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SUSCEPTIBILITY TO VENTRICULAR FIBRILLATION DURING CHLOROFORM AND CYCLOPROPANE ANAESTHESIA

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The experimental production of ventricular fibrillation during chloroform anaesthesia has been investigated often on several species of animals. There are, however, few studies in which both chloroform and cyclopropane have been used and compared in the same experimental series. In this study the susceptibility of various species of animals to the production of ventricular fibrillation by adrenaline under chloroform and cyclopropane anaesthesia was investigated. The effect of depth of anaesthesia under cyclopropane was also studied in cats and dogs and a few experiments were done on the influence of morphine and of Dibenamine (N: N-dibenzyl-β-chloroethylamine) on the response to adrenaline in guinea-pigs and dogs.

METHOD

Chloroform anaesthesia was induced and maintained by bubbling air through chloroform into a cylinder covering the head of the animal. By changing the rate of flow of the air bubbled through the chloroform, the concentration of the vapour could be controlled easily. Cyclopropane was administered from a spirometer; soda lime removed carbon dioxide from the system.

Small doses of adrenaline were injected during light and deep anaesthesia, the stage of anaesthesia being judged by the presence or absence of the corneal reflex, by the rate and depth of respiration, and by the amount of relaxation. Light anaesthesia comprised the lower part of Stage II and first plane of Stage III, and deep anaesthesia the fourth plane of Stage III and the upper part of Stage IV. Changes in the heart rate and rhythm were observed by means of a stethoscope or an electrocardiograph which consisted of a vacuum tube amplifier operating an ink-writing oscillograph. In the smaller species, if respirations ceased and the heart sounds became inaudible, an autopsy was performed at once and the state of the heart and lungs was noted. A diagnosis of ventricular fibrillation was made by the observation of rapid, tremulous contractions of minute areas of the ventricular myocardium.

RESULTS

In guinea-pigs adrenaline (0.1 mg. per kg. intramuscularly) caused ventricular fibrillation during light chloroform but not during light cyclopropane anaesthesia (Table I). Smith (1949) found that adrenaline did not lead to ventricular fibrillation in guinea-pigs under deep cyclopropane. With both anaesthetics increased depth of anaesthesia caused bradycardia, missed beats, and heart block, while decreased

depth of anaesthesia restored the cardiac rate and rhythm to normal. Death from overdosage was due to respiratory failure, since the breathing ceased while the heart was still beating vigorously. The dose of adrenaline employed was not considered to be toxic to the unanaesthetized guinea-pig, because doses up to 1.0 mg. per kg. were not lethal. However, adrenaline in doses of 2.0 mg. per kg. caused death in three of six guinea-pigs, death being due in two animals to ventricular fibrillation and in one to acute pulmonary oedema.

Adrenaline did not cause ventricular fibrillation in rats or rabbits under light or deep cyclopropane or chloroform anaesthesia (Table I).

TABLE I

OCCURRENCE OF ADRENALINE-INDUCED VENTRICULAR FIBRILLATION IN VARIOUS SPECIES DURING CHLOROFORM AND CYCLOPROPANE ANAESTHESIA

Species	Adrenaline mg. per kg	Chloroform		Cyclopropane	
		Number	V.F.	Number	V.F.
Rats	0.2 i.m.	12	0	10	0
Guinea-pigs	0.1 i.m.	12	4	14	0
Rabbits	0.02 i.v.	10	0	5	0
Cats	0.04–0.08 i.v.	12	3	12	0
Dogs (light)	0.01–0.02 i.v.	10	5	13	0
,, (deep)	0.01–0.02 i.v.			8	5

In three of twelve cats during light chloroform anaesthesia, ventricular fibrillation was induced by the intravenous injection of adrenaline (0.04 to 0.08 mg. per kg.). A transient tachycardia developed in all the other cats after the adrenaline. Spontaneous ventricular extrasystoles occurred frequently during cyclopropane anaesthesia. Of thirteen cats anaesthetized with cyclopropane, one died of ventricular fibrillation during the induction period. Adrenaline (0.04–0.08 mg. per kg.) injected intravenously into the remaining cats during light and deep cyclopropane resulted in a tachycardia which never progressed to fatal ventricular fibrillation.

Of ten dogs injected intravenously with 0.01–0.02 mg. adrenaline per kg. during light chloroform anaesthesia, five died of ventricular fibrillation (Fig. 1). A short run of ventricular tachycardia preceded the fibrillation. Of the five animals that survived, four developed a multiple focus ventricular tachycardia (Fig. 1) and one developed an auricular tachycardia after adrenaline; these rapid cardiac rates lasted from 26 to 54 seconds. Intravenous injections of 0.01–0.02 mg. adrenaline per kg. into thirteen dogs during light cyclopropane anaesthesia resulted only in ventricular extrasystoles or a transient ventricular tachycardia. However, when eight of these dogs were anaesthetized to the stage of slow shallow respirations and were then injected with the same dose of adrenaline, five developed ventricular fibrillation and died (Fig. 1).

