

Organic phosphorus insecticides may cause mild illnesses in persons working closely with the materials, but they did not constitute any hazard for residents surveyed recently in Wenatchee, Wash.

Exposure to Organic Phosphorus Sprays and Occurrence of Selected Symptoms

WAYLAND J. HAYES, Jr., M.D., Ph.D., ERNEST M. DIXON, M.D.,
GORDON S. BATCHELOR, M.S., and WILLIAM M. UPHOLT, Ph.D.

PESTICIDES are used intensively in agriculture in the vicinity of Wenatchee, Wash. Direct measurement of dermal and respiratory exposure of sprayer operators in this area to parathion was reported by Batchelor and Walker in 1954 (1). A survey designed to evaluate the hazard of organic phosphorus insecticides was carried out in this same locality during 1951 (2). It was found that definitely exposed persons showed a significant reduction

in average cholinesterase values and an increase in illnesses consistent with poisoning during the period of their exposure. There was no evidence of either reduced cholinesterase activity or increased illness during the spray season in persons with little or no exposure to insecticides.

This survey was continued during the 1952 and 1953 seasons. The present paper presents the results of that work.

Dr. Hayes is chief of the Toxicology Section, Technical Development Laboratories, Communicable Disease Center, Public Health Service, Savannah, Ga. Dr. Dixon was stationed at the CDC Wenatchee Field Station, Wenatchee, Wash., when this study was made. He is now at the Kettering Laboratory, University of Cincinnati College of Medicine. Mr. Batchelor was the entomologist for the Wenatchee Field Station, and is now with the Allied Chemical and Dye Corp. in Wenatchee. Dr. Upholt is chief of the Wenatchee Field Station.

Kenneth C. Walker, a chemist at Wenatchee, determined the cholinesterase activity of the blood samples for the study, and Dr. William F. Durham, a biochemist at the CDC laboratories in Savannah, assisted in preparing the report. Dr. J. Monte Johnston and Dr. W. T. Sumerford participated in the early phases of the surveys while they were stationed at Wenatchee.

Materials and Methods

The procedure was essentially the same as that used in the 1951 survey (2). The subjects were again grouped according to decreasing potential exposure as follows: mixing-plant personnel (MPP), commercial applicators (CA), part-time applicators (PTA), workers in orchards (WO), fieldmen, warehousemen, and miscellaneous workers (FWM), residents living near orchards (RNO), residents of Wenatchee area living far from orchards (RFO), and a control group of residents living completely outside the agricultural area (ROA).

The four exposure periods were again based on the best information which could be obtained regarding exposure to insecticides for each individual. The observations on the potentially

exposed groups (RNO and RFO) and the definitely unexposed group (ROA) were divided into periods based on the observed periods of exposure for the exposed groups. The periods were preexposure, exposure, recovery (arbitrarily taken as the 30-day period immediately following the last exposure of the season), and postrecovery. Also included in the recovery period were any data obtained from a person known to be in a convalescent state following poisoning, provided that he avoided further exposure.

In 1952, 228 persons were studied, including 100 of the same subjects studied in 1951. A total of 923 blood samples were analyzed for erythrocyte and 927 for plasma cholinesterase activity, using the electrometric method of Michel (3). Two hundred and twenty of the subjects were interviewed periodically for symptoms, as well as history of exposure.

In 1953, 239 persons in four of the groups were studied: commercial applicators (34 persons), residents near orchards (62 persons), residents far from orchards (107 persons), and residents outside the area (38 persons). These groups were selected to represent occupationally exposed (CA), potentially environmentally exposed (RNO and RFO), and definitely unexposed (ROA) populations. Cholinesterase determinations were not carried out on these subjects. In this year an effort was made to achieve greater statistical significance for the survey of symptoms by (a) increasing the number of observations in each group and (b) equalizing, insofar as possible, the number of observations from the various exposure periods. Most of the participants were interviewed each month, starting in some instances as early as March and extending through November or December. In an effort to assure as much uniformity of sampling as possible between the exposure periods, no individual participant was included in the final tabular summary unless he had been interviewed at least once in each of three periods, including both the preexposure and the exposure periods.

