Aspects of Pesticidal Use of Endrin on Man and the Environment

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Introduction

Endrin is the most acutely toxic member of the groups of cyclodiene insecticides which includes aldrin, dieldrin, isodrin, and telodrin.

Endrin has been used as an agricultural pesticide for more than 20 years to control a variety of chewing and sucking insect pests which inhabit the soil and infest crops. It is also used to control mice populations in deciduous orchards, as an avicide, and as a rodent repellent in the reseeding of forest.

Endrin is highly toxic, it is persistent, and residues in the soil, water and animal tissues have resulted from uses to control insects, birds, and rodents. Records show substantial reductions in populations of non-target species in some areas where endrin has been used. These factors have aroused serious concern among various groups of conservationists.

Prior to 1965, when large quantities of endrin were used on sugar cane and cotton, substantial fish kills in the lower Mississippi River were attributed to endrin contamination from industrial effluent and by runoff and drift from nearby agricultural uses.

Since 1965 the number of registered uses for endrin have declined probably due in part to the high toxicity, the lack of tolerances greater than zero and the development of insect resistance to the pesticide. However, since the cancellation of the use of DDT on cotton, the cotton use of endrin has increased 2.5 times during the past year. Large fish and bird kills have been associated with this increase in use on cotton.

Summary

Endrin is the common name for the insecticide which contains at least 92 percent 1, 2, 3, 4, 10, 10-hexachloro-6,7-epoxy-1, 4, 4a, 5, 6, 7, 8, 8a-octahydro-1, 4, 5, 8 endo endo-dimethanonaphthalene. Endrin was first synthesized in the 1940's and has been used as an insecticide since 1951.

During the 1970-1971 growing season, endrin was registered for foliar and soil applications as an insecticide on cotton, corn, small grains, sugar cane, potatoes, sorghum, and sugar beets. Other uses included seed treatment, post-harvest use in orchards as a ground spray for orchard mouse control, as an avicide, and for use on ornamentals in greenhouses and nurseries. The uses on corn, potatoes, sorghum and sugar beets have subsequently been cancelled because of lack of tolerances.

The quantities of endrin used in 1970-1971 were 43 percent of that used in 1966 with 34 percent of the total used on cotton, 14 percent on corn, 16 percent on small grain and 28 percent for control of the orchard mouse. During 1971-1972, the amount used was more than twice that used during the prior year; the use on cotton accounted for this increase.

Endrin is the most acutely toxic of the cyclodiene pesticides in use today, having an acute oral LD_{50} in rats of approximately 7.5 mg/kg and an acute dermal toxicity in the same species of 15 mg/kg. However, unlike the other cyclodienes, endrin is rapidly metabolized and excreted and neither endrin or its metabolites appear to be accumulating in adipose tissue of the general population or in occupationally exposed workers.

The pharmacological action of endrin is similar to that of the other cyclodienes with central nervous stimulation being the predominant effect. In laboratory animals, there appears to be a latent period of about one hour before the onset of convulsions, regardless of the amount of endrin ingested. Hepatic enzyme induction has been noted in long-term feeding studies in the rat.

Pathologic findings associated with life-span feeding of high levels (25-100 ppm) of endrin in the diet were diffuse degeneration of the brain, liver, kidneys and adrenal glands. No significant toxicological effects were associated with levels of 1 ppm or less. The dogs are approximately twice as sensitive to the toxic effects of endrin as the rat. No increase in the incidence of malignant tumors in the test groups was noted over the control animals of either species. In a three generation reproduction study in rats, levels of endrin up to 2.0 ppm had no effect on fertility, gestation, viability, and lactation indices. While no teratogenic studies, per se, have been carried out on endrin, no teratogenic effects were noted in the reproduction studies cited above. However, this can not be taken as conclusive evidence of the lack of teratogenic potential of endrin. No mutagenic studies on endrin have been reported.

Endrin has been included in most of the surveys of chlorinated insecticide levels in adipose tissue and blood. Even in those areas where endrin is most extensively used (e.g., India and the Lower Mississippi area) endrin was not found in human subcutaneous fat or in blood from the general population at a limit of detection of 0.03 ppm and lower. Levels of the 9-keto metabolites of endrin in

four human fat samples were all less than 0.0004 ppm. Studies carried out on occupationally exposed workers have revealed harmful physiological effects only in those instances where absorption of endrin has occurred from careless handling.

The Joint Expert Committee on pesticide residues has determined the FAO/WHO "no effect" levels for endrin in the rat and the dog to be 1 ppm. This is equivalent to 0.05 mg/kg body weight/day for the rat and 0.025 mg/kg body weight/day for the dog. The acceptable daily intake for man (ADI) has been estimated to be 0.0002 mg/kg body-weight.

Adequate methodology has been developed for monitoring endrin in food, water, air, and wildlife. During the period from 1964-1969, 111,296 samples of domestic food were examined for endrin residues. No residues of endrin were found in finished or crude corn oil or cottonseed oil, milk, dairy products, or baby foods. However, there was an increase in the percentage of endrin residues found in samples of small fruits, root vegetables meat, poultry, and grains for animal use during this period. The highest incidence of endrin residues were found in domestic samples of crude soybean oil followed by fish and root vegetables.

The average dietary intake of endrin for the period of 1964-1970 was calculated to be 2.5 percent of the ADI (0.00000.5 mg/kg body weight/day). The average daily intake of 0.0011 mg/kg body weight was reported for all chlorinated organic pesticides for the same period. The maximum dietary intake of endrin from a well-balanced-diet was approximately 0.001 mg/day (7 percent of the ADI). This was attributed to levels found in meat, poultry, potatoes, leafy vegetables, and garden fruit for the

period June 1968 to April 1969. During the period June 1969 to April 1970 similar amounts of endrin were ingested in the balanced diet, but the highest levels of contamination were found in potatoes, root vegetables, and garden fruits.

Volatilization is considered to be a major factor in the disappearance of endrin from treated soil. Although endrin has not been identified as an air contaminater from distant sources, detectable amounts have been measured as drift following spraying and dusting operations. A recent fish-kill in Alabama was attributed to drift from applications to cotton by aircraft.

Occurrence of endrin in water has been related to agricultural uses on adjacent soil and to industrial contamination from chemical plants. Endrin has not been detected in water from the major drainage basins since 1968, but the detection of endrin in fish taken from these waterways suggest periodic contamination from point sources particularly in the Mississippi, Arkansas, and White Rivers of the Southern States. Results of intensive studies indicate that the major portion of water burden of endrin is from that absorbed on suspended microparticulates which possibly result from agricultural run-off.

Endrin is less persistent than dieldrin, but detectable amounts may remain through several growing seasons. Endrin is lost from soil through erosion by water and wind, volatilization from soil surfaces, direct uptake by plant roots and biological conversion. Residues in agricultural soils have not been detected below 12 inches. Endrin degrades rapidly in flooded soils with high organic matter. Endrin

ketone, endrin aldehyde and an unidentified hydrophilic product have been detected in soil.

Amounts of endrin which is translocated into growing plants is directly related to amounts in the soil. Residues have been detected in stems on leaves of cereal grains but none have been reported in the grain or seed portion. Amounts detected in grasses, alfalfa, root crops, peanuts and soybeans were greater than the amounts in the soil in which the crops were grown.

Effects of endrin on fishes and other wildlife is related to high toxicity of this pesticide. Several fish kills have resulted from run-off following treatment of sugar beets and cotton. The LC_{50} for most fish is within the range 0.05-3.1 ppb. Levels of 5 ppb in water caused embryonic death during the gastrula and blastula stages. In some species 0.0001 ppb induce changes in behavior patterns which interferes with courtship fertilization processes. Reported changes in LC_{50} values and bioaccumulation by lower members of the aquatic food web at rates 920-2800 times the level found in water indicates the development of resistance to endrin. Results of field and laboratory testing indicate that endrin is the most toxic chlorinated hydrocarbon pesticide to wild mammals and birds. Trace amounts detected in fat of game animals are not considered a dietary hazard for humans. Dietary levels of 1 ppm are lethal for several species of birds, and < 0.1 ppm caused cessation of egg production.

CHAPTER I

Chemistry and Methodology of Endrin

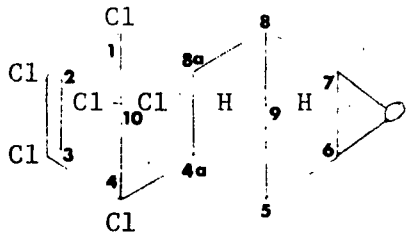
I.A. Introduction

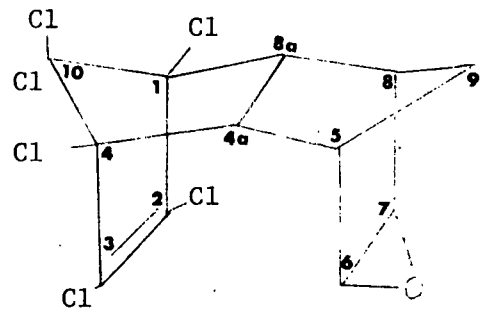
Endrin was first synthesized in the 1940's and has been used as an insecticide since 1951. It is one of a series of chlorinated cyclodienes which has insecticidal properties. In an attempt to determine the chemical nature of the toxic moiety, Soloway (1965) examined 106 cyclodienes. He found high insecticidal action only in those compounds in which there were two electronegative centers, close to each other, and on a plane of symmetry defined by the dimethano-bridge. In this respect there appears to be remarkably little difference in the insecticides aldrin, dieldrin, endrin and telodrin. The similar effects caused by these substances on the central nervous system suggest that they act on similar sites. The electron-rich sites of these molecules which are not believed to be chemically active, are considered likely locations for strong electrostatic interaction---possibly on nerve cell membrane (Benson, 1969). The epoxides are believed to be the active compounds since only those compounds in which the double bond on the nonchlorinated side of the molecule is readily epoxidized, display insecticidal activity. The rigid case configuration with the electronegative centers of the chlorine atoms of these lipid-soluble substances is thought to be important to the passage across membranes and to their molecular action (Hathaway, 1965). Because of the similarity in structure of the molecules, and similarity of clinical effects from acute

exposure in most animals and man, it is likely that the toxicological action occurs on similar, if not the same sites, in the central nervous system.

I.B. General Chemistry

Endrin is the common name for the insecticide which contains at least 92 per cent 1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro-1,4,5,8 endo endo-dimethanonaphthalene (Jager, 1970). The empirical formula $C_{12}H_8Cl_6O$, is described by the following graphic and spacial presentations





I.B.1. Physical properties: Crystalline and technical endrin are stable to light and air.

Endrin is a sterioisomer of dieldrin; a fact borne out by the wide differences in melting points of the two substances--dieldrin 150°C, Endrin 235°C. In the convention of the American Chemical Society, Endrin has the endo, endo configuration with respect to the two methano moities of the molecule. The chlorinated "left" side which represents about 75 percent of the mass of the molecule is identical in aldrin,dieldrin,isodrin, telodrin, heptachlor and chlordane. Solubility of endrin (Kirk-Othmer, 1963) is different solvents is presented in Table I.B.1.

Table I.B.1.

Solubility of Endrin

Solvent	Solubility in % by Weight at 25°C
Acetone	28
Amylacetate	24
Benzene	37
Butyl Alcohol	7
Carbon Tetrachloride	24
Cyclohexanone	44
Diesel Oil	11
Ethyl Alcohol	4
Ethylene Dichloride	41
Fuel Oil	11
Heavy Aromatic Naphthalene	32
Isopropyl Alcohol	4
Kerosene	6
Methyl Alcohol	3
Methyl Cellosolve	10
Methyl Ethyl Ketone	33
Mineral Spirits	9
Toluene	46
Trichloroethylene	41
Turpentine	19
Velsicol AR-50	35
Xylene	39
Water	>0.1 ppm

Other physical properties of endrin (Martin, 1961; Terriere, 1964; Richardson and Miller, 1960) are presented in Table I.B.2.

Table I.B.2.

Physical Properties of Endrin

Molecular weight	380.93
Physical State	Pure: white crystalline solid powder. Technical - light tan flowable
Vapor pressure	Technical: 2.7×10^{-7} mm Hg at 25°C
Flammability	Non-flammable
Melting point	235°C decomposes
Bulk density (lb/ft^3)	55-60
Specific gravity	1.70 20°C

I.B.2. Available forms

The following preparations are available commercially:

Wettable powders	-	Contain 25-50 percent active ingredient.
Dust Concentrates	-	Contain 20-75 percent active ingredient to be diluted with inert filler prior to field use.
Field strength dusts	-	Contain 0.5 - 1.0 percent active ingredient.
Emulsible concentrates	-	Contain 15-48 percent active ingredient to be mixed with water before use.
Granules	-	Contain 2-5 percent active ingredient ready for field use.
Combinations with organic phosphates	-	As emulsible concentrates to be diluted with water before use.

I.C. Synthesis

Endrin is manufactured by the following procedure (Shell, Velsicol, 1970):

(1) Hexachlorocyclopentadiene (*i*) is adducted with vinyl chloride (*ii*) by the Diels-Alder process to yield the hexachlorocyclopentadiene-vinyl chloride adduct (*iii*) (1,2,3,4,5,7,7-heptachlorobicyclo[2.2.1]hept-2-ene).

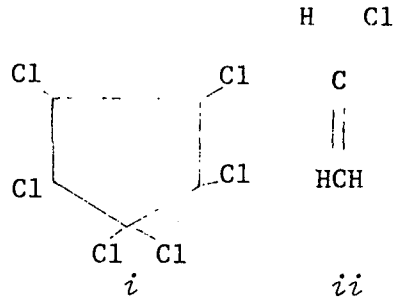
(2) The adduct (*iii*) is dehydrohalogenated with alcoholic base to yield 1,2,3,4,7,7,-hexachlorobicyclo[2.2.1]hepta-2,5-diene (*iv*).

(3) The chlorinated bicycloheptadiene is adducted with cyclopentadiene (*v*) to yield isodrin (*vi*)(1,2,3,4,10,10-hexachloro-1,4,4a,5,8,8a-hexahydro-*endo*-*endo*-1,4:5,8-dimethanonaphthalene).

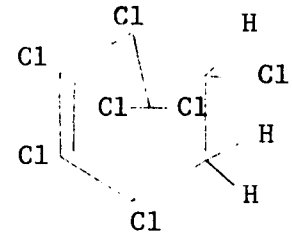
(4) Isodrin is treated with peracetic acid to yield endrin (*vii*).

This process of synthesis may be represented symbolically as follows:

(1) Adduction:

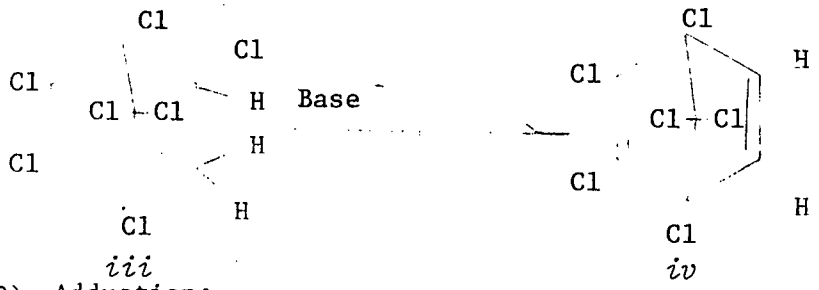


i *ii*



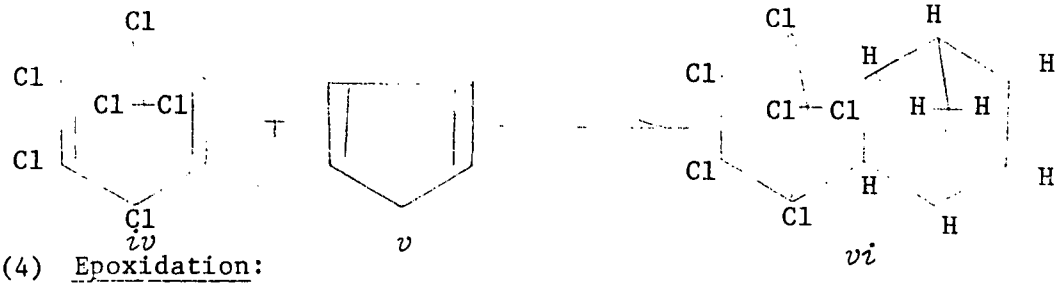
iii

(2) Dehydrohalogenation:



iii *iv*

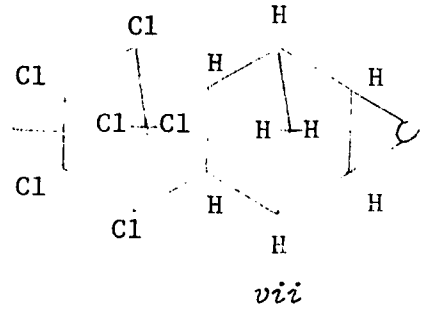
(3) Adduction:



iv *v* *vi*

(4) Epoxidation:

vi oxidation



vii

I.D. Chemical reactions

Crystalline and technical grade preparations of endrin are stable to light and air. However under biological conditions, or by exposure to sunlight, ultraviolet light, Lewis acids, or heat, products shown in Figure I.D. may be formed.

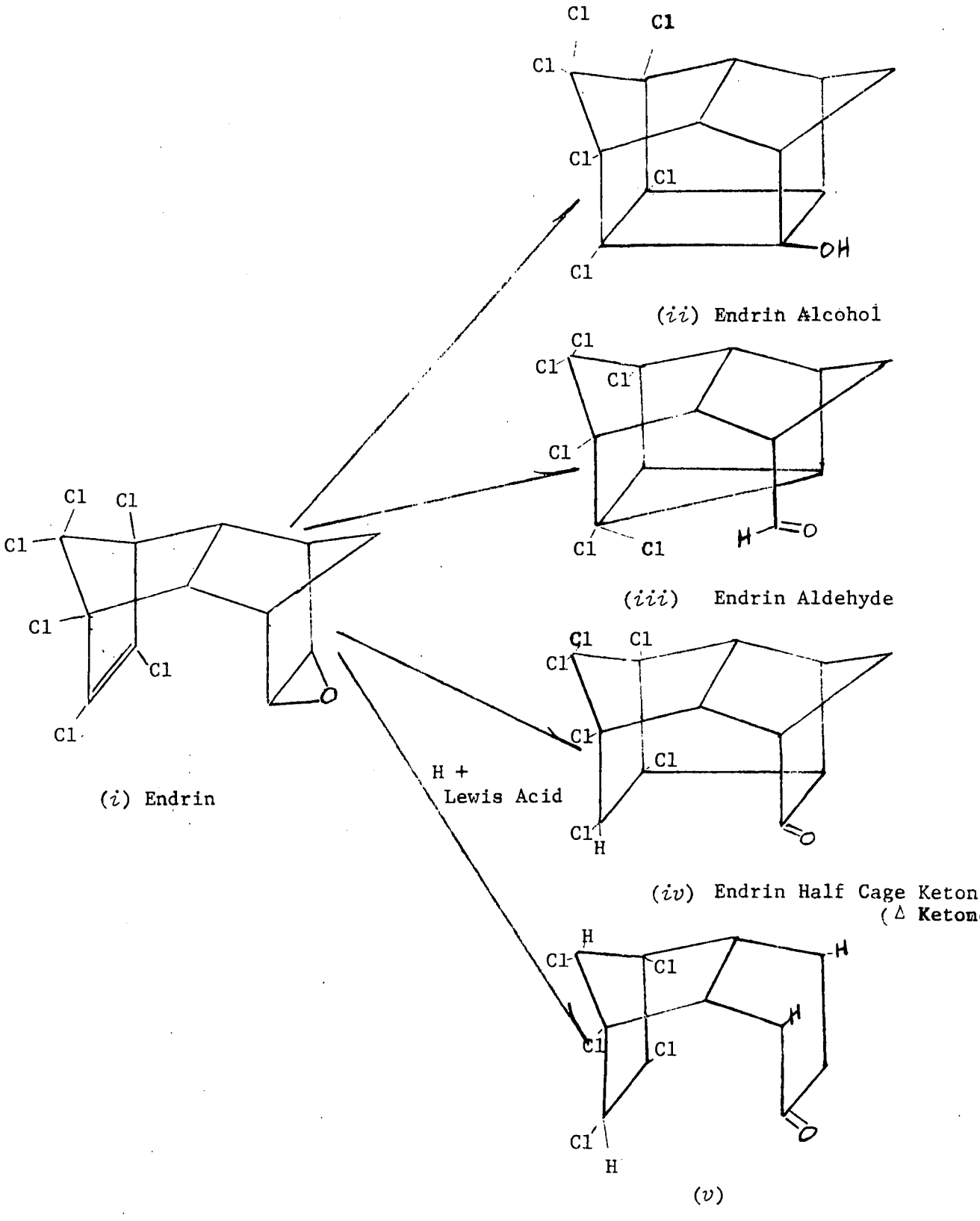


Figure I.D. Degradation products of Endrin

I.D.1. Derivatives

During analysis by GLC on conventional support media endrin tends to tail and decompose (MacDonell, 1968). After suitable support media and operating conditions had been determined, elution patterns from known preparations and preparations from experimental sources suggested that the molecule was changed prior to extraction of during cleanup. Heat induces formations of I.D. (*iv*) (Benson, 1969). Treatment with concentrated sulfuric acid for 10-15 minutes at room temperature causes isomerization of endrin to I.D. (*iii*) and I.D. (*iv*) (Chou and Cochrane, 1969). Treatment with zinc chloride in hydrochloric acid converted endrin to I.D. (*iv*) without other by-products (Weincke, 1969). When treated with aqueous solutions of chromous chloride endrin is converted to I.D. (*v*) (Chou and Cochrane, 1971).

I.D.2. Photochemistry

Endrin in hexane and cyclohexane was converted by irradiation at 253.7 mm, 300 mm and sunlight to I.D. (*v*) in yields up to 80 percent (Zabik, 1971). This product which is highly resistant to oxidation reduction procedures has been detected in fields where endrin has been used. When applied to growing bean leaves, which were subsequently exposed to sunlight for 1 hour, rotenone enhanced photoconversion of endrin to the aldehyde and ketone isomers (Ivie, 1970. Exposure to ultraviolet light induces formation I.D. (*iv*) (Benson, 1969).

I.D.3. Degradation Products

Endrin is converted to more hydrophilic substances by plants, animals and bacteria. The Δ ketone I.D. (*iv*) and the alcohol I.D. (*ii*)

have been recovered from soybean plants which were grown in soil treated with ^{14}C-endrin (Nash and Beall, 1971). Within four weeks following foliar application of ^{14}C-endrin to white cabbage two hydrophilic metabolites and unaltered endrin were found in plant tissue and soil, one metabolite was tentatively identified as I.D. (*iv*) (Weisgerber, 1969). Five conversion products were found in soil and plant tissue 12 weeks after topical application of endrin to collard plants. One group of these was slightly more hydrophilic than endrin, and the other two products were strongly hydrophilic. Two of the first group had GLC retention times similar to endrin ketone; one of these had chlorine structure similar to endrin but a higher molecular weight (Bayless et al., 1970). Of 150 microbial isolates from various soil samples, 25 degraded endrin. At least 7 metabolites were isolated from a mass culture of Pseudomonas. Most of the metabolites were ketones and aldehydes with 5 or 6 chlorine atoms.

One metabolite which occurred in all samples was I.D. (*v*) (Matsurma et al., 1971). Twenty microbial cultures such as Trichoderma sp., Pseudomonas sp. and Bacillus sp., capable of degrading dieldrin, degraded endrin to keto-endrins (Patil et al., 1971).

Two unidentified compounds and I.D. (*ii*), I.D. (*iii*), and I.D. (*iv*) have been identified in tissue and feces from rats dosed orally with ^{14}C-endrin (Richardson, 1970). Compound I.D. (*iv*) has been recovered from human and animal tissue (Schultz, 1964).

I.E. Methods for Analysis

Quantities of endrin have been determined by biological and chemical methods. Biological methods are relatively insensitive and nonspecific and have been replaced by faster more specific chemical procedures. Chemical procedures include analysis of chlorine, infra red and visible spectrophotometric measurement, and separation and quantitation by thin layer and gas chromatography.

Samples submitted for analysis are extracted with solvents such as benzene, toluene, and mixtures of benzene, toluene, hexane, or pentane which contain alcohols or acetone. Treatment of the extracts include concentration and cleanup by solvent fractionation or chromatography on flurosil, celite, aluminum or "David-dow" columns. The type of material in the sample, and the method used for detection indicate the solvent mixture to be used for extraction and the degree of cleanup required prior to analysis. The following is a brief description of accepted methods of analysis.

I.E.1. Bioassay - Living populations of insects or crustaceans such as Drosophilia sp., house flies, cray fish, daphnia and aphids, were exposed for predetermined periods of time to extracts from samples suspected of containing endrin. Mortality of text organisms caused by unknown concentrations of endrin was compared with mortality produced by known amounts. Although this method was used widely before more accurate methods were developed, it lacks specificity and sensitivity. Greatest value of bioassay is at low residue levels, provided sample history is known and contamination with other insecticides can be excluded (Tew and Sillibourne, 1961, 1961a; Heusman, 1961; Luedemann and Neuman, 1961; Bringmann and

Not in ref list.

and Kühn, 1960; McDonald, 1962; Sun and Sanjean, 1961).

I.E.2. Total Chlorine - Organic chlorine (White, 1961) is reduced to inorganic chloride by such means as sodium alcohol reduction, sodium-biphenyl reagent, quartz tube or Parr bomb combustion. Inorganic chloride is then determined by several methods such as Volhard titration, potentiometric or amphrometic titration. Specificity of this method depends on effective separation of the substance to be analyzed from interfering substances.

I.E.3. Spectrophotometric Methods - Several colorimetric methods are available for residue analysis.

I.E.3.a. After cleanup, the sample is reacted with phenylazide. The resulting dehydrophenyltriazole derivative is coupled with a diazotized amine to form a colored complex (White, 1961; Shell, 1957). Endrin must be reduced with sodium alcohol before it will react with phenylazide. The method is slow and reagents are unstable.

I.E.3.b. Infra red method - This method is based on the comparisons of the heights of absorption bands at 11.4 - 11.8 microns of an unknown with a calibration curve prepared from materials of known purity (White, 1961). Since dieldrin has similar absorbance, careful cleanup is required for this method. This rapid, versatile method is used extensively for quality control, but initial expense for instrumentation, maintenance of instrument and training are high.

I.E.4. Chromatographic methods

I.E.4.a. Thin-layer chromatography - Extract of samples is reduced in volume and purified, either by chromatography or florisil, magnesium oxide or aluminum oxide (activated at 270°C for 3 hours) or by solvent portioning. After concentration a portion of the extract is applied

to a restricted area of a plate containing an inert adsorbent and developed with a suitable solvent. In one instance endrin in alfalfa hay was measured with silica Gel H; benzene was developing solvent, and detection was with standard indophenal blue spray (Archer, 1968).

TLC has been used to detect metabolites of endrin and as a preparative procedure for GLC. Solvent systems and Rf values for alumina thin layer chromatography of hydroxychlordane and some endrin metabolites are presented in Table I.E.1. (Nash and Beall, 1971).

Table I.E.1.

Solvent systems and Rf values for alumina thin layer chromatography of hydroxychlordene, endrin delta keton, endrin aldehyde, and endrin alcohol

Solvent Systems		Hydroxy-chlordene	Endrin Ketone	Endrin Aldehyde	Endrin Alcohol
(1)	Heptane-acetone (80 + 20)	0.21±0.01[a]	0.49±0.04	0.17±0.03	0.22±0.01
(2)	Hexane-ethylacetate-acetic acid (70 - 30 + 2)	0.59±0.05	0.74±0.07	0.38±0.04	0.50±0.03
(3)	Ethyl acetate	0.47±0.03	0.76±0.02	0.37±0.02	0.41±0.02
(4)	Hexane--acetone--methanol (80 - 10 + 10)	0.55±0.04	0.72±0.02	0.41±0.03	0.36±0.04
(5)	Acetone	0.87±0.02	0.93±0.01	0.66±0.05	0.87±0.03

[a] Mean and standard deviation of 4 replications.

I.E.4.b. Gas liquid chromatography

GLC is the presently preferred analytical method. The technique permits measurements with greater than 100 times the sensitivity of other methods. This procedure requires extensive cleanup but permits

the quantitation of multiple components in each sample. Different types of samples are extracted with polar solvents and purified by column chromatography on florisil or oxides of magnesium and aluminum. Micro-liter quantities of concentrates are introduced into chromatographic systems which consist of an inert gas flowing at a constant rate in one direction over a stationary phase maintained under predetermined temperature conditions. Components are separated by their relative afinities for the solid phase and are elicited and at characteristic time intervals after addition to the system. Quantitation is obtained with highly sensitive electronic devices which monitor and record changes in the characteristics of the gas as it leaves the column. Types of samples and differences in components to be measured determine type of solid phase used in the column (Dale et al., 1966; Sessions et al., 1968: Woodham et al., 1970; Taylor, 1970; Nash and Beall, 1971).

Retention times on different stationary phases relative to aldrin of some organochlorine pesticides are presented in Table I.E.2. (Sessions et al., 1968).

Table I.E.2.

Retention Data for Three Types of Stationary Phase

Pesticide	Stationary phase		
	SE_{30}	QF_1	XE_{60}
Lindane	0.44	0.85	1.32
Heptachlor	0.78	0.9	0.95
Aldrin	1.00 (5′)	1.00 (4′)	1.00(2 1/2′)
Heptachlor epoxide	1.30	1.90	2.33
Endosulfan A	1.67	2.59	2.60
Dieldrin	2.01	3.10	3.60
p,p′-DDE	2.15	2.06	2.97
Endrin (major peak)	2.27	>6	4.05
Endosulfan B	2.33	4.77	7.65
p,p′-DDT	2.89	2.72	4.03
p,p′-DDT	3.74	4.33	7.13

When electron capture detectors are used,it is essential to determine the linear response range of each individual pesticide because of the characteristics of each detection. Detection limits and linear resonse ranges with one electron capture detector are presented in Table I.E.3. (Sessions et al., 1968).

Table I.E.3.

Linear Dynamic Range of Pesticides

Pesticide	Detection limit* (ng)	Linear response range (ng) min.	studied	max.
Lindane	0.0007	0.003		0.5
Aldrin	0.0013	0.005		0.75
Heptachlor	0.0012	0.005		0.6
Heptachlor epoxide	0.0015	0.006		0.7
Dieldrin	0.002	0.008		2.5
Endosulfan A	0.002	0.008		0.7
Endosulfan B	0.0025	0.01		1.0
p,p'-DDE	0.003	0.01		1.5
Endrin	0.015	0.05		3.5
p,p'-DDT	0.015	0.05		5.0
p,p'-DDT	0.015	0.05		5.0

* Equivalent to a peak of height 2% fsd on attenuation setting 1 x 4 (1.2×10^{-9} A full scale)

Retention times on several solid phases of different degradation products of endrin and hydroxychlordene recovered from soybean leaves and stems, relative to retention time of aldrin, are presented in Table I.E.3. (Nash and Beall, 1971).

Gas-liquid chromatographic identification of degradation products in extracts from leaves and stems of soybeans grown in endrin- and heptachlor-treated soil

	Standard or Cleanup Fraction	Endrin	Endrin Alcohol	Endrin Aldehyde	Endrin Ketone	Hydroxychlordene
15% QF-1-10% DC-200	standard	2.46	3.33	3.80	5.80	1.12
	fraction (c)	2.46	3.33	3.80	5.80	1.12
	chloroform (d)	none	none	none	5.80	--
3% OV-17	standard	2.95	4.89	4.45	7.64	1.25
	fraction (c)	2.95	4.89	none	7.64	1.25
	chloroform (d)	none	none	none	7.64	--
1.5% OV-17-2% QF-1	standard	2.98	4.77	4.82	7.85	1.24
	fraction (c)	2.98	4.77	none	7.85	1.24
	chloroform (d)	none	none	none	7.85	--
5% SE-30	standard	2.28	2.51	2.28	3.42	--
	fraction (c)	2.28	2.51	none	3.42	--
	chloroform (d)	none	none	none	3.42	--

The GLC method is highly sensitive and may be used to corroborate TLC measurements. Instrumentation and maintenance are expensive and highly trained technicians are needed for successful analysis.

CHAPTER I

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Chapter II

Pharmacology, Toxicology, and Epidemiology

Endrin is the most acutely toxic of the cyclodiene pesticides in use today. However, unlike the other cyclodienes, endrin is rapidly metabolized and excreted and neither endrin or its metabolities appear to be accumulating in the adipose tissues of the general population or in occupationally exposed workers.

II.A. Pharmacology of Endrin

As with the other cyclodienes, the principal pharmacological action of endrin is that of central stimulation. The rate of metabolism and excretion of endrin is rapid when compared to that of its stereoisomer dieldrin, or other chlorinated hydrocarbons.

II.A.1. Absorption, Distribution, and Excretion

The pertinent literature on the absorption, distribution, and excretion of endrin, when fed or exposed to various laboratory animals has been reviewed.

II.A.1(b) Absorption

In the toxicity section, it is noted that endrin is toxic to all animals regardless of route of exposure. It may, therefore, be concluded that endrin is absorbed through all the various routes. Endrin is virtually non-soluble in water and readily soluble in lipids. This differential solubility is a factor determining endrin's absorption by different routes. As shown in Table II. 1, the absorption by the dermal route, the liquid formulation is more toxic than are the powdered forms of endrin. A comparison of LD_{50} values for the various routes of administration may give an indication of their relative efficiencies as a route of absorption. The possible biotransformation to a non-toxic or more toxic compound than the parent compound must be, however, considered in such LD_{50} values with dermal LD_{50} values for identical formulations of endrin do not show any striking differences. The inhalation data is inadequate; but it is suggestive that complete absorption could occur via this route. There is very little information regarding either the amount of the rate of absorption of endrin through different routes of entry to the organism.

TABLE II.1. ACUTE DERMAL TOXICITY OF ENDRIN

SPECIES	Carrier	LD50(mg/kg)	ref.
Rat	Peanut oil solution	5.6	Worden, A. N. et al., (1958)
Rat	19.2% (w/v) emulsifiable concentrate containing xylenes	11.3	Worden, A. N. et al., (1958)
		15.0	Gaines, T. B. (1960)
Rat	Xylene Solution	60 male, 120 female	Lade, B. I., (1960)
Rat	20% emulsifiable concentrate in xylene	100	Newell, G. W. (1960)
Rabbitt	Dry crystalline powder		Newell, G. W. (1960)
	20% emulsifiable concentrate containing xylenes.	50	Letter to Shell Bulletin (1960).

II.A.1(b) Distribution and Storage

Endrin, like other chlorinated pesticides, when fed to animals, is partly stored unchanged in the tissues, particularly in the adipose tissues (Kiigemagi et al., 1958; Street et al., 1957; Terriere et al., 1958, 1959, and Treon et al., 1955). When fed at high levels, endrin is excreted in milk and eggs (Ely et al., 1957; Street et al., 1957, and Terriere et al., 1958). The ratio of the level in fatty tissue to the dietary level has been estimated at 0.5-2.0, depending upon the dietary level (Kiigemagi et al., 1958; Terriere et al., 1958, and Treon et al., 1955).

Unlike the situation with its stereoisomer, dieldrin, the extent of storage of endrin is relatively small, and the compound is eliminated more quickly, due probably to its rapid biliary excretion (Cole et al., 1970). Levels of the 9-keto metabolite of endrin in four human fat samples were all less than 0.0004 ppm (<0.4 ppb), (Richardson, 1970).

The maximum concentration of endrin in various tissues of animals maintained on experimental diets are summarized in Table II. 2.

Korte et al., (1970) reported that when endrin was given orally to rats at a daily dose corresponding to 0.4 ppm in the diet, a steady state of storage was reached after about six days for male and female rats. The storage level for females (27 percent) is about twice as high as for the males (14 percent). These figures are based on the total amount of radioactivity administered. Four days after cessation

TABLE II. 2

MAXIMUM CONCENTRATION OF ENDRIN IN TISSUES OF ANIMALS MAINTAINED ON DIETS CONTAINING ENDRIN

Animal	Endrin in Diet, ppm	MAXIMUM ENDRIN CONTENT OF TISSUE AT END OF FEEDING PERIOD, ppm							Reference
		Body Fat	Liver	Kidney	Muscle	Heart	Brain	Spleen	
Dog[a]	3	3.4	1.2	0.3		1.5	3.0	1.6	Treon, J. F. (1956).
"	1	3.5	1.2	1.1		1.5	2.0	1.3	Treon, J. F. (1956).
Cattle[b]	5.0	2.5							Claborn, H. V. et al., (1960).
"	2.5	1.3							Claborn, H. V. et al., (1960)
"	2.0	1.0	0.2	0.1	0.3	0.1	0.1		Terriere, L. C. et al.,(1958), and Kiigemagi et al.,(1958).
"	0.75	0.4	0.2	0.1	0.1	0.1	0.1		Terriere, L. C. et al.,(1958), and Kiigemagi et al.,(1958).
"	0.25	0.2	0.1	0.1	0.1	0.1	0.1		Terriere, L. C. et al.,(1958), and Kiigemagi et al.,(1958).
"	0.10	0.1	0.1	0.1	0.1	0.1	0.1		Terriere, L. C. et al.,(1958), and Kiigemagi et al.,(1958).
Sheep	5.0	1.2							Claborn, H. V. et al., (1960).
"	2.0	1.5							Claborn, H. V. et al., (1960).
"	2.5	2.8							Street, J. C. et al., (1964).
"	0.75	0.5	0.1	0.1	0.1				Terriere, L. C. et al.,(1958), and Kiigemati et al., (1958).
"	0.25	0.1	0.1	0.1	0.1				Terriere,L.C. et al.,(1958), and Kiigemagi et al., (1958).
"	0.10	0.1	0.1	0.1	0.1				Terriere, L.C. et al.,(1958), and Kiigemagi et al.,(1958).
Hogs[b]	0.75	0.1	0.1	0.1	0.1				Terriere, L.C. et al.,(1958),
"	0.25	0.1	0.1	0.1	0.1				Terriere, L.C. et al.,(1958).
"	0.10	0.1	0.1	0.1	0.1				Terriere, L.C. et al.,(1958).
Chickens[c]	2.25	18.0							Terriere, L.C. et al.,(1959).
"	0.75	4.0			0.3				Terriere, L.C. et al.,(1959).
"	0.25	1.0			0.1				Terriere, L.C. et al.,(1959).
"	0.10	0.6			0.1				Terriere, L.C. et al.,(1959).

a/Feeding period for dogs was 18 months.
b/Feeding period for cattle, sheep and hogs was 12 weeks.
c/Feeding period for chickens was 6 weeks.

Phenylazide method of analysis--sensitive to 0.1 ppm. [Terriere et al., 1958 and Kiigemagi et al., 1958]

of dosing, the males contained only 5.3 percent, and females, 15 percent of the administered radioactivity. The biological half-life of endrin in male rats, at the storage level investigated, is 2-3 days; in females, it is approximately 4 days. The radioactivity was mainly excreted in the feces, which contained during the first 24 hours after oral administration, 70 to 75 percent of the radioactivity as hydrophilic metabolites. After the first 24 hours, only metabolites were present in the feces. Following intravenous injection of 200 ug ^{14}C endrin/kg bodyweight in two doses, male rats retained 5.2 percent and females 12.1 percent of the administered radioactivity after 24 hours.

Walsh (1971) reported the distribution patterns of endrin or dieldrin in brain, liver, fat, and blood after an i.v. injection of an LD_{90} of endrin in male CF#1 mice. He found that endrin equilibrates sooner in liver, fat and blood, while dieldrin equilibrates sooner in brain tissues. The rate of accumulation of dieldrin and endrin in the brain did not correlate with the onset and development of the convulsive seizure pattern.

II.A.1(c) Excretion

A male rat was fed a dietary level of 30 ppm of ^{14}C-labelled endrin for eight days (Ludwig, 1965 and 1966). About 60-70 percent excretion was noted from the first day, and after three days the feces contained more than 80 percent of the administered radioactivity. On day 9, 84 percent had been excreted; and, there appeared to be a level of saturation after 6-7 days of feeding. The feces contained about 75-80

percent metabolites, of which there were at least two different compounds. The fatty tissue stored 3-4 ppm of endrin, giving a storage ratio of about 10:1. Compared to 84 percent excretion in the feces, only about 0.5 percent was found in the urine.

Korte et al., (1970) measured the excretion rate of ^{14}C-endrin after oral administration. The biological half-life after a dose of 16 or 64 ug/kg body weight was one to two days. However, at a dose of 128 ug/kg, the half-life increased to approximately six days, indicating a decreased excretion at higher dosage levels.

The rapid rate of metabolism and excretion of endrin compared to that of other chlorinated hydrocarbon insecticides has been confirmed by a study on rats, with and without bile fistula, and on isolated perfused rat liver (Cole et al., 1970; Altmeier et al., 1969). In rats receiving a daily oral administration of 32 ug/kg, the storage reached a state of equilibrium after 5-6 days. Under these conditions, the half-life was three days in male rats and four days in female rats, (Klein and Drefahl, 1970).

Klevay (1970) studied the excretion of endrin by the isolated perfused liver of male and female rats. The excretion of the radioactivity by the bile duct of the male livers was significantly greater than the female livers. The ^{14}C-endrin appeared two to twelve time more rapidly in the bile of the male livers than in that of the female livers and the author thought that this explained the lesser toxicity and lesser adipose tissue storage of endrin in male rats.

II.A. 2 Biotransformation (Metabolism)

There is considerable indirect evidence that endrin degrades to a less toxic derivative. It has also been assumed that endrin either is metabolized and stored in a chemical form not detected by analytical methods or is rapidly metabolized and excreted.

The information available on the metabolism of endrin up to 1967 have been reviewed previously (Soto and Deichmann, 1967; Brooks, 1969). The following experimental data summarizes the pertinent information leading to the current knowledge on the metabolism of endrin (see Figure II.1).

In rats, Klein et al., (1968) and Richardson et al., (1970) found that endrin is rapidly metabolized and excreted, principally in the feces. The feces contain two metabolites as well as endrin itself. Baldwin et al., (1970) found that the major fecal metabolite is a secondary alcohol formed by substituting a hydroxyl group for one of the hydrogens of the methano-bridge of endrin (II). The other fecal metabolite is also an alcohol. Three days after a single oral dose of ^{14}C-labelled endrin, approximately half of the ^{14}C radioactivity remained in the bodies of the rats. This material was principally one metabolite which was identified as 9-keto endrin (I), an oxidation product of the secondary alcohol found in feces.

