AgEcon SEARCH
RESEARCH IN AGRICULTURAL & APPLIED ECONOMICS

The World's Largest Open Access Agricultural & Applied Economics Digital Library

This document is discoverable and free to researchers across the globe due to the work of AgEcon Search.

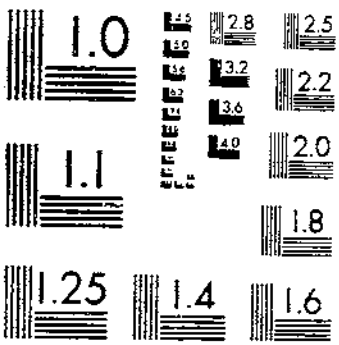
Help ensure our sustainability.

Give to AgEcon Search

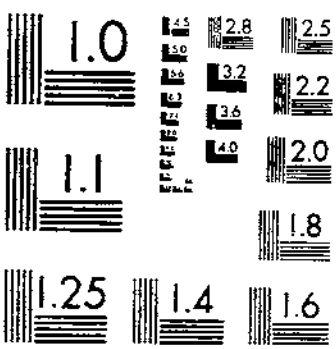
AgEcon Search
http://ageconsearch.umn.edu
aesearch@umn.edu

*Papers downloaded from **AgEcon Search** may be used for non-commercial purposes and personal study only. No other use, including posting to another Internet site, is permitted without permission from the copyright owner (not AgEcon Search), or as allowed under the provisions of Fair Use, U.S. Copyright Act, Title 17 U.S.C.*

START



MICROCOPY RESOLUTION TEST CHART
NATIONAL BUREAU OF STANDARDS-1963-A



MICROCOPY RESOLUTION TEST CHART
NATIONAL BUREAU OF STANDARDS-1963-A

RC 30.
A53-1
#1122

The Acute Toxicity of Chlorinated Hydrocarbon and Organic Phosphorus Insecticides to Livestock

DEPOSITORY
NOV 22 1955
Los Angeles Public Library

R. D. Radeleff, George T. Woodard
W. J. Nickerson, and R. C. Bushland

Technical Bulletin 1122

UNITED STATES DEPARTMENT OF AGRICULTURE

CONTENTS

	Page
Introduction	1
General considerations	2
Animals	5
Materials and methods	6
Part I	7
Chlorinated hydrocarbon insecticides	7
Chlordane	7
BHC	10
Toxaphene	15
Strobane	18
Aldrin	19
Heptachlor	21
Dieldrin	22
DDT	25
TDE	27
Methoxychlor	28
Perthane	29
Dilan	30
Symptoms of poisoning	30
More toxic compounds	30
Less toxic compounds	31
Autopsy findings	32
Micropathology	32
Part II	34
Organic phosphorus insecticides	34
Parathion	34
EPN	35
Malathion	36
Diazinon	37
Bayer compounds	38
Symptoms of poisoning	40
Autopsy findings	41
Summary	42
Literature cited	45

For sale by the Superintendent of Documents, U. S. Government Printing Office
Washington 25, D. C. - Price 20 cents

Washington, D. C. Issued November 1955

The Acute Toxicity of Chlorinated Hydrocarbon and Organic Phosphorus Insecticides to Livestock

By R. D. Radeleff, George T. Woodard, and W. J. Nickerson,[1] *veterinarians, Animal Disease and Parasite Research Branch*, and R. C. Bushland, *entomologist, Entomology Research Branch, Agricultural Research Service*

INTRODUCTION

Since 1947 the Bureau of Entomology and Plant Quarantine and the Bureau of Animal Industry (now Entomology Research Branch and Animal Disease and Parasite Research Branch, respectively) have been conducting cooperative investigations on the toxicity of certain insecticides to livestock. These studies have covered the insecticides developed for commercial use since 1940.

Portions of these studies have been published from time to time (*3, 4, 15, 16, 17, 18, 19, 20, 21*)[2] but it now seems desirable to have a compilation of all the data obtained concerning the acute dermal and oral toxicity of these materials. The experiments [3] reported here were conducted at the Kerrville, Tex., laboratories of the United States Department of Agriculture.

The experimental approach used in the investigations at Kerrville deviates somewhat from that of researchers who make use of laboratory-size animals and strive for a clearcut median lethal dosage as their product. Our objective has been to determine the maximum dosage that might be applied or administered to an animal without producing observable symptoms of poisoning, and to determine the minimum dose that might be expected to produce such poisoning. The numbers of animals available for our experiments were fewer than we would like, but we believe we have obtained enough data to indicate safe doses for livestock.

While our primary concern was to establish safe doses of insecticides to apply externally for the control of parasites feeding on animals, we also attempted to determine the oral doses which might cause poisoning should an animal drink insecticidal formulations or otherwise ingest the insecticides. Many of the insecticides discussed have not been recommended for use on animals, but may be available to them on treated feeds, or through careless storage of insecticide concentrates.

[1] Dr. Nickerson resigned from the Bureau of Animal Industry in 1952.

[2] Italic numbers in parentheses refer to Literature cited, p. 45.

[3] Portions of the experiments reported in this bulletin were supported by grants-in-aid of various amounts under formal cooperative agreements between the Department of Agriculture and the following industrial groups: William Cooper and Nephews, Hercules Powder Company, Humble Oil and Refining Company, Julius Hyman and Company, and the Velsicol Corporation.

The potential hazards of continued exposure of animals to insecticides, and the residues appearing in meat and milk following treatment with or ingestion of these insecticides, are discussed in other reports (*3, 6, 17, 20, 21*), or will be discussed in the near future. This report concerns only the acute oral and dermal toxicity of these insecticides.

GENERAL CONSIDERATIONS

Toxicity has been defined as the quality, state, or degree of being poisonous, and a poison has been defined as an agent which, when introduced (especially in small amounts) into an organism, may produce an injurious or deadly effect. These definitions will be accepted for the purposes of this report, particularly in that the word "toxic" will be used to denote an injurious effect, whether lethal or not. Lethality will be stated in positive manner.

An insecticide may gain entry into the body by way of the digestive tract, the respiratory tract, or the skin. In the experiments described in this report only two channels are involved—the skin and the digestive tract.

The toxic effects of the insecticides discussed are exerted primarily after absorption from the skin or digestive system has occurred. In most, if not all cases, normal functioning of certain tissue, especially that of the nervous system, is impaired, leading to numerous secondary effects. While it is possible for some of these compounds to produce direct irritation of the epithelial surface of the skin and digestive tract, it is only in occasional cases that they are observed to do so.

Our understanding of the process by which these insecticides are absorbed from the skin or digestive tract is by no means complete. It may be simple diffusion; indeed, this seems important to at least the initiation of the passage. Absorption may take place in a more complicated manner, such as temporary chemical alteration, or conjugation with natural compounds in the body.

Whatever the process, the passage is accomplished rapidly. Symptoms of poisoning have appeared in our animals in as short a time as 6 minutes after treatment, but most frequently within 2 to 6 hours. Passage seems to begin the moment that contact is made with the skin or digestive membrane and continues for a period of time sufficient to exhaust the immediate supply of insecticide unless death by poisoning occurs before absorption is complete. Exceptions have been noted. For instance, with certain compounds evidence of toxicity may not appear until several days after dermal application.

The rate of absorption of insecticides, as of other chemicals, is influenced by the physical state of the compound. We observed in a series of experiments with toxaphene that emulsions were absorbed more rapidly than suspensions of wettable powders. Emulsions containing toluene were absorbed more rapidly than those containing xylene or kerosene. In turn, those made with xylene were absorbed more rapidly than those containing kerosene. Absorption was determined by the time from treatment to onset of symptoms. Among the wettable powders used in our experiments no significant differences were noted in speed of absorption. Observations were made when toxaphene ground with a wettable clay was used with no added wetting agent, with a moderate amount of wetting agent, and an

excess of wetting agent. There were no differences in toxicity of the three powders.

Although there are meager confirmatory data in the published literature, dusts of insecticides are probably absorbed to a lesser extent than suspensions, emulsions, or solutions.

It must be emphasized that although the speed of absorption is influenced by the physical state of a given compound it does not follow that the total amount of insecticide absorbed is similarly influenced. That the total amount absorbed from emulsions and from suspensions is probably the same is shown in the experiments reported in this publication, in that formulations, when used at identical concentrations on similar animals, show no significant differences in toxicity—first one and then the other being slightly more toxic.

The equivalent toxicity of emulsions and suspensions may have two possible explanations. The amount of insecticide deposited on the hair of an animal may be greater from a suspension than from an emulsion because of a filtering action of the hair coat, while the absorption of insecticide into the body may be less, the combined net effect being equal total absorption into the body and equivalent toxicity. On the other hand, the amount of insecticide deposited and the amount absorbed may be fully equivalent initially, in which case the equivalent toxicity would be expected. Our present data do not resolve these possibilities.

If we were to put the same number of grams of insecticide upon similar animals, using these two types of formulations, some differences in absorption might appear. We have observed little, if any, difference in toxicity between emulsions and suspensions given orally. In giving insecticides to laboratory animals, many workers have observed wide differences in toxicity according to the physical state of the insecticide. Ely and Moore (7) demonstrated significant differences in the DDT content of milk from dairy cattle when the physical state of the DDT administered was varied.

Regardless of the disposition eventually made of the debate we must face the realities offered by the present experiments, in which equivalent concentrations of insecticides in emulsions or suspensions have produced approximately equivalent toxicity in equally susceptible animals.

In describing the dermal-application experiments in this publication, we have expressed the dosage in terms of the percentage of the insecticide in the spray or dip used. In some ways this is an empirical dosage incapable of accurate measurement because, although the animals were thoroughly wetted in every case, the amount running off during spraying and draining off after either dipping or spraying was a variable quantity. There will also be other differences, such as in the length of hair of various animals and in the methods of various operators. That these variables are of no great consequence is exemplified by the general uniformity of results obtained at given concentrations of insecticides.

One exception of consequence to this uniformity of results has been found in the treatment of animals by dipping in vats or tanks, particularly when emulsifiable materials are used. Initial studies by Radeleff,[4] in which a radioactive iodine compound was used as a

[4] Unpublished data

label for emulsion particles, established the important point that as the particles increased in size (the concentration of insecticide in the emulsion remaining uniform) the amount of insecticide deposited on animal hair was increased. This was not a new concept of insecticide-emulsion behavior, the mechanism having been used by entomologists for many years to obtain deposits of poisons on plants by means of emulsions composed of large particles, often called quick-breaking emulsions. The experiments did make us aware that the principle applied equally for emulsions used on animals, and did help to explain the losses of cattle after dipping in emulsions of insecticides at concentrations known to be safe when applied as sprays or fresh dips. The increased deposition will occur from any emulsion, whether used as a spray or as a dip, but is of greatest importance in dipping because in this operation the animals pass through hundreds and frequently thousands of gallons of emulsion while traversing a vat, and may extract the larger particles of as many gallons.

When an animal is sprayed, it is exposed to a limited quantity of the emulsion, generally not exceeding 2 gallons, depending on the operator's judgment of when the animal has been thoroughly wetted. The sprayed animal is not exposed to more insecticide than the total amount contained in those 2 gallons. An exception is when the emulsion is allowed to "cream" or partially separate in the sprayer, thereby increasing the insecticide content of one portion of the total volume at the expense of the other portion. If insufficient agitation follows this "creaming", some animals will receive a reduced dose while others may receive a toxic dose. Sparr, Clark, and Vallier (*22*) demonstrated under practical dipping conditions that a stable emulsion is required for safety and that an increased particle size increases deposition upon cattle hair. The rate at which the particle size and deposition increase are in turn influenced by the composition of the formulation and probably by other factors.

Because of the influence of particle size on toxicity, it is not sufficient to have a method of accurately determining the concentration of insecticide in a dip or spray such as has been developed by Littler (*12*) and by Bowen (*2*); some knowledge must also be had of the size of the emulsion particles and of the uniformity of the emulsion.

Manufacturers of insecticide formulations are generally aware of these effects and have taken steps to provide emulsifiable concentrates, which form emulsions that remain stable for long periods of time. In spite of this, care needs to be constantly exercised to see that the emulsion is of proper stability and consistency before spraying or dipping is begun.

It is feasible to conduct experiments in which the dosage is carefully applied to the skin and related to body weight. Such experiments yield accurate comparisons of the toxic effects of insecticides; however, even with such data at hand, we are still faced with the evaluation of the toxicity of the compounds under practical control conditions when used by farmers and ranchers.

Toxicologists have long recognized the variations in toxicity of a given compound due to species of animal, age, general health, and idiosyncrasy. The present insecticides are not exceptions.

