There appeared to be little physiological plausibility in the symptoms comprising some of the factors. There was also little association between these symptom groupings and the estimate of recent OP exposure (flock size), although this may be due either to the statistical problem of having almost as many symptom variables (73) as cases in the analysis (n=82) or to the simplicity of the exposure estimation. Overall therefore, factor analysis provided little clarification of the data.

A preferred method of symptom grouping emerged from k-means cluster analysis (essentially providing a number of clusters, most distinct from each other as possible) of the 21 symptoms reported most frequently by the exposed workers at 24 hours post-dip. This analysis identified 5 distinct symptom clusters which appeared to have a measure of plausibility. Significance testing between scores of exposed and control groups showed significantly more symptoms were reported by dippers at 24 hours post-dip, on 3 of these and in the total of the 5 clusters.

This provides some tentative support for the view that certain symptoms can be identified which occur more frequently in those recently exposed to OPs (symptoms contained in clusters 2, 4 and 5)and that these symptoms are consistent with a flu-like illness. Our initial identification of such symptoms points to the need for further verification of these findings in studies specifically targeted at definition of symptom groups following OP exposure.

8. REFERENCES

1. DEPARTMENT OF HEALTH. COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT (1999). Organophosphates, Chapter 5. Crown Copyright.

2. STEPHENS,R., SPURGEON,A., AND BERRY, H. (1996) *Organophosphates: the relationship between chronic and acute exposure effects.* Neurotoxicology & Teratology 18(4): 449-453.

3. REES H. Exposure to sheep dip and the incidence of acute symptoms in a group of Welsh sheep farmers. Occupational Environmental Medicine 1996;53: 258-263.

4. STEPHENS R, SPURGEON A, CALVERT IA, BEACH J, LEVY LS, BERRY H, HARRINGTON JM. (1995) Neuropsychological effects of long-term exposure to organophosphates in sheep dip. Lancet, 345: 1135-1139.

5. STEPHENS,R., SPURGEON,A., BEACH,J., CALVERT, I.A., BERRY, H., LEVY, L., AND HARRINGTON, J.M. (1995) *An investigation into the possible chronic neuropsychological and neurological effects of occupational exposure to organophosphates in sheep farmers.* HSE Contract Research Report No. 74/1995.

6. KAISER, H.F. (1960) *The application of electronic computers to factor analysis.* Education and psychological measurement, 20: 141-151.

7. CATTELL, R.B. (1966) *The scree test for the number of factors.* Multivariate Behavioural Research 1: 245-276 in Statistica Manual, Vol.III Statistics II. StatSoft 1995, Tulsa OK.

8. HAKSTIAN, A.R., ROGERS, W.D., AND CATTELL, R.B. (1982) *The behaviour of numbers of factors rules with simulated data.* Multivariate Behavioral Research, 17: 193-219.

9. APPENDICES

Appendix 1

List of symptoms reported at 24 hours post dip (ranked by frequency in exposed dippers)

	Exposed				Controls			
Symptom	**No**	**Yes**	**%**	**Rank**	**No**	**Yes**	**%**	**Rank**
Gen. cramp	57	53	48.1	1	96	10	9.4	38
Lethargy	63	46	42.2	2	66	41	38.3	4
Headache	67	43	39	3	83	24	22.4	15
Shiver	69	41	37.2	4	99	8	7.5	48
Runny nose	70	40	36.3	5	67	41	38	5
Weak muscles	70	39	35.7	6	90	18	16.7	21.5
Stiff joints	74	34	31.4	7	74	33	30.8	8
Excess sleep	77	32	29.3	8	80	28	25.9	10
Dry mouth	78	31	28.4	9	82	25	23.4	13.5
Sneezing	80	29	26.6	10	57	50	46.7	2
Sleep walking	81	28	25.6	11	106	1	0.9	71.5
Thinking problems	82	28	25.4	12	95	13	12.0	32.5
Productive cough	81	27	25	13	62	45	42.1	3
Judging distance	82	27	24.7	14	104	4	3.7	64
Numb toes	84	26	23.6	15	100	8	7.4	51.5
Sore throat	83	25	23.1	16	84	24	22.2	16
Cough	84	25	22.9	17	62	45	42.1	3
Nose bleeds	87	23	20.9	18	102	5	4.7	60
Feeling down	88	22	20	19	82	25	23.4	13.5
Excess sweating	90	19	17.4	20.5	91	17	15.7	24
Judging time	91	19	17.2	20.5	91	17	15.7	24
Skin eruptions	94	16	17	22	100	8	7.4	51.5
Cough blood	92	18	16.3	24	62	45	42.1	3
Dizziness	92	18	16.3	24	98	9	8.4	43
Ear ache	92	18	16.3	24	104	4	3.7	64
Blurred vision	94	16	15.5	26	98	10	9.3	40.5
Problems seeing	92	16	14.8	27	98	10	9.3	40.5
Forgetfulness	93	16	14.6	28	74	34	31.5	7
Poor libido	94	15	13.7	29	95	13	12	32.5
Stomach pain	95	15	13.6	30	100	8	7.4	51.5
Sore feet	96	14	12.7	31	97	11	10.2	36
Heartburn	95	13	12	32	89	19	17.6	19.5
Upset stomach	97	13	11.8	33	95	13	12	32.5
Breathlessness	98	11	10	36	91	17	15.7	24
Watery eyes	99	11	10	36	87	21	19.4	17
Stiff muscles	99	11	10	36	81	27	25	11
Twitching muscles	99	11	10	36	94	13	12.1	30
Speech difficulty	98	11	10	36	99	9	8.3	45.5
Fever	99	10	9.1	39	106	2	1.9	68
Generally unwell	100	10	9	40	91	16	15	26
Tight upper stomach	100	9	8.3	41	98	10	9.3	40.5
Discoloured urine	100	9	8.2	43	101	7	6.5	55.5
General ache	100	9	8.2	43	54	54	50	1
Light headedness	100	9	8.2	43	97	11	10.2	36
Increased Saliva	101	9	8.1	45	100	8	7.4	51.5
Chest pain	101	8	7.3	47	99	9	8.3	45.5
Irregular heartbeat	101	8	7.3	47	94	14	13	28.5
Weeping	101	8	7.3	47	107	1	0.9	71.5
Feelings of nausea	102	8	7.2	49.5	100	8	7.4	51.5

