

Experimental Study on the Mechanism of Cardiac Failure in the Diffuse Anoxia and Acute Local Ischemia of Myocardium in Dogs

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During the last decade there have been several reports on the mechanism of ventricular fibrillation in coronary diseases in man (2, 5). Beck from the results of his experiments on dogs has concluded that ECG changes and ventricular fibrillation are caused by an oxygen differential in the adjacent areas of myocardium (Trigger area) (2,3,4).

Coffman (6) has demonstrated occurrence of ventricular fibrillation in the uniform hypoxic heart in dogs. Warren and Saurbery(12) and some others (5,6,7,) have refuted the Beck's hypothesis on the ventricular fibrillation. Attempts were made in our laboratory to find out if the ECG changes and ventricular fibrillation were merely due to the oxygen differential.

Methods

A total of 117 acute experiments were performed on mongrel dogs by the three following methods:

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1- *General hypoxia*: 21 dogs weighing from 6 to 15 Kg were anesthetized with 35 mg/kg sodium pentobarbital. The trachea was connected to an automatic respirator (Palmer Ideal Pump Type AC) set at an average frequency of 35 strokes/min. and a tidal volume of 250 ml/kg B.W./min. The hypoxia was performed by connecting the respirator to a 100 liter-spirometer containing a mixture of 8% oxygen and 92% nitrogen. Blood pressure of the right carotid artery was recorded continuously by a mercury monometer. The ECG was recorded by the Visette Electrocardiograph (Sanborn, Model 300) on leads 1,2, and V_3 . The arterial oxygen saturation was measured in the left ear by the Oximeter (Water X-70) before and through the course of each experiment.

2- *Ligation of the coronary arteries*: 76 dogs weighing 5.5 to 17 kg were used for these experiments. Under the pentobarbital anesthesia and artificial respiration the chest was opened in the 4th intercostal space and the coronary arteries (anterior descending, posterior, and circumflex) were ligated separately in each series (8). Ligation on the anterior descending artery was done about 3 to 5 mm below the origin of septal branch (10). The carotid blood pressure and ECG were recorded as in the first method. The animals were sacrificed after two hours if fibrillation or cardiac arrest did not occur up to that time.

3- *Perfusion of the coronaries in the hypoxic hearts*: 40 dogs weighing 8 to 22 kg were used for this method. Each experiment was performed on two anesthetized equiponderant dogs connected to each other by the femoral-coronary anastomosis. Blood pressure of the donor's left femoral artery and the receiver's left carotid artery were recorded simultaneously. ECG was taken from the receiver dog. In the receiver dog under artificial respiration, the chest was opened, the anterior descending in one series and the circumflex in the other series were dissected out, and heavy ligatures were passed under the vessels. The blood was perfused from the right femoral

artery of the donor through a rubber tubing into the coronary artery of the receiver (9), and it was circulated back from the left femoral artery of the receiver to the right femoral vein of the donor. The rate of perfusion was regulated by adjusting the clamps applied on the rubber tubes and checking the systemic blood pressure of the donor and receiver. After the blood pressures were stabilized, time was allowed for 15 to 20 minutes before general hypoxia was induced in the receiver dog as the first method. Both donor and receiver were heparinized.

Results

The results are summarized in Table 1.

1- *General hypoxia*: The ECG changes, consisting of decrease in amplitude of R waves, increase in the amplitude of T waves (8 ± 3.1 mm), elevation (2.6 ± 1.2 mm) or depression (2.1 ± 0.9 mm) of ST segments, were observed in 80% of the cases starting 11-13 minutes after induction of the hypoxia. The arterial oxygen saturation decreased from a control level of 97% to 92-93% at the beginning of ECG changes. The average arterial oxygen saturation just before the occurrence of ventricular fibrillation and standstill was 88 ± 3 and 87.6 ± 3.3 respectively. The arterial blood pressure was first increased up to 9 minutes coinciding with an oxygen saturation of 91% and then gradually decreased as hypoxia was progressing. The cardiac arrest was always preceded by a short episode of a marked sinus bradycardia (Fig. 1 and 2).