The useful insecticides developed since 1940 may be classified into two major groups—the chlorinated hydrocarbons and the organic

phosphorus compounds. The chlorinated hydrocarbons are typified by DDT, TDE, methoxychlor, BHC (benzene hexachloride), chlordane, dieldrin, aldrin, heptachlor, endrin, isodrin, toxaphene, Strobane, Dilan (CS–708), and Perthane (Q–137). They may be divided into two groups according to their acute toxicity for livestock. The group of low order of toxicity includes DDT, TDE, methoxychlor, Dilan, and Perthane.

The insecticidal activity and mammalian toxicity of chlorinated hydrocarbons are so dependent on molecular structure that rearrangement without addition or removal of atoms (isomerism) may completely nullify the insecticidal activity, as well as alter the toxicity to animals.

The chlorinated hydrocarbon insecticides are principally neurotoxic in their activity, and generally produce a diffuse stimulation of the central nervous system, resulting in numerous neuromuscular expressions of that stimulation. The small quantities or absence of these compounds in the central nervous system during poisoning has been a subject for conjecture. Some workers have hypothesized that a second, endogenous compound is produced or released which is the actual toxicant. Sternburg and Kearns (*24*) demonstrated such a substance in DDT-poisoned roaches.

In addition to the neurotoxic effects there may be deleterious effects on the functional elements of the liver, kidneys, and other organs.

The organic phosphorus compounds might appropriately be classed as inhibitors of cholinesterase, since all members of this group appear to express their primary activity in this manner. The organic phosphorus compounds discussed in this publication are parathion, EPN, malathion, Diazinon, chlorthion, and Bayer compounds L 13/59 and 21/199.

Because of the large volume of data to be presented, and because of the group similarities of symptoms and lesions, we believe that it will make for conciseness and better understanding to discuss the manner of application, the experimental animals, and experimental technique for all experiments first and then the symptoms and lesions for each of the groups rather than to repeat these for each compound.

Animals

The animals used in these experiments were typical farm animals—cattle, hogs, sheep, goats, and horses—in average health and condition, housed, fed, and cared for as farm animals would be in the warmer sections of the United States, without special isolation or other abnormal arrangement. All were free from disease at the time of treatment as determined by clinical examinations. The only exceptions to this freedom from disease were among the baby dairy calves, which were subject to enteric disorders just as are such calves wherever raised. Affected animals were discarded from the tests when the development of such disorders after treatment could influence the results.

It will be noted that more dairy-type calves, 1 to 2 weeks of age, were used in these tests than any other type or species of animal.

We learned in the early studies that such calves were far more susceptible to poisoning than were other farm animals or other types of calves. The 1- to 2-week-old dairy calf was then adopted as the standard farm animal for toxicity screening of new insecticides for the two reasons, higher susceptibility and lower cost. Insecticides that can safely be applied to baby dairy calves at twice the dosage employed for insect control have thus far been found to have an equal or wider margin of safety for all other farm animals except poultry. It is important that the reader understand that these calves are of a specific type and age. Resistance to poisoning increases with age so that older (1 to 2 months) calves are not harmed by the doses toxic for the very young.

Materials and Methods

Initial studies with each insecticide were generally conducted with emulsifiable concentrates prepared in the laboratory and composed, by weight, of: Insecticide 25 parts, xylene 65 parts, and emulsifier (Triton X–100) 10 parts. Later, other emulsifiable concentrates were used, as were wettable powders when available. All the wettable powders were obtained from the manufacturers. Dilutions of all concentrates were prepared on a weight/weight basis in tap water, using 8.3 pounds as the weight of 1 gallon of water.

Spray applications of insecticides were made with a variety of equipment ranging from the simple garden-type compressed-air devices to high-pressure orchard-type sprayers. Accordingly, the operating pressure varied from approximately 60 to 300 pounds per square inch. Since no differences were noted in the results obtained with the various devices, the compressed-air sprayer was used for most of the applications because it permitted the use of smaller quantities of insecticide. Each animal sprayed was wetted as completely as possible, the operator making certain that the liquid penetrated to the skin of all parts of the animal's body.

The smaller animals were dipped in a portable metal vat of 100-gallon capacity. Each animal was held in the vat long enough to insure complete wetting of the hair or wool.

Oral doses of insecticides were administered as freshly prepared emulsions or suspensions by means of dosing syringes or stomach tubes.

Observations of the treated animals were made at regular, frequent intervals, day and night, for such periods as were indicated by the particular experiments. Symptoms were recorded as they occurred, and autopsies were conducted as soon after death as possible. Selected tissues were preserved for histological study.

PART I

Chlorinated Hydrocarbon Insecticides

CHLORDANE

Technical chlordane is a thick, syrupy liquid of pungent odor. For use on livestock, emulsifiable concentrates, wettable powders, and dry dusts are available. The same formulations are available for crop usage. Chlordane is effective against a number of ectoparasites of livestock at concentrations of 0.25 to 0.5 percent in emulsions and suspensions.

The available data on the toxicity of chlordane are confused by the fact that changes have been made in its manufacture, the product becoming less toxic as developments took place. For that reason the data in the tables have been divided into two groups, according to whether or not they were obtained prior to 1953. No essential differences in symptoms have been noted between the two products.

The results of single dermal applications of chlordane to various animals are given in table 1. The symptoms of poisoning in these animals appeared in as short a time as 5½ hours after treatment, but most of the animals did not become affected until 24 to 36 hours after spraying. Deaths occurred in 2 to 9 hours after the appearance of symptoms. The minimum toxic concentration of the older chlordane for baby calves appeared to be 1 percent, but was 2 percent with that produced in 1953. The minimum toxic single dose for older cattle appeared to be in excess of 2 percent with either new or old material. Except as already noted, all types of livestock tolerated 1.5-percent concentrations, three times the concentration usually suggested for insect control.

The newer chlordane has not been used in our experiments on horses, hogs, sheep, or goats, but its toxicity for these animals would be expected to be less than was observed with the old material, increasing an already adequate margin of safety.

The results of multiple dermal applications of chlordane given in table 2 indicate that the older chlordane was cumulative in action, while the 1953 product did not appear so. All livestock except baby calves, lambs, and kids tolerated at least 3 applications of 1.5-percent chlordane of old manufacture. Lambs and kids were poisoned by 3 such applications, while all others tolerated 8 treatments, even when applied at 4-day intervals. Of 10 cattle, however, 3 were poisoned and died after 3 applications of 2 percent of the older chlordane, applied at 2-week intervals. With the 1953 chlordane, 8 cattle were treated 12 times at 2-week intervals with 2-percent sprays without evidence of any harm. This illustrated the improvement made in the chemical.

The calf listed as having been sprayed 8 times with 1.5-percent chlordane at 4-day intervals became affected on the day after the seventh treatment, was convulsive 3 days after the eighth treatment, and died 31 days after the eighth treatment.

The results of administering technical chlordane (1953 manufacture) as emulsions or suspensions orally to baby dairy calves and to sheep

344495—55——2

TABLE 1.—*Results of single dermal applications of emulsions and suspensions of chlordane to various farm animals*

CHLORDANE PRODUCED PRIOR TO 1953

Kind of animal	Age	Concentration in spray	Formulation type [1]	Animals			
				Treated	Affected severely, recovered	Died	Unaffected
		Percent		*Number*	*Number*	*Number*	*Number*
Calves	1–2 wk.	8.0	Em	1	0	1	0
		4.0	Em	3	0	1	2
		2.0	Em	10	1	4	5
		1.0	Em	8	0	1	7
Calf	4 mo.	1.5	Em	1	0	0	1
Cattle	1 yr.	1.5	Em	2	0	0	2
		1.5	WP	2	0	0	2
	1–5 yr.	2.0	WP	18	0	0	18
Lamb	3 wk.	1.5	Em	1	0	0	1
Sheep	1–2 yr.	1.5	Em	10	0	0	10
		1.5	WP	10	0	0	10
Kid	3 wk.	1.5	Em	1	0	0	1
Goats	1–2 yr.	1.5	Em	5	0	0	5
		1.5	WP	5	0	0	5
Pigs	3–4 mo.	4.0	Em	2	0	0	2
		1.5	Em	2	0	0	2
		1.5	WP	2	0	0	2
Horses	4 yr.	1.5	Em	1	0	0	1
	5 yr.	1.5	WP	1	0	0	1
CHLORDANE OF 1953 PRODUCTION							
Calves	1–2 wk.	2.0	Em	6	0	1	5

[1] Em = emulsion; WP = wettable powder suspension.

are given in table 3. All 3 calves receiving 100 mg./kg. doses were affected within 4 hours of treatment and all 3 died. The calves given 50 mg./kg. were affected within the same time although 1 recovered, 2 died, and 1 was not affected. Two calves given 25 mg./kg. showed symptoms of poisoning; one recovered. Five calves given 10 mg./kg. of chlordane were unaffected. Of the 6 sheep given 100 mg./kg. there were no fatalities, but 5 were definitely poisoned. Only 1 sheep was given 50 mg./kg. and it was not poisoned. In addition to the sheep listed in table 3, one sheep was given 50 mg./kg. of chlordane in an emulsion daily, 4 days a week until 17 doses had been given, without showing gross disturbances. This sheep was rested 1 week and then given daily doses of 250 mg./kg. each, the second such dose producing symptoms of poisoning. The sheep was then destroyed to obtain fat for chemical study.

Marsh, Johnson, Clark, and Pepper (*13*) found the minimum toxic dose of chlordane for cattle to be 91 mg./kg. and the minimum lethal

TABLE 2.—*Results of applying 1.5-percent chlordane emulsions and suspensions dermally every 4 days to various farm animals*

CHLORDANE PRODUCED PRIOR TO 1953

Kind of animal	Age	Formulation type [1]	Treatments	Animals		
				Treated	Died	Unaffected
			Number	*Number*	*Number*	*Number*
Calf	4 mo.	Em	8	1	1	0
Cattle	9 mo.	Em	8	2	0	2
		WP	8	2	0	2
Lamb	2 mo.	EM	5	1	1	0
Sheep	1–2 yr.	Em	8	5	[2] 1	4
		WP	8	10	0	10
Kid	2 mo.	Em	6	1	[3] 1	0
Goats	1–2 yr.	Em	8	5	[4] 2	3
		Em	8	5	[5] 1	4
Pigs	3–4 mo.	Em	8	4	0	4
		WP	8	4	0	4
Horse	4 yr.	Em	8	1	0	1
		WP	8	1	0	1

[1] Em=emulsion; WP=wettable powder suspension.
[2] Affected by and died after the 6th dipping.
[3] Affected by the 3d dipping and died after the 6th dipping.
[4] One died after the 6th dipping; the other was affected by the 7th, and died after the 8th dipping.
[5] Died after the 6th dipping.

dose to be 129 mg./kg. when given in the form of a grasshopper bait. Welch (*26*) administered 50 mg./kg. of chlordane to cattle with no harmful effects noted, while sheep were poisoned by 500 mg./kg. and killed by 1,000 and 2,000 mg./kg. One sheep was given 3.5 grams of chlordane (approximately 100 mg./kg.), and was poisoned by the dose.

The symptoms of chlordane poisoning observed by Marsh and coworkers, and by Welch, were similar to those given in this report and those previously described by Radeleff (*15*).

From the foregoing results we believe that the use of chlordane on or around livestock is not without some attendant hazards to the animals, but that under regular usage in accordance with recommended procedures there should be no harm to any species of livestock. Any condition which would increase the concentration of a spray or dip, or increase the rate of deposition on the hair, could produce poisoning; this may have been a factor in the cases reported by Arnold (*1*). Accidental poisonings may result if animals have access to chlordane in grasshopper baits or other forms through carelessness.

Emaciation and lactation will increase the susceptibility of sheep to chlordane poisoning, as determined by Radeleff and Bushland (*19*). Under such conditions ewes may be poisoned by 1.0-percent dips of chlordane, while their lambs are unaffected by the same dipping. A summary of a study of this type appears in table 4.

