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Sequelae of Acute Organic Phosphate Poisoning

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WITH THE WIDESPREAD and increasing use of chemicals to control insects, rodents, and weeds in our environment, clinical studies which may contribute to our learning more about possible residual or chronic effects from human exposures are badly needed. Such studies, however, present serious difficulties, stemming from the numbers of compounds in use, the many combinations of concurrent and sequential exposures, and differing routes of entry and effective dosages. Nevertheless, a start has to be made, as only through clinical studies will some of the evidence necessary for evaluation become available. The study to be reported will represent one approach to the problem: a follow-up, 3 years after acute insecticide poisoning, of a group of 235 individuals reported as occupationally exposed to organic phosphates in California in 1960. The follow-up was begun in the summer of 1963 and completed 1 year later.

The Study Population

The source of the study population was the 283 individuals reported by physicians to the California Department of Industrial Relations in 1960 as having had occupational disease attributed to organic phosphate insecticides.[1] The group was reduced to 235 for follow-up and to 232 for final study by application of criteria to be presented below.

Cases reported in 1960 were chosen for 1963–64 follow-up because (1) the 3-year interval was deemed adequate to establish the presence or absence of sequelae; (2) the time interval of 3 years was sufficiently short to permit location of most of the patients; (3) litigation related to compensation would probably be completed; and (4) the cases reported in 1960 had been the subject of an earlier follow-up by the Department of Public Health of the State of California, in the form of questionnaires to the treating physicians 1 month after the poisoning episodes (as part of a study of Doctor's First Report of Work Injury).[2]

Some comment on the work force in California's industry is necessary for an understanding of the composition of the group at risk from which this study population was drawn. About two-thirds of the occupational diseases attributed to pesticides in 1960 occurred in workers in the agricultural industry, the remainder being scattered among manufacturing (e.g., chemical companies), government (state and local), trade (e.g., nurseries, packing houses) and service (e.g., pest-control operators). In 1960 there were about 455,000 agricultural workers in California. Of these, 153,000 were self-employed farmers and unpaid family labor, not covered by Workmen's Compensation and therefore not reportable to the Department of Industrial Relations. Of the approximately 302,000 covered by Workmen's Compensation, about 43,000 were contract foreign laborers (mainly Mexican nationals). The impossibility of follow-up in these people led to their exclusion from the study. The study population was thus drawn from about 259,000 hired permanent and temporary domestic workers in the agricultural industry and an undetermined number of nonagricultural workers. Because the size of the labor force is uncertain and reporting incomplete, no attempt should be made to translate the number of reported cases into an estimate of incidence.

Review of the 283 reports in 1960 of systemic poisoning by organic phosphate pesticides led to elimination of 48 individuals because of obvious misdiagnosis (brought out in replies to

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gestive of organic phosphate poisoning and increased in exposed groups. The groups were constituted as follows:

Group 1 (87 patients). those with signs and symptoms of parasympathetic stimulation (miosis or three or more of the following: headache, nausea, weakness, chest pain, abdominal cramps, vertigo, vomiting, nervousness, sweating, disturbed vision, shortness of breath, wheezing, salivation) confirmed by a depressed blood cholinesterase level;

Group 2 (91 patients). those with signs and symptoms of parasympathetic stimulation, but without laboratory confirmation ("borderline" or normal results or no cholinesterase test performed);

Group 3 (57 patients). those reported as having organic phosphate poisoning, but with inadequate data on symptoms and laboratory findings.

Patients Located and Examined

The number of individuals located and those examined, classified in this preliminary manner (before follow-up), are shown in Table 1.

Of the 57 "located but not examined," 4 were dead at the time of the follow-up, 8 were in the armed services, and 6 were known to have left California. The other 39 could not be reached during the available time of November through April, a period when exposures to organic phosphates were minimal, and evaluation could be made without the complicating factors of fatigue and acute exposures.