2- *Coronary ligation*: The relative percentage of fibrillation and standstill varied according to the different coronaries (Table 1), but the total average incidence was 26.3% fibrillation and 23.6% standstill. The changes in T and ST segments were developed in 95% of the total cases after 8.6 minutes as average. In the joint ligation of anterior descending and circumflex, in two cases A-V block, and in two other cases the bundle branch block was developed.

METHODS		Total No. of Expt.	Fibrillation		Time in min		Standstill.		Time in min.	
			No.	%	Range	Mean	No.	%	Range	Mean
General Hypoxia		21	2	9.5	55-75	65	19	90.5	55-145	86
Ligation of Coronaries	Ant. Desc.	15	2	13.34	19-41	36				
	Post.	15	1	6.67	14	14	2	13.34	30-30	30
	Circ.	15	4	26.6	25-35	31				
	Circ. + Ant.	31	13	42	1.5-7	3.2	16	51.6	2.5-24	8
Perfusion + Hypoxia	Ant.	10	2	20	27-62	44	8	80	25-70	40
	Circ.	10	7	70	1-18	6	3	30	15-27	20

Table 1. The incidence of fibrillation and standstill in general hypoxia, ligation and perfusion of the coronaries.

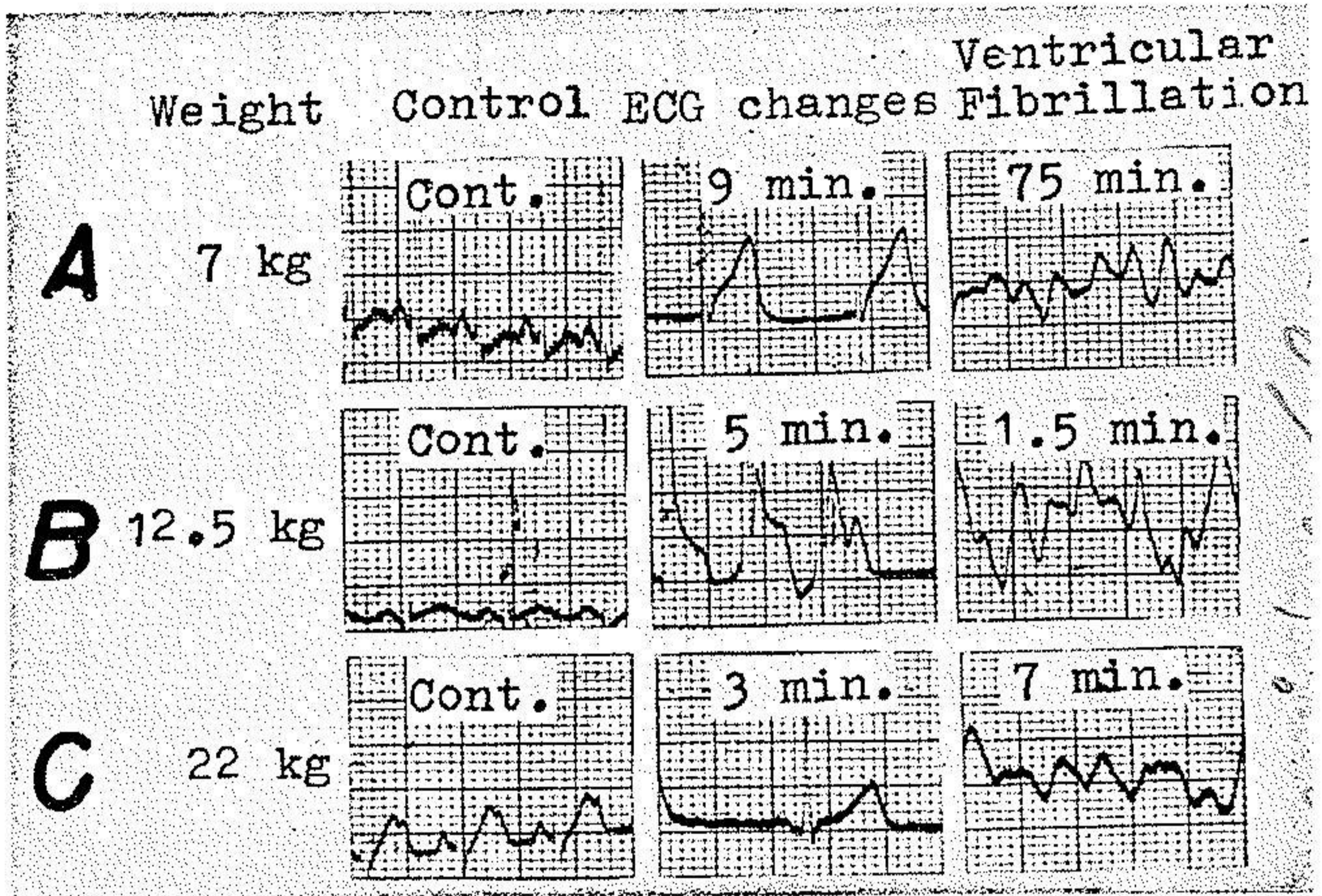


Fig. 1- The ECG sample of V₃ (A; general hypoxia, B; ligation of the anterior descending and circumflex, C; perfusion of the circumflex).

