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The Toxicity of the Vapors of Aroclor 1242® and Aroclor 1254®

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INVESTIGATION of the physiological response of animals to the inhalation of two Aroclors, namely 1242 and 1254,® was undertaken because in the earlier literature[1] dealing with the toxic effects of Aroclors, no distinction has been drawn between the toxic effects of chlorinated biphenyls and those of chlorinated naphthalenes, despite the differences in the chemical composition, physical characteristics, and industrial applications of these classes of compounds. In the case of the chlorinated biphenyls, at least, further toxicological investigation and consideration were required to demonstrate the relationship between the extent of their chlorination and their toxicity.

Properties

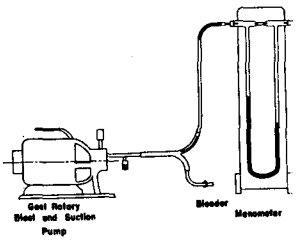
AROCLOR 1242 is a light, straw-colored, mobile liquid. According to Benignus, of Monsanto Chemical Company, it contains 42.0 ± 0.5% of chlorine, an amount which corresponds to a chlorinated biphenyl with three chlorine atoms in unassigned positions. The physical and chemical properties are given in Monsanto Application Bulletin No. O-P-115. Its specific gravity at 25°/25°C is 1.378 to 1.388; it has a distillation range of 325° to 360°C; a refractive index (D-line at 20°C) of 1.627 to 1.629; a Saybolt Universal viscosity at 100°F of 80 to 93 seconds, and a flash point (Cleveland Open Cup) of 176°-180°C. Its vapor pressure is about 4 mm at 150°C and about 30 mm at 200°C. Although insoluble in water and glycerine, it is soluble in most organic substances. At 745 mm of mercury and 25°C, the concentration of 1 mg of the vapor of Aroclor 1242 per liter of air is equivalent to 96.9 ppm by volume.

Aroclor 1254, which corresponds to pentachlorobiphenyl, is a light, straw-colored, viscous liquid. The positions of the chlorine atoms have not been established. The molecular weight of pentachlorobiphenyl is 326.445, of which 54.3% is chlorine. Benignus has reported that Aroclor 1254 contains 55.0 ± 0.5% of chlorine. Bulletin No. O-P-115 describes Aroclor 1254 as having a specific gravity at 25°/25°C of 1.538 to 1.548; a distillation range of 365° to 390°C, a refractive index (D-line at 20°C) of 1.639 to 1.641, and a Saybolt Universal viscosity at 100° F of 1,800 to 2,500 seconds. The vapor pressure at 150°C is about 1.3 mm, and at 200°C is about 9 mm. The material is soluble in most organic substances, but it is insoluble in water and glycerine. At 745 mm of mercury and 25°C the concentration of 1 mg of Aroclor 1254 per liter is equivalent to 76.5 ppm by volume.

Experimental Method

EXPOSURE TO THE VAPOR: In a preliminary experiment (No. 1) with the vapor of Aroclor 1242, a group of animals was confined for seven hours on each of five days per week in a rectangular plywood chamber (volume 600 liters), of which the inner metal lining was coated with a baked chemically resistant plastic, through which was passed a stream of air laden with Aroclor 1242 in a known concentration. The stream of air, conditioned with respect to temperature (75° ± 3°F inside the chamber), dust and humidity, entered the chamber through an "Anemostat," located at the center of its top, at the rate of 500 liters per minute, as measured by an inclined manometer attached

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Schematic diagram of e
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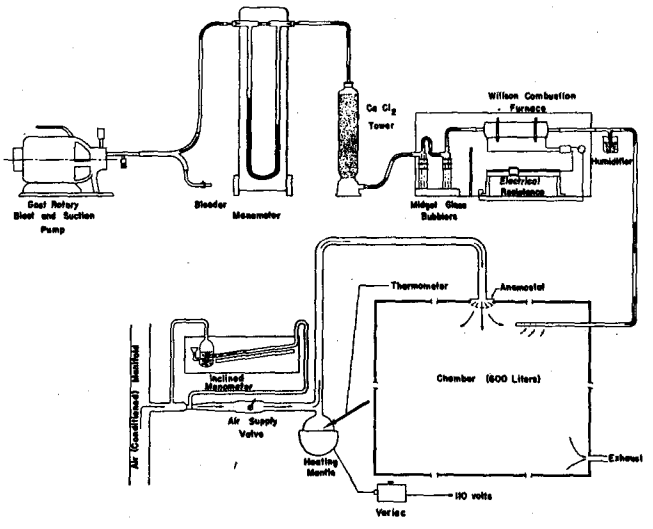


Fig. 1.
Schematic diagram of equipment for volatilizing Aroclor, chamber, and equipment for combustion and collection of samples.

to a venturimeter (Fig. 1). The air was withdrawn by suction from the chamber through an exit tube located on the rear wall near the floor, equidistant from the sides.

Aroclor 1242 was volatilized from a heated glass well maintained at 132° to 138°C. The air passed over the surface of the liquid before entering the chamber (Fig. 1).

In a second similar experiment performed on the same Aroclor (No. 2), the temperature of the liquid was kept at 100° to 105°C.

