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JOURNAL TITLE: J CHRONIC DISEASE
VOLUME, NUMBER, PAGES, YEAR: 26:105-118, 1973
AUTHOR: NELSON WC, LYKING MH, MACKEY J, NEWILL V
TITLE: MORTALITY AMONG ORCHARD WORKERS EXPOSED TO LEAD ARSENATE SPRAY: A COHORT STUDY.

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J Chron Dis 1973, Vol. 26, pp. 105–118. Pergamon Press. Printed in Great Britain

MORTALITY AMONG ORCHARD WORKERS EXPOSED TO LEAD ARSENATE SPRAY: A COHORT STUDY

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(*Received 6 June* 1972; *in final form* 26 *September* 1972)

INTRODUCTION

BEFORE the discovery and heavy use of DDT in the mid-1940's, lead arsenate insecticide spray was used in huge quantities. Total lead arsenate usage in the United States peaked in 1945 at 80 million lb and over 5 million lb were still applied on fruit and tobacco in 1968 [1, 2]. The majority of its use was and is on apple orchards.

Both lead and arsenic have long been known to be toxic to humans. Clinical lead poisoning is manifested by severe abdominal colic, headaches, anemia, loss of appetite, fatigue, constipation, motor-nerve paralysis, and encephalopathy. Chronic excessive exposure is characterized by acute symptoms superimposed on a background of progressive renal insufficiency and cerebral incompetence [3–7]. Many children with acute encephalopathy, the most severe clinical symptom of lead poisoning, also have acute renal injury [8, 9]. Almost exclusively confined to children, lead induced encephalopathy often leaves permanent brain damage after both exposure and acute illness have ceased [10–12]. High lead exposure may also be harmful to reproduction [13, 14] and may aggravate some pre-existing diseases such as cirrhosis of the liver [15]. Whereas the previous effects occur at elevated blood lead concentrations, lead can inhibit the activity of an enzyme controlling heme synthesis even when blood lead levels are within the normal range of 10 to 40 μg per 100 g [16]. Several excellent summary articles exist on the health effects of lead [2, 8, 17, 18].

Symptoms of acute and chronic arsenic poisoning may include dermatitis, nasal and throat irritation, nasal septum perforation, nausea, vomiting, stomach pain and coughing [19]. Cancer of the skin, lung and liver have been attributed to arsenic exposure while cancers of the mouth, esophagus, and larynx are also suspected [19, 20]. Several studies attempting to show increased prevalence of cancer in industrially exposed workers and to induce cancer in laboratory animals by arsenic exposure have proven negative. A summary of these studies and other health effects information appears in [21].

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Most effects studies for both lead and arsenic have explored the acute or chronic morbidity effects of high exposures. There is a lack of information regarding chronic effects at lower enviromental levels of exposure, especially at levels that do not produce clinical poisoning. As yet, no cases of clinical acute lead poisoning have been reported in adults with blood lead levels below 80 μg per 100 g or in children with blood lead levels below 50 μg per 100 g. Although it is known that lead accumulates with age in the skeleton, kidneys, liver, aorta, pancreas and lungs, few follow-up studies have been made on the present health status of people exposed to high lead levels 20–50 yr ago [22]. This study of orchard workers exposed to lead arsenate spray fills a portion of this major gap in the knowledge of lead and arsenic health effects by examining the effects of lead arsenate exposure on life expectancy. That excess mortality might be expected is indicated by one study claiming an association between excess deaths from kidney disease and lead exposure among an adult cohort with a history of childhood plumbism [23].

SUMMARY OF THE EARLIER STUDY

In 1968–1969, the mortality experience of a cohort of Wenatchee area residents who participated in an earlier morbidity study of the health effects of lead arsenate spray exposure was studied.

In 1938–1939 an epidemiologic study was conducted in the Wenatchee Valley of Washington by the United States Public Health Service. This prolific apple-growing region was selected as the study location because of its long use of large quantities of lead arsenate spray and its isolation from industrial exposures to lead and arsenic.

In 1938, the 1231 study members were classified into three exposure groups. 'Orchardists' prepared and applied lead arsenate sprays during 1938. 'Consumers' included persons whose occupations did not bring them into contact with lead arsenate. This group included most children and a large number of women. 'Intermediates' were less homogeneous comprising former orchardists, warehouse workers, and those with infrequent lead arsenate spray exposure. For each intermediate and orchardist, the number of years of spray exposure was recorded.