In view of the fact that 174 (74%) of the study population of 235 were "located," and only 117 (50%) were "located and examined," the major characteristics of the groups "located and examined," "located but not examined," and "not located" should be compared. From the basic records available at the beginning of the study, some information, such as the county of injury, age, sex, toxic agent, and hospitalization, was known for most individuals in all groups.

Geographical Distribution The counties in which the acute poisonings occurred in the 235 cases selected for follow-up were grouped in five major geographical areas of the state (Table 2). Most of the reported cases came from the San Joaquin Valley and the Northern California coastal counties, and it was in these areas that the majority were located and examined. There was some migration from county of injury to county of interview, but the majority of subjects located were found in the county of injury.

Logistical problems in follow-up did not permit contact with many of the subjects poisoned in the Southern California coastal counties or in the Imperial Valley, so that 84 (72%) of those interviewed came from the San Joaquin Valley, where 63% of the acute episodes had occurred, and 30 (26%) came from Northern California coastal counties which had contributed 21% of the study group. Conversely, a large proportion of the located-and-not-examined group came from Southern California and the Imperial Valley.

Age Distribution The group located and not examined was younger than the other two (Table 3). Part of the explanation for this finding is the number of workers in this group in the Armed services (there were 8 such individuals,

TABLE 1. PRELIMINARY CLASSIFICATION AS TO LIKELIHOOD OF PROPER DIAGNOSIS AND NUMBERS OF INDIVIDUALS LOCATED AND EXAMINED

*Group**	*Total*	*Located*	*Examined*	*Located, not examined*	*Not located*
I	87	70	47	23	17
II	91	63	42	21	28
III	57	41	28	13	16
TOTAL	235	174	117	57	61

*For definition of groups, see text.

TABLE 2. GEOGRAPHICAL DISTRIBUTION OF ACUTE EPISODES

Area	*Located*				*Not located*		*Total in area*	
	Examined		*Not examined*					
	No.	*% of area*	*No.*	*% of area*	*No.*	*% of area*	*No.*	*% of area*
San Joaquin Valley	84	57	30	20	34	23	148	100
Northern California coast	30	61	8	16	11	22	49	99
Southern California coast	0	0	10	48	11	52	21	100
Imperial Valley	0	0	7	78	2	22	9	100
Other	3	38	2	25	3	38	8	101
TOTAL	117	50	57	24	61	26	235	100

TABLE 4. TOXIC AGENTS REPORTED AS RESPONSIBLE FOR ACUTE EPISODES

	Located and examined		*Located and not examined*		*Not located*		
Toxic agent	*No.*	*%*	*No.*	*%*	*No.*	*%*	*Total (no.)*
Parathion	39	33	12	21	39	64	90
Phosdrin	17	15	11	19	7	11	35
Thimet	11	9	1	2	5	8	17
Systox	8	7	5	9	0	0	13
More than one	17	15	9	16	7	11	33
Other	7	6	9	16	0	0	16
Not known	18	15	10	18	3	5	31
TOTAL	117	100	47	101	61	99	235

TABLE 5. DISTRIBUTION OF CASES EXAMINED BY AGE AND SEX

Age (years)	*Female*	*Male*	*Total*
Under 20	0	15	15
20-29	1	38	39
30-39	1	23	24
40-49	1	17	18
50-59	2	10	12
60-69	1	5	6
TOTAL	6	108	114

The median age was 31 years; the mean, 34.

tions such as cultivating, irrigating, and harvesting in previously sprayed areas, handling impregnated seeds, etc. Incidental activities are those in which accidental contacts occurred to persons not normally exposed in the course of their work.

Signs and Symptoms in Acute Episodes Table 8 shows a summary of the symptoms and signs recorded in the 114 cases regarded as valid for the study, and a breakdown for 3 of the agents involved. These data represent a compendium of the positive findings obtained upon interrogation and from those medical records available to us. The accuracy from subject to subject varies with their recollections and the thoroughness with which findings were recorded. We were impressed, however, with how vivid most of the poisoning episodes were in the patients' memories and the good agreement between their descriptions and hospital and medical records.

