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Exposure to Parathion

Effect on General Population and Asthmatics

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There has been much lay and medical concern regarding toxic effects of insecticides on the general population. In addition to direct toxic effects, it is suspected that insecticidal application has deleterious physical effects on persons with respiratory diseases. To evaluate some of these problems, the authors have attempted to quantitate actual absorption, symptoms, and laboratory evidence of intoxication in persons with varying degrees of exposure to parathion. By means of controlled observations, the respiratory effect of application of this compound on persons with bronchial asthma was also measured. The results suggest that the effect of this chemical on the general population is negligible.

THE ORGANIC phosphorus insecticides have become firmly established in agricultural use. Although the high toxicity of some of them to man is well known, it is recognized that proper safety precautions may obviate the dangers to persons with heavy occupational exposure.[1-3] However, concomitantly with the rapidly increasing use of insecticides, concern has been expressed by public health officials, insecticide appliers, farmers, and members of the general population about the hazard of poisoning to unprotected persons receiving small or incidental exposure. This has been of particular concern where residential areas are in juxtaposition to fields under cultivation.

Between 1951 and 1953, studies in Wenatchee, the apple-growing district of Washington,[4,5] led to the conclusions that depression of cholinesterase activity and symptoms of organic phosphorus poisoning occurred only after definitive exposure, and that persons without occupational or gross accidental exposure to insecticides were not affected by them. Although those conclusions were considered valid, a similar study was instituted in the Phoenix, Ariz area because of numerous complaints of poisoning from the general population and because of the differences between the Phoenix and Wenatchee areas which could conceivably lead to different results. These differences were (1) the preponderance of aerial rather than ground application of insecticides in the Phoenix area; (2) the large number of persons with respiratory, allergic, and other chronic diseases in the Phoenix area; and (3) differences in temperature, relative humidity, and other environmental factors.

Agricultural insecticides are used in the Phoenix area during most of the year. However, the heaviest applications are made to the cotton crop, especially in July, August, and September. Applications during June and October are smaller and the amounts of insecticides used for cotton in May, November, and December are almost negligible.

Methods

One hundred twenty-two volunteer subjects were placed in approximately equal groups in the following manner:

Group No.	Description of Group
1	Nonasthmatic, no exposure to organophosphorus insecticides
2	Nonasthmatic, environmental exposure to organophosphorus insecticides
3	Asthmatic, no exposure to organophosphorus insecticides
4	Asthmatic, environmental exposure to organophosphorus insecticides
5	Nonasthmatic, occupational exposure to insecticides, including organophosphorus compounds

Unexposed subjects lived and worked in the city of Phoenix and had no known contact with insecticides. Persons with environmental exposure lived less than 500 yards (less than 50 yards in the majority of cases) from cotton fields being treated by aerial application of insecticides. Asthma refers to the allergic type with unequivocal wheezing. The occupationally exposed group was composed of

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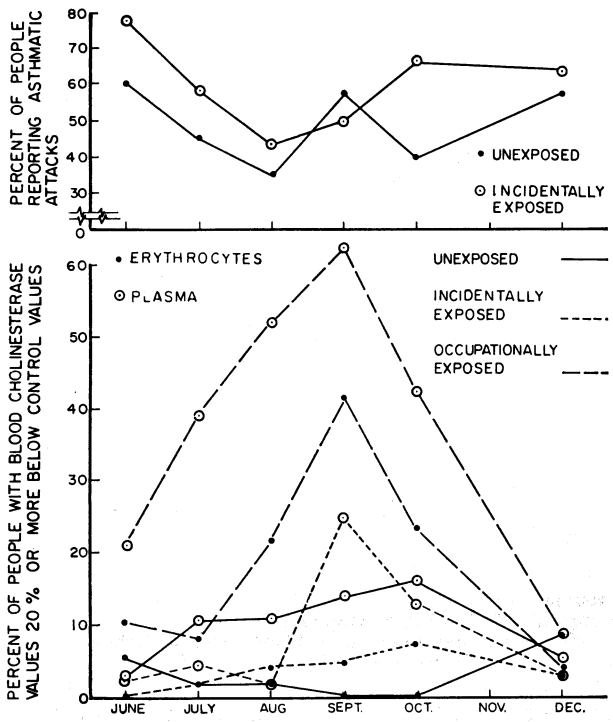

Incidence of asthma and blood cholinesterase depression in people with different degrees of exposure to organophosphorus insecticides.

formulators, crop-dusters, loaders, and mechanics.