Cholinesterase Values

The results of the cholinesterase activity determinations are given in table 1. The groups

with occupational exposure (MPP, CA, PTA, and WO) showed a definite decrease in plasma cholinesterase levels and some diminution in erythrocyte enzyme values during the exposure period. Though the decrease in mean values was not great in any group, it was largest in the group with the heaviest exposure, the mixing-plant personnel. The lowest values (cells, 0.05; plasma, 0.09) encountered during the exposure period were in a person living near an orchard. These extremely depressed cholinesterase activity levels were the result of a near-fatal, acute case of organic phosphorus poisoning suffered by a 2-year-old child who had played with a can from which the original contents of 25 percent emulsifiable parathion concentrate had not been completely removed. The poisoning incidents reported by Johnston (4) and Dixon (5), as well as several unpublished cases, support the conclusion that, although extensive day-to-day exposure is regularly associated with reduced blood cholinesterase activity, the only fatal and near-fatal cases of poisoning which were found were associated not with long-standing exposure but with brief, massive exposure and gross carelessness.

In the recovery period, the average plasma enzyme values of 3 of the 4 occupationally exposed groups (MPP, PTA, and WO) had returned essentially to their normal levels. The commercial applicators still showed a somewhat depressed average plasma cholinesterase level at this time. For two of the groups with greatest exposure (MPP and CA), the erythrocyte enzyme levels were still significantly subnormal during the recovery period.

Few postrecovery samples were obtained. The values found were all in the expected range except for one low plasma value for a single resident near an orchard. This low plasma value, which was associated with a normal red cell value, must be considered characteristic of the individual in question because it continued low after an appreciable time with no possible exposure.

It is of interest to note that the average pre-exposure cholinesterase levels of individuals living in an intensively sprayed area are essentially the same as those of individuals living in unsprayed areas. The three less-exposed

Table 1. Cholinesterase values for various occupational and control groups in relation to exposure to organic phosphorus insecticides, Wenatchee, Wash., 1952

Group	Number of people	Number of samples	Cholinesterase values (Δ pH/hour)					
			Red blood cells			Plasma		
			Range	Mean	Standard error	Range	Mean	Standard error
Preexposure period								
MPP	7	11	0.60-0.92	0.73	0.03	0.50-1.18	0.74	0.06
CA	16	28	.61-.81	.70	.01	.66-1.26	.91	.03
PTA	39	49	.57-.90	.71	.01	.40-1.18	.85	.01
WO	14	14	.57-.84	.70	.02	.54-1.12	.83	.04
FWM	12	21	.58-.86	.73	.02	.53-1.36	.90	.04
RNO	21	31	.61-.90	.72	.01	.45-1.17	.80	.04
RFO	12	26	.50-.84	.72	.01	.61-1.02	.85	.01
ROA ¹	14	38	.64-.88	.73	.01	.54-1.28	.92	.04
Exposure period								
MPP	8	24	0.15-0.80	0.62	0.03	0.14-0.81	0.57	0.04
CA	30	84	.21-.92	.64	.03	.14-1.10	.67	.03
PTA	59	² 165	.41-.90	.68	.01	.26-1.26	.79	.01
WO	13	³ 36	.54-.84	.68	.01	.49-1.05	.74	.02
FWM	29	79	.45-.89	.71	.01	.36-1.62	.86	.03
RNO	28	110	.05-.94	.69	.03	.09-1.19	.76	.06
RFO	15	59	.50-.86	.69	.01	.58-1.02	.81	.02
ROA ¹	14	⁴ 59	.58-.84	.70	.01	.48-1.27	.90	.03
Recovery period								
MPP	2	2	0.52-0.70	0.60	0.07	0.75-0.81	0.78	0.03
CA	16	22	.09-.86	.53	.05	.05-1.15	.69	.05
PTA	14	⁵ 14	.38-.82	.67	.03	.52-1.09	.79	.05
WO	3	3	.62-.72	.69	.20	.59-0.92	.78	.10
FWM	5	5	.61-.82	.72	.04	.46-1.08	.83	.10
RNO	6	7	.18-.80	.55	.09	.26-1.14	.70	.12
RFO	2	2	.71-.74	.72	.02	.96-0.98	.97	.00
ROA ¹	9	9	.60-.86	.73	.04	.59-1.26	.94	.08
Postrecovery period								
MPP								
CA	7	7	0.48-0.90	0.66	0.18	0.68-1.15	0.83	0.06
PTA	4	4	.55-.78	.66	.05	.76-1.02	.92	.07
WO	1	1		.78			.87	
FWM	4	4	.59-.80	.70	.04	.67-1.32	.97	.14
RNO	1	1		.64			.48	
RFO	1	1		.76			.69	
ROA ¹	11	11	.66-.92	.75	.02	.60-1.27	.98	.07

¹ The averages for the year in this group were 0.72 for cells and 0.92 for plasma. Although this group was not exposed to the spray chemicals under investigation, the cholinesterase values were distributed on the basis of collection date to the four periods set up for the exposed groups. This distribution provided a control for any potential seasonal variation in cholinesterase values.