TABLE 3.—*Results of administering single oral doses of chlordane to baby dairy calves and to adult sheep*

CHLORDANE PRODUCED IN 1953

Kind of animal, and age	Dose	Animals				
		Treated	Affected mildly	Affected severely, recovered	Died	Unaffected
	mg./kg.	*Number*	*Number*	*Number*	*Number*	*Number*
Calves, 1–2 wk	100	3	0	0	3	0
	50	4	0	1	2	1
	25	2	1	1	0	0
	10	5	0	0	0	5
Sheep, 4–5 yr	100	6	3	2	0	1
	50	1	0	0	0	1

TABLE 4.—*Results of dipping emaciated ewes and their lambs in emulsions of chlordane*

Kind of animal	Concentration in dip	Animals			
		Treated	Affected mildly, recovered	Died	Unaffected
	Percent	*Number*	*Number*	*Number*	*Number*
Ewes	2.0	5	0	1	4
Lambs	2.0	5	0	0	5
Ewes	1.0	15	1	0	14
Lambs	1.0	15	0	0	15
Ewes	.5	10	0	0	10
Lambs	.5	10	0	0	10

BHC

BHC, or benzene hexachloride, is a highly effective parasiticide widely used on livestock. Five isomers of this compound are present in the technical material, of which the gamma isomer is the most insecticidal and most acutely toxic to mammals. A highly refined product containing 99 percent or more of the gamma isomer is called lindane. The BHC used in the experiments reported here ranged in gamma isomer content from 12 to 99+ percent. The toxicity observed was directly associated with the gamma content and was entirely independent of the presence or absence of other isomers.

The results of single applications of sprays and dips to baby dairy calves, given in table 5, show that BHC is toxic to such calves at 0.05 percent, but not at 0.025 percent, of the gamma isomer. There was little difference in toxicity between suspensions and emulsions.

TABLE 5.—*Results of single dermal applications of BHC on 1- to 2-week-old dairy calves*

Kind of animal and age	Gamma concentration	Formulation type [1]	Animals			
			Treated	Affected severely, recovered	Died	Unaffected
	Percent		*Number*	*Number*	*Number*	*Number*
Calves, 1-2 wk.	0.15	Em	1	0	1	0
	0.1	Em	11	1	2	8
	0.1	WP	2	0	2	0
	0.05	Em	10	0	3	7
	0.05	WP	9	2	0	7
	0.025	Em	5	0	0	5

[1] Em=emulsion; WP=suspension of wettable powder.

Single applications of smears of lindane to the skin of baby dairy calves were made to study the possible hazards associated with the use of lindane in screw-worm treatment. From the results shown in table 6 we would expect 25 mg./kg. of lindane, applied dermally in a localized area, to be occasionally toxic for such calves.

Older animals appear more resistant to BHC poisoning. When we used technical BHC of 12-percent gamma content, calves 6 to 8 months of age were unharmed by sprays containing 0.15 percent of gamma; lambs 6 weeks of age and pigs 3 months of age were not harmed by 0.5 or 1.0 percent, a single treatment being applied in each case. A concentration of 0.15-percent gamma is 5 to 6 times that sprayed on livestock for ectoparasite control and 3 times that used as a scabies treatment.

TABLE 6.—*Results of single dermal applications of lindane formulations to baby dairy calves 1–2 weeks of age*

Formulation, percent	Dose of lindane	Animals				
		Treated	Affected mildly	Affected severely, recovered	Died	Unaffected
	mg./kg.	*Number*	*Number*	*Number*	*Number*	*Number*
EQ–335 screw-worm smear lindane 3.0	25	7	1	0	0	6
Lindane 5.0, Tween 20, 15, and xylene 80	100	6	0	1	5	0
Lindane 5.0, pine oil 47.5, and mineral oil 47.5	100	6	0	1	3	2

Ely, Underwood, Moore, Mann, and Carter (*9*) reported on an accidental spraying of adult dairy cattle with a 0.3-percent lindane suspension used for spraying barn walls. A total of 240 cows were sprayed, resulting in 11 cases of poisoning, of which 5 terminated fatally. The spraying of barn and cattle was accomplished with 50 gallons of spray, allowing a maximum of just over 0.2 gallon per animal, if it were all used on the cows, but in actuality the spray was only allowed to strike the cattle as a part of the normal barn spraying, making the dosage anything but uniform. Apparently the dose was less than 1 quart per cow.

The results of repeated applications of BHC are given in table 7. As was observed with chlordane, older calves and most other livestock were more resistant than baby dairy calves to poisoning by repeated applications. Kids and lambs were poisoned by 1 and 2 applications, respectively, while all others treated were unaffected by a total of 8 applications of 0.15-percent gamma (from technical BHC of 12-percent gamma content) at 4-day intervals.

TABLE 7.—*Results of repeated dermal applications of BHC (12-percent gamma) containing 0.15 percent of gamma at 4-day intervals for a total of eight treatments*

Kind of animal	Age	Animals			
		Treated	Affected, recovered	Died	Unaffected
		Number	*Number*	*Number*	*Number*
Calves	6–8 mo.	2	0	0	2
Lamb	3 wk.	1	[1] 1	0	0
Sheep	1 yr.	5	0	0	5
Goat kid	3 wk.	1	0	[2] 1	0
Goats	1 yr.	5	0	0	0
Pigs	3 mo.	2	0	0	2
Horse	5 yr.	1	0	0	1

[1] Affected by 1st treatment; unaffected by 7 additional treatments.
[2] Affected by 2d application; died after 5th treatment.

Results of administering single oral doses of BHC or lindane to calves, cattle, and sheep are given in table 8. The minimum toxic dose for baby dairy calves appeared to be between 2.5 and 5 mg./kg. of gamma, the lower dose producing no intoxication while the higher dose caused death. The minimum toxic dose for yearling Hereford cattle appeared to be between 10 and 25 mg./kg., the lower dose producing no symptoms while the higher dose was lethal. Because only a single animal received the 10 mg./kg. dose it is unwise to conclude that this dose could not be toxic. Sheep appear to tolerate 10 mg./kg. but are poisoned by 25 mg./kg. (See table 8.) Sheep were poisoned by 50 and by 75 mg./kg. doses, but were not killed until the dose was raised to 100 mg./kg.

TABLE 8.—*Results of administering single oral doses of lindane to baby dairy calves, adult sheep, and cattle*

Kind of animal	Age	Dose	Animals				
			Treated	Affected mildly	Affected severely, recovered	Died	Unaffected
		mg./kg.	*Number*	*Number*	*Number*	*Number*	*Number*
Calves	1–2 wk	15	5	0	0	4	1
		5	3	0	1	2	0
		2.5	9	0	0	0	9
Sheep	1–2 yr	100	4	0	3	1	0
		50	12	3	6	0	3
		25	8	6	1	0	1
		10	10	0	0	0	10
Cattle	1 yr	25	1	0	0	1	0
		10	1	0	0	0	1

Sheep were given 25 mg./kg. of lindane orally once a week until 6 doses had been given, the results being tabulated in table 9. All the sheep so treated were affected by at least 1 of the doses but none of the sheep were affected by all 6 doses.

One sheep was given 5 mg./kg. of gamma from technical BHC (12-percent gamma) 4 days a week until 22 such doses had been given without producing symptoms of poisoning. Two daily doses of 50 mg./kg. were then given, causing poisoning and death. A second sheep was given 50 mg./kg. of BHC (6 mg./kg. of gamma) 4 days a week for 15 doses without producing poisoning but the 16th dose initiated symptoms of poisoning and the 17th caused death.

While the foregoing results apply for well-fed animals, Radeleff and Bushland (*19*) have found that emaciated sheep are more susceptible to poisoning by the gamma isomer of BHC than well-nourished ones, and that lactation also increases the susceptibility. Results of those studies were published in detail in 1953 (*21*) and summaries are given in tables 10 and 11 for purposes of comparison with the present data.

TABLE 9.—*Results of orally administering 25 mg./kg. of lindane as an emulsion to sheep once a week for 6 weeks* [1]

Sheep No.	Week of treatment					
	1	2	3	4	5	6
1	N	AR	AR	AR	AR	N
2	N	AR	N	AR	AR	N
3	AR	N	AR	N	AR	AR
4	AR	AR	AR	AR	N	AR
5	N	AR	N	N	N	N
6	N	AR	N	N	N	N

[1] N=not affected; AR=showed definite symptoms of poisoning and recovered.

TABLE 10.—*Results of dipping emaciated ewes and their lambs in benzene hexachloride*

Kind of animal	Formulation from technical BHC, gamma content—	Animals				
		Treated	Affected mildly	Affected severely, recovered	Died	Unaffected
	Percent	*Number*	*Number*	*Number*	*Number*	*Number*
0.06 PERCENT GAMMA ISOMER IN DIP						
Ewes	14	30	3	4	7	16
Lambs	14	30	0	0	0	30
Ewes	12	30	0	2	3	25
Lambs	12	30	0	0	1	29
Ewes	[1] 99+	30	3	0	1	26
Lambs	[1] 99+	30	0	0	0	30
0.03 PERCENT GAMMA ISOMER IN DIP						
Ewes	14	10	1	1	0	8
Lambs	14	10	0	0	0	10
Ewes	12	10	2	0	0	8
Lambs	12	10	0	0	0	10
Ewes	[1] 99+	10	0	1	0	9
Lambs	[1] 99+	10	0	0	0	10

[1] Lindane.

TABLE 11.—*Results of dipping well-fed ewes and their lambs in BHC dip containing 0.25 percent of gamma, 10 ewes and 10 lambs for each treatment*

Kind of animal	Formulation prepared from BHC gamma content	Animals		
		Affected mildly	Affected severely, recovered	Unaffected
	Percent	*Number*	*Number*	*Number*
Ewes	14	3	0	7
Lambs	14	0	0	10
Ewes	12	1	0	9
Lambs	12	0	0	10
Ewes	[1] 99+	0	2	8
Lambs	[1] 99+	0	1	9

[1] Lindane.

It is highly probable that similar increases in susceptibility occur in cattle, a strikingly similar phenomenon having been reported from Australia [5] where emaciated adult cattle were poisoned by normal and previously routine concentrations of gamma BHC. The mechanism by which the susceptibility is increased in such animals is not understood.

[5] Graham, Norman H., of William Cooper and Nephews, and Ian Montgomery of Imperial Chemicals, personal communications.

Ely, Moore, and Carter (*8*) fed dairy cows 6.22 mg./kg. of crystalline lindane daily for 110 days without producing symptoms of poisoning. Welch (*26*) gave cattle 125 mg./kg. of BHC (12.5 mg./kg. of gamma) without producing symptoms. In his work, sheep given 750, 1,000, and 2,000 mg./kg. of BHC (10 percent gamma) were poisoned but deaths did not occur. One of the sheep was given 2.25 grams of BHC daily, showed symptoms on the twentieth day, but survived 60 such daily doses. The symptoms described by Welch for BHC poisoning agree with those presented in this and preceding papers (*4, 18, 19*) and with those described by Ely and coworkers (*9*).

TOXAPHENE

Toxaphene is a waxy chemical produced by the chlorination of camphene. It is prepared for livestock use as an emulsifiable concentrate and as a wettable powder. It is effective against a wide range of pests at the strengths of 0.25 to 0.5 percent in sprays. Some results of treating animals with toxaphene have been published by the Kerrville staff (*3, 4, 5, 6, 16, 18, 20*).

Results of treating cattle of various ages with single applications of toxaphene are given in table 12. The minimum toxic concentration for baby calves appears to be about 0.75 percent and the minimum lethal dose 1.0 percent. Older cattle are mildly affected by 4.0 per-

TABLE 12.—*Results of single dermal applications of toxaphene to cattle of various ages*

Kind of animal	Age	Concentration of toxaphene	Formulation type [1]	Animals			
				Treated	Affected, recovered	Dead	Unaffected
		Percent		*Number*	*Number*	*Number*	*Number*
		0.5	Em	12	0	0	12
		.75	Em	20	4	0	16
		.75	WP	4	0	0	4
Jersey	2 wk	1.0	Em	21	3	8	10
		1.0	WP	3	0	0	3
		1.5	Em	8	3	0	5
		1.5	WP	4	1	0	3
		1.5	Em	2	0	0	2
Jersey	4–6 mo	1.5	WP	2	0	0	2
Jersey	2 wk	2.0	Em	6	0	6	0
Jersey	3–4 mo	2.0	Em	14	4	5	5
Hereford	3–4 mo	2.0	Em	25	1	0	24
Jersey	2 wk	3.0	Em	1	0	1	0
		4.0	Em	5	1	3	1
Jersey	1 mo	4.0	WP	1	1	0	0
Jersey and Herefords	6–8 mo	4.0	Em	13	1	0	12
		4.0	WP	7	0	0	7
		8.0	Em	2	0	2	0
Jersey	1 mo	8.0	WP	1	1	0	0
Hereford	4 yr	8.0	Em	1	1	0	0

[1] Em=emulsion; WP=suspension of wettable powder.

344495—55——3

cent while one steer survived poisoning by an 8.0-percent spray. Jerseys were more susceptible than Herefords at each age level.

Onset of symptoms in the poisoned cattle occurred in from 30 minutes to 24 hours after treatment, with deaths occurring in 15 minutes to 48 hours after onset of symtoms.