While the second experiment with Aroclor 1242 was in progress, an experiment involving the vapor of Aroclor 1254 (No. 1) was carried out in a second chamber similar to the first except for the absence of a plastic inner lining. The rate at which air flowed over liquid Aroclor 1254, which was maintained at 130° to 135°C, was 400 liters per minute.

In order to accustom the animals to the experimental procedure, they were kept in their respective chambers for seven hours on each of four consecutive days during the week prior to the introduction of the Aroclor vapor into the chamber. For purposes of control (No. 1), a third group of animals was confined, throughout a like period before and during the period of the exposure to the Aroclors, in another chamber supplied only with conditioned air.

A second set of experiments with each of the Aroclors at lower concentrations was conducted in the same chambers. In the third experiment with Aroclor 1242, which was heated to 55° to 60°C, the air passed over the liquid at the rate of 800 liters per minute. In the second experiment with Aroclor 1254, the liquid was maintained between 115° and 125°C while 700 liters of air per minute passed over its surface before entering the chamber. The animals exposed in each of these experiments, as well as a second group of controls, were confined in separate 600 liter chambers during a seven hour period on each of five days per week during the week preceding the initial exposure of the test animals to the vapor of the respective Aroclors.

In all experiments, the period of exposure or confinement (controls) was seven hours per day on five days per week for several weeks. In all instances, the original group consisted of one cat, six guinea pigs, ten mice, four rabbits, and ten rats. Among both the experimental and control groups, several animals died from extraneous causes during the course of these experiments and were replaced very soon thereafter. In the second experiment with Aroclor 1242, in the first experiment with Aroclor 1254, and in the comparable group of controls, representative animals were killed throughout the experiment.

METHOD FOR THE DETERMINATION OF THE AROCLORS IN AIR: These materials were determined quantitatively by virtue of the fact that, on thermal decomposition, they yield hydrochloric acid which with silver nitrate, forms a suspension, the density of which could be measured by means of the Beckman spectrophotometer at 500 mμ.

On each day, two samples of air from each chamber were collected by passing air at the rate of one liter per minute (for 15 minutes in the case of the higher concentrations and for 45 minutes in case of the lower concentrations) through a fused silica combus-

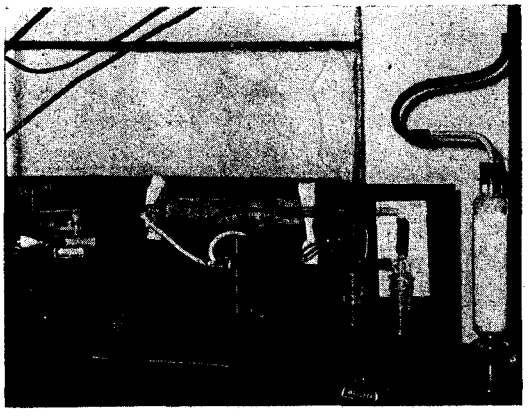


Fig. 2.
Humidifier, furnace, and sampling towers.

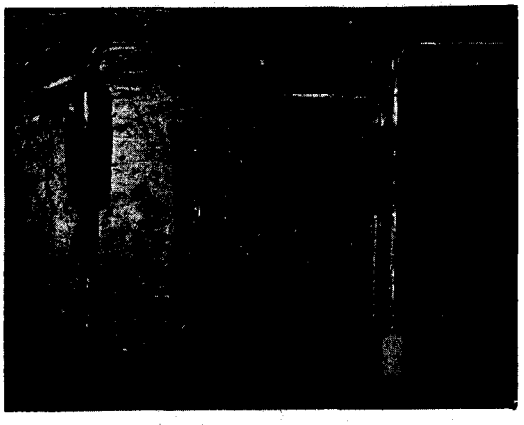


Fig. 3.
Sampling towers. (Midget Bubblers)

tion furnace, and then through two midget bubblers, in series, each containing 10 ml of 0.1 N sodium hydroxide. A quartz tube (13 mm outside diameter, 7 mm inside diameter and 16.25 inches in length) contained several strips of folded platinum foil. The middle nine inches of the tube were wrapped with a heating unit. The heating unit of the furnace (Fig. 2) consisted of 20 feet of B. and S., gauge 22, nichrome wire (1 ohm per foot), and was covered with asbestos cement. The sample of air was humidified by a cotton wick saturated with water placed 0.5 inch upstream from the quartz tube. With the furnace maintained at 850°C, the Aroclor was decomposed in the presence of H_2O to form HCl; this was absorbed in 0.1 N sodium hydroxide in midget bubblers (Fig. 3) equipped with fritted-glass bubblers (Mine Safety Appliance Company No. 43867).

The 0.1 N sodium hydroxide was prepared by dissolving 4.0 g of pellets (ACS specifications 0.01% Cl) in about 50 ml of double-distilled water. To this were added 10 g of arsenic trioxide (chloride-free) dissolved in water and filtered through Whatman No. 42 filter paper. The combined solutions were diluted to 1,000 milliliters.