There is no question but that the nonspecificity of the commonest symptoms can lead to difficult diagnostic problems. It is only by studying the sequence and combinations of symptoms in individual cases and their timing relative to a possible exposure that a sound clinical judgment is possible. When one reviews individual case histories, one's convictions as to the accuracy of many of the diagnoses is enhanced by the patient's clear recognition that he was having an experience unique for him. Particularly vivid and unusual were the visual disturbances that many subjects noticed. Another outstanding feature was the profound weakness that accompanied the episode in many instances.

No sweeping conclusions should be drawn from comparison of the symptoms with various agents because of differences in dose and route of administration. In our series, however, Phosdrin and parathion did not appear to differ significantly in the symptoms recalled by the patients. Thimet poisoning was characterized in all 12 cases by nausea and vomiting; headaches were frequent, but there were less miosis, sweating, and weakness. Characteristically there ap-

TABLE 6. SEASONAL DISTRIBUTIONS OF ACUTE EPISODES IN 1960 IN 114 INDIVIDUALS LOCATED AND EXAMINED IN 1964

Agent	*Jan.*	*Feb.*	*Mar.*	*Apr.*	*May*	*June*	*July*	*Aug.*	*Sept.*	*Oct.*	*Nov.*	*Dec.*	*Total*
Parathion	—	1	1	3	5	3	5	3	15	—	—	—	36
Phosdrin	—	—	—	—	3	13	2	4	5	3	—	—	30
Thimet	—	—	1	9	—	2	—	—	—	—	—	—	12
Systox	—	—	—	—	—	1	1	3	—	—	—	—	5
More than one	—	—	—	—	1	3	5	11	2	1	—	—	23
Other	—	1	—	—	4	—	—	3	—	—	—	—	8
TOTAL	0	2	2	12	13	22	13	24	22	4	0	0	114

TABLE 8. SYMPTOMS AND SIGNS DURING ACUTE EPISODES IN 1960 IN INDIVIDUALS LOCATED AND EXAMINED IN 1964

Symptom or sign	Individuals manifesting symptom (%)			
	Total series ($N = 114$)	Parathion ($N = 36$)	Phosdrin ($N = 30$)	Thimet ($N = 12$)
Nausea	84	84	70	100
Miosis	55	67	83	8
Vomiting	54	55	53	75
Weakness	53	55	67	60
Sweating	37	42	43	48
Dizziness, etc.	36	33	40	33
Disturbed vision	36	30	43	50
Abdominal cramps	25	28	27	25
Headache	24	19	10	58
Chest pain or tightness	20	28	10	42
Salivation	10	3	13	0
Nervousness, insomnia	9	3	23	0
Diarrhea	9	6	6	8
Loss of appetite	8	14	6	17
Cough, expectoration	4	0	3	0
Shortness of breath	1	3	0	8

coming home from work at the height of the spraying season, and according to fellow workers had been working that day with organic phosphate pesticides. Since many workers have volunteered the information that blurring of vision, restricted visual fields, and "fuzziness" were extremely common at the end of the work day, the relationship between such accidents and disturbed function due to insecticide poisoning would be worth investigating. Durham *et al.*[7] have reported interesting studies pertinent to this question.

Possible Sequelae

For all individuals interviewed, a period of at least 3 years had elapsed since the acute poisoning episode. As indicators of possible chronic sequelae, all symptoms or signs which persisted longer than 6 months were reviewed, with special consideration to those which had continued until the time of our examination.

Symptoms in the 43 individuals whose complaints lasted longer than 6 months after poisoning were grouped into a few major categories (Table 11). It should be stressed that these complaints were based on responses elicited during a systems review and were not necessarily attributed or related to the poisoning either by the patient or by the examining physician. They supplied the leads for further inquiry as to possible sequelae. As many individuals had more than one symptom, totals are greater than 43.