² Only 164 red cell values available.

⁴ Only 58 red cell values available.

³ Only 35 red cell values available.

⁵ Only 13 red cell values available.

Table 2. Occurrence of illness and of selected symptoms among various occupational and control groups in relation to exposure to organic phosphorus insecticides, Wenatchee, Wash., 1952

Group	Number of people	Number of illnesses	Percent of persons with illness	Percent of observed illnesses exhibiting—															At least 1 selected symptom	Myosis or at least 3 other selected symptoms
				Selected symptoms																
				Headache	Nausea	Weakness or fatigue	Pain or tightness in chest	Abdominal pain	Vertigo, fainting, or incoordination	Vomiting	Nervousness, drowsiness, or insomnia	Sweating	Cough or expectoration	Disturbance of vision	Loss of appetite	Shortness of breath	Nasal discharge, including postnasal drip	Myosis		
Preexposure period																				
MPP	8	2	25													50		50	0	
CA	30	13	43	31			8				8	15	8		8	31		62	0	
PTA	39	19	53	5	5		11	11				21				5	5	32	5	
WO	7	4	57	50										25				75	25	
FWM	12	5	41								20			20				20	0	
RNO	83	77	93	26	4	5	8	3	5	3	21	1	14	5	3	6		40	16	
RFO	119	116	97	30	6	10	8	9	5	4	23	1	22	3	5	3		30	17	
ROA	57	47	82	19	4	4	2	8		2	23		13	2		6		19	13	
Exposure period																				
MPP	8	6	75	17		33	50									33		50	50	
CA	68	60	88	52	13	13	33	5	5	2	10	2	23	15	8	15		20	55	
PTA	59	48	81	50	25	54	14	12	23	12	19	14	25	12	14	10		10	12	
WO	12	7	58	28	28	28			28	14	28	28	71	28	28	14		28	14	
FWM	28	20	75	30	5	20	40	15	15		20	20	25	10	10	25		25	5	
RNO	90	90	100	30	6	14	3	3	4	3	22		26	4		3		40	1	
RFO	122	117	96	40	8	15	9	12	3	6	26	3	24	2	5	6		43	3	
ROA	59	49	83	12	6	8		12	2	4	18		14	2				26	2	
Recovery period																				
MPP	2	0	0																	
CA	38	22	58	23	55	18	18	9	5	5		9	23	9	5			18	5	
PTA	14	8	57	75	12	50		12	12	25	12	12	25	12		12		12	12	
WO	3	3	100										33					67	33	
FWM	5	2	40				50						100					50	100	
RNO	54	48	89	23	2	10	2	6	4	4	25		12			2		31	2	
RFO	98	93	95	11	4	10	3	8		1	12	2	13	1	4	3		24	2	
ROA	49	37	76	11		5		8			8		11					19	3	
Postrecovery period																				
MPP	0	0	0																	
CA	41	21	51	14			5	5					24					33	71	
PTA	4	4	100				25		25				25					25	75	
WO	1	0	0																	
FWM	4	1	25																0	
RNO	63	61	97	26	10	20	2	11	2	10	2		25	2	2			48	66	
RFO	101	94	93	21	10	14	3	13		7	10		24	2	3			50	71	
ROA	61	54	89	15	13	13	2	13		13	9	2	22		11			37	56	

NOTE: Values are zero unless otherwise indicated.

groups (FWM, RNO, and RFO) as well as the definitely unexposed population (ROA) remained normal during all periods.

Symptomatology

The symptoms recorded during the 1952 survey are tabulated in table 2 in the same form used in the earlier study (2). The distribution of the nonspecific symptoms throughout the various groups and throughout the four periods showed no particular pattern. In contrast the selected symptoms listed in the table were noted much more frequently during the exposure period. This finding indicates that mild illnesses involving symptoms similar to those characteristic of organic phosphorus intoxication were significantly increased during the exposure period. However, on the basis of the 1952 survey, as was also true for the 1951 study, it was not possible to differentiate clearly among the various potentially exposed groups with respect to the incidence of this type of illness. In an effort to solve this problem, the protocol of the survey was modified somewhat for 1953, as described above.