The sample was transferred to a 25 ml graduated cylinder to which one drop of a solution of phenolphthalein was added (1 g of phenolphthalein dissolved in 100 ml of CP methanol). The solution was neutralized with 3N nitric acid (190 ml CP concentrated nitric acid diluted to 1,000 ml with double-distilled water) and diluted to 23 ml with double-distilled water. One ml of 3N nitric acid was added to obtain a pH of 1. After adding 1 ml of a solution of silver nitrate (3 g of $AgNO_3$ diluted to 1,000 ml with double-distilled water), the suspension was mixed by inversion. After standing 30 minutes, the transmission of wave-length 500 mμ was measured in a 50 cm cell by means of a Beckman spectrophotometer which was set against a corresponding cell containing a reagent blank.

The amount of Aroclor was estimated by means of a standardized curve prepared from known quantities of sodium chloride. A curve presenting the transmission values at 500 mμ of suspensions prepared from sodium chloride ranging from 5.0 to 120 micrograms per 25 ml of final suspension is shown in Fig. 4. On the basis of 42.0% of chlorine in Aroclor 1242 and 55.0% in Aroclor 1254, one microgram of sodium chloride is equivalent to 1.442 micrograms of Aroclor 1242 or to 1.1028 micrograms of Aroclor 1254.

Experimental Results

MORTALITY—AROCLOR 1242: No signs of intoxication were observed in any of the members of a group of 31 animals (Experiment No. 1), all of which survived throughout a period of 24 days, on 17 of which they were subjected to the inhalation of air bearing 8.6 micrograms of Aroclor 1242 per liter (0.83 ppm) for seven hours (Table I).

One cat, four guinea pigs, six mice, two rabbits, and eight rats survived without

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signs of intoxication throughout their exposure (Experiment No. 2) for seven hours on each of 82 days over a period of 120 days to air bearing the vapor of Aroclor 1242 in the concentration of 6.83 micrograms per liter (0.66 ppm). Certain other survivors (two guinea pigs, three mice, one rabbit, and two rats) were subjected to fewer periods of exposure (cf. Table I). The deaths from extraneous causes among the exposed animals were fewer than those which occurred among the corresponding group of controls (No. 1, Table I). One cat, three mice, three guinea pigs, three rabbits, and eight rats survived following confinement for seven hours on 84 days over a period of 122 days, in a chamber in which the air, conditioned with respect to dust, humidity and temperature, contained no vapor of either Aroclor. Ten more survivors (three guinea pigs, four mice, one rabbit, and two rats) were subjected to fewer periods of confinement (cf. Table I).

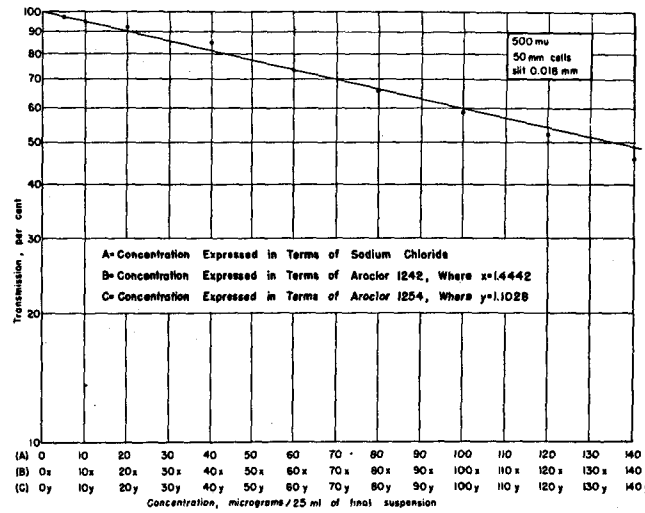


Fig. 4.
Standard curve for the determination of Aroclor 1242 and Aroclor 1254.

In another experiment (No. 3, Table I-A) in which animals were exposed to air bearing Aroclor 1242 in the concentration of 1.9 micrograms per liter (0.18 ppm) for seven hours per day on 150 days over a period of 214 days, the incidence of mortality among

TABLE I.
SUMMARY OF DATA ON MORTALITY AMONG ANIMALS EXPOSED TO THE VAPOR OF AROCLOR 1242 OR AROCLOR 1254 IN AIR
(Higher concentrations)

Material	Concentration γ/l	Concentration ppm	Duration of Exposure (hours)	Number of Animals that Survived: Cats	Guinea Pigs	Mice	Rabbits	Rats	Expt. No.
Aroclor 1242	8.60	0.83	17 x 7	1	6	10	4	10	1
Aroclor 1242	6.83	0.66	82 x 7	1	6[1,1]	9[1,2,2]	3[1]	10[1,3]	2
Aroclor 1254	5.40	0.41	83 x 7	1	6[1,1,1]	10[1,4]	4[1,3]	10[1]	1
Control	0	0	84 x 7	1	6[1,1,3]	7[1,5]	4[6]	10[1,2]	1

[1]One of the animals was exposed on only 65 to 77 days
[2]One of the animals was exposed on only 41 to 58 days
[3]One of the animals was exposed on only 20 to 33 days
[4]Five of the mice were exposed on only 74 days
[5]Three of the mice were exposed on only 14 to 19 days
[6]One of the rabbits was exposed on only 19 days