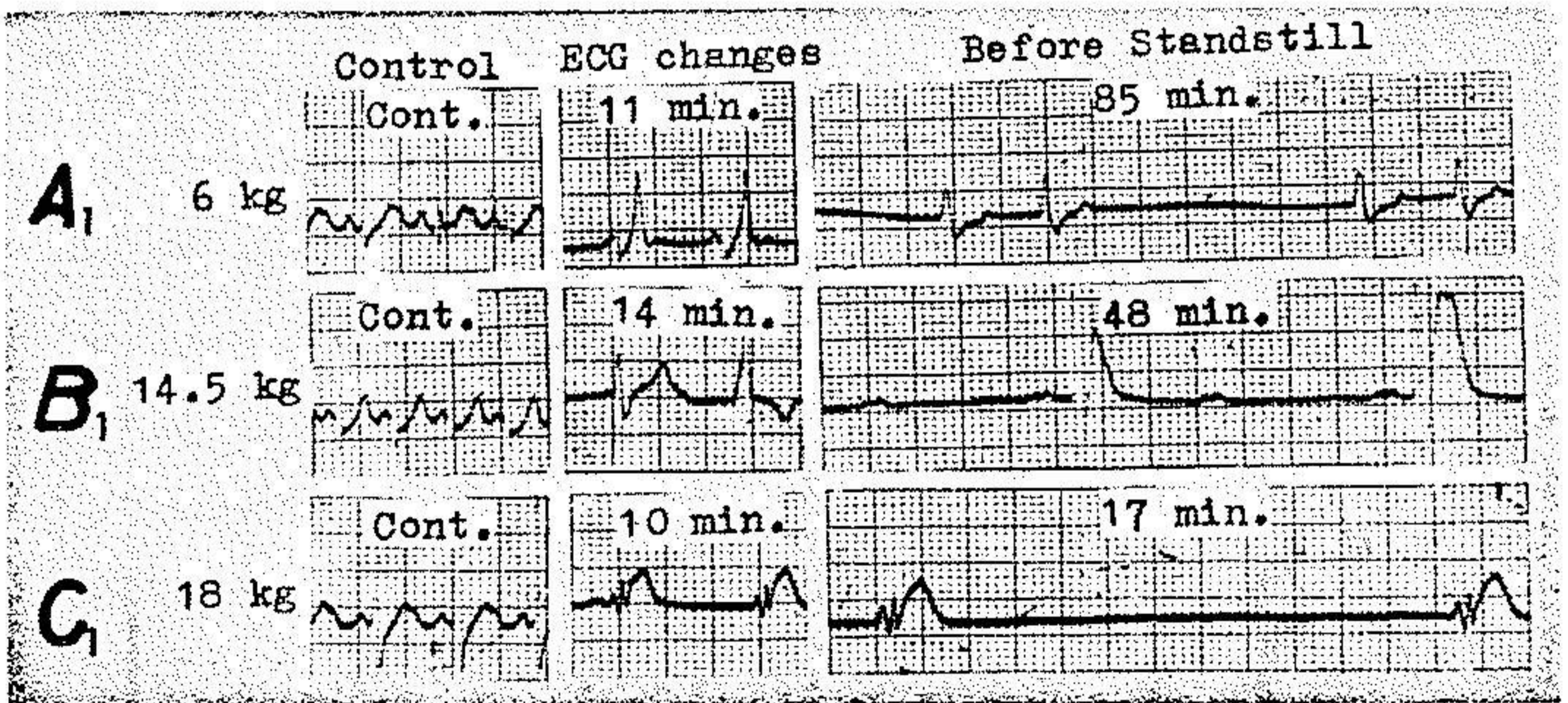


Fig. 2- The ECG sample of V₃ (A₁; general hypoxia, B₁; ligation of the anterior descending and circumflex, C₁; perfusion of the circumflex).

3- *Cross perfusion*: In this series of experiments the blood pressure of the receiver dogs increased and then decreased as the hypoxia was progressing until the occurrence of fibrillation or standstill, when it fell abruptly to zero level. The blood pressure of the donor remained unchanged in 12 cases but in seven cases (5 in anterior and 2 in circumflex) it gradually fell to 40% of the initial level at the moment of occurrence of fibrillation or standstill in the receivers. Six of these cases ended in standstill after an average time of 30 minutes and only one in fibrillation after 62 minutes.

Discussion

The occurrence of T and ST changes in 80% of the diffuse hypoxic hearts is a significant finding which is in sharp contrast with the theory of oxygen differential (4). The occurrence of about 10% fibrillation in the diffuse hypoxic heart and also an equivocal percentage of 30% standstill and 30% fibrillation in the local ischemic hearts (the total cases of ligation and perfusion) is also good evidence against the mechanism of oxygen differential. The difference between the average arterial oxygen saturation in the two groups of fibrillation and standstill was not statistically significant. The bigger ratio of standstill to fibrillation in joint ligation of the anterior coronary and circumflex ($\frac{51.6}{42}$) and particularly