When ^{14}C-labelled endrin was administered orally to rabbits at 0.5 mg/kg body-weight at three and four day intervals, four metabolites were isolated from the urine which appear to have the following chemical

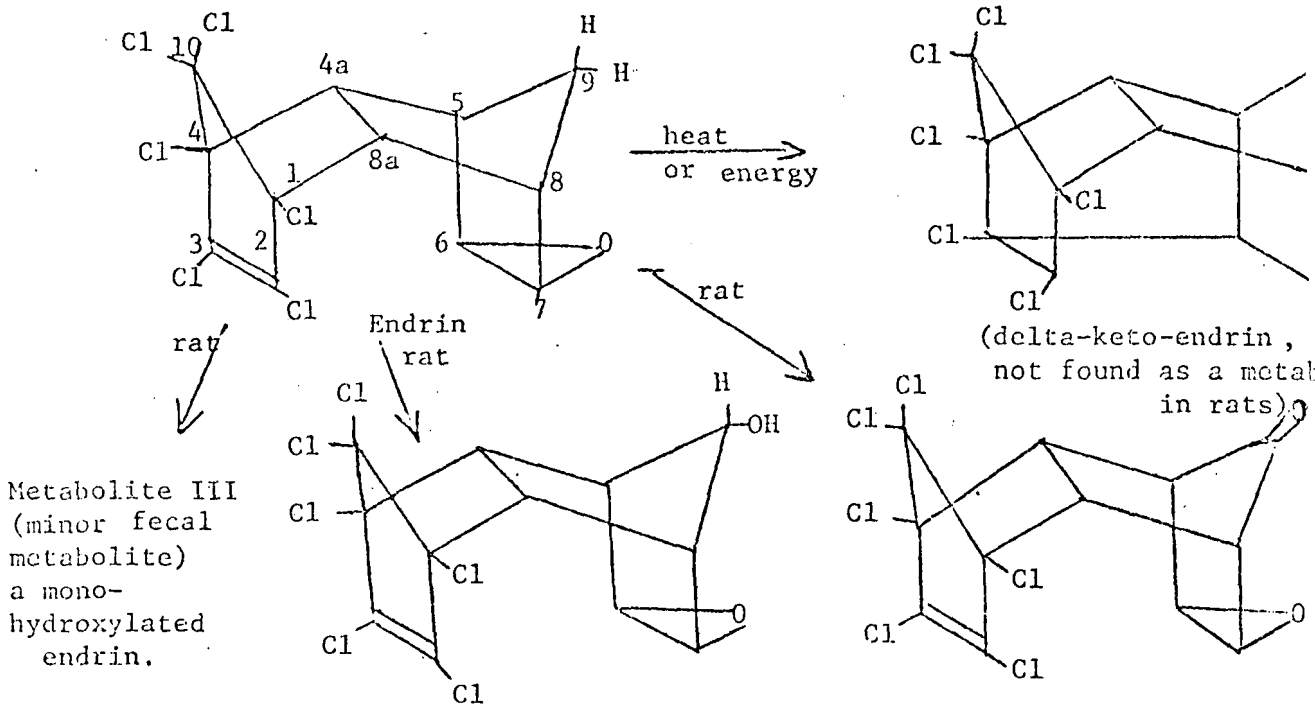

Figure II.1. METABOLISM OF ENDRIN IN THE RAT

natures: A (40 percent of excreted radioactivity) is a conjugate compound of a hydroxy derivative of endrin; B (12 percent) is a monohydroxy derivative of an unbridged endrin isomeric ketone; C (40 percent) is the 4a-hydroxyendrin; D (8 percent) has a molecular weight of 420 and the C-C double bond intact in the chlorinated ring. None of these compounds is the delta-keto endrin (Korte and Porter, 1970).

The acute oral LD_{50} for delta-keto 153, a metabolite of endrin formed in plants, has been found to be 62.1 mg/kg and 23.6 mg/kg for male rats and mice, respectively (Newell, 1964). For the aldehyde, the acute oral LD_{50} in male mice is 500 mg/kg (Newell, 1964). The lethal dose of delta-keto 153 for three routes of administration has been reported by Witherup (1964); the results are summarized in Table II. 3.

TABLE II. 3

LETHAL DOSES OF DELTA-KETO ENDRIN FOR VARIOUS ROUTES OF ADMINISTRATION

Animal	Route of Administration	Vehicle	Lethal dose mg/kg
Rabbits	Intravenous	Peanut oil	5
Rats	oral (acute)	"	M 120-280 F 10-36
Rats	cutaneous	"	> 940 in M and F*

* At dosages of 180-940 mg/kg applied to the skin and washed off 6 hours later; all rats survived and exhibited no ill effects, except transient losses in body weight.

II.A. 3 Effect on Enzymes and other Biochemical Parameters

In monkeys which had received exposure to an unspecified quantity of endrin, there were significant changes in the enzymes serum glutamic-oxaloacetic transaminase and serum glutamic-pyruvic transaminase (Barth, 1967).

Elevation of serum alkaline phosphatase has been observed in rats fed 25 ppm, and possibly in rats fed 5 or 1 ppm of endrin for 16 weeks (Nelson et al., 1956), but not in dogs feed 4 ppm of endrin for two years (Jolley et al., 1969), nor in human subjects occupationally exposed to unspecified levels of endrin (Shell, 1965).

Weil and Russells (1940) have reported a decrease in alkaline phosphatase in rats after eight hours fasting; these observations indicate some degree of enzymatic abnormality and functional liver damage. Hart (1964) has noted a stimulatory effect of chlorinated hydrocarbons resulting in increased hepatic drug enzyme activity, and this suggests a possible biochemical alternation involving liver.

Daugherty et al., (1963) reported that there was no effect of endrin on substrate-linked phosphorylation, and Weikel et al., (1968) noted no effect from endrin on the phosphate exchange rate. Nelson et al., (1956) showed that endrin, unlike aldrin, dieldrin, and DDT, does not inhibit the phosphate exchange rate in whole blood.

There are no specific studies on hepatic enzyme induction, however, enhancement of enzyme(s) are indicated in the long-term feeding studies of rats (Nelson et al., 1956; Treon et al., 1955) and dogs (Treon et al., 1955; Richardson et al., 1967). Based on these data, a 1 ppm dietary

level of endrin may be regarded as the "no effect" level in the rat and the dog. This no-effect level can also be applicable to the enzyme induction level in the rat and the dog.

II.A. 4 Pharmacodynamics

Reins et al., (1964) noted an increase in peripheral blood pressure and in renal vascular resistance after intravenous infusion of endrin in dogs. Adrenalectomy partially offset the marked drop in renal blood flow after endrin infusion, although systemic hypertension was unaffected. It was suggested that endrin stimulates the sympatho-adrenal system accounting for the increased peripheral vasoconstriction. The results were by no means conclusive, however, and considerable work involving the effect of endrin on the kidney remains to be done.

Emerson et al., (1963) have reported a possible scheme of the mechanism of action of acute endrin intoxication (See Figure II. 2). While most of the effects of endrin appear to be caused by direct action on the central nervous system, some may result secondarily from altered cerebral hemodynamics.

Speck and Maaske (1958) noted a latent period of 45-60 minutes before the appearance of convulsions in rats, regardless of the amount of endrin dose. It was shown that injections of trypan blue sufficient to color the choroid plexus prevented the convulsions which was interpreted to be an indication the "blood-brain barrier" permeability was increased by endrin. The validity of this interpretation is questionable.

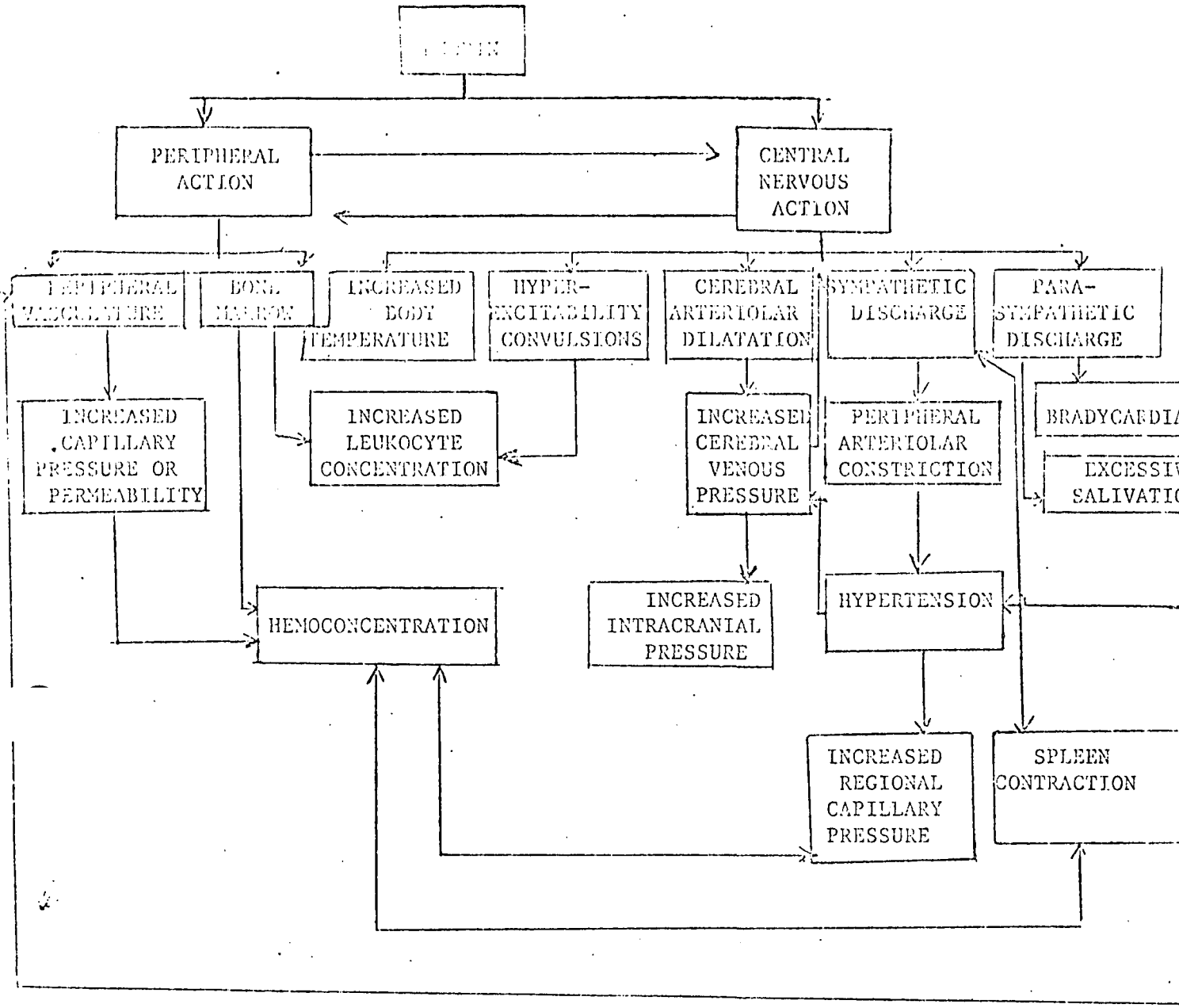

Figure II.2. A POSSIBLE SCHEMA OF ACTION OF ENDRIN

Electroencephalograms made after the administration of large doses of endrin showed irregular slowing, irregular spikes. and frequent convulsive discharges. Severe chronic convulsions could be produced by auditory or tactile stimulation of the rats. It was noted that a tolerance appeared to develop during subacute exposure to endrin in long-term feeding period, the electroencephalograms appeared normal although convulsions were produced (Speck and Maaske, 1958).

Degenerative changes, which were not described, have been noted in the brain after lethal intoxication by endrin, but there is no record of any lesion in the peripheral neural tissues (Treon et al., 1955).

Intravenous injections of endrin in anesthetized pigeons, produced a number of changes in telencephalic neuronal functions (Revizin, 1966).

Emerson et al., (1964) observed that dogs treated with a lethal dose of endrin followed the usual pattern of symptoms and that their tolerance for barbiturates increased greatly during intoxication even though the barbiturates decreased the arterial blood pressure. Emerson (1965) reported that endrin administered to beagle dogs produced cardiovascular alterations such as hypertension and severe bradycardia. Decreased glomerular filtration rate and renal blood flow with hypertension and bradycardia were observed by Reins et al., (1964). Endrin caused an increase in the venous return and corresponding elevation of cardiac output with no change in peripheral resistance (Reins et al., 1966).

A noticeable rise in cardiac flow coincided with a steady drop in resistance (Hinshaw et al., 1966); the left arterial pressure increased strikingly within 15 minutes after treatment with endrin, but the right arterial pressure held steady. Gourdey et al., 1954, reported that the chlorinated hydrocarbon insecticides exerted their effects through central rather than peripheral stimulation. Convulsions apparently originate from a direct action of endrin on the central nervous system. Sowell et al., (1968) summarized the physiological changes produced by endrin as shown in Figure II. 3.

Effect on Liver, Kidney and Other Organs

There have been reports of possible impairment in liver (Nelson et al., 1956) and kidney function (Reins et al., 1964). An increased serum alkaline phosphatase level due to ingestion of endrin indicates impaired liver function, but the data used to arrive at this conclusion is statistically insignificant and, therefore, open to criticism. The impairment of kidney function, particularly the decreased glomerular filtration rate, is indicated to result secondarily from alteration in peripheral hemodynamics.

Diets containing endrin in the concentration of 8 ppm, when fed for almost six months, did produce enlargement of the liver, kidneys and brain of dogs. After 19 months of feeding diets containing 3 ppm of endrin, the kidneys and hearts of dogs were significantly enlarged. Other viscera were unaffected at the 3 ppm level and no visceral weight changes were noted at the feeding level of 1 ppm (Treon et al., 1955; Treon et al., 1966) unpublished report of Kettering Laboratory, May 9, 1955).

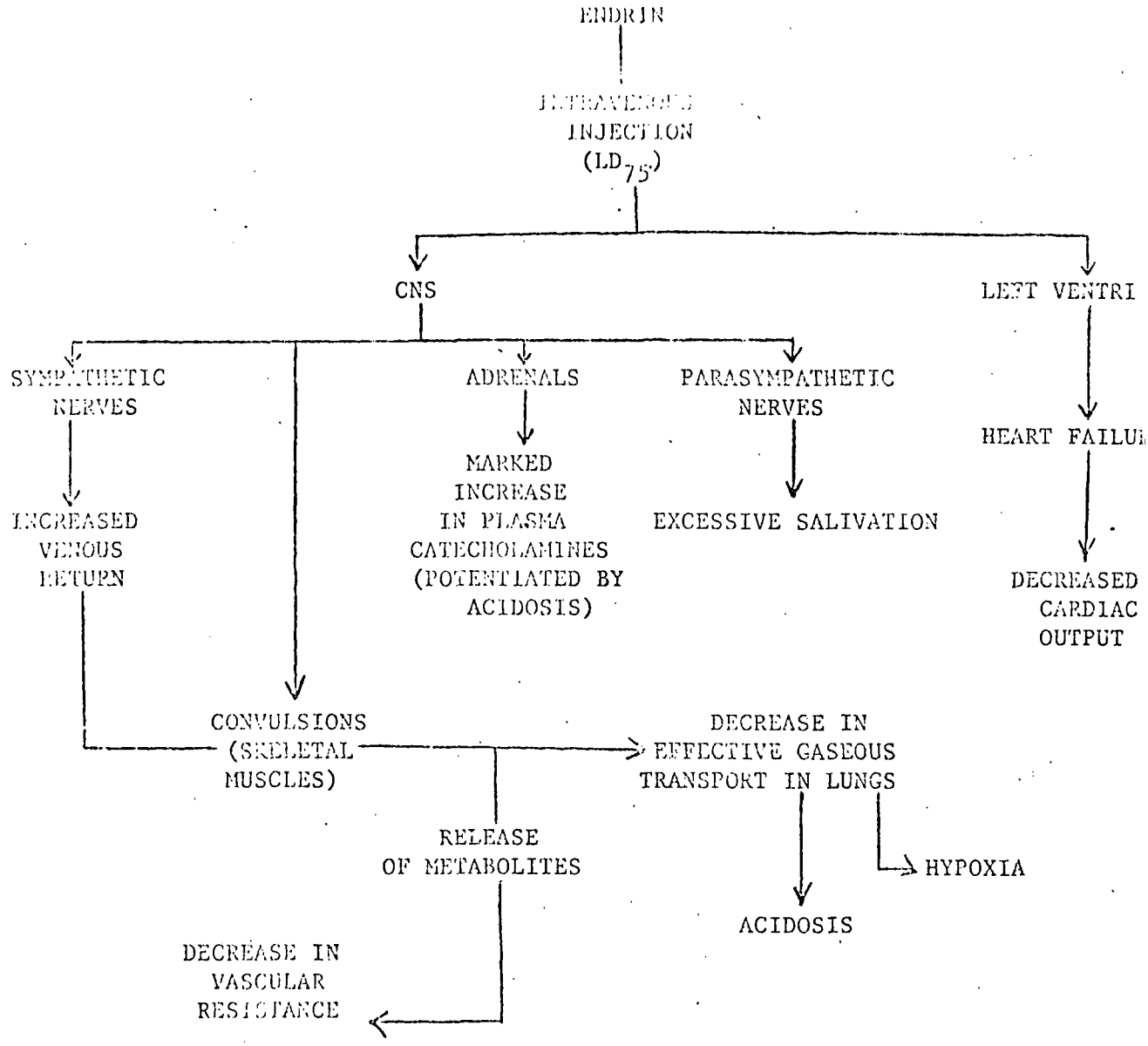

Figure II.3. PHYSIOLOGICAL CHANGES PRODUCED BY ENDRIN

Male rats showed a significant enlargement of their livers in relation to total body weight after two years of feeding endrin at levels of 25 ppm and 5 ppm. This phenomenon was not noted in female rats nor in male rats fed levels of 1 ppm endrin. Female rats which were fed a diet containing 5 ppm of endrin showed an increase in the weight of the kidneys as compared to body weight. This was not noted in males nor at other feeding levels in females. No other changes in the weight of viscera were noted (Treon et al., 1955).

II. B. Toxicology

Endrin has the highest acute toxicity by all routes of exposure to mammals of all of the chlorinated hydrocarbon pesticides in use today. Dermal absorption is apparently rapid and complete. However, endrin is rapidly metabolized and excreted and adipose storage does not present a problem. The level of endrin causing no toxicological effects for the rat is 1 ppm in the diet, equivalent to 0.05 mg/kg body weight/day; for the dog is 1 ppm in the diet, equivalent to 0.025 mg/kg body weight/day. The FAO/WHO estimate of acceptable daily intake for man is 0.0002 mg/kg body weight.

II. B. 1 Acute Toxicity

Acute oral, dermal, and inhalation toxicity studies have been carved out for endrin.

II. B. 1(a) Acute Oral Toxicity

The acute LD_{50} toxicity (single dose) of 4-dimethanonaphthalenes (aldrin, isodrin, dieldrin and endrin), when given orally to non-fasted rats or rabbits, has been shown to be more closely related to the spatial configuration than to the empirical composition of these compounds.

Isodrin or endrin having the endo, endo configuration are more toxic than those which have the endo, exo configuration (aldrin, dieldrin). The LD_{50} values of acute oral toxicity in various species of laboratory animals are summarized in Table II. 4.

The laboratory animals that absorbed endrin at a lethal oral dose exhibited the following pattern of toxic symptoms: stimulation, hyperexcitability, hyperactivity, uncoordination and exaggerated body movements, ultimately leading to convulsions, depression, and death. It was also noted that there is an interval of up to an hour or so following oral dosing before the onset of lethargy prefacing the tremors (Speck and Maaske, 1958 and Zavon 1961).

The LD_{50} values shown in Table II. 4 for cats, rabbits, monkeys and guinea pigs are less accurate than those for rats, because of smaller numbers of animals used. It is apparent, in general, monkeys and cats are more susceptible than of rats and guinea pigs are more resistant. Rabbits, are also somewhat more resistant.

TABLE II. 4

ACUTE ORAL TOXICITY OF ENDRIN

SPECIES	Strain or Breed	Age	Number of Animals Used M	Number of Animals Used F	Dosage Form 0.1 to 1.0% W/V in Peanut Oil	LD_{50} (mg/kg) M	LD_{50} (mg/kg) F	Reference
Rat	Carworth	29-31 days	10	10	Solution	28.8 (27.8-28.8)	16 (16.4-16.8)	Treon et al., 1955.
Rat	Carworth	6 mos.	10	10	Solution	43.4 (42.1-43.4)	7.3 (7.3-11.7)	Treon et al., 1955.
Rat	----	6 mos.	--	--	----	---	40-43	Speck and Macke, 195
Cat	Tabby	Adult	1	1	Solution	5	5	Treon et al., 1955.
Rabbit	Dutch	Adult	--	4	Solution	---	7 (7-10)	do
Guinea Pig	Albino	Adult	2	2	Solution	36 (24-36)	16 (10-16)	do
Dog					Water-Suspension	10		Kettering, 1955, Shell Document K-55-1
Monkey		Adult	2	2	Solution	1-3	1-3	Treon et al., 1955.
Monkey		Adult	--	--		12	12	Barth, 1967
Goat		Adult	--	--	96% Technical		25-50	Tucker, 1970.

Adult female rats (6 months of age) are more susceptible to the toxic effects of endrin than are younger immature female rats. The difference in susceptibility of guinea pigs, in relation to sex, appears to be similar to that of rats. Females are more susceptible than males.

The acute toxicity of endrin appears to be influenced by the diet. Three groups, each comprising about 100 male rats, were fed for 28 days either a normal diet, a normal protein diet containing protein only as casein, or a low protein diet. The acute toxicity to endrin was then determined by a single oral administration of the pesticide. The LD_{50} values were 27, 17, and 7 mg/kg for the animals fed the respective diets, indicating an approximately fourfold increase in toxicity between the normal and low protein diet as well as an effect due to the type of protein fed (Boyd and Stefec, 1969).

II.B. 1(b) Acute Dermal Toxicity

The acute toxicity of endrin upon application to the intact or abraded skin of female rabbits for 24 hours according to the sleeve method of Draize, Woodard and Calvery (1944) are summarized in Table II. 5. The minimum lethal dose was found to be greater than 60 mg and less than 94 mg per kg. body weight. Neither gross nor microscopic evidence of damage to the skin of these animals was found (Treon et al., 1955).

TABLE II. 5

IMMEDIATE TOXICITY OF ENDRIN MAINTAINED IN CONTACT WITH INTACT SKIN OF FEMALE RABBITS BY METHOD OF DRAIZE, WOODARD AND CALVERY (APPLIED AS RECRYSTALLIZED DRY POWDER THAT PASSED 100-MESH SCREEN MAINTAINED UNDER RUBBERSLEEVE FOR 24 HOURS)

Dosage, G./Kg.	No. of Animals That Died/No. of Animals Given Dose
0.25-3.6	8/8
0.16	2/3
0.125	1/3
0.094	1/3
0.060	0/3

Treon et al., (1955) also reported the effects of the intermittent cutaneous contact of endrin to intact skin of rabbits and their findings are summarized in Table II. 6.

These data indicate endrin is rapidly and completely absorbed from intact skin.

II. B. 1(c) Acute Inhalation Toxicity

Treon et al., (1955), exposed several species of animals to air containing the sublimed vapor of endrin in the concentration of 5.44 Mgrams per liter (0.36 ppm). The results are summarized in the Table II. 7. The endrin concentration of the air in the inhalation chambers was determined 4 times daily.

TABLE II. 6

EFFECTS OF ENDRIN ADMINISTERED UPON SKIN OF FEMALE RABBITS FOR 2 HOURS ON EACH OF 5 DAYS PER WEEK OVER SEVERAL DAYS.*

No. of Doses Applied	Daily Dosage		Condition of Skin	No. That Died/No. Given Material
	G.	G./Kg.		
19-25	0.150	0.067-0.091	Intact	3/3
40-70	0.075	0.020-0.042	Intact	1/3
25-45	0.075	0.027-0.044	Abraded	1/4

* Treon et al. (1955)

TABLE II. 7

FATE OF ANIMALS EXPOSED INTERMITTENTLY TO VAPOR OF ENDRIN IN AIR
(EXPOSED FOR 7 HOURS PER DAY 5 DAYS PER WEEK. CONCENTRATION, 5.44 Mgrams/liter, i.e., 0.36 ppm)

Species	Duration of Exposure (Hours)	No. of Animals That Died/No. of Animals Exposed
Cat	130 x 7	0/1
Guinea pig	130 x 7	0/2
Hamster	(101 -- 130) x 7	0/2
Rat	130 x 7	0/3
Rabbit[a/]	118 x 7	2/4
Mouse[b/]	107 x 7	1/3

a/ Three additional rabbits survived 12 7-hour periods of exposure.

b/ Six additional mice survived 18, 18, 42, 58, 64, and 64 7-hour periods of exposure.

* Treon et al. (1955)

II. B. 2 Subacute Toxicity

Worden (1969) reported the mortalities of rats during the first 37 days of feeding diets containing various levels of endrin. The data are summarized in Table II. 8. He found that there were no further deaths among the groups of survivor rats at 37 days when those rats were transferred from an experimental to a control diet. One of the males continuing to receive the experimental diet of 25 ppm of endrin died on day 50. The symptoms induced by endrin included: hypersensitivity, audiogenic seizures (which occurred frequently during the cleaning of the room), swelling of the subcutaneous tissues of the head, staring eyes, bloody incrustations over the eyelids, sporadic mild convulsions lasting over 30 seconds, and, in fatal cases, violent convulsions resulting in death. The symptoms were more marked during the earlier stages of the study and were less severe in animals that survived. This may have reflected loss of more susceptible animals, but may also have been due to tolerance.

Groups consisting of five male and five female rats were fed dietary levels of 0, 1, 5, 25, 50 or 100 ppm of endrin for up to 16 weeks. All of the group fed 100 ppm died within the first two weeks and only two rats fed 50 ppm and three fed 25 ppm survived. Three males fed 5 ppm also died; the other animals were continued on the test diet for the full 16 weeks. Weight loss was roughly dose related but was evident in all test groups, as was hypersensitivity to tactile stimuli.

TABLE II. 8

MORTALITY DURING 37 DAYS OF SUBACUTE ADMINISTRATION OF ENDRIN TO RATS.*

Endrin	25	2/5	3/5	1F,1M,3F,4F,4M
	35	5/5	4/5	1F,1F,3F,3M,4M,5M,5M,6F,6M
	50	5/5	5/5	1F,1F,1M,1M,3F,3M,3M,4F,6F,6M
	100	5/5	5/5	1F,1F,1M,2F,2F,2M,3F,3M,4M,4M

* Worden (1969)

There was an initial drop in serum alkaline phosphatase during the first three to eight weeks; feeding, which was then followed by an increase at all dose levels. At the end of the 16 weeks, the phosphatase level was elevated above the controls in all the test groups, the levels being highest in the groups fed 25 and 50 ppm (Nelson et al., 1956). However, other statisticians have considered that the elevation of serum alkaline phosphatase was not significant in the groups fed 1 and 5 ppm of endrin (Williams, 1966).

In a series of experiments by Treon et al., (1955), dogs were fed diets containing from 1 to 50 ppm endrin along with control groups for periods of time up to 47 days.

Two of the four dogs fed diets containing 8 ppm and the one fed 5 ppm died. The data are shown in Table II. 9.

The two surviving dogs on 8 ppm were kept on the diet for about six months and then sacrificed; increased organ to body-weight ratios for the liver, kidney and brain were found (See Table II. 10), and histopathological examination showed degeneration of kidney tissue. Three of the four dogs on 4 ppm of endrin survived and there were no symptoms in dogs fed 1 or 3 ppm.

Cattle and sheep were not affected by 5 ppm of endrin their diet for 112 days (Radeleff, 1956).

Groups of 20 seven-day old chicks each were unaffected by feeding diets for 12 weeks containing 0, 1.5 or 3 ppm of endrin. When the concentration was increased to 6 or 12 ppm, the birds became highly excitable, failed to gain as much weight as the controls, and the

TABLE II. 9

FATE OF DOGS GIVEN ENDRIN IN DIET*
(Insecticide introduced into diet 6 days of each week)

Daily Dosage in Relation to Food ppm	Body weight, mg./kg.	Sex and (no. of dogs)	Duration of Period of Feeding on Diet Containing Endrin, Months	Fate
50	2.50-4.00	M(1). F(1)	18-20 days.	Both died.
25	1.21-2.20	F(2)	18-30 days	Both died.
5) a/	0.25-0.36)			
20)	0.97-1.27)	F(1)	4.7	Died.
10	0.49-0.81	M(1), F(1)	24-44 days	Both died.
8	0.29-0.62	M(1), F(1)	5.7	One died.
2) b/	0.09-0.17)			
8)	0.31-0.65)	M(1), F(1)	9.9	One died.
5	0.20-0.27	M(1)	47 days	Died.
4	0.15-0.21	M(1), F(2)	5.7	All survived.
3	0.12-0.25	M(2), F(2)	18.7	All survived.
1	0.045-0.12	M(1), F(1)	18.7	All survived.
0 b/	0	M(1), F(1)	18.7	All survived.

a/ Smaller dosage given during first portion (2.9 months) of feeding period, larger dosage during remainder of period.

b/ Three additional control dogs survived 5.7 months.

* Treon et al., (1955)

TABLE II. 10

RATIO OF WEIGHT OF FAT AND ORGANS TO BODY WEIGHT OF DOGS FED ALMOST 6 MONTHS ON DIETS CONTAINING ENDRIN

Endrin in Diet, ppm	n	Grams per 100 Grams Body Weight			
		Liver	Kidneys	Brain	Fat
8	3	3.16	0.52	1.16	0.20
4	3	3.06	0.36	0.92	0.30
0	3	2.66	0.37	0.85	0.43

* Treon et al. (1955)

survival rates over a 12 week period were 85 and 5 percent, respectively, compared to 100 percent in the control (Sherman and Rosenberg, 1954).

Groups of 40 quail, each were fed dietary levels of 0, 0.5, 1, 5, 10, 20 or 50 ppm endrin in their diet, starting when one day old. Survival was adversely affected in all the test groups, and there were no survivors beyond two weeks in the birds fed 10 ppm or more. Food consumption was abnormally low. Symptoms involved lack of muscular coordination, tremors, bedraggeled appearance and rigidity with occasional convulsive movement (DeWitt, 1956).

Day-old pheasants, in groups of 40, did not survive beyond eight days when fed dietary levels of 5 or 20 ppm endrin. Reduced food consumption occurred, and the symptoms were the same as those seen in quail (DeWitt, 1956).

II. B. 3 Chronic Toxicity

The pathologic findings associated with the life-span feeding of endrin to rats at various dosage levels are shown in Table II. 11.

In a two-year experiment, groups of 20 male and 20 female rats each were fed diets containing 0, 1, 5, 25, 50 and 100 ppm of endrin. Concentrations of 50 and 100 ppm were lethal within a few weeks. The concentration of 25 ppm increased the mortality rate of the females (See Table II. 12). Non-survivors at the three higher levels exhibited diffuse degeneration of the brain, liver, kidneys and adrenal glands.

TABLE II.11 PATHOLOGIC FINDINGS ASSOCIATED WITH THE INCORPORATION OF ENDRIN IN THE DIETS OF RATS*

Level of Exposure, ppm	Time (maximum), years	Pathologic Findings
100	2	Diffuse degeneration of brain, liver and kidney; 6 rats with diffuse degeneration and necrossis of proximal and distal convoluted tubules.
50	2	Diffuse degeneration of brain, liver, kidneys and adrenals; no specific renal lesions; slight fatty vacuolization of hepatic cells in two animals.
25	2	Diffuse degeneration of brain, liver, kidneys and adrenals; remainder of viscera normal.
5	2	Normal viscera.
1	2	Normal viscera.

* Treon et al. 91955)

TABLE II.12

MORTALITY AMONG GROUPS OF CONTROL RATS AND RATS FED 2 YEARS ON DIETS CONTAINING ENDRIN*

	No. That Died/No. Fed on Diet			
	MALES		FEMALES	
P.P.M.	80 weeks	106 weeks	80 weeks	106 weeks
100	18/20 a/	18/20	18/20 a/	19/20 a/
50	13/20 b/	16/20	19/20 a/	20/20 a/
25	5/20	9/20	12/20 c/	15/20
5	5/20	13/20	7/20	12/20
1	5/20	9/19	4/20	9/20
0	7/20	12/20	5/20	13/20

a/ P. $\angle$ 0.01.

b/ This value is only slightly above 0.05.

c/ P. 0.05-0.01.

* Treon, et.al. (1955)

The survivors in the two higher levels showed degenerative changes in the liver only, while those fed at the lower levels had normal viscera. At a level of 5 ppm or higher, an increase in lever to body-weight ratio in males was observed. (See Table II. 13). This effect was not observed in males fed 1 ppm or in females fed at either 1 or 5 ppm endrin. Too few observations were made upon other groups to provide statistically significant data. Treon et al., (1955) concluded from the results of this experiment that the "no effect" level of endrin is at the level of 1 ppm in diet.

A total of 1600 mice in equal numbers of each sex, consisting of one inbred and one hybrid strain, were divided into four groups, two of which were fed a control diet and the other two fed 0.3 or 3.0 ppm of endrin. Feeding of the test diet was started at five weeks of age and continued throughout their normal lifespan, or until sacrifice. Because of an early high incidence of fibroadenomas occurring in both control and test groups in the hybrid strain, all the females of that strain were sacrificed after 72 weeks for pathological examination. A few of the mice, fed 3.0 ppm only, displayed convulsions in the early stages of feeding but recovered and survived. Mortality was not adversely affected by endrin, nor was body-weight or food intake. No hematological abnormalities were evident in two males in the hybrid group fed 0.3 ppm, which had severe leukemia. In either sex, the total number of neoplasms was not influenced by the endrin content of the diet, except in the case of hepatomas in the females of the hybrid strain, which were significantly higher than the controls in the mice of the group

TABLE II.13

RATIO OF WEIGHT OF LIVER TO BODY WEIGHT OF RATS FED 2 YEARS ON DIETS CONTAINING ENDRIN*

Endrin in Diet ppm	Sex	n	Ratio of Weight of Liver to Body Weight G./100 G.	P
100	M	2	3.26	a/
50	M	4	3.08	a/
25	M	11	3.03	0.02-0.01
5	M	7	3.14	0.05-0.01
1	M	10	2.82	> 0.05
0	M	8	2.66	. . .
25	F	5	3.43	a/
5	F	8	3.22	> 0.05
1	F	11	3.08	> 0.05
0	F	7	3.01	. . .

a/ Too few for statistical determination.

* Treon et al. (1955)

fed 3.0 ppm, and sacrificed between weeks 53 and 60 of the feeding period. Because of a relatively high incidence of hepatomas in one group of controls of this strain, the increase at the 3.0 ppm level was considered not due to endrin. It was noted that in no animals of either sex were there any metastases of the hepatomas into the lungs (Witherup et al., 1970).

In an experiment of about 19 months' duration, groups comprising two male and two female dogs were placed on diets containing 0, 1 or 3 ppm of endrin. All dogs on 3 ppm had increased organ to body-weight ratios for the kidneys and heart. On the other hand, the ratios of the weights of the livers, brains, spleens and fat to body-weight of dogs fed either 3 or 1 ppm were not significantly different from those of control beagles (See Table II. 14). Some female dogs fed 1 or 3 ppm of endrin had a renal abnormality characterized by a slight tubular vacuolation; this change was also observed in the female control dog. Male dogs in both control and test groups had normal viscera.

From these series of experiments, Treon et al. (1955), summarized the dog experimental results as follows:

(1) Dogs can consume safely about one-half the concentration of endrin in their diets that rats can tolerate, if comparison is made on the basis of comparably prolonged periods of time.

(2) Dogs are at least ten times as susceptible to the toxic effects of endrin as to those of DDT, if judged by the histopathological findings in certain organs of these animals, when fed upon diets containing endrin or DDT in comparable concentrations.

Groups comprising seven male and seven female dogs were fed dietary levels of 0, 0.1, 0.5, 1.0, 2.0 or 4.0 ppm of endrin for two years. Scheduled autopsies were performed on two dogs of each sex from the 0, 1.0 and 4.0 ppm groups at six and 12 months. There were no deaths due to the treatment nor were there any differences in body-weight increase or food consumption between the group. The only clinical abnormalities noted were in one female and two male dogs fed 4.0 ppm, and one female fed 2.0 ppm. These animals showed evidence of, or were observed having, convulsions; the earliest incidence was observed in a male dog after five months on 4.0 ppm. The only change in organ weights were occasional slight increases in liver or liver-to-body-weight ratios in the dogs fed 2.0 and 4.0 ppm. After two years, histopathological examination showed slight vacuolation of hepatic cells in the females and diffuse pigmentation of the hepatic cells in one male and all females. At 4.0 ppm, vascular degeneration and diffuse brown pigment in the hepatic cells was evident in all dogs, without any sex differentiation. In two of the dogs, which had convulsions, autopsies revealed some pathological changes in the brain. All other organs in the dogs fed 2.0 or 4.0 ppm and all organs in the dogs fed 1.0 ppm or less, showed no morphological changes which were considered to be attributable to feeding endrin. There were no significant changes in the blood picture or in the chemical or physical characteristics of the urine attributable to endrin. After two years, levels of liver enzymes, prothrombin time, bromsulphthalein clearance, serum protein

electrophorosis, glucose, urea nitrogen, cholesterol, calcium, inorganic phosphorus, total bilirubin or uric acid showed no changes attributable to endrin feeding (Jolley et al., 1969).

II. B. 4 Carcinogenic Studies

In the chronic studies carried out in mice, rats, and dogs, endrin was not reported to cause an increase in the occurrence of malignant tumors over that of the control animals. Similar results were used by Diechmann, et al., (1970) in the study reported below.

Beginning with weanling rats, varying numbers of rats of both sexes were fed dietary levels of 0, 2, 6, or 12 ppm of endrin throughout their lifetime. No primary malignant hepatic tumors were found in any animals upon histological examination. Two benign hepatic tumors (haemangiomas) were found in one male control rat and the other in a female fed 6 ppm of endrin. Tumor incidence in other tissues also was not significantly different between the control and experimental animals (Diechmann et al., 1970).

TABLE II. 14

RATIO OF WEIGHT OF FAT AND ORGANS TO BODY WEIGHT OF DOGS FED ALMOST 19 MONTHS ON DIETS CONTAINING ENDRIN*

Endrin in Diet, ppm	n	Grams per 100 Grams Body Weight					
		Liver	Kidneys	Brain	Fat	Heart	Spleen
3	4	2.92	0.52[a]	0.91	0.45	0.84[a]	0.41
1	4	3.07	0.39	0.91	0.45	0.76	0.33
0	6[b]	2.86	0.42	0.92	0.52	0.67	0.30

a/ P.0.05 - 0.01

b/ Includes 2 additional male beagles and 2 additional female beagles, less than 2 months older and also eligible for AKC registration, employed as controls in overlapping experiments.

* Treon, et al., (1955)

II.B. 5. Reproduction Studies

Groups of male and female mice were fed endrin at dietary levels of 0 or 5 ppm for 30 days. Test and control mice were than randomly paired and continued on the test diet for a further 90 days, there being a total of 101 pairs in the group fed endrin. The first litters from test animals were significantly smaller than those from the control group. The time taken to produce the first litter was not significantly different between the two groups (Good and Ware, 1969).

Five groups, each comprised of 13-14 pairs of Saskatchewan deer mice (Peromyscus manicalatus) of varying ages, were fed dietary levels of 0, 1, 2, 4, or 7 ppm of endrin over intermitten periods between which times the animals were either fed a normal diet or were subjected to 48 hours starvation. The animals were sacrificed by exposing them to cold stress at -16^{o}C, and the time of death recorded. During feeding, parental mortality increased in proportion to the level of endrin. Young animals were more susceptible than old. Starvation increased mortality in all test groups but not in the controls; this effect was more evident with increasing dose levels. Litter production frequency and mean litter size before and during experimental feed were similar. However, post-natal mortality prior to weaning increased in the young from parents fed 4 or 7 ppm. Endrin adversely affected the survival time during cold stress in the females but not in the males (Morris, 1968).

Groups of ten male and 20 female rats were fed dietary levels of 0, 0.1, 1.0 and 2.0 ppm of endrin over a period of three generations. The F_0 generation was mated after 79 days on the test diets, and the males were rotated. The young from the first litter were discarded at weaning and the parents mated again after ten days to form the F_1b generation. Young from this generation were mated when 100 days old, and this protocol was followed for three generations, using the second litter in all cases. The size of the litter in the F_3 generation from the 2.0 ppm group was significantly larger than that from the controls. Mortality was high in the controls which resulted in a greater percentage survival in the F_3a litter in the 0.1 ppm group and in all F_3b litters in the test groups. The weights of weanlings were comparable to the controls except in the F_3 a litters from the 0.1 ppm, which were significantly less due probably to the larger litter sizes in that group. Examination of the F_3b weanlings revealed no differences in organ to body-weight ratios. It was stated that were no histological abnormalities, but details of the pathology were not available. Fertility, gestation, viability and lactation indices did not indicate that endrin affected any of these parameters (Hine et al., 1968).

No eggs were produced from quail which received 1 ppm of endrin in their diet either as winter maintenance or during the reproductive period (DeWitt, 1955).

misplaced data

There was reduced egg production in pheasants, fed 10 ppm of endrin, but not at 2 ppm or less. Survival of the chicks to two or six weeks was also markedly reduced at 10 ppm but not at lower doses (DeWitt, 1965).

Hen eggs were injected with 0.5 or 5 mg of endrin per egg. The hatching rate was 40 or 20 percent, respectively (Dunachie and Fletcher, 1966).

When 0.2 or 2.0 mg of endrin was injected into the yolk of fertile eggs incubated for seven days, the hatchability was 40 and 6.9 percent, respectively (Smith et al., 1970).

The reproduction studies with endrin in various mammalian and avian vertebrate species, including chicken egg injection hatchability data, indicate that endrin had no influence on maturation but fetal and postnatal mortality were increased.

II. B. 6. Teratogenic Studies

No teratogenic studies, per se, have been carried out on endrin. No teratogenic effects were noted in the reproduction studies cited above. However, this can not be taken as conclusive evidence of the lack of teratogenic potential of endrin.

II. B. 7. Special Studies on the Photoisomerization Product of Endrin

When endrin is irradiated with short wavelength ultraviolet light, the delta-keto compound is formed in 37 percent yield as well as an aldehyde in 9 percent yeld. Under the influence of sunlight, only the ketone is formed. The ketone is about a quarter as toxic to rats as endrin and, like endrin, is more toxic to the male than to the female (Soto and Diechmann, 1970).

II. C. Human Toxicity

II. C.1. Signs and Symptoms of Poisoning

The major clinical manifestation of endrin intoxication in man are convulsive seizures of several minutes duration followed by semi-consciousness. More serious symptoms are continuous convulsions, high fever, and decerebrate rigidity prior to death. Mild symptoms of poisoning include dizziness, weakness of the legs, abdominal discomfort, and nausea. Temporary deafness and insomnia may also occur. It has been estimated, based upon reports of outbreaks of poisoning, that 0.2-0.25 mg/kg bodyweight will produce a single convulsion in man, and that repeated convulsions will result from 1 mg/kg (Hayes, 1963).

II. C.2. Treatment and Prognosis of Intoxication

First aid in the case of accidental skin contamination should consist of immediate removal of all contaminated clothes, including underwear, and washing of the contaminated skin and hair with soap and water. All contaminated clothing should be changed and laundered before re-use.

In the case of ingestion, vomiting should be induced and the stomach emptied as quickly as possible.

If the patient is unconscious, a free airway should be ensured. If respiration has stopped, aritficial respiration should be employed.

Medical treatment is largely symptomatic and supportive and directed against convulsions and anoxemia. Carbonadsorbens may be given. Sodium sulphate may be administered as a laxative. Oily laxatives or milk should not be given. Morphine, epinephrine, and

noradrenaline are contra-indicated .

An unobstructed airway must be maintained. When needed, oxygen and/or artificial respiration must be given.

If prompt and adequate treatment is given, then death can be prevented and even the severest intoxication will recover completely within some weeks (Princi, 1957). Furthermore, EEG's will return to a normal pattern within months (Princi, 1957; Hoogendam et al., 1962 and 1965).

Administration of phenobarbitone may both control prodromal symptoms and prevent convulsions. When convulsions do occur barbiturates should be given by slow intravenous infusion, e.g., thiopentone sodium, 10 mg/kg, with a maximum of 750 mg for an adult. The administered dose should be sufficient to control convulsions.

II. C. 3. Observation of Intoxication in Man

In one incident 59 people became ill from the ingestion of bread accidentally containing up to 150 ppm of endrin, but there were no fatalities (Davies and Lewis, 1956). Calculations based on the amount of bread consumed suggested that an intake of 0.2-0.25 mg/kg could produce a convulsion (Hayes, 1963), whereas the maximum amount consumed was estimated to have been 1 mg/kg body weight (Zavon, 1961).