TABLE I-A.
SUMMARY OF DATA ON MORTALITY AMONG ANIMALS EXPOSED TO THE VAPOR OF AROCLOR 1242 OR AROCLOR 1254 IN AIR
(Lower concentrations)

Material	Concentration γ/l	Concentration ppm	Duration of Exposure (hours)	Number of Animals that Survived: Cats	Guinea Pigs	Mice	Rabbits	Rats	Expt. No.
Aroclor 1242	1.90	0.18	150 x 7	1	6[1]	8[2,3]	3[1,4,4]	10[5]	3
Aroclor 1254	1.50	0.11	150 x 7	1	7[2,3,5]	10[2,2,5,6]	4	11[3]	2
Control	0	0	150 x 7	1	6[2]	10[1,2,4,5,5,6]	5[1,5,5]	10[5]	2

[1]One of the animals was exposed on only 26 to 37 days
[2]One of the animals was exposed on only 41 to 55 days
[3]One of the animals was exposed on only 130 to 139 days
[4]One of the animals was exposed on only 5 to 13 days
[5]One of the animals was exposed on only 107 to 120 days
[6]One mouse was exposed on only 66 days

the various species, with the exception of the rabbits (which died during an epidemic of pneumonia), was no greater than that encountered among a similarly constituted control group (Experiment No. 2, Table I-A).

One cat, five guinea pigs, six mice and nine rats survived throughout the entire period of their subjection to the vapor of Aroclor 1242. Seven additional survivors (one guinea pig, two mice, three rabbits, and one rat) were exposed intermittently to the vapor of Aroclor 1242 over a shorter period of time (cf. Table I-A). Among the group of controls (Experiment No. 2, Table I-A), one cat, five guinea pigs, four mice, two rabbits, and nine rats survived throughout the entire period of confinement, for seven hours on each of 150 days over 213 days in a chamber supplied with conditioned air. Eleven other control animals (one guinea pig, six mice, three rabbits, and one rat) survived during a shorter total period of intermittent confinement (Table I-A). No signs of intoxication were observed among experimental or control animals.

MORTALITY—AROCLOR 1254: One cat, three guinea pigs, four mice, two rabbits, and nine rats survived throughout their exposure, for seven hours on each of 83 days over a period of 121 days, to air containing Aroclor 1254 in the concentration of 5.40 micrograms per liter (0.41 ppm). Certain other animals (three guinea pigs, six mice, two rabbits, and one rat) were killed for examination after 33 to 74 periods of exposure (Table I). The incidence of mortality from extraneous causes among the exposed and control animals (Experiment No. 1), with the exception of the rabbits, was comparable (Table I).

One cat, four guinea pigs, six mice, four rabbits, and 10 rats survived (Experiment 2, Table I-A) following their exposure for seven hours on each of 150 days over a period of 213 days to air containing Aroclor 1254 in the concentration of 1.5 micrograms per liter, (0.11 ppm). Eight other animals (three guinea pigs, four mice, and one rat) survived through 30 to 139 periods of exposure. The incidence of fatalities among the exposed group was slightly less than that encountered among the controls (Experiment 2, Table I-A).

TABLE II.
THE AVERAGE CHANGES IN WEIGHT OF EXPERIMENTAL AND CONTROL ANIMALS
(Higher concentrations)

Species of Animal	Number of Animals	Average Initial Weight (kg)	Average Change in Weight Expressed as Percentage of Initial Weight
Aroclor 1242 - 8.60 γ/l - Experiment No. 1			
Cat	1	2.863	+ 8.1
Guinea Pig	6	0.649	− 2.0
Mouse	10	0.024	+ 9.1
Rabbit	4	3.901	+ 7.7
Rat	10	0.328	+ 2.1
Aroclor 1242 - 6.83 γ/l - Experiment No. 2			
Cat	1	2.271	+22.2
Guinea Pig	6	0.404	+56.4
Mouse	9	0.021	+21.2
Rabbit	3	2.587	+50.5
Rat	10	0.212	+17.6
Aroclor 1254 - 5.40 γ/l - Experiment No. 1			
Cat	1	2.320	+22.1
Guinea Pig	6	0.409	+40.7
Mouse	10	0.021	+28.9
Rabbit	4	2.722	+39.7
Rat	10	0.227	+ 6.9
Conditioned Air - Controls - Experiment No. 1			
Cat	1	2.388	+ 6.6
Guinea Pig	6	0.418	+56.6
Mouse	7	0.022	+17.4
Rabbit	4	2.764	+44.5
Rat	10	0.211	+16.4

TABLE II-A.
THE AVERAGE CHANGES IN WEIGHT OF THE SURVIVORS AMONG THE ORIGINAL GROUPS
(Lower Concentrations)