Eye Complaints Blurring of vision accompanied over one-third of the episodes of acute poisoning. Acute symptoms lasted only a very short time; most patients had no complaints after a day or two.

TABLE 9. PRELIMINARY GROUP CLASSIFICATION AND FINAL ESTIMATE OF SEVERITY OF ACUTE EPISODES IN INDIVIDUALS LOCATED AND EXAMINED

Group*	Final estimate of severity (No. of cases)				
	Severe	Moderate	Mild	None	Total
I	3	29	15	0	47
II	2	20	20	0	42
III	1	5	19	3	28
TOTAL	6	54	54	3†	117

*For definition of groups, see text.
†Excluded from subsequent analyses.

TABLE 10. SEVERITY OF ACUTE 1960 ATTACK AND CHOLINESTERASE ACTIVITY AT THAT TIME IN 114 INDIVIDUALS LOCATED AND EXAMINED IN 1964

Cholinesterase activity	Severity of attack (No. of cases)			
	Severe	Moderate	Mild	Total
No record of determination	0	12	25	37
Low	4	37	16	57
Borderline	2	2	5	9
Normal	0	0	6	6
No report found	0	3	2	5
TOTAL	6	54	54	114

hospital for 2 days and received 5.3 mg. of atropine. Subsequently he had two more mild poisoning episodes, for one of which he was hospitalized (July 1963). His only residual complaints are difficulty in vision ("I can't see so well") and photophobia. Eyes showed injected conjunctivae, bilateral pterygia and arcus senilis, and presbyopia.

Case II-92

A 27-year-old Negro farm laborer was poisoned in 1960 with Thimet, which he dumped from boxes into a spreader without using gloves or respiratory protection. About 5 hr. after an 8-hr. work day he became nauseated and vomited, his "eyes weakened," and he had abdominal cramps. Examination showed pinpoint pupils. Cholinesterase activity was not determined. He was given atropine and returned to work in 1 month. He continues to have intermittent abdominal distress and frequent headaches, and says that his left eye is weaker than it used to be. He was a nervous, intense young man, and examination of his eyes revealed no objective evidence for his minor complaint.

Several patients exhibited chronic conjunctivitis, accompanied in 2 (including one of the above) by photophobia. Some attributed this to the pesticide exposures, but all were constantly exposed to wind, dust, and glare, and it is extremely unlikely that the organic phosphate was the explanation. Another individual had a cataract under periodic surveillance, but there was no suggested relationship to poisoning.

It appears that the episode of acute poisoning, which in so many patients was characterized by miosis and blurring of vision, focused the patient's attention on his eyes, and that this emphasis was sometimes accentuated by the side-effects of atropinization. In the older worker it was natural that hitherto latent or developing visual difficulties would be attributed to the poisoning. The fact that in our series of 114 cases there were so few permanent visual disturbances attributed to the poisoning, and the fact that so many occurred in very mild or borderline cases, leads us to discount the likelihood of any causal relationship in these cases between organic phosphate poisoning and permanently disturbed vision. In only 1 patient (II-49) does there seem to have been any strong probability of a cause-and-effect relationship between the acute poisoning and a subsequent visual field defect. Although a consulting neurologist made a tentative diagnosis of basilar artery insufficiency, whether transient anoxia or atropine intoxication precipitated the episode cannot be answered at this late date.

Gastrointestinal Complaints Nausea, vomiting, and abdominal cramps were very prominent features of the acute poisoning episodes, but they characteristically cleared up with recovery from the acute illness.