Results of single applications of toxaphene to sheep, goats, pigs, and horses are summarized in table 13. Both sheep and goats appear less resistant than cattle to toxaphene poisoning, the minimum toxic and lethal concentration being between 1.5 and 4.0 percent. Pigs were resistant to 4.0-percent sprays. Minimum toxic concentrations were not determined for these animals.

Results of multiple applications to animals other than baby calves are given in table 14. All animals were treated with 1.5-percent toxaphene sprays or dips at 4-day intervals for 8 applications. No toxic effects were noted.

Results of the oral administration of toxaphene to calves, sheep, and goats are given in table 15. The minimum toxic dose for baby calves appears to be about 5 mg./kg. For sheep the minimum toxic dose is 25 mg./kg. and for goats approximately the same.

One adult sheep was given 50 mg./kg. of toxaphene orally in a xylene emulsion 4 days a week and was not affected by the first 7 doses. The 8th dose initiated symptoms of poisoning and the 14th dose produced death.

TABLE 13.—*Results of single dermal applications of toxaphene on sheep, goats, pigs, and horses*

Kind of animal	Age	Concentration of toxaphene	Formulation type [1]	Animals			
				Treated	Affected, recovered	Dead	Unaffected
		Percent		*Number*	*Number*	*Number*	*Number*
Lambs	6 wk	4.0	Em	2	0	0	2
Sheep	1–2 yr	1.5	Em	5	0	0	5
		1.5	WP	5	0	0	5
		4.0	Em	3	3	0	0
		4.0	WP	1	0	0	1
		8.0	Em	2	0	2	0
Kids	6 wk	4.0	Em	4	0	4	0
Goats	1–2 yr	1.5	Em	5	0	0	5
		1.5	WP	5	0	0	5
		4.0	Em	3	1	0	2
		4.0	WP	1	0	0	1
		8.0	Em	3	1	2	0
Pigs	8–10 wk	4.0	Em	2	0	0	2
Pigs	3–4 mo.	1.5	Em	2	0	0	2
		1.5	WP	2	0	0	2
Horse	5 yr	1.5	Em	1	0	0	1
		1.5	WP	1	0	0	1

[1] Em=emulsion; WP=suspension of wettable powder.

TABLE 14.—*Results of multiple dermal applications of toxaphene at 1.5-percent concentration every 4 days for 8 treatments*

Kind of animal	Age	Formulation type [1]	Animals	
			Treated	Unaffected
			Number	*Number*
Cattle	6–8 mo.	Em	2	2
		WP	2	2
Sheep	1–2 yr.	Em	5	5
		WP	5	5
Goats	1–2 yr.	Em	5	5
		WP	5	5
Pigs	3–4 mo.	Em	2	2
		WP	2	2
Horse	5 yr.	Em	1	1
		WP	1	1

[1] Em=emulsion; WP=suspension of wettable powder.

TABLE 15.—*Results of single oral doses of toxaphene emulsions and suspensions administered to baby dairy calves, cattle, sheep, and goats*

Kind of animal	Age	Dose	Animals				
			Treated	Affected mildly	Affected severely, recovered	Died	Unaffected
		mg./kg.	*Number*	*Number*	*Number*	*Number*	*Number*
Calves	1–2 wk.	50	5	0	0	3	2
		25	6	0	0	2	4
		10	3	0	1	1	1
		5	2	1	0	0	1
Calves	3 mo.	50	3	0	2	1	0
Sheep	1–2 yr.	250	3	0	2	1	0
		170	3	0	3	0	0
		100	3	0	2	1	0
Sheep	4–5 yr.	50	7	1	1	0	5
		25	10	0	1	0	9
		10	9	0	0	0	9
Goats	1–2 yr.	250	3	0	1	2	0
		170	3	0	2	1	0
		100	3	0	3	0	0
		50	3	0	3	0	0

Marsh, Johnson, Clark, and Pepper (*13*) found that the minimum toxic dose of toxaphene for cattle was 35 mg./kg., while deaths occurred at 144 mg./kg., when toxaphene was given in the form of a grasshopper bait. The symptoms and lesions described by those workers agree closely with those observed by us, and as previously described in detail by Radeleff (*16*).

Emaciation and lactation apparently increases the susceptibility of ewes to poisoning by toxaphene as shown in table 16. From those results it would appear that under such conditions ewes may be poisoned by dips containing 1.0 percent of toxaphene. It would also appear from those results that their lambs could be poisoned by the same dip.

TABLE 16.—*Results of dipping emaciated ewes and their lambs in toxaphene emulsions*

Kind of animal	Toxaphene concentration	Animals		
		Treated	Affected severely, recovered	Unaffected
	Percent	*Number*	*Number*	*Number*
Ewes	1.0	15	1	14
Lambs	1.0	15	3	12
Ewes	0.5	10	0	10
Lambs	0.5	10	0	10

From the foregoing results it appears that toxaphene and chlordane are of approximately equal toxicity when applied dermally to baby calves, but that toxaphene is considerably more toxic than chlordane when administered orally.

STROBANE

Strobane is an amber liquid with a rather pleasant odor, similar to toxaphene in chemical, insecticidal, and toxicological activity. As yet, its full usefulness as an insecticide has not been established, but it seems desirable to publish the available toxicological data.

The results of dermal applications are given in table 17. From these limited numbers of treated calves it would appear that Strobane is about one-half as toxic as toxaphene. Results of single oral administrations of Strobane to baby calves and to sheep are given in table 18. In these very limited trials the minimum toxic dose appeared to be very close to 10 mg./kg., the calves appearing overly sensitive and suggesting minimum intoxication. For sheep, the minimum toxic dose appeared to be under 50 mg./kg., although the studies were not completed before this manuscript was prepared. On the basis of this limited study of oral toxicity, Strobane again appears to be somewhat less toxic than toxaphene.

The symptoms exhibited by the animals poisoned by Strobane were essentially the same as those for toxaphene and other members of the more toxic group of chlorinated hydrocarbon insecticides.

TABLE 17.—*Results of single dermal applications of Strobane upon dairy calves 1 to 2 weeks old*

Kind of animal and age	Concentration in spray	Animals			
		Treated	Affected severely, recovered	Died	Unaffected
	Percent	*Number*	*Number*	*Number*	*Number*
Calves, 1–2 wk.	4.0	2	0	2	0
	2.0	2	0	1	1
	1.0	6	0	0	6

TABLE 18.—*Results of single oral doses of Strobane administered to dairy calves 1 to 2 weeks of age, and to adult sheep*

Kind of animal	Dose	Animals				
		Treated	Affected mildly	Affected severely, recovered	Died	Unaffected
	mg./kg.	*Number*	*Number*	*Number*	*Number*	*Number*
Calves	25	2	0	0	1	1
	10	3	0	0	0	3
Sheep	150	2	0	2	0	0
	100	2	0	2	0	0
	50	11	2	4	0	5

ALDRIN

Aldrin is a white crystalline solid, insoluble in water but soluble in most organic solvents. It is a highly effective insecticide, presently used chiefly for the control of plant pests. While it is effective against a number of parasites preying upon livestock it is a relatively highly toxic compound, as will be shown in the following data, and it has a definite tendency to accumulate in body fat, the combination making it less desirable for use on animals than some of the other compounds.

Results of single spray treatments with aldrin are given in table 19. Symptoms of poisoning appeared in calves 3 to 34 hours after treatment. Deaths occurred in from 15 minutes to 24 hours after onset of symptoms. The lambs showed symptoms of poisoning within 18 hours after treatment and died 10 hours later. The Angora kids were affected within 12 hours of treatment and died 16 hours later.

The minimum toxic concentration of aldrin applied as a spray to calves appears to be 0.25 percent or slightly less, making it more toxic, on a percentage basis, than toxaphene or chlordane and about one-half

TABLE 19.—*Results of single dermal applications of aldrin emulsions to calves, lambs, and kids*

Kind of animal	Age	Concentration in spray	Animals			
			Treated	Affected severely, recovered	Died	Unaffected
		Percent	*Number*	*Number*	*Number*	*Number*
Calves	2 wk	4.0	1	0	1	0
		2.0	1	0	1	0
		1.0	1	0	1	0
		0.75	2	1	1	0
		0.5	14	2	8	4
		0.25	7	1	0	6
Lambs	3 wk	4.0	2	0	2	0
Kids	3 wk	4.0	2	0	2	0

as toxic as dieldrin. Minimum toxic concentrations for sheep and goats were not determined.

A summary of the results obtained by administering aldrin orally to baby calves and to adult cattle and sheep is given in table 20. From these data it would appear that the minimum toxic dose of aldrin is just under 5 mg./kg. for baby calves, and between 10 and 25 mg./kg. for cattle. The minimum toxic dose for sheep appears to be between 10 and 15 mg./kg.

Kitselman, Dahm, and Borgmann (*11*) fed small amounts of aldrin to cattle and sheep and produced symptoms of poisoning as follows.

TABLE 20.—*Results of single oral doses of aldrin administered to baby dairy calves and to adult sheep and cattle*

Kind of animal	Age	Dose	Animals				
			Treated	Affected mildly	Affected severely, recovered	Died	Unaffected
		mg./kg.	*Number*	*Number*	*Number*	*Number*	*Number*
Calves	1–2 wk	15	2	0	2	0	0
		5	7	2	0	0	5
		2.5	2	0	0	0	2
Steers	1 yr	25	1	0	0	1	0
		10	1	0	0	0	1
Sheep	1–2 yr	28.5	1	0	1	0	0
		15	1	0	1	0	0
		10	1	0	0	0	1
		5	1	0	0	0	1
		2.5	1	0	0	0	1

Cattle were killed by 10 daily doses of 1.9 mg./kg. of aldrin, by 21 daily doses of 0.84 mg./kg., and by 33 daily doses of 0.686 mg./kg. One heifer was poisoned by 29 daily doses of 0.52 mg./kg. but recovered. In a second series, a heifer was given 4 mg./kg. daily, developed symptoms on the 8th day, and died on the 21st day. A second heifer received 2 mg./kg. daily and developed symptoms after 29 doses, recovered, and survived a total of 64 doses. Heifers fed 1.0 or 0.5 mg./kg. daily for 64 days were unaffected.

In the same series of studies one ewe died after receiving 20 daily doses of aldrin at 0.414 mg./kg. One ewe receiving 6 mg./kg. daily, lost her appetite after 15 doses and died after 28 doses.

The symptoms and lesions of aldrin poisoning observed by Kitselman and coworkers (*11*) are similar to those we observed at the Kerrville laboratory.

In the studies by Kitselman and coworkers it is interesting to note that most of the doses which proved toxic totalled from 15 to 30 mg./kg., and are roughly the amounts required for toxic effect from single doses. This is in keeping with our knowledge that aldrin has a great tendency to be held in the body after ingestion.

HEPTACHLOR

Heptachlor is at present used against insects other than those attacking livestock, but could in the future have a place in livestock pest control.

Results of single spray applications of heptachlor are given in table 21. Symptoms appeared in poisoned animals in from 23 to 44 hours after treatment. In every case death occurred within 2 hours after the onset of symptoms. No recoveries were noted in this series. The minimum toxic concentration for baby calves appears to be between 0.25 and 0.5 percent, making heptachlor more toxic than chlordane and toxaphene but slightly less toxic than aldrin for these animals. Lambs appeared to be resistant to as much as 4.0-percent concentrations but a minimum toxic dose was not established.

The results of administering heptachlor orally to sheep and calves are given in table 22. Those sheep that recovered from poisoning

TABLE 21.—*Results of single dermal applications (sprays) of heptachlor emulsions to calves and lambs*

Kind of animal	Age	Concentration in spray	Animals		
			Treated	Died	Unaffected
		Percent	*Number*	*Number*	*Number*
Calves	1–2 wk	4.0	1	1	0
		2.0	3	3	0
		1.0	6	4	2
		.75	2	0	2
		.5	7	1	6
		.25	11	0	11
Lambs	3 wk	4.0	2	0	2

TABLE 22.—*Results of single oral doses of heptachlor administered to baby dairy calves and to adult sheep*

Kind of animal	Age	Dose	Animals			
			Treated	Affected severely, recovered	Died	Unaffected
		mg./kg.	*Number*	*Number*	*Number*	*Number*
Calves	1–2 wk	50	7	2	5	0
		25	6	1	2	3
		15	5	0	0	5
Sheep	1–2 yr	150	2	0	2	0
		100	2	0	2	0
Sheep	4–5 yr	100	2	0	1	1
Sheep	1–2 yr	75	1	0	0	1
		50	1	0	0	1
Sheep	4–5 yr	50	2	1	0	1
		25	11	0	0	11

did so without complications. The minimum toxic dose for calves appeared to be between 15 and 25 mg./kg.