Species of Animal	Number of Animals	Average Initial Weight (kg)	Average Change in Weight Expressed as Percentage of Initial Weight	P
Aroclor 1242 - 1.9 γ/l - Experiment No. 3				
Cat	1	1.730	+115.0	—
Guinea Pig	5	0.514	+ 43.1	>0.05
Mouse	6	0.0238	+ 21.5	>0.05
Rat	9	0.214	+ 39.9	>0.05
Aroclor 1254 - 1.5 γ/l - Experiment No. 2				
Cat	1	2.858	+ 15.2	—
Guinea Pig	4	0.487	+ 32.5	>0.05
Mouse	6	0.0243	+ 17.0	>0.05
Rabbit	4	2.958	+ 44.4	>0.05
Rat	10	0.222	+ 28.7	>0.05
Conditioned Air - Controls - Experiment No. 2				
Cat	1	3.329	− 7.8	—
Guinea Pig	5	0.500	+ 54.7	—
Mouse	6	0.0257	+ 13.2	—
Rabbit	4[1]	2.622	+ 52.2	—
Rat	9	0.218	+ 33.7	—

[1]Includes two early replacements.

No general or specific
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animals during or after

GROWTH: The pertine
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SUMMARY OF THE DATA
THE BODY WEIGHT OF
Aroclor 1242
Aroclor 1254
Controls - 0

Compound	Organ
Aroclor 1242	Liver
Aroclor 1242	Liver
Aroclor 1242	Liver
Aroclor 1254	Liver
Aroclor 1254	Liver
Aroclor 1254	Liver
Aroclor 1242	Kidneys
Aroclor 1242	Kidneys
Aroclor 1242	Kidneys
Aroclor 1254	Kidneys
Aroclor 1254	Kidneys
Aroclor 1254	Kidneys
Control	Liver
Control	Liver
Control	Liver
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Control	Kidneys
Control	Kidneys

I.
WEIGHT OF EXPERI-
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erage Weight kg)	Average Change in Weight Expressed as Percentage of Initial Weight
Experiment No. 1	
.863	+ 8.1
.649	— 2.0
.024	+ 9.1
.901	+ 7.7
.328	+ 2.1
Experiment No. 2	
.271	+22.2
.404	+56.4
.021	+21.2
.587	+50.5
.212	+17.6
xperiment No. 1	
.320	+22.1
.409	+40.7
.021	+28.9
.722	+39.7
.227	+ 6.9
- Experiment No. 1	
.388	+ 6.6
.418	+56.6
.022	+17.4
.764	+44.5
.211	+16.4

-A.
WEIGHT OF THE SUR-
RIGINAL GROUPS
trations)

ge ight	Average Change in Weight Expressed as Percentage of Initial Weight	P
periment No. 3		
0	+115.0	—
4	+ 43.1	>0.05
38	+ 21.5	>0.05
4	+ 39.9	>0.05
xperiment No. 2		
3	+ 15.2	—
7	+ 32.5	>0.05
13	+ 17.0	>0.05
3	+ 44.4	>0.05
2	+ 28.7	>0.05
- Experiment No. 2		
9	— 7.8	—
0	+ 54.7	—
57	+ 13.2	—
2	+ 52.2	—
3	+ 33.7	—

No general or specific signs of intoxication were noted among the experimental animals during or after their exposure.

GROWTH: The pertinent data relating to the changes in weight of the animals of the various groups are presented in Table II and II-A.

Although comparable controls were not weighed during the first experiment with Aroclor 1242 (17 x 7.0 hrs.—8.60 micrograms per liter) all of the animals, except the guinea pigs, appeared to gain normally in weight during the period of exposure. Despite a small net loss by the guinea pigs in this experiment, they were actually gaining weight at the termination of the period of exposure.

The animals exposed to the vapor of Aroclor 1242 in the concentration of 6.83 micrograms per liter (Experiment No. 2) or to Aroclor 1254 in the concentration of 5.40 micrograms per liter (Experiment No. 1), with the exception of the guinea pigs that were exposed to the vapor of Aroclor 1254, grew equally as well as the controls (Experiment No. 1, Table II).

The growth of the surviving experimental animals in the groups initially exposed to the lower concentrations of the vapor of Aroclor 1242 (Experiment No. 3, 1.9 micrograms per liter) and Aroclor 1254 (Experiment No. 2, 1.5 micrograms per liter) was unaffected. No significant differences in the average change in weight of the experimental and the control groups were found by the use of the "t" test (Table II-A).

WEIGHT OF LIVER AND KIDNEYS: The weights of the livers and kidneys and the relationships of their weights to the body weights (expressed as grams per 100 grams of body weight) of the animals that survived following exposure to the vapor of Aroclor 1242 in the concentration of 6.83 micrograms per liter, are shown in Table III, which also gives the corresponding data on the controls. Comparison by the "F" test of the variances of the ratios of the livers or kidneys to the body weights of rats, guinea pigs and rabbits exposed to the vapor of Aroclor 1242 (6.83 micrograms/liter), with those of the controls, revealed no significant differences ($P>0.05$) except in the case of the livers of the rats. Application of the "t" test to the mean values (Table III) revealed no significant differences between the test and control groups of guinea pigs, rats, and rabbits.

Comparable values for rats, guinea pigs and rabbits exposed to Aroclor 1254 in the concentration of 5.40 micrograms per liter

TABLE III.