Data on the pathology of 60 fetal cases of endrin poisoning, 41 of which involved suicide, have been published by Reddy et al., (1966). No specific histopathological organ changes were observed. These data do not include any reference to the size of the doses ingested. However, the toxic doses of endrin were estimated to be 5-50 mg/kg by the oral route; the lethal dose of endrin was estimated to be about 6 grams (Reddy et al., 1966).

Endrin has been found at concentrations of up to 400 mg/kg in the fat and up to 10 mg/kg in other tissues of people who have been fatally poisoned poisoned. Hates (1963 and 1966).

Van Raalte (1965) extracted from the world literature all cases of fatal endrin poisoning known at the time. A total of 97 cases were reviewed of which 69 cases were suicide, 24 accidental ingestion, 4 occupational cases from endrin spraying. No fatalities were reported as a result of endrin manufacture and formulation.

Coble et al., (1967) reported 3 cases of non-fatal convulsive endrin poisoning in the United Arab Republic resulting from the consumption of bread made from endrin-contaminated flour. In the first case, the serum endrin level was 0.053 ug/ml; 30 minutes after the convulsion endrin could not be detected ($<$ 0.004 ug/ml) in samples of the cerebrospinal fluid. Twenty hours after the onset of convulsions, the serum endrin level had fallen to 0.038 ug/ml; 10 hours later, it was 0.021 ug/ml. In cases 2 and 3, no endrin was detected in the blood 8-1/2 and 19 hours, respectively, after convulsions.

A total of 874 persons were hospitalized, and there were 26 deaths in several outbreaks of poisoning in Saudi Arabia in 1967 due to consumption of bread containing endrin. Approximate average levels in the bread in various outbreaks were 48, 1500, or 400 ppm, corresponding to a percentage of fatalities of 1.4, 9.5, and 0.4, respectively, among those poisoned. Blood from patients contained 0.007-0.032 ug/ml endrin. Signs and symptoms were typical of central nervous system stimulation, and all survivors rapidly returned to normal (Weeks, 1967).

II.C. 4. Symptomatology, Treatment, and Prognosis of Intoxication

Frequently, the first indication of acute endrin poisoning is a sudden epileptiform convulsions, occurring from 30 minutes to up to 10 hours after exposure (Weeks, 1967). The convulsions last for several minutes and are usually followed by a semi-conscious state for 1/4-1 hour (Coble et al., 1967). Death or permanent brain damage may ultimately occur resulting from anoxemia due to prolonged convulsions (Jacobziner et al., 1959, Coble et al., 1967). In less severe cases of endrin poisoning, the primary complaints are headache, dizziness, abdominal discomfort, nausea, vomiting, insomnia, agressiveness and, rarely, slight mental confusion (Coble et al., 1967; Week, 1967). The prognosis is good if cerebral damage by prolonged anoxemia is avoided. Recovery to full normal health in such cases is rapid and usually complete within a few days (Davies et al., 1956). No specific findings from acute endrin poisoning have been reported at autopsy (Reddy et al., 1966; Coble et al., 1967; Weeks, 1967). The rapidity of the onset of signs and symptoms, predominantly of central nervous system stimulation, and the rapid return to normal among those who survive is typical for an intoxication with an organochlorine insecticide (Weeks, 1967). The recovery from an endrin intoxication is quicker than that from the other cyclodiene insecticides.

Studies in human subjects experiencing intoxication from endrin (Coble et al., 1967; Weeks, 1967) and from occupational workers (Hayes and Curley, 1968; Jager, 1970) have demonstrated that endrin

rapidly disappears from the blood in cases of acute intoxication and cannot be detected in the fat or blood of people exposed to endrin unless symptoms of intoxication are evident.

II.D. Epidemiology

Endrin has been included in most of the surveys of chlorinated insecticide levels in adipose tissue and blood. Even in those areas where endrin is most extensively used (e.g., India and Lower Mississippi area) endrin could not be found in human subcutaneous fat or in blood from the general population at the limit of detection of 0.03 mg/kg and lower (Kunze et al., 1953; Hoffman et al., 1964; Dale et al., 1965; Zavon et al., 1965; Novak et al., 1965; Robinson et al., 1965; Wiswesser, 1965; Hayes et al., 1965; Brown 1967; Hayes, 1967; Wasserman et al., 1968; Hayes et al., 1968; Robinson, 1969). Levels of the 9-keto metabolite of endrin in four human fat samples were all less than 0.0004 ppm (Richardson, 1970).

II.D.1. Surveillance Studies of Occupationally Exposed Workers

In Treon's review of the toxicology of endrin (1956) he states: "These studies (on workers handling endrin) reveal that harmful physiological effects to workers are found only in those instances where excessive absorption has occurred either in the form of an acute dose or subacute doses from unusually careless handling. No established cases of chronic illness from exposure to endrin are on record".

In a manufacturing plant in the U.S.A., medical supervision of workers exposed for a period of 1-19 years (average 12 years) failed to reveal any unreasonable adverse effects (Hayes et al., 1967).

In these occupationally exposed workers no endrin could be found in the subcutaneous fat.

Van Dijk (1968) examined serum alkaline phosphatase levels of 15 endrin operators in November 1964, July 1965 and February 1966 respectively. Some of these operators had been working in the endrin plant for periods up to 8 years. No significant change in the alkaline phosphatase was found.

Among workers in a plant manufacturing endrin and a number of other pesticides, no detectable amounts of endrin were found in samples of plasma, fat, or urine. Exposure was for an average time of 2,106 hours. Based upon the limit of detection, the levels of endrin were below 0.0030 ppm in plasma, 0.03 ppm in fat and 0.0016 ppm in urine. Endrin has, however, been detected in the serum and urine of people who received amounts sufficient to produce intoxication (Hayes and Curley, 1968).

Serum alkaline phosphatase was determined in 30 workers who had been exposed to endrin for periods from six weeks to eight years. There was no difference in the levels found in the exposed group and those found in a group comprising nine unexposed individuals, nor was there any relationship detected between the phosphatase levels and the duration of exposure of the workers (Shell, 1965).

In 45 operators of the endrin plant, of Shell International Ltd., blood concentrations have been determined at least once a year since 1964. Endrin has never been found in the blood at a detection level

of 0.01 ug/ml (since December 1965, 0.005 ug/ml. No worker has ever been transferred because of an elevated endrin level in blood (Jager, 1970).

Jager (1970) reported the occurrence of endrin in the blood of formulators handling endrin.

Twenty percent endrin was accidentally splashed with emulsifiable concentrate on the hand of a worker filling a drum. He immediately took a shower with soap and water and changed clothes. A blood sample taken one hour after the accident contained: endrin, 0.09 ug/ml; dieldrin and telodrin below detection level. This man developed no signs or symptoms of intoxication. Five days later the endrin level in his blood was $\leq$ 0.005 ug/ml.

A formulator handled technical endrin powder carelessly, producing a lot of dust, disobeying instructions to wear a dust mask. After having worked for 4 hours he sustained a convulsive seizure which was treated with phenobarbital, 60 mg every 3 hours for one day. Afterwards, he complained of headache only. The next day, he felt well. The following blood levels of pesticides were found:

Directly after the convulsive seizure:	0.08 ug/ml endrin, 0.11 ug/ml dieldrin;
24 hours later:	0.02 ug/ml endrin, 0.11 ug/ml dieldrin;
4 days after the 2nd samples:	$\leq$ 0.005 ug/ml endrin, 0.10 ug/ml dieldrin.

Four colleagues working next to the worker cited above, but who had been wearing dust-masks were examined at the same time and showed endrin levels in the blood of 0.01, 0.01, 0.005, and $\leq$0.005 ug/ml, respectively. None of these workers had signs or symptoms of intoxication, notwithstanding the fact that one of them had in addition to 0.01 ug/ml endrin, a dieldrin level of 0.18 ug/ml in the blood.

An operator was accidentally splashed with 20% endrin emulsifiable concentrate. He showered and changed clothes 10 minutes after the accident. Treatment consisted of prophylactic oral doses of phenobarbital 60 mg every 4 hours for 24 hours and close observation. No signs or symptoms of intoxication were noted. The following blood levels were found: 40 minutes after the accident: 0.027 ug/ml endrin, 0.01 ug/ml dieldrin; 12 hours after the accident: 0.025 ug/ml endrin, 0.01 ug/ml dieldrin.

The endrin blood levels probably peaked between the first and second samples , i.e., twtween one and twelve hours after the accident.

It is estimated that the blood level of endrin below which no signs or symptoms of intoxication occurs is in the range of 0.05 - 0.100 ug/ml. Measurable blood levels (detection level 0.005 ug/ml) occur only after gross overexposure. The half-life of endrin appears to be approximately 24 hours. Medical control of a group of workers exposed over periods up to 13 years has failed to show any effects of long-term exposure. The blood picture, results of urinalysis, SGOT and SGPT, alkaline phosphatase and lactic dehydrogenase remained all

within normal limits. Electroencephalographic changes which were occasionally noted returned to normal. Absenteesism due to disease or accidents was comparable to that of a control group. Because of the short half-life of endrin, it is (unlike dieldrin) impossible to calculate the average level of exposure of the workers to endrin (Jager, 1970).

II.D.2. Steroid Hormonal Metabolism of Endrin Workers

6-B-Hydroxycortisol Excretion in Urine

Many drugs and chemicals may stimulate the hydroxylation of steroids in the body, amongst them phenobarbital, diphenylhydantoin, phynylbutazone, and N-phenylbarbital (Werk et al., 1964; Burstein et al., 1965; Kuntzman et al., 1966; Conney, 1967; Kuntzman et al., 1968).

The studies of these investigators suggest that the measurement of the urin ary excretion of 6-B-hydroxycortisol, a metabolite of cortisol, compared with the excretion of total 17-hydroxycorticosteroids, which is not changed by the inducers, might be a useful index for the induction of hydroxylase in liver microsomes in man. Kuntzman et al., (1968) found that 6-B-OH-cortisol excretion in man is normally below 400 ug/day, whereas in situations in enzyme induction, such as in N-phenylbarbital treated human volunteers, excretions exceeding 400 ug/day were found.

For this study, excretion of 6-B-OH-cortisol and 17-OH-corticosteroids were determined in 20 non-insecticide exposed four-shift workers.

All urine samples were collected between 8 a.m. and 11 a.m. on the last day of the morning shift. Hormone determinations were made by Searle Scientific Services, Lane Road, High Wycombe, Buck, U.K., who also added their own control group of 10 men. By determining the ratio between the excretion of 6-B-hydroxycortisol and 17-OH-corticosteroids, the factor of diuresis is eliminated and there is no need for examining 24 hour urine samples. Therefore, this method is convenient for use in healthy workers.

The results of these determinations are summarized in the Figure II.4. From this it is clear that geometric means and ranges of the ratio in aldrin-dieldrin workers do not differ from those in the control groups. In this group of 13 aldrin-dieldrin workers the range of p, p'DDE in the blood was 0.006-0.042 ug/ml with an arithmetic mean of 0.015 ug/ml, which is in the same range as in the general population. Dieldrin levels in the blood of these 13 workers ranged from 0.018-0.110 ug/ml with an arithmetic-mean of 0.051 ug/ml. In these workers, who had reached a steady state level as far as dieldrin is concerned, the mean leave corresponds, according to the formula of Hunter and Robinson (1969), to an average equivalent oral daily intake of 593 ug/man/day, which is at least 85 times the intake of the general population in the U.K. and the U.S.A. for this insecticide. But even the man with highest dieldrin level in this group (0.h10 ug/ml, or 183 times the present blood level of the general population--showed, apart from a p,p"DDE level of 0.014 ug/ml, a 6-B-hydroxycortisol ratio of $\frac{166}{5.6} = 29.6$, both values being

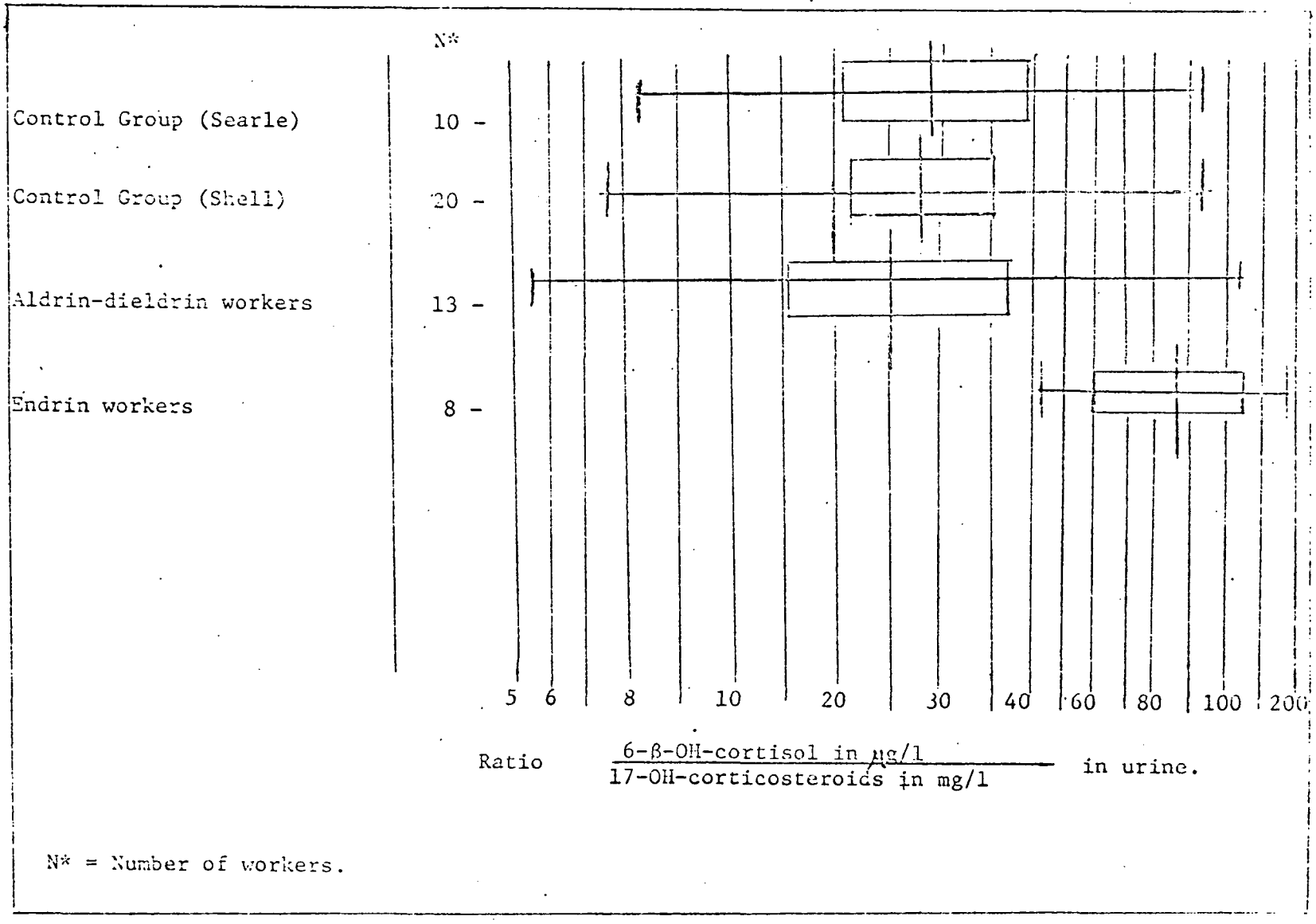

Figure II.4. Ratio $\frac{\text{6-β-cortisol in µg/l}}{\text{17-OH-corticosteroids in mg/l}}$ in urine. (Geometric mean and 95% confidence limits of this mean and of all observations).

quite normal in comparison with the control groups.

The ratio between the excretion of 6-B-OH-cortisol and 17-OH-corticosteroids was also determined in 8 endrin workers.

It was found that the range and the geometric mean of this ratio, was significantly higher when compared iwth those of the control groups and the aldrin-dieldrin workers. The 6-B-OH-cortisol levels in urine were higher in this group, whereas 17-OH-corticosteroids and 17-keto-steroids did not show marked differences between groups. Of course, these levels expressed in mg/l are dependent on the total urine production per day.

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Chapter III

Toxicity, Fate, and Significance of Endrin in the Environment

III.A. Introduction - Endrin is the most toxic chlorinated hydrocarbon pesticide. It is persistent and residues in soil, water and animal tissue have resulted from uses to control insects, birds and rodents. Records show substantial reductions in populations of non-target species in some areas where endrin has been used. These factors have aroused serious concern among various groups of conservationists and other interested individuals lest some non-target wildlife populations become decimated or extirpated.

III.B. Toxicity to Fish - Acute toxic effects observed under field conditions generally have resulted from careless application, disposal, or accidental spillage (Johnson, 1968). Environmental variables such as the types pH and temperature of soil or the mineral and oxygen content, turbidity and pH of water influence persistence in soil and the acute toxicity threshold of fishes.

Pesticides have been used in such quantities that they have become pollutants of terrestrial and aquatic environments which ranks second in importance to all other industrial wastes. Surveys of fish kills carried out by the U.S. Public Health Service (1960, 1961, 1962),demonstrated that pesticides were the cause of 32 percent of all fish kills in 1960, 21 percent in 1961, and 18 percent in 1962. Numerous fish kills have been reported in some areas of the Mississippi Delta adjacent to lands where, on a 10-year average, 10 lb. endrin per acre were applied each year (Tangwell, 1965). Thus, fish killed by pesticides exceeded in number those killed by refinery, paper mill, or plating wastes.

III.B.1. Acute Studies - Results of laboratory studies are usually reported as LC_{50} or TLm values for exposure periods of 1, 2, 3, or 4 days. Tests by Iyatomi, et al., (1958) were conducted on young carp; (Cyprinus carpio), and goldfish, (Carassius auratus). LC_{50} values for carp exposed for 48 hours varied from 0.004 to 0.008 ppm at 17-28°C and 0.002 ppm for goldfish at 27-28°C. Endrin becomes less toxic to fish as water temperature is lowered, and fish eggs and larvae are more resistant than adults. Lethal concentrations determined by Henderson, et al., (1959) were 0.006 ppm for bluegill (Lepomis macrochirus) and 0.00196 ppm for goldfish at 96-hour exposure.

Static 96-hour bioassays with 12 insecticides were conducted at 24°/00 salinity, 20°C and pH8 with the following seven species of estuarine teleosts (American eel, Anguilla rostrata; mummichog, Fundulus heteroclitus; striped killifish, Fundulus majalis; bluehead, Thalassoma bifasciatum; striped mullet, Mugil cephalus; Atlantic silverside, Menidia menidia; and northern puffer, Sphaeroides maculatus. Endrin was consistently the most toxic compound tested. The LC_{50} values of each species in 96 hour tests with endrin is shown in Table III.B.1. ranged from 0.05 to 3.1 micrograms per liter. The range in LC_{25} (96 hrs.) and LC_{75} (96 hrs.) for endrin in seven species of estuarine teleosts in ppb were: LC_{25}-0.03 to 1.9; and LC_{75}-0.08 to 4.5. When the relative toxicity of organochlorine insecticides to marine organisms were compared, it was concluded that teleosts were less resistant than mollusks and about equal in sensitivity to decapod crustaceans (Eisler, 1970b).

Table III.B.1.

ACUTE TOXICITY OF ENDRIN TO ESTUARINE FISHES*

SPECIES	TOTAL NUMBER FISH	LC_{50} in Micrograms Per Liter (ppb) Active Ingredients At--		
		24 hr.	48 hr.	96 hr.
Atlantic silverside	50	0.5	0.08	0.05
Bluehead	25	0.6	0.5	0.10
Striped killifish	60	1.8	0.7	0.30
Striped mullet	40	0.7	0.3	0.30
American eel	70	1.1	0.6	0.60
Mummichog	49	1.8	0.7	0.60
Northern Puffer	60	3.1	3.1	3.10

*Data from Eisler, 1970b

Toxicities of endrin to spring chinook (Oncorhynchus tshawtscha) and coho (Oncorhynchus kisutch) salmon, rainbow trout (Salmo gairdneri), bluegill, mosquitofish (Gambusia affinis), guppies (Lebistes reticulatus), and marine threespine sticklebacks (Gasterosteus aculeatus) were reported by Katz and Chadwick (1961). Coho salmon were the most sensitive with a 96-hour TLm of 0.27 ppb; rainbow trout were 0.90; chinook salmon, 0.92; guppies, 0.90; bluegills, 0.60; and stickleback, 0.75 (all ppb).

Screenivasan and Natarajan (1962) tested endrin as a fish toxicant to eliminate undesirable species. Their data showed the following LC_{50} values for 24-hours: Tilapia mossambica, 0.01 to 0.013 ppm; Channa spp., 0.01 to 0.08; Barbus spp., 0.008 to 0.01; Danio acquipinnatus, 0.006 to 0.008; Rasbora daniconius, 0.006 to 0.009; mosquitofish, 0.010 to 0.012; and carp, 0.008 to 0.11.

The toxicity of some insecticides to the Indian catfish, Heteropneustes fossilis, was studied by Saxena and Aggarwal (1970). This species died within 5 hours in an aqueous solution containing 0.12 ppm endrin. At a concentration of 0.014 ppm, fish could survive only for 12 to 16 hours, while exposure to 0.00598 ppm caused death within 24 hours. The greatest concentration at which the fish could survive was 0.00578 ppm.

The effect of potential mosquito larvae control chemicals upon mosquitofish, a natural predator, was evaluated by Mulla (1963). When applied at rates of 0.1 lb./acre, endrin produced a complete kill for 2-3 days, and moderate mortality up to a week post-treatment. Endrin applied at 0.5 lb/acre produced 100% mortality up to 20 days after treatment.

A major obstacle in insecticide use for rice borer control in paddy fields is the high toxicity of many insecticides to fish growing in paddy fields under natural or artifical conditions. The Department of Agriculture, Malaya, studied the toxicity of various insecticides to fish and found that exposure for 20 hours to 0.45 ppb endrin was lethal for young Ophicephaius striatus. These results support an earlier opinion that endrin is too toxic for use at the normal rate of application (1/2-1 pound per acre). Endrin was found, from tests in Selangor, to be highly toxic to ducks as well as to fish. The solvent oil also appeared to be a contributing factor in the toxicity of insecticides (Anon, 1957). With marine species, spot (Leiostomus xanthurus), the lethal concentration of endrin was 0.1 ppb after 5 days exposure (Lowe, et al., 1966).

Brungs and Bailey (1966) studied the influence of suspended solids on the acute toxicity of endrin to fathead minnows (Pimephales promelas). TLm values for controls (clear water) ranged from 0.47 to 0.52 ug/l.; while those containing clay in suspension were 0.37 to 0.50 ug/l. Similar work by Ferguson, et al., (1965) indicates that little of the endrin associated with bottom sediments becomes available to fish within a short time.

Blood levels of endrin in gizzard shad (Dorosoma cepedianum) and channel catfish (Ictalurus punctatus) were studied to determine threshold levels of acute toxicity. The blood from dead shad had endrin levels greater than 0.14 ug/g (av. 0.24) blood from live fish contained less than 0.10 ug/g (av. 0.06). Two gizzard shad with levels above 0.10 ug/g

survived. Similar results were observed in shad exposed under field conditions (Brungs and Mount, 1966). Results obtained when channel catfish were exposed to continuously renewed water containing endrin indicated blood threshold at approximately 0.30 µg/g, with minimal overlap between living and dead fish (Mount, et al., 1966). A continuous flow laboratory system, where pesticide concentrations were kept constant, was used by Mount and Putnicki (1966) to examine accumulation of endrin by fathead minnows. Fish exposed to water containing 0.000015 ppm endrin had total body concentrations 10,000 times those in the water. These authors also verified the presence of endrin in concentrations from 2 to 4 µg/g in approximately 40 muscle samples of dying channel catfish. Blood samples taken from dying channel catfish in the 1963 Mississippi River fish-kill area ranged from 0.40 to 0.56 µg/g (Annon., 1964).

Endrin toxicity to resistant and susceptible mosquitofish was assessed by Burke and Ferguson (1960) in both static and flowing solutions. Resistant fish were obtained from cotton field drainage ditches while susceptible ones came from insecticide-free ponds. The toxicity of a given concentration of endrin was greater than constantly renewed solutions than under static conditions. In flowing-water rates of mortality of susceptible specimens exposed at 2.0 ppb was roughly comparable to mort. rates in the resistant forms exposed to 200.0 ppb.

Relative toxicity of endrin to four salmonid species was tested by Post and Schroeder (1971). Species used included brook trout (Salvelinus fontinalis), rainbow trout, cutthroat trout (Salmo clarki), and coho salmon. TLm figures in ppb were: brook trout

0.355 to 0.59; cutthroat trout, 0.113 to 0.192; rainbow trout, 0.405; and coho salmon, 0.77. The two values each given for brook and cutthroat trout showed the effects of different average body weights. Endrin was 66% more toxic to 1.15 g brook trout than to 2.04 g brook trout and 70% more toxic to 0.37 g cutthroat trout than to 1.25 g fish.

Earnest and Benville (1972) provided data on acute toxicity of endrin to two surf fishes from the estuarine region of San Francisco Bay. With the shiner perch (Cymatogaster aggregata), 96-hour TLm_{50} was 0.8 ug/1 in static and 0.12 in intermittent flow bioassays. Comparable data for the dwarf perch (Micrometrus minimus) were 0.6 ug/1 for static and 0.13 for intermittent flow tests.

Another study compared results of simultaneous static and dynamic bioassays of endrin in Pimephales promelas (fathead minnow) which were acclimated to the laboratory for one month before testing. Endrin was used at concentrations of 1.0, 0.5, 0.34, and 0.22 ppb. The LC_{50} (48 hour, 18°C) for endrin was 0.77 ppb (static) and 0.5 ppb (dynamic) or 0.74 times greater for dynamic as compared with static conditions. The LC_{50} (96-hour) for endrin was 0.77 ppb (static) and 0.39 (dyanamic). LC_{50}'s from static tests were slightly higher than those from dynamic tests (Lincer, et al., 1970).

Carp eggs, stripped and fertilized in vitro, were subjected to a commercial formulation of endrin at concentrations of 0.001, 0.01, 0.10, 1.0, 5.0, and 10.0 ppm active ingredient. Embryo viability was not signficantly affected at concentrations less than 1 ppm. However, embryo death at the gastrula and blastula stages resulted at concentrations of 5 and 10 ppm, respectively (Malone and Blaylock, 1970).

Lowe (1966) measured 24-hour LC_{50}'s in flowing seawater for spot, striped mullet (Mugil cephalus), menhaden (Brevoortia patronus), longnose killifish (Fundulus similis), and sheepshead minnows (Cyprinidon variegatus). Acute toxicities for these five species in ppb were: striped mullet, 2.6; spot, 0.45; menhaden, 0.80; sheepshead minnow, 0.32; and longnose killifish, 0.23. The 24-hour TLm for previously non-exposed bluegills from Louisiana showed 2.0 ± 0.27 ppb, and 2.0 ppb was reported as the "lethal exposure concentration" (Bennett and Day, 1970).

Ferguson, et al., (1965) measured TLm values to endrin were for black bullheads (Ictalurus melas) and mosquitofish in the Mississippi River. Values for four populations of mosquitofish varied from less than 0.5 to 120 ppb and for the black bullhead from 0.37 to 2.5 ppb. The acute 36-hour TLm values were measured by Ferguson and Benghan (1966) for yellow bullheads (Ictalurus natalis) taken from sprayed and unsprayed areas in Mississippi. The results show a 60-fold endrin resistance in fish from treated areas but both levels are well within the established "highly toxic range" (up to 1.0 ppm) uses as a "rule of thumb" in pesticide label cautions.

Monthly insecticide tests on two Yazoo-Mississippi Delta oxbow lakes were made by Bingham (1970). Varying adjacent agricultural use patterns resulted in high pesticide levels in one lake and much lower levels in the other. Thirty-six hour bluegill bioassays in endrin showed TLm values of Wolf Lake fish 20-fold greater than Mossy Lake fish, or 300 ppb and 15 ppb, respectively.

Butler (1969) discussed the significance of residues in estuarine fauna. He stated that test procedures showed that 48-hour TLm_{50} values for endrin for various species of crustaceans and fishes were usually 1 ug/g or less within normal ranges of environmental salinity and temperature.

Adult northern puffers, Sphaeroides maculatus, were exposed to graded concentrations of endrin. All fish subjected to 10.0 ppb of endrin died within 24 hours. At concentrations of 1.0 ppb or lower, no mortality occurred within 96 hours (Eisler and Edmunds, 1966).

Eight extensive fish kills occurred in agricultural drains of the Sacramento Valley in July, August and September, 1963. Field investigations revealed that five kills were associated with using endrin in apple pomace bait to control cutworms in sugar beets. Growers applied the endrin bait and then irrigated the field to force cutworms to the soil surface where they could find the bait. Heavy fish losses were attributed to water draining from the field. In one of the five reported endrin-related kills, as many as 30,000 fish were estimated to have been killed (Hunt, 1964).

III.B.2. Chronic Studies - Effects of endrin on aquatic animals and fish eggs exposed for long periods has been studied. Lowe, et al., (1966) observed spot, Leiostomus xanthurus) which were reared to sexual maturity in sea water containing sublethal concentrations of 0.05 ppb. These fish showed no symptoms of poisoning during 8 months exposure. No pathology was found at this exposure level. In contrast, a 3-week exposure to a

near-lethal concentration (ca 0.075 ppb) produced systemic lesions to the brain, spinal cord, liver, kidneys, and stomach. Test fish surviving long-term exposure to endrin were not affected by subsequent stress situations, such as rapid salinity change or periods of starvation. Separate groups of spot were exposed to several concentrations of endrin for periods up to 19 days. After five days exposure, all fish were dead in concentrations of 0.1 ppb and above. A lower concentration of 0.075 ppb killed no fish until the ninth day of exposure and 19 days were required to kill 57% of the population. The 0.05 ppb concentration was sublethal (Lowe, 1966).

Effects of endrin on egg hatching of the longnose killifish (Fundulus similis) were studied by placing fertilized eggs in petri dishes containing 0.001 and 0.0001 ppm endrin with daily changes in solution. Hatching started 15 days after fertilization and continued for 1 week. Hatching rates were 40 and 45% of the control at these concentrations while mortality of fry was 6% for each group.

Static bioassays with endrin were conducted on mummichogs Fundulus heteroclitus, at 24°/oo salinity, 20°C and ph 8.0. Most mummichogs that survived high LC_{75}, 24 hr.) levels of organochlorine insecticides for more than 120 minutes died by day 21 post-exposure. Shorter exposures produced fewer deaths. In holding studies, mortality was high during a 240-hour observation period following 96-hour exposure (Eisler, 1970a).

Temperature, salinity, and pH of the medium all influence pesticide-induced mortality. Toxicity of organochlorine insecticides to mummichogs

was greatest at intermediate temperatures (20°- 25°C.), and least at intermediate pH (7-8) within the ranges tested. Salinity of the medium had little or no measurable effect on toxicity. Concentrations of endrin fatal to 50 percent of mummichogs at 96 and at 240 hours were 0.60 and 0.33 ppb, respectively. The LC_{50} ratio (96 hrs./240 hrs.) was 1.8. Mortality of mummichogs following sublethal exposure to endrin showed a ratio of LC_{50} (96 hrs.) to LC_{50} (96 hrs./240 hrs. post-treatment) of 1.09.

A study was made on effects of short-term immersion in high concentrations of pesticides. The organochlorine compounds tested produced similar mortality patterns by day 21 post-exposure. These consisted of high survival when exposure was less than 120 minutes, partial survival when exposed between 120 and about 360 minutes, and few or no survivors at exposures of 720 minutes and greater. Loss in toxicity occurred with several insecticides after the test medium had been aerated for 96 hours before adding fish. However, this treatment caused endrin to be more toxic to mummichogs.

Mummichogs survived immersion in high (LC_{75}, 24 hrs.) concentrations of various pesticides without apparent effects, when exposure did not exceed 120 minutes for organochlorine compounds. Animals that survive exposure to various concentrations of different toxicants with no signs of external damage frequently exhibit abnormal rates of growth, reproduction, or death during the post-exposure period. These observations suggest that in areas of extensive tidal flushing, aerial spraying immediately before very high tides could be accomplished with relatively minor consequences to non-target species (Eisler, 1970a).

Chronic endrin poisoning in goldfish was examined by Grant and Mehrle (1970). They found that endrin incorporated into the diet of male goldfish for 3-4 months affected growth, thyroid activity, serum characteristics, body fat, gonad development, behavior and mortality. Response to endrin dosage differed according to concentration. Low doses (4.3 - 43 µg/kg body weight/day) either caused no discernible effect or stimulated growth rate and higher body fat content. Highest doses (143 and 430 ug/kg) caused mortality, decreased growth, and other chronic symptoms of endrin intoxication.

Bennett and Day (1970) investigated the absorption at sublethal concentrations of endrin by bluegills which were obtained from a non-agricultural area and probably had no prior exposure to endrin. Absorption was measured for the entire body, skeletal muscle and liver. Initial exposure showed a sharp increase in endrin levels followed at at 7 to 8 hours by a decline to a low at 12 hours. Later the concentration in body tissue increased to a high at 24 hours. The decrease between 7-12 hours suggests that the fish were metabolizing and/or excreting endrin. but why the 12-24 hr. effect?

The effects of endrin upon reproduction of a fresh water fish, the medaka (Oryzias latipes), were studied by Johnson (1967). Sexually mature fish were exposed continuously for 23-45 days to renewed solutions containing 0.04-1.32 µg/l endrin. Concentrations of 0.6 µg/l were lethal to most adult fish. Concentrations of 0.3 µg/l and lower had no apparent effect on adults, and survival, growth and spawning activity corresponded

to that of the controls. Medaka affected at higher concentrations displayed behavior patterns that made courtship and fertilization impossible. Spawning behavior was not affected at lower concentrations but endrin accumulated in the eggs. Resulting mortalities affected reproduction as completely as disruption of behavior of the adults. Depending upon the concentration to which the parent was exposed, fry died or failed to develop normally. Eggs from non-exposed parents were incubated directly in endrin solutions. Massive doses of endrin (10 mg/1 and greater) in the water had no apparent effect on embryo development until the 8th or 9th day when they were about to hatch. Embryos developed tremors, convulsed within the chorion and usually died before hatching. Eggs incubated in solutions containing 15 ug/1 or greater suffered severe endrin toxicity at hatching. Concentrations of 10 ug and less caused hyperactivity and erratic behavior in the hatching fry.

In an experiment with stickleback, the eggs absorb endrin in proportion to the concentrations to which they are exposed, but to a lesser degree than fish. The concentrations in eggs were directly related to effects on hatching fry. Concentration in the egg of 1.8 mg/kg caused erratic fry behavior; 7.8 mg/kg or greater caused severe muscle tetanus.

The chronic toxicity of endrin to bluntnose minnows (Pimephales notatus) and guppies was studied intensively by Mount (1962). Neither species could withstand concentrations greater than 0.5 ppb in water for more than a few of the 29 days of the tests. Less than 50% of the

test fish could live in 0.5 ppb more than 30 days. At the level of 0.4 ppb, about 65% of the fish could survive for more than 30 days. Little mortality was detected at levels of 0.25 and 0.1 ppb in the water. Cumulative effects or tissue damage did not occur in fish which survived in water containing endrin. Fish seemed to recover completely from a single exposure. However, increased activity caused by very low endrin concentrations could be very damaging to fishes in natural waters. This could disrupt spawning and make fish more vulnerable to predation and other decimating factors.

Grant and Mehrle (1973) studied the effect of sub-lethal doses of endrin on rainbow trout (Salmo gairdneri). The authors concluded that endrin caused dysfunction of physiologic processes critical to survival. Mature trout receiving sublethal doses of endrin (4.3 - 145 mg/kg body wt./day in 0.215-7.25 mg/kg of food) were then forced to swim for 1 hour. The insecticide affected serum electrolytes, osmolatily, total protein, cholesterol, cortisol, lactate, glucose, liver glycogen, and growth. Forced swimming alone altered 9 of 16 serum parameters examined. Growth was inhibited appreciably by 145 mg/kg but not by lower doses. Visceral fat accumulated 4.8-8.7 mg endrin/g tissue in the 43 and 145 mg/kg exposures.

III.B.3. Special Studies:

III.B.3.a. Residue - Frost (1969), in discussing the contamination of the world environment by stable pesticides, mentioned that a British study of refined cod liver oil from fish caught close to or north of the

Arctic Circle showed the presence of 0.09 ppm BHC, 0.02 ppm heptachlor, 0.16 ppm dieldrin, 1.65 ppm DDT and derivatives and 0.03 ppm endrin. The spread of pesticide contamination can be partially explained by transfer of the poisonous compounds by river and ocean currents as well as by migratory animals.

Spot (Leiostomus xanthurus) that survived an eight-month exposure to 0.05 ppb endrin were analyzed for residue accumulation. Whole-body analyses showed a residue to 67.0 ppb. Samples subjected to 5-month exposure to the same concentration gave 78.0 ppb residues. No endrin could be detected in fish from this chronic exposure after being replaced for 13 days in uncontaminated water (Lowe, 1966).

The extreme toxicity of endrin to fish causes conjecture as to what the specific action of the toxicant might be. Symptoms appearing during poisoning indicate that the effect is mediated through the nervous system. Mount (1962) attempted to determine the point of entry and the movement of endrin through the body by exposing carp to concentrations of 2.5 to 10 ppb endrin for periods of 2.5 to 28 days. The digestive tract, liver, heart-spleen-blood, and kidney contained the highest accumulations. Maximum concentrations were approximately 160 times greater than in the test solutions. The heart-spleen of a carp exposed 28 days to 2.5 ppb contained endrin residues of 400 ppb. Muscle tissue was low in endrin content. Gills were low or negative. Since the digestive tract was consistently high, Mount concluded that the endrin probably entered the body through the intestine.

Crab and seven species of edible marine fish in the Pacific Northwest were monitored for pesticide levels (Stout, 1968). Endrin levels detected were considered to be an occasional sample contained 0.006 ppm.

Chlorinated hydrocarbon residues were reported for eight representative species of fishes of the lower Colorado River Basin of southern Arizona (Johnson and Lew, 1970). The estimated 345,000 acres of cotton land in the drainage in 1965 received average an application of 1.2 lb./acre of endrin. Despite this usage only trace amounts of endrin were recovered as fish residues. Much higher levels of other chlorinated hydrocarbons occurred. ~ therefore ?

A preliminary report on pesticide monitoring in Louisiana was given by Epps, et al., (1967). Extensive sampling occurred in five separate drainage basins each distinguished by a different type of farming. The areas were: (1) Six Mile Creek, a forested area never cultivated, which served as the control; (2) Tensas River, a large cotton and soybean producing area of the Mississippi Delta with heavy usage; (3) Mermentau River, a rice growing area in Southwest Louisiana; (4) Bayou Chevreuil, an area with heavy usage where sugarcane is the only crop; and (5) Bayou Courtableau, an intensely farmed area in the south-central part of the State where cotton, sugarcane, and rice are grown. Amounts of endrin found in 22 samples of bluegills, 17 shad and 27 catfish are presented in Table III.B.2. In a given stream, variation of residue levels in fish was not wide. No pesticides were used in the Six Mile area. Usage was heavy in the Tensas and Courtableau areas. Endrin was used more extensively in the Chevreuil area; consequently, levels in fish from this area were relatively higher.

Table III.B.2.

Endrin Residues in Fresh Water Fish from Different Drainage Basins in Louisiana (ppm)*

	Angola	Chevreuil	Courtableau	Mermentaus	Six Mile	Tensas
BG	P	P	0.03	N	N	P
Shad	N	0.87	0.04	N	N	P
Cat	0.05	0.31	0.06	N	N	0.01

BG Bluegill, Lepomis macrochirus

Shad Gizzard Shad, Dorosoma cepedianum

Cat Channel Catfish, Ictalurus punctatus

P Present at minimum level of detection

N Not detected

A monitoring program was inaugurated at the Tule and Lower Klamath Lake Wildlife Refuges in Northeastern California because of pesticide poisoning of fish-eating birds. This contamination presumably resulted from irrigation return flow, run-off or leaching of pesticides from adjoining agricultural lands. Samples were collected over a two-year period and endrin occurred frequently. Tui chubs (Siphateles bicolor) accumulated up to 198 ppb. Largemouth bass (Micropterus salmoides) exposed to live-boxes for periods ranging from 80 to 209 days accumulated 15.3 to 107.0 ppb endrin residues. The lower figure was in January when pesticide runoff was at a minimum. The maximum figure occurred in September near the end of the pesticide use season (Godsil and Johnson, 1968).

Pesticide residues from an estuary near Pensacola, Florida were monitored for about 1.5 years. Residues in fish from the estuary rarely exceeded 0.1 ppm. Endrin was found in some samples up to 0.02 ppm (Hansen and Wilson, 1970).

A national pesticide monitoring program sampled residues in fishes from 50 stations located in the Great Lakes and in major river basins throughout the United States. Endrin was reported consistently in samples from only three stations: Luling, Louisiana (Mississippi River); Pine Bluff, Arkansas (Arkansas River); and De Valls Bluff, Arkansas (White River). Thirty of the 50 collection sites recorded endrin-contaminated fish but levels were generally in the 0.01 - 0.10 ppm range. A few higher values recorded were: 1.5 ppm for carp from the Susquehanna River, Maryland; 0.27 ppm for spotted sucker (Minytrema melanops) from Apalachicola River, Florida; 0.14 ppm for striped mullet and also channel catfish from the Mississippi River, Louisiana; 0.11 ppm for smallmouth buffalo (Ictiobus bubalus) and flathead catfish (Pylodictis olivaris) from the Arkansas River, Arkansas; and 0.71 ppm for channel catfish from a Colorado River reservoir in Arizona (Henderson, et al., 1969).

Snead (1970) presented a preliminary report on pesticide residues in commercially produced catfish. Edible portions of the catfish from 147 commercial catfish farms in Mississippi and Arkansas also were analyzed. Pesticide residues were found in small amounts in virtually all fish samples. Endrin residues were detected in 70.6 percent of the

fish from Arkansas and 61.0 from Mississippi. Average endrin residue levels in catfish were .0265 ppm for Arkansas and .0266 from Mississippi. The percentage of endrin residues greater than or equal to the 0.3 ppm level was 2.1 for Arkansas and 1.3 for Mississippi.

Pesticide influence in channel catfish culture in 4 southern states was reported by Grant (1970). Problems in the culture of catfish included reproductive failure, excessive mortality, and abnormal growth and morphogenesis. In a general agricultural area with extensive history of organic chlorine pesticide use, widespread mortalities of both immature and adult fish followed an unseasonable, two-week duration of sub-freezing weather in December. Terminal symptoms were similar to those of pesticide intoxication.

Fish, fish food, and mud were contaminated with endrin, dieldrin and DDT (plus its breakdown products). Endrin concentrations ranged from trace amounts to 0.2 µg/kg, and DDT levels were about 1 µg/kg, based on whole fish weight. Mud contained trace amounts of insecticide, but all three toxicants were found in about 75 % of the diets sampled. Observations of spring spawning revealed high mortality of embryos before hatching, and malformed axial skeletons in hatchlings. Skeletal structure was aberrant - most terata were "tailless," and some had lordosis or scoliosis. The only other conditions known to produce scoliosis in fishes are vitamin C deficiency and maintenance in total darkness. The total body endrin residues in pond-reared channel catfish from 18 sources was within the range < 0.005, 1.01 µg/g (av. 0.13). Contamination of channel catfish

food from 7 sources was < 0.005-0.14 ug/g (av. 0.03). Average value of endrin residues in fat and ovaries of mature channel catfish were, fat--0.5 ug/g (0.1-1.0) in eight samples and ovaries - 0.02 ug/g (ND-0.08) in five samples.