The animals poisoned by heptachlor demonstrated symptoms and lesions considered typical for chlorinated hydrocarbon insecticides.

DIELDRIN

Dieldrin is another of the chlorinated hydrocarbon insecticides used at present principally against pests other than those feeding on livestock. Certain applications to these pests may be made in the future. Dieldrin is a white crystalline solid. It is soluble in some of the organic solvents, but rather insoluble in most of the aliphatic petroleum solvents and insoluble in water.

Results of single applications of dieldrin as external treatments are given in tables 23 and 24. Symptoms of poisoning appeared in as short a time as 3 hours and as long as 14 days after treatment. Deaths occurred in from 3 hours to 14 days after symptoms appeared. This extremely long delay in onset of symptoms and of death after onset is without parallel in our experience. The animals that recovered from poisoning did so at a much slower rate than did animals poisoned by the other insecticides. One lamb was affected over a period of 18 days, during which time recovery slowly took place. In several cases the animals displayed typical symptoms of poisoning, apparently recovered completely, then relapsed after several days into typical symptoms followed by death.

The minimum toxic dose of dieldrin for baby calves appeared to be between 0.1 and 0.25 percent, making it roughly twice as toxic as aldrin and 8 to 10 times as toxic as toxaphene or chlordane.

Results of repeated applications of dieldrin are given in table 25. From the results with cattle sprayed with 0.5 percent dieldrin we feel that dieldrin is accumulative in action, since the 3 sprayings at 3-week intervals produced a greater reaction than did a single application of 1.0 percent (table 24).

TABLE 23.—*Results of single dermal applications of dieldrin to young animals*

Kind of animal	Age	Concentration in spray	Formulation type [1]	Animals			
				Treated	Affected severely, recovered	Died	Unaffected
		Percent		*Number*	*Number*	*Number*	*Number*
Calves	2 wk	1.0	Em	8	0	8	0
		0.75	Em	4	0	3	1
		0.5	Em	4	0	2	2
		0.5	WP	5	1	2	2
		0.25	Em	8	0	5	3
		0.25	WP	3	0	1	2
		0.1	Em	8	0	0	8
Lambs	2 wk	3.0	Em	3	0	3	0
		3.0	WP	5	1	4	0
Pigs	8 wk	2.0	Em	2	0	0	2
		4.0	Em	4	0	0	4

[1] Em=emulsion; WP=suspension of wettable powder.

TABLE 24.—*Results of single dermal treatments of adult animals with dieldrin*

Kind of animal	Age	Concentration of dieldrin	Formulation type [1]	Animals			
				Treated	Affected, recovered	Died	Unaffected
		Percent		*Number*	*Number*	*Number*	*Number*
Hereford cattle	9 mo	0.5	Em	2	0	0	2
		0.5	WP	2	0	0	2
		0.25	Em	4	0	0	4
		0.25	WP	4	0	0	4
Jersey cattle	1 yr	4.0	Em	2	2	0	0
		3.0	Em	2	2	0	0
		2.0	Em	2	0	2	0
		2.0	WP	2	2	0	0
		1.0	Em	2	0	0	2
Sheep	1 yr	4.0	WP	2	2	0	0
		4.0	Em	2	2	0	0
Goats	2 yr	4.0	Em	3	0	1	2
Horse	4–15 yr	1.0	Em	3	0	0	3

[1] Em=emulsion; WP=suspension of wettable powder.

TABLE 25.—*Results of repeated dermal applications of dieldrin upon adult cattle*

Breed	Age	Concentration of dieldrin	Formulation type [1]	Treatments	Interval between treatments	Animals		
						Total treated	Affected, recovered	Unaffected
		Percent		*Number*	*Weeks*	*Number*	*Number*	*Number*
Hereford	8 mo.	0.5	Em	3	2	2	1	1
		.5	WP	3	2	2	1	1
		.25	Em	8	3	4	0	4
		.25	WP	8	3	4	0	4
Jersey	4 yr.	.5	Em	2	3	1	0	1
		.5	WP	2	3	1	0	1

[1] Em=emulsion; WP=suspension of wettable powder.

Results obtained with oral doses of dieldrin are given in table 26. The poisoned calves developed symptoms in 3 to 5 hours after treatment. Deaths occurred in from 15 minutes to 5 hours after appearance of symptoms. Two pigs showed symptoms 2 hours after treatment, one dying 4 days after treatment, while the other recovered in the same period. The affected horse showed symptoms 3 hours after treatment and recovered in 12 hours. The onset of symptoms and occurrence of death were not as delayed as they were in the externally treated animals. The significance of this difference is not understood.

The minimum toxic dose of dieldrin for baby calves appeared to be between 5 and 10 mg./kg. The minimum toxic dose for pigs was between 25 and 50 mg./kg., while for horses 25 mg./kg. was definitely toxic.

TABLE 26.—*Results of single oral doses of dieldrin administered to baby dairy calves, pigs, adult cattle, and horses*

Kind of animal	Age	Dose	Animals			
			Treated	Affected severely, recovered	Died	Unaffected
		mg./kg.	*Number*	*Number*	*Number*	*Number*
Calves	1–2 wk.	25	1	0	1	0
		15	2	0	2	0
		10	3	0	2	1
		5	2	0	0	2
Steer	1 yr.	25	1	0	1	0
		10	1	0	0	1
Pigs	3 wk.	50	2	1	1	0
		25	2	0	0	2
		10	2	0	0	2
		5	2	0	0	2
Horse	8 yr.	25	1	1	0	0

DDT

DDT was the first of the chlorinated hydrocarbon insecticides to have widespread use on man, animals, and plants. At present, on a world-wide basis, it is still the basic insecticide of this family. Considering its widespread use on man and animals and the lack of authentic cases of poisoning other than gross accidents or attempts at suicide, it remains as one of the safest economic poisons ever introduced. Both experimental work and practical use have demonstrated that it is not acutely toxic in fairly high doses except to a few kinds of animals and plants. Particularly is this true of livestock. In our experiments we have been unable to produce poisoning of cattle, sheep, goats, hogs, or horses by external application, the experiments conducted being summarized in tables 27 and 28.

TABLE 27.—*Results of single dermal applications of DDT to various kinds of livestock*

Kind of animal	Age	Concentration in spray	Formulation type [1]	Animals	
				Treated	Unaffected
		Percent		*Number*	*Number*
Calf	2 wk.	1.5	Em	1	1
		8.0	WP	2	2
Steers	6–8 mo.	1.5	Em	2	1
		1.5	WP	2	2
Lambs	6 wk.	1.5	Em	1	1
		8.0	WP	2	2
Sheep	1–2 yr.	1.5	Em	5	5
		1.5	WP	5	5
Kid	6 wk.	1.5	Em	1	1
Goats	1–2 yr.	1.5	Em	5	5
		1.5	WP	5	5
Hogs	3–4 mo.	1.5	Em	2	2
		1.5	WP	2	2
Horse	5 yr.	1.5	Em	1	1
		1.5	WP	1	1

[1] Em=emulsion; WP=suspension of wettable powder.

The results of oral administration of DDT to baby calves and to sheep are given in table 29. Interesting comparisons can be made with methoxychlor in the baby calves where methoxychlor was approximately one-half as toxic as DDT and did not enjoy the wider margin of safety generally attributed to it by workers using laboratory animals.

A lactating Jersey cow was given 100 mg./kg. of DDT daily for 23 days. The first 16 doses produced no evidence of toxic disturbance. The last 7 doses caused the cow to lose weight rapidly. Some slight evidence of nerve stimulation was noted on the last 3 days of feeding. The cow was destroyed to obtain fat for chemists to recover the original DDT from the fat. There were no gross lesions observed at autopsy.

TABLE 28.—*Results of repeated dermal applications of DDT at 1.5-percent concentration every 4 days until 8 treatments were given*

Kind of animal	Age	Formulation type [1]	Animals	
			Treated	Unaffected
			Number	*Number*
Cattle	6–8 mo	Em	2	2
		WP	2	2
Sheep	1–2 yr	Em	5	5
		WP	5	5
Goats	1–2 yr	Em	5	5
		WP	5	5
Hogs	3–4 mo	Em	2	2
		WP	2	2
Horse	5 yr	Em	1	1
		WP	1	1
Calf	2–6 wk	Em	1	1
Lamb	3–7 wk	Em	1	1
Kid	3–7 wk	Em	1	1

[1] Em=emulsion; WP=suspension of wettable powder.

Howell, Cave, Heller, and Gross (*10*) sprayed dairy cows with 5.0-percent suspensions of DDT daily for 14 days without producing symptoms of poisoning. The same dosage was attempted, using emulsions, but skin injury resulted from the solvents and the spraying had to be discontinued.

Orr and Mott (*14*) fed 3 dairy cows 100 mg./kg. of DDT daily for 6 days, then increased the dose for 2 of the cows to 150 mg./kg. daily for 6 days and then to 200 mg./kg. for 6 days, while the third cow received the 100 mg./kg. dose for the three 6-day periods. All 3 cows showed nervous disturbances during the first week but all survived the treatment. A fourth cow was given 200 mg./kg. of DDT daily for 6 days and survived, although very severely affected. The same workers fed sheep 100 mg./kg. daily for 6 days, followed by 150 mg./kg. for 6 days, and 200 mg./kg. for the third 6-day period.

TABLE 29.—*Results of single oral doses of DDT administered to baby dairy calves and to adult sheep*

Kind of animal	Age	Dose	Animals			
			Treated	Affected mildly	Affected severely, recovered	Unaffected
		mg./kg.	*Number*	*Number*	*Number*	*Number*
Calves	1–2 wk	500	1	0	1	0
		250	1	1	0	0
		100	8	0	0	8
Sheep	4–5 yr	1,000	2	0	2	0
		500	4	0	3	1

These sheep showed no evidence of poisoning other than a loss in weight. Individual sheep were given 500, 1,000, 1,500, or 2,000 mg./kg. of DDT as a single dose. The sheep receiving 2,000 mg./kg. was the only one affected and showed only slight nervous disturbances. Orr and Mott also fed horses DDT. One horse was given 200 mg./kg. daily for 6 days and did not show symptoms other than weight loss. A second horse was given 100 mg./kg. daily for 6 days, then 150 mg./kg. daily for 6 days, and 200 mg./kg. for the third 6-day period. This horse lost weight but showed no other evidence of poisoning.

Telford and Harwood (*25*) administered 150 grams of DDT to a horse weighing 1,405 pounds (234 mg./kg.) without producing symptoms of poisoning.

Spicer, Sweeney, Von Oettingen, Lillie, and Neal (*23*) fed DDT to goats. They found that single doses of 500 and 1,000 mg./kg. produced definite poisoning followed by recovery, and concluded that the minimum lethal dose was in excess of 1,000 mg./kg. Of 4 goats given 1,000 mg./kg. daily, 2 were sacrificed in a moribund state after 6 doses, 1 died after 9 doses, and the fourth died after 11 doses. These authors concluded that the susceptibility of goats to DDT poisoning was dependent, in part at least, on the amount of body fat, the goats in best condition surviving the greater number of doses.

Welch (*26*) produced poisoning in cattle with DDT at 500 mg./kg. but the animals recovered. In his work sheep showed slight symptoms after a single dose of 500 mg./kg. and definite symptoms with recovery at 1,000 and 2,000 mg./kg. One sheep given 4.5 grams of DDT daily (approximately 100 mg./kg.) was poisoned after 10 daily doses.

The symptoms of poisoning by DDT observed at the Kerrville laboratory agree with those described by Orr and Mott, Spicer *et al.*, and Welch.

TDE

TDE is a white crystalline solid that is similar to DDT in physical and chemical properties and, in our work, toxicity to livestock. As with DDT, we have been unable to induce poisoning by external applications of this compound. The results obtained in our experiments are summarized in tables 30 and 31.

TABLE 30.—*Results of single dermal applications of TDE to calves, lambs, and kids*

Kind of animal	Age	Concentration in spray	Formulation type [1]	Animals	
				Treated	Normal
		Percent		*Number*	*Number*
Calves	2 wk	1.5	Em	1	1
		8.0	WP	2	2
Lambs	6 wk	1.5	Em	1	1
		8.0	WP	3	3
Kid	6 wk	1.5	Em	1	1

[1] Em=emulsion; WP=suspension of wettable powder.