It is recognized, of course, that the entire population has some dietary exposure to insecticides.[6] However, in contrast to the chlorinated hydrocarbons, the active organophosphorus compounds, which hydrolyze very rapidly, are rarely found in detectable amounts on marketed crops. Thus it is felt that dietary exposure to organophosphorus compounds is negligible, and that groups 1 and 3 are truly "no exposure" groups.

In order to obtain pre- and postexposure observations, as well as data during the time of exposure, study members were visited monthly (except in November) from May through December, 1958. At each interview, blood and overnight urine samples were collected and the subject was questioned about insecticidal exposure and symptomatology. Symptoms investigated were asthma (as indicated by wheezing) and also disorders commonly associated with organic phosphate poisoning, namely, headache, blurring of vision, excessive lacrimation, nausea, weakness or fatigue, tightness in the chest without wheezing, insomnia, diaphoresis, fainting, and convulsions.

Table 1.—Reports of Any Combination of Three Symptoms* During Month Preceding Interview

Groups 1 and 3 (Unexposed)			Groups 2 and 4 (Environmentally Exposed)		
Month	No. of Persons Interviewed	No. With Three Symptoms	Month	No. of Persons Interviewed	No. With Three Symptoms
June	34	3	June	40	1
July	46	2	July	43	3
Aug	45	4	Aug	42	6
Sept	42	0	Sept	40	4
Oct	43	0	Oct	38	3
Dec	35	1	Dec	33	2

*Headache, blurring of vision, excessive lacrimation, nausea, weakness or fatigue, tightness in chest without wheezing, insomnia, diaphoresis, fainting, and convulsions (asthma excluded).

Cholinesterase activity of red blood cells and plasma was measured by a standard microelectrometric technique[7,8] following separation of red blood cells and plasma by centrifugation at 10,000 rpm for three minutes. Urinary p-nitrophenol was measured by the method of Elliott et al[9] and was expressed as a parathion equivalent.

Results

Symptoms of Organophosphorus Poisoning.—Table 1 presents the number of persons with no exposure or with environmental exposure who reported any combination of three symptoms (excluding asthma) for the month preceding each interview. Although the number complaining of symptoms was higher for the exposed groups, the differences are not significant for any month. No person reporting three symptoms appeared clinically to have organophosphorus poisoning; only three had depressions of cholinesterase activity of red cell and plasma of 20% or more; none had depression of both red cell and plasma cholinesterase activity concomitantly with his symptoms. There was no report of three symptoms from the occupationally exposed group (between 19 and 23 were interviewed each month), although a few gave histories of miosis and headache which were related to exposure.

Cholinesterase Depression.—The percentage of persons with a decrease of 20% or more from their own pre-exposure cholinesterase activities is shown by month in the lower portion of the Figure. As no significant differences were found between asthmatics and nonasthmatics in either the exposed or unexposed groups, the data are combined according to exposure. The differences between unexposed and incidentally exposed persons were small and not significant ($P<0.05$), while the differences between the occupationally exposed group and the other two groups combined were significant for plasma in June and July and for both plasma and red cells in August, September, and October.

Excretion of p-Nitrophenol.—Of the 320 urine samples collected from persons in groups 1, 2, 3, and 4, only one contained material which gave a reaction for p-nitrophenol. This positive specimen was from a farmer in group 4 who was excreting 8μg per hour. He had no known exposure during the previous month, no symptoms of poisoning, and no decrease of cholinesterase activity of the blood.