III.B.4. Resistance - The sensitivity to pesticides in three generations of sheepshead minnows was examined by Holland and Coppage (1970). The purpose was to determine whether succeeding generations exposed to DDT could develop resistance to DDT, and "cross-resistance" to endrin. Experimental fish were offspring of survivors of exposures to concentrations of DDT that killed 70% or more of the fish in the previous generation. Control fish were offspring of unexposed fish. Among controls, and the F_1 generation of fish freshly treated with DDT, mortality was 100 percent following exposure to 1 ppb endrin, but only 5% of an equal number in the F_2 generation succumbed. When fish with long history of exposure to DDT received similar treatment with endrin 80 fish from the F_1 generation died, as opposed to a loss of 40 from 70 tested from the F_2 generation. The authors suggest that lipid metabolism and maturation of ova were greatest when parent fish were exposed and that incorporation of insecticides into the ova may be the factor that increased sensitivity.

The susceptibility and resistance of mosquitofish to several insecticides were studied by Boyd and Ferguson (1964). Approximate LD_{50} values for DDD, endrin, aldrin, dieldrin, toxaphene, heptachlor, and lindane were determined for four populations of mosquitofish, Gambusia affinis. Results showed resistance and cross-resistance in populations

having past exposure to insecticides. Evidence favoring a genetic basis for resistance was presented wherein toxicity levels remained constant in progeny of resistant fish reared in the absence of insecticides.

Thirty-six hour LD_{50} values (ppm active ingredient) for endrin to four populations of mosquitofish are presented in Table III.B.3. In these trials 50 fish were used on each level tested.

Table III.B.3.

36-Hour LD_{50} values (ppm) for endrin in four populations of mosquitofish

	Locality			
Insecticide	State College	2 miles South State College	Indianola	Sidon
Endrin LD_{50} (ppm)	0.001	0.008	0.006	0.12

These values indicate a stong correlation between past exposure to insecticides and decreased susceptibility to the test compounds. The values for the untreated State College fish were within the range of those reported for other species of fish (Rudd and Genelly, 1956).

The observed resistance resulting from the selective action of insecticides is probably genetic. Toxicity values for fish at least one and perhaps as many as three generations removed from exposure to insecticides remained essentially unchanged from those of the original selected parental population.

Resistance to endrin in three species of freshwater fish was investigated by Ferguson, Culley, et al., (1964). Mosquitofish (Gambusia affinis) from cotton producing areas in the Mississippi Delta were previously found resistant to most commonly used chlorinated hydrocarbon insecticides. As much as 300-fold resistance persisted among the first few generation of resistant fish reared in insecticide-free environments. Continuing concern prompted additional investigation to determine whether resistance was peculiar to mosquitofish, or an adaptation also possessed by other fishes living in heavily treated areas. Tolerances of Mississippi Delta golden shiners (Notemigonus crysoleucas), bluegill sunfish (Lepomis macrochirus), and green sunfish (Lepomis cyanellus) were determined for endrin. Delta fish were obtained from Twin Bayou near Indianola, Sunflower County, Mississippi which is bordered for several miles by large cotton plantations and subject to insecticide contamination by runoff, drift, and possibly some direct application. Comparative dosage-mortality data were collected for fish with minimal prior exposure to insecticides from non-agricultural areas near State College, Oktibbeha County, Mississippi.

Tests conducted in March and April indicated much higher tolerances than those of June and July. A change was most apparent in tolerances of green sunfish to endrin where the 36-hour TLm declined from 575 ppb to 160 ppb. The fish community at Twin Bayou apparently consisted of 7 species, some of which were represented by incredibly large numbers of individuals, e.g., mosquitofish. During nearly 100 hours of collecting, no upper trophic level carnivores such as largemouthed bass or crappie were observed. This may be the result of biological magnification of

insecticides having a more severe effect on animals occupying a position at the top of a food chain.

Comparative toxicity of endrin to resistant (Twin Bayou) and non-resistant (State College) populations of three species of freshwater fish is presented in Table III.B.4.

Table III.B.4.

36-hour TLm values to endrin (ppb) observed in resistant and non-resistant fish

Golden Shiners		Bluegills		Green Sunfish	
State College	Twin Bayou	State College	Twin Bayou	State College	Twin Bayou
3.0	310	1.5	300	3.4	160

omit 2nd time used

Patterns of insecticide resistance in mosquitofish, (Gambusia affinis) were evaluated by Culley and Ferguson (1969). The extent of insecticide resistance in a resistant population from Belzoni, Mississippi, was compared with that of a susceptible population from State College, Mississippi, using 28 insecticides from five major groups. Spray records for the Belzoni area and insecticide characteristics such as stability and toxicity were used to evaluate patterns in the resistant population. Comparative 48-hour LC_{50} values with endrin from resistant (Belzoni) and susceptible (State College) populations of mosquitofish were 0.6 ppb for the State College sample and 314.0 ppb for the Belzoni group, or a 523X difference. Resistance was observed with pesticides related to toxaphene and endrin with patterns of resistance similar to those in arthropods.

Resistant mosquitofish tolerate as much as 214.28 ppm endrin in their tissues, and one such fish is able to release sufficient endrin into 10 liters of tapwater to kill five susceptible mosquitofish and still survive (Ferguson, Ludke, et al., 1966). Resistant green sunfish survived after each consumed a live mosquitofish containing 24.93 ppm endrin, but susceptible sunfish died in 15.5 hours. Many green sunfish regurgitated the endrin-contaminated mosquitofish but died later. Most regurgitated Gambusia showed no effects of digestion, an indication that endrin was absorbed superficially as suggested by Ferguson and Bingham (1966a).

The first report of resistance in a natural population involved DDT-resistant mosquitofish from an intensively-sprayed cotton-producing area (Vinson, et al., 1963). Since then, resistance to various organochlorine toxicants has been recorded in at least seven other species.

Results of 36-hour TLm measurements and gas chromatographic analyses showed that mosquitofish in waters near heavily-treated cotton fields and from an uncontaminated site removed endrin from static test solutions at the same rate. In susceptible fish with a 500 ppb endrin solution caused 32% mortality in 25 minutes, but hours were required in resistant fish. Relative mortality of fed and starved fish in endrin solutions and the rate of endrin uptake discounted swallowing as a primary route of entry. Six times as much endrin was taken up by the exposed head region as by the general body surfaces. Oxygen demands of the two populations were similar, but increased for susceptible fish at low endrin concentrations and for resistant fish at high concentrations coincident with the appearance of endrin poisoning symptoms. The

authors conclude that the mechanism of resistance is physicological toleration of massive endrin accumulations (Ferguson, Ludke, et al., 1966).

It was previously stated that resistance to endrin has been observed in yellow bullheads. Specimens of this fish from contaminated waters had a 36-hour TLm values of 75 ppb, whereas specimens from an unpolluted source were extremely sensitive - 1.25 ppb. This indicates a 60-fold endrin resistance in fish in waters subjected to cotton field drainage (Ferguson, Bingham, 1966). how calculated

Possible selective mechanisms in the development of insecticide resistant fish were evaluated by Finley, et al., (1970). Resistant and susceptible green sunfish populations fed endrin-exposed resistant mosquitofish had a 45X difference in endrin tolerances. Susceptible and resistant green sunfish each consumed one mosquitofish, all susceptible green sunfish died in 6.25 to 21.50 hours (an average of 11.75 hours) and all resistant and control fish survived the 96-hour test. Results of bioassays and gas chromatographic analyses showed that insecticide-resistant fish living near heavily treated cotton fields at Belzoni, Mississippi were subjected to relatively brief, irregular periods of exposure after rains. Runoff from cotton fields increased mortality among caged susceptible and native resistant fish. Feeding of endrin-exposed and field-collected resistant mosquitofish (Gambusia affinis) to resistant and susceptible green sunfish (Lepomis cyanellus) showed that selective pressure from residues in the food chain among resistant consumers was minimal compared with direct exposure. No insecticide stratification in the water was indicated by live-cage bioassays conducted at top and bottom depths.

Susceptible fish showed symptoms of poisoning (e.g., hyperactivity) soon after consuming the mosquitofish, and 36 of 40 regurgitated the mosquitofish prior to death without apparent correlation between predator weight and survival time. Resistant green sunfish exhibited no symptoms of poisoning, and all retained the ingested mosquitofish. Three samples (10 whole mosquitofish each) from the group that were consumed contained an average of 180 ppm endrin. not lethal ? ? ? to mosq. fish ?

Residues in whole body samples of individual susceptible green sunfish that died ~~on~~ from a continuous diet of field-collected resistant mosquitofish (1966-1967) showed 0.28, 0.10 and 0.312 ppm endrin. Monthly residue analyses of pooled samples (about 2 g) of native resistant mosquitofish from the Belzoni caging area (1966-1967) had endrin residues of 0.54, 0.40 and 0.058 ppm.

These observations suggest that insecticide contamination resulting from relatively brief period of runoff from adjacent cotton fields constitutes the principal selective mechanism in the development of resistant fish populations in adjacent waters. Both residue analyses and mortality of caged fish reflect the increase in pesticide content of streams after rains.

Succinic dehydrogenase activity on resistant and susceptible mosquitofish was investigated (Yarbrough and Wells, 1971). In perfusion studies no difference in enzymic activity was observed between susceptible and resistant brains, but with liver homogenates higher enzymic activity was observed in material from susceptible fish. The higher fat content of

the resistant liver homogenates probably explains the lower values observed with resistant fish. Endrin inhibition of succinic dehydrogenase was reported in homogenized brains of susceptible fish whereas varying degrees of stimulation were observed in resistant brain homogenates. Similar results were obtained with liver mitochondria from resistant and susceptible fish. Comparisons of results of liver and brain in which the mitochondria preparations had been disrupted showed endrin inhibition at every level tested in both resistant and susceptible samples. This study suggests that vertebrate resistance involves a cellular membrane barrier since inhibition of succinic dehydrogenase activity in resistant tissue was demonstrated only after mitochondrial membrane was disrupted.

In a later paper Wells and Yarbrough (1972) compared the *in vivo* and *in vitro* binding patterns of endrin - ^{14}C in susceptible and resistant mosquitofish brain and liver cellular fractions. Cell membrane fractions of resistant fish bind more endrin than susceptible fish, while the resistant mitochondria binds less endrin than susceptible fish mitochondria. Differences between endrin uptake in susceptible and resistant fish, retention of endrin by brain cell membranes, a blood-brain barrier, and a structural difference in myelin could account for endrin resistance in mosquitofish.

Oxygen consumption of endrin-resistant mosquitofish was significantly lower (26%) than that of a susceptible strain. Susceptible fish had an increased oxygen uptake at the onset of poisoning symptoms, and a decrease prior to death. Resistant fish showed no consistent change. At higher

concentrations of exposure (20 and 75 ppb endrin), total oxygen consumed by susceptible fish decreased significantly from controls (McIngvale, et al., (1968).

Ludke, et al., (1968) checked endrin resistance in resistant and susceptible populations of golden shiners. A 1,000 ppb endrin solution killed 50 of 50? susceptible fish in 75 minutes but only 40 of 50 resistant shiners in 40 hours. Endrin residues in whole bodies of resistant shiners killed in endrin-treated water were as much as 82 times those of susceptible shiners. Endrin concentrations in the blood of living resistant shiners were as much as 64 times greater than those of endrin-killed susceptible shiners.

Day (1968) found that the longnose killifish exhibits an apparent tidal rhythm of susceptibility to endrin and sodium chloride. Fish were more resistant to the chemicals at high tide. The tidal rhythm was not evidenced after three days. It is possible that the rhythm of susceptibility is endogenous and is phased by an external tidal factor.

Ferguson (1967) concluded that pesticide-resistant fishes and vertebrates may pose a major hazard to natural ecosystems. Although selection of a resistant fishery may permit exposed populations to survive, it may eventually produce a biological component dangerous to all consumers, including man (Ferguson, Ludke, et al., 1967).

III.B.3.c. Biological Magnification - All fish and wildlife are part of the food chain or web which may start with lower lifeforms which concentrate persistent pesticides in their bodies. When the lower forms are consumed,

a higher dosage is passed on to predatory fish and thence to fish-eating birds and mammals. Food chains in the aquatic environment are especially vulnerable since they maybe exposed to pesticides in runoff as well as to pesticides applied directly to water (Anon., 1964).

Bridges (1961) reported fish kill in Colorado caused by runoff of endrin applied to sugar beets. A field adjacent to the affected pond was sprayed at 6 ounces of active ingredient per acre, and four days later numbers of dead yellow perch (Perca flavescens), pumpkinseed (Lepomis gibbosus), bluegill, black carppie (Promoxis nigromaculatus), largemouth bass and carp were observed. Pond water contained 0.04 ppm a month later. Vegetation residues reached a maximum of 0.55 ppm 15 days post-treatment. Residues in the bluegill were 1.00 ppm nearly two months later. Endrin disappeared from the water about a month after application, six weeks in vegetation, two months in bottom mud and less than 3 months in fishes.

Johnson (1967), in his report on the effects of endrin on the medaka, gave some data on residue concentrations in adult fish. After 28 days exposure these were approximately proportional to the concentration to which they were exposed. Calculated accumulation factors showed fish concentrated endrin in their body from approximately 17,000 to 26,000 times the concentration in the water.

The food chain of protozoa to crustacea to fish was studied by Priester (1966) after the toxicity of endrin to each organism had been determined. Each species was treated with a sublethal dose, and

crustacea were fed to fish. Endrin which was concentrated 920 times by Daphnia during a 14-day exposure was not detected in fish after ingestion of treated daphnia and was not detected in protozoa following a 7-day exposure to 50 ppb.

The toxicity of endrin-resistant mosquitofish to natural predators was ascertained by Rosato and Ferguson (1968). These resistant specimens were exposed to 2 ppm endrin for 7 days. A single survivor was force-fed to each of several carnivorous fish, including red fin pickerel (Esox a. vermiculatus), largemouth bass and bluegills. Mortality of all predator species was 100 percent within 7.1 and 12.6 hours. Resistant mosquitofish accumulate endrin residues sufficient to kill potential predators several hundred times their own weight.

The mass death of fish in the lower Mississippi River in 1963 led to speculation concerning the accumulation of insecticide residues in the environment and rumors of increasing concentration of endrin in the fauna of the food chain. Buildup of endrin in soil and water was postulate. However high concentration or time ordered changes in endrin concentrations were observed in twelve successive monthly samplings of representative fish, shellfish, mud and water from the lower Mississippi River. Oysters and shrimp were negative throughout. Catfish yielded 0.01, 0.02, and 0.01 ppm of endrin in July 1964; and one reading of 0.01 ppm in each of August and October 1964 and June 1965. Bream yielded one reading of 0.01 ppm in each of July and October 1964 and February 1965. Mud and water were negative throughout apart from two readings

of 0.01 ppm in July 1964 and one of 0.01 ppm in each of February and June 1965 (Novak and Rao, 1965).

III.B.3.d. Other Studies of Pathological or Physiological Effects - A study was initiated to determine the pathway of entry into exposed fish. A comparison was made of mortality rates of normal black bullheads and others rendered incapable of swallowing endrin. In one group the gut was tied off in the region of the upper esophagus. A second group was subjected to the same operation with thread in place but omitting the ligature. These constituted a sham-operated control. A third group served as unimpaired controls. In every test, all fish from all three groups were dead after a 23-hour exposure to 50 ppb endrin. Mortality rates were nearly identical. These results showed that fish unable to swallow endrin died as rapidly as those free to swallow (Ferguson and Goodyear, 1967).

The effects of endrin on the oxygen consumption of the bluegill sunfish, Lepomis macrochirus, were studied by Huner, et al., (1967). Katz (1961) and Henderson, et al., (1959) found endrin to be the most toxic insecticide tested on various fishes. Effects of sublethal (0.1 ppb) and lethal (1.0 ppb) endrin concentrations on oxygen consumption were measured. Increase in oxygen consumption occurred within 5-hour and 24-hour exposures to 0.1 ppb while at 1.0 ppb oxygen consumption was less. Exercise had no significant effect on oxygen consumption at either concentration but it did affect mucus production and hastened death.

Adult northern puffers, Sphaeroides maculatus, were exposed to various concentrations of endrin and blood and tissue samples from fish surviving

a 96-hour exposure were studied. Mean hemoglobin content and relative liver size of puffers exposed to 1.0 and 0.05 ppb differed littled from controls. Concentrations of sodium, potassium, calcium and cholesterol in serum were consistently higher in exposed fish, but amounts of magnesium and zinc in the livers of test animals were consistently lower. Exposure to sublethal concentrations of endrin impaired liver function has shown elevation in serum content of major cations and cholesterol (Eisler and Edmunds, 1966). Serum cholinesterase was 2-8 percent of normal were reported in carp exposed to lethal concentration (0.05 to 0.005 ppm) of endrin (Hayama and Kuwabara, 1962; together with changes in serum Transaminase Lue-Hurg, 1966).

Inhibition by endrin of succinate dehydrogenase and cytochrome oxidase, two enzymes involved in mitochondrial electron transport in the catfish, Ictalurus melas, was shown by Colvin and Phillips (1968). Extent of inhibition depended upon endrin concentration and the specific activity of the enzyme preparation. No appreciable effect of endrin on acetylcholinesterase or NADH - cytochrome-c-reductase was reported. Binding to lipoprotein components essential for mitochondrial oxidation was proposed as a logical site for endrin action.

The effect of endrin on uptake of phospholipids, neutral lipids, and cholesterol by embryos of steelhead trout (Salmo Gairdeneri) was checked by Grajcer (1968). Pathways by which endrin is distributed between the egg yolk and the developing embryo were studied. In one trial, fertilized and unfertilized eggs were cocharged with endrin. Another involved

exposing hatching steelhead eggs to 10 ppb endrin. Exposure stopped after hatching but endrin assay of of both embryos, yolk sacs and young continued to 25 days after hatching when the last specimens expired. In a third experiment, eggs and alevins were continuously exposed to endrin.

A small but steady uptake and accumulation of endrin occurred in all eggs. Fertilized eggs accumulated more endrin (0.40 µg/day) than the unfertilized eggs (0.30 µg/day). Major uptake occurred within a 24-hour period of hatching during which time alevins increased their endrin content up to 40 times. Initially most of the endrin was stored in the yolk. Results of assays indicated an irregular accumulation of endrin in the embryos. The challenged alevins expired by the 13th day after hatching. At this time, endrin content in alevins increased but the uptake of endrin shifted from materials in the extracted dry weight and phospholipids to the fraction containing neutral lipids and cholesterol.

Histopathological lesions in cutthroat trout chronically exposed to endrin were described by Eller (1971). Pathological conditions were found in the gill, liver, pancreas, brain and gonads. Edema, hemorrhage, and possibly intracapillary congestion characterized gill damage after exposure to highest concentrations of 0.04 mg/l water. Hepatic lesions in young trout were similar to those preceding the development of hepatomas in nutritionally deficient fish. Increased incidence and severity of hepatic degenerative changes in fish exposed to high endrin levels suggested nutritional difficiency. Marked hyperplasia of pancreatic islets and irregular, atypical oocytes were observed after exposure to high endrin levels.

III.C. Toxic Effects on Wildlife - Extensive data from laboratory tests corroborate hazards to birds and mammals resulting from agricultural use of endrin. Losses among populations of non-target birds, mammals and fish have been caused from registered uses such as for orchard mouse control. Residues in moderate amounts may accumulate in animal tissues and may reach toxic levels in aquatic birds. Residues of endrin in animal tissues recede further than DDT, dieldrin or heptachlor epoxide under withdrawal conditions.

III.C.1. Acute Toxicity - Extensive data from both laboratory tests and field studies substantiate the highly toxic effects of endrin on both mammals and birds. Even some registered uses for rodent control have created losses among non-target bird and mammal species. Residue accumulation in animal tissues is moderate, but may reach toxic levels in aquatic birds. Bioaccumulation has been demonstrated.

The acute oral LD_{50} toxicity of endrin tabulated by Schafer (1972) was 2.4 mg/kg for red-winged blackbirds (Agelaius phoeniceus) and the same for starlings (Sturnus vulgaris), 5.6 mg/kg for the common grackle (Quiscalus quiscula), 5.6 for the common pigeon (Columba livia); and 1.8 for the house sparrow (Passer domesticus). DeWitt, et al., (1960) listed the approximate LD_{50} of endrin to bobwhite quail as 5.0, and to ring-necked pheasants - 14.0.

Arasan (thriam) - endrin-coated pine seed is used to repel birds and rodents for direct seeding to reestablish conifers. Hamrick (1969) determined the lethal dosage of treated seeds to several species. Force-feeding of one treated slash pine seed each to 10 bobwhite quail (Colinus

virginianus) resulted in 100% mortality. Of seven gray squirrels (Sciurus carolinensis) offered a known number of treated seed, five died; these five gnawed an average of 85 seeds. If completely consumed, this meant ingestion of 29.7 mg. endrin. Of two others given a mixture of treated and untreated seed, one died and the other exhibited symptoms of poisoning. One chipmunk (Tamias striatus), offered treated seed, was found dead twelve hours later. Possible maximum endrin intake was 1.4 mg. Wild cotton rats (Sigmodon hispidus) had access to treated seed spilled under cages. One was observed in severe tremors a day after treated seed became available. No spilled seeds were touched after the third night. Twelve pen-reared wildstock turkeys (Meleagris gallapavo) also were tested. Of 10 turkey hens force fed treated seed, 3 died. Two that died received 30 seeds (about 2.5 mg/kg of endrin) and the other 36. The average treated slash pine seed containing 0.35 mg endrin. For an average-sized adult quail, this would be a dosage in excess of the estimated 1.5 mg/kg LD_{50} value.

Luckens and Davis (1965) measured acute toxicity figures for the big brown bat (Eptesicus fuscus). Endrin administered in the feed induced mortality at doses as low as 4 mg/kg. The LD_{100} was 12 mg/kg although there was one survivor at 20 mg/kg. Results indicated an approximate LD_{50} of 5-8 mg/kg.

In laboratory studies on Japanese quail (Coturnix c. japonica made by Bakos, et al., (1968), the lethal dose of endrin was 0.02 µg/ml per g live weight. The authors cautioned that at rates, used for rodent control afforded an imminent danger to feathered game.

Treon, et al., (1955) reported acute oral LD_{50} values (mg/kg) as follows: monkey - 3; 6-month old rats - 7.5 (F) - 43.4 (M); cats - minimum LD_{50} less than 5; 26-31 day old rats - 28.8 (M) and 16.8 (F); and guinea pigs - 16 (F) and 36 (M).

Negherbon (1959) listed acute oral toxicities for endrin in mg/kg as follows: female rabbit (MLD) - 5 to 7; female guinea pig (MLD) - 10 to 16; male guinea pig (MLD) - 24 to 36; monkey (both sexes) - MLD of 1 to 3; and the LD_{50} for a 7-day old chick as 3.5.

Toxicity of endrin determined by Tucker and Crabtree (1970) gave an acute oral LD_{50} figure of 5.64 mg/kg for 10-13 month old female mallard ducks. Young female ring-necked pheasants (3-4 mo.) were 1.78 mg/kg. Pigeons of both sexes were 2-5 mg/kg. Four-year old sharptailed grouse were highly sensitive at 0.75 - 1.5 mg/kg.

In a study of the effects of endrin on the pigeon, Revzin (1966) found the i.v. LD_{50} was 1.5 mg/kg. The slope of the dose-response curve was very steep; 1.2 mg/kg was an LD_0 whereas 2.0 mg/kg approximated an LD_{100}.

Rudd and Genelly (1956) found the LD_{50} for adult female pheasants to lie between 3.6 (LD_{25}) and 5.6 (LD_{80}) mg/kg.

Allard (1971) described wildlife poisoning resulting from an approved pesticide use. Death of chukar partridges was attributed to consumption of endrin treated wheat used in a rodent control program in an orchard. Results of tissue analysis are presented in Table III.C.1.

Table III.C.1.

Endrin in Tissues from Chukar Partridges
(ppm)

Bird No.	Tissue	Total DDT	Endrin
1	Fat	1.01	4.58
	Liver	0.50	0.84
	Muscle	N.D.	0.05
2	Fat	1.15	1.79
	Liver	0.26	0.88
	Muscle	N.D.	0.06
3	Fat	0.08	6.24
	Liver	0.39	1.28
	Muscle	N.D.	0.04

Waterfowl were selected for acute toxicity tests because they frequent alfalfa fields in winter when mice are controlled with endrin (Keith, et al., 1962). Four cackling geese orally administered single ~~oral~~ doses of 5 to 10 mg/kg of endrin died, while two others subjected to 2.5 mg/kg were alive after 9 days.

Results of single, oral doses of endrin given to eight widgeon showed 3 birds at 5, 2 birds at 10, and 1 bird at 20 mg/kg succumbed. Two others at 2.5 mg/kg were alive after 9 days. In a ~~chronic~~ subacute feeding trial scheduled for five days, widgeon given daily doses of 1.0, 2.0 and 2.5 mg/kg per day? died before the fifth day. Similar results were obtained with white-fronted geese wherein 4 birds given 5 to 10 mg/kg per day? died while two others receiving 2.5 mg/kg were alive after 9 days.

The effect of age on sensitivity (acute oral toxicity) of pesticides to mallard ducks was recorded by Hudson, et al., (1972). Acute LD_{50} values determined on mallards 36 hr., 7 days, 30 days and 6 months after ~~hatching~~ hatching are presented in Table III.C.2. Central nervous system stimulants produced LD_{50} values that decreased from 36 hr. to 7 or 30-day old birds, and increased from birds aged 7 or 30 days to 6 months. The results of these tests show that young animals are not always more susceptible to pesticides than adults and age-susceptibility factors should be considered important in developing standardized toxicologic protocols.

Table III.C.2.

Acute Oral LD_{50} (mg/kg) of Endrin to Mallards of Various Ages

	Age			
Chemical	36 ± hr.	7 ± 1 Days	30 ± 3 Days	6 Mo. ± 3 Days
Endrin	22.3	3.37	2.90	5.33
	(9.88-50.3)	(2.36-4.80)	(2.17-3.88)	(3.67-7.73)

III.C.2. Subacute and ? Chronic Toxicity - Chronic toxicity to quail and pheasants of endrin was studied by DeWitt (1956). Inclusion of 1 ppm endrin in diets fed growing quail resulted in high mortality rates. Young pheasants failed to survive on diets containing 5 ppm endrin. No ill effects were noted among quail fed winter diets containing 1 ppm endrin. Egg production, fertility, and hatchability were relatively unaffected

= how high ?

by inclusion of insecticides in diets fed breeding quail, but their chicks showed high mortality rates even when reared on insecticide-free diets. Hatchability of pheasant eggs and viability of chicks were adversely affected by endrin in the reproduction diets.

Comparative dietary toxicities of 89 pesticides to birds were examined by Heath, et al., (1972). Toxicity was expressed as the LC_{50} of active chemical in 5-day ad libitum diet followed by 3 days on untreated diet. Endrin, consistently the most toxic chemical tested, gave LC_{50} values of: bobwhite - 14; Japanese quail - 18; pheasant - 14; and mallard - 22 ppm.

Hamrick (1964) reported on chronic tests of endrin-coated conifer seed on wildlife. Six turkeys force-fed sublethal dosages of treated seed and surviving until the study was completed averaged 5 lb., 2 oz. in weight. Two birds not force-fed treated seed but offered both treated and untreated seed averaged 7 lb., 9 oz. or 2 lb., 7 oz. more.

DeWitt, et al., (1963) established an "LD_{50}" for adult bobwhite quail, fed 10 ppm endrin in the diet, as 1 mg/kg. In an earlier study, DeWitt (1955) reported that adult pheasants all died within 23 days when fed 100 ppm endrin in their diet. All young pheasants died when 5 ppm of endrin was incorporated in their diet. Bobwhite quail all died within 6 weeks when fed 2 ppm or more. Young quail fed 5 and 0.1 ppm suffered 70 and 26 percent mortality, respectively, during two one-week exposures, 28 days apart.

III.C.3. Special Studies

III.C.3.a. Residues - There is concern that insecticide residues may be accumulating in wild animals used as food by humans. Moore, et al.,

(1968) made analyses of renal fat from 45 antelope (Antilocapra americana) collected in South Dakota. Combined chlorinated insecticide residues were only 0.08 ppm. No samples had endrin above 0.03 ppm.

Pesticide analyses were run on 21 whitetail deer (Odocoileus virginianus) from the Mississippi Delta Region (Cotton and Herring, 1971). Only six deer from one collection point contained trace amounts endrin residues in the fat.

Pesticide residue concentrations in Colorado mule deer (Odocoileus hemionus) were studied by Jewell (1966). In muscle tissues from nine deer, endrin residues ranged from none ~~determined~~ detected to 0.072 ppm. In the adipose tissues of two deer, endrin residues were trace and 0.059 ppm.

Wilson (1967) mentioned pesticide residues from two dead porpoises. These aquatic mammals represent one of the top trophic levels in a marine food chain. More than 200 ppm of DDT and its metabolites were found in the blubber of both animals, and 0.05 to 2.0 ppm of endrin and dieldrin residues.

Snyder (1963) obtained endrin residue data on vole (Microtus pennsylvanicus) in relationship to reproduction. Voles which consumed from 5.4 to 126.0 mg/kg endrin in the laboratory contained from 0.16 to 1.92 ppm in their tissues. Endrin applied at 0.6 lb/acre did not produce residues in resident meadow mice while from less than 0.15 to 0.73 ppm was detected in 11 of 17 animals taken 2 months after treatment with 2.0 lb/acre. Mean concentration was 0.34 ppm. Difference in reproductive rates between females of endrin-treated and control groups varied only 0.25 or less for corpora lutea, implantation sites, and viable embryos.

Harrison (1966) pointed out that endrin was used in Great Britain to a much lesser extent than aldrin, dieldrin, DDT or BHC. When endrin was present in avian tissue and eggs in Great Britain, the ratio of endrin residue to pp'-DDE seldom exceeded 1 to 500, and of endrin to dieldrin 1 to 100. The following observations from birds at the top of aquatic or terrestrial food chains are endrin residues in eggs (ppm): hen harrier (Circus cyaneus) - 0.01; merlin (Falco columbarius)- 0.32; heron (Ardea cinerea) - 0.03; cormorant (Phalacrocorax carbo) - 0.01; shag (Phalacrocorax aristotelis) - 0.01; peregrine (Falco peregrinus)- 0.09; osprey (Pandion haliaetus) - 0.002; and sparrow hawk (Accipiter nisus) - 0.003 - 0.04. Liver samples from the kingfisher (Alcedo atthis) were 0.24 and from the kestrel (Falco tinnunculus) - 0.13.

A British study by Jefferies and Prestt (1966) mentioned finding residues of 0.01 ppm endrin in organs of the mallard (Anas platyrhynchos), a prey species of the lanner (Falco biarmicus).

Other studies in eight British species of adult birds were conducted by Gramp and Olney (1967). Forty-five analyses were positive for endrin in mixed viscera (liver, hear, spleen and gut). Highest amounts found were 6.4 ppm in greenfinch (Carduelis chloris), 2.4 ppm in red-legged partridge (Alectoris rufa), and 1.53 ppm from a rook (Corvus frugilegus).

Koeman and van Genderen (1966) published on pesticide residues of birds found dead or dying in a coastal Netherlands habitat. The spoonbill (Platalea leucorodia) showed 0.6, 2.0 and 3.0 ppm for liver

and 0.4 and 0.5 for breast muscle. The oystercatcher (Haematopus ostralegus) had trace and 0.3 for liver. Liver tissue from the sandwich tern (Sterna sandvicensis) ranged from 0.4 to 0.9 ppm. The common tern (Sterna hirundo) gave values of present, 0.5 and 3.0 ppm for liver; 0.9 and 3.9 for breast muscle; 2.6 and 7.9 for kidney; and 1.2 and 1.5 for brain. Spoonbills, oystercatchers, and terns feed predominantly on crustaceans, mollusks and fish, respectively.

Later Koeman, et al., (1967) reported upon endrin residues in livers of sandwich terns found dead in the Dutch Wadden Sea. Mean values of 2 groups each (33 bird total) were chicks - 0.42 to 0.47 ppm; juveniles - 0.12 to 0.43; and adults - 0.29 to 0.67. Residues in the eggs of several tern species from the Netherlands, Great Britain, Ireland and Germany (total 69 eggs) ranged from not detectable (Ireland), 0.03 in only 1 of 5 eggs from Great Britain, 0.08 to 0.24 in Germany, and 0.17 to 0.20 in the Netherlands. Significant endrin residues were confined to the Dutch and adjacent German Coasts. Very likely the contamination originated at least in part from factory effluent.

Numerous birds of prey, owls and other birds were reported dead in the Netherlands in the winter of 1968-1969 (Koeman, et al., 1969). Onset of mortality coincided with sowing winter cereals, which, owing to unfavorable weather, occurred late in 1968 and early in 1969. Birds possibly were poisoned by pesticides used in seed-dressing practice. Only dieldrin was present in lethal concentrations in the tissues. However, endrin residues were recorded from liver and kidney tissue the buzzard (Buteo buteo) - 0.16 ppm, and the long-eared owl (Asio otus) - 0.13 ppm.

Reichel, et al., (1969) found residues of less and 0.1 and 0.1 ppm in carcass, liver and brain of a bald eagle (Haliaeetus Leucocephalus) from Florida.

Risebrough, et al., (1968a), in their study of residues among various raptorial and fish eating birds, found several positive endrin analyses. Two eggs Craveri's murrelet (Endomychura craveri) from Baja California, Mexico, contained 0.17 ppm endrin (lipid weight). Three brown pelican (Pelecanus occidentalis) eggs collected from the Gulf of Panama contained 0.06, 0.07 and 1.13 ppm endrin (lipid weight). Two brown booby eggs (Sula leucogaster), also collected off Panama, had endrin residues of 0.06 and 0.011 ppm (lipid weight). One osprey egg (Pandion haliaetus) collected in the Gulf of California showed an endrin residue of 0.25 ppm.

South Dakota pheasants (Phasianus colchicus), was described by Linder and Dahlgren (1970), showed less than 0.03 endrin in brain tissue and crop contents of 14 juveniles and similar levels in adults. Pheasants and sharp-tailed grouse (Pedioecetes phasianellus campestris) of South Dakota were analysed by Greichus, et al., (1968). Endrin residues in the fat were not found above 0.05 ppm.

The Bureau of Sport Fisheries and Wildlife, United States Department of the Interior, reported on "Pesticide Residues in Whooping Crane Specimens", in 1964). Analyses were made for residues in tissues, eggs, and food supplied to captive birds. Low levels of pesticidal residues were found in all whooping crane samples examined. Endrin was found only in two eggs at 0.509 and 0.611 ppm. Concentrations of 0.283 and 0.087 ppm were found in diet samples.

Residues in insects and birds found in Louisiana cotton fields were recorded by El Sayed, et al., (1967). They found 0.46 ppm endrin in mayflies but no endrin in six species of birds.

Recommended control for cutworm in Colorado wheatlands has been 3-4 oz. endrin/acre. Bird Census begun in 1969 showed little effect on numbers the first two weeks after spraying. From 16 to 70-80 days post-spray birds declined significantly. Twelve dead birds were found in sprayed fields, none in unsprayed. Sick and dead black-tailed and white-tailed jackrabbits were observed on sprayed fields as well as three dead cottontails, two prairie voles and one deer mouse. Three or more domestic sheep ewes and a lamb died with toxic symptoms after accidentally grazing sprayed areas at least twice within a two-week period. Residues in cutworms collected 1-16 days post-spray averaged 2.5 ppm and ranged from 0.2 to 10.8 ppm. Birds found dead and most collected alive around treated fields up to several weeks post-spray had from less than 0.1 to 0.4 ppm whole carcass residues (McEwen and Blomberg, 1970).

Organochlorine residues in 21 aquatic bird species from 31 locations in Alberta, Saskatchewan and Manitoba were determined by Vermeer and Reynolds (1970). Endrin was among the compounds screened but not detected.

Forty-five bald and 21 golden eagles found sick or dead in 18 states and Canada during 1964-1965 were analysed for pesticide residues (Reichel, et al., 1969). Endrin residues were detected only in six bald eagles. Median residue values in ppm were: carcass - 0.09; liver - 0.09; and brain - trace.

Keith, et al., (1962) examined endrin residues in heart, kidney, liver, brain and breast muscle tissues from experimental birds and from those found dead in alfalfa fields in central California treated for mouse control. Artificial exposure of caged birds to alfalfa treated with 0.8 lb/acre of endrin resulted in some mortality. Residues in 4 cackling geese ranged from 1.8 to 2.4 ppm. A ring-necked pheasant gave 2.8 ppm. These were from birds found dead on a treated field. Dead cackling geese (4) from another treated field showed residues of 1.7 to 4.1 ppm. Liver birds (4) had residues of 0.8 to 2.4 after 7 days.

Pesticide residues in the common egret (Casmerodius albus) in California were reported by Faber, et al., (1972). Five specimens found dead or moribund had endrin residues in the brain of less than 0.10 to 0.28 ppm. Endrin residues were not recovered from liver or breast muscle.

Wildlife lossess in the field in California were reported by Hunt (1964). Several small birds observed falling from trees and dying at the Cotton Research Station in Shafter, Kern County, included doves, finches, sparrows and mocking birds. Endrin had been applied to cotton for control of cabbage looper the previous day. The birds apparently had been feeding on cabbage looper larvae that were abundant in the sprayed plots.

Endrin residue was found in a composite sample of three birds at levels of 1.29 ppm in flesh and 1.45 ppm in the gizzards. The recommended rate for cabbage looper control was 0.5 pounds endrin/acre.

Residues found indicate that endrin was probably responsible for the bird die-off.

III.C.3.b. Bioaccumulation and Reproductive Effects - Cramp and Olney (1967) related the occurrence of up to 6.4 ppm endrin residues in British birds, and that worms and slugs from an endrin-sprayed field contained 10.3 ppm, indicating route by which some birds could receive relatively large amounts. — bioaccum cut off by death here!

Bioaccumulation of endrin from natural food sources in the eastern bobwhite quail, (Colinus virginianus), was discussed by Gregory (1969) in a simplified food chain situation involving soybeans, Glycine Max, Mexican bean beetles, Epilachna varivestis, and bobwhite quail. One group of quail exposed to acute and chronic endrin concentrations was force-fed contaminated beetles at 1 mg endrin/kg/bird. Another test group exposed to acute and chronic dosages was force-fed contaminated beans at 0.015 mg endrin/kg/bird. Two days following treatment, all birds were sacrificed. Fat, liver, and gonadal tissues, from both acute and chronic dosages, involving beans and beetles, consistently contained endrin residues. Fat tissue from acute dosage involving beetles contained 0.682 ppm endrin, while the same tissue from chronic dosage contained 0.421. Liver and gonadal tissues from acute dosage utilizing beetles contained 0.145 and 0.113 ppm endrin, respectively, while those from chronic dosage contained 0.201 and 0.245 ppm, respectively. Fat tissue from acute dosage utilizing beans contained 0.014 ppm endrin, while the same tissue from chronic dosage contained 0.01[6] ppm. Liver tissue from

the acute test averaged 0.004 ppm endrin, and from the chronic phase - contained 0.007 ppm. Gonadal tissue contained endrin only in trace amounts.

Analyses of whole birds, from all tests, revealed retention of approximately 16% of the total acute dose, and 21% of the total chronic dose. Apparently the compound was not metabolized by any component of the food chain, but accumulated and was transferred in the original form.

The effects of endrin on parental survival and fertility, litter size, and young survival to weaning of field-captured deer mice (Peromyscus maniculatus) were evaluated by Morris (1968). Endrin was fed at intervals over a 7-month period with standard pellets containing 0, 1, 2, 4 and 7 ppm endrin. Adult mortality during feeding, starvation and cold stress periods was directly proportional to endrin levels in the food. Within each group, litter production frequency and mean litter size before and during experimental feeding were similar. Mortality of young before weaning apparently occurred at higher endrin levels. Post-natal mortality of young up to weaning may be the main effect of endrin on reproductive performance.

Morris (1970) later studied the effects of endrin on unenclosed field populations of meadow voles and deer mice. Treated area was sprayed at 0.5 lb/acre. Immediate and significant post-spray declines in meadow voles occurred but no long-term toxicological effect was demonstrated. Population on the treated area recovered rapidly, eventually exceeding pre-spray numbers in two years. The experimental vole population seemingly responded to endrin as it would to local depopulation by removal trapping.

Although deer mice were more abundant on the sprayed than on the control area before endrin application, their numbers were significantly reduced after spraying and never did recover. Recruitment by immigration or breeding did not occur. All individuals captured on the spray plot the following two years remained there for only one trapping period. A long-term toxicological effect on deer mice seemed evident. This showed a differential response of the two small mammal populations to endrin.

Intravenous injection of endrin in the anesthetized pigeon induced changes in telencephalic neuronal function. Dosages of 4 mg/kg or more caused seizure activity throughout the telencephalon. At 2-3 mg/kg, endrin caused seizure activity largely limited to the ectostriatum, a telencephalic visual projection area. At 0.5-2.0 mg/kg, endrin caused a specific increase of potentials evoked in the ectostriatum by stimulation of the nucleus rotundus, a diencephalic visual projection area. Reticular formation functions tested were little affected. Relatively low brain levels of endrin may impair visual function in birds. Visual impairment could be a major factor underlying the well known sensitivity of birds toward endrin (Revzin, 1966).

III.C.3.c. Endrin as a Ground Spray for Rodent Control - Endrin has been used both here and abroad for limited agricultural and forestry purposes in control of various rodents, particularly mice or voles. Damage may consist of girdling or gnawing the bark of lower limbs, trunk or roots of forest platings, fruit trees and ornamentals, damage to forage crops, or by consuming the seed of forest trees.

Endrin is a compound of choice because of its greater toxicity and apparent effectiveness against rodents. However, opinion has been divided upon the risk to humans, domestic animals and wildlife. Thus, in some European countries such as Denmark, West Germany and Czechoslovakia, endrin may be used for vole control without restriction, whereas in others such as the U.S.S.R., Belgium and the Netherlands, its use is not permitted for this purpose.

Cook (1964) reports that only limited experiments have been made in Great Britain for vole control with endrin. Vole populations there may fluctuate widely from one year to another and many years may pass before a population reaches a harmful density. When this occurs, damage in fruit orchards and forest plantations may be heavy. The author did not comment on the efficacy of the compound.

A unique situation prevails in Switzerland regarding use patterns (Schneider, 1966). There, endrin is forbidden as an insecticide because of its high toxicity and persistence. On the other hand, it may be employed under restricted conditions and close supervision for the destruction of voles (Arvicola terrestris) at a rate of 400 g/hectare. An emulsion is sprayed on short-cut grass under the trees from mid-October to mid-November. Only young enclosed orchards are treated. The following year, 1.9 ppm endrin was found in grass cut for the first time, and 0.27 ppm in the third cutting (Hurter, 1965). Therefore, the use of this grass was not permitted for fodder.

Areas treated must be enclosed for 5 months by a wire netting-fence at least 1.2 m high and with a mesh no greater than 5 cm. This precaution

was taken to prevent the poisoning of humans, domestic animals and game. Schneider further indicates that cats and hares have been poisoned in cases where this regulation was disobeyed.

