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Acute Effects of Aroclor 1254 on the Feline Cardiovascular System

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Aroclor 1254 was administered intravenously at 30-minute intervals to anesthetized cats at a dosage of 100 mg/kg body weight. Arterial and venous blood samples were taken at 10 minute intervals for determination of oxygen tension (pO_2), carbon dioxide tension (pCO_2), and pH. Electrocardiograms, blood pressure, and respiration were recorded as well. The pO_2 of the blood was reduced rapidly and markedly with concurrent changes in pCO_2 and pH characterizing a respiratory acidosis. Respiratory rate increased to a sizable degree with development of cardiac arrhythmias. All animals died within 60 minutes following initial dosing. Severely hemorrhagic lungs in conjunction with edema were observed in all cats at necropsy.

The Aroclors are members of a group of compounds called polychlorinated biphenyls (PCBs). The Aroclors, which have many industrial uses, are utilized as components in heat exchange units of fishmeal processing plants. In 1971, a leaking heat exchange unit resulted in the contamination of poultry fishmeal by Aroclor 1242. This incident and others focused attention on the potential toxicity of the PCBs, since they persist as environmental contaminants.

The various Aroclors are reported to be one-quarter to one-fifth as toxic as DDT (Peakall and Lincer, 1970). Some of the major toxic effects of PCBs in fowl (Flick *et al.*, 1965; Harris, 1971; McCune *et al.*, 1962; Vos and Koeman, 1970) and rats (Food and Drug Administration, 1971; Grant *et al.*, 1971) have been described and include the development of edema, lowered hemoglobin levels, enlarged kidneys, and liver damage. Vos *et al.* (1970) have suggested that a toxic factor or impurity may be present in PCBs and may cause the toxic effects.

In preliminary studies in our laboratory, we observed that a high degree of hypoxia and markedly darkened arterial blood occurred in dogs administered intravenously Aroclor 1254 in dimethyl sulfoxide (DMSO) carrier at dose levels of 100–250 mg/kg. This observation and the lack of information on the toxic effects of PCBs in the cat emphasized the need to initiate this study. Consequently, the primary purpose of this study was to evaluate the action of Aroclor 1254 on selected parameters of the feline cardiovascular system.

MATERIALS AND METHODS

Aroclor 1254 (FDA sample 370 71-698) was warmed in a beaker of hot water to reduce viscosity. A 25-ml glass-stoppered graduate was tared on a top-loading balance, and 5.0 g (3.25 ml) of Aroclor was pipetted into the graduate and diluted

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to a volume of 10 ml with 99.9% DMSO. A clear solution was produced with agitation, and there was no evidence of separation of the two phases throughout the study. All utensils containing Aroclor 1254 were rinsed with hexane and ethyl alcohol and the rinses were placed in a plastic jug for proper disposal.

Each of seven mongrel cats (three males and four females), weighing between 2.6 and 4.1 kg, was anesthetized with sodium pentobarbital (25–30 mg/kg) via the cephalic vein. The right and left femoral veins and the left carotid artery were catheterized, following a procedure of blunt dissection, with intramedic polyethylene tubing (0.034 in. i.d.; 0.060 in. o.d.). The catheterized vessels were kept patent by flushing them with heparinized saline solution before and after administration of the compound and blood sampling. Anesthesia was maintained by administering sodium pentobarbital into the right femoral vein as required. The Aroclor-DMSO solution was administered into the left femoral vein at a dosage of 100 mg Aroclor/kg at 30-minute intervals to six of the seven cats; the fluid volume averaged 0.6 ml. The remaining cat received three doses of 0.6 ml of DMSO alone at 30-minute intervals followed by two doses of Aroclor-DMSO, also at 30-minute intervals. The catheter used for administration of Aroclor 1254 was rinsed with hexane and ethyl alcohol and was used in all cats for Aroclor administration only.

Blood samples were taken with 1-ml glass syringes coated with Vaseline to reduce gas loss and purged with sodium heparinate (1000 units/ml) to prevent coagulation. Approximately 0.5 ml of blood was taken at each sampling time. Arterial and venous samples were taken from the carotid artery and right femoral vein, respectively, just prior to the first dose and at 10 and 20 minutes after each dose. All samples were analyzed for pH, oxygen tension (pO_2), and CO_2 tension (pCO_2) by using the blood microsystem and digital acid base analyzer.[2]

Arterial pressure was monitored through a physiological pressure transducer and recorded along with respiration and an electrocardiogram by using an eight-channel recording system.[3] Respiration was recorded with a bellows type pneumograph, and a lead I or II electrocardiogram was obtained by using a standard five-wire patient cable. Recordings of the above physiological parameters were obtained at two intervals prior to the initial dose and just preceding and following each dose thereafter. Tracings were also taken at various intervals during the dosing period when a change was observed in the electrocardiographic tracing. Record tracings were taken at a chart speed of 25 mm/second.