TABLE 31.—*Results of repeated dermal applications of emulsions of TDE at 1.5-percent concentration every 4 days until 8 treatments were given*

Kind of animal	Age	Animals	
		Treated	Normal
		Number	*Number*
Calf	2–6 wk	1	1
Kid	6–10 wk	1	1
Lamb	6–10 wk	1	1
Cattle	6–8 mo	2	2
Sheep	1–2 yr	5	5
Goats	1–2 yr	5	5
Pigs	3–4 mo	2	2
Horse	4 yr	1	1

The results of oral administration of TDE to baby calves and to sheep are given in table 32. By this route TDE appears to be about equivalent in acute toxic effects to DDT and approximately twice as toxic as methoxychlor. The symptoms observed in TDE poisoning are basically the same as those seen with DDT and will be described at the end of this publication.

TABLE 32.—*Results of single oral doses of TDE administered to baby dairy calves and to adult sheep*

Kind of animal	Age	Dose	Animals				
			Treated	Affected mildly	Affected severely, recovered	Died	Unaffected
		mg./kg.	*Number*	*Number*	*Number*	*Number*	*Number*
Calves	1–2 wk	500	1	0	1	0	0
		250	1	1	0	0	0
		100	4	0	0	0	4
Sheep	4–5 yr	1,000	5	0	0	0	5

METHOXYCHLOR

Methoxychlor is a white crystalline solid having many of the physical properties of DDT and TDE. It is one of the least toxic of the chlorinated hydrocarbon insecticides studied at the Kerrville laboratory. As with DDT and TDE, we have been unable to induce poisoning of calves, cattle, sheep, goats, hogs, or horses by external applications of methoxychlor. The treatments employed and the results obtained are shown in tables 33 and 34.

To date we have been able to produce poisoning only in baby dairy calves by the oral administration of suspensions of methoxychlor.

TABLE 33.—*Results of single dermal applications of methoxychlor to young livestock*

Kind of animal	Age	Concentration	Formulation type [1]	Animals	
				Treated	Unaffected
		Percent		*Number*	*Number*
Calves	2 wk	1.5	Em	1	1
		8.0	WP	2	2
Kid	6 wk	1.5	Em	1	1
Lambs	6 wk	1.5	Em	1	1
		8.0	WP	3	3

[1] Em=emulsion; WP=suspension of wettable powder.

TABLE 34.—*Results of multiple dermal applications of methoxychlor emulsions of 1.5 percent concentration at 4-day intervals until 8 treatments were given*

Kind of animal	Age	Animals	
		Treated	Unaffected
		Number	*Number*
Calf	2–6 wk	1	1
Kid	2–6 wk	1	1
Lamb	2–6 wk	1	1
Cattle	6–8 mo	2	2
Sheep	1–2 yr	5	5
Goats	1–2 yr	5	5
Hogs	3–4 mo	2	2
Horse	4 yr	1	1

A summary of the results of oral administrations will be found in table 35 and includes doses given to calves and to sheep.

In addition to the doses tabulated, 1 sheep was given oral doses of a xylene emulsion of methoxychlor 4 days each week, each dose being 50 mg./kg., until a total of 21 such doses had been given, without producing symptoms. Two doses, each of 250 mg./kg., and one dose of 500 mg./kg. were then given and no symptoms appeared. The sheep was then destroyed and the fat collected for chemical studies.

Welch (*26*) did not induce poisoning in cattle by a single dose of 500 mg./kg. of methoxychlor. Sheep given 1,000 and 2,000 mg./kg. were unaffected, and 1 sheep failed to show symptoms after 60 daily doses of 4.5 grams of methoxychlor.

PERTHANE

Perthane, also known as Q–137, is another compound closely related to DDT. It has been applied to baby dairy calves as an 8-per-

TABLE 35.—*Results of single oral doses of methoxychlor administered to baby dairy calves and to adult sheep*

Kind of animal	Age	Dose	Animals		
			Treated	Affected severely, recovered	Unaffected
		mg./kg.	*Number*	*Number*	*Number*
Calves	1–2 wk	1,000	1	1	0
		500	1	1	0
		250	5	0	5
Sheep	4–5 yr	1,000	4	0	4

cent suspension, 3 being treated, without producing symptoms of poisoning. No further studies have been made at this time. It is believed that its general toxicological picture is similar to DDT, TDE, and methoxychlor in being one of the safest of the chlorinated hydrocarbon insecticides.

DILAN

Dilan, also known as CS–708, is a mixture of 1 part of Prolan and 2 parts of Bulan. As was the case with Perthane, only 3 baby calves have been treated, and these were treated with 8-percent suspensions without producing symptoms of poisoning. Dilan should also be placed among the safest of the chlorinated hydrocarbon insecticides.

Symptoms of Poisoning

MORE TOXIC COMPOUNDS

The more toxic chlorinated hydrocarbon insecticides including BHC, chlordane, toxaphene, Strobane, dieldrin, aldrin, heptachlor, and isodrin, are diffuse stimulants of the central nervous system. The expressions of such diffuse stimulation are of extreme variety but are predominately neuromuscular. While is it unlikely that a single animal will demonstrate all of the possible symptoms, there is a sufficient similarity between animals to permit recognition and identification of a definite syndrome.

The onset of symptoms may occur in from a few minutes to days after exposure, depending on the chemical and the dose applied or ingested. Most animals show symptoms within the first 24 hours after exposure. The symptoms displayed may be progressively severe in nature or may be explosive and fulminating.

An affected animal may first be apprehensive and hypersensitive or may become belligerent. Soon blepharospasms and fasciculations of the facial and cervical muscles will appear, followed by clonic spasms of the cervical muscles, then those of the forequarters, and, finally, those of the hindquarters. These spasms may be rapidly repeated or may appear intermittently at regular or irregular intervals. Concurrently with the appearance of muscular spasms the secretion of saliva begins to increase and the animal begins to perform chewing or champing movements of the jaws, thereby producing a froth that appears at and adheres to the lips and muzzle.

As the action of the insecticide grows more intense the animal is increasingly agitated, often frenzied, and begins to lose coordination. The animal may stumble while walking, jump imaginary objects, walk aimlessly about, or move in close circles. Abnormal postures may be assumed, such as resting the sternum on the ground while the hind legs remain in the standing position; others persist in keeping the head between the forelegs.

These various symptoms may progress to convulsions which are clonic-tonic in nature, accompanied by periods of paddling movements, nystagmus, grinding of the teeth, and groaning or grunting. Convulsive seizures may be repeated at regular or irregular intervals, or, once begun, may persist until death.

Occasionally an animal will be struck by a maniacal seizure and plunge headlong into a fence, wall, trough, or other object before falling in a convulsion. A few animals have been observed to select an area of skin and lick at it until the hair and epidermis are removed, usually leaving a raw and bleeding surface.

In some instances the onset of symptoms is explosive, the animal leaping into the air as if stung and then backing or twisting into a convulsion without exhibiting any premonitory symptoms.

Poisoned animals have been observed to become comatose and remain so for several hours before death.

Convulsive seizures, if prolonged for more than a few minutes, cause the body temperature to rise sharply and remain as high as 114°–116° F. Much of this increase in temperature is naturally due to the muscular activity involved in the seizures, but it is our opinion that there is probably a concommitant interference with the heat regulatory centers and mechanisms distinct from the factor of work. In such prolonged seizures dyspnea occurs and death follows respiratory failure. The cessation of pulmonary ventilation before cardiac arrest establishes a generalized cyanosis.

During the symptomatic period many animals will show an exaggerated response to sudden stimuli such as noises or movements. This is particularly true with toxaphene and strobane.

In marked contrast to these active symptoms are those shown by some animals wherein there is severe depression, drowsiness, inappetence, and reluctance to move about, followed by emaciation and dehydration. Such symptoms may persist until death, or there may be an alternation of depression and activity.

The severity of the symptoms displayed is definitely not an index of the chances of an animal for survival. In our work we have seen animals die after a single, brief convulsion, while others have survived numerous seizures of apparent equivalent severity.

LESS TOXIC COMPOUNDS

The less toxic insecticides which produced symptoms in our experiments were DDT, TDE, and methoxychlor, and the discussion following is confined to these three insecticides.

In this type of poisoning the animals first show restlessness and are excitable and hypersensitive, much as are the animals poisoned by the more toxic group. Fasciculations of the facial muscles then appear, particularly in those of the eyelids, which are very rapid, ap-

proaching the character of tremors. This movement is much more rapid than with the more toxic compounds and is not as coarse. Tremors then appear in other muscles of the body, finally involving every skeletal muscle simultaneously. These tremors become coarser with the progress of time, finally causing the animal to shake violently. Such seizures may be provoked almost at will by slight external stimuli. Dyspnea occurs with such attacks.

Following seizures, the animal is depressed and stiff.

In the milder cases of poisoning, tremors are absent or inconspicuous, the animal walking with the pasterns extended stiffly, appearing as though on "tip-toes," and walking with short choppy steps. This is followed by a period of apparent laminitis during which the animal walks as though all four feet were extremely sore. During this period the reflexes are slow and the animal loses weight rapidly.

Autopsy Findings

In acute poisoning the lesions found are nonspecific. Due to the high activity usually preceding death and the coeval rise in body temperature there is cloudy swelling of most viscera and blanching of the intestines. Small hemorrhages occur at random throughout the body but are more consistently found on the heart. The epicardium usually shows from a few to several hundred petechial or larger hemorrhages tending to occur primarily in the areas adjacent to the major coronary vessels. There may be diffuse endocardial hemorrhages. As a rule the heart is in systole and the myocardium is whitish in color. There may be excessive pericardial fluid.

Generally, although there have been exceptions, the lungs are congested, dark in color, and show some hemorrhages. In some cases blood-tinged exudate is present in the bronchioles. The lungs may be edematous. In some cases the involvement is lobular or lobar rather than diffuse.

In cases of oral dosage there may be a mild gastroenteritis.

The brain and spinal cord are usually congested and frequently edematous. There is frequently an excess of cerebrospinal fluid attaining high pressure.

In chronic cases the foregoing lesions occur, together with degenerative lesions of the liver and kidneys. There is usually a loss of weight immediately before death, accompanied by dehydration and gelatinization of or absence of fat depots.

Micropathology

Summations of microscopic findings are to be found in table 36. As may be expected, the microscopic lesions follow those observed in the gross specimens—congestion, cloudy swelling, hemorrhages, and edema in the acute cases, with necrosis, fatty changes, and varying degenerations of the liver and kidney being the most frequently observed in those surviving for the longest periods. Congestion with cloudy swelling and small hemorrhages occur in the brain and spinal cord.

TABLE 36.—*Microscopic lesions found in cases of acute poisoning by chlorinated hydrocarbon insecticides*

Findings	Organs and total number examined					
	Liver 47	Kidney 42	Lung 9	Cerebrum 28	Cerebellum 24	Spinal Cord 19
Congestion	29	27	9	21	18	13
Hemorrhages	0	14	6	6	10	4
Cloudy swelling	26	29	0	8	7	7
Fatty changes	21	2	0	0	0	0
Necrosis	11	2	0	1	0	0
Degenerative changes	2	10	0	1	0	1
Increased cellularity	1	12	0	0	0	0
Exudates present	0	20	0	0	0	3
Edema	0	2	0	0	1	1
Pericellular vacuolation	0	0	0	18	11	5

PART II

Organic Phosphorus Insecticides

PARATHION

Parathion has found wide acceptance for use against insects feeding on plants. In some countries its use on livestock has been advocated. At this time its usefulness in the United States is chiefly against plant-feeding insects. Dangers to livestock are the consumption of parathion-treated plants and residues spilled by operators of spraying and dusting machinery. To obtain comparative toxicity data we have treated a number of animals with this material.

Results of single dermal applications of parathion are given in table 37. Poisoning may be expected to occur in baby Jersey calves at concentrations as low as 0.01 percent while definite lethal effects will be noted at 0.025 percent, whether the insecticide is applied as an emulsion or as a suspension.

TABLE 37.—*Results of single dermal applications (sprays) of parathion to baby dairy calves, sheep, and goats*

Kind of animal	Age	Concentration in spray	Formulation type [1]	Animals			
				Treated	Affected mildly	Died	Unaffected
		Percent		*Number*	*Number*	*Number*	*Number*
Calves	1-2 wk.	0.25	WP	4	0	4	0
		.1	Em	1	0	1	0
		.05	Em	3	0	3	0
		.05	WP	4	0	0	4
		.025	WP	4	0	2	2
		.025	Em	3	0	2	1
		.02	Em	1	0	1	0
		.01	Em	3	1	0	2
Sheep	1-2 yr.	1.0	Em	1	0	1	0
Goats	1-2 yr.	1.0	Em	1	0	1	0
		.1	Em	2	0	0	2

[1] Em = emulsion; WP = suspension of wettable powder.