Field voles (Microtus agrestis) created considerable concern in Germany during the period of reforestation following World War II. They caused serious damage to tree bark in extensive plantations and also in naturally regenerated forests. Repellents at stem bases proved impractical over large areas. Field voles only occasionally accepted poisoned grain, and coumarin (warfarin) preparations failed entirely. Little was achieved with other bait materials. Failure of traditional control methods led to experiments with chlorinated hydrocarbons starting in 1954 (Schindler, 1956). Toxaphene and endrin proved effective in these tests. However, a five-fold dose was used as compared with the rate commonly used for insects. Dead voles and ones showing affected movements were found only a few hours after application and two or three days later the areas were considered free from field voles. The most effective method was spraying grasses and other surface growth with 1.0 to 1.7 kg of 30 percent endrin emulsion in 400 to 600 liters of water per hectare. This method was recommended originally only for fenced areas free of wild game. However, this restriction was later removed when no injury to game, birds or domestic livestock was observed.

The control of orchard mice (voles) in the United States has been studied most intensively over many years by personnel of the Fish and Wildlife Service, U.S. Department of the Interior, and with endrin,

specifically, by Horsfall and associates of the Virginia Polytechnic Institute, Blacksburg, Virginia. Studies by both groups started in the early 1950's. Horsfall's first recorded studies with endrin were published in 1954 wherein he reported that rates of 2.5 lb/acre required precautions and that ground spray rodenticides were hazardous to animals but gave no data.

Personnel of the Bureau of Sport Fisheries and Wildlife and predecessor agencies, meanwhile, worked on a wide array of potential orchard mouse rodenticides between 1934 and the present time. Studies of endrin apparently were conducted only during the period of 1955-56 and some reservations were made on this use because of potential hazards to man and other non-target species. The U.S. Department of Interior now does not advocate continued use of chlorinated hydrocarbons nor does it permit their use on lands under its jurisdiction.

During the period 1949-1969, Horsfall and his co-workers published more than 40 articles related to orchard mouse control. Those published since 1955 dealt almost entirely with endrin as a control agent. Rates used experimentally or operationally varied from 1.2 to 2.7 lb/acre. There was a rapid decline in mouse activity to near zero levels in 6 days or less in 1954. For 1953, 3 to 6 weeks were required for a similar reaction, apparently associated with differences in moisture conditions (Horsfall, 1956). Little or no evident deleterious effects were noted on men or game animals but no quantitative data were presented.

States bordering the Atlantic Seaboard from New England to Georgia plus Tennessee, Kentucky and Ohio have commercial apple orchards subject

to attack by two species of voles, the meadow mouse (Microtus spp.) and the pine mouse (Pitymys pinetorum). Elsewhere in the fruit growing sections of northern and western states most damage problems are associated with Microtus alone. This latter species, being primarily a surface feeder, can generally be effectively controlled with poisoned baits placed in runways and burrows. However, the subterranean dwelling pine vole damages orchard trees by gnawing and girdling tree roots at sites where baits presumably are more difficult to place or are less effective. The pine vole is the principle apple orchard pest from North Carolina northward to the southern New England states. Endrin ground sprays at currently recommended rates evidently help control both meadow and pine voles but are predominately designed to control the latter species.

In his various reports, Horsfall found that endrin reduced mouse activity in orchards generally, at times suddenly, sometimes gradually, and occasionally a failure occurred. His "signs of activity" index to vole numbers was used to demonstrate endrin effectiveness under some conditions. However, as pointed out by Hayne (1970), this method is inadequate for exploring why endrin sometimes fails, or for comparing other candidate control methods with endrin on a quantitative basis. A research program should develop laboratory and field methods adequate to support quantitative studies. Such methods already exist for some small mammals. It should be determined how endrin controls the pine vole, and why treatments sometimes fail. Then the relative effectiveness can be appraised for candidate methods to replace endrin. Concurrently,

there is need for accurate before- and after-treatment wildlife censuses on treated areas plus residue analyses of dead or dying animals to determine precisely what caused their demise. Endrin is extremely toxic to birds, mammals and fish yet documentation on non-target losses from endrin orchard spray operations is practically non-existent. Rollins and Horsfall (1956, 1961), in observing many orchard sprayings, mentioned that some quail and rabbits had been killed. However, most orchards had only an occasional dead animal and many had none. Wolfe (1957) recommended 1.2 to 1.4 pounds actual endrin per acre for orchard Microtus control in the State of Washington. He stated that possibly an occasional quail or pheasant is killed by endrin sprays, but noted little evidence of such deaths the previous three years. Fitzwater (1953) recommended against the use of ground sprays in Michigan due to uncertainty of effectiveness, especially against pine mice, and danger to wildlife and domestic animals.

Effects of endrin applications on three Fairfield County, Ohio orchards were observed by Beck (1957). One 100-acre orchard containing a pond was treated at about 3 lb/acre. Six hundred walleye pike averaging 1 lb. each were stocked in the pond 1 month after spraying and all apparently died within 3 days. None of the previous resident fish (minnows, bluegills) were found the following summer. Frogs still occurred but the tadpoles reportedly died. Terrestrial forms found dead on the three orchards included rabbits, birds, woodchucks, cats and a dog.

Forbes (1968) discouraged orchard use of endrin in New York because of danger to wildlife and the development of resistant mice in

the Hudson Valley. Webb and Horsfall (1967) also reported upon a laboratory study of endrin resistance in pine mice. Wild pine mice with a history of treatment with endrin from a Berryville, Virginia orchard showed a 12-fold greater tolerance to the pesticide than did mice from an untreated orchard near Hagerstown, Maryland. Pooled data indicated LD_{50} values of 2.97 and 36.12 mg/kg in this study. Horsfall and Webb (1966) pointed out that a poison with a median lethal dose of 30 mg/kg should still provide adequate control if properly exposed. Hayne (1970) cited Tietjen (1970) that in 1968 in New York orchards, the acutal oral LD_{50} for pine mice from an orchard where endrin had been applied for 11 consecutive years at 3.2 lb/acre was 5.4 mg/kg, as compared with 1.84 mg/kg where endrin had not been used.

Excretion of ^{14}C-endrin and its metabolites in endrin susceptible and resistant pine mice (Microtus pinetorum) was studied by Petrella and Webb (1973).

It was hypothesized that endrin metabolism may partially contribute to the greater protection of resistant (R)animals from the toxic effects of endrin as opposed to susceptible (S) animals. F_1 offspring born of endrin resistant and susceptible parents, and having LD_{50}'s of 18.97 $\pm$ 1.78 mg/kg and 2.56 $\pm$ 0.23 mg/kg, respectively, were dosed for 9 days with 0.51 mg/kg/day ^{14}C-endrin (specific activity 2.19 mCi/mmole) and feces and urine were collected. R animals excreted 71% of the administered radioactivity (18% in urine, 53% in feces), whereas S animals excreted 51% of the dose (23% in urine, 27% in feces). Fecal metabolite (s), expressed as percent of the dose, were compared for the two strains.

Where is p 13748 ? None ?

An approximate 2-fold greater amount was observed in the R animals. The increased rates of excretion and metabolism may play a part in the mechanism of resistance observed in these animals.

MacNay (1965) discussed the control of mice, rabbits and deer in the orchards of Ontario and Quebec. He listed a number of possible control methods but indicated that ground sprays of DDT, toxaphene or endrin should be used only as a last resort.

Effects of endrin on vole (Microtus pennsylvanicus) reproduction in blue grass meadows was studied by Snyder (1963). Endrin spray was applied at rates of 0.6, 0.9, 1.3 and 2.0 lb/acre. Censusing was done 2 to 4 months after application. The 0.6 lb/acre application caused no population decline. Applications at 0.9, 1.3 and 2.0 lb/acre caused reductions of 95, 92 and 71 percent, respectively. Application of 0.6 and 2.0 lb/acre caused a reduction in the number of litters.

A hazard related to endrin ground cover spray use involves fish losses due to runoff into farm ponds or adjacent stream drainages. Such incidents may be related to heavy rains immediately following application, or spraying of endrin on frozen ground where penetration is adequate. Studholme (1958) contacted owners of 15 farm ponds in Pennsylvania orchard spray areas and found that 6 had experienced partial or complete loss of fish. A 1959 news release (N.H.F. & G. Dept.) states that the first fish kill in Pennsylvania attributed to water pollution by endrin employed to control mice occurred on Yellow Breeches Creek in Cumberland County. The stream kill appeared to be complete and included

suckers, chubs and minnows. Some endrin had accidentally been spilled while being mixed in a sprayer alongside the stream. Tarzwell (1958) commented on apparent endrin contamination of a spring used as a domestic water supply. The source was in a drainage area in Menallen Township, Pennyslvania planted to fruit trees. Bioassay studies showed a complete kill of fathead minnows in 4 hours, indicating a concentration of 10 ppb.

The North Carolina Water Quality Division (1971) issued a report of a fish kill in Lake Tunaluska, Haywood County. This loss resulted from endrin used for rodent control by apple growers in the lake drainage basin just a few days prior to the kill. Endrin residues were washed into an inlet stream by a heavy rain on November 20. Fish mortalities occurred from November 21, 1970 to the latter part of March, 1971. Endrin concentration in the water (less than 0.001 mg/l) was less than the TLm value for carp. However, the long exposure time created by confinement to the lake permitted accumulation of sufficient endrin to cause death. As An estimated 15,776 fish of 8 species perished. Up to 0.66 ppm endrin was found in bottom mud. One fish contained 3.3 ppm endrin in the liver, while another showed endrin residues of 1.62 ppm for flesh and 1.10 ppm for kidney tissue.

Rogers (1972) gave data on water samples from 8 ponds located near Hancock, Maryland orchards where endrin was applied. Five of these proved negative while the other contained 0.32, 0.21 and 2.90 ppb.

Wolfe, et al., (1963) reported upon the possible health hazards of agricultural uses of endrin in the Pacific Northwest. Analyses of

residues on 17 samples of windfall apples ranged from 0.3 to 1.2 ppm. This average residue of 0.6 ppm would appear to present little hazard to children or others. Endrin residues on sprayed orchard grass and fescue were very persistent.

A study was undertaken during 1957 to determine the most effective method of controlling meadow mice (Microtus sp.) that were girdling trees in a 140-acre commercial holly grove in Santa Cruz County, California (Dana and Shaw, 1958). A small one-quarter acre test plot was treated in June with endrin at a rate of 2 lb/acre. Subsequent trapping and visual observation showed that this treatment kept the area free of mice for about 58 days. Another test in October at the same rate gave protection for 71 days.

Alfalfa is a major crop in the southern Sacramento Valley, California and fields are frequently plagued with irruptions of meadow mice (Hunt and Keith, 1962). Tests were made to determine the efficacy of endrin for mouse control in dormant alfalfa. This area is also an important wintering stie for migratory ducks and geese, and contains an abundant pheasant population. Alfalfa is one of the few sources of green feed available to these birds in winter. Sites treated for mouse control were observed to determine if treatments resulted in wildlife mortality. Four dead cackling geese, a dying house cat, a dead jack rabbit, a dead killdeer and a dead long-eared owl were found on or near a 30-acre treated area. A dead pheasant, a dying pheasant and a dead cackling goose were found on other treated areas.

Tests were begun to find if birds suffered mortality while held on treated fields. Eight cackling geese, seven pintails, seven widgeon and ten pheasants were placed in cages on a field treated with 0.8 lb/acre of endrin. Within one week, four geese, two pintails and one widgeon had died, while birds held under similar conditions on untreated fields all survived. Endrin residues on alfalfa during this test ranged from 23 to 120 ppm.

These data were also reported upon by Keith, et al., (1962). Laboratory studies showed this chemical to be apparently equally toxic to widgeon, cackling geese and white-fronted geese. The acute oral LD_{50} of endrin to these species is between 2.5 and 5.0 mg/kg. Residues extracted from birds found dead on alfalfa fields treated with endrin showed 1.8, 2.0, 2.4 and 2.4 ppm for cackling geese and 2.8 ppm for ring-neck pheasant.

Hunt and Keith (1962) also reported upon residue analyses of cackling geese exposed to endrin on a plot treated for mouse control. Four wild birds found dead contained from 1.8 to 2.4 ppm, four captive birds dying after exposure in cages contained 1.7 to 4.1 ppm, and four captive birds surviving exposure in cages showed 0.8 to 2.4 ppm. All analyses were based upon composite samples of heart, liver, brain, kidney and muscle.

These authors reported upon effects to wildlife of another endrin use. Seven valley quail, submitted for examination from the Watsonville area, were found dead on berry fields sprayed with endrin at 0.3 lb/acre for blackfly control. Residue analysis of a composite of seven quail livers showed 3.35 ppm endrin and 4.30 ppm dieldrin.

Two reports of pheasant mortality were received from farmers in the Tule Lake area. Two dead pheasant chicks were found in one potato field, and 20 dead hens and 10 dead chicks in a second field. Both fields had been treated with 9 ounces of endrin/acre for the control of aphids just before the losses occurred.

Ferrel (1963) reported that an investigation was made of a die-off of jackrabbits and cottontail rabbits near San Lucas, Monterery County, California. By actual count, 147 jackrabbits and 18 cottontails were found dead in the vicinity of a 92-acre alfalfa field. Endrin was applied to this field for the control of cutworm at 0.8 lb/acre just prior to the die-off. Endrin residues of 1.6 ppm were present in the composite sample of liver and kidney tissue of one affected jackrabbit, thus implicating endrin as the cause of this die-off.

To recapitulate the data on mouse control with endrin in orchards, an account by Krestensen (1972) gives a brief synopsis of difficulties encountered with pine mice. He mentioned the experimental use of a 24-acre block in a 300-acre abandoned orchard near Hancock, Maryland. The area had been abandoned 4 years previously. Endrin was applied in the fall of 1967 to bring a heavy population of mice under control. Since 1968, approximately 35 trees were lost due to damage occurring between abandonment and the 1967 application of endrin. No endrin was applied after 1967 and now approximately 80 percent of the remaining orchard is dead with most dead trees showing mouse damage. This may be an extreme case but shows that some orchardists would be placed at a severe financial

disadvantage if endrin was banned for use in mouse control. It is claimed by most orchardists within the pine mouse range that endrin may provide effective if not complete control of pine voles under proper soil and weather conditions, although failure do occur. Withdrawal of this endrin use could well create a crisis in pine mouse control since other baits or ground sprays generally prove less effective. It may be well to consider a limited extension of this endrin use pending completion of trials on an anti-coagulant chemical which poses less hazard from the standpoint of acute toxicity. This compound shows some promise in preliminary testing and is being used under experimental permit. To our knowledge, no other adequate substitute is currently available for this specialized use.

Attempts at substitute methods of orchard mouse control were reported by Tietjen (1969). In the search for new poisons, Gophacide,(R) an experimental organophosphate coded DRC-714, was first investigated in 1961. Gophacide has a potential for broad use against many agricultural pests including meadow mice and pine mice. In laboratory tests it was effective against both with an LD_{50} of 3.6 mg/kg for meadow mice and approximately 10.0 mg/kg for pine mice. In field tests conducted against meadow mice in Colorado, Gophacide in an oat groat bait at a concentration of 0.08 percent, gave better than a 90 percent reduction in activity one week after treatment.

With the pine mouse, he failed to come up with a grain well enough accepted to be used as a bait. An additive was found to make grain bait more palatable. A fruit extract, DRC-470, proved effective. When 0.2 percent of this material was added to Gophacide-treated oat groat baits

acceptance increased four-fold (from a mean of 0.23 g/animal/day to 0.97 g/animal/day), no mice refused the baits, and all died. During November 1968, two large-scale field tests were conducted in Ohio with the trail-builder and the oat groat bait plus additive. Pre- and post-treatment trapping periods were 3 days each with post-treatment trapping commencing 7 days after treatment. These tests resulted in a 91 and 94 percent reduction in activity of mixed populations of meadow and pine mice.

Hazards to men and wildlife must be ascertained before Gophacide can be registered for operational use in orchards.

III.C.3.d. Use of Endrin-coated Conifer Seeds in Reforestation - For about the past 15 years, endrin-coated conifer seeds have been used to reestablish forests on burned-over or clear-cut areas. The method is used extensively for fir, pine and redwood reforestation in the Pacific Coast States and also for pine regeneration in the Southeast. As pointed out in Chapter VIII, there are numerous published reports that seed-eating rodents or birds may consume large quantities of conifer seed and adversely affect reforestation efforts. White-footed mice, chipmunks, ground squirrels, shrews and certain seed-eating song birds all have significant effects on reseeding.

It is now common practice to protect conifer seed from such destruction by coating seeds with endrin at a concentration of 1 lb. actual endrin per 100 lb. conifer seed. Endrin is used in conjunction with Arasan (thiram) or a latex-like adhesive to bind the endrin to the seed. Also a dye or aluminum powder coating is added in an attempt to make the seed less attractive to birds.

Morton (1967) reported upon the effects of aerial distribution of endrin-coated Douglas fir seeds upon the aquatic life of an Oregon coastal stream. A forest fire destroyed or damaged 46,000 acres of timber in the upper Smith River drainage, a Pacific coastal stream located in west central Oregon. Federal and State agencies were concerned over the possible effects of endrin-coated seed on trout and salmon in streams of the treated Oxbow Burn area. Earlier study had shown that each treated seed carried about 0.11 milligram endrin per seed. In the laboratory aquarium, under static conditions, it was found that six treated seeds placed in 15 l water at 55°F. would kill half the rainbow trout in 2 days and all of them in 3 days.

Results of field observations and analyses of samples of live-boxed and wild salmon, trout and other native species showed no mortality or residue deposition in tissues over a 6-week period following application. Seeds were applied at a rate of 3/4 lb/acre of 1 percent formulation endrin coating. This gave a calculated rate of 0.0075 pounds actual endrin per acre, or 4.8 lb. per square mile. Analyses of 4 water samples taken 1-10 days after seeding gave 2 readings of less than 0.04 ppb endrin, one of 0.05 ppb and one of 0.556 ppb. The only fish with endrin in their tissues were red-sided shiners (Richardsonius balteatus) which showed 30 ppb. Residues of 25 ppb also were found in Pacific crayfish (Astacus trowbridgi). While this study indicated no serious threat to game fish, it was suggested that every effort be made to keep treated seed out of streams.

Marston, et al., (1969) described the reseeding of a 175-acre "clear-cut" watershed in the headwaters of the Alsea River, Oregon. This followed

the conventional practice of aerially broadcasting endrin-coated Douglas fir seed. Seeding produced measurable amounts of endrin in the streamflow for 2 hours after seeding started and again during the peak flow of a winter freshet 6 days after seeding. Total endrin detected during these two runoff periods amounted to only 0.12 percent of that theoretically applied to the entire watershed. This was much lower than laboratory results (11.3 percent) from soaking endrin-treated seed in distilled water for 32 days. No data were given on wildlife effects.

Hooven (1957) reported upon a field test of endrin-treated Douglas fir seed. The experiment sought to check the effectiveness of endrin for the control of seed-eating mammals. The experiment utilized three 10-acre plots, broadcast seeded at the rate of 0.5 lb. Douglas fir seed an acre. Two plots were covered with endrin-treated (1 percent) seed and one with untreated seed. Plots were located in the Tillamook burn of northwestern Oregon.

A census of small animals through live trapping and marking was taken prior to seeding. Two species of mice (Peromyscus sp. and Microtus thomasi) and one of shrews (Sorex sp.) were captured. Trapping, prior to seed application, showed 47 and 19 small mammals on endrin-treated plots and 26 on the control. Seeding was in January with post-treatment census in May. Only 2 mammals were captured on one treated plot and none on the other. Six deer mice and nine shrews were caught on the control area.

An examination of each plot for seedlings was made in June. Of 100 mil-acre samples per experimental plot, an average of 51 percent were stocked on treated areas and only 13 percent on the control.

Reseeding on the north coast area of California covered 2,200 acres in 1965-66 and 7,613 acres in 1966-67. Three-fourths to one pound per acre of Monterey pine or Douglas fir seed was applied per acre. Most was treated with 1 percent endrin although part received only 0.5 percent (Hunt, 1967). There was concern over possible harm to anadromous fisheries and wildlife resources.

Bioassay with 1 percent endrin-treated seeds and rainbow trout showed that two or more endrin-treated seed in a 5-gallon aquarium were fatal (5 fish--66 hour LC_{100}). Residue levels in flesh and in fat at various exposures are given in Table III.C.5. Tests were also made on California valley quail. A single seed with a calculated 0.219 mg endrin content produced 73 percent mortality. Two seeds (0.438 mg) gave 100 percent kill.

Post-treatment collections of birds and mammals were made in 1966 on two reseeded areas. Six of 15 samples positive for endrin residues are shown in Table III.C.3.

Table III.C.3.

Endrin Residues in Wildlife from Ingesting Treated Conifer Seeds

Species	Tissue Analyzed	No. In Sample	Endrin ppm
Blue Jay	Intestine	2	3.18
Mountain Quail	Intestine	1	1.24
Varied Thrush	Intestine	4	.78
Valley Quail	Intestine	1	.79
Chickaree	Intestine	1	.56
Gray Squirrel	Stomach	1	1.17
Gray Squirrel	Intestine		1.55

In 1967, collections were made subsequent to reseeding treatments. Residue checks were made also on two mountain and three valley quail taken miles from any source of endrin. No background levels of endrin were found in these birds. From treated areas, whole body analysis of Steller's Jay and flicker showed .13 ppm endrin and another jay--.15 ppm. Other checks on three jays showed .03 ppm and on five miscellaneous small birds--.47 ppm.

A study was made to determine the toxicity of endrin treated seed to steelhead fingerlings placed in live cars of a small creek (.45 cfs). Endrin treated pine seeds were put in cheese cloth bags and placed in the stream above each live car. Results are shown in Table III.C.4.

Table III.C.4.

Endrin Residues from Treated Seed in Steelhead Fingerlings

Live Car Number	Lbs. seed/cfs cumulative total	Endrin Residue (ppm) whole fish*	fat	water
1	0	.001	.045	ND
2	.32	.013	.64	.000016
3	1.0	.036	3.05	.000041
4	1.8	.051	2.00	.000039
5	3.2	.102	7.39	.000243
6	5.6	.156	8.76	.000208

*Composite of 10 fingerlings.

Total amount of seed used above was more than 26 times the theoretical amount that would result from the prescribed application rate of .75 lb/acre, indicating little hazard from acute effects.

In an earlier paper on the same studies, Hunt (1966) gave the data in Table III.C.5 on fish from bioassay. Levels of endrin residue found in control fish and water make these data somewhat questionable.

Table III.C.5.

Endrin Residues in Rainbow Trout Exposed to Treated Seeds in Water

Fish Exposed to No. of Seeds	Endrin (ppm) Based on Whole fish	fat content
0	1.5	98.8
1	1.9	139.0
2	1.6	93.2
4	1.9	192.0
16	2.6	290.0
32	2.9	408.0
64	2.8	327.0

Another more recent report from the California Division of Fish and Game (1968) discusses studies related to endrin-treated conifer seedings on 20 different areas in Humboldt County. A pine seed reforestation project was treated with endrin-coated seed on January 15, 1968. On February 5, 41 dead varied thrush and 2 dead Oregon junco were found. where? On February 8-9, another field search revealed 37 varied thrush, 2 juncos, 1 valley quail, 1 hairy woodpecker and an affected flying squirrel.

Samples checked gave endrin residues as shown in Table III.C.6.

Table III.C.6.

Endrin Residues in Animals Exposed to Field Application of Treated Conifer Seed

Species	No. In Sample*	Tissue	Residues In ppm Endrin
Varied thrush	10*	Digestive tract	11.0
" "	"	gizzard	134.0
Varied thrush	10	Digestive tract	16.5
" "	10	" "	8.6
" "	6	" "	10.2
" "	"	gizzard	18.8
Oregon junco	2	whole	1.397
Varied thrush	8	flesh	0.32
	"	fat	1.71
Varied thrush	1	Digestive tract	71.5
" "	1	" "	85.8
" "	1	Brain	0.081 not dead ? ?
" "	1	"	0.591 <
" "	1	Fat	8.17
" "	1	"	6.08
" "	1	Flesh	3.82
" "	1	"	7.50
Flying Squirrel (sick)	1	Stomach & Intestine	0.30
Varied thrush	1	Whole bird	3.6
" "	1	" "	1.1
" "	1	" "	N.D.
Oregon junco	1	" "	0.572
Steller Jay	1*	Whole bird	0.44
Varied thrush	3*	" "	2.08
Oregon junco	1*	" "	2.26
Jay	1**	" "	0.006
Black-backed three-toed woodpecker	1*	" "	N.D.
Varied thrush	1**	" "	1.5
Brown headed-cowbird	1**	" "	N.D.

Table III.C.6 (continued)

Species	No. In Sample*	Tissue	Residues in ppm Endrin
Sparrow	1**	" "	.0084
H. thrush	2**	" "	N.D.
Oregon junco	3**	" "	N.D.

*=Found dead

**=Shot

Cotton and Herring (1972) discussed another incident of wildlife losses from reforestation efforts. Five bobwhite quail were found dead in clear-cut area in Stone County, Mississippi directly treated with endrin-coated longleaf pine seeds. Contents of three quail crops from treated areas showed 14.4 percent pine seed by weight. GLC analyses of pine seeds from these crops showed:

Endrin	48.906 ppm
Δ - keto endrin	18.920 ppm
Total endrin	67.826 ppm
dieldrin	0.453 ppm

Contents of crops from 3 quail collected several weeks later from treated areas, one-third pine seed by weight, analyzed 37.84 ppm endrin and 16.58 Δ-keto endrin or 54.42 ppm total endrin. Soybeans composed 100 percent of two quail crops from an untreated area. No endrin residues were found in the crop contents or gut but brain tissue showed 0.3 ppm endrin.

Studies by Hamrick (1969) are reported in greater detail under the wildlife acute studies section. However, it should be mentioned here that he found that the force-feeding of one endrin-treated slash pine seed each to 10 bobwhite quail resulted in 100 percent mortality within 60 hours.

These data demonstrate that, on occasion, the aerial distribution of endrin-coated conifer seed can have a deleterious effect on seed-eating birds. One might consider this a hazard to "non-target" species since forest-dwelling rodents are evidently responsible for a major part of seed losses.

Concern over wildlife losses must be tempered by the fact that, prior to the use of endrin, direct seeding attempts generally failed. Hazards related to endrin seed treatment are minimized by the low total poundage used, low application rate per acre, and infrequent use on managed forests where the harvest cycle may extend from 30 to 100 years or more.

Some alternative compounds are being tested as potential replacements for this endrin use. At present, there are no registered substitute materials available. Substitution with a control agent of lower acute oral toxicity would be desirable.

The loss of Douglas fir (Pseudotsuga menziesii) seed to small mammals is a major obstacle to the success of natural and artificial seeding. Baiting with 1080 and treating seed with endrin have been used to prevent lossess but these materials are now subject to Federal and State restrictions. Pank and Matschke (1972) reported on the

decline and reinvasion of deer mouse populations after baiting Douglas fir clear-cuts with 6-aminonicotinamide. Oat groats treated with 1.0% active ingredient by weight were broadcast at 1/2 lb/acre on three 40-acre clear-cuttings. Livetrapping one week after baiting indicated a 100% reduction of resident deer mouse populations. After one month reinvasion had brought enough population to justify rebaiting according to the criterion of five mice captured per 100 trap nights. Laboratory tests showed good acceptance and effectiveness with 12 species (new and old world mice, rats, nutria, pocket gophers and jack rabbit). Initital studies indicated no secondary poisoning hazard.

Deer mice (Peromyscus maniculatus) have long been considered a major problem in conifer forest replacement, especially where direct seeding methods are employed. Over the past several decades strychnine, thallium sulfate, endrin and sodium fluoroacetate (1080) have been used for control. However, these are highly toxic and there is need for a safer rodenticide. Howard, et al., (1970) found this species susceptible to diphacinone, an anticoagulant. Consumption of 0.01% diphacinone-treated crimped oat groat bait for at least 3 days was fatal to 80% of the mice. Longer exposures frequently produced 100% mortality. When the 0.01% bait was broadcast at 2 lb/acre in field tests, no deer mice tagged prior to treatment were recaptured. The susceptibility of deer mice to diphacinone suggests that it might become a satisfactory substitute for endrin in control of conifer seed damage.

III.C.4.a. Toxicity to Domestic Animals - There has been an increased need for determining toxicity to poultry and livestock for pesticides

used on forage crops or for parasite control. In 1953, Sherman and Rosenberg checked the oral toxicity of 96% endrin to New Hampshire chicks at 7, 21, 45 and 64 days old. The LD_{50} for 7-day old chicks was 3.5 mg/kg. Older birds were more resistant. At 4.3 mg/kg, there was 50% mortality among 21-day old birds, 40% mortality at 45 days, and 10% mortality at 64 days.

The subchronic toxicity of endrin to New Hampshire chicks was investigated by Sherman and Rosenberg (1954). Endrin added to a starter chick ration at rates of 12, 6, 3 and 1.5 ppm for week-old chicks was continued on test for 42 days. Death occurred rapidly in lots fed endrin at higher levels, the majority succumbing during the first week. The two highest endrin dosages caused chicks to become highly excitable during the first week. Slight disturbances produced flightiness, nervous chirping and convulsion. Effects on mortality or growth of chicks to 7 weeks old showed 95% mortality with 12 ppm endrin, 15% mortality at 6 ppm and no losses at lower exposure levels. Significantly lower weight gains were made by female survivors of treatments containing 12 and 6 ppm endrin. Among male survivors, lower weight gains resulted from feeding rations containing 6 ppm endrin.

Phillips (1973) discussed a case of suspected endrin poisoning in poultry. The ration was fed to a group of day-old chicks and also to 28-week-old hens. All day-old chicks died within 72 hours of initial exposure. One hen died in 13 days, and two others in 20 days. Analysis showed 21 ppm endrin in the diet; 3.9 to 4.9 ppm in carcasses; and tissues 0.7 to 2.5 ppm. These concentrations were considered sufficient to have caused the observed clinical signs and deaths.

Toxicity data for 21 pesticides, obtained by the chick embryo technique, were compared with acute oral LD_{50} values obtained with rats. A rank correlation was established between these two sets of data. Endrin toxicity to the chick embryo correlated well with the rat data (Marliac, et al., 1965).

Accidental endrin poisoning was encountered in seven commercial chicken flocks in the Ottawa Valley, Quebec (Morin, et al., 1970). Both endrin contaminated feeds and endrin compounded rations proved toxic for chickens. Losses of 74, 80 and 90% occurred in flocks fed rations contaminated with 19, 32 and 35 ppm endrin, respectively. Effect of rations containing known levels of endrin showed losses on the seventh day in groups fed 30 ppm or more endrin, leading to 100% mortality in 21 days. In a group fed a ration containing 15 ppm endrin, losses occurred later and totaled 62.5%. The LD_{50} for broiler chickens, 5 weeks of age, was between 2 and 4 mg/kg.

Tucker and Crabtree (1970) indicated the acute oral toxicity of endrin to 1-2 year old domestic goats to be 25-50 mg/kg. The reference test "Garner's Veterinary Toxicology," revised by Clarke and Clarke (1967), states that endrin has been found effective as a systemic acaricide in cattle. However, at a dose rate of 10 mg/kg of body weight administered subcutaneously, it was toxic to the host.

Steers, lambs and hogs fed endrin at dietary levels of 0.1 ppm for 12 weeks showed little tendency to deposit endrin in body tissues in concentrations higher than in their diets. After 12 weeks of endrin feeding at 0.25 ppm, the endrin content of the fat of these animals was not higher than 0.2 ppm. Other tissues

showed no detectable endrin at this intake level. At the 2.0 ppm level, steers showed 0.9 ppm in both body and renal fat at 12 weeks. These residues dropped to 0.3 ppm at 18 weeks (Terriere, et al., 1958).

Radeleff (1964) recorded results of various feeding levels of insecticides to cattle and sheep for various times, and maximum fat residues resulting from such dosages. Endrin fed at 2.5 ppm in the diet for 16 weeks resulted in a maximum fat residue of 1.6 ppm for cattle and 3.2 ppm for sheep. Feeding at 5.0 ppm produced maximum fat residues of 2.4 ppm in cattle and 2.2 ppm in sheep.

Endrin was recommended in 1958 for sugarcane borer control. A few growers grazed sheep in their fields for grass control. Studies were made on endrin residues found in lamb fat from animals allowed to graze for 55 days on endrin-treated pasture. One-fourth pound endrin was applied to a 0.5 acre pasture at intervals of roughly 1 week apart for a total application of 0.75 lb/acre. On removal, 2 animals showed residues of 18.3-23.4 ppm endrin for internal fat and 11.5 to 14.0 ppm for external fat. Two animals sacrificed at 14 days after removal had 20.3 - 23.7 internal and 14.6 - 20.1 ppm endrin in external fat. Final figures after 42 days on untreated pasture were 8.9 - 13.8 ppm internal and 6.4 - 11.0 ppm endrin residues in external fat. Appreciable endrin residues were still present in lamb fat 42 days after removal from the treated pasture (Long, et al., 1961).

Endrin was administered to bred ewes in order to determine toxicant storage by the ewe and transferral to the lamb from various dietary intakes.

Treatments were at zero, 0.75 and 2.0 ppm of the roughage consumed. The toxicant feeding period was 12 weeks, at which time one ewe on each treatment level was slaughtered. Remaining sheep were carried an additional 6 weeks on the same ration without endrin added. The only source of toxicant to the lamb was through the ewe's milk. Lambs were slaughtered when approximately 40 days old. Milk samples were collected at 2, 7, 20 and 40 days post-partum.

Ewes sacrificed after 12 - weeks exposure showed from 0.2 to 1.5 ppm endrin in the fat. All samples had less than 0.1 ppm in flesh. Fat content of endrin in lambs whose dams received endrin showed 0.3 to 0.5 ppm. Milk samples from ewes receiving endrin gave values of 0.2, 0.4, 0.13 and 0.21 ppm at 2 days. Figures for 7 days were 0.6, 0.7, 0.12 and 0.18 ppm. Residues in milk 20 days after birth were 2 samples less than 0.01, 2 at 0.01, and 1 at 0.08 ppm. Finally, the data at 40 days showed one sample at less than 0.01, 1 at 0.02, 2 at 0.03 and 1 at 0.05 ppm (Street, et al., 1957).

does this study deal with skin?

Chlorinated hydrocarbon insecticides are fat soluble and when sprayed on cattle and sheep to control parasites may be absorbed through the skin. Studies were made at Kerrville, Texas over a 6-year period to determine whether or not similar dosages used in feed would lead to meat and milk contamination and how long residues might persist (Claborn, 1956). Fat samples were obtained by biopsy, and the data are presented in Table III.C.5.

similar to what?

Table III.C.7.

PPM of Endrin Stored in the Fat of Domestic Animals

Dosage (ppm)	Animal	Weeks After Continuous Feeding			
		4	8	12	16
5	Steer	1.4	-	2.5	1.9
		-	2.2	-	-
"	Heifer	1.2	-	2.4	1.3
		-	0.8	-	3.6
	Av.	1.3	1.5	2.4	2.3
"	Wether	1.9	-	0.5	3.5
		-	1.5	-	1.4
"	Ewe	1.1	-	1.2	1.7
		-	2.4	-	-
2.5	Steer	0.9	-	0.4	1.6
		-	2.8	-	1.0
2.5	Heifer	1.6	-	1.3	0
		-	2.3	-	0.6
"	Wether	3.4	-	2.8	0.9
		-	1.8	-	0.3
		-	-	-	1.6
		3.1	-	1.8	2.7

Ely, et al., (1957) reported upon endrin found in milk of cows fed endrin-sprayed alfalfa and technical endrin. Hay made during 2 seasons from alfalfa sprayed with 2.7, 6.6 and 7.8 oz. endrin/acre, harvested one week after spraying and stored dry in bales for 6 months, had 2.8, 3.7 and 1.9 ppm endrin, respectively, when fed to dairy cattle. Cows receiving hay containing endrin residues of 1.9, 2.8 and 3.7 ppm produced milk with less than 0.15, 0.14 and 0.15 ppm endrin, respectively. When feeding endrin dissolved in soybean oil to milking cows, higher intakes were required to detect endrin in the milk than when feeding endrin residues on alfalfa hay. Toxic symptoms were noted in two cows receiving more than 1.5 mg/kg of endrin in soybean oil.

Dairy cows were given daily doses of endrin ranging from 0.1 to 2.0 total dietary concentration for 12 weeks. Milk samples were analyzed for endrin residues during and after the endrin intake period. Various tissue samples were also analyzed for endrin content at the end of the 12-week period. Small amounts of endrin (less than 0.01 to 0.10 ppm) were detected in milk at all levels of intake. Concentrations of endrin up to 1.0 ppm were found in the body fat (Kiigemagi, et al., 1958).

Residues in milk cows fed rations containing low concentrations of five chlorinated hydrocarbon pesticides were studied by Williams et al and Mills (1964). The study involved 16 lactating dairy cows in which mixtures of five pesticides were fed at approximately 0.05, 0.15 and 0.30 ppm of each pesticide. The study included 2-week prefeeding, 5-week pesticide-treated feeding, and 3-week postfeeding periods. Heptachlor epoxide and dieldrin transferred in the milk in the highest concentration with endrin next in order. Plateau endrin residue concentrations in milk for the three feeding

levels were 0.004, 0.010 and 0.018 ppm, respectively. This study showed that very low endrin feeding levels will result in measurable residues in cow's milk.

In the period 1964 through 1967, various chlorinated hydrocarbon residues were detected above the actionable level in milk production of 40 Wisconsin dairy herds. Endrin was detected in milk produced by one herd. The herd had been treated with an old dust? formulation of rotenone for louse control. Shortly after application, three animals went into convulsions and one eventually died. Approximately 30% endrin was detected in a small dust sample. Endrin detected in extracted milk fat at 3 intervals over a 5-week period was 6.76, 0.81 and 0.13 ppm (Moubry, et al., 1968).

Endrin and four other organochlorine pesticides were fed in combination at low levels (0.05, 0.15 and 0.45 ppm) to hens. Residues were determined in abdominal fat, breast muscle and livers. Tissue samples, taken from birds at each feeding level and a control at regular intervals during a 5-month period, included 2 weeks pre-~~fortification~~ treatment, 14 weeks on the ~~forti-~~ treated ~~fied~~ feed, and 1 month withdrawal. Endrin levels in fat ranged from about 0.3 to 3.0 ppm and correlated directly with levels in the diet. Residues in breast muscle all were very low-below 0.03 ppm. Residue plateau really levels in livers after 14 weeks of fortified diet were 0.1, 0.2 and 0.35 for the 3 levels fed (Cummings, et al., 1967).

A companion study by Cummings, et al., (1967a), recorded residues in chicken eggs from low level feeding of five insecticides. Sixty laying hens were carried for a 20-week period to show residue levels in eggs from birds maintained on feed containing 0.05, 0.15 or 0.45 ppm

of linden, heptachlor epoxide, dieldrin, endrin and DDT in combination. The rate of decline of residue in eggs also was measured over a one-month withdrawal period. While dieldrin and heptachlor epoxide showed greatest storage in eggs, endrin was third among five compounds. The "background" or prefeeding levels of endrin were less than 0.01 ppm. Within 3 days after feeding pesticide-fortified rations higher levels were observed. There was a direct relation between the plateau level and the level of pesticide in the feed. All endrin residues were found in the yolk. Peak residues after 96 days on treated feed were nearly 0.03 ppm at the 0.05 ppm feeding level; about 0.09 at 0.15 ppm dosage; and 0.03 at the 0.45 ppm treatment rate. In the latter case residues dropped about 45 percent after a 30-day return to the uncontaminated diet.

Effects of endrin on the cardiovascular system of the dog were examined by Hinshaw, et al., (1966). Experiments were carried out on anesthetized dogs administered endrin (3 mg/kg b.wt., i.v.). A marked and progressive increase in venous return (cardiac output) occurred within 30 minutes following administration. Total peripheral resistance fell significantly and remained low. No changes in pulmonary vascular resistance were observed. Endrin appeared to exert a toxic action on the left ventricle; left heart failure shown by elevated left arterial pressure regularly occurred. Animals given endrin exhibited large increases in blood catecholamine concentration. Adrenalectomy significantly decreased catecholamine which, however, remained elevated above pre-endrin values.

III.C.5.b. Effects on Eggs and Embryos - Analysis of egg yolk and poultry tissues for chlorinated hydrocarbon residues was conducted by Stemp, et al., (1964). Recovery of endrin from egg yolk varied from 80 to 84 percent while that from chicken fat was 84 to 86 percent.

Leghorn laying hens were orally administered endrin at three levels by capsule. Hens were later slaughtered, and abdominal fat samples collected. Both carcasses and fat were pressure cooked in an autoclave for 3 hours at 15 p.s.i. Over 95 percent of the insecticide residues were rendered from the body tissues within one hour and detected in the fat drippings. Only a trace of residue remained in both white and dark meat at 2 and 3 hours of processing. Continued heating of fat drippings produced some destruction of endrin (Stemp, et al., 1965).

Known quantities of various pesticides were injected directly into the yolk of incubating eggs. Most compounds tested at 10 ppm had little effect except endrin which showed only a 40 percent hatch. At 100 ppm the hatching rate for endrin-treated eggs was only 20 percent (Dunachie and Fletcher, 1966).

The extraction efficiencies, based on the amount of endrin removed by an exhaustive extraction of four procedures, were compared for effectiveness in removal of residues incurred in eggs from hens fed endrin (Wessel, 1969). Endrin residues in eggs from the various samples and methods tested gave readings of 0.01, 0.02-0.03, 0.09, and 0.18 - 0.20 ppm.

Twenty-five insecticides were tested for their toxicity to hen embryos at various concentrations, using an egg injection technique. Most organochlorines did not harm the embryo at high dosages (up to 500 ppm), with notable exceptions to this among the cyclodienes. Results expressed as percent endrin-treated eggs hatching compared with a control group were 30 percent at 100 ppm; 39 percent at 50 ppm; 23 at 25 ppm;

103 at 10 ppm; and 109 at 5 ppm. Endrin did show inconsistent results. The terminal stage of incubation was the most susceptible. Effects of time of administration of 100 ppm on the hatching of hen's eggs, expressed as percentage of survival compared with the control were at day 5-4; at day 8-75; and at day 10-100 percent. A delay of 8 and 10 days in injecting greatly reduced the toxicity. In a starvation experiment at a dose of 5 ppm all chicks were dead by the fifth day; with the same dose and feeding, there was complete survival (Dunachie and Fletcher, 1969).

The effect of injection of chlorinated hydrocarbon pesticides on hatchability to eggs also was studied by Smith, et al., 1970. Injection of 0.2 mg of endrin into fertile eggs after 7 days of incubation decreased hatchability to 40 percent. Higher levels were very toxic and resulted in as low as 1.8 percent hatchability. The concentrations of endrin used were 0, 0.2, 0.4, 0.8, 1.6 and 2.0 mg/egg.

III.D. Toxicity to Other Organisms of Land and Water

III.D.1. Toxicity to Microflora - Vance and Drummond (1969) reported the biological concentration of pesticides by algae. Algae, the base constituents of the aquatic food web, concentrate pesticides many fold and generally are more resistant to toxic effects than higher members of the food chain. Unialgal culture of two blue-green algae, (Microcystis aeruginosa and Anabaena cylindrica, and two green algae, (Scenedesmus quadricauda and Oedogonium sp., were grown under continuous florescent lighting in aqueous solutions of endrin dissolved in acetone. Comparative LC_{100} values for the four species listed above were < 5, > 15, > 20, and > 20 ug/ml respectively. Concentration factors of pesticide residues extracted after 7 days exposure were in the order 200, 222, 156 and 140X, respectively.