RESULTS

The most noticeable and immediate effects of Aroclor 1254 were an increased respiratory rate, a reduction in the pO_2 of the blood (Table 1), and the production of cardiac arrhythmia. Respiratory rates increased from a predose rate of 15 to between 40 and 60 respirations/minute over an approximate 1-hour dosing period. The effect was immediate in that a two- to three-fold increase in respiratory rate usually occurred within about 2 minutes after the initial administration of Aroclor 1254. The pO_2 was reduced by 50% in both arterial and venous blood (Table 1);

[2] Radiometer-Copenhagen, The London Company, Cleveland, Ohio.
[3] Hewlett-Packard, Sanborn Division, Waltham, Massachusetts.

TABLE 1

EFFECTS OF INTRAVENOUS ADMINISTRATION OF AROCLOR 1254 ON BLOOD ACID-BASE COMPONENTS IN THE CAT[a]

Time	Arterial blood			Venous blood		
(min)	pH	pO_2	pCO_2	pH	pO_2	pCO_2
0	7.40 ± 0.03(6)	106.3 ± 3.3(6)	34.0 ± 2.8(6)	7.33 ± 0.02(7)	39.0 ± 2.7(7)	41.8 ± 2.2(7)
10	7.28 ± 0.01(6)	70.3 ± 5.1(7)	45.6 ± 3.2(7)	7.26 ± 0.01(6)	31.3 ± 2.9(5)	51.6 ± 3.0(6)
20	7.29 ± 0.03(6)	60.1 ± 4.7(6)	44.5 ± 3.1(7)	7.23 ± 0.02(5)	26.5 ± 1.7(5)	55.2 ± 2.9(7)
40	7.31 ± 0.03(5)	52.4 ± 5.5(6)	36.2 ± 2.8(6)	7.20 ± 0.01(5)	23.0 ± 0.9(6)	52.1 ± 3.1(6)
50	7.31 ± 0.01(3)	42.3 ± 4.8(4)	35.1 ± 5.3(4)	7.13 ± 0.03(3)	18.5 ± 4.1(4)	54.8 ± 6.1(4)
70	7.26 (1)	50.0 (1)	41.3 (1)	7.21 (1)	23.8 (1)	54.1 (1)

[a] Aroclor 1254 was administered at doses of 100 mg/kg at 0, 30, and 60 minutes. Values are given as means ± SE. Numbers in parentheses are the number of animals in each group.

60% of that reduction occurred in the first 10 minutes following the initial administration. Acid-base changes were reflected by an increased pCO_2 with a concurrent reduction in pH; this effect was more noticeable in venous blood than in arterial blood.

The most predominant feature of the electrocardiograms taken after Aroclor 1254 administration was the development of premature ventricular contractions (Fig. 1, A and B). These arrhythmias occurred generally as multiple unifocal contractions with or without coupling. Occasionally, ventricular extrasystoles occurred singly with compensatory pause followed by a normal sinus rhythm. Multifocal premature ventricular contractions were evident to a lesser degree. Ventricular tachycardia usually preceded expiration in association with rapidly declining blood pressure and loss of respiration. T wave flattening was observed in all cats immediately after the initial dosing with Aroclor 1254. S–T segment deviations were observed at various times throughout the dosing period.

Blood pressure remained relatively constant throughout the study with the average pressure for all cats over the 1-hour dosing period ranging between 91 and

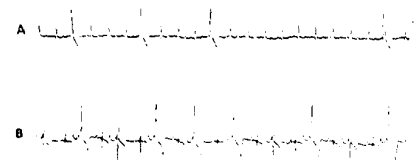

FIG. 1. Cardiac arrhythmias in cats administered Aroclor 1254. (A) Lead I electrocardiogram 5 minutes following administration of 350 mg Aroclor 1254. Beats 3, 7, 11, and 21 are unifocal ventricular or premature contractions. Attn. ×5, 25 mm/sec. (B) Lead I electrocardiogram 2.5 minutes following administration of 300 mg Aroclor 1254, demonstrating multifocal ventricular or premature contractions. Beats 3, 7, 9, 11, 15, and 19 are aberrant complexes. Beats 1, 5, 13, and 17 are also abnormal beats arising from a different focus. Attn. ×2, 25 mm/sec.

105 mm Hg. Body temperature was difficult to maintain within the normal range of this study in all cats and, therefore, this parameter could not be accurately evaluated; however, there did not appear to be any increased loss of body heat throughout the experimental period that could be attributed to administration of Aroclor 1254. Loss of body heat was ostensibly associated with general anesthesia and appeared to be a slow continuous process from the beginning of preparation for the experiment to expiration of the animal. Application of heat lights and drapes did assist in stabilizing the body temperature.

Postmortem examination of all cats revealed grossly hemorrhagic and mottled lungs with severe congestion of the dorsal lobes. Incision of the trachea, bronchi and lung parenchyma revealed the presence of pulmonary edema. The epicardial and endocardial surfaces of the heart were all grossly normal, as were the liver and kidneys.