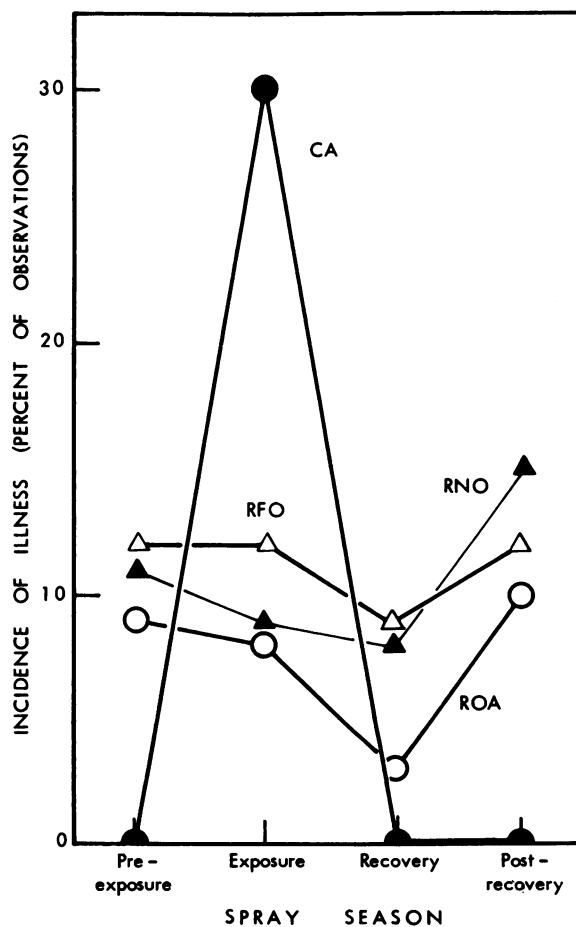
The symptoms recorded during the 1953 survey are shown in table 3. In this tabulation the incidence of symptoms and of illnesses is based on the number of observations, not on the number of illnesses or the number of persons as in table 2.

The incidence of all illnesses revealed that the commercial applicators were generally "healthier" than either the environmentally exposed groups or the unexposed group. The unexposed group had a slightly lower incidence of symptoms and of illnesses in all four periods than did the environmentally exposed groups (RNO and RFO). This lower incidence, however, is considered to be unrelated to exposure since these groups were different with respect to their potential contact with insecticides only during the exposure period.

The increase in illnesses among the commercial applicators during the exposure period was a result of an increase during this period in the selected symptoms known to be associated with intoxication by organic phosphorus compounds. The difference between periods was most apparent for the frequency of headache, nausea,

pain or tightness in the chest, and myosis. The significance of this trend can be seen by considering the incidence of myosis or of illnesses involving three or more of the other selected symptoms. As explained in the earlier report, the occurrence of myosis or of three or more other selected symptoms is a stronger indication of intoxication from organic phosphorus insecticides than is the occurrence of unselected symptoms or of any single symptom other than myosis. Each of the selected symptoms other than myosis occurs quite commonly as a result of conditions unrelated to exposure to insecticides, but they are not so likely to occur in combination without easily recognized etiology.

Incidence of illness involving myosis or at least three other selected symptoms among groups occupationally exposed (CA), environmentally exposed (RNO and RFO), or unexposed (ROA) to organic phosphorus insecticides, Wenatchee, Wash., 1953.



The incidence of myosis or of three or more of the other selected symptoms is shown in figure 1, as well as in table 3, for each of the groups. Especially in view of the generally lower incidence of symptoms of any kind among the commercial applicators, the great rise in this group in the incidence of illnesses involving myosis or three or more other selected symptoms during the exposure period is striking. Actually, 7 of the 8 illnesses in this group could be clearly correlated with known heavy exposure to either parathion or tetraethyl pyro-

phosphate. Six of them included myosis as well as two or more other selected symptoms. The eighth case was presumably a respiratory infection that was epidemic at that time.