Some chlorinated hydrocarbon pesticides can be converted in natural environments to forms more stable and sometimes more toxic than the parent compounds which have been called "terminal residues," (Eagan, 1969). Batterton, (1971) tested the effects of endrin and metabolites on the growth rates of two bacteria-free, blue-green algal species, Anacystis nidulans a fresh water species and Agmenellum quadruplicatum a marine species. Both species were tolerant to ketoendrin than endrin. Growth rate of marine species was inhibited by all endrin concentrations tested (0.2, 19, 95, 475 and 950 ppb) whereas the fresh water form was affected only at high concentrations. In fresh water algal cultures with 950 ppb insecticide, lag in growth rate was observed for as much as 12 hours preceeding exponential growth. The marine form was generally more tolerant than the freshwater species.

III.D.2. Toxicity to Microfauna and Miscellaneous Invertebrates - Residues of chlorinated cyclodiene insecticides, as a result of their extensive use and high stability, may remain in the soil for extended periods. Evidence has been found, however, to indicate that some micro-organisms from soil are capable of degrading even the highly persistent pesticides. Matsumura, et al., (1971) studied the ability to degrade endrin of about 150 isolates from various soil samples. Of all cultures tested, 25 degraded endrin and ketoendrin, called metabolite IV was formed by all 25 with mass cultures of Pseudomonas sp. Major metabolites were designated as III, IV and V and minor metabolites II and VI.

Bollen and Tu (1971) studied the effects on the activity of soil organisms of endrin applied at rates used with Douglas fir seeds. In commom practice 0.5 - 1 lb. of pine seeds that have been treated with 1-4 grams of endrin per pound acre are applied per acre. At this rate of application 1 seed occurs in each 2-4 square foot with a maximum application of endrin at 3-6 ppm per cubic inch of soil under each seed. Endrin applied to soil at more than three times the maximum that might be expected from application of endrin-treated tree seed exerted no appreciable effect on numbers of soil microbes or on ammonification, nitrification, or sulfur oxidation.

Drake, et al., (1971) studied the effects of insecticides on soil arthropods at Tucson, Arizona. Invertebrates were removed from soil samples in an irrigated pasture treated two years previously at 4 lb/acre endrin. Residue in soil at the time of sampling was 0.60 ppm endrin. Mites and Collembola represented 63 and 31 percent, respectively, of

the invertebrates collected from 15 test plots treated with various insecticides. Analysis of variance indicated no significant differences between plots in total counts of mites and Collembola. There were differences among the treatment means for the other arthropods. Eighty to 90 percent of the mites in the plot treated with endrin were oribatids. Ground pearl crawlers (Margarodes sp.) occurred in samples from each test plot except one treated with DDT-Strobane. Insecticidal residue remaining in the soil apparently had no significant effect on total numbers and kinds of invertebrates in the soil community. Homoptera were greatly decreased in all insecticidal plots. There were no significant differences in numbers and kinds of soil invertebrates from control plots with those treated with endrin two years previously.

Bottom organisms were collected from a drainage stream located adjacent to a commercial orchard which had been treated with endrin for rodent control in Wisconsin (Moubry, et al., 1968). Organisms containing endrin residues included alder fly larvae (Sialis sp.) -- 0.009 ppm; caddis fly larvae (Limnephilus rhombicus) -- 0.003 ppm; and freshwater shrimp (Gammarus sp.) -- 0.013 and 0.025 ppm.

Sanders and Cope (1968) determined the relative toxicity of various pesticides to naiads of three species of stoneflies Pteronarcys californica, Pteronarcella badia, and Claassenia sabulosa collected from Colorado mountain streams, were used. Toxicity of endrin measured for 24-, 48-, and 96-hour exposures at 15.5°C are presented in Table III.D.1.

Table III.D.1.

LC_{50} Values for Stonefly Naiads to Endrin (ppb)

Species	Exposure Time		
	24-hr.	48-hr.	96-hr.
P. californica	4.0	0.96	0.25
P. badia	2.8	1.7	0.54
C. sabulosa	3.2	0.84	0.76

Two species of stonefly naiads, Pteronarcys californica and Acroneuria pacifica also were investigated by Jensen and Gaufin (1966) to evaluate acute and long-term effects of organic insecticides. The two species were exposed to concentrations of insecticides equal to or less than their 4-day TLm. Comparative 4-day TLm values for the two test organisms showed 0.32 ppb for for A. pacifica and 2.4 ppb for P. californica. A progressive reduction of TLm figures occurred for both species exposed to endrin for 30 days. The 30-day TLm for Pteronarcys naiads exposed to endrin was approximately one-half the value for static, 4-day exposures. The 30-day TLm values of Acroneuria naiads represented concentrations more than 10 times less than those of the 4-day static values. Results indicate that endrin has a cumulative effect, and that a relatively large application factor would be necessary when using static 4-day bioassay results for estimating safe concentrations over extended periods.

Tolerances of selected freshwater invertebrates to pesticides were examined by Naqvi and Ferguson (1969). In 48-hour exposures, six species

of cyclopoid copepods from a pesticide contaminated ditch near Nelzoni, Mississippi, were resistant to high concentrations of nine pesticides than the same species from areas of minimal pesticide contamination near State College, Mississippi. Similarly, a clam Eupera singleyi, and a snail, Physa gyrina, from the Belzoni locality had higher tolerances to endrin than the same species from State College. High concentrations of 20 insecticides which killed fish within 3 minutes failed to kill the worm, Tubifex tubifex, from Belzoni in 72-hour tests. The potential hazard of increased tolerances in these invertebrate species is the increase in amount of pesticide residues available to higher trophic levels.

III.D.3. Earthworms - A comprehensive literature review on the effects of chemicals on earthworms was prepared by Davey (1963) which showed that these animals may accumulate persistent pesticides in quantities sufficient to cause toxic effects in predators that feed upon them. Pesticide concentration by animals in terrestrial situations has not been demonstrated as frequently as for the aquatic environment. However, Barker (1958) found that earthworms from areas treated for control of Dutch elm disease contained amounts of DDT that would be fatal to robins. Cramp and Olney (1967) reported that a sample of worms and slugs from an endrin sprayed field contained 10.3 ppm endrin and from this source some birds could receive relatively large exposures.

Earthworms are surprisingly resistant to different pesticide formulations. Endrin dust tested in pot experiments at 5 lb/acre produced no mortality among Eisenia foetida after 2 months exposure

that much?

(Hopkins and Kirk, 1957) and 1024 lb/acre of endrin gave erratic results. Endrin applied as a 0.01 percent emulsion of about 27 lb/acre successfully controlled earthworms in tobacco seed beds in India (Patil, 1960).

Slugs and earthworms in a cotton field accumulated 18 and 11 times the soil residues of organochlorines. Slugs contained 53 ppm DDT and its metabolites, 0.4 ppm dieldrin and 1 ppm endrin. Earthworms contained 32 ppm DDT complex residues and traces of dieldrin and endrin (Dustman and Stickel, 1969).

Soil and earthworms and other soil invertebrates were collected from 67 agricultural fields in 8 states. Total organochlorine residues in soils averaged 1.5 ppm, and in earthworms, 13.8 ppm. Amounts of insecticides in earthworms varied directly with amounts in the soils. Nearly 24 percent of all soil samples contained endrin, but the amount exceeded 0.1 ppm in only 6. Endrin occurred in 39 percent of the earthworm samples. Twenty percent of the samples exceeded 0.1 ppm endrin. Perhaps the most dramatic biomagnification was shown by endrin residue data from a Maryland apple orchard. Endrin ppm values were: soil, 3.47; earthworms, 11.04; slugs, 95.81 - 134.06; and snails, 2.72. Earthworms from another Maryland orchard contained 5.13 ppm endrin. Presumably the endrin was applied for orchard mouse control. Earthworms in this study were represented by four genera: Allolobophora, Diplocardia Helodrilus, and Lumbricus. The amount of residues found in worms from 15 fields was within the range found to kill birds in short-term feeding studies. However, this assumption was based upon invertebrate

residues of DDT and metabolites. The effect of reported endrin levels on animals higher in the food chain is a possible matter of concern, but remains to be adequately evaluated (Gish, 1970).

The effects of endrin on the numbers and biomass of earthworms were studied after application to trefoil pasture which had not been previously treated with herbicides or insecticides for at least five years. Endrin treatment was made at the rate of 1 lb. ai/acre. Numbers and biomass of earthworms three weeks after 20 quadrats were treated ranged from 1 to 17 in numbers and 132.2 gms total biomass. The biomass in treated plots was less than 50 percent that in untreated plots. Endrin lessened numbers in the treated quadrats by 52 percent (Thompson, 1971).

III.D.4. Plankton -- Results from experiments at Woods Hole, Massachusetts cited by Vogt (1970) emphasized the dangers of chlorinated hydrocarbon pollution to the balance of marine life. Some varieties of marine phytoplankton were highly sensitive to some chlorinated hydrocarbon pesticides, but the green flagellate Dunaliella tertiolecta was not sensitive to 1000 ppb endrin. The carbon uptake of Skeletonema costatum and Coccolithus huxleyi was significantly inhibited with 10 ppb endrin. More than 100 ppb DDT blocked cell division in S. costatum after two or three divisions, but had no influence on C. huxleyi. The reverse of these effects was observed with endrin. The carbon uptake of Cyclotella nana, the most sensitive, was inhibited with as little as 1 ppb endrin. Endrin stopped cell division completely. High concentrations of pesticides could affect the regeneration of phytoplankton and their subsequent domination by a single species.

The species assayed above by Menzel, et al., (1970) were obtained from diverse sources. S. costatum is a coastal centric diatom isolated from

Long Island Sound. The naked green flagellate D. tertiolecta is typical of tide pools and estuaries. The other two species, C. huxleyi, and the ccentric diatom C. nana both were obtained from the Sargasso Sea. Sensitivity and response to environmental pollutants may vary considerably among species of marine planktonic algae as shown by the above data. The greater resistance of one estuarine species, in comparison with the susceptibility of coastal and open ocean forms may reflect the need for adaptability. Chlorinated hydrocarbons may not be universally toxic to all species, but may exert a dramatic influence on the succession and dominance of certain forms.

The metabolic transformation of endrin by marine microorganisms was studied by Patil, et al., (1972). Samples of sea water, bottom sediments from both ocean and estuaries, surface films, algae and marine plankton were collected and treated with radioactive insecticides and incubated for 30 days in the laboratory. Seventeen samples were exposed directly to radioactive endrin. Ketoendrin is known to form by either photochemical reaction or microbial actions. Although no photolytic reaction could be observed in control tubes illuminated in the absence of microorganisms, a photosensitizing substance possibly was present among the microbial products and the reaction may have been of a photochemical-biochemical nature. The only water sample which showed degradation was from Hawaiian fish ponds, which contained algae populations. Fish pond water formed 35.5 percent of an unknown metabolite of endrin while an algae collection from a stagnant fish pond formed 24.4 percent ketoendrin.

Stickel (1968) pointed out that aquatic animals can be adversely affected by a reduction in their food supply. Phytoplankton communities

are an important food base in aquatic environments whose productivity can be seriously affected by exposure to small amounts of pesticides. In controlled 4-hour exposure to 1.0 ppm of endrin, lindane and mirex, phytoplankton productivity was reduced 28 to 46 percent (Butler, 1963).

III.D.5. Bees and other Pollinating Insects - Twenty chemical treatments were tested for aphid control in red clover raised for seed in eastern Washington (Johansen, 1960). Predators and parasites of the clover aphid in the control plot were sampled after the applications. During the first six days after application, endrin was the least destructive to beneficial insects. This material reduced predator-parasite populations 38 percent as compared with checks. However, percent honey bee mortalities from treatments on red clover at 0.4 lbs. endrin/acre were 64 percent in one hour, 80 percent in three hours, and 100 percent in ten hours.

Sixty-one pesticides were tested against 5 parasitic hymenopterans and 6 predatory coccinellids. Data served as guides in selecting the best materials for destroying pests without undue harm to natural enemies (Bartlett, 1963). Single dosages applied were those commonly used on orchard crops. The data suggest that the effect of each pesticide upon most adult parasitic hymenoptera may be anticipated with a high degree of reliability. The effect upon predatory coccinellids was much less predictable.

At the high dosage used, many materials were broadly toxic to most entomophagous species tested. Among these was endrin applied as a 50 percent wettable powder at 0.5 lb/100 gal. water. Rate of deposition was 6.44 µg/sq. cm. Toxicity ratings were high for 9 and medium for 2 of the 11 species tested. High toxicity was expressed as an LT_{50} of less than 24 hours.

Medium toxicity was delineated as an LT_{50} of greater than 24 but less than 100 hours. ~ both can be equally dead

Endrin used at low concentration (.0447 percent) represented the dilution customarily applied to orchard crops as a complete coverage spray. The high concentration was 10-fold that of the low to simulate possible dehydration of a 10 percent honey bait applied in a water spray.

Toxicity data were presented as H (high)-50 percent mortality within 1 day or less of first exposure; M (medium)-LD_{50} between 1 and 4 days; L (low)-appreciable, but less than 50 percent kill after 4 days; and (0)-no detectable mortality in 4 days. At the lower concentration, endrin-treated bait showed acceptance of 61 and 35 percent for the 2 coccinellid predators with toxicity of 0-L for both. The parasitic hymenoptera showed 45 and 56 percent acceptance and toxicities of L and L-M.

At high dosage level acceptance was lower and toxicities rated higher. For coccinellids, these were 6 and 10 percent acceptance and L and M toxicity. Comparable data for hymenoptera were 17 and 29 percent acceptance with high toxicity in both instances. Stomach poison activity of the chlorinated hydrocarbon group was peculiar. With the exception of endrin, methoxychlor and lindane, which killed certain species, chlorinated hydrocarbons were not generally potent stomach poisons (Bartlett, 1966).

Comparative field studies on the toxicity of pesticides to honey bees (Apis mellifera) were begun by Anderson and Atkins (1967) in 1952 in California and continued to the time of publication. They rated endrin in the moderately toxic group which included compounds having LD_{50} values of 2 to 10 micrograms per bee. Field tests were mainly on alfalfa, cotton, citrus, ladino clover and sweet corn.

Atkins and Anderson (1967) also issued another paper dealing exclusively with laboratory tests. Again they referred to endrin as being moderately toxic. It ranked 58th among 217 compounds tested. The endrin LD_{50} in µg/bee was 2.018.

III.D.6. Crustaceans - A study was designed to determine relative toxicities of several widely used pesticides to the scud, Gammarus lacustris, a crustacean commonly found in small streams and ponds of western United States. Toxic effects were measured by median lethal concentration (LC_{50}) for 24-, 48-, and 96-hour exposures at 70°F. In static bioassays at 70°F, estimated LC_{50} values in micrograms per liter for endrin were 24-hour, 6.4; 48-hour, 4.7; and 96-hour, 3.0 (Sanders, 1969).

The activity in water of 14 pesticides used in Utah was determined by a modified bioassay method using G. lacustris as a test animal. Concentrations (ppm in water) for 96-hour LD_{50} values for endrin were 0.0115 (Nebeker and Gaufin, 1963-64).

Reduction in shell growth, loss of equilibrium, and death are used as criteria of toxicity in oysters, shrimp, and fish, respectively. Since insecticides are designed to kill terrestrial arthropods, there is much concern about the effects of these chemicals on marine crustaceans which have commercial value such as crabs and shrimp. These animals spend much time in shallow estuarine waters occasionally polluted with insecticides. In laboratory studies performed with continuously flowing sea water a small percentage of juvenile brown shrimp, Penaeus aztecus, tolerated a very low concentration (0.025 ppb) of endrin for 60 days; shrimp survive

only a few days at endrin concentrations greater than 0.05 ppb (Lowe, 1966). In Korean shrimp (Palaemon macrodactylus) at temperatures ranging between 13 and 18 degrees C, the 96-hour TL_{50} values (µg/l) for endrin were 4.7 for static bioassays and 0.12 for intermittent-flow bioassays (Earnest, 1970).

Massive fish kills occurred in the lower Mississippi and Atchafalaya Rivers and the Gulf of Mexico, in the fall and winter months after 1960, and were particularly severe in the winter of 1963-64. In fresh waters, primarily bottom-feeding fish were affected, while in brackish waters bottom and surface-feeding species were involved. Analysis of fish revealed that endrin was consistently found in all tissue extracts examined. Endrin was present in lethal amounts in the blood of dead fish taken from the Mississippi River. Specimens of dead or moribund catfish collected from the Mississippi River at Baton Rouge in December 1963 were found to be toxic to mice. In similar tests oysters taken in good condition from Grand, Quarantine, American Bays and other shellfish growing areas were not found to be toxic. Living shrimp collected from the delta of the Atchafalaya River were found to contain 360 ppb endrin as well as other insecticides (U.S. Dept. of H.E.W., Publ. Health Ser., 1964).

In 24-hour bioassays, fresh-water shrimp, Palaemonetes Kadiakensis, from 3 areas of intensive pesticide use in the Mississippi delta were 1 to 25 times more resistant to 7 organochlorine, 3 organophosphorus, and 1 carbamate insecticides than shrimp from Noxubee National Wildlife Refuge (Bluff Lake). Toxicity, ranked in descending order, was: most toxic-endrin, DDT, methyl parathion, parathion; medium toxicity-guthion, lindane, toxaphene, strobane; least toxic-chlordane, sevin and heptachlor.

The mortality of susceptible shrimp caged in a canal near cotton fields, was 66 percent greater than resistant shrimp (Naqvi and Ferguson, 1970).

The importance of daphnids as part of the fresh-water biota, and their sensitivity to toxic substances, stimulated many investigators to use them as assay organisms. The acute toxicity of endrin to Daphnia magna, as indicated by 96-hour bioassays and expressed as TLm, was 0.352 ppm (Anderson, 1959). Organophosphates generally were more toxic than chlorinated hydrocarbons to Daphnia pulex and Simocephalus serrulatus. Toxicity of hydrocarbons to D. pulex varied greatly with 48-hour EC_{50} values ranging from 0.36 to 460 ppb. Estimated 48-hour EC_{50} immobilization values, in micrograms per liter, for daphnids exposed to endrin were: (1) S. serrulatus -26 µg/1 at 60°F and 45 at 70°F; and for D. pulex -20 µg/1 at 60°F. Endrin was 9(6-14) times more toxic than dieldrin to S. serrulatus, while D. pulex showed endrin 12 (8-19) times more toxic than dieldrin (Sanders and Cope, 1966).

Toxicities of pesticide ingredients to some fresh water organisms were reported by Nishiuchi and Hashimoto (1967). Their TLm values for 3 hours exposure to two fresh water daphnids were listed as greater than 10 ppm for both Daphnia pulex and Moina macrocopa. This was a relatively short exposure period. Fresh water fish and daphnids are clearly different in susceptibility to pesticides. It is impossible to presume the susceptibility of the fish to pesticides from that of daphnids and vice versa. A high correlation was recognized between the susceptibilities of the two daphnids.

Specimens of Daphnia magna, killed by extremely small quantities of pesticides also were killed by small amounts of extracts of common plants, such as lettuce, radishes, and beets. Even following rigorous

cleanup, these plant extracts were toxic enough to the test organism to mask any mortality caused by pesticide residues. Although D. magna is extremely sensitive to many pesticides, its sensitivity to certain plant extracts and possibly to other ingredients in commercial insecticide formulations make its use as a bioassay organism of doubtful value. Gas chromatographs equipped with electron capture detectors had an equal or better sensitivity to the insecticides tested, and gave more reproducible and more accurate results on field-treated samples of carrot tops (Frear and Kawar, 1967).

Fish and invertebrates frequenting coastal areas are especially vulnerable to chemical insecticides which tend to diffuse in drainage systems and to concentrate in estuaries (Butler, 1966). Several studies on the effects of insecticides on marine organisms demonstrate that concentrations which are not sufficient to control many species of pestiferous insects, including several species of salt-marsh mosquitoes, can kill eggs and larvae of bivalve mollusks (Davis, 1961) and alter the tissue chemistry of clams (Eisler and Weinstein, 1967). Acute endrin toxicity tests to sand shrimp, (LC_{50} in µg/l) was 2.8 for 24 hours, 1.8 for 48 hours and 1.7 for 96 hours.

For grass shrimp LC_{50}'s for endrin were 10.3 ug/l at 24 hours, 4.3 at 48 hours and 1.8 for 96 hours. Endrin was the most toxic of all organochlorines tested on this species. LC_{50}'s of endrin to the hermit crab were 27 µg/l at 24 hours, 18 at 48 hours and 12 at 96 hours. Lindane, p,p'-DDT and methoxychlor were more toxic among the organochlorines (Eisler, 1969).

Red crawfish, Procambarus clarki, collected at Baton Rouge, Louisiana were exposed to endrin for periods of 24-, 48-, and 96 hours. TLm values were 0.4 ppm for 24 hours, 0.3 ppm for 48 hours and 0.3 ppm for 96-hour exposure. Endrin was the most toxic organochlorine compound checked (Muncy and Oliver, 1963).

III.D.7. Mollusks - A nationwide program was initiated in 1965 to monitor residues of chlorinated hydrocarbon pesticides in estuarine shellfish. About 160 stations were established and samples were collected at thirty-day intervals. Despite the wide array of persistent pesticides used in the United States, only DDT, dieldrin, and endrin occurred most frequently in monitored samples. Estuarine mollusks were collected at monitoring stations in five states in 1967. Endrin residues were detected in samples taken from Texas and California; the maximal level detected was 19 ug/kg. The Gulf Breeze, Florida laboratory accumulated data on relative toxicity of commonly used pesticides when exposed to estuarine test animals for one to four days. In such tests, 48-hour TL_{50} values for various crustacean species usually were 1 µg/kg or less within normal ranges of environmental salinity and temperature (Butler, 1969).

Residues of chlorinated hydrocarbon insecticides in the North Sea environment were studied by Koeman, et al., (1967-1968). In 1964, residues were detected in Sandwich terns and spoonbills seen dying or found dead at Texel in the Dutch Wadden Sea (Koeman and van Genderen, 1966). The symptoms, tremors and convulsions, suggested poisoning, probably by neurotoxic compounds. Distribution of insecticides in the Dutch and

West Germany coastal environment was studied further by using the mussell (Mytilus edulis) as an indicator organism. Mollusks concentrate chlorinated hydrocarbon insecticides as a consequence at their filter-feeding habit. In August 1965, mussels were collect at 20 places along the Dutch coast. Highest residues of chlorinated hydrocarbons were found near the mouth of the Rhine, and at sites to the northeast. This corresponds with the outflow of river water as it moves along the Dutch coast and enters the Wadden Sea. Residues of chlorinated hydrocarbon insecticides in sprat (Clupea sprattus), juvenile herring (Clupea harengus), and sand eel (Ammodytes lanceolatus), captured in the Dutch Wadden Sea in 1965 and 1966 are shown in Table III.D.2.

Table III.D.2.

Endrin in Fishes from The Wadden Sea

Year	Number of fishes	Residue in ppm of body weight (geometric mean and ranges)
		Endrin
1965	103 (11 samples)	0.14 (0.07-0.45)
1966	37 (28 samples)	0.09 (0.01-0.29)

The samples contained telodrin, an insecticide not used in Europe which was manufactured by a chemical industry near the mouth of the Rhine. It is likely that some endrin was discharged in the effluents from the plant. Residues of endrin in mussel (Mytilus edulis) samples along the Dutch and West German Coast, and at one place on the British Coast during the summer, 1966 are shown in Table III.D.3.

Table III.D.3.

Endrin in Mytilus edulis taken near Holland

Sampling Place	Residue in ppm of body weight Endrin
Scheveningen	0.36
Katwijk	0.07
IJmuiden	0.19
Den Helder	0.05
Griend	0.02
Mellum	0.02
Oldeoog	0.01
Scolt Head	< 0.01

Residues of endrin in mussels (Mytilus edulis) sampled at Scheveningen between 1965 and 1967 are shown in Table III.D.4.

Table III.D.4.

Endrin in Mytilus edulis taken at Different Times of the Year

Date	Residue in ppm of Body Weight Endrin
August 1965	0.05
January 1966	0.20
August 1966	0.36
January 1967	0.26
August 1967	0.04

Chlorinated hydrocarbon pesticide residues in California bays and estuaries were studied as a part of a nationwide monitoring program. Endrin was found only at West Island in the Sacramento-San Joaquin estuary. It was reported during three different months at this site. Analyses of clams revealed endrin at 10 ppb or less for the Asiatic clam, Corbicula fluminea. All samples were screened for 10 organochlorine pesticides but only DDT, DDD, and DDE were routinely found. Significantly higher pesticide pollution occurred in estuaries receiving runoff from large agricultural and urban areas than in other estuaries (Modin, 1969).

The effects of pesticides on oyster growth and presence of residues as a public health problem were studied. Growth rate of oysters was

reduced 35 to 100 percent following exposure to 0.1 mg/l endrin. A residue of 0.033 mg/l endrin in sea water caused 50 percent reduction in oyster shell growth. In a 1965 progress report, a Gulf Coast research center indicated 90 oyster samples positive for chlorinated hydrocarbons. Residues in water from which oysters were taken ranged from 0.01 to 0.07 mg/l for endrin. In another study, six oyster samples were taken from Indian River, Brevard County, Florida. Sampling stations coincided with commercial fishing sites and within flowing streams considered highly subject to pesticide runoff. For endrin, the range in water was 0.0013-0.005 mg/l which was below that which inhibit oyster growth (Mason and Rowe, 1969).

Monthly sampling and analyses for endrin residues of mud and water, top-water fish (bream), bottom-water fish (catfish), shrimp, and oysters from the lower Mississippi River were carried out for 1 year. Oysters and shrimp contained less than 0.005 ppm (Novak and Rao, 1965).

Samples of oysters, water, and bottom sediment were collected from the lower Mississippi River region and southern Barataria Bay. Highest endrin concentrations found in water and bottom sediment samples were less than 0.001 and 0.01 ppm, respectively. No endrin residues were reported from oysters (Hammerstrom, et al., 1967).

In a similar study Mobile Bay, Alabama, 82 samples of oyster, of water and 65 of bottom sediment were collected from sites where shellfish were growing. Median residue levels of endrin in positive oyster bottom sediment samples were <0.01 and < 0.001 ppm, respectively. Median

pesticide concentration in positive water samples 0.001 ppm for all chlorinated pesticides (Hammerstrom, et al., 1969).

Wilson (1966) studied the amount of residual pesticides found in oysters under laboratory conditions at Gulf Breeze, Florida. After exposure for 10 days in water containing 1.0 ppm had accumulated in oyster tissue. This indicates a biological magnification of 1000X.

Oysters collected from estuarine areas in South Carolina, Georgia, Florida, Mississippi, Louisiana and Texas were analyzed for pesticide residues. Chlorinated pesticides generally were either not detected or found at relatively low levels in Atlantic and Gulf Coast area samples. Endrin was detected in 27 of 115 oyster samples within the range < 0.01 to 0.07 ppm (Bugg, et al., 1967).

Studies were made to determine endrin concentrations in water, bottom sediment, and oysters in a Louisiana estuarine area, and to determine interaction with bottom sediment. The species concerned was the Eastern oyster, (Crassostrea virginica. The study area was near Barataria Bay, located some 40 miles south of New Orleans. A total of 111 samples were collected on a bi-monthly basis for eight months in 1968 and 1969, in Grand Bayou, Hackberry Bay and Creole Bay. Endrin was not detected in 34 samples (31 percent of the total). Of 62 positive samples, one yielded less than 6 ppb, 10 less than 5 ppb, five less than 4 ppb, one less than 2 ppb, 32 samples less than 1 ppb, one less than 0.8 ppb, and 12 less than 0.5 ppb (Rowe, et al., 1970). Comparison of pesticide concentrations found in 1968-1969 with similar surveys in

1964-1966 and 1965-1966 indicated that pesticide influx into the study area had decreased. The 1968-1969 maximum endrin concentration was 29 times less than in 1965-1966 (Rowe, et al., 1971).

The tendency for molluscs to accumulate aquatic pollutants is well known. This results from their method of feeding which involves filtration of large amounts of water. For this reason, Ryan, et al., (1972) studied use of the mussel Hyridella australis as a biological monitor of endrin in fresh water from a creek in Victoria, Australia. The mussels carried less than 0.01 ppm endrin when collected. Caged specimens were subjected to endrin in the stream. Water samples did not contain more than trace amounts (< 0.01 ppm), but mussels reached a tissue concentration of 0.38 ppm endrin after 24 days. Residue levels later decreased to 0.05 ppm at 68 days. Mussels in an experimental tank with 0.5 ppm endrin in solution reached a tissue residue level of 3.44 ppm in 3 days, a seven-fold increase. When experimental and control mussels were placed together in fresh water, the experimental group quickly lost endrin while the control group took up some of the excreted residues.

Indigenous of coastal areas are especially vulnerable to chemical insecticides which tend to accumulate in estuaries and inshore environments. Mollusks are considerably more resistant to insecticides than either teleosts or decapod crustaceans according to results of 96-hour bioassays with selected groups of marine fauna (Eisler, 1969 and 1970). Test animals were adult quahaug clams (Mercenaria mercenaria), and mud snails (Nassa obsoleta) collected from Sandy Hook Bay, New Jersey. All mollusks

were held 14 days prior to testing in aquaria containing 1,000 liters of sea water. All clams survived for 133 days following exposure for 96 hours to concentrations up to 10 mg/l of the four organochlorine insecticides, including endrin. No deaths occurred among snails during 96-hour exposure to any concentration of endrin or during the remainder of the 33-day observation period. However, gastropods initially exposed to 0.1 mg/l and higher of endrin exhibited a marked reduction in egg case deposition when compared to controls.

Detoxification of pesticidal residues in fish and shellfish was studied by Hallab (1968). The objective was to determine detoxification agents in vivo and in vitro that would lessen or minimize toxicity of chlorinated pesticides with special reference to shellfish. Oysters and shrimp were used as experimental animals. Aminopyrine, orinase, and pyralgin used in 1 and 10 ppm concentrations as detoxification agents were applied to experimental animals with sublethal doses of chlorinated pesticides. Orinase at 1 and 10 ppm showed most promise in degrading pesticides in oysters and shrimp.

In the in vitro studied, oysters spiked with 0.1-2 ppm of chlorinated pesticides were irradiated at different levels of irradiation with CO^{60}, X-ray and ultraviolet rays. X-ray irradiation was ineffective in degrading the pesticide molecule. CO^{60} irradiation showed highly significant effects ($P < 0.01$) in degrading the pesticide molecule at 0.2 and 1.0 Megarad.

III.D.8. Amphibians - Eleven organochlorine insecticides were tested against tadpoles of the bullfrog, Rana catesbeiana, in field ponds. Endrin was

applied at 0.1 and 0.5 lb/acre. With 0.1 lb. endrin/acre a 50 percent mortality occurred at 24 hours and 90 percent loss after 48 hours. Application of 0.5 lb/acre caused 100 percent mortality in 24 hours (Mulla, 1963).

Relative toxicities of several halogenated hydrocarbon insecticides was measured for grass frogs (Rana pipiens) immersed in contaminated solutions. Endrin concentrations of 0.015 and 0.02 ppm showed no lethal effect after 30 days exposure, while 6 of 20 frogs were dead after 30 days at 0.03 ppm. Those immersed at the highest concentration changed skin color and became grayish. Neuro-muscular changes were characteristically produced with 0.03 ppm. Endrin was more toxic than similar amounts of dieldrin, aldrin, chlordane, toxaphene, methoxychlor or BHC (Kaplan and Overpeck, 1964).

Ferguson and Gilbert (1967) tested cricket frogs and Fowler's toads from several localities with differing degrees of insecticide contamination with endrin. The approximate 36-hour TL_{50} values (Mg/ml) for several populations were: northern cricket frog (Acris crepitans) --0.4 to 0.6 ppm, southern cricket frog (Acris gryllus)--0.02 to 0.045 ppm, and for Fowler's toad (Bufo w. fowleri)--0.03 to 0.095 ppm. Anuran populations captured near treated cotton fields showed up to 200-fold resistance compared with populations from pesticide-fee areas. Toads were generally more tolerant than cricket frogs.

Mulla (1962) used insecticides to control excessive populations of frogs and toads in California. Endrin was found to be highly toxic to tadpoles of the bullfrog. A complete kill occurred at 0.1 lb/acre.

Static bioassays were conducted to determine the relative acute toxicities of various pesticides to week-old tadpoles of the western

chorus frog (Pseudacris triseriata) and five-week-old tadpoles of Fowler's toad (Bufo w. fowleri). Endrin was the most toxic to Pseudacris tadpoles, and the second most toxic to Bufo tadpoles. TLm values in mg/1 at 15°C for the chorus frog were: 24 hours-0.29; 48 hours-0.29; and 96 hours-0.18 and for Fowler's toad 0.57, 0.46 and 0.12 at 24, 48, and 96 hours, respectively (Sanders, 1970).

III.E. Fate in Air - Environmental pollution has received great public concern but little research has been done on atmospheric pollution by pesticides. In 1961, Harris and Lichtenstein showed that volatilization of aldrin, dieldrin, heptachlor and lindane was a major factor in their disappearance from treated soils. Movement and distribution of pesticides have been attributed to both atmospheric and hydrospheric currents. The limited literature available suggests air contamination by evaporation or codistillation of chlorinated hydrocarbons with water and verified by occurrence in atmospheric dust, and rainwater. Risebrough, et al., (1968) detected chlorinated hydrocarbons, primarily dieldrin, DDT and DDE in dust borne by trade winds from European-African land mass to Barbados, West India. The amounts detected, < 1-164 ppb, suggest that movement on contaminated dust particles may contribute to contamination of water and land far distant from sites of use. A study of airborne particulate pesticides in urban atmospheres was conducted in 1963 and 1964 (Tabor, 1965). Aldrin was detected in measurable amounts in only one location. No traces of endrin, commonly used in combination with other pesticides, were found in any samples. Similar observations were made by Abbott, et al., (1965, 1966) in dust samples taken in central London and its suburbs which contained traces of BHC, DDT, DDE, TDE and dieldrin but not endrin.

In a pilot study designed to measure atmospheric contamination by 19 pesticides air samples were obtained from 9 urban and agricultural areas in the United States. Most pesticides present in the atmosphere were particulates. Only DDT was detected at all localities. Twenty-five samples taken at Stoneville, Mississippi were positive for endrin with a maximum level of 58.5 ng/cubic meter (Stanley, et al., (1971).

Attempts to use a "balance-sheet" approach to pesticide persistence have been unsuccessful. Large amounts remained unaccounted for even in carefully controlled studies. Volatilization losses to the atmosphere may partially explain such discrepancies.

Volatilization accounted for a significant net loss of 2 percent endrin applied at 2 lb. ai/acre to sugar cane. Half was applied to the cane and half to the soil surface. Mean atmospheric concentration of endrin reached 540 ng/cubic meter during the 3-day period after application and decreased asymptotically to 30 ng/cubic meter 77 days later (Willis, et al., 1969).

Jegier (1965) studied the hazards of insecticide applications in Quebec. A field survey of spraying was conducted to measure respiratory and dermal exposure of spray operators during application of insecticides to orchards, small fruits, vegetables and grain. The mean concentration of endrin in air determined in air inside aircraft to which pilots were exposed during spraying, was 0.01-0.05 mg per cubic meter. Respiratory exposures were determined by checking filters of respirators worn by observers sitting beside spray operators on tractors. Mean respiratory and dermal exposures of 3 subjects to endrin were 2.4 and 0.15 mg per man hour. Mean dermal exposure to endrin during aircraft spraying was 1.1 mg per hour, but under high pressure ground spraying conditions, 0.15 mg per hour. The latter value was attributed to the direct injection of endrin into the ground.

Reports of humidity on residue persistence are meager. Kalkal, et al., (1961) found that the fumigant action of some insecticide residues increased significantly under similar temperature between 55 and 80 percent relative

humidity. Under high humidity, there was a rapid change of insecticide into the vapor phase and in amounts high enough to account for the fumigant effect. Heptachlor epoxide loss was approximately 2 times greater at the higher humidity. Lyon and Davidson (1965) measured residue losses under high and low humidity conditions. Test conditions were 80 $\pm$ 2 F. and relative humidity at 8$\pm$5 and 80 $\pm$ 5 percent. Heptachlor epoxide again showed residue losses two times greater under high humidity. However, both endrin and coumaphos showed a greater loss at low humidity. Endrin weight loss was 2.0 mg at 8 percent relative humidity but only 1.1 mg at 80 percent. The exact cause of this variation is unknown.

Organochlorine pesticides were measured in rainwater collected continuously during 12 months at 7 widely distributed sites in the British Isles (Tarrant and Tatton, 1968). BHC, lindane, dieldrin, DDT, and DDE and TDE were found at all sites throughout the year, but endrin was not detected. How if it was used there?

Vaporization of chlorinated hydrocarbon insecticides from soil surfaces may be an important source of plant contamination. Aerial plant parts were contaminated by insecticide volatilization from soil surfaces as well as by root absorption and translocation. These included tests on soybeans with four pesticides, including endrin. With all chemicals tested, seeds always showed the lowest residue concentrations (Anon., 1970).

Investigations of climatic effects on insecticide toxicity were conducted in Texas by Mistric and Gaines (1953). High temperatures and humidities, rainfall, dew and sunlight proved important in reducing the

toxicity of certain insecticides. Tests also were conducted to determine effects of wind and other climatic factors. The boll weevil, cotton leafworm and salt-marsh caterpillar were used as test insects.

Field cage toxicity tests for boll weevil control indicated that normal climatic factors reduce endrin toxicity when applied at 0.33 lb. ai/acre. Temperature range was from 64° to 95°F., and relative humidity from 28 to 74%. Toxicity (% mortality) decreased to 84.7% immediately after release, 64.5% after 24 hours, and 43.2% after 48 hours.

In a laboratory study on residual toxicity conducted under assimilated normal climatic conditions no appreciable loss of mortality from endrin was observed after 48 hours. Simulated rain applied immediately after treatment with endrin caused no appreciable reduction in endrin toxicity to boll weevils. Percent mortality with "no rain" controls was 95.7, while those subjected to rain showed 93.6. Similar results were obtained with cotton leafworm.

High and low temperatures had minimal effects on endrin toxicity to boll weevil. Mortality caused after residues were treated at low temperatures for 24-hours was 98 percent and 100 percent after similar delay at high temperatures. Movement of air at 5.9 m.p.h. produced by an electric fan caused reduction in toxicity to cotton leafworm of endrin applied at 0.1 lb/acre.

III.F. Fate in Water - The chief hazard of pesticide residues in aquatic environments is biological accumulation in the food chain. Organochlorine insecticides may be absorbed selectively by plankton which are later consumed by small fish which, in turn, are eaten by larger fish. Biological

accumulation does not appear to be an immediate problem with human food but some evidence indicates possible harmful effects in fish, birds and marine mammals at the higher trophic levels.

Trace amounts of endrin and other organochlorine compounds can be removed from waters by treatment with large amounts of activated carbon (Chesters and Konrad, 1971). Quantities associated with low level chronic contamination are difficult to remove and available evidence suggests that current water treatment practices are inadequate to avoid long-term, low-level contamination (Mrak, 1969).

Lichtenberg, et al., (1969) summarized five annual surveys (1964 through 1968) for chlorinated hydrocarbon pesticides in surface waters of the United States. Data collected at 110 stations on all major drainages showed widespread occurrence of these compounds. The reduction of endrin occurrences from nearly 50% in 1964 to zero in 1968 was considered significant in light of its association with major fish kills in the lower Mississippi prior to 1964. It ranked fourth in occurrence after dieldrin, DDT and DDD. Highest recorded levels for each year in µg/l were: Potomac-0.094 and Rio Grande-0.067 in 1964; Mississippi (Arkansas)-0.116 and Atchafalaya (Louisiana)-0.019 in 1965; Hudson-0.069 and South Platte (Colorado)-0.063 in 1966; Kansas-0.133 and Maumee (Ohio)-0.036 in 1967, and none recorded for the entire country in 1968.

In another program, fish were collected from 50 sampling stations located in Great Lakes and in major river basins throughout the United States. Endrin was reported consistently in samples from only three stations--one on the Mississippi River in Louisiana, and the Arkansas and White Rivers

in Arkansas. These were all at relatively low levels (<0.1 ppm). Scattered higher values were reported from other stations such as the Susquehanna River, Maryland, Roanoke River, North Carolina, Savannah River, Georgia, Apalachiocola River, Florida, Lake Ontario, New York, Missouri River, North Dakota, Green River, Utah, Colorado River, Arizona and The Sacramento River, California. This constitutes presumptive evidence of widespread contamination of water or aquatic food organisms with endrin (Henderson, et al., 1969).

Microparticulates suspended in Lake Erie water were collected by continuous centrifugation and were examined directly or placed on a sucrose density gradients. Residues were examined by both gas and thin-layer chromatography. Endrin was shown by both methods to be associated with microparticles contained in the various fractions of the gradient. The first gradient fraction of one sample contained endrin equilavent to 0.69 nanograms/1 of lake water (Pfister, et al., 1969).

Pesticide monitoring of the aquatic biota of Tule Lake National Wildlife Refuge was established because of pesticide poisoning of fish-eating birds (Godsil and Johnson, 1968). Endrin found regularly in samples of both water and aquatic biota presumably resulted from irrigation return flow, runoff or leaching from crop lands. Water contained a maximum 0.1 ppb endrin in 1965 while tui chubs accumulated up to 198 ppb the same year.

Effects of pesticide applications in the Houston, Texas area were measured on shellfish and shellfish-growing waters of Galveston Bay. Pesticide levels in both water and oysters were low at all times. All

oyster samples contained trace amounts of endrin, but no endrin was detected in water samples. The occurrence in oysters indicated presence in water at some previous date (Casper, 1967).

Endrin content of marine fish of the northeast Pacific was generally insignificant--up to 0.006 ppm (Stout, 1968). Larger pesticide residues occurred in fish taken at the mouth of the Columbia River than in those from Hecate Strait, British Columbia, where no major river enters the ocean. Agricultural runoff was considered to be a factor causing higher residues in the former sample.

The effects of aerial distribution of endrin-coated Douglas fir seeds on the aquatic life of Oregon coastal streams were studied. Morton (1967) evaluated effects on game fish of re-seeding a burned-over area in the Smith River basin. In laboratory tests six treated seeds placed in 15 liters of water at 55°F. killed half the rainbow trout in an aquarium in two days and all of them in three. Leaching from these seeds after 3 days contained 0.32 µg/1. Many water samples were taken from several creeks draining the re-seeded area but only four showed endrin residues--two were 0.04 ppb one was 0.05 ppb, and the fourth--0.556 ppb. Samples of live-boxed and wild trout, salmon and other native fishes indicated no observed mortality or residue accumulation in tissues over a six-week period following application. Observed mortality did occur in crayfish (Astacus trowbridgi) and the red-sided shiner (Richardsonius balteatus).

A 175-acre "clear-cut" area of watershed in the headwaters of the Alsea River, Oregon was re-seeded by aerially broadcasting endrin-coated Douglas fir seed. Measurable amounts of endrin (up to 0.10 µg/1) were

detected in the stream flow for 2 hours after seeding started and again during the high flow of a winter freshet the sixth day after seeding. Total amounts of endrin detected during these two runoff periods amounted to only 0.12% of that theoretically applied to the entire watershed. Endrin leached off a subsample of seed, covered with distilled water for 32 days, was 28.2 ppb, or 11.3% of the total calculated endrin seed coating (Marston, et al., 1969).

Samples of a water-suspended sediment mixture from 11 streams in western United States were analyzed monthly in 1965 and 1966 (Brown and Nishioka, 1967). A total of 12 insecticides was detected. Slightly more than 50 percent of the positive samples contained 5 ppt or less total pesticides. Positive occurrences were most frequent from February through May. Of 165 positive results, only 7 contained endrin which occurred in samples from the Missouri, Colorado, Rio Grande and Snake Rivers within the range 5-40 ppt. In a follow-up study the network was increased to 20 sampling stations during the October, 1966 to 1968 period (Manigold and Schulze, 1969). Of 235 positive samples, four contained endrin; these were from stations on the Brazoa, Colorado and Gila Rivers at concentrations of .02, .07, .01, and .01 ppb.