Cont

Cont

	Exposed				Controls			
Symptom	**No**	**Yes**	**%**	**Rank**	**No**	**Yes**	**%**	**Rank**
Loss of appetite	102	7	6.4	51.5	97	11	10.2	36
Diarrhoea	102	7	6.4	51.5	102	6	5.6	58
Impotence	104	6	5.4	53.5	104	4	3.7	64
Pins and needles	104	6	5.4	53.5	90	18	16.7	21.5
OP smell sensitivity	105	5	4.5	55	105	2	1.9	68
Tingling toes	104	4	3.7	56	100	8	7.4	51.5
Bowel problems	106	4	3.6	59	107	1	0.9	71.5
Buzzing ears	106	4	3.6	59	89	19	17.6	19.5
Itchy skin	106	4	3.6	59	80	25	23.8	12
Stomach cramps	106	4	3.6	59	102	6	5.6	58
Sore hands	106	4	3.6	59	99	9	8.3	45.5
Flaking skin	107	3	2.7	62	95	13	12	32.5
Trouble reading	106	3	2.7	62	97	10	9.3	40.5
Trouble sleeping	107	3	2.7	62	88	20	18.5	18
Swollen ankles	108	2	1.8	66.5	104	4	3.7	64
Flushes	108	2	1.8	66.5	94	14	13	28.5
Hallucinations	107	2	1.8	66.5	107	1	0.9	71.5
Vomiting	107	2	1.8	66.5	103	5	4.6	61
Feeling aggressive	109	1	0.9	70.5	78	30	27.8	9
Bluish skin	108	1	0.9	70.5	104	4	3.7	64
Mouth ulcer	108	1	0.9	70.5	100	7	6.5	55.5
Pale skin	108	1	0.9	70.5	102	6	5.6	58
General weakness	108	0	0	73	93	15	13.9	27

Appendix 2

List of Symptom Grouping Items from the original study. Reproduced from HSE 74/1995

Cardio-respiratory
Bluish discolouration of parts of the skin
Chest pain
Coughing
Coughing up phlegm
Difficulty breathing
Paleness of the skin
Reddening of the face or neck (flushing)
Runny nose
Slowing down or speeding of heart beats
Sneezing

Visual
Blurred vision
Eye irritation – redness, watering, burning
Problems seeing

Global
Feeling dizzy
Feeling lethargic, or slowed down generally
Feeling of weakness
Headache
Impotence
Increased sense of smell for sheep dip chemicals
Light headedness
Loss of sexual appetite
Shakiness
Sleep walking
Sleeping a lot
Trouble sleeping

Cognitive
Experiencing difficulty reading
Experiencing difficulty speaking
Forgetting things
Losing thought trends
Losing track of time
Problems with judging distance

Non-specific
Fever
General aches and pains
Generally feeling unwell
Nosebleeds
Shivering
Skin eruptions
Sweating (without physical exercise)

Sheep Dip flu
(*items also appear in above categories*)
Feeling of weakness
Feeling of weakness in muscles
Fever
General aches and pains
Headache
Loss of appetite

Gastro-intestinal
Diarrhoea
Dry mouth
Heartburn
Inability to control bowel movements
Increased saliva in the mouth
Loss of appetite
Nausea – feeling sick
Sore throat
Stomach cramps
Stomach pain
Tight feeling in the upper part of the stomach
Upset stomach
Vomiting – being sick