in perfusion of the anterior descending artery ($\frac{80}{20}$) compared to that of a separate ligation of each coronary ($\frac{13.3}{6.6}$) and perfusion of the circumflex ($\frac{30}{70}$) can be explained on the basis of difference in the total blood flow supplied to the corresponding areas of the myocardium. The larger area of ischemia, or the more severe diffuse hypoxia, has more chance for cardiac arrest and less incidence of fibrillation. Our results confirm essentially the findings reported by Coffman (6), Warren and Saurbery (12), Danese (5), and Wallon (11).

Summary

The acute diffuse hypoxia and local ischemia of heart were induced in dogs by general hypoxia, ligation of the coronary arteries and perfusion of the coronaries in the diffuse hypoxic hearts. The results of our experiments suggest that the quantitative diminution of oxygen and blood supply to the myocardium is, rather than oxygen differential, a determining factor for development of ventricular fibrillation or cardiac arrest.

Resumé

L'hypoxie diffuse aigüe et ischemie locale du myocarde a été induite chez les chiens, par hypoxie générale, ligature des artères coronaires et perfusion des Coronaires dans les cœurs hypoxiques. Les résultats de nos expériences suggèrent qu'une diminution quantitative d'oxygène et le flux sanguin dans le tissu myocardique, plutôt qu'une différence de taux d'oxygène est responsable pour développement de fibrillation ventriculaire et arrêt cardiaque.

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