Pesticides in water and sediments of the lower Mississippi River and its tributaries were analyzed by Barthel, et al., (1969). Pesticide residues were detected from both agricultural and non-agricultural sources. There was no indication of a general buildup of chlorinated hydrocarbon pesticide residues in stream sediments from farm use. Significantly higher residues in water and sediment were found in tributary streams

near manufacturing or formulating plants in Tennessee and Mississippi. Water samples from Wolf River and Cypress Creek near Memphis, Tennessee contained 0.25-2.03 ppb endrin and 5.04-6.5 ppb ketoendrin. No contamination was found in 1966 in Mississippi River sediments upstream from the confluence with Wolf River which suggests that manufacturing wastes were the source of pollution. Traces of some of these pollutants were found in sediments 500 miles downstream near Baton Rouge, Louisiana.

These findings are related to a summary report of the 1963 Mississippi fish kill which led to the announcement that endrin was the cause of 1963-65 fish losses in the lower Mississippi River (Mount and Putnicki, 1966). Beginning in November, 1960, large numbers of dying fish were observed in the Mississippi and Atchafalaya Rivers and associated bayous. There were few mortalities in 1961 and 1962, but a heavy kill occurred again in 1963. Fresh, brackish water and marine fish species were affected. Lethal threshold concentrations of endrin in the blood were determined from dying bullheads, buffalo and gizzard shad. Blood samples of these species were well above the lethal level measured in the laboratory. Water concentrations of endrin in the Mississippi River varied from 0.1 to 0.2 µg/l at West Memphis and New Orleans. This concentration was acutely lethal in laboratory tests on channel catfish, largemouth buffalo and gizzard shad. It may be difficult to understand that such minute quantities of endrin such as 0.1 ppb could be acutely toxic to fish. However, in 2 hours the blood of a catfish has attained an endrin concentration more than 1,000 times that of the surrounding

water, and fathead minnows exposed to .015 µg/1 had total body concentrations 1,000 that of the water.

A creek flowing into Lake Erie and a controlled drainage system (the water of which is pumped into Lake Erie) were monitored for insecticide residues during 1970 (Miles and Harris, 1971). Residues in water, mud, and fish were most pronounced in the more abundant DDT complex and dieldrin. Endrin was determined in chubs and suckers (10-18 ppb) although it was not detectable in the water or mud.

Samples of oysters, sediment and water were checked from an estuarine area of Louisiana (Rowe, et al., 1971). '70 in ref. list Water samples from all stations on every sampling date contained less than 1 ppb of endrin. However, samples of sediment and oysters showed a chain buildup to levels five times as great. Oysters, water and bottom sediments were checked for endrin from the lower Mississippi River region and southern Barataria Bay. Collections were made during three separate 6-8 month periods between 1964 and 1966. Highest endrin concentrations in water were less than 0.001 ppm with median values being the same. Bottom sediments were less than 0.01 ppm and oysters had a similar median value (Hammerstrom, et al., 1967).

The ecological distribution of pesticides in Lake Poinsett, South Dakota was studied by Hannon, et al., (1970). DDT and metabolites were found at all trophic levels and heptachlor, aldrin, dieldrin and lindane were present in most sample types. Endrin was not detected above analytical confidence limits in any sample.

After accidental spillage of the agricultural pesticides nabam and endrin into Mill River, Prince Edward Island, there were extensive mortalities among brook trout and juvenile Atlantic salmon. Abnormal behavior including unseasonal downstream movements in summer and unusual response to an electric field were observed among surviving trout and salmon (Saunders, 1969).

Sparr and Appleby (1966) determined the concentration of endrin in waterways, fish and mud from a cotton field treated three times with endrin at 0.3 lb. per acre. Endrin in the soil did not exceed 0.04 ppm, even after subsequent sprayings. Traces of endrin were found in fish but not in mud. Runoff water from the cotton field showed only 0.05 ppm after the last spraying. Pesticides in drinking water from 10 selected municipal water supplies whose source was either the Missouri or Mississippi River was assayed by Schafer, et al., (1969). Over 500 grab samples of finished drinking water were checked for 10 chlorinated pesticides and about 1/3 of the samples contained endrin.

Studies were conducted in Louisiana to assess methodology of measurement and to determine the extent and duration of surface water contamination by endrin used in sugar cane culture. In 1961, up to 360 ppt of endrin was recovered from water. Endrin was recovered from each of six streams sampled, three of which were at sites of fish kills attributed to endrin. In 1964 with more efficient sampling techniques 700-820 ppt were detected. Surface runoff was the main source of endrin contamination (Lauer, et al., 1966).

Average annual applications of 7.5 ? lb/A? from repeated applications at 0.03 lb/acre had been made to cotton fields near Greenville, Mississippi since 1956. During 1965, endrin residues in soil averaged 0.3 ppm in the spring and 0.32 ppm in the fall. Water accumulating in a nearby slough was sampled 19 times between April and February. Measurable endrin residues were detected on only 6 sampling dates in amounts ranging from 0.07 to 1.49 ppm. Samples of slough sediment showed endrin residues on 3 of 19 collection dates, ranging from 0.27 to 0.91 ppm (Iverson, 1967).

Effects of pesticides on raw waste water were studied by Canter, et al., (1969). Reagent grade endrin in concentrations up to 50 mg/l had no effect on the B.O.D. of sewage. Commercial endrin caused an increase in chemical oxygen demand (C.O.D.) of 20 mg/l per mg of endrin. in each liter? Escherichia coli cultures could grow on nutrient agar containing commercial endrin in concentrations up to 500 mg/l. E. coli suspensions did not show viability after 1 hour exposure to 3000 mg. per 1. endrin.

III.G. Fate in Plants - Amounts of endrin taken up by soybean, wheat, corn, alfalfa, bromegrass and cucumber seedlings from five soils treated with 0.5 or 5.0 ppm C-14 labeled insecticide were determined in greenhouse experiments (Beall and Nash, 1969). Residue concentrations in plants usually were well below soil treatment rates, although endrin residues in alfalfa and bromegrass exceeded the treatment rate of some soils. Mean concentrations of residues taken up (regardless of soils) showed endrin second only to heptachlor among insecticides tested. Data suggested linearity of residue uptake with soil concentration at low soil treatment rates. Silt negatively affected endrin uptake. No degradation products

of endrin were detected. Persistence in soil was positively correlated with organic matter.

The persistence of endrin in sassafras loam soil in New Jersey and translocation into potatoes were determined. Test plots were treated at 3 and 6 lb/acre of 2% endrin granules. Damage to the tuber from wireworm decreased as the endrin residue increased. Residues were detected in potatoes from the first two plantings but none from the third. Potatoes grown the first year after treatment (1963) contained endrin residues at 84-117 ppb in soil treated with 3 lb/acre and 100-133 ppb at 6 lb/acre. The following year (1964) 17 ppb endrin was found at 3 lb. treatment and 12-17 ppb at 6 lbs. (Winnett and Reed, 1968).

Residues of cyclodienes were found in the foliage of wheat grown in soil treated with aldrin and endrin, but no residues were found in the grain (Saha and McDonald, 1967).

Field and laboratory studies determined contamination of several commercially important crops grown in soil containing known concentrations of endrin was investigated by a regional committee in six states, Florida, Mississippi, North and South Carolina, Texas and Virginia. Problems of low residues were associated with soybeans grown in soils containing relatively high levels of endrin in turnips and in green tobacco leaves. Since the tolerance for endrin is zero in turnip greens, the small amounts detected were illegal. The low residues of endrin found in green tobacco leaves presented no food residue problems (Van Middelem, 1969).

Forty-nine fields of peanuts, potatoes and carrots were monitored for chlorinated hydrocarbon pesticides in soil and root crops in seven

Eastern states (Seal, et al., 1967). With methods of detection sensitive to 0.01 ppm endrin was found in the soil from about one-fifth of the fields, but no residues of endrin were identified in crop samples.

Samples of soil and turnips grown in Florida in fine, loamy sand soils fortified with 1,2 and 4 lb/acre endrin were analyzed for endrin. Soil samples were taken within 24 hours after planting and on the day of harvest. Levels of endrin in planting soils treated with 0,1,2 and 4 lb/acre were 0.01, 0.64, 0.74, and 1.98 respectively and at harvest soil levels were 0.03, 0.77, 1.59 and 3.71 ppm. Endrin was translocated from soil into the turnip plant to only a limited extent. At rates of 4 lb/acre turnip peel contained the highest insecticide level (0.12 ppm) and peeled turnips and turnip greens contained 0.04 and 0.02 ppm. Above ground plant parts could have been contaminated by vaporization, co-distillation and splashing or blowing of contaminated soil onto the leaves and stems (Wheeler, et al., 1969).

Soybeans grown in Mississippi soils fortified with 2,4 and 8 lb/acre of endrin were analyzed to determine possible crop contamination (Barrentine and Cain, 1969). Following applications at 0,2,4, and 8 lb/acre, levels of endrin in planting soil were 0, 0.59, 1.20 and 1.49 ppm respectively, and 0, 0.34, 1.04 and 1.79 ppm in harvest soil. Endrin levels in soybeans were 0.01, 0.04, 0.08 and 0.12 ppm for the respective application levels.

Peanuts and soybeans grown in Texas soils fortified at planting with endrin were analyzed to determine crop contamination (Dorough and Randolph, 1969). Endrin residues in peanut planting soil treated with 0, 1, 2, and

means >1ft. deep soil sample = very deep

4 lb/acre were 0.15, 0.32, 0.90 and 2.08 ppm, respectively; harvest soil contained 0.13, 0.23, 0.51 and 0.60 ppm and harvested peanuts contained 0.00, 0.02, 0.07 and 0.10 ppm. Soybean planting soil treated similarly contained 0.18, 0.47, 1.11 and 1.49 ppm, harvest soil contained 0.12, 0.17, 0.49 and 0.48 ppm, and harvested soybeans contained 0.00, 0.00, 0.02, and 0.03 ppm, respectively.

Absorption of insecticides by soybeans through the roots and through the aerial portion of the plant from vaporized soil application was studied. Surface and subsurface soils were separated by a sealed disk with no part of the plant above soil touching the surface-treated soil. Treated surface and subsurface layer (250 and 1500 g., respectively) soils contained 0.5 mcc of C-14 labeled endrin. Plants were allowed to grow for 53 days, harvested, and separated into upper leaves, stem and lower leaves and stem, pods and seeds. In subsurface studies, larger amounts of endrin residues transmitted by root sorption were found in the lower stem. In surface treatment studies, lower leaves contained most residues with upper leaves containing the next largest amounts. Residues of endrin resulted from root uptake and translocation, and to a lesser degree from vaporization from soil surfaces (Nash and Beall, 1970).

gm per what? how much active endrin?

The action of endrin on the bean stem miner, a destructive pest on young soybeans in Formosa was studied by Lee (1962) in connection with its translocation in soybean plants. Summer plants, 8-11 days old were completely protected for 15 days with foliar spray applied at relatively low dosages such as 90 g. ai/hectare. Endrin emulsion showed some degree of repellency to ovipositing flies, but its persistent effect caused the

kill of newly hatched larvae through translocation into the post-treatment growth of plants in which the eggs were laid.

In 1966, comparative samples of soil and soybean seed and plants were collected for analysis from Greenville, Mississippi and Mobile, Alabama, and from 27 sites in 3 other Southern states and 3 Midwestern states. Endrin residues were found in about three-fourths of the samples from Arkansas and Mississippi. Endrin had been used extensively for cotton insect control at the Greenville, Mississippi study area prior to planting soybeans. Soybean seed, plants and soil sampled from 10 blocks totaling 219 acres, contained an average of 0.38 ppm, 0.28 ppm, and 0.07 ppm, respectively. Endrin residues which appeared in soybean samples collected in Mississippi and Arkansas and were apparently related to the use of endrin for cotton insect control. When endrin soil concentrations ranged from 0.10 ppm to 0.20 ppm, residues frequently were detected in soybeans grown in such soil. This contamination may have resulted partly from translocation from the soil and partly from drift or inadvertent overspray (U.S. Dept. of Agriculture, 1968).

Information was obtained on pesticide levels in crops and soils over a 3-year period on approximately 1 square mile study areas at Grand Forks, North Dakota; Yuma, Arizona; and Mobile, Alabama. Endrin found in about half the soil samples, averaged 0.26 ppm. what about other ½ ? Actual soil residue levels changed little during the 3-year period. Endrin was found in 13% of the small grain, corn and sorghum samples at an average of 0.08 ppm. Endrin residues averaged 0.23 ppm in 17% of the samples from soils where alfalfa and grass were grown. An average of 0.07 ppm endrin was found in 15% of the forage samples (Sand, 1968).

Knutson, et al., (1971) measured insecticide residues in corn planted in an irrigated area in Kansas. At harvest, levels from 0.06 to 2.43 ppm endrin were detected in foliage following foliar applications in early August. No residues were found in the grain following either soil or foliage application.

A study was conducted in Colorado by Jewell (1966) to determine whether pesticides sprayed in or around orchards might cause contamination of transect vegetation. Samples of willow, bigtoothed sage, antelope bitterbrush, orchard grass, alfalfa, clover, serviceberry, mountain mahogany, rabbitsbrush, chokecherry, apple, rose and scrub oak were tested for endrin.

Endrin was used to control voles in orchards of Switzerland (Schneider, 1966). An emulsion was sprayed on shortcut grass under the trees in October and November. The following year, 1.9 ppm endrin was traceable to grass of the first cutting, and 0.27 ppm in the third cut. For this reason use of such grass was not permitted for domestic animal fodder.

Organochlorine insecticide soils from southwestern Ontario were analyzed for organochlorine pesticides to determine if residues were sufficient to cause unacceptable residues in crops used for animal feed. Alfalfa, oats, corn, sugar beets, potatoes, and carrots were planted in soil containing insecticide residues. Soil B, a fine sandy loam soil (1.4% organic matter) contained 0.76 ppm cyclodiene insecticides, with the predominant material being dieldrin. Soil D, a muck soil (66.5% organic matter) contained 10.44 ppm cyclodiene insecticides. In soils B and D, small amounts of endrin were detected in most crops tested (Harris and Sans, 1969).

Fourteen lb. endrin/acre incorporated 4 to 6 inches into a sandy loam soil at Riverside, California resulted in 2.3 to 4.7 mcg/g of 0-6 inch soil layer. Nine carrot varieties, Daucus carota, were compared for uptake of endrin residues. This varied from 1 to 4 ppm of apparent endrin among the varieties studied. Most endrin residue occurred in carrot skin (Hermanson, et al., 1970).

The effects on the macro- and micro-element constituents of corn and beans growing in soil containing 1, 10 and 100 ppm endrin were examined by Cole, et al., (1968). After 8 weeks 100 ppm endrin caused a decrease in the weight of corn plants, and at 10 and 100 ppm decreased the weight of bean plants. All pesticides tested caused significant changes in macro- and micro-element levels of above-ground tissues of corn and beans after 4 and 8 weeks growth. Endrin produced changes in P, K, Mg, Mn, Fe, Cu, B, N and Zn levels, ~~were observed~~, but produced no significant changes occurred in Ca, Al, and Sr levels. Both N and Cu levels in corn decreased with increasing endrin after 4 and 8 weeks.

Endrin has been recommended for European corn borer control, and farmers in the Corn Belt frequently pasture their cattle after harvest in treated corn fields. The cattle pick up ears missed in harvesting and also feed on the stover. The following experiment was conducted to determine if endrin residues would accumulate in the milk of dairy cattle, pasteurized in areas treated with endrin. Endrin was applied at 0.25 lb/acre to a 4.4-acre field of dent corn as a 2.5 percent granular preparation. In the fall, after the corn had been picked, cows were randomly assigned to pasture in treated and control areas. Milk samples were collected twice

weekly over 38 consecutive days. Fifty-gram butterfat samples were used for the following analyses: (1) 11 samples from the control cows, (2) 11 samples from animals on the endrin-treated plot, and (3) 11 samples of control butterfat fortified with 2 ppm endrin. The absorbance values of the 11 samples from (2) were not greater than the values for the corresponding control samples (Johnsen, et al., 1961).

After foliar applications to white cabbage, C-14 endrin partially evaporated from the surfaces and was also partially taken up by the plant and released in a few weeks via transpiration. Two to four weeks after application unaltered endrin and two hydrophilous metabolites A and B, were found in both plants and soil. Metabolite B was identical to endrin-ketone (Weisgerber, et al., 1968).

Cotton plants treated with ^{14}C endrin, were analyzed to determine distribution and behavior of residues. Upper surfaces of leaves from cotton plants grown in the greenhouse were treated 3 times with 600 µl of a solution of 17 mg 14-C endrin (1.85 mCi/mM) and 313 mg unlabeled endrin in 50 ml acetone. Plants were harvested 12 weeks after the last application and separated into samples of leaf, stem, roots, seed pod, seed fiber and seed. One-third of the radioactivity applied was recovered in the combined plant and soil samples. Of total activity: 30.5% (36.6 ppm) was found in and on living leaves, 49.2% (201.2 ppm) in and on dead leaves, 0.27% (0.33 ppm) in stems, 0.06% (4.9 ppm) in seed pods, 0.003% (0.36 ppm) and trace amounts in fibers, seeds, and the soil. No activity was detected in root samples. Five conversion products detected represented 24% of the total endrin recovered. One group of three was only slightly

more hydrophilic than endrin and the other two products were strongly hydrophilic. Two conversion products of the first group had retention times identical with endrin ketone. One was later positively identified as endrin ketone. The ohter had a slightly higher molecular weight and had the chlorine structure of endrin (Bayless, et al., 1970).

The effects of cultivation conditions on residues and metabolism of C-14 labeled endrin were tested with tobacco (Weisgerber, et al., 1969). After 6 weeks, 32 to 47 percent of the topically applied endrin remained on tobacco leaves in the plants. One extremely hydrophilic degradation product was found in plants and on the soil but was not characterized because of low concentration. This substance which differed from photodegradation products was similar in chromatographic behavior to the metabolite earlier reported for white cabbage. The percentage of metabolites increases with better cultivation conditions, lower endrin dosage, and increases with time after treatment.

Experiments with endrin - ^{3}H on cotton were made by Korte, et al., (1970). Low amounts of the keto-rearrangement product were detected on the leaf surfaces, but no penetration was detected. This keto-compound probably was formed by UV rearrangement of endrin on the leaf surface. Later these authors observed uptake and metabolism of endrin by cabbage, tobacco, carrots and wheat germ buds. After application of endrin ^{14}C in acetone to leaf surfaces or to the soil, material from leaves, roots, stalks, and soil was extracted at various intervals.

In a greenhouse experiment with cabbage four weeks after application 0.8 percent of the applied radioactivity was found on the leaf surfaces,

4.4 percent in the plants, and 0.2% in stalks and roots. Hydrophilic metabolites were found at an increasing rate from leaves to soil.

A disappearance of residues by transpiration, corresponding to that of the cabbage experiments, was also found in carrots and tobacco. Four weeks after application of ^{14}C endrin to tobacco leaves, 29 percent of the applied radioactivity remained present on leaf surfaces, and 7% in the plants. The slower disappearance of residues from tobacco probably is due to a lower rate of transpiration. Metabolic rates on carrots strongly depended upon the form of application. Three weeks after application of ^{14}C endrin into the soil, the metabolic rate, based upon recovered radioactivity, was 12 percent after injection into the roots and 32 percent after application on the leaves near the vegetation point.

Four different treatments of endrin ground spray were applied on Virginia orchards of two varieties of apples during two different seasons. Application rates were at 2 and 4lb/acre. Both picked and dropped fruits from the succeeding apple crop were analyzed for endrin. Amounts of endrin detected in picked apples was 0--.005 ppm and 0.028 ppm in the dropped fruits (Horsfall, et al., 1970).

Health hazards of endrin in some agricultural uses in the Pacific Northwest were examined by Wolfe, et al., (1963). Each fall, many orchardists in that area spray their orchard cover crops with 1.2-1.4 lbs. endrin per acre for control of meadow mice (Microtus). Residues on windfall apples in endrin-sprayed orchard cover crops were obtained on 17 samples taken soon after spraying. Endrin residues ranged from 0.3 to 1.2 ppm with an average of 0.6 ppm. This average value agrees

quite closely with residue tests reported by Wolfe (1957) where residues on windfall apples following endrin spraying ranged from 0.3 to 0.5 ppm. Orchard grass and fescue samples contained 60, 240 ppm endrin during the first month after application. From 25 to 100 ppm was still present at the end of the fifth month. Gyrisco and Huddleston (1961) noted similar persistence and variability for endrin residues following a single application on an alfalfa-brome grass mixture.

The morphological and somatic chromosomal aberrations induced by pesticides in barley were examined by Wuu and Grant (1966). The percentage germination of barley seeds treated with solutions of endrin containing 500, 1000, and 1500 ppm for 6, 12 and 24 hours was evaluated. In general, germination of seeds treated with endrin for 24 hours was 55 percent of the treated for 6 hours. Chromosome aberrations induced by endrin in root tip cells of C_1 seedlings were 6.01 to 9.05 percent greater than abnormal seedlings. The most common cytological aberration observed was chromosome breakage. Occurrence of these chromosome irregularities and malformations suggest that hereditary constitution of seeds of some plants may be changed if the plants are subjected to chance pesticide treatment.

III.H. Fate in Soil - The fate of pesticides in soil is influenced by environmental processes (1) adsorption and degradation (2) leaching into lower soil strata (3) direct uptake by plant roots (4) evaporation or volatilization from soil surface and (5) erosion of the soil by water or wind.

Insufficient monitoring data are presently available to assess the extent of endrin contamination of soils. It is not well known whether contamination is confined to areas where endrin is used extensively.

The organochlorine insecticide content of 40 mineral soils and 16 organic soils and sediments was determined from random samples collected from Wisconsin and eight states west of the Mississippi River. Approximately half the samples contained no detectible residues. None of the soil samples examined contained endrin. It is not known whether this was due to relatively rapid degradation or simply to lack of use on the soils sampled (Trautmann, et al., 1968).

A comprehensive review paper was presented on insecticide residues in soils by Edwards (1966). According to Edwards, Foster, et al., (1956), found endrin the most persistent chlorinated hydrocarbon, almost 100 percent remaining after two years. Kincaid, et al., (1960) stated that 11 percent endrin disappeared in a year. These workers found that residues as percentage of amount applied were much less for larger doses than for smaller doses than for smaller ones, e.g., after 5-1/2 years at 15 lbs. ai/acre, 40% of the endrin remained, but at 75 lbs. ai/acre, only 37% could be detected.

Another study was conducted on insecticide residues on 16 southwestern Ontario farms at three intervals over a 5-year period. Residues of some organochlorine pesticides were present in soils on all 16 farms during each of the 3 years sampled. Of 48 samples taken, 18 contained endrin residues ranging from 0.1 to 6.55 ppm. The higher values all occurred on muck soils where chemicals were used to control vegetable pests. Endrin was found on only two farms in 1964; by 1969, residues were present on nine farms, indicating increased use as other pesticides were phased out in 1969 (Harris and Sans, 1971).

Menzie (1972) in his paper on the fates of pesticides in the environment listed the approximate "half-life" of Isodrin/endrin in the soil as 4-8 years. The persistence and fate of endrin in soil is dependent both upon chemical and a variety of environmental factors. The above range merely indicates that half the endrin may have volatilized or degraded within that period.

From 1953 to 1957, annual applications of endrin at rates of 4.9 to 5.4 lb/acre were applied to Holtville sandy clay soil in California (Hermanson, et al., 1971). Measurable enduring soil insecticide residues occurred in soils receiving endrin at 5 lb/acre/year. A rank of decreasing persistence (a persistency index:1.00=no degradation or disappearance during the first year) over an 11-year period listed endrin as 0.20. Consequences derived from regression analysis showed that endrin had a persistence "half-life" of 4 years.

The percentage of technical endrin remaining in Congaree sandy loam soil after 4 years was 41. Treatments and maintenance of the soils were such that leaching, volatilization, photodecomposition, mechanical removal and probably biological decomposition (because of high initial application rate) were at a minimum. This value may approach an upper limit of endrin persistence in soil (Nash and Woolson, 1967).

The 38 cm profile distribution in 1966 of several chlorinated insecticides in cultivated Congaree sandy loam soil was recorded by Nash and Woolson (1968). Tests were made 13 years after the last applications in 1953. Test areas had received accumulations of

pesticides of 73 or 146 kg/ha from frequently repeated foliar applications during three growing seasons (1951-53). Endrin was found throughout the soil profile. Eighty percent of the total endrin residues were concentrated in the upper 23 cm of soil, which probably corresponds to the cultivated layer. The quantity of insecticide in the top 7.6 cm of soil was less than the mean quantity between 7.6 and 23 cm depths. This indicates that volatility and photodecomposition may play an important part in dissipation. The degree of persistence ~~can be visualized~~ is indicated by the fact that, 12 years after application, 28 percent of the foliar applications and 44 percent of the soil-incorporated endrin remained in the soil of test plots.

Insecticides were used extensively on shadegrown tobacco crops in the Florida-Georgia area for many years. Experimental work was undertaken to determine: (1) amounts of chlorinated hydrocarbon insecticides which may accumulate in soil without apparent detriment to tobacco; (2) their rate of disappearance under shade conditions; and (3) the amounts of organic chlorine which had accumulated in the soil of commercial fields (Kincaid, et al., 1960).

Endrin at 15 and 75 pounds a.i. in an emulsifiable concentrate, was applied March 6, 1953, to triplicate plots. Data on insecticide residues were given. The major portion of each insecticide disappeared during the test period of 5-2/3 years. Calculated from linear equations best fitted to the data, the percentage of endrin which disappeared during any one year was 11%.

Commercially grown onions and the soils on which they were grown were evaluated in 10 major onion-producing states for pesticide residues. It was found that soil from 15.5 % of the sites contained endrin. Soil residues in ppm ranged from 0.01 to 2.05 but averaged only 0.06. No residues were detected in onion samples (Wiersma, et al., 1972).

Forty-one agricultural soil samples from 21 vegetable farms in Saskatchewan were analyzed for insecticide residues. All but 2 of 41 samples had more than 0.01 ppm of total organochlorine pesticide residues. However, endrin was present in only one sample at 0.48 ppm (Saha and Sumner, 1971).

Soil samples were collected on 31 farms located throughout southwestern Ontario. The soil types ranged from sand to muck. Endrin was detected at a concentration of 3.8 ppm in 1 sample, and trace amounts in 2 other samples. Highest organochlorine residues occurred in tobacco, vegetable and orchard soils. Development of cyclodiene resistance by soil insects in southwestern Ontario can be correlated with levels of cyclodiene residues in the soil (Harris, et al., 1966).

A unique opportunity to study insecticide usage and resulting residue was provided by creation of a new irrigation district in central Kansas. During the period 1960-1969, this site developed from dry-land farming with little use of insecticides to intensified crop production and pesticide usage. Endrin foliar sprays were applied in early August to corn at silking time. Endrin levels on foliage collected soon after spraying were 0.9-6 ppm. Endrin residues at harvest ranged from 0.06 to 2.43 ppm. No endrin residues were detected in corn grain sampled at

harvest. Capped wells, from 13 to 71 feet deep, contained no residues at the 0.1 ppb level. Vertical penetration of other soil-applied pesticides did not exceed 12 inches, nor was there evidence of lateral contamination of ground water from adjacent lands. Surface waters from the adjoining reservoir and river contained no residues at the 0.1 ppb level. Endrin was detected in surface waters at trace levels (<0.1 ppb) (Knutson, et al., 1971).

Mullins, et al., (1971) studied the presence and persistence of organochlorine insecticide in Colorado soils. Fifty samples of orchard and cultivated soils were collected from eleven sites which had a history of endrin use. Endrin residues were detected in trace amounts from only two sites.

Organochlorine insecticide residues in agricultural soil and legume crops were measured in northeastern Saskatchewan by Saha, et al., (1968). Soil samples from 20 fields were analyzed. Endrin was present in 15 percent of the fields at 0.01 to 0.02 ppm. Residues of endrin in legume crops were either undetectible or present in only trace amounts.

Soil samples from 67 fields in 22 counties of 8 states in the South and Midwest were analyzed for organochlorine pesticide residue. Total organochlorine insecticides in soils averaged 1.5 ppm. Nearly 24% of the samples contained endrin, but only in six samples contained more than 0.1 ppm. Samples positive for endrin were obtained from cotton fields in Alabama, Arkansas, Louisiana and Mississippi. Other crop areas with endrin soil residues were sugar cane fields in Louisiana,

corn fields in Illinois and apple and peach orchards in Maryland. Maximum readings on cotton land were in Alabama (0.11 ppm), while Maryland orchard soils contained ~~1.29-3147~~ 0.25 – 3.47 ppm (Gish, 1970). this much!??

Results from bioassay and gas chromatographic techniques indicated that amounts of endrin lethal to fish occurred in bottom muds from a Leflore County, Mississippi bayou. Cotton fields adjacent to these waters had been treated with endrin. Aerial applications in 1963 totaled 14 lbs. endrin/ac. and for 1964, 4.8 lb/acre. Several mud samples from this locality contained 6.1-48.2 ppb endrin. Acetone extracts from such muds killed test fish (Ferguson, Ludke, et al., 1965). use a, b, c etc. as appropriate

Chlorinated pesticide residues in an aquatic environment located adjacent to a commercial apple orchard in Wisconsin where endrin had been used for rodent control were studied by Moubry, et al., (1968). Silt and organic debris obtained from a stream located in the drainage area showed 0.002-0.013 and 0.011-0.025 ppm, respectively.

The degradation of organochlorine insecticides in the Philippines was investigated by Castro and Yoshida (1971) under upland and flooded conditions. Endrin was degraded only in flooded Casiguran soil which had the highest organic matter content. After 2 months, only 8.4 percent of the chemical was recovered in the flooded soil while 88.24 percent was recovered in upland soil.

The mobility of 11 insecticides in 6-inch soil columns was studied according to standard procedures. Chlorinated hydrocarbon insecticides were considered immobile. Endrin did not move out of the layer to which it had been applied at a rate of 4 lb/acre despite upward movement of

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Several insecticides, including endrin, were applied to Pullman clay loam soil in Texas at 1.6 lb/acre. Chlorinated hydrocarbons gave satisfactory control of wireworm and grubs for five years after treatment. Neither grain sorghum or wheat yields were affected by the insecticides (Daniel, 1966). Endrin residues in the soil varied from 0.06 ppm in the upper six inch layer to 0.009 ppm at 12 inches.

In another study of pesticide residues in soils and crops in Southwestern Ontario, Harris and Sans (1969) reported endrin values of 0.14 ppm before planting and 0.11 ppm after harvest on dandy loam soil. However, comparable figures on muck soils were much greater, being 5.94 and 5.80 ppm respectively.

Monitoring for chlorinated hydrocarbon pesticide residues was conducted in seven Eastern states by Seal, et al., (1967). Endrin occurred in the soil of about one-fifth of 49 fields checked. Range of amounts detected in carrots and potaotes was 0.05-0.50 ppm.

Wiersma, et al., (1971) reported on a later phase of the national soils monitoring program. Endrin was not detected, but results of their analyses of 242 cropland and 117 non-cropland samples from 6 states indicated widespread in occurrence of several other organochlorine pesticides.

The effect of 29 pesticides, including endrin, on the production of CO_2 and nitrification by soil microorganisms was determined. A few compounds were stable but without significant effect in soil. Some (including cyclodienes) persisted and depressed respiration and nitrification, and others displayed toxicity but were transformed by soil

microorganisms (Bartha, et al., 1967). CO_2 production in soil containing endrin 250 and 2500 ppm endrin was inhibited 20 percent but these treatment levels had no effect on soil fortified with glucose.

It was apparent that endrin did not influence nitrification. At the 250 ppm soil treatment level, NO_3 production for endrin-treated soils was 15.7 mg at 6 days, 47.2 mg at 12 days, and 70.5 mg at 18 days.

The persistence and moderate toxicity of the cyclodiene compounds in soil, described by others, also was observed in these studies. No indication of microbial degradation was obtained. Biological epoxidation of endrin would not have been detected by the analytical methods employed.

Chapter III

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Chapter IV

Residues in Crops and Food Items

IV.A. Introduction - Residues of endrin in food and feed crops may result from the direct application of the pesticide to the crop, translocation to growing plants from contaminated soils, or by drift from application to adjacent areas. Foliar application of endrin may dissipate by weathering; but limited absorption and translocation can occur in some plants. Soil applications are more likely to persist from one growing season to the next depending on the type of soil and the amount of material applied. The occurrence of residues in certain crops such as soybeans, vegetables and peanuts may be contingent upon crop rotation practices and prior pesticide usages.

Some endrin residues are removed from human food by processing prior to consumption. Substantial quantities of endrin have not been reported in commercially processed vegetable oils. However, the seed meal formed by removal of the crude oil may contain pesticide residues which appear as contaminants in meat, milk and eggs following use of the meal as animal feed. Endrin residues in tobacco are not removed by curing or by subsequent manufacture of tobacco products. Endrin residues occur in sediment or lees after fermentation of wines, but none has been reported in the wine. The processing of crops for human consumption may affect the removal of endrin residues depending on the type of crop, the location of the residue in the plant and the severity of the procedure used. During the commercial processing of oil seed products, endrin is not detected in the refined oil of any of the oil

seed crops. However, the residue content in the oil seed meal is important because of its general use in animal feeds. Endrin residues in tobacco were not significantly reduced.

Endrin in contaminated food and feed is deposited in fatty tissue of animals or excreted in milk and eggs in amounts proportional to levels of intake. Following withdrawal of contamination, the levels of endrin in the fatty tissue and in eggs and milk dissipated over a period of time related to amounts detected and types of fatty tissue involved.

IV.B. Tolerances - Tolerances are established to control the amount of pesticide residue that may remain in or on food so that pesticides can be used effectively in the production of food without harm to the consumer. The presence of some pesticide residue in selected foodstuffs is allowed in amounts demonstrated to be no higher than those resulting from "good agricultural practice" provided that the final amount of residue in the daily food is no greater than the amount accepted as safe for long-term consumption for man.

In establishing safe limits for chemicals used in post-harvest treatment of raw agricultural products, numerical tolerances are established by the Environmental Protection Agency for regulatory purposes. These are listed in Table IV.B.I for endrin on raw agricultural commodities. The regulations provide that processed foods prepared from raw foods containing residues within legal tolerances will not be illegal if the residues have been removed to the extent possible in good manufacturing practices and if the remaining residue

does not exceed the tolerances on the raw product. These tolerances are at levels that permit the use without danger of excessive residue occurring. A summary of recommendations of FAO/WHO for tolerances and practical residue limits as applied to raw agricultural products moving in commerce are presented in Table IV.B.2. The figures include the sum of endrin and delta-keto endrin (FAO/WHO, 1971).

Table IV.B.1.

TOLERANCES FOR ENDRIN ON RAW AGRICULTURAL COMMODITIES

COMMODITY	TOLERANCES (ppm)	ANALYTICAL METHOD	REFERENCE
Soybeans	0.2 (proposed)	gas chromatographic procedure with an electron capture detector.	FR Feb. 5, 1971
Cottonseed	0.1 (proposed)		
Eggs and the fat of cattle, goats, hogs, horses, milk, poultry and sheep	0.05 (proposed)		
Apples, sugarcane grain of barley, oats rye and wheat	0.02 (proposed)		
Crude soybean oil	0.5 (proposed)		
Broccoli, brussels sprouts, cabbage, cauliflower, cottonseed, cucumbers, eggplant, peppers, potaotes, sugarbeet tops, summer squash and tomatoes	0.0		FR Jan. 1, 1972

Table IV.B.2.1

Recommendations for Endrin Concerning Acceptable Daily Intakes, Tolerances, and Practical Residue Limits, as of November 1971 (FAO/WHO)

Maximum Acceptable Daily Intake (mg/kg body wt.)	Tolerances and Guideline Levels		Practical Limit	
	Commodity	ppm	Commodity	ppm
0.0002	Cottonseed		Milk and Milk products (fat basis	0.02
	Crude Cottonseed oil	0.1		
	Edible cottonseed Maize oil	0.02		
	Apples, Wheat, Barley, Sorghum, rice (husk and/or polished)	0.02	Eggs (shell-free)	0.2

Policy Consideration for Residues - With recent advances in analytical methodology, more sensitive and sophisticated procedures have been developed for detecting presticide residues in levels as low as parts per billion. The President's Science Advisory Committee recommended in a report, "Use of Pesticides", dated May 15, 1963, that the accretion of residues in the environment be controlled by an orderly reduction in the use of persistent pesticides. Tolerances for those insecticides were to represent residual amounts resulting from recommended operational procedures which were considered to be without hazard when consumed in the daily diet. In addition, tolerances should be rescinded for those crops on which there are no registered uses and on those crops which may result in residues in other commodities for which tolerances are not established.

Acceptable Daily Intake - The daily dosage of a chemical which during an entire lifetime appears to be without appreciable risk on the basis of all facts known at this time. Without appreciable risk is taken to mean the practical certainty that injury will not result even after a lifetime of exposure. The maximal acceptable daily intake of endrin for man is estimated to be 0.0002 mg/kg of body weight. This value was derived from minimal daily dosage which caused no detectable changes in experimental animals. In rats, the 1.0 ppm level of endrin in the daily diet is equivalent to 0.05 mg/kg of body-weight was determined as causing no significant toxicological effect.

In dogs, the 1.0 ppm of endrin in the daily diet is equivalent to 0.025 mg/kg of body-weight was determined as causing no significant toxicological effect (FAO/WHO, 1970). For calculation of tolerances, the ADI must be considered in relation to the acutal quantities of food items containing the economic posion which are being eaten by a given population.

IV.B.1. Monitoring Programs - The Food and Drug Administration, Department of Health, Education, and Welfare, monitors pesticide residues in the Nation's food supply through two programs. One program, commonly known as the "total diet program" involves the examination of food ready to be eaten. The total diet samples are purchased from retail stores, bimonthly, in five regions of the United States. The food items and proportion used represent a two-week diet of high consumption level for a 16-19-year-old male which was constructed with the advice and assistance of U.S. Department of Agriculture. The average intake is based on consumtion of 4 kg food/day, which is almost twice that consumed by the "average" man. The foods are prepared for consumption and composited into 12 classes of similar foods.

The purpose of the second program is to determine the compliance with tolerances of residues on raw agricultural products shipped in interstate commerce and imported into the United States. The Consumer and Marketing Service of the U.S. Department of Agriculture obtains and monitors meat and poultry samples from animals and poultry slaughtered in all federally inspected establishments and from shipments imported into the United States.

During the five-year period from 1964 to 1969, 111,296 samples of domestic foods were examined for residues. A summation of the rates of endrin residues in various commodities is presented in Table IV.B.3. No endrin residues were found in finished or crude corn oil or cotton-seed oil, milk, dairy products or baby foods. However, there appears to be an increase in the percentage of endrin residue found in samples of small fruits, root vegetables, meat, poultry and grains for animal use during the 1964 to 1969 period. An average of the incidence and levels of endrin found in domestic and imported commodities is presented in Table IV.B.4. The highest incidence of endrin residues were found in domestic samples of crude soybean oil followed by fish and root vegetables. The highest incidence of endrin residue was in imported samples of large fruit followed by vine and ear vegetables and small fruit. The highest incidence of endrin residue in meal composite sample occurred in potaotes (Duggan, R,E., 1971).

Table IV.B.3.

Percent of Commodities with Endrin Residue, 1964-1969

	Domestic			Imported		
	1964-67	1968	1969	1964-67	1968	1969
Large Fruits	1.37	4.02	1.30	32.50	20.86	--
Small Fruits	0.52	1.75	6.01	1.37	10.34	--
Grain and Cereals for human use	0.20	0.90	0.34	1.09	--	--
Vegetables Leaf and Stem	4.56	3.84	1.46	2.46	--	--
Vine and Ear	3.25	5.07	3.54	9.52	9.33	5.00
Root	5.17	4.39	10.23	0.28	--	--
Beans	0.31	--	--	1.17	--	4.17
Fluid Milk						
Dairy products	(1965-67	--		(1965-67		
Meat	0.10)	0.77	1.54	0.79)	0.24	3.61
Poultry	--	3.28	8.57	--	--	--
Eggs	1.15	0.60	0.50	--	--	--
Fish	8.20	3.97	4.79	2.67	4.92	2.20
Shellfish	3.47 (1966-67	0.60	--	1.53 (1966-67	--	15.88
Grain-animal use (1966-69)	0.43)	0.28	0.96	--)	--	--
Baby Food						
Tree Nuts	0.81	--	--	--	--	--

Table IV.B.3 (Cont'd)

Percent of Commodities with Endrin Residue, 1964-1969

	Domestic				Imported			
	1964-69	1967	1968	1969	1964-66	1967	1968	1969
Peanut Oil								
Crude	2.78	--	--	--	--	--	--	--
Meal	--	--	--	--	--	--	--	--
Refined	--	--	--	--	--	--	--	--
Cotton Seed Oil								
Crude	--	--	--	--	--	--	--	--
Meal	--	6.56	--	--	--	--	--	--
Refined	--	--	--	--	--	--	--	--
Soybean Oil								
Crude	6.12	29.41	--	--	--	--	--	--
Meal	--	1.72	3.12	--	--	--	--	--
Refined	--	--	--	--	--	--	--	--
Corn Oil								
Crude	--	--	--	--	--	--	--	--
Meal	--	--	--	--	--	--	--	--
Refined	--	--	--	--	--	--	--	--

Table IV.B.4

Incidence of Endrin Residues for 1964-1969

	Domestic		Imported		Meal Composite	
	Incidence %	Ave. ppm	Incidence %	Ave. ppm	Incidence %	Ave. ppm
Large Fruit	2.0	T	30.6	0.01	--	--
Small Fruit	1.5	T	4.4	T		
Grain and Cereals	0.3	T	1.0	T	1.5	TT
Vegetables Leaf and Stem	4.0	T	2.0	T	3.7	0.001
Vine and Ear	3.5	T	8.8	T	3.0	TT
Root	5.5	T	1.5	T	2.2	TT
Potatoes				14.2	0.001	
Beans	0.3	T	1.4	T	--	--
Fluid Milk (fat)						
Dairy Products (fat)						
Meat (fat)	0.4	T	1.0	T	1.5	TT
Poultry (1968-1969)	4.4	T				
Eggs	0.9	T	--	--		
Fish	5.7	T	2.9	T		
Shellfish	2.5	T	2.4	T		
Grain (animal) (1966-1969)	0.4	T	--	--		
Tree nuts	0.7	--	--	T		
Baby Food						

Table IV.B.4. (cont'd)

Peanut Oil		
Crude	2.4	0.007
Meal Cake	--	---
Refined	--	---
Cotton Seed Oil		
Crude	--	---
Meal Cake	1.4	TT
Refined	--	--
Soybean Oil		
crude	9.3	0.028
Meal Cake	0.8	TT
Refined	--	--
Corn Oil		
crude	--	--
Refined	--	--

T = 0.005 ppm

TT = 0.001 ppm

The average dietary intake of endrin for the period of 1964-1970 was calculated to be 2.5 percent of the ADI (0.000005 mg/kg body weight/day). The average daily intake of 0.0011 mg/kg body weight was reported for all chlorinated organic pesticides for the period of 1964-1970. Dairy products, meat, fish and poultry classes comprise the source of approximately half of the intake of total chlorinated residues while grains, fruits and garden fruits account for about 40% of the intake of chlorinated hydrocarbon insecticides. The maximum dietary intake of endrin from a well-balanced diet was approximately 0.001 mg/day (7 percent of the ADI). This was attributed to levels found in meat, poultry, potaotes, leafy vegetables and garden fruit for the period of June 1968 to April 1969. During the period of June 1969 to April 1970, similar amounts of endrin were ingested in the balanced diet, but highest levels of contamination were found in potaotes, root vegetables and garden fruits (Duggan, R.E., 1972).