Air monitoring was done to determine exposure associated with various orchard activities. The results are summarized in Table 1. Unfortunately, particle size, a major determinant of respiratory retention, was not determined. For comparison, nonoccupational ambient air lead levels range from 0.01 to 0.05 mg of lead per 10 m^3 of air. All orchard operations except sorting and packing involved lead exposures equal to or greater than those experienced in industrial environments such as battery manufacturing, a hazardous lead trade. However, orchardists experienced less annual exposure duration to lead in their seasonal tasks than do constantly employed industrial workers.

Urinary lead and arsenic and blood lead measurements were obtained for most participants, though the individual values are no longer available. Samples were collected during most months and showed some seasonal variation. Table 2 displays the average concentrations by exposure group and sex. These values verify an exposure gradient for the three groups. In nearly every case, the consumers had the lowest average values and the orchardists the highest average values. Men consistently had higher levels than women.

TABLE 1. ARSENIC AND LEAD CONCENTRATION IN THE ORCHARD AIR IN 1938 [24]

Insecticide operation	Length of exposure: Hours per day	Length of exposure: Weeks per year	Concentration, milligrams per 10 m³ (a): Arsenic Average	Arsenic Range	Lead Average	Lead Range
Mixing insecticide	1	8–12	18.5	0.2–110.7	57.4	0.9–467.3
Burning containers	NA(b)	NA	166.7	48.6–261.2	35.8	10.2–76.5
Spraying orchard	8–14	8–12	1.4	0.4–4.8	4.5	1.3–14.3
Thinning fruit	8–14	2–3	0.8	0.1–3.2	3.0	0.4–17.0
Picking fruit	8–14	6–10	5.8	2.6–19.0	29.3	7.7–75.2
Dumping fruit	8–12	8–12				
(October)			0.6	0.1–1.9	1.9	0.4–6.9
(December)			0.1	0.02–0.2	0.3	0.01–1.1
Sorting and packing (October)	8–12	4–12	0.06	0.03–0.08	0.16	0.07–0.22

(a) This volume of air, 10 m³, is approximately the amount that is inhaled during the working day, although the actual amount will vary with the degree of physical activity. Approximately 20–50 per cent of the total metal inhaled will be retained, primarily as a function of particle size.

(b) NA=not available.

TABLE 2. AVERAGE CONCENTRATIONS OF URINARY AND BLOOD LEAD AND URINARY ARSENIC IN 1938 [24]

	Urinary lead µg per l		Blood lead µg per 100g		Urinary arsenic µg per l	
Adult (≥ 15 yr) Consumers	n	x̄	n	x̄	n	x̄
Men	146	35.3	148	26.3	140	62.0
Women	123	27.8	124	25.8	121	56.3
Adult intermediates						
Men	102	43.3	108	29.5	123	71.0
Women	25	27.4	27	21.9	25	58.0
Adult orchardists						
Men	386	88.3	329	43.9	305	140.5
Women	61	46.0	58	43.4	58	97.9
Children (< 15 yr)						
Boys	81	52.9	17	36.9	78	106.3
Girls	65	54.5	14	36.1	67	113.3

Children's values were higher than consumers and intermediates. To determine if children normally have higher levels than adults, a comparison was made of the urinary lead and arsenic and blood lead levels of Bethesda, Maryland children with Bethesda adults and Wenatchee children. The Bethesda children were lower than both groups. The high levels of the Wenatchee children were attributed to their playing in the orchards and eating unwashed apples.

Although the blood and urine analyses showed a consistent gradient for groups, no significant differences were observed for clinical symptoms. Whereas seven individuals in the orchardist group did have a low grade of lead arsenate intoxication, they were not numerous enough to be significant in group comparisons of symptoms. The orchardists showed no tendency for the signs of lead and arsenic intoxication to occur in combination.

Despite the negative findings of the morbidity study, this population afforded a rare opportunity for a follow-up mortality study of individuals exposed to non-toxic levels of lead and arsenic.

FOLLOW-UP METHODS

While many records from the 1938 study had been lost, three important information sources were available: the final report of the earlier study, a set of punched cards (hereafter the 1938 cards) containing for each of 1231 study members the exposure group, exposure duration, age, sex, various clinical findings, and some miscellaneous data, and a typed list (hereafter the 1938 list) giving the names of the first 1229 study members, as well as each age, sex, exposure group, and (for orchardists) the exposure duration. The addresses of the study members were unavailable, as were the names of the last two from the original group.