Table 2.—Rate of Excretion of Urinary p-Nitrophenol* by Occupationally Exposed Persons

No. of Persons	May, μg/hr	June, μg/hr	July, μg/hr	Aug, μg/hr	Sept, μg/hr	Oct, μg/hr	Dec, μg/hr
Pilots							
2	0†	12‡	6	71	31	0	0
3	....	....	47	65	0	45	0
5	0	....	2	29	0	8	0
7	0	....	0	16	10	0	0
10	0	0	0	4	4	....	0
13	....	0	....	106	....	0	0
14	0	....	6	86	10	18	0
15	trace	....	94	53	259	....	2
18	0	....	....	118	8	0	0
19	0	....	0	....	....	....	0
24	0	....	4	12	37	0	0
25	0	....	10	35	4	0	0
26	....	....	46	14	6	0	....
Loaders and Mechanics							
4	0	....	....	80	73	22	0
8	trace	....	....	....	14	0	1
9	0	0	16	0	8	0	0
12	trace	....	24	88	392	35	....
16	0	....	14	33	24	12	2
20	0	....	0	....	....	0	0
Formulators							
17	0	....	0	8	4	6	0
21	....	....	0	12	4	24	0
23	0	....	12	145	6	86	18

*Expressed as parathion equivalent in μg/hr.
†Value of zero means that any quantity present was below sensitivity of method.
‡The rates have been "rounded" to the nearest whole number.

The data in Table 2, however, show that the persons in the occupationally exposed group frequently excreted p-nitrophenol, particularly during the peak periods of July, August, and September. During August, only one person, a formulator, did not excrete measurable p-nitrophenol.

Symptoms of Asthma.—The upper portion of the Figure shows the percentage of persons in groups 3 and 4 who complained of asthma at any time during the month preceding interview. The amount of asthma was remarkably similar in the two groups except in October, a month of comparatively little insecticidal exposure for group 4. A somewhat higher proportion of persons with incidental exposure reported asthma except during September, the month when the effects of exposure as measured by cholinesterase were greatest in men with occupational exposure.

Comment

The results of this study support the conclusions of others [5,7,10,11] that hazards of insecticidal poisoning to persons with environmental or incidental exposure are negligible. The environmentally exposed persons in this study probably had as much exposure as any individuals not occupationally involved with insecticides. Most of their homes were directly across a road from the fields being treated and were frequently enveloped by drift following application. Although the occupants, whether asthmatic or not, frequently complained about the insecticides, primarily because of odor and irritation of mucous membranes, there was no individual who had symptoms resembling those of organophosphorus poisoning.

In addition to the lack of symptoms of poisoning, two other factors indicated that hazard of environmental exposure was negligible. First, there was not a significant incidence of cholinesterase depression in groups 2 or 4 when compared with their controls. A 20% decrease was chosen because it has been recognized that variation between measurements on different samples from the same unexposed person may be as high as 23% for red blood cells and 25% or more for plasma.[12,13] That depressions of 20% are not necessarily significant of poisoning is indicated by the fact that there were as many such depressions in unexposed persons as in those with some exposure. Lack of any cholinesterase depression in these subjects when they had symptoms is, however, corroboration of the clinical impression that the few symptoms reported were not related to insecticides.

Second, measurement of the p-nitrophenol excretion indicates that the actual insecticidal exposure of all persons other than those in the occupational group was extremely small. Since parathion was the organophosphorus insecticide used almost exclusively in the area under study, information concerning it or its measurable metabolite should be representative of exposure to all insecticides used. We have found that excretion of p-nitrophenol during the first 24 hours after exposure appears to be a more sensitive index of exposure than either symptoms or cholinesterase activity; many of the specimens from groups 2 and 4 were collected within that interval. In persons with occupational exposure, significant amounts of this metabolite were found almost uniformly.

Evaluation of the effect of insecticides on asthma is much more difficult than evaluation of its effect as a poison. The asthmatics with environmental exposure were generally older than their controls, had asthma longer, and had a higher incidence of chronic respiratory disease, such as pulmonary emphysema and bronchiectasis. These factors would tend to make the incidence of asthma higher in the exposed group. Despite this, the incidence in the two groups was remarkably similar and roughly followed the same seasonal occurrence. This similarity suggests that the morbidity may have been due to common factors such as molds, grasses, and weeds in June, and house dusts and bacterial antigens in the winter months.

However, it is difficult to disregard the fact that many of the exposed asthmatics unequivocally indicated temporal relationships between exposure to insecticides and asthmatic attacks. One defect in evaluating the data is that no attempt at quantitating the asthmatic attacks was made. This, plus the complexity and the variability of the disease, makes it impossible to draw definitive conclusions regarding the relationship between environmental

exposure to insecticides and exacerbation of asthma. However, these similarities in occurrence do indicate, despite the drawbacks of the method, that if insecticides do affect pre-existing bronchial asthma, the effect is a relatively minor one.

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