Effect of morphine.—In guinea-pigs, the intraperitoneal injection of morphine sulphate (10 mg. per kg.) 15 min. before induction with chloroform did not prevent the development of ventricular fibrillation. Of ten animals so treated and given 0.1 mg. adrenaline per kg. intramuscularly five died of ventricular fibrillation.

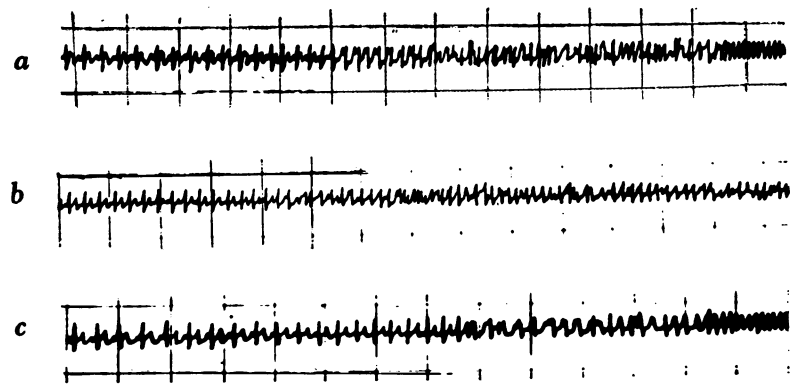

FIG. 1.—Electrocardiograms (lead IV) of dogs injected intravenously with adrenaline (0.02 mg. per kg.). Adrenaline induced in (*a*) ventricular fibrillation during light chloroform, in (*b*) multiple focus ventricular tachycardia during light cyclopropane, and in (*c*) ventricular fibrillation during deep cyclopropane. Time intervals 1 sec.

Effect of dibenamine.—Eight dogs were injected intravenously with dibenamine (12–30 mg. per kg.) and lightly anaesthetized with chloroform. When adrenaline (0.01 mg. per kg.) was injected two died of ventricular fibrillation while the other animals developed a transient tachycardia.

DISCUSSION

It is believed that ventricular fibrillation is likely to develop when impulses pass into the myocardium containing some fibres in a refractory state. Such fibres may be excited to contract a little later when an impulse reaches them by a more devious pathway than normal. If conditions are suitable a circus movement in the ventricle may become established. When the myocardium contains localized blocks to the transmission of the impulses, and the frequency of the impulses is high, the conditions are favourable to the production of fibrillation. Garb and Chenoweth (1948) found that the excitability of the papillary muscle of the ventricle is markedly decreased by chloroform in contrast to ether, which decreases it only slightly, so that during chloroform anaesthesia it is conceivable that localized blocks in the myocardium may occur. Robbins and Baxter (1937) believed that the cardiac irregularities that occur during deep cyclopropane anaesthesia were due to anoxaemia and not to cyclopropane, but Lee, Orth, Wangeman, and Meek (1943) found that arrhythmias developed even in the presence of a normal oxygen saturation of the blood. It appears, therefore, that a high concentration of cyclopropane also depresses the myocardium and results in localized blocks to the transmission of impulses.

Adrenaline is also an important aetiological factor in the precipitation of ventricular fibrillation, because it causes this arrhythmia not only during chloroform and cyclopropane anaesthesia but, in larger doses, in normal unanaesthetized guinea-pigs. Cardiac sympathectomy (Allen *et al.*, 1945) and adrenergic blocking agents, e.g., dihydroergotamine methanesulphonate (DHE 45) and dibenamine, are said to prevent ventricular tachycardia and fibrillation during cyclopropane anaesthesia

(Orth and Ritchie, 1947; Nickerson and Nomaguchi, 1949). In this work dibenamine was tried, and it was not entirely successful in preventing adrenaline-induced ventricular fibrillation in dogs under chloroform.

Summary

1. Under light chloroform anaesthesia the injection of adrenaline resulted in ventricular fibrillation in guinea-pigs, cats, and dogs. Under cyclopropane, adrenaline induced ventricular fibrillation only in dogs during deep anaesthesia.

2. In rabbits, adrenaline did not lead to ventricular fibrillation during chloroform or cyclopropane anaesthesia.

3. Dibenamine did not always protect dogs under chloroform from ventricular fibrillation.

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