The follow-up was begun in 1968, 30 yr after the original study, with the aim of locating either the original study member himself or an informant who could give information leading to the location of the death certificate. For a given study member, field efforts continued until there was reasonable certainty that the person located or described by the informant or death record was indeed the participant in the previous study. Most living study members remembered participating. For others, occupational background was sought and current age or age at death was checked for consistency against the age recorded on the 1938 cards. Names had to check with the 1938 list, or be obvious deviations.

Since addresses were lacking, valuable information for follow-up was obtained from the 1937 Wenatchee city directory, the current Wenatchee telephone book, State vital statistics records, school records, and local birth and death records.

ANALYSIS METHODS

The following data for each study member were available for analysis: age in 1938, sex, exposure group, exposure duration as of 1938, years of orchard work after 1938, age at follow-up or age at death or age last known alive, and primary and associated causes of death. Death causes listed on the death certificates were coded according to the International Classification of Diseases (ICD), 1965 Revision. Primary cause of death was chosen using the Rules for Classification of the World Health Assembly.

The Standard Mortality Ratio (SMR) technique was used to assess mortality experience. This ratio is calculated by dividing the observed number of deaths by the expected number of deaths. Washington State was chosen as the standard population from which expected deaths were calculated. Life tables for Washington were obtained for the years 1939–1941, 1949–1951, and 1959–1961.

The advantage of the life table method in the computing of expected deaths is the division of the total time period into smaller (yearly) intervals for which expected deaths are obtained. All follow-up information is utilized since any post-1938 experience, even if only a short time interval, is used in the analysis. For each member of the 1938 cohort, use of the life tables enabled the calculation of each individual's contribution to the years-at-risk and hence expected death category.

Expected deaths were calculated in the following manner. The three time periods (1938–1948, 1948–1958, 1958–1968) are centered on 1943, 1953 and 1963. The Wash-

gton life tables were centered on the years 1940, 1950 and 1960. Linear interpolation as used to obtain life tables for 1943 from the 1940 and 1950 tables and also to btain tables for 1953 from the 1950 and 1960 tables. Since mortality rates have mained essentially unchanged over the last decade, the 1960 tables were used r 1963.

This process provided sex-specific tables for 10-yr age groups. Values for the 5+ age groups were extrapolated using a fourth degree polynomial. Individual ge death rates were obtained by a graduation formula which used a fifth degree olynomial (Jenkins fifth difference modified osculatory formula) [25].

In addition to the above tables for total mortality, similar tables were constructed eparately for the following three specific cause groups: heart disease (ICD 390–29), cancer (ICD 140–209), and stroke (ICD 430–439).

The expected death contribution for an individual of a given age is the death ate for that age (sex and time-specific). For example, the expected death contribution for a male age 30 in 1947 is found from the male table for 1938–1948 using the death rate for age 30.

The exposure group categories never changed. Regardless of subsequent orchard work or retirement from orchard work, these categories were retained at their 1938 designations. It was felt better not to mix people who were in different exposure groups in 1938. Their changing exposure would be reflected better by changing exposure duration categories than by changing group categories.

FOLLOW-UP RESULTS

By the cut-off date of 1 October 1969, the current status of 1175 of the 1229 possible study members was determined. Of these 1175, 452 had died and 723 were located alive. In addition, 26 were located at some time after 1938 but lost before 1968. Only 28 (2 per cent) were not located. This latter group included three members who were located but were excluded from the current study; one because he was not a Wenatchee resident but had participated in the earlier study while visiting relatives, the other two because of large age discrepancies. A classification of the 1201 study members followed-up appears in Table 3.

Upon contact with the study member or informant, the information obtained included name, birthdate, follow-up age, sex and current status (dead or alive). For deaths, follow-up age was age at death. For those followed for a time but lost before 1968, follow-up age was the age last known alive. Information on orchard experience after 1938 and the reason for leaving orchard work was also obtained.

Death certificates were obtained for 442 of the 452 deaths. Five of the other ten were war deaths. For the other five, the date of death was not specific enough to locate the death certificate.