SUMMARY OF THE DATA ON THE RELATIONSHIP OF THE WEIGHT OF THE LIVER OR THE KIDNEYS TO THE BODY WEIGHT OF ANIMALS EXPOSED TO THE VAPOR OF AROCLOR 1242 OR AROCLOR 1254

Aroclor 1242 - 6.83 γ/l - 82 x 7 hrs.
Aroclor 1254 - 5.40 γ/l - 83 x 7 hrs.
Controls - 0 γ/l - 84 x 7 hrs.

Compound	Organ	Species of Animal	n	Average Organ Weight (g)	Average Body Weight (g)	Ratio of Weight of Organ x 100 to Body Weight	t	P
Aroclor 1242	Liver	Rat	9	11.2	240	4.64	1.2381	0.20-0.30
Aroclor 1242	Liver	Guinea Pig	6	29.6	640	4.68	0.4291	>0.50
Aroclor 1242	Liver	Rabbit	3	122.0	4,023	3.04	1.5085	0.10-0.20
Aroclor 1254	Liver	Rat	10	12.8	239	5.34	3.3992	<0.01
Aroclor 1254	Liver	Guinea Pig	6	25.9	581	4.51	0.0000	>0.50
Aroclor 1254	Liver	Rabbit	4	120.0	3,537	3.53	1.0122	>0.50
Aroclor 1242	Kidneys	Rat	9	1.85	240	0.773	0.5842	>0.50
Aroclor 1242	Kidneys	Guinea Pig	6	5.0	640	0.805	0.7257	0.40-0.50
Aroclor 1242	Kidneys	Rabbit	3	18.6	4,023	0.468	0.4177	>0.50
Aroclor 1254	Kidneys	Rat	10	2.1	239	0.770	0.4199	>0.50
Aroclor 1254	Kidneys	Guinea Pig	6	4.6	581	0.808	0.5411	>0.50
Aroclor 1254	Kidneys	Rabbit	4	15.8	3,537	0.464	0.3163	>0.50
Control	Liver	Rat	10	9.0	243	4.15	—	—
Control	Liver	Guinea Pig	6	30.3	266	4.51	—	—
Control	Liver	Rabbit	4	102.3	3,993	2.61	—	—
Control	Kidneys	Rat	10	2.0	243	0.807	—	—
Control	Kidneys	Guinea Pig	6	4.8	666	0.731	—	—
Control	Kidneys	Rabbit	4	19.5	3,993	0.504	—	—

are also given in Table III. Application of the "t" test to the differences in the mean values which characterized the experimental and control animals (Table III) shows that the weights of the livers of the exposed rats were significantly greater than those of the controls, the ratio of the liver to the body weight of the former being 5.34 g per 100 g of body weight, that of the latter being 4.15 g per 100 grams. In all other instances tested (livers and kidneys of both guinea pigs and rabbits and kidneys of rats) the differences were statistically insignificant.

The organs of the animals exposed to the lesser concentrations of the vapor of the Aroclors were not examined in this manner because of the borderline character of the results associated with the higher concentrations.

LIVER FUNCTION: Data were obtained as to the apparent prothrombin activity of the blood (measured by the method of Kato[2]) of certain animals that had been exposed (1) to the vapor of Aroclor 1242, in the concentration of 6.83 micrograms per liter; (2) to the vapor of Aroclor 1254 in the concentration of 5.40 micrograms per liter; and (3) to conditioned air alone. In Table IV the percentile relationships of the clotting power have been calculated arbitrarily by dividing 100 times the average clotting time of the blood of the control animals by the clotting time of the blood of the experimental animals on the same day. No diminution in the clotting power of the blood, as a measure of the impairment of the function of the liver, was induced by the exposure of the animals to the vapor of Aroclor 1242 in air in the concentration of 6.83 micrograms per liter, or to the vapor of Aroclor 1254 in the concentration of 5.40 micrograms per liter.

This functional test was not applied to animals subjected to the lower concentrations, because of the negative results obtained when the animals were subjected to the higher concentrations.

HEMATOLOGICAL RESULTS: Determina-

TABLE IV.

THE EFFECT OF EXPOSURE TO THE VAPOR OF AROCLOR 1242 OR AROCLOR 1254 IN AIR FOR SEVEN HOURS PER DAY ON FIVE DAYS PER WEEK OVER A PERIOD OF SEVERAL MONTHS UPON THE APPARENT PROTHROMBIN CONTENT OF THE BLOOD OF CATS AND RABBITS

Relation of "Prothrombin Time" of Control and Exposed Animals Expressed Arbitrarily in Terms of Percentage Change in Clotting Time of Blood 100 x Clotting Time of Blood of Control Animals		Time of Sampling in Relation to Period of Exposure	
Clotting Time of Blood of Exposed Animals		Days Before First Period	Serial Number of Period After Which Blood Was Drawn
Aroclor 1242 - 6.83 γ/l - Experiment No. 2			
Cat A-445	Rabbits (Average)		
100.0	89.6	3	
90.3	93.8	2	
113.6	105.1		10
101.5	99.0		30
97.4	98.0		45
116.2	103.7		59
	101.5		82
	100.0		[1]
Aroclor 1254 - 5.40 γ/l - Experiment No. 1			
Cat A-444	Rabbits (Average)		
100.0	97.1	3	
100.0	96.9	2	
	81.8		9
98.5	90.0		10
	99.6		15
113.6	102.0		30
	112.1		32
101.5	97.0		45
92.5	95.4		59
90.0	95.2		83
	100.0		[2]

[1]Determination made 15 days after 82nd period of exposure.
[2]Determination made 14 days after 83rd period of exposure.

