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Effect of Quinidine on Ventricular Fibrillation in Hypothermic Dogs.* (24978)

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Ventricular fibrillation occurs regularly during profound hypothermia in dogs(1). Gollan(2) has prevented this arrhythmia by a combination of quinidine, slow rewarming period, prevention of left heart distention, and control of rate of coronary perfusion. In experiments reported below we tested the efficacy of quinidine alone as a means of preventing V. F. in hypothermic dogs.

Methods. Hypothermia was induced in healthy, mongrel dogs anesthetized with pentobarbital. Extracorporeal circulation was carried out with a pump-oxygenator-heat exchanger device as described elsewhere(3). A thermistor was placed in the esophagus and flow through the extracorporeal circuit set at 50 ml/min/kg until esophageal temperature fell to 20°C. Flow was then reduced to 25 ml/min/kg. E. K. G., E. E. G. and femoral blood pressure were recorded. The chest was opened only when electrical defibrillation was needed or when other direct procedures on the heart were carried out.

Methods. Eleven dogs (Group I) were cooled to temperatures of 6-10°C without receiving quinidine. Fifteen dogs (Group II) were similarly cooled but received 28-30 mg/kg quinidine: HCl 10-15 minutes before start of cooling period. The quinidine was given i.v. in doses of 100 mg every 5 minutes until QRS interval doubled or until PR interval increased to 40-60 mS.

Result. All 11 dogs in Group I developed ventricular fibrillation either during cooling, rewarming, or both periods. In all dogs, electrical defibrillation was successfully accomplished at temperatures of approximately 30°C. Dog 4, placed on a pacemaker, fibrillated at 16° on rewarming, even though heart continued to respond up to point of fibrillation. In 5 runs where cooling fibrillation did not occur, the heart spontaneously stopped. When it fibrillated on rewarming, there were usually 3 or 4 slow rhythmical beats before ventricular fibrillation began. Acetylcholine (3 mg/kg) Mecholyl (3.5 mg/kg) and TEA (3 mg/kg) were ineffective in preventing onset of ventricular fibrillation in single experiments. Maintenance of left auricular pressure below 15 mm Hg was similarly ineffective in one experiment.

In 15 dogs in Group II, there were only 2 instances (dogs 6 and 7) of fibrillation. One was due to inadequate initial dose of quinidine and second was probably due to too low quinidine blood levels on the fourth hypothermic episode. Complete cardiac standstill occurred at about 8.5°, though in one instance this was at 13°C. On rewarming, cardiac action returned at about 16° varying from 11° to 19°. Following rewarming, there were no EKG abnormalities to suggest residual quinidine toxicity; 11 dogs were allowed to survive.

Discussion. Large doses of quinidine have proven effective in preventing ventricular fibrillation during profound hypothermia of 10°C or lower, when this is accomplished by core cooling with pump-oxygenator-heat exchanger system. Quinidine, to achieve this effect, was administered intravenously until suppressive effect was noted in the EKG as shown by changes in QRS and PR intervals (4). This occurred well before any signifi-

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TABLE I. Prevention of Ventricular Fibrillation with Quinidine during Profound Hypothermia.

Dog	Period of hypothermia	Low temp., °C	Cardiac arrest, min.	I.V. quinidine, mg/kg	V.F.
9	1	9	13	30	0
10	1	6	22	35	0
11	1	6.5	20	28	0
13	1	5	26	32	0
6	1	1	19	20(I.M.)	Rewarm
	2			25	0
7	1	8.8	9	30	0
	2	9	8		0
	3	8.2	7		0
	4	9	9		Rewarm
8	1	8.2	19	30	0
	2	8.8	13		0
	3	9.5	11	10	0
	4	10	10		0
18	1	7	60	30	0
21	1	7	74	30	0
22	1	7	68	30	0
23	1	7	69	30	0
24	1	7	74	30	0
26	1	7	60	30	0
27	1	5.5	65	30	0
28	1	6	68	30	0

V.F.—Ventricular fibrillation.

cant hypotensive effect of drug.

The mode of action of quinidine in prevention of ventricular fibrillation in profound hypothermia is not known. It is possible that suppressive action of quinidine may prevent premature firing of a stimulus or premature response to stimuli when there are still critical temperature gradients in heart that prevent uniform myocardial response(5).

Complete circulatory standstill for as long as one hour is tolerated at temperatures below 10°C. This with demonstration of simple method of preventing ventricular fibrillation suggests many possibilities for surgical applications of this technic.

Summary. In a series of animals with esophageal temperatures reduced to 10°C or lower by core cooling, ventricular fibrillation has been regularly prevented with intravenous infusion of quinidine.

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Exogenous Timing of Rat Spontaneous Activity Periods.*† (24979)

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While numerous investigations have resulted in descriptions of periodic patterns of spontaneous locomotor activity in mammals in constant conditions, particularly those with periods approximately 24-hours in length, very little progress has been achieved in resolving the mechanism by which these mammalian periodisms are timed. Brown, Shriner and Ralph(1), studying a male white rat, both in conditions of constant darkness and constant low illumination, found 24-hour cycles under the former conditions and 25¼-hour cycles under the latter. Utilizing the rat's 25¼-hour overt rhythm of running to randomize the overt running relative to time of solar day (24-hours) and lunar day (24.8-hours), these investigators found, underlying the overt 25¼-rhythm, both solar-day and lunar-day rhythmic components. The more conspicuous was lunar-day one, with rat running about 3 times as much at lunar nadir as at lunar zenith. It was postulated that these natural-period cycles constituted reference

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