The characteristics of the 28 study members lost to follow-up were investigated. Those people having little (ten years or less) or no orchard exposure were more likely to be lost than those with more exposure (3.0 per cent against 0.7 per cent). Females were more likely to be lost than males (3.3 per cent vs 1.7 per cent). For both sexes, orchardists were lost frequently and consumers most frequently.

A similar classification study of the 26 study members who were followed briefly but lost before 1968 yielded almost identical results. It is quite unlikely due to the small number of members lost or withdrawn and the small number of orchardists

TABLE 3. CLASSIFICATION OF THE 1201 FOLLOW-UP STUDY MEMBERS

	Males									Females								
	Consumers			Intermediates			Orchardists			Consumers			Intermediates			Orchardists		
1938 age	0–44	45–64	65+	0–44	45–64	65+	0–44	45–64	65+	0–44	45–64	65+	0–44	45–64	65+	0–44	45–64	65+
0 yr	106	23	7	6	3	1	0	0	0	127	46	12	38	30	5	0	0	0
1–10 yr	0	0	0	65	28	7	146	32	0	0	0	0	44	30	5	28	10	0
11–20 yr	0	0	0	10	18	8	101	53	14	0	0	0	1	10	1	3	11	0
21+ yr	0	0	0	0	13	10	27	90	28	0	0	0	0	1	0	2	0	1
Total	106	23	7	81	62	26	274	175	42	127	46	12	83	71	11	33	21	1
Total		136			169			491			185			165			55	
Total					796									405				

ithin these categories, that these people would have significantly affected the analysis sults had they been completely followed.

ANALYSIS RESULTS

For all study members combined, the SMR was 0.70. It is substantially below 00 due to the choice of a standard population, Washington State, which includes ·ban and disabled populations, both higher-risk mortality groups not included in .e Wenatchee area.

No consistent differences were observed in the SMR by exposure group category. he overall SMR was 0.74 for the consumers, 0.78 for the intermediates, and 0.65 ·r the orchardists. Orchardists certainly gave no evidence of increased mortality.

Analysis by time period also showed no consistent differences. The overall SMRs ere 0.68 for 1938–1948, 0.74 for 1948–1958 and 0.68 for 1958–1968. The time period ·ecific SMRs were very similar even for smaller classes. For example, for males age 5+, the time period ratios were 0.98, 1.02, and 0.94 respectively, for intermediates id 0.59, 0.70 and 0.64, respectively, for orchardists.

Analysis by exposure duration showed inconsistent differences. There was no ·idence of increasing mortality risk due to longer exposures. For example, the ·tegory males age 55+ contained 78 per cent of the deaths in the two positive ·posure groups. Restricting attention to this age-sex category, the SMR for ex-osure duration 1–5 yr was 1.25, for 6–10 yr was 0.93, for 11–15 yr was 0.92, for 5–20 yr was 1.95 and for 21+ years was 0.65 for intermediates. For orchardists ·e SMRs were 0.40, 1.61, 0.60, 0.81, 0.61, respectively.

Analysis by sex gave an overall SMR of 0.69 for males, 0.73 for females. Sex-ecific analysis by exposure groups showed that male intermediates had the highest MR, 0.89 compared with 0.62 for consumers and 0.64 for orchardists while female ·chardists had the highest SMR, 0.86 (only 18 deaths), compared with 0.79 for onsumers and 0.67 for intermediates.

Age-specific analysis added no dramatic insight. At the younger ages, 0–54, females ·d exhibit some increased mortality (SMR of 1.03 based on only 19 deaths), primarily · the consumer category. The male SMR for the 0–54 group was 0.51. For ages 5+ the male SMR was 0.72, the female SMR was 0.70.

Table 4 summarizes the observed and expected deaths and the SMR for total ·ortality. The classes shown include consumer (total), intermediate (3 exposure urations and total), orchardists (3 exposure durations and total), 3 age groups, id total for all groups. The expected deaths were 447; the 5 war deaths were ex-·uded from the analysis. The only category suggestive of excessive mortality is the ·termediates with 11–20 yr of exposure.

Table 5 shows the SMR for intermediates and orchardists adjusted to the overall onsumer SMR of 0.74. The p values shown are found from the chi-square statistic ·ne degree of freedom) equal to (observed deaths—expected deaths)^2/expected deaths. ·nly the 3 orchardists categories: age 45–64, exposure 21+; age 46–64, all exposures; id total were statistically significant. In all three cases the observed deaths were gnificantly *fewer* than expected. The intermediate categories of age 65+, 11–20 yr id all ages. 11–20 yr are suggestive of excess deaths but are not different from ·pected at the 5 per cent significance level.