Since the number of commercial applicators was very small, data for 18 such workers not included in the above analysis because they were missed in the preexposure period were also examined. These 18 were observed in the exposure period and at least once in the recovery or postrecovery periods. As shown in table 4, the inclusion of the observations for

Table 3. Occurrence of illness and of selected symptoms among various occupational and control groups in relation to exposure to organic phosphorus insecticides, Wenatchee, Wash., 1953

Group	Number of people	Number of observations	Percent of observations revealing—																		
			Selected symptoms														Any illness	At least 1 selected symptom	Myosis or at least 3 other selected symptoms		
			Headache	Nausea	Weakness or fatigue	Pain or tightness in the chest	Abdominal pain	Vertigo, fainting, or incoordination	Vomiting	Nervousness, drowsiness, or insomnia	Sweating	Cough or expectoration	Disturbance of vision	Loss of appetite	Shortness of breath	Nasal discharge, including postnasal drip				Myosis	Wheeze
Preexposure period																					
CA.....	16	20	15				5							15	5			70	30	0	
RNO.....	62	108	17	2	3	5	2	2	17				12	3	1	6	32	3	98	61	11
RFO.....	107	178	22	4	8	7	6	2	21	4	4		18	2	2	2	25	2	97	67	12
ROA.....	38	56	16	5	7	2	2		9				14	2		4	20	2	82	45	9
Exposure period																					
CA.....	16	27	37	11	4	18		4	4				7	4		4	22	18	81	56	30
RNO.....	62	159	19	2	6	1	2	3	1	18			15	1		1	26		98	57	9
RFO.....	107	268	23	3	7	4	6	1	2	19			14		3	2	24		94	62	12
ROA.....	38	65	9	5	6		6	2	3	12			8				22		86	42	8
Recovery period																					
CA.....	11	11	9			18	9										27		91	64	0
RNO.....	48	48	20	2	8		6	2	2	22			10			2	28	2	88	52	8
RFO.....	96	96	9	4	7	3	7		1	11	1		13	1	4	3	22		95	51	9
ROA.....	32	32	9		3		6			6			6				16		78	34	3
Postrecovery period																					
CA.....	16	26					8						4				15		65	31	0
RNO.....	62	110	20	6	12		8	1	6	1			17	1	1		35		95	49	15
RFO.....	100	184	13	5	10	2	7		4	7			15	1	2	2	28		89	49	12
ROA.....	38	70	11	9	7		7		9	3			10				20		84	31	10

NOTE: Values are zero unless otherwise indicated.

Table 4. Occurrence of illness and of selected symptoms among persons occupationally exposed to organic phosphorus insecticides, Wenatchee, Wash., 1953

Item	Exposure period	Recovery period	Post-recovery period
Number of individuals...	34	22	34
Number of observations...	55	22	51
Percent of observations revealing any illness...	87	86	63
Percent of observations revealing at least 1 selected symptom...	67	59	33
Percent of observations revealing myosis or at least 3 other selected symptoms.....	36	5	0

this group with those for the original group increases somewhat the incidence of illnesses involving at least one selected symptom and the incidence of myosis or of at least three other selected symptoms during the exposure period. Thus it strengthens the conclusion that there was a highly significant increase in this type of illness among occupationally exposed individuals during the period of exposure.

The occurrence of three or more selected symptoms was slightly more frequent among the environmentally exposed groups (RNO and RFO) than among the unexposed group (ROA) in all periods. (None of these groups reported myosis.) As suggested above, however, this difference was probably due to uncontrolled variables. Twelve of the eighteen illnesses involving three or more selected symptoms in the unexposed group were fairly definitely associated with etiologies unrelated to intoxication. Ten of the twelve were diagnosed as influenza or upper respiratory infection. One person had an operation for an intestinal obstruction, and another had cardiovascular disease. It is significant that of the 6 illnesses that were not adequately explained, 3 occurred in the preexposure period, 2 in the postrecovery period, and only 1 in the exposure period.

Of the 46 illnesses with three or more selected symptoms (but no myosis) found in the residents near orchards, 35 were fairly clearly associated with etiologies unrelated to insecticide exposure. These included upper respira-

tory infection, known allergies, pregnancy, peptic ulcer, and scarlet fever. The 11 that were not adequately explained were distributed 3 in the preexposure period, 3 in the exposure period, 1 in the recovery period, and 4 in the postrecovery period.

There were 84 illnesses revealing three or more selected symptoms (but no myosis) among the residents far from orchards; of these illnesses, 42 could be associated with etiologies unrelated to insecticide exposure, including about the same ones as those found in residents near orchards. Of the 42 illnesses that were not adequately explained, 15 occurred in the preexposure period, 16 in the exposure period, 6 in the recovery period, and 5 in the postrecovery period. With such a distribution there would seem to be little, if any, basis for associating these unexplained illnesses with exposure to insecticides.