THE AVERAGE NUMBERS O
OF HEMOGLOBIN IN T

Compound	Concentratio (γ/l)
Aroclor 1242	6.83
Aroclor 1254	5.40
Controls	0

[1]Value significantly less than
[2]Value significantly greater th

tions of the numbers
leucocytes and of the h
the peripheral blood of
rabbits subjected to inh
of Aroclor 1242 in the
micrograms per liter,
V, which also includes c
control animals. Applic
to differences in the r
experimental and cont
borderline evidence o
ences in the number
the concentration of th
blood of the guinea pi
were small and of opp
bers of leucocytes in t
animals were low, while
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individual variations,
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Somewhat comparable
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PATHOLOGICAL FINDI
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15 days after the final

In the first experime
(8.60 micrograms per
mals were examined p
gross examination of
reveal any significant
sues of only represe
cat, four guinea pigs,
and six rats) were se
microscopically. No
found in the viscera c

In the second expe
1242 (6.83 microgram

grams per liter; (2) 1254 in the concen- ams per liter; and alone. In Table IV ıips of the clotting ated arbitrarily by verage clotting time trol animals by the ood of the experi- ame day. No dimin- er of the blood, as a ıent of the function l by the exposure of or of Aroclor 1242 tion of 6.83 micro- ıe vapor of Aroclor ion of 5.40 micro-

was not applied to ıe lower concentra- ıegative results ob- s were subjected to ns.

ULTS: Determina-

l IN AIR FOR SEVEN NTHS UPON THE AP- RABBITS

in Relation to Period of kposure	Serial Number of Period After Which Blood Was Drawn
	10
	30
	45
	59
	82
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	10
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	30
	32
	45
	59
	83
	2

TABLE V.

THE AVERAGE NUMBERS OF ERYTHROCYTES AND LEUCOCYTES AND THE AVERAGE CONCENTRATION OF HEMOGLOBIN IN THE PERIPHERAL BLOOD OF EXPERIMENTAL AND CONTROL ANIMALS

Compound	Concentration (γ/l)	Experiment Number	Species of Animal	Erythrocytes: (Thousands) per mm³	Leucocytes: per mm³	Hemoglobin: g/100 ml
Aroclor 1242	6.83	2	Guinea Pig	5,701	10,112[1]	14.4[2]
			Rabbit	6,088	9,755	12.1
Aroclor 1254	5.40	1	Guinea Pig	5,886	12,927	14.5[2]
			Rabbit	6,486[2]	10,811	13.2
Controls	0	1	Guinea Pig	5,729	12,124	13.9
			Rabbit	5,909	11,590	12.2

[1]Value significantly less than that yielded by controls.
[2]Value significantly greater than that yielded by controls.

tions of the numbers of erythrocytes and leucocytes and of the hemoglobin content in the peripheral blood of the guinea pigs and rabbits subjected to inhalation of the vapor of Aroclor 1242 in the concentration of 6.83 micrograms per liter, are given in Table V, which also includes comparable results on control animals. Application of the "t" test to differences in the mean values for the experimental and control animals yielded borderline evidence of significant differences in the number of leucocytes and in the concentration of the hemoglobin in the blood of the guinea pigs. These differences were small and of opposite sign (the numbers of leucocytes in the blood of the test animals were low, while the hemoglobin content was high), as well as being subject to individual variations, and they cannot be regarded as of physiological significance. Somewhat comparable results were obtained when guinea pigs and rabbits were subjected to Aroclor 1254 in the concentration of 5.40 micrograms per liter. No physiological significance is attached to the slightly elevated hemoglobin content of the guinea pigs.

PATHOLOGICAL FINDINGS: In all of the experiments, animals were killed from one to 15 days after the final period of exposure.

In the first experiment with Aroclor 1242 (8.60 micrograms per liter), all of the animals were examined postmortem, and since gross examination of the viscera did not reveal any significant alterations, the tissues of only representative animals (one cat, four guinea pigs, six mice, four rabbits and six rats) were sectioned and examined microscopically. No abnormalities were found in the viscera of these animals.

In the second experiment with Aroclor 1242 (6.83 micrograms per liter), and in the first experiment with Aroclor 1254 (5.40 micrograms per liter), which were carried out simultaneously, the deaths that occurred among the test and control animals were the apparent result of an appreciable incidence of pneumonia. The lesions of certain of the animals were those of frank pneumonia; in others such lesions were not fully developed. Degenerative changes in the viscera were usually found, in varying degrees of severity, in association with the pneumonia, but in certain animals, test and control alike, the degenerative changes were more evident than the pneumonia. The similarity of the lesions in test and control animals, and the lack of characteristic evidence of chemical pneumonitis, led to the reasonable, but not altogether certain, conclusion that all of these fatalities resulted from intercurrent disease among the animals, and not from the effects of their exposure to the Aroclors. For practical purposes, this conclusion was subjected to the critique of further experiments involving more prolonged exposure of animals to somewhat lower concentrations. Except in the case of the rats exposed to Aroclor 1254, the survivors subjected to the higher concentration of either Aroclor had normal viscera.