Table 4. Observed and expected deaths and SMRs for total mortality

Years of exposure	Cohort	Age 0–44	45–64	65+	Total
0	Consumers				
	Observed	11	29	73	113
	Expected	10.38	38.48	103.69	152.56
	SMR	1.06	0.75	0.70	0.74
1–10	Intermediates				
	Observed	3	16	40	59
	Expected	4.62	26.01	50.15	80.78
	SMR	0.65	0.62	0.80	0.73
	Orchardists				
	Observed	7	16	26	49
	Expected	9.17	28.36	28.18	65.71
	SMR	0.76	0.56	0.92	0.75
11–20	Intermediates				
	Observed	0	8	26	34
	Expected	0.31	8.24	25.48	34.03
	SMR	0.00	0.97	1.02	1.00
	Orchardists				
	Observed	2	26	49	77
	Expected	4.05	41.56	77.04	122.65
	SMR	0.49	0.63	0.64	0.63
21+	Intermediates				
	Observed	0	1	19	20
	Expected	0.00	2.51	27.46	29.97
	SMR	—	0.40	0.69	0.67
	Orchardists				
	Observed	0	13	82	95
	Expected	0.68	30.62	121.31	152.60
	SMR	0.00	0.42	0.68	0.62
All years	Intermediates				
	Observed	3	25	85	113
	Expected	4.93	36.76	103.09	144.7
	SMR	0.61	0.68	0.82	0.78
	Orchardists				
	Observed	9	55	157	221
	Expected	13.90	100.54	226.53	340.97
	SMR	0.65	0.55	0.69	0.65
	All groups				
	Observed	23	109	315	447
	Expected	29.21	175.79	433.31	634.03
	SMR	0.79	0.62	0.73	0.70

The analysis was also performed separately for each of three principal causes of death, heart disease, cancer, and stroke. The cause-specific life tables were used with other deaths treated as withdrawals. Tables 6, 7 and 8 summarize these results.

It is seen that for classes suggestive of excess mortality for all causes, the excess cannot be attributed to any specific cause. In most cases each of the three specific causes are reasonably consistent. For example, for intermediates, all ages, 11–20 yr exposure, the heart disease SMR is 0.97, the cancer SMR is 1.6, and the stroke SMR

TABLE 5. TOTAL MORTALITY SMR ADJUSTED TO CONSUMER DEATH RATE AND ASSOCIATED p VALUES

Years of exposure	Cohort	Age 0–44	45–64	65+	Total
1–10	Intermediate				
	SMR	0.88	0.83	1.08	0.98
	p value	—	0.47	0.65	0.92
	Orchardists				
	SMR	1.03	0.76	1.24	1.01
	p value	0.97	0.28	0.27	0.97
11–20	Intermediates				
	SMR	0	1.31	1.38	1.35
	p value	—	0.44	0.10	0.08
	Orchardists				
	SMR	0.67	0.84	0.86	0.85
	p value	—	0.39	0.29	0.15
21+	Intermediates				
	SMR	—	0.53	0.93	0.90
	p value	—	—	0.75	0.64
	Orchardists				
	SMR	0	0.57	0.91	0.84
	p value	—	0.04	0.41	0.09
All years	Intermediates				
	SMR	0.81	0.92	1.11	1.05
	p value	—	0.67	0.32	0.59
	Orchardists				
	SMR	0.87	0.74	0.94	0.87
	p value	0.69	0.02	0.40	0.04
	All groups				
	SMR	1.06	0.84	0.98	0.95
	p value	0.76	0.06	0.73	0.29

is 0.65 (only 3 deaths). The overall SMR is 0.65 for heart disease, 0.73 for cancer, and 0.79 for stroke. Less common causes of death, including kidney disease, liver disease, and lung cancer, were also studied but were not found to be unusually prevalent. The normal-prevalence measures were obtained from relative cause-specific Vital Statistics from Washington State for 1953, the midpoint in the follow-up period.

Data were also collected on reason for leaving orchard work. Responses included health, death, retirement, other employment, and other. This information did not prove useful. The female response rate was too low to allow any use of the reasons. While the response rate was slightly better for males, no additional information on the contribution of lead arsenate spray exposure to mortality was gained.