Ten patients complained of gastrointestinal problems that persisted more than 6 months, and in 4 they were present at the time of examination. These patients are distinct from those individuals who became nauseated or had other symptoms upon transient re-exposure to pesticides or their accompanying solvents; those will be discussed below under *Repeated Exposures.*

Seven individuals in the series had peptic ulcer or its symptoms at some time subsequent to the poisoning; in 4 of these, the ulcer was reported to us as having been confirmed by X-ray. Persistent and recurrent epigastric pain diagnosed as due to peptic ulcer immediately followed the acute poisoning in 2 of these patients. These symptoms lasted 9 months in one case and 12 months in another, but both individuals have now been symptom-free for over 2 years. Five others have had ulcer symptoms in the period subsequent to poisoning. Two had had such symptoms prior to the poisoning; in all cases there were problems connected to family and job responsibilities to which the patients attributed their difficulties. In 2, symptoms had started before poisoning; in 1, 8 months after poisoning; and 1, 2 years afterward; and in 1, 2½ years afterward. No conclusion as to relationship seems justified.

Five other patients had less well-defined gastrointestinal symptoms, expressed in terms such as "cramps in the evenings," "cramping abdominal pains," "nausea and abdominal pain occasionally," "indigestion," and "cramps and nausea."

Headaches Headache was not a prominent symptom in our series during the acute episodes; it was usually overshadowed by gastrointestinal and visual disturbances. In 7 patients, however, headache was a persistent symptom after the acute poisoning. These cases are described below.

Case I-4

A 33-year-old white man, while mixing and loading for an aerial sprayer, manifested severe headaches, constricted pupils, weakness and sweating of hands for several days, and lost consciousness on his way home from work. The plasma cholinesterase enzyme activity was 0.42 Δ pH/hr.; in RBC, 0.09 Δ pH/hr. He had ambulatory treatment with atropine. He did not feel well for 2 months, and for 2 years had severe recurrent headaches which he had not had before. He finally consulted a neurologist and after examination findings and electroencephalograms were normal, symptoms disappeared. He now has no complaints.

used for crop dusting with parathion. Flagging planes 48 hr. later, he became nauseated, vomited, and could not keep his balance, reeling as though drunk. He was hospitalized for 3 days. Cholinesterase levels were determined to be low but laboratory results were not included in the reports. The patient felt very weak after hospitalization; otherwise. he was completely well and continued crop dusting during the subsequent 2 summers without manifesting symptoms. Two years after the original episode he had the first of four seizures in which he lost consciousness for 5–10 min. There was no aura or tongue biting, but some tensing of muscles and shaking at the end of each attack. Detailed studies, including a glucose tolerance test, X-ray, electroencephalogram, electrocardiogram, and neurological examination have been negative. Taking analeptic drugs he had no attacks in 1½ years, but experienced an attack in mid-1965 when drug therapy was discontinued. There is no apparent causal relationship between these episodes and the acute poisoning.

It is significant that none of the 114 patients examined had had any episode which could be described as a psychotic reaction during the 3 or more years after poisoning. In the entire 232 cases there was a record of only 1 individual being admitted during this period to a mental institution in California; we have so far been unable to interview that man. Several of the severe episodes of poisoning resulted in periods of unconsciousness lasting hours to days. In no case were there symptoms suggesting residual brain damage from anoxia.

It would be indeed surprising if some psychiatric sequelae did not occur occasionally in association with severe episodes of acute organic phosphate poisoning. The cerebral anoxia which may occur, the nonspecific stress of a dangerous illness, and the fears regarding earning power and job changes could all lead to neuropsychiatric symptoms in a susceptible individual.

Other Signs and Symptoms Three patients never regained the weight lost during the acute episode. For 2 of them there was no explanation and they did not appear ill. In the third there were respiratory symptoms, and follow-up studies for tuberculosis have been recommended.

Acquired Intolerance to Pesticides Of the 114 individuals who were examined, 20 stated that they could no longer tolerate smelling or contact with insecticides. In 12 individuals nausea or nausea and vomiting resulted after even a whiff of pesticides; in 5 others, headache was the major symptom; 1 has "spasm of the pupils"; 1, itching of the skin and blurring of vision; and 1, "a shaky feeling." Almost invariably the symptom of intolerance was the same as the major symptom experienced in the acute attack.