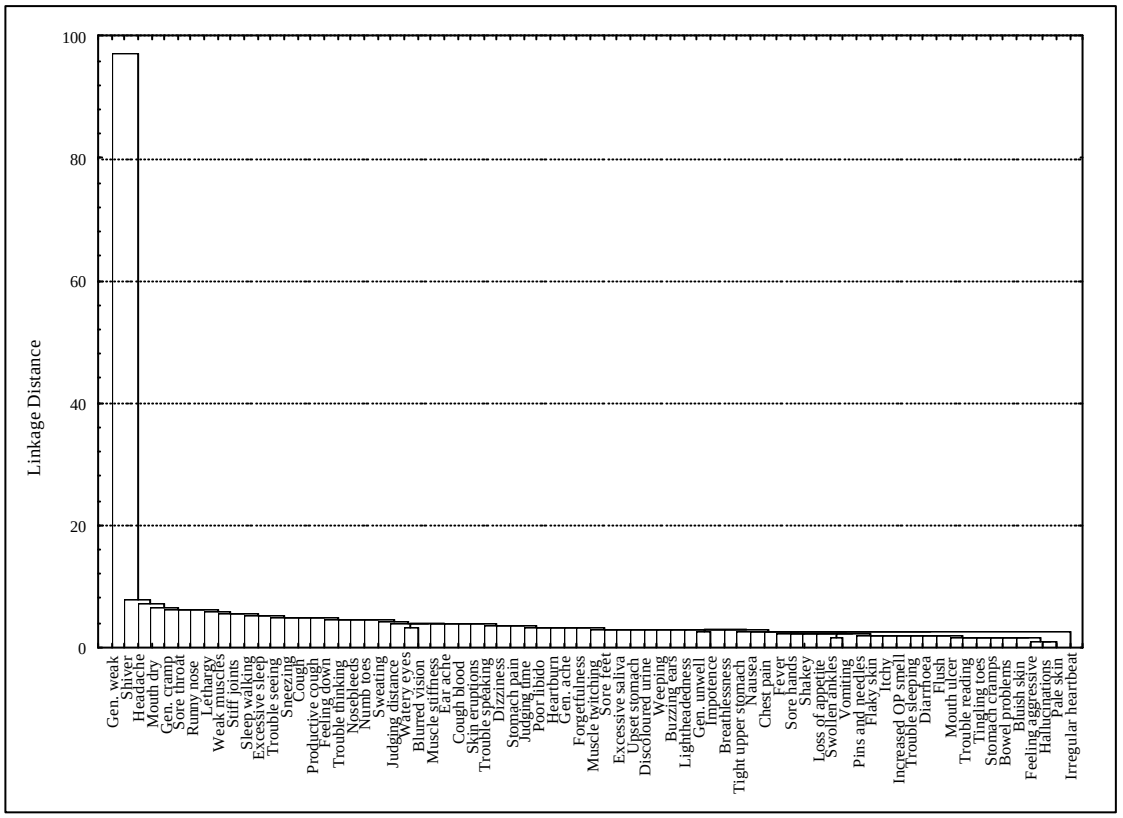
Localised
Cramps other than in the stomach
Earache
Feeling of weakness in muscles
Itching or skin rashes
Muscle twitching
Numbness of toes
Pins and needles
Ringing or buzzing in the ears
Sore feet
Sore hands
Stiffness in the muscles
Tingling of toes

Psychiatric
Feeling aggressive
Feeling down or depressed
Hallucinating
Weeping for no apparent reason

Distractors
Ankle swelling
Coughing up blood
Mouth ulcers
Peeling or flaky skin
Stiffness in the joints

Typical Acute OP Exposure Symptoms
(*items also appear in above categories*)
Slowing down or speeding up of heart beats
Difficulty breathing
Paleness of the skin
Stomach cramps
Tight feeling in the upper part of the stomach
Diarrhoea
Increased saliva in the mouth
Heartburn
Nausea – feeling sick
Vomiting – being sick
Loss of appetite
Muscle twitching
Eye irritation – redness, watering, burning
Sweating (without physical exercise)

Appendix 3



Vertical hierarchical tree plot of euclidian distances between the 73 symptoms reported by exposed dippers at 24 hours post dip

Printed and published by the Health and Safety Executive
C1 10/01

MAIL ORDER
HSE priced and free
publications are
available from:
HSE Books
PO Box 1999
Sudbury
Suffolk CO10 2WA
Tel: 01787 881165
Fax: 01787 313995
Website: www.hsebooks.co.uk

RETAIL
HSE priced publications
are available from booksellers

HEALTH AND SAFETY INFORMATION
HSE InfoLine
Tel: 08701 545500
Fax: 02920 859260
e-mail: hseinformationservices@natbrit.com
or write to:
HSE Information Services
Caerphilly Business Park
Caerphilly CF83 3GG

HSE website: www.hse.gov.uk

CRR 371

£10.00

ISBN 0-7176-2111-1