The control cat given DMSO alone developed an increase in respiratory rate from 10 to 25 respirations per minute during the dosing regimen. Blood pressure was essentially unchanged. The pO_2 of arterial and venous blood was not decreased following administration of DMSO alone at 30-minute intervals (Table 2); in fact, it increased over control levels by 7 and 10% in arterial and venous blood, respectively, over the dosing period. In general, the pCO_2 and pH levels were conversely affected compared with values for the test animals, as shown by the decreased pCO_2 and increased pH.

The electrocardiogram from the cat receiving DMSO alone prior to Aroclor 1254 showed a short series of synchronous ventricular premature contractions after the first and second doses of DMSO. Flattening of the T wave was observed in both cases prior to initiation of the arrhythmias.

The administration of Aroclor 1254 after the DMSO injections resulted in a pO_2 reduction of 35–40% in arterial and venous blood; pCO_2 was increased and pH was decreased, demonstrating a response similar to that of the test animals.

TABLE 2

THE EFFECT OF INTRAVENOUS ADMINISTRATION OF DIMETHYL SULFOXIDE (DMSO) ALONE AND AROCLOR 1254-DMSO MIXTURE ON BLOOD ACID-BASE COMPONENTS IN THE CAT*

Time	Arterial blood			Venous blood		
(min)	pH	pO_2	pCO_2	pH	pO_2	pCO_2
0	7.45	90.0	33.5	7.39	29.1	41.0
10	7.44	84.5	30.9	7.39	36.5	37.8
20	7.44	91.5	29.9	7.42	41.1	37.7
40	7.45	90.0	29.5	7.41	40.0	38.5
50	7.47	97.0	27.2	7.41	35.0	38.8
70	7.53	102.5	21.8	7.42	33.7	35.0
80	7.54	111.5	20.9	7.43	36.5	33.1
100	7.43	67.5	28.9	7.32	23.7	40.3
110	7.42	57.0	28.9	7.22	22.0	47.5
130	7.40	65.0	25.0	7.22	24.5	48.8

* DMSO alone (0.6 ml) was administered at 0, 30, and 60 minutes. Aroclor 1254 (100 mg/kg) in DMSO was administered at 90 and 120 minutes.

Changes in the electrocardiogram were also similar to those of the test animals following administration of Aroclor 1254; i.e., T wave flattening, reduced heart rate, and ventricular extrasystoles occurred.

DISCUSSION

Aroclor 1254 is a viscous and highly irritating material and, although it appears to be miscible in the blood when administered in DMSO, the possibility of its separation or precipitation must be considered. If separation does take place, physical blockage of semipermeable membranes and/or tissue irritation may occur. The development of pulmonary edema would also produce a physical blockage to an interchange of oxygen and carbon dioxide at the alveolar level.

The marked and immediate reduction in oxygen tension (hypoxia) and the classical respiratory acidosis syndrome (low pH and elevated CO_2), as well as the apparently compensating and marked increase in respiration rate, would seem to indicate a physical impairment of gaseous exchange. The increased respiratory rate appeared to have no effect in improving pO_2 levels nor did it affect to any great degree the acid-base balance (Table 1).

The marked hemorrhagic condition of the lungs of all cats observed at postmortem examinations would indicate that the primary blockage or impairment may occur at this site. To examine the possibility of interference with the hemoglobin mechanism by Aroclor 1254, a sample of arterial blood from one of the test animals was aerated in a flask containing glass beads. After the blood had been shaken vigorously, it changed from a dark brownish color to bright red. Subsequent analysis of this sample revealed a marked increase in pO_2 levels. This demonstrated that the hemoglobin mechanism was functional *in vitro* and that oxygen uptake by the blood was not impaired.

Electrocardiographic patterns were remarkably similar in all cats. A very definite ventricular arrhythmia predominated, and was always preceded by flattening of the T wave and in some cases S–T segment deviation. T wave changes are known to occur under conditions of hypoxia (Lamb, 1965). The ability to produce cardiac arrhythmia with DMSO alone, even for short periods, implies that the more severe and lasting arrhythmias which developed following administration of the Aroclor-DMSO mixture were not totally due to Aroclor 1254 alone.

That the arrhythmias which did develop were prompted by an inability of the ventricle to repolarize must be considered since T wave changes usually preceded development of the arrhythmias.

This study suggests that a blockage or interference of the pulmonary alveolar capillary interface had occurred in the cats and resulted in a general hypoxemia. A gradual physiological deterioration, including cardiac impairment, eventually occurred, leading to death of the animal. All of these effects would appear to be directly related to those produced by Aroclor 1254 and not to the vehicle or solvent (i.e., DMSO) for Aroclor 1254. The effects of DMSO in the control animal of this study are similar to those previously reported in the dog (Peterson and Robertson, 1967). For example, intravenous administration of graded doses of DMSO from 5 to 10,000 mg/kg produced few alterations in cardiopulmonary dynamics and in arterial pH, pO_2, and pCO_2, only at the high dose levels of DMSO were physiological alterations detected.

It should be emphasized that the effects demonstrated in this study resulted from an Aroclor dosage of a sizable magnitude (100 ppm) chosen to produce an acutely toxic effect. Such levels do not normally occur in the environment.

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