Two individuals, not included above, indicated that they felt they were intolerant to insecticides in that they appeared to develop symptoms and depressed cholinesterase levels under working conditions in which others were not affected. Both had changed employment because of this. There were no laboratory indications, such as lowered cholinesterase or pseudocholinesterase levels, to support their claimed sensitivity.

Of all 22, 16 said that they had given up work involving contact with agricultural chemicals because of their intolerance. Six continued to work as farm laborers, but avoided contacts as much as possible.

It appears likely that this so-called sensitivity is a psychogenic phenomenon. As stated above, the symptoms induced on recontact were those of the outstanding symptoms suffered during the acute episode. In at least 3 instances in which Phosdrin was implicated, the patients stated that upon even minimal exposure they were immediately aware of blurring of vision or localized sweating.

It should be reemphasized that practically all patients had a very vivid recollection of the acute illness. The odors of the organic phosphates are quite characteristic and the patients volunteered that such an odor or similar odors, including that of the accompanying solvent in some cases, would induce symptoms. This intolerance, psychogenic or not, appears to be a real aftereffect.

Repeated Exposures

In view of the occupations of most of the individuals studied (agriculture or supporting services), it would be expected that the acute episodes reported were not their only exposures to pesticides. In many workers the acute poisoning occurred after a history of exposure and symptoms suggestive of borderline poisoning for some time. Over two-thirds of those located and examined (78 of 114) returned to activities involving frequent, intermittent, or potential exposures to organic phosphates. Many indicated that they carefully avoided exposures; others that they had changed jobs to avoid contacts.

Of those who returned to possible exposures, 10 experienced subsequent attacks of acute poisoning requiring medical attention, and an additional 17 reported that they had experienced

TABLE 13. DIBUCAINE NUMBERS AND OTHER FACTORS (TOTAL GROUP)

Dibucaine number	Ethnic origin		Severity of acute attack		Return to exposure		Subsequent intolerance to pesticides	Total
	Mexican or Spanish-American	Other white	Severe	Moderate or mild	Within 1 week	Never		
60-64	0	2	0	2	0	0	1	2
65-69	1	2	0	3	0	1	0	3
70-74	1	6	0	9	0	3	1	9
75-79	7	15	1	22	3	8	4	22
80-84	8	39	3	47	3	20	11	51
85-89	2	13	2	13	0	8	4	15
90-94	1	4	0	6	1	2	1	6
TOTAL	20	81	6	102	7	42	22	108
Mean dibucaine number	80.0	80.8	82.8	80.4	81.3	81.4	81.0	80.6

Individuals who complained of persistent symptoms did not differ in average dibucaine numbers from those with no persistent symptoms. The former averaged Dibucaine No. 80.2 (range, 61–92) and those with no persistent symptoms averaged Dibucaine No. 80.1 (range, 63–93).

Other Tests No abnormal results were obtained in thymol turbidity tests for 105 individuals or in serum glutamic oxaloacetic transaminase determinations, for 88 individuals. Urinary paranitrophenol determinations, for 30 individuals who had possible recent exposures, were all negative.

Comment

It was realized at the beginning of the study that there would be inherent difficulties in making definitive conclusions from examinations of individuals poisoned 3 or more years before. These difficulties included biases arising out of incomplete response to follow-up efforts, the uncertainty of accurate diagnosis of poisoning (in retrospect), the wide range of toxic agents, exposures, and intercurrent factors in a relatively small study population, and the lack of any group for valid comparisons if possible sequelae were found. The study was regarded as a probing effort, aimed at appraising the practicability of such a follow-up, and seeking leads which could be studied definitively under more nearly ideal circumstances.

That only 74% of the study group was located and only 50% examined, of course leads to qualified conclusions. The importance of some of the differences in the groups "located and examined," "not examined," and "not located" can be exaggerated, as they apparently resulted as much from concentration of effort on the San Joaquin Valley and the northern California coastal counties as on selective responses by patients. The population we studied was older than those not studied and in general we found that older subjects have more complaints than younger ones.