All of the animals exposed to the vapor of Aroclor 1242 in the concentration of 1.9 micrograms per liter were examined postmortem, and the viscera of most of them were examined microscopically. The few deaths among the exposed group were attributed to incidental infectious pulmonary disease. All exposed survivors, except two rabbits that had hepatic lesions of coccidiosis, had normal viscera. The control animals (Experiment No. 2) that died were found to have had pneumonia. Of those that sur-

vived, one rat, two guinea pigs, and one mouse had focal or diffuse cytoplasmic vacuolation of the hepatic cells. The remaining control animals had normal viscera.

All of the animals exposed to the vapor of Aroclor 1254 in the concentration of 1.5 micrograms per liter were examined postmortem, and the viscera of most of them were examined microscopically. A guinea pig that died exhibited chronic pyelonephritis, pulmonary hyperemia and edema, and degenerative lesions in the brain and liver. The visceral lesions were related, no doubt, to the renal infection. The deaths of four mice were attributable to acute bronchitis and pneumonia. The viscera of the cat that survived were normal. Of the seven guinea pigs that were living when the experiment was terminated, three had normal viscera and four had slight alterations of hepatic cells characterized by cytoplasmic vacuolation. Ten mice survived, and of these six had normal viscera and four had slight degenerative changes in the liver. Four rabbits killed one to 15 days after the last period of exposure had diffuse hepatic degeneration. The character of the lesions varied from cloudy to hyaline or hydropic degeneration and included varying degrees of fatty metamorphosis. The other viscera of these animals were normal. All of the rats were examined and found to have slightly to moderately severe degenerative lesions of the liver. The lesions of greatest severity were found in the rat that was killed and examined on the first day after the last period of exposure. Two rats had chronic pyelonephritis, and the remainder had slight degeneration of the renal tubules.

Discussion: In terms of mortality, growth (except that of guinea pigs) and non-occurrence of pathological changes, the vapor of Aroclor 1242 in the concentration of 8.6 micrograms per liter (approaching saturation) appeared to be non-injurious to experimental animals subjected thereto for seven hours on each of 17 days over a period of 24 days.

Experimental animals subjected to but a slightly lower concentration of Aroclor 1242 (6.83 micrograms per liter) for seven hours per day on each of 82 days over the period of 120 days suffered no injury on the basis of any of the following criteria: mortality, growth, pathology, organ enlargement, liver function or hematological changes.

More prolonged exposure of animals to a lower concentration of Aroclor 1242, (1.9 micrograms per liter) over the period of seven months was likewise without harm in terms of growth, mortality and the absence of pathological changes.

In view of this evidence it is suggested that the tentative allowable concentration of the vapor of Aroclor 1242 should be at least two micrograms per liter (2 mg per cu meter), which is twice that recommended by the American Conference of Governmental Industrial Hygienists[3] for a chlorinated diphenyl of unstated chlorine content.

The exposure of animals to the vapor of Aroclor 1254 in the concentration of either 5.40 or 1.5 micrograms per liter failed to induce harmful effects in the form of retardation of growth (except in the case of guinea pigs exposed to the higher concentration), or of mortality, but histopathologic evidence of apparently reversible hepatic cellular injury was found in the animals. These findings cannot certainly be attributed to the effects of Aroclor 1254 because of the appreciable incidence of pneumonia among both experimental and control animals. When these nonspecific toxic changes in the viscera of the animals were associated with pneumonia, they were readily explained thereby, but they were also found in animals that had been exposed to the vapor of Aroclor 1254 and were free of pneumonia. That these may have represented toxic effects of exposure to Aroclor 1254 finds support in the fact that the livers of the exposed rats (5.40 micrograms per liter) were significantly heavier in relation to their body weight, than were those of control rats. It would appear that this material, which is reported to contain 55% of chlorine, is somewhat more toxic than is Aroclor 1242, which contains only 42% of chlorine. Therefore it is suggested that the threshold concentration of 1 mg per cu meter of air recommended tentatively for safe industrial practice by the American Conference of Governmental Industrial Hygienists[3] is reasonable.

It should be noted that it was necessary to heat these Aroclors in order to increase the rate of volatilization sufficiently to attain the concentrations maintained in these

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Summary

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experiments. To the extent that their industrial usage is carried out at ordinary temperatures, the hazard of their inhalation may well be slight or entirely absent.

Summary

PROLONGED intermittent exposure of animals to the vapor of Aroclor 1242 (1.90 to 8.63 micrograms per liter) demonstrated no injury. Prolonged exposure to comparable concentrations of Aroclor 1254 resulted in reversible degenerative changes in certain viscera.

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