DISCUSSION

The main conclusion of this study is that excess mortality does not occur consistently from exposure to lead arsenate insecticide spray. While the results are suggestive of excess deaths at some lesser exposures, the evidence is that many lives including those with the longest exposures are not being affected. An exhaustive set of class-specific analyses did not incriminate the lead arsenate exposure as a consistent factor in the observed deaths.

Table 6. Observed and expected deaths and SMRs for heart disease mortality

Years of exposure	Cohort	Age 0–44	45–64	65+	Total
0	Consumers				
	Observed	1	8	26	35
	Expected	1.52	14.29	44.70	60.50
	SMR	0.66	0.56	0.58	0.58
1–10	Intermediates				
	Observed	1	8	17	26
	Expected	0.90	10.29	21.39	32.59
	SMR	1.10	0.78	0.79	0.80
	Orchardists				
	Observed	0	4	10	14
	Expected	1.77	11.94	12.37	26.08
	SMR	0.00	0.34	0.81	0.54
11–20	Intermediates				
	Observed	0	4	10	14
	Expected	0.07	3.44	10.88	14.40
	SMR	0.00	1.16	0.92	0.97
	Orchardists				
	Observed	0	9	19	28
	Expected	0.95	18.29	34.60	53.84
	SMR	0.00	0.49	0.55	0.52
21+	Intermediates				
	Observed	0	0	10	10
	Expected	0.00	1.08	12.29	13.38
	SMR	—	0.00	0.81	0.75
	Orchardists				
	Observed	0	8	39	47
	Expected	0.18	13.40	54.32	67.90
	SMR	0.00	0.60	0.72	0.69
All years	Intermediates				
	Observed	1	12	37	50
	Expected	0.98	14.82	44.56	60.36
	SMR	1.02	0.81	0.83	0.83
	Orchardists				
	Observed	0	21	68	89
	Expected	2.90	43.63	101.29	147.82
	SMR	0.00	0.48	0.67	0.60
	All groups				
	Observed	2	41	131	174
	Expected	5.40	72.73	190.56	268.69
	SMR	0.37	0.56	0.69	0.65

Several caveats are necessary. Information on important covariables such as individual cigarette smoking or lead-arsenic exposure from diet is unfortunately not available. The local water supply was investigated as a possible source of lead or arsenic and found not to be a problem.

It is difficult to be sure of the exposure dosage categories. It is unfortunate that the individual blood and urine concentrations were lost. While the group averages

TABLE 7. OBSERVED AND EXPECTED DEATHS AND SMRS FOR CANCER MORTALITY

Years of exposure	Cohort	Age 0–44	45–64	65+	Total
0	Consumers				
	Observed	4	9	3	16
	Expected	1.68	9.12	13.68	24.48
	SMR	2.38	0.99	0.22	0.65
1–10	Intermediates				
	Observed	0	3	7	10
	Expected	0.62	5.57	7.02	13.21
	SMR	0.00	0.54	1.00	0.76
	Orchardists				
	Observed	0	6	3	9
	Expected	0.98	5.46	4.19	10.63
	SMR	0.00	1.10	0.71	0.85
11–20	Intermediates				
	Observed	0	2	6	8
	Expected	0.03	1.47	3.48	4.98
	SMR	0.00	1.36	1.72	1.60
	Orchardists				
	Observed	0	9	3	12
	Expected	0.38	7.16	10.82	18.36
	SMR	0.00	1.26	0.28	0.65
21+	Intermediates				
	Observed	0	0	3	3
	Expected	0.00	0.38	3.40	3.78
	SMR	—	0.00	0.88	0.79
	Orchardists				
	Observed	0	1	11	12
	Expected	0.07	4.87	16.20	21.14
	SMR	0.00	0.21	0.68	0.57
All years	Intermediates				
	Observed	0	5	16	21
	Expected	0.65	7.42	13.90	21.98
	SMR	0.00	0.67	1.15	0.96
	Orchardists				
	Observed	0	16	17	33
	Expected	1.43	17.48	31.21	50.13
	SMR	0.00	0.92	0.54	0.66
	All groups				
	Observed	4	30	36	70
	Expected	3.76	34.02	58.80	96.58
	SMR	1.06	0.88	0.61	0.73

followed the suspected exposure gradient, considerable individual variation was present. We cannot be positive who the most exposed study members were. The dosage level is particularly a problem for the intermediates, who have the most heterogeneous exposure.