The incidence and daily intake in milligrams of endrin found in the total diet for the five-year period of 1964 to 1969 are presented in Table IV.B.5 (Duggan, R.E., et al., 1971), and Table IV.B.6 summarizes a distribution of the level of endrin residues found in domestic samples for the period of 1963 to 1966 (Duggan, R.E., 1969).

IV.C. Residues in Crops from Direct Application - Maturing cabbage was treated with endrin at the rate of 0.8, 0.5, and 0.25 pounds of actual pesticide per acre. Residue levels were determined at intervals of 0, 1, 3, 5, 7, 10, 14, and 21 days after application by gas chromatography. The residue levels of endrin for the 0.8 pound per acre application were reported as 4.17 ppm on the day of application followed by a decrease

Table IV.B.5.
Average Incident and Daily Intake of Endrin
(T=< 0.001 mg)

1964-1965		1965-1966		1966-1967		1967-1968		1968-1969	
% Positive Composites	Daily Intake Mg.	% Positive Compo-sites	Daily Intake Mg.	% Positive Compo-sites	Daily Intake Mg.	% Positive Compo-sites	Daily Intake Mg.	% Positive Compo-sites	Daily Intake Mg.
2.8	T	2.0	T	1.7	T	1.1	0.001	3.3	T

Table IV.B.6
Percent of Endrin in Domestic Food Samples for 1963-1966

Range (ppm) :	T-0.03	0.04-0.10	0.11-0.50	0.51-1.0	1.01-1.50	1.51-2.0	Above 2.01	Excessive Residues	Number of Residues
	72.0	20.1	7.5	0.2	0.2	---	---	29.8	1,212

to 0.81, 0.30, and 0.13 ppm by the 7th, 14th, and 21st day, respectively. The residue levels of endrin for the 0.5 pounds per acre application were reported as 2.26 ppm on the day of application followed by decrease to 0.32, 0.17, and 0.10 by the 7th, 14th, and 21st day, respectively. The residue levels of endrin for the 0.25 pound per acre application were as 0.21, 0.09, and 0.004 for the 7th, 14th, and 21st day, respectively, after application. Residue values of endrin were not reported for the initial 0.25 pound per acre sample (Mattick, L.R., 1963).

Tomatoes, snapbeans, and collards were dusted with a two percent endrin formulation at the rate of 30 pounds per acre. Residue levels were determined by the phenyl azide colorimetric method from samples taken immediately after treatment and daily thereafter. Endrin residues in tomatoes were reported as 0.31 ppm on the day of application and were not detected on the first day after application. Endrin residues on snapbeans were reported as 0.48 ppm on the day of application and were not detected on the third day after application. Endrin residues on collards were reported as 17.3 ppm on the day of application and were not detected on the fourth day after application (C.H. Brett, 1958).

Emulsifiable concentrates of aldrin, dieldrin and endrin were applied to alfalfa at the rate of four ounces per acre to determine their relative persistence on fresh forage. The resulting endrin residue on the green samples were determined photometricly at 0, 7, 14, 21, and 28 days following application. Endrin residues were reported as 63.3 ppm on the day of application followed by a decrease to 7.1, 3.43 > 0.25 and < 0.11

ppm by the 7th, 14th, and 21st and 28th day respectively. Endrin residues were usually at about the limits of the level of detection in 28 days on the fresh alfalfa. The author concludes that endrin residues were more persistent than those of aldrin but somewhat less than dieldrin residues (G.G. Gyrisco, 1961).

The foliar application to apple trees of 0.05 percent endrin resulted in an initial deposit of 104 ppm with 13 percent of the initial deposit remaining after one week and 2 percent after 7 weeks. Endrin residues were determined by gas-liquid chromatography from apple leaf samples taken prior to spraying, one hour after spraying and at 1, 3, 7, and 11 weeks afterward. The ketone isomer of endrin was detected after one week, but not in later samples. The aldehyde isomer was present to the extent of 15 percent of the total residue on the leaves in the sample taken after 7 weeks, but it was not detected in the samples taken 4 weeks later (Harrison, R.B., et al., 1967).

Residues of endrin on windfall apples and orchard cover crops were determined following a single October application of 1.2 pounds endrin per acre for mouse control. After spraying, the endrin residues on windfall apples were reported to range from 0.3 to 1.2 ppm with an average of 0.6 ppm. During the first month after application, the endrin residues on orchard grass and fescue ranged from 60 to 240 ppm. At the end of the fifth month, the endrin residues on orchard grass and fescue were 100 ppm. The authors conclude that there is little residue deterioration on orchard grass during the cool conditions encountered in the fall and winter months (Wolfe, H.R., 1963).

Two ground spray applications of endrin were applied to apple orchards for mouse control. The first application was made during the fall after harvest and the second in spring of the following year when the leaves and fruit were forming. Endrin was applied at two and four pounds per acre to the width of limb-end to limb-end ground strip for the length of the tree line of two separate orchards. Residues were determined by gas-liquid chromatography from samples of both dropped and hand-picked fruit taken from the treated and control areas. The neighboring control orchards had never been ground sprayed with endrin. Traces of endrin > 0.0005 ppm were reported in samples of the neighboring control orchards. Dropped apples from the spring spraying of 2 and 4 pounds endrin per acre showed a residue range of 0.005 to 0.028 ppm. The quantities of endrin on picked fruit from spring application of either 2 or 4 pounds per acre were trace 0.005 ppm of endrin. The authors conclude that as judged by the permissible residue standard of 0.04 ppm actionable level, no significant endrin residue persisted in either picked or dropped fruits harvested from any of the ground sprayed plots (Horsfall, et al., 1970).

The foliar application of 12.6 mg of ^{14}C-labeled endrin to the leaf surfaces of cotton plants resulted in a recovery of 33 percent of the labeled material 12 weeks after the last application. Twenty-six percent of the labeled material was found in the leaves with the remainder found in the stalks, pods, fibers, seed and oil. The recovered

activity consists of endrin and at least, five conversion products, one of which is identical with the keto-rearrangement product of endrin (Bayless, A., et al., 1970).

Tobacco plants grown under covered conditions so to protect the plants from rain were treated with 2.08 mg of ^{14}C-labeled endrin per plant. Six weeks after the foliar application, a residue of 32 to 47 percent of the initial deposit of endrin remained on the tobacco leaves and in the plant. In addition to the unchanged endrin, at least one hydrophilic degradation product was reported in the plants and soil. It was not identical with the photodegradation products of endrin (Weisgerber, I., et al., 1969).

TDE and endrin were reported as the major organic insecticides used on flue cured tobacco for the control of the tobacco hornworm. The modified Schechtor-Hallor method was used for DDT and the dechlorination sulfanilic acid-phenyl azide method was used to determine the endrin residue on tobacco. TDE and endrin residues on green tobacco during priming time were reported above 50 and 10 ppm, respectively. These residues are dissipated about 45 percent during processing. Auction market tobacco contains approximately 37 ppm of TDE and 1.8 ppm of endrin. An average of 13µg of TDE and 0.2µg of endrin are found per commercial cigarette (T.G. Bowery, 1959).

IV.D. Residues after Processing - Crude soybean and cottonseed oil were spiked with 1.0 ppm endrin and processed by stimulated commercial

processing procedures. Samples of crude oil and products were analyzed by gas-liquid chromatography. The unit processes in edible oil manufacture are alkali-refining bleaching, hydrogenation and deodorization. Neither alkali-refining or bleaching reduce the endrin contamination. Endrin is eliminated from the edible oil by either hydrogenation or deodorization or by both procedures. The presence of rearrangement or unknown breakdown products of endrin were not detected in the hydrogenated oil. The data indicates that endrin or its isomerization products appear to be removed from the neutral oil during deodorization by forced volatilization. The authors conclude that normal commercial processing of crude vegetable oils for human consumption effectively removes any chlorinated pesticides which may be present in crude oils (Smith, K.J., et al., 1968).

Endrin residues in vegetable oil seeds and products of soybeans, cotton, peanut, and corn were reported for the fiscal period 1964 to 1966. Endrin residues were reported in the raw products of soybeans, peanut and corn, but none in cottonseed. Of the three commodities containing residues in the raw products, only soybeans and peanuts were reported to contain endrin in the crude oil. Only soybean meals or cakes were reported to contain endrin residue. Endrin was not detected in the refined oil of any of the four oil seed crops (Duggan, R.E., 1968).

Endrin residues in sugarbeets and processing products were determined by gas chromatography from sugarbeets grown in endrin treated soil. The soil surface was sprayed with an endrin emulsion applied at the rate

of five pounds actual per acre and double-disced within three hours of application. The treated and control area was seeded on the following day and the sugarbeets grown to maturity. The resulting endrin residues were reported as 2.790 ppm in soil (at harvest), 0.244 ppm in raw sugarbeets, 0.195 ppm in cossettes (sliced sugarbeet prior to extraction), 1.621 in dried pulp, 0.360 ppm in carbonation mud, 0.008 in raw juice and 0.004 ppm in first carbonation juice. The dried pulp contained the major portion of endrin that was found in the processing method. The processing did not include the molassess and sugar product. Sugarbeets grown in soil of this test area are generally considered to contain an average of 14 percent crude sugar (sugar plus molasses). The endrin content of the treated soil at the time of harvest was reported as 5.06 pounds per acre (K.C. Walker, 1965).

To determine the distribution of endrin through the preparation of wines, 1.0 ppm of endrin was added to the grape musts. The samples of musts lees, wines and distillates were analyzed by paper chromatography for endrin residues. At this level of endrin contamination there was no measurable effect on fermentation. None of the endrin residues was detected in the finished wine or distillate of the lees. Endrin was reported in the sediments or lees removed after fermentation at 0.9 ppm (Painter, R.R., et al., 1963).

Irish and sweet potatoes were spiked with 100 ppm of endrin. The effects of irradiation, storage, potato type and processing on the residue content of endrin in potatoes was determined by gas-liquid chromatograph. The two methods of processing were: (1) heat processing,

with and without water; and (2) frozen, blanched and unblanched. Irradiation did not significantly affect the quantity of the endrin residue. Storage for 6 weeks did not significantly decrease the endrin residual level while storage for 12 weeks did significantly decrease level of endrin. The decrease in pesticide residue from processing was dependent on the potato type. Residues of endrin from processing were reduced 49.75 percent in sweet potatoes and 65.12 percent in Irish potatoes. Heat processing effectively reduced the endrin residue content by 27.0 percent. Endrin was affected to a greater extent by heat processing with water than heat processing alone. Blanching significantly reduced the endrin residue levels in the potatoes (J.M. Solar, 1971).

Field-cured alfalfa hay samples were contaminated with endrin and subjected to various extraction techniques for the removal of endrin residues. By analysis, the contaminated hay contained a residue of 900 ppb of endrin. Residues were determined by thin-layer chromatography and gas-liquid chromatography. Endrin residues were not removed by washing with hot or cold water. Oven heat removed approximately 35% of the residue. The residue removal was increased to 73% when the hay was saturated with water and heated. The residue was not loosely deposited nor chemically bound to the plant materials. It was found mainly in the wax-like material of the plant cuticle. Endrin was 93 percent removed by vapor washing with common solvents such as benzene or water. The author concludes that the vapor treatment of contaminated hay with steam before dehydration may have some practical application for pesticide removal (Archer, T.E., 1968).

The concentration of endrin in commercial tobacco in 1956 was barely detectable with the methods available. Levels as high as 1.3 ppm were reported by 1964. During harvesting of the tobacco leaves, applications of insecticides are recommended immediately after priming to provide a maximal period of seven days between application and priming. Endrin residues from 5 to 13 ppm were reported on the green leaf after weathering for 7 days. Forty percent of the chlorinated hydrocarbon residues are lossed during the flue-curing process. Storage or aging of tobacco had little effect on the residue content of organochlorine residue in tobacco. In experimental cigarettes impregnated with endrin approximately 20% of the applied insecticide appeared in the mainstream of smoke with approximately 80% endrin dissipated during the smoking process.

Residues were measured in flue-cured tobacco, the principal ingredient of cigarettes, which was obtained from the auction markets in North Carolina, South Carolina, Georgia and Florida. Residues in cigar wrapper tobacco in Florida and residues in manufactured tobacco products on the 1962 retail market were also determined. All samples were analyzed by electron capture gas chromatograph. High residues of endrin were found on some of the samples of flue-cured tobacco in North Carolina as well as the cigar wrapper tobacco in Florida. All of the cigarette samples contained endrin, with half containing 1 ppm or more. The maximum residue of 2 ppm endrin found in one filter brand was 7 times greater than the maximum found in cigarettes in 1957. Endrin was detected in 7 of the 9 samples of pipe tobacco and snuff, with one sample of snuff running as high as 2 ppm (Lawson, F.R., et al., 1964).

Representative samples of six brands of cigarettes were purchased on the retail market during 1966 and 1967. The tobacco was analyzed by electron-capture gas chromatography. In tobacco samples taken in 1966, endrin was reported in concentrations of 0.49-1.57 ppm. In 1967, the concentration of endrin in the same brands of cigarettes was reduced to 0.31 to 1.20 ppm. The average level of endrin in 1967 was only 61% of that reported in 1966 (Sheets, T.J., 1968).

King-sized cigarettes of a standard brand were purchased on the open market and separated from the paper. Residues were determined by electron-capture gas chromatographic method. Tobacco from a commercial cigarette was shown to contain 43 ppm DDT-TDE and no endrin residues (Skrentry, R.F., et al., 1971).

Cigarette tobacco from Japanese, German and American brands were analyzed for chlorinated hydrocarbon pesticide residues by gas chromatography. The average pesticide contents for the three Japanese brands were as follows: α-BHC 0.1 ppm; β-BHC 0.2 ppm; γ-BHC (lindane) 0.1 ppm; δ-BHC 0.1 ppm; p,p'-DDT 0.4 ppm; aldrin 0.1 ppm; dieldrin 0.2 ppm; endrin 0.5 ppm. The West German and American cigarettes, similar in pesticide content, showed no detectable contamination with β-BHC, δ-BHC or aldrin. They contained average quantities of 0.02 ppm α-BHC, 0.1 ppm γ-BHC, 5 ppm p,p'-DDT, 0.2 ppm dieldrin and 1.5 ppm endrin (Karvahara, T., et al., 1971).

IV.E. Residues in Animals from Direct Application - Milk samples containing endrin were taken from dairy animals dusted with a rotenone formulation

contaminated with approximately 30 percent endrin. Endrin residues were determined by gas-liquid chromatography. Shortly after application, three cows went into convulsions, and one animal died. Endrin was detected in extracted fat of the initial milk samples at 6.76 ppm. This level of endrin was reduced to 0.81 ppm in 14 days followed by a further reduction to 0.13 ppm in 36 days after the initial sample was taken. The authors conclude that the retention time of chlorinated hydrocarbons in milk follow the order of dieldrin> DDT and its analogues> BHC> lindane> endrin> methoxychlor (Moubry, R.J., 1968).

IV.F. Residues in Animals from Feed Contamination - Feed contaminated with endrin at the levels of 2.5 and 5.0 ppm were fed to cattle for 16 weeks. Tissue samples of fat were taken from both groups at 4,8, 12, and 16 weeks during the feeding period. Levels of endrin in the fatty tissue of cattle fed the 2.5 ppm level averaged 1.2, 2.6, 0.8, and 0.8 ppm at 4,8,12, and 16 weeks respectively. Levels of endrin in the fatty tissue of cattle fed 5.0 ppm 1.3, 1.5, 2.4 and 2.3 ppm at 4,8,12, and 16 weeks respectively. Endrin was not reported in the tissue samples taken four weeks after the last feeding of either dosage level. In comparing endrin to other pesticide contaminates likely to occur in the feed of cattle and sheep the authors report the order of storage in fat as follows: aldrin > dieldrin > heptachlor epoxide> BHC > DDT > chlordane > lindane> endrin> heptachlor > toxaphene, (Claborn, et al., 1960).

The cumulative results of several studies on the propensities of various organochlorine insecticides to be excreted in the milk of

cows fed known amounts of contaminated feed were reported by J.G. Saha (1969) in the order of heptachlor epoxide > aldrin > dieldrin > kelthane > endrin > γ-BHC> DDT > heptachlor > toxaphene > chlordane> methoxychlor. Endrin residue in milk per ppm residue in feed was reported in the ratio of 0.07 ppm to one. The author concludes that the relative rate of detoxification of these insecticides should follow the reverse order, methoxychlor being most readily detoxified and heptachlor epoxide the least readily detoxified. Similar order has been found to prevail for storage in body fat (Ganon, et al., 1959).

Lactating dairy cows received an average daily dose of endrin from 0.06 to 0.11 mg per kilogram of body weight gave average concentrations of endrin in the milk of approximately 0.1 to 0.2 ppm. Alfalfa sprayed with 2.7, 6.6, and 7.8 ounces of endrin per acre was harvested one week after spraying and stored for six months. The hay treated at 2.7 and 6.6 ounces per acre was fed for 48 days while the hay treated with 7.8 ounces per acre was fed for 63 days. Residues of endrin in milk and hay were determined by the amperometric silver nitrate titration method. Hay made from the alfalfa plots sprayed with 2.7, 6.6, and 7.8 ounces of endrin per acre had an average endrin residue of 2.8, 3.7, and 1.9 ppm, respectively, at the time of feeding. The average endrin content of the milk of cows receiving hay contaminated with 1.9, 2.8, and 3.7 ppm was 0.05, 0.14, and 0.15 ppm, respectively. A daily intake of approximately 0.05 mg per kilogram of body weight of endrin and below did not result in the excretion of measurable amounts of endrin into the milk (Ely, R.E., et al., 1957).

A mixture of five pesticides (heptachlor epoxide, dieldrin, endrin, lindane and DDT) were added to the grain rations of lactating dairy cows at the levels of 0.05, 0.15, and 0.30 ppm. All samples were examined by the electron-capture gas chromatographic method. Residues of endrin and lindane were found in the milk at all three feeding levels, although at lower concentrations than heptachlor epoxide and dieldrin. No endrin or lindane was found in the milk of the control animals. The residue of endrin in milk reached a maximum at the end of the 35-day feeding period for all three dosage levels. The plateau concentrations of endrin residue in milk were 0.004, 0.010, and 0.018 ppm for the three respective feeding levels. During the three week withdrawal period the residue level of endrin in the milk samples returned to baseline values in approximately 8, 17, and 23 days after the last exposure to the three respective feeding levels. Feed consumption and milk production were very uniform for the entire duration of this study (Williams, S., et al., 1964).

Endrin was fed to steers, lambs and hogs at 0.1, 0.25, and 0.75 ppm in their diet for 12 weeks to determine the extent of tissue residue likely to result from feeding contaminated forage crops to livestock. All tissue samples were analyzed for endrin by the spectrophotometric method. The general appearance and weight gains were considered normal for both the treated and control animals. Only endrin residue levels of 0.25 ppm or higher were present in amounts that could be consistently detected by the analytical method. Steers accumulated the highest level and hogs showed the least tendency to store endrin in the fatty tissue. Residues of endrin

in the fatty tissue of hogs and lambs were reduced below the level of detectability within six weeks after the last exposure. The endrin content of the fat of steers was reduced 60 percent within six weeks of the last exposure. There was no decrease in the endrin content of the meat as the result of cooking (Terriere, L.C., et al., 1958).

Lactating dairy cows were fed daily doses of 0.1, 0.25, 0.75, and 2.0 ppm of endrin in their grain ration for 12 weeks. All of the milk and body tissue samples were analyzed for endrin by the spectrophotometric method. The lower levels of endrin fed were of the same order of magnitude as those expected from actual field use of endrin on forage crops. The general appearance, weight gained and milk production were considered normal for the treated and control animals. Endrin residues in the milk were reported for those animals receiving endrin at 0.25 ppm and above. These residues were apparent in the milk within the first week and except for the 2.0 ppm level had disappeared from the milk within one month after the feeding had ceased. The endrin residue in milk reached a plateau within a month and remained at this level for the remainder of the exposure. Endrin residues in fat were reported at the 0.25 ppm level and above the maximum concentration being 1.0 ppm. These residues had disappeared within one month after the feeding had ceased. This study indicates that in dairy cows the ratio of storage in body fat to intake is about 1 to 2 for all levels tested (Kiigemagi, Ulo, et al., 1958).

To demonstrate the relationship between the low level pesticide residue commonly found in commercial poultry feed and the resultant residues in eggs, lindane, heptachlor, dieldrin, endrin and DDT were

fed in combination at levels of 0.05, 0.15 and 0.45 ppm to hens for a 14-week period. Residues were determined in eggs by the electron-capture gas chromatography method of analysis. The level of storage in eggs approached a plateau at the end of the 14-week period. Endrin residues in eggs were reported in the range of 0.03 to 0.3 ppm for the the three dosage levels. The plateau level of endrin residue in eggs is proportional to the level of pesticide in the feed for all pesticides except DDT. Endrin residues in eggs slowly declined but were still present at the end of the month withdrawal period. The distribution of pesticides between egg yolk and white were reported in the following ratios in yolk to white; lindane 90/10; p,p'-DDT 93/7; DDE 95/5; heptachlor epoxide 99/1; dieldrin 99/1 and endrin 100/0. The average egg production was approximately 60 percent (Cummings, J.G., 1966).

To demonstrate the relationship between low level pesticide residues commonly found in commercial poultry feeds and the resultant residues in poultry tissue, lindane, heptachlor, dieldrin, endrin and DDT were fed in combination at the levels of 0.05, 0.15, and 0.45 ppm to hens for a 14-week period. Residues were determined in abdominal fat, breast muscle and liver by electron-capture gas chromatography. The tendencies of the pesticides to store in the abdominal fat and eggs were in the order of dieldrin < heptachlor < epoxide < endrin < DDT < lindane. With the exception of heptachlor epoxide, the level of storage in fat had approached a plateau at the end of the 14-week period. The storage levels for heptachlor epoxide and dieldrin in fat were about 10 times that of the respective levels of pesticides added to the feed. With the exception

of DDT, the residue plateau levels in the fat were proportional to the feeding levels. The plateau residues in the abdominal fat were about 10 times greater for each pesticide than the respective amounts found in eggs. The endrin residues in breast tissue were reported in the range of 0.01 to 0.03 ppm. Endrin residues in fatty tissue were reported in the range of 0.035 to 3.5 ppm for the three dosage levels. Lindane residue showed the greatest decline rate while endrin residues were still evident during the one-month withdrawal period (Cummings, J.G., et al., 1967).

Laying pullets and broiler chickens were fed doses of 0.1, 0.25, 0.75, and 2.25 ppm of endrin in their daily diet for periods of six to eight weeks. Tissues and eggs were examined for endrin residues using a specific spectrophotometric method of analysis sensitive to 0.1 ppm. Weight gain, egg production, feed consumption and mortality appeared normal. The results indicate that a dietary level of 0.10 ppm endrin fed for 8 weeks will be deposited in the fat without danger of contaminating the eggs with endrin. At 0.25 ppm level and above, definite deposition of endrin in egg tissue occurs after 2 to 4 weeks and it is evident for about a month after exposure to endrin is stopped. Endrin residues in the eggs of pullets were reported as 0.2 and 0.3 for the 0.25 and 0.75 ppm dietary level at the end of the eight weeks feeding. Four weeks after the feeding ceased, the residue in eggs for the 0.25 and 0.75 ppm dietary level had decreased to < 0.01 and 0.2 ppm respectively. Four weeks after the feeding had ceased the residue in fat for the 0.25 and 0.75 ppm dietary level were reported at 0.3 and 1.1 ppm respectively.

When broilers received 0.75 ppm in their diet for six weeks, endrin residues were reported in fat at 3.1 ppm in breast tissue at 0.2 ppm and in drumstick at 0.3 ppm. Feeding of 2.25 ppm of endrin resulted in residues of 17 and 18 ppm in fatty tissue. Cooking failed to eliminate the residues (Terriere, L.C., 1959).

Tissue levels of endrin were reported in the fat of lambs 42 days after the last exposure to an endrin-treated pasture. Six lambs were grazed on a 0.5 acre of endrin-treated pasture for 55 days and then removed to graze on the untreated pasture for 42 days. On the day the animals entered the test area, two percent granules were applied at 0.5 lb. actual endrin to the treated pasture. This rate of application was repeated for a total of six applications over a six-week period. No toxic symptoms were observed during the experimental period. No significant difference in average weight increase was reported between the two groups. Endrin residues in the fat were determined by the chromatographic dechlorination phenyl azide method from samples obtained at 0, 14, and 42 days after the last exposure. The calculated average levels of endrin residue in the fatty tissue at 0, 14, and 42 days were 16.8, 19.7, and 10.0 ppm, respectively. The author concludes that there was apparently no measurable loss of endrin from fat 14 days after lambs were transferred from the treated to the untreated pasture although there is an indication of some loss from fat after 42 days (Long, W.H., et al., 1961).

Feed contaminated with endrin at the levels of 2.5 and 5.0 ppm were fed to sheep for 16 weeks. Tissue samples of fat were taken

from both groups at 4,8,12 and 16 weeks during the feeding period. Levels of endrin, in the fatty tissue of sheep fed the 2.5 and 5.0 ppm level averaged 3.2, 1.8, 2.3, and 1.4 ppm and 1.5, 2.0, 0.8 and 2.2 ppm, respectively. Endrin was not reported in the tissue samples taken four weeks after the last feeding of either dosage level. In comparing endrin to other pesticide contaminates likely to occur in the feed of cattle and sheep, the authors report the order of storage in fat as follows: aldrin > dieldrin > heptachlor epoxide > BHC > DDT > chlordane > lindane > endrin > heptachlor > toxaphene (Claborn, et al., 1960).

Pregnant ewes were dosed with gelatine capsules containing a one percent endrin dust formulation at the levels of 0.75 and 2.0 ppm for 12 weeks as shown in Table IV.F.I. Samples were analyzed by the phenylazide spectrophotometric method for endrin. Most lambs were born during the first and second week of feeding. Fat samples were taken from lambs slaughtered at 6 to 8 weeks of age. The only source of toxicant to the lambs was that contained in the mother's milk.

The meat samples were reported to contain 0.1 ppm endrin.

Table IV.F.1.

ENDRIN RESIDUES IN FATTY TISSUE OF SHEEP AND LAMBS (ppm)

Dosage Level	Ewes at 12 weeks	Ewes at 18 weeks	Lambs at 6 weeks
0	0.1	0.4	0.1
0.75	0.5	0.4	0.5
2.00	1.5	0.2	0.3

The excretion of endrin once stored in body tissues appears to be a rather slow process. Endrin concentrations in the fat samples taken from lambs at 6 to 8 weeks of age were nearly as great as those found in the fat tissue of the parent. Appreciable amounts of endrin were found in the fat of ewes after 12 weeks of treatment. After withholding the toxicant for six weeks, the endrin content of the fatty tissue of the ewes was lower but still present in significant amounts (Street, J.C., et al., 1957).

Residue in Animal Products Processing - The effects of processing and storage on endrin residues in dairy products was determined by either adding the pesticide prior to processing the milk or by adding endrin to the daily diet of cows until the resulting residues in the milk reached 0.6 to 0.8 ppm endrin. The contaminated milk was then processed into butter, ice cream, Swiss-type cheese, condensed milk and dry whole powdered milk. After separation of the whole milk, endrin was found only in the cream and none was detected in the skim milk. Endrin was not affected by condensing. Some loss of endrin was reported during the spray and drum drying process. No significant changes were observed in the structure or amount of endrin during storage of butter, cheese, ice cream, and sterilized milk (Langlois, B.E., 1965).

The effects of processing and preparation methods on pesticide residues was determined on contaminated chicken tissue. Lindane, endrin, heptachlor, dieldrin and aldrin were fed at 10 ppm to broilers throughout an eight week growing period. The determinations for tissue residues were made by electron-capture gas chromatographic method.

Weights of birds receiving endrin and aldrin were lower than the other groups. Several birds died in the endrin group indicating that the level of endrin fed was near the maximum amount of residue which could be tolerated by the bird. Tissues from these birds were cooked by baking, frying or steaming in closed containers for 30, 60 and 90 minutes. Residues calculated on a dry matter basis were lowered during cooking but the reduction in concentration was not significant in most cases. Lindane concentration was reduced considerably when tissues were heated in closed containers. Heptachlor epoxide residues were reduced during heating in closed containers. Heating had no effect on the residues of endrin, dieldrin, or aldrin. Any loss which occurred in the cooked samples of endrin, dieldrin and aldrin was apparently through leaching of fat and water (Ritchey, S.J. et al., (1972).

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Chapter VI

The use of Endrin in Relation to the Hazards or Safety of Continued Use

Endrin is a synthetic chlorinated hydrocarbon which has been used as a pesticide (economic poison) for more than 15 years to control a variety of chewing and sucking insect pests which inhabit soil and infest crops. It is also used to control mice populations in deciduous orchards as an avicide, and as a rodent repellent in the reseeding of forests. Prior to 1965, when the largest quantities of this pesticide were used, especially on sugar cane and cotton, large fish kills in the lower Mississippi River were attributed by some to endrin contamination from industrial effluent and by runoff and drift from nearby agricultural uses. However, periodic fish which have resulted from a number of complex factors have been reported in the Mississippi River over many decades. Several additional factors, including industrial pollution could easily have been involved in these unfortunate events.

Since 1966 the number of registered uses for endrin have declined probably due in part to its relatively high toxicity, the lack of tolerances greater than zero and the development of resistance to endrin.

Relative amounts of endrin used since 1970 are presented in Table VI.A. by insect pests. During the 1970-1971 season, amounts of endrin used was approximately one-third of the amount used in 1966. Inspite of the cancellation of endrin on corn and other food

crops, amount level during 1971-1972 season was over twice the amount during the prior season with the increase attributed solely to use on cotton. Registered uses, rates of application, limitations and registered alternates are presented in Table VI.B. Registered uses of endrin for which there is no registered alternate or for which registered alternates are not as effective as endrin are presented in Table VI.C. Insects from different areas known to be resistant to endrin are presented in Table VI.D.

TABLE VI A

Relative Quantities of Endrin Used During 1970 - 1972.**

Field Crop	1970 - 1971* (%)	1971 - 1972 (%)
Cotton	34.1	82.14
Corn	14.9	Cancelled
Small Grain	16.0	6.4
Sugar Cane	2.2	0.009
Seed Treatment	2.1	0.008
Potatoes	0.5	Cancelled
Sorgum, Sugar Beets	0.9	Cancelled
Orchard (deciduous)		
Mouse Control	28.6	11.44
Other		
Greenhouse, nursery, bird control	0.7	0.003

*For these uses 132 labels were registered by Shell Chemical Co and Vilsicol Chemical Corp.

**Amount used in 1971 was 43 percent of that used in 1966. In 1971 amount used on cotton was 18.7 percent of the amount used in 1966, and in 1972 82 percent of the amount used in 1966. Quantities used for orchard mouse control have increased seven fold since 1966.

TABLE VI B

Summary of Registered Endrin Uses and Alternates

Crop or use	Tolerance (ppm)	Dosage (lbs. a/A)	Limitations	Pests	Possible Substitutes
Barley Oats Rye Wheat	Extended	0.25	Single application. Do not apply within 45 days of harvest or of feeding. Do not graze livestock on treated forage. Do not feed threshings to livestock.	Armyworm	Carbaryl Chlordane Malathion Methyl parathion Parathion Toxaphene Trichlorfon
				Chinch bugs	Parathion Toxaphene
				Cutworms	Toxaphene Thiodan Trichlorfon
				Fall armyworm	Parathion Toxaphene
				Pale western cutworm	Toxaphene Thiodan Trichlorfon

Crop or Use	Tolerance	Dosage	Limitations	Pests	Substitutes
Cotton	0 Extended	0.7	Apply for control of cutworms. Do not graze dairy animals or animals being finished for slaughter on treated fields. Workers entering fields within 5 days after treatment should be protected.	Cutworms	Carbaryl Strobane Toxaphene Trichlorfon
		0.5	Do not graze dairy animals or animals being finished for slaughter on treated fields. Workers entered fields within 5 days after treatment should be protected.	Boll weevil	Azodrin Carbaryl Chlordane EPN Guthion Malathion Methyl parathion Methyl trithion Strobane Toxaphene

Crop or Use	Tolerance	Dosage	Limitations	Pests	Substitutes
Cotton (cont.)					
				Brown cotton leafworm	Guthion Malathion Parathion
				Cabbage looper	Azodrin Bacillus thuringiens Methyl parathion Thiodan
				Cotton fleahopper	Bidrin Carbaryl Chlordane Guthion Malathion Methyl parathion Methyl trithion Phosphamidon Strobane Thiodan Toxaphene Trichlorfon

Crop or Use	Tolerance	Dosage	Limitations	Pests	Substitutes
Cotton (cont.)				Cotton leaf perforator	Bidrin Carbaryl Malathion Methyl parathion Methyl trithion Parathion Trichlorfon
				Cotton leafworm	Carbaryl Guthion Malthion Methyl parathion Methyl trithion Parathion Trichlorfon
				Garden webworm	Carbaryl Guthion Malathion Methyl parathion Strobane Toxaphene

Crop or Use	Tolerance	Dosage	Limitations	Pests	Substitutes
Cotton (cont.)				Greenhouse leaf tier	
				Grasshoppers	Carbaryl Chlordane Malathion Methyl parathion Strobane Toxaphene
				Fall armyworm	Carbaryl Methyl parathion Strobane Toxaphene
				False wireworms (adults)	Carbaryl
				Field crickets	Dieldrin

Crop or Use	Tolerance	Dosage	Limitations	Pests	Substitutes
Cotton (cont.)				Lygus bugs	Bidrin Carbaryl Chlordane Guthion Malathion Methyl parathion Phosphamidon Strobane Toxaphene Trichlorfon
				Sale-marsh caterpillar	Bidrin Diazinon Methyl parathion Parathion Trichlorfon

Crop or Use	Tolerance	Dosage	Limitations	Pests	Substitutes
Cotton (cont.)				Tarnished plant bug	Bidrin Carbaryl Chlordane Guthion Malathion Methyl parathion Phosphamidon Strobane Toxaphene Trichlorfon
				Thrips	Bidrin Carbaryl Chlordane Guthion Malathion Methyl parathion Methyl trithion Parathion Phosphamidon Strobane Toxaphene

Crop or Use	Tolerance	Dosage	Limitations	Pests	Substitutes
Cotton (cont.)				Celery leaf tier	
				Rapid plant bug	Aldrin Guthion Heptachlor
				Crickets	Aldrin
				Darkling ground beetles	Chlordane Heptachlor Toxaphene
		2 oz./100 lb. seed	Seed treatment Do not use as food or feed.	False wireworms	Aldrin Dieldrin Lindane
				Wireworms	Aldrin Dieldrin Lindane
Deciduous Fruits: Apples Apricots Cherries Nectarines Peaches Pears Plums Prunes	Extended	2.4	Postharvest application to orchard floor in Oct. or Nov. Apply to 500 psi pressure. Do not cultivate prior to application or within 2 months thereafter. Do not treat areas where runoff will	Mouse control	

Crop or Use	Tolerance	Dosage	Limitations	Pests	Substitutes
Cotton (cont.)					
Deciduous fruits: (cont.)					
Quinces					
Apples only			contaminate streams, ponds, or domestic water supplies. Do not graze orchards, cut forage for hay, or allow drop fruit to be utilized for any purpose. Post or otherwise prevent entry to treated area within 30 days after treatment.		
Sugarcane	Extended	0.25 (granular)	45 days. 4-8 applications at 14-day intervals. 2.0% granular formulation only. Do not feed bagasse or field trimmings to livestock. OR	Sugarcane borer	Carbaryl Guthion Thiodan

Crop or Use	Tolerance	Dosage	Limitations	Pests	Substitutes
Sugarcane (cont.)	0.5	45 days.	4 aplications at 21 day intervals. Do not feed bagasse to livestock.		
		0.5	Apply to seed pieces in open row.	Sugarcane beetle	Aldrin
Reforestation Seed Treatment, Direct Seeding			NF	Birds and Mammals (Repellent	
Avian Control Buildings			NF	Pest Birds (Contact Poison)	Fenthion
Ornamentals and Nursery Stock Foliage			NF	Cicadas	Carbaryl
				Cyclamen mite	Diazinon Thiodan
				Spittlebugs	Methoxychlor

Table VI.C.

Registered use of endrin for which there is no registered alternate or registered alternate is not as effective as endrin.

Crop or Use	Pest	Registered Alternate
deciduous fruit (primarily apples and peaches)	meadow mouse	* None
	pine mouse	*none
Cotton	leaf perforator	none satisfactory
forest seed	bird and rodents	none
small grains	cutworms	none satisfactory

*Experimental permits have been issued for diaphacinone and chlorophacinone, however, no data is available as yet on the efficacy of these compounds.

Table VI.D.

Pest known to be resistant to individual insecticide in one or more areas of the United States.

Pest	Insecticide	States
Band-wing white fly	Methyl parathion	La.
Beet army worm	organochlorine compounds	Ariz. Ark. Cal. Miss.
Boll weevil	organochlorine compounds	Ala., Ark., Ga., La., Miss., N.C., Okla., S.C., Tenn., Texas.
Bollworm	DDT	Ala., Ark., Ariz., Cal. Ga., La., Miss., Mo., Okla., Tenn., N.C., Texas
	Endrin	Ark., La., Miss., Okla., Tenn.
	Carbaryl	Ariz., La., Okla.
	Methyl parathion	Ark., Okla.
	TDE	Texas
Cabbage looper	DDT	Ariz., Ga., Tenn., Texas
	Organochlorine compounds	Ala., Ark., Cal., La., Miss., Okla.
	Endrin and toxaphene	Ariz.
	Organophosphorous compounds	Ark.
Cotton aphid	benzene	Ark., Ala., Ga., La., Miss., Tenn.
Cotton fleahopper	Organochlorine compounds	Texas
Cotton leaf perforator	Organochlorine compounds	Cal.
	DDT	Army
	Organophosphorous compounds	Cal.
Cotton leafworm	organochlorine compounds	Ark., La., Texas
Lygus bug	organochlorine compounds	Cal.
	trichlorfon monocratophos	Cal.
	DDT	Ariz.

Table VI.D. (cont'd)

Pest	Insecticide	State
Pink bollworm	DDT	
Salt-marsh caterpillar	Toxaphene, DDT, Endrin	Ariz., Cal.
Southern garden leaf-hopper	DDT	Cal.
Spider mites		
Tetranychus turkestan,	organophosphorous compounds except phorate seed or soil treatment	Ala., Cal.
T. cinnebarinus, *T.*	organophosphorous compounds	Ala., Ariz., Cal.
Pacificus	Except phorate seed or soil treatment	Texas
T. urticae	organophosphorous compounds except phorate seed or soil treatment	Ala., Ark., Cal., La., Miss., N.C.
T. Pacificus	dicofol	Cal.
Stink bug	organochlorine compounds	Cal.
Thrips		
Frankliniella (mixture	dieldrin	Cal.
	endrin	
	Toxaphene	
T. Occidentalis	organochlorine compounds	Texas
T. Tabaci	organochlorine compounds	Texas
Tobacco budworm	Carbaryl	La., Texas
	DDT	Ala., Ga., La., Miss. N.C., Texas, Ark.
	Endrin	La., Miss., Texas,
	Strobane plus DDT	Texas.
	TDE	Texas
	Toxaphene plus DDT	La., Miss., Texas
	organophosphorous compounds	Texas, La.

CHAPTER VII

General Discussion of the Hazards of Endrin in Relation to Use Patterns

Endrin is a relatively persistent snythetic chlorinated hydrocarbon pesticide with a high acute toxicity. When ingested or absorbed into a mammalian organism, it tends to accumulate in fatty tissues. There are zero tolerances on thirteen specific food crops that are covered by registration; other registrations have also been issued. The principal formulations are granular products, baits, wettable powders, and emulsifiable concentrates. Dust formulations are not common and are difficult to handle because of drift factors. The following is a summary of benefit/risk relationships pertaining to the principal registered patterns of use.

1. Foliage Treatments (Small Grains)

The pesticidal benefits from uses to control cutworms and armyworms are relatively high since most of the effective alternates such as aldrin, chlordane and heptachlor are under review for cancellation. Other alternates tend to be less effective and more costly. Relatively low dosages and early season usage are required. The application of spray and granular proportions affords moderate to low risk to the applicator and low risk of environmental pollution. The principal risks involved are feed and forage contamination, hazards to wildlife in the treated fields and in field margins, and possible contamination of water from run off. Container disposal may also be

a problem in many cases. There are no residue tolerances on food and feed crops.

2. Foliage Application (Cotton) but also including Seed Treatment

The benefits of this use are relatively low to moderate since substitute pesticides are for the most part readily available. However, these substitutes which include methyl parathion, azinphos methyl, EPN and monocrotophos (Azodrin) are more costly. Mixtures of endrin and methyl parathion are widely used; no antidote has been proposed for this mixture. Human health hazards from endrin spray applications are low to moderate and low for granular application. Hazards related to environmental pollution are moderate. Moderate hazards are involved in the treatment site and field margins so far as fish and wildlife are concerned. There is a zero tolerance on cotton seed which can easily be violated. Container disposal problems can be serious. Seed treatments have low to moderate benefits; application and environmental risks are low.

3. Soil and Foliar Applications (Sugarcane)

The pesticidal benefits involved are quite low at this time, since reasonably adequate substitutes are now available. However, the environmental and application risks also appear quite low with spray and granular formulations except with respect to exposed fish and wildlife. There are, of course, no tolerances in sugar and related products. Container disposal problems also may be serious.

4. Seed Treatment (Forest)

The pesticidal benefits involved in this use are quite high because of rodent feeding on treated seeds. The dosages are quite low and the seeds are usually broadcast over large uninhabited areas by aircraft. The risks of these treatments to applicators flying the aircraft or regulating the treatment from the ground appear to be quite minimal since all of these applications are on a professional basis usually by State or Federal official agencies or by large lumber companies. Environmental pollution may be a factor to some extent but is probably minimal because of low dosage and the infrequency of repeated applications. This use affords a substantial danger to selected types of wildlife since the purpose of the treatment is to kill various rodents and birds which would otherwise eat the treated seed. The seeds also are treated to some extent to make them at least partially repellent to seed-eating birds. Container disposal may also be somewhat of a problem.

5. Deciduous Orchards (Mouse Control)

The pesticidal benefits from orchard treatments for mouse control are high since there is no registered substitute. Some promising alternates are being investigated. Substantial dangers are involved with this use especially from the standpoint of environmental pollution and hazards to fish and wildlife in or near the treatment area. There are no tolerances for residues of endrin on deciduous fruit. Applicator hazards are relatively low to moderate. Container disposal problems involve a relatively high risk since large dosages are involved and a number of containers require disposition.

6. Foliage Application (Nursery Stock and Ornamentals)

The pesticidal benefits involved are low to moderate since there are a number of substitutes that are equally effective and not necessarily expensive. The risk from this use of endrin is low to moderate. No food commodities are involved and environmental pollution problems do not appear to be serious. Container disposal could be a problem.

7. Perch Solution (Bird Control)

The benefits from use are moderate to high. Fenthion as a registered alternate has a high degree of acute toxicity and is subject to about the same benefit/risk relationship as endrin. However, present data suggest that fenthion may not be as effective as endrin under all conditions of use. The risks of application are relatively low and risks of environmental pollution are moderate as are the risks to wildlife especially songbirds and other nonpest birds. Container disposal and disposal of the used perches can be a relatively serious problem.