Onset of symptoms was as early as 1 hour after treatment and as late as 8 hours. Death occurred from 4 hours to 5 days after treatment. Because of the edema and congestion which develop during the course of parathion poisoning there is danger of subsequent pneumonia, and death may occur several weeks after treatment.

Results of oral administrations of parathion to baby calves, cattle, and sheep are summarized in table 38. Parathion is the most toxic of all the insecticides studied at this laboratory. A single dose of 0.5 mg./kg. was sufficient to poison baby calves. For cattle, the toxic dose is many times that for calves and no poisoning resulted from doses of 25 mg./kg. Sheep were poisoned by 20 mg./kg. but not by 10 mg./kg.

TABLE 38.—*Results of administering single oral doses of parathion suspensions to dairy calves, cattle, and sheep*

Kind of animal	Age	Dose	Animal				
			Treated	Affected mildly	Affected severely, recovered	Died	Unaffected
		mg./kg.	*Number*	*Number*	*Number*	*Number*	*Number*
Calves	1–2 wk	1.5	3	0	1	2	0
		0.5	8	3	2	0	3
		0.25	4	0	0	0	4
		25	2	0	0	0	2
Steers	1 yr	4	1	0	0	0	1
		2	1	0	0	0	1
Sheep	1–2 yr	100	1	0	0	1	0
		75	2	0	1	1	0
		50	5	0	2	1	2
		20	5	0	0	1	4
		10	10	0	0	0	10
		5	1	0	0	0	1

EPN

EPN is another phosphorus compound similar in many respects to parathion. At present its uses are limited to the control of insects other than those on animals, and the principal sources of poisoning will probably be treated forage, or materials spilled during control operations or otherwise left exposed.

Results of single applications of sprays of EPN to baby dairy calves are given in table 39. From those data we may conclude that EPN

TABLE 39.—*Results of single dermal applications (sprays) of EPN applied to dairy calves 1 to 2 weeks of age*

Kind of animal and age	Concentration in spray	Formulation type [1]	Animals			
			Treated	Affected severely, recovered	Died	Unaffected
	Percent		*Number*	*Number*	*Number*	*Number*
Calves, 1–2 wk	1.0	Em	2	0	2	0
	0.5	Em	2	0	2	0
	0.25	Em	3	0	3	0
	0.25	WP	4	2	2	0
	0.1	Em	3	2	0	1
	0.05	WP	5	0	0	5
	0.05	Em	5	2	0	3
	0.025	Em	6	0	0	6
	0.025	WP	3	0	0	3

[1] Em=emulsion; WP=suspension of wettable powder.

is roughly equivalent in acute toxicity to gamma benzene hexachloride, occasionally producing poisoning at concentrations of 0.05 percent. The results of oral administration of EPN to calves, cattle, and sheep are given in table 40.

TABLE 40.—*Results of single oral doses of EPN administered to baby dairy calves, adult cattle, and sheep*

Kind of animal	Age	Dose	Animals			
			Treated	Affected severely, recovered	Died	Unaffected
		mg./kg.	*Number*	*Number*	*Number*	*Number*
Calves	1–2 wk.	10	1	1	0	0
		2.5	2	1	0	1
		1.0	2	1	0	1
		0.5	3	0	0	3
Steer	1 yr.	10	1	0	0	1
		5	1	0	0	1
Sheep	1–2 yr.	100	1	0	1	0
		75	2	0	2	0
		50	3	2	1	0
		20	4	1	2	1
		10	10	0	0	10

The symptoms and lesions exhibited by the animals poisoned in this series are similar to those shown by parathion and other members of the cholinesterase-inhibiting series. Onset of symptoms varied from 30 minutes to 24 hours after treatment. Death usually occurred within 24 hours of the onset of symptoms. Recoveries from sublethal doses were complete in 24 to 96 hours after the onset of symptoms.

MALATHION

Malathion, like parathion and EPN, produces cholinesterase inhibition. Its acute toxicity is less than either parathion or EPN, being equivalent to toxaphene.

At present there seems to be a wide field of application for malathion, and its use on animals has been suggested. The dangers for the present are those associated with the ingestion of treated forage and carelessly exposed material in concentrated form.

The results of dermal applications of malathion to baby calves are given in table 41. The minimum toxic concentration would appear to be between 0.5 and 1.0 percent. Such applications have not been made to other animals. The results of oral administration of malathion to baby calves and to sheep are given in table 42. The minimum toxic dose for baby calves appears to lie between 10 and 20 mg./kg. By this route malathion seems much safer than toxaphene. However, the number of animals treated was small and the figures must be accepted accordingly. Sheep tolerated 50 mg./kg. doses but were poisoned by 100 mg./kg. and all higher doses.

The symptoms and lesions of malathion poisoning are basically the same as for the rest of the organic-phosphorus family of insecticides.

TABLE 41.—*Results of single dermal applications (sprays) of malathion applied to baby dairy calves 1 to 2 weeks of age*

Kind of animal and age	Concentration in spray	Formulation type [1]	Calves		
			Treated	Died	Unaffected
	Percent		*Number*	*Number*	*Number*
Calves 1–2 wk.	1.0	Em	21	0	21
	1.0	WP	4	3	1
	0.5	WP	4	0	4
	0.25	WP	3	0	3

[1] Em = emulsion; WP = suspension of wettable powder.

TABLE 42.—*Results of single oral doses of malathion administered to baby calves and to adult sheep*

Kind of animal	Age	Dose	Animals				
			Treated	Affected mildly	Affected severely, recovered	Died	Unaffected
		mg./kg.	*Number*	*Number*	*Number*	*Number*	*Number*
Calves	1–2 wk.	50	1	0	1	0	1
		20	9	1	2	0	6
		10	5	0	0	0	5
Sheep	1–2 yr.	300	2	0	1	1	0
		200	2	1	1	0	0
		150	3	0	1	1	1
		100	3	0	1	0	2
		50	10	0	0	0	10

DIAZINON

Diazinon is one of the most recently developed phosphorus insecticides. The results of single dermal applications to baby calves are given in table 43. The results of administering single doses of Diazinon to calves, cattle, and sheep are given in table 44. The minimum toxic dose for baby calves seems to be just under 1.0 mg./kg., that dosage causing definite sleepiness in half of the calves so treated. However, Diazinon appeared to give the animals a better chance of recovery than did parathion when the calves were affected to approximately the same extent. The minimum toxic dose for sheep was just under 30 mg./kg., that dosage producing only very mild symptoms of poisoning. For adult cattle the minimum toxic dose seems to be between 10 and 25 mg./kg.

Diazinon was repeatedly observed to differ slightly from the other members of this group in the production of symptoms, in that the intoxicated animals always passed through a period of drowsiness before exhibiting the more typical symptoms.

TABLE 43.—*Results of single dermal applications of Diazinon as sprays to dairy calves 1 to 2 weeks of age*

Kind of animal and age	Concentration in spray	Formulation type [1]	Animals				
			Treated	Affected mildly	Affected severely, recovered	Died	Unaffected
	Percent		*Number*	*Number*	*Number*	*Number*	*Number*
Calves, 1-2 wk	0.5	Em	3	1	2	0	0
	0.25	Em	5	2	0	1	2
	0.1	Em	5	0	0	0	5
	0.1	WP	5	2	0	0	3
	0.05	WP	10	0	0	0	10

[1] Em=emulsion; WP=suspension of wettable powder.

TABLE 44.—*Results of administering single oral doses of Diazinon to baby dairy calves, cattle, and sheep*

Kind of animal	Age	Dose	Animals				
			Treated	Affected mildly	Affected severely, recovered	Died	Unaffected
		mg./kg.	*Number*	*Number*	*Number*	*Number*	*Number*
Calves	1-2 wk	10	1	0	0	1	0
		2.5	2	0	2	0	0
		1.0	8	6	0	0	2
		0.5	2	0	0	0	2
Steers	1 yr.	25	1	0	1	0	0
		10	2	0	0	0	2
		5	1	0	0	0	1
Sheep	3-4 yr.	30	3	3	0	0	0
		20	9	0	0	0	9
		10	2	0	0	0	2

BAYER COMPOUNDS [6]

The Bayer Company of Germany has produced several new phosphorus insecticides. Only one of these materials has received a common name, the remainder still being known by numbers. Because of promising experimental results in the entomological field, and in

[6] Mention of trade names or companies does not constitute endorsement by the Department of Agriculture.

order to present the data presently available on these compounds, the following data are included in this report.

Bayer L/13/59 is one of the more promising of this group. Results of administering single oral doses of this compound to baby calves and to cattle are given in table 45. From those data it appears that the minimum toxic dose for baby calves is between 5 and 10 mg./kg.; for cattle, between 50 and 100 mg./kg. Five baby dairy calves have been sprayed with this compound at 1 percent, 4 at 0.25 percent, and 1 at 0.1 percent without producing symptoms of poisoning. No higher doses have been applied.

TABLE 45.—*Results of administering single oral doses of Bayer compound L 13/59 to dairy calves and cattle*

Kind of animal	Age	Dose	Animals			
			Treated	Affected mildly	Affected severely, recovered	Unaffected
		mg./kg.	*Number*	*Number*	*Number*	*Number*
Calves	1–2 wk.	10	1	0	1	0
		5	5	0	0	5
Cattle	1 yr.	200	1	0	1	0
		100	1	1	0	0
		50	2	0	0	2
		25	2	0	0	2

Chlorthion, also known as Bayer 22/190, is one of the least toxic of this group. Results of single oral doses of chlorthion are given in table 46. It appears that the minimum toxic dose of chlorthion for baby dairy calves is between 50 and 100 mg./kg. One yearling Hereford heifer was given 50 mg./kg. of chlorthion without producing symptoms.

Bayer compound 21/199. Results of single dermal applications of this compound are given in table 47. From the data there pre-

TABLE 46.—*Results of administering single oral doses of chlorthion (Bayer 22/190) to baby calves and adult cattle*

Kind of animal	Age	Dose	Animals		
			Treated	Died	Unaffected
		mg./kg.	*Number*	*Number*	*Number*
Calves	1–2 wk.	100	1	1	0
		50	1	0	1
		25	1	0	1
		10	1	0	1
Heifer	1 yr.	50	1	0	1

sented, the minimum toxic concentration for baby calves appears to be between 0.25 and 0.5 percent. One yearling Hereford heifer was given 50 mg./kg. of compound 21/199 and died of poisoning; a similar heifer given 25 mg./kg. was unaffected.

These phosphorus compounds produced symptoms and lesions similar to those observed with the other cholinesterase-inhibiting compounds.

TABLE 47.—*Results of single dermal applications of Bayer 21/199 to dairy calves 1–2 weeks of age*

Kind of animal and age	Concentration in spray	Formulation type [1]	Animals		
			Treated	Affected severely, recovered	Unaffected
	Percent		*Number*	*Number*	*Number*
Calves, 1–2 wk	1.0	WP	2	0	2
	0.5	WP	5	1	4
	0.25	WP	5	0	5
	0.2	WP	2	0	2
	0.1	WP	3	0	3
	0.1	Em	1	0	1

[1] Em=emulsion; WP=suspension of wettable powder.

Symptoms of Poisoning

All the phosphorus compounds used in our experiments produced symptoms of poisoning that, to us, are indistinguishable. The symptoms shown are those associated with destruction of or interference with the enzyme that destroys esters of choline.

Poisoned animals generally first show excessive salivation. The flow is abundant and the consistency of the saliva approaches that of water. The animal then usually encounters respiratory difficulty and breathes with the mouth open and with greatly exaggerated respiratory movements. As the respiratory effort increases the animal walks stifflegged and wanders about restlessly. Fasciculations of all skeletal muscles are present. Eventually exhaustion forces the animal to lie down. As death approaches there are loud rales from the lungs and the animal grunts softly. Death appears to occur by suffocation. Only with the very highest doses have convulsions been seen.

Compounds that inhibit cholinesterase vary widely in that activity. For that reason results of experiments may be drastically affected by the presence of other closely related compounds as impurities. Since commercial production will rarely be a chemically pure product we may expect that occasionally there may be poisonings resulting from entirely rational doses.

A second factor in producing variable results with these materials goes back to individual susceptibility, recognized for all species of animals and most, if not all, poisons. In the case of the organic phosphates, a part of the individual susceptibility is due to the

cholinesterase reserve of the animal. It is possible to lower the reserve progressively by small doses of inhibitors to a threshold beyond which poisoning will be produced by minute additional doses of inhibitor. Thus it is that animals maintained alongside of or on frequently treated fields or pastures may gradually have their cholinesterase reserves reduced to the vanishing point, thereby increasing their susceptibility to cholinesterase inhibitors as well as to cholinergic drugs that may be employed in the therapy of certain conditions.