It is interesting to speculate on factors leading to individuals not being located. Migrants were, of course, the ones most difficult to find; failure to respond to written inquiries led to direct attempts aimed at the last reported address and employer. Although all inquiries were phrased so as not to arouse alarm, there nevertheless is the strong possibility of over-response by individuals who felt that they had permanent injuries, since there did not in most cases appear to be any counteracting fear of reprisal from an employer. Our impression is that the effect of all these factors probably would have led to overstatement rather than understatement of sequelae.

There were some uncertainties, but enough useful information was gained on the nature and circumstances of exposure and on the clinical course of organic phosphate poisoning to permit most cases to be classified in a manner useful for analysis. With respect to exposures, a great body of information was obtained on the many ways these individuals come into contact with chemicals while at work and the number of different compounds many of them had used during the period of 5 or 10 years prior to our study. We were also impressed by the difficulties of adequate protection of workers without revision of attitudes, techniques, and supervision.

preferable to observations in an uncontrolled environment.

Summary and Conclusions

1. A group of 235 individuals reported by California physicians as occupationally poisoned by organic phosphate insecticides during 1960 was selected for a study of possible sequelae.
2. Follow-up was carried out 3 or more years after acute poisoning. Of the 235 individuals, 175 (74%) were located and 117 (50%) were examined.
3. Comparison of the "examined" with the "located and not examined" and the "not located" groups, using data in the original reports, showed that the individuals examined were relatively older than those in the other groups. Other differences between the groups could be explained by the greater proportion of cases followed in the San Joaquin Valley and northern California coastal counties than in the Imperial Valley and southern California coastal counties.
4. Of the 117 individuals examined, 114 were regarded as having had definite organic phosphate poisoning. After appraisal of the course of the acute illness, 6 were graded as having had severe poisoning, 54 moderate, and 54 mild.
5. Interrogation and examination of the 114 individuals disclosed that 43 had complaints which persisted more than 6 months after poisoning and that 33 still had complaints. These complaints fell into several major categories: optic, gastrointestinal, cephalalgia, cardiorespiratory, neuropsychiatric, and miscellaneous.
6. Eight individuals complained of continued disturbed vision; 6 attributed it to the acute episode. In 4 the difficulty involved only near vision and was diagnosed as presbyopia; another had a nonincapacitating visual field defect tentatively diagnosed as due to a basilar arterial insufficiency unrelated to poisoning.
7. Seven individuals had symptoms of peptic ulcer at some time subsequent to poisoning, but the time relationships and the existence of a variety of family and job stresses made it improbable that the pesticide poisoning played a major role.
8. Headaches in 7 individuals had no consistent pattern.
9. Nine individuals had chest complaints, and in 2 coronary occlusion had occurred (1 year and 2 years after poisoning). No causal relationship was apparent.
10. Ten individuals had persistent symptoms that seemed primarily referrable to the central nervous system. None felt that his problem was a result of acute poisoning, and in at least 6 there were other etiologic factors (trauma in 2, alcoholism in 3, and a history of encephalitis in 1). In none of the 114 was there any episode which could be described as psychotic during the 3 or more years after poisoning.
11. Intolerance to the odor of pesticide preparations was mentioned by 20 subjects. It was manifested by nausea, vomiting, headache, or other symptoms. The intolerance symptom was usually the same as the major symptom of the acute attack and was probably psychogenic or represented a conditioned reflex.
12. Cholinesterase activity in the red blood cells and plasma was determined for 110 of the group. The major finding of interest was the distribution of pseudocholinesterase levels, which showed more than the expected proportion of higher levels of activity.
13. Our general conclusion is that a study of this type would have detected serious sequelae of high incidence, but would not reveal minor aftereffects or those of low incidence, especially if related to specific compounds, high exposures, or highly susceptible individuals. Needed are additional longitudinal studies of people after severe poisonings. Studies of hypersusceptibility and longitudinal appraisal of enzyme responses demand controlled observations in controlled environments, preferably with volunteers.

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