Summary and Conclusions

A study of the effect of exposure to organic phosphorus insecticides carried out during 1952 and 1953, using some of the same subjects as those observed by Sumerford and his colleagues in 1951 (2), confirmed the previously demonstrated relationships between blood cholinesterase levels, exposure, and illness. It also provided further evidence that the occurrence of myosis or three or more other selected symptoms is a criterion for the differential diagnosis of mild poisoning. None of the results of the new investigation contradicted any conclusion stated in the first report.

In addition to these confirmatory findings, the present study showed clearly for the first time that illness resembling mild poisoning was not significantly more common in persons living in an agricultural community who had no occupational or gross accidental exposure than it was in persons living in a nonagricultural area, where insecticides were not used.

REFERENCES

- (1) Batchelor, G. S., and Walker, K. C.: Health hazards involved in use of parathion in fruit orchards of north central Washington. *A. M. A. Arch. Indust. Hyg.* 10: 522-529, December 1954.
- (2) Sumerford, W. T., Hayes, W. J., Jr., Johnston,

J. M., Walker, K., and Spillane, J.: Cholinesterase response and symptomatology from exposure to organic phosphorus insecticides. *A. M. A. Arch. Indust. Hyg.* 7:383-398, May 1953.

(3) Michel, H. O.: An electrometric method for the determination of red blood cell and plasma

cholinesterase activity. *J. Lab. & Clin. Med.* 34:1564 (1949).

(4) Johnston, J. M.: Parathion poisoning in children. *J. Pediat.* 42:286-291, March 1953.

(5) Dixon, E. M.: Dilatation of pupils in parathion poisoning. *J. A. M. A.* 163:444-445, February 1957.

PHS films

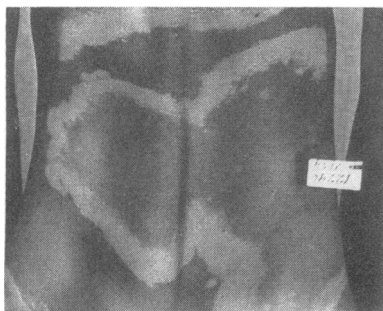
Clinical Manifestations of Leprosy

Part I. Tuberculoid Type

Part II. Lepromatous, Indeterminate, and Borderline Types

35-mm. filmstrip, color, silent with captions, 50 and 54 frames, respectively, 1956.

Audience: Physicians, public health officers, nurses, and medical students.



Part I of the filmstrip consists of a series of examples of tuberculoid lesions, each with a brief descriptive caption. The examples are limited to those found in the Westfort Institution, Pretoria, South Africa, and nearly all the patients are Negroes.

Part II shows 20 cases of the lep-

romatous type, 17 indeterminate, and 7 borderline, all Negro patients in the same institution. Each has its appropriate caption.

Refuse Disposal by Sanitary Landfills

16-mm. film, color, sound, 13 minutes, 472 feet. 1957.

Audience: Environmental sanitation personnel and other public health workers, municipal officials and civic groups.

The contributions of the sanitary landfill to community progress and public health are contrasted in this film with the faults of other disposal methods, such as open dumps, carrying vectorborne disease and nuisance hazards.



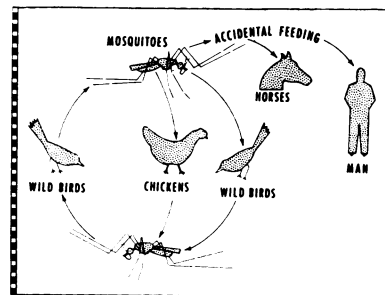
Children play on site of former landfill.

How to select a site, types of equipment used in landfilling, how to construct the fills, and different types of operating procedures are delineated.

Arthropod-Borne Encephalitis

16-mm. film, color, sound, 17 1/2 minutes, 629 feet. 1957.

Audience: Epidemiologists, sanitary engineers, insect and rodent control personnel, and medical students.



The nature, significance, distribution, and known control measures for arthropod-borne encephalitis are delineated in this introductory film. The definition and importance of the disease, the three types and where they are found, human and equine cases, and temporary and permanent control measures are covered. The usual cycle of encephalitis transmission is from mosquitoes to wild birds. Infection of man and horses is believed accidental.

PHS films may be obtained on LOAN from the Communicable Disease Center, Public Health Service, 50 7th Street NE., Atlanta 5, Ga., or PURCHASED from United World Films, Inc., 1445 Park Avenue, New York 29, N. Y.