Several speculations which can be neither proved nor disproved are possible. One might claim that orchardists who were most vulnerable to lead arsenate spray left orchard work before 1938 so were either not in this study or were classed as

Table 8. Observed and expected deaths and SMRs for stroke mortality

Years of exposure	Cohort	Age 0–44	45–64	65+	Total
0	Consumers				
	Observed	1	2	23	26
	Expected	0.35	3.68	18.49	22.52
	SMR	2.85	0.54	1.24	1.15
1–10	Intermediates				
	Observed	0	1	5	6
	Expected	0.16	2.24	8.59	10.99
	SMR	0.00	0.45	0.58	0.55
	Orchardists				
	Observed	0	1	6	7
	Expected	0.26	2.03	4.27	6.55
	SMR	0.00	0.49	1.41	1.07
11–20	Intermediates				
	Observed	0	0	3	3
	Expected	0.01	0.71	3.88	4.60
	SMR	0.00	0.00	0.77	0.65
	Orchardists				
	Observed	0	1	10	11
	Expected	0.12	2.99	11.70	14.82
	SMR	0.00	0.33	0.85	0.74
21+	Intermediates				
	Observe	0	0	0	0
	Expected	0.00	0.23	4.24	4.47
	SMR	0.00	0.00	0.00	0.00
	Orchardists				
	Observed	0	0	14	14
	Expected	0.02	2.41	18.01	20.44
	SMR	0.00	0.00	0.78	0.68
All years	Intermediates				
	Observed	0	1	8	9
	Expected	0.17	3.17	16.72	20.06
	SMR	0.00	0.32	0.48	0.45
	Orchardists				
	Observed	0	2	30	32
	Expected	0.41	7.43	33.97	41.82
	SMR	0.00	0.27	0.88	0.76
	All groups				
	Observed	1	5	61	67
	Expected	0.93	14.28	69.18	84.40
	SMR	1.07	0.35	0.88	0.79

intermediates. Thus, those who remained in orchard work were a self-screened group who were relatively resistant to any harmful effects.

Similarly, the people most susceptible to the lead arsenate spray might either have died or moved away before 1938 leaving behind a selected group of better mortality risks. This theory would account for the extremely favorable mortality experience of the entire cohort in comparison with the total state.

Another difficulty with interpretation of study results is the relatively small number of study members. Some of the suggestive excess deaths are not significant because of small numbers. Many of the volunteers in 1938 are still too young to have reached high risk mortality age. Large numbers of subjects are needed in studies involving subtle effects of environmental exposures rather than mortality, which is a rather crude index.

To eliminate the possibility that those most affected by a potential hazard may drop out before a formal study begins, future effects studies should identify and follow all individuals from their first exposure to a possible health risk. In the future, too, the expense of better defining individual exposure is obviously justified. Exposure can be better handled in prospective studies than in follow-up studies.

From the beginning of the study, the limitations of the small size of the study group, the paucity of exposure information, and the possible bias of the study population were apparent. However, the availability of such a highly-exposed group afforded a unique opportunity to obtain a mortality analysis. A large gradient in mortality experience would have overcome these recognized difficulties; that this did not occur only emphasizes the importance of these limitations for future studies.

SUMMARY

A follow-up mortality study was conducted for a cohort of 1231 individuals in Wenatchee, Washington, who had participated in a 1938 morbidity survey of the exposure effects of lead arsenate insecticide spray. The individuals were classified by spray exposure and duration as well as by age and sex. An 'orchardist' group had highest exposure to the lead arsenate spray while a 'consumer' group had no direct spray exposure. A third group had intermediate exposure. Duration of the exposure was categorized into 0, 1–10, 11–20 and 21+ yr.

Over 97 per cent of the original group was located in the follow-up which took place in 1968–1969. There were 452 deaths. A life table method of analysis of the standard mortality ratio (SMR) was used. The standard population for calculating expected deaths was the state of Washington. Rate analysis was done for total deaths and for the specific primary causes of heart disease, vascular lesions, and cancer.