Autopsy Findings

In acute poisoning by cholinesterase-inhibiting insecticides the lesions found at autopsy are never outstanding and never pathognomonic. In many cases the autopsy findings are entirely negative.

In those cases showing lesions, there may be hemorrhages of varying sizes on the heart, lungs, or gastrointestinal tract, not consistent in their location. The lungs may be congested, and are often edematous and heavy. Frothy exudate is often present in the bronchi and trachea.

In cases where the animal was affected over a prolonged period, pneumonia may be observed. In our experience several cases have suggested pneumonia by the character of breathing only to present a perfectly clear pair of lungs at autopsy.

SUMMARY

Studies of the acute toxicity of 12 chlorinated hydrocarbon insecticides for livestock have been presented, including DDT, TDE, methoxychlor, Perthane, Dilan, BHC, toxaphene, chlordane, heptachlor, aldrin, dieldrin, and Strobane. The studies were designed to determine the minimum toxic and maximum safe doses of these compounds when applied to the skin as sprays or dips, or ingested. Results have been tabulated for the sake of brevity.

These 12 compounds were used to treat 1,441 head of livestock, of which number 171 were definitely poisoned but recovered completely, while 184 poisoned animals died. The symptoms displayed by these 355 intoxicated animals have been summarized in two sections, one concerning the more toxic and the other the less toxic compounds. Lesions observed in the 184 animals that died of poisoning have been summarized in a like manner, while the histological findings in a proportion of these animals have been presented in tabular form.

In a similar manner the minimum toxic and maximum safe dosages of seven organic phosphate insecticides have been determined on livestock, including malathion, EPN, parathion, Diazinon, Bayer L 13 59, Bayer 21 199, and chlorthion. The treatments were applied as sprays or administered orally, to a total of 288 head of livestock. In this total of 288 animals, 54 were poisoned but made complete recoveries, while 45 were poisoned and died. The symptoms displayed by these 99 intoxicated animals have been summarized for the entire group. A similar summary is given of the lesions observed in the 45 fatal cases.

A summary of minimum toxic and maximum safe doses appears in tables 48 and 49.

TABLE 48.—*A summary of the minimum toxic and maximum nontoxic doses of insecticides*[1] *applied as sprays to livestock through January 15, 1954*

Chemical	Animals	Age	Maximum nontoxic dose tested	Minimum toxic dose found
			Percent	*Percent*
Aldrin	Calves	1–2 wk	0. 1	0. 25
	Lambs	3 wk		4. 0
	Kids	3 wk		4. 0
BHC, gamma	Calves	1–2 wk	0. 025	0. 05
	Calves	6–8 mo	0. 15	
	Cattle	Adult	0. 1	0. 25
	Lambs	6 wk	1. 0	
	Sheep	Adult	1. 0	
	Pigs	3 mo	1. 0	
	Horses	Adult	0. 15	
Chlordane	Calves	1–2 wk	0. 5	1. 0
	Cattle	Adult	2. 0	
	Lambs	3 wk	1. 0	2. 0
	Sheep	Adult	3. 0	4. 0
	Goats	Adult	3. 0	4. 0
	Horses	Adult	1. 5	
Dieldrin	Calves	1–2 wk	0. 1	0. 25
	Cattle	Adult	1. 0	2. 0
	Lambs	2 wk	2. 0	3. 0
	Sheep	Adult		4. 0
	Pigs	8 wk	4. 0	
	Goats	Adult		4. 0
	Horse	Adult	1. 0	
Heptachlor	Calves	1–2 wk	0. 25	0. 5
	Cattle	1 yr	0. 5	
	Lambs	3 wk	4. 0	
Strobane	Calves	1–2 wk	1. 0	2. 0
Toxaphene	Calves	1–2 wk	0. 5 0. 75	1. 0
	Cattle	Adult	2. 0	4. 0
	Lambs	6 wk	4. 0	
	Sheep	Adult	1. 5	4. 0
	Kids	6 wk	4. 0	
	Goats	Adult	1. 5	4. 0
	Hogs	Adult	4. 0	
	Horses	Adult	1. 5	
Bayer 21 199	Calves	1–2 wk	0. 2	0. 5
Diazinon	Calves	1–2 wk	0. 05	0. 1
EPN	Calves	1–2 wk	0. 025	0. 05
Malathion	Calves	1–2 wk	0. 5	1. 0
Parathion	Calves	1–2 yr		0. 01
	Sheep	1–2 yr		1. 0
	Goats	1–2 yr	0. 1	1. 0

[1] DDT, TDE, methoxychlor, Dilan, and Perthane were nontoxic to baby calves at 8.0 percent concentration. Bayer L 13/59 was nontoxic at 1 percent. Higher doses have not been applied. Data on chlorthion as a spray are inconclusive.

TABLE 49.—*A summary of the minimum toxic and maximum nontoxic single doses of various insecticides*[1] *administered orally to livestock through January 15, 1954*

Chemical	Animals	Age	Maximum nontoxic dose tested	Minimum toxic dose found
			mg./kg.	*mg./kg.*
Aldrin	Calves	1–2 wk	2.5	5.0
	Cattle	1 yr	10	25
	Sheep	1–2 yr	10	15
BHC, gamma	Calves	1–2 wk	2.5	5.0
	Sheep	1–2 yr	10	25
Chlordane	Cattle	1 yr	10	25
	Calves	1–2 wk	10	25
	Sheep	4–5 yr	50	100
DDT	Calves	1–2 wk	100	250
	Sheep	4–5 yr		500
Dieldrin	Calves	1–2 wk	5	10
	Cattle	1 yr	10	25
	Pigs	3 wk	25	50
	Horse			25
Heptachlor	Calves	1–2 wk	15	25
	Sheep	4–5 yr	25	50
Methoxychlor	Calves	1–2 wk	250	500
	Sheep	4–5 yr	1,000	
Strobane	Calves	1–2 wk	10	25
	Sheep	1–2 yr		50
Toxaphene	Calves	1–2 wk	2.5	5.0
	Sheep	4–5 yr	10	25
	Goats			50
TDE	Calves	1–2 wk	100	250
	Sheep	4–5 yr	1,000	
Bayer L 13/59	Calves	1–2 wk	5	10
	Cattle	1 yr	50	100
Chlorthion	Calves	1–2 wk	50	100
	Cattle	1 yr	50	
Diazinon	Calves	1–2 wk	0.5	1.0
	Cattle	1 yr	10	25
	Sheep	3–4 yr	20	30
EPN	Calves	1–2 wk	0.5	1.0
	Cattle	1 yr	10	
	Sheep	1–2 yr	10	20
Malathion	Calves	1–2 wk	10	20
	Sheep	1–2 yr	50	100
Parathion	Calves	1–2 wk	0.25	0.5
	Cattle	1 yr	4.0	
	Sheep	1–2 yr	10	20

[1] One yearling Hereford given 50 mg./kg. of Bayer compound 21/199 died of poisoning; a similar heifer given 25 mg./kg. was unaffected. Perthane and Dilan were applied to baby dairy calves as an 8-percent suspension only, without producing symptoms of poisoning.

LITERATURE CITED

(1) Arnold, R. M.
1949. Deaths of calves following dipping in chlordane. Amer. Vet. Med. Assoc. Jour. 115 (873): 462–463.

(2) Bowen, C. V.
1950. A rapid vat-side test for assaying toxaphene in cattle dips. U. S. Bur. Ent. and Plant Quar. ET–285, 5 pp.

(3) Bushland, R. C., Claborn, H. V., Beckman, H. F., Radeleff, R. D., and Wells, R. W.
1950. Contamination of meat and milk by chlorinated hydrocarbon insecticides used for livestock pest control. Jour. Econ. Ent. 43: 649–652.

(4) ——— Wells, R. W., and Radeleff, R. D.
1948. Effect on livestock of sprays and dips containing new chlorinated insecticides. Jour. Econ. Ent. 41: 642–645.

(5) Choudhury, B., and Robinson, V. B.
1950. Clinical and pathological effects produced in goats by the ingestion of toxic amounts of chlordane and toxaphene. Amer. Jour. Vet. Res. 11 (38): 50–57.

(6) Claborn, H. V., Bowers, J. W., Wells, R. W., Radeleff, R. D., and Nickerson, W. J.
1953. Meat contamination from pesticides. Agr. Chem. 8 (8): 37–39, 119, 121.

(7) Ely, Ray E., Moore, L. A., Carter, R. H., Mann, H. D., and Poos, F. W.
1952. The effect of dosage level and various methods of administration on the concentration of DDT in milk. Jour. Dairy Sci. 35: 266–271.

(8) ——— Moore, L. A., Mann, H. D., and Carter, R. H.
1952. The effect of various dosage levels of crystalline lindane on the concentration of lindane in cow's milk. Jour. Dairy Sci. 35: 733–737.

(9) ——— Underwood, P. C., Moore, L. A., Mann, H. D., and Carter, R. H.
1953. Observations on lindane poisoning in dairy animals. Jour. Amer. Vet. Med. Assoc. 123 (920): 448–449.

(10) Howell, D. E., Cave, H. W., Heller, V. G., and Gross, W. G.
1947. The amount of DDT found in the milk of cows following spraying. Jour. Dairy Sci. 30: 717–721.

(11) Kitselman, C. H., Dahm, P. A., and Borgmann, A. R.
1950. Toxicologic studies of aldrin (compound 118) on large animals. Amer. Jour. Vet. Res. 11 (41): 378–381.

(12) Littler, Clarence A.
1950. A vat-side test for assaying DDT–BHC in dipping vats. Vet. Med. 45: 480–482, 484.

(13) Marsh, Hadleigh, Johnson, L. H., Clark, R. S., and Pepper, J. H.
1951. Toxicity to cattle of toxaphene and chlordane grasshopper baits. Mont. Agr. Expt. Sta. Bul. 477, 11 pp.

(14) Orr, L. W., and Mott, L. O.
1945. The effects of DDT administered orally to cows, horses, and sheep. Jour. Econ. Ent. 38: 428–432.

(15) Radeleff, R. D.
1948. Chlordan poisoning: symptomatology and pathology. Vet. Med. 43: 342–347.

(16) ———
1949. Toxaphene poisoning: symptomatology and pathology. Vet. Med. 44: 436–442.

(17) ———
1951. Effects of various levels of lindane in the feed of beef cattle. Vet. Med. 46: 105–106, 119.

(18) ——— and Bushland, R. C.
1950. Acute toxicity of chlorinated insecticides applied to livestock. Jour. Econ. Ent. 43: 358–364.

(19) RADELEFF, R. D., and BUSHLAND, R. C.
1953. BENZENE HEXACHLORIDE POISONING OF EMACIATED SHEEP. Vet. Med. 48: 53–58.
(20) ——— CLABORN, H. V., BECKMAN, H. F., WELLS, R. W., and BUSHLAND, R. C.
1951. TOXAPHENE RESIDUES IN FAT OF SPRAYED CATTLE. Vet. Med. 46: 305–308.
(21) ——— CLABORN, H. V., WELLS, R. W., and NICKERSON, W. J.
1952. EFFECTS ON BEEF CATTLE OF PROLONGED TREATMENT WITH A DDT SPRAY. Vet. Med. 47: 94–96.
(22) SPARR, B. I., CLARK, J. C., VALLIER, E. E., and BAUMHOVER, A. H.
1952. STUDIES ON THE STABILITY OF TOXAPHENE EMULSIONS IN DIPPING VATS. U. S. Bur. Ent. and Plant Quar. E–849, 11 pp., illus.
(23) SPICER, S. S., SWEENEY, T. R., VON OETTINGEN, W. F., LILLIE, R. D., and NEAL, P. A.
1947. TOXICOLOGICAL OBSERVATIONS ON GOATS FED LARGE DOSES OF DDT. Vet. Med. 42: 289–293.
(24) STERNBURG, JAMES, and KEARNS, C. W.
1952. THE PRESENCE OF TOXINS OTHER THAN DDT IN THE BLOOD OF DDT-POISONED ROACHES. Science 116 (3006): 144–147.
(25) TELFORD, H. S., and HARWOOD, PAUL D.
1945. DDT FAILS TO REMOVE HORSEBOTS. Jour. Econ. Ent. (Sci. Note) 38: 399.
(26) WELCH, HOWARD
1948. TESTS OF THE TOXICITY TO SHEEP AND CATTLE OF CERTAIN OF THE NEWER INSECTICIDES. Jour. Econ. Ent. 41: 36–39.

U. S. GOVERNMENT PRINTING OFFICE: 1955

END