For all study members combined, the SMR was 70 per cent, demonstrating that this cohort experienced less mortality than the Washington average. While several of the analysis sub-categories had significant SMRs, the pattern of these differences was not consistent. Exposure group mortality ratios were not consistent with the exposure gradient. Intermediates had the highest SMR (0.78) and orchardists the lowest (0.65). The mortality pattern for increasing duration of exposure also was not consistent. The highest mortality was experienced by the intermediate group in the 11–20 yr duration category. For the cause-specific analyses, the pattern of mortality was reasonably consistent for each analysis sub-category implying that excess deaths were not solely due to any of these three specific principal causes.

Acknowledgements—The authors wish to thank Ms. Janet Daling, Research Analyst, and Dr. Jack Allard, Chief, Office of Laboratories, both of the Washington State Department of Social and Health Services; and Dr. Charles Dobrovolny, Division of Pesticide Community Studies, Pesticide Office and Mr. Frederick Sher, Division of Health Effects Research, Office of Research and Monitoring, both of the Environmental Protection Agency, for their invaluable and dedicated efforts on this study.

REFERENCES

1. The Pesticide Review—1968. U.S. Department of Agriculture, Stabilization and Conservation Service, ...ington, D.C., 1968
2. Engel RE, Hammer DI, Horton RJM *et al*: Environmental Lead and Public Health. Environmental Protection Agency, Research Triangle Park, North Carolina, 1971
3. Henderson DA: Chronic nephritis in Queensland. Aust Ann Med 4: 163–177, 1955
4. Lane RE: Health control in inorganic lead industries. Arch Environ Hlth 8: 243–50, 1964
5. Byers RK, Lord EE: Late effects of lead poisoning on mental development. Am J Dis Child 66: 471–494, 1943
6. Moeschlin S: Poisoning: Diagnosis and Treatment. First American edition, Grune & Stratton, New York and London, pp. 45–71, 1965
7. Aub JC *et al*: Lead poisoning, Medicine Monographs, Vol. 7, Baltimore, Williams & Wilkins, 1926
8. Chisholm JJ, Leaky NB: Aminoaciduria as a manifestation of renal tubular injury in lead intoxication. J Pediat 60: 1–17, 1962
9. Chisholm JJ: The use of chelating agents in the treatment of acute and chronic lead intoxication in childhood. J Pediat 73: 1–11, 1968
10. Smith HD: Pediatric lead poisoning. Arch Environ Hlth 8: 256–266, 1964
11. Chisholm JJ: Harrison HE: The exposure of children to lead. Pediatrics 18: 943–954, 1956
12. Byers RK: Lead poisoning, review of the literature and report of 45 cases. Pediatrics 23: 585–597, 1959
13. Hamilton A: Industrial Toxicology. New York, Hoeber, pp. 43–44, 1934
14. Cantarow A, Trumper M: Lead Poisoning. Baltimore, Williams & Wilkins, pp. 97–98, 1944
15. Seven MJ, Ed: Metal-Binding in Medicine. Philadelphia, Lippincott, Chapter 4, 1960
16. Hernberg S, Nikkanen J, Mellin G, *et al*: Delta-aminolevulinic acid dehydrase as a measure of lead exposure. Arch Environ Hlth 21: 140–145, 1970
17. Grundy R: Toxicologic and epidemiologic bases for air quality criteria: carbon monoxide and lead. J Air Pollut Contr Ass 19: 729–32, 1969
18. Kehoe RA: The metabolism of lead in health and disease. Roy Inst Public Hlth 24: 81–97, 129–143, 177–203, 1961
19. Buchanan WD: Toxicity of Arsenic Compounds. New Jersey, Van Nostrand, 1962
20. Hueper WD: Environmental carcinogenesis in man and animals. Ann NY Acad Sci 108: 963–975, 1963
21. Sullivan RJ: Preliminary Air Pollution Survey of Arsenic and its Compounds. National Air Pollution Control Administration APTD 69-26, 1969
22. Schroeder HA, Tipton IH: Human body burden of lead. Arch Environ Hlth 17: 965–978, 1968
23. Henderson DA: The aetiology of chronic nephritis in Queensland. Med J Aust: 377–386, 1958
24. Neal PA *et al*: A study of the effect of lead arsenate exposure on orchardists and consumers of sprayed fruit. Public Health Service Bulletin No. 267, 1941
25. Miller D: Elements of Graduation. Philadelphia, Actuarial Society of America, pp. 22–24, 1946