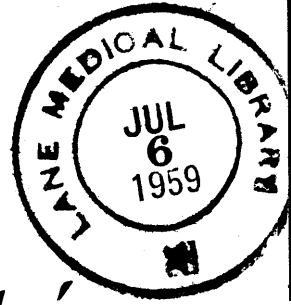


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# SELECTIVE HYPOTHERMIA OF THE HEART IN ANOXIC CARDIAC ARREST

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ANOXIC CARDIAC ARREST is taking its place among methods of elective cardioplegia. Despite Wesolowski's early observations that cardiac activity could be re-established after prolonged anoxia, resuscitation is uncertain after more than 20 minutes of continuous myocardial anoxia at normal temperature. Cross and his associates have extended the period of safe anoxia by perfusing the coronary arteries with cold blood after induction of potassium arrest. This work introduced the concept of selective cardiac hypothermia.

Gollan, Sealy, and their associates incorporated heat exchangers into their extracorporeal circulatory systems to accomplish general hypothermia in combination with the heart-lung machine. Selective hypothermia has appeal because of the rapidity with which the myocardial temperature can be restored to normal. Refinements in artificial heart-lung apparatus have rendered obsolete the low flows permitted with adjunctive general hypothermia. Moreover, indictment of potassium arrest is now substantiated well enough to justify a systematic search for methods to enhance the safety and duration of anoxic arrest. Again, selective hypothermia of the heart emerges as a logical route to prolonged, reversible myocardial anoxia.

This investigation was designed to study selective hypothermia of the heart induced by simple perfusion of the suspended pericardial sac with cold isotonic saline. Suture fixation of a small catheter at several points

along the rim of the pericardial cradle provided a satisfactory method for irrigating the heart. Saline at 0 to 5 degrees C. accomplished the heat transfer when administered at a rate of about 30 milliliters per minute through the multiholed catheter. The solution in no way obscured the operative field and in fact contributed to identification of structures by washing away whatever blood was present.

Periods of cardiac anoxia as long as 1 hour were well tolerated in dogs during selective hypothermia of the heart while the remainder of the body was perfused with blood at normal temperature.

## METHOD

Adult mongrel dogs of either sex were anesthetized with intravenous pentobarbital sodium and submitted to right thoracotomy through the fourth intercostal space. The caval cannulations were carried out after approximately 1.75 milligrams per kilogram of body weight of heparin were given into the right atrium. The pericardium was sutured to the muscular edges of the incision to exclude lung tissue from the operative field and to provide a reservoir for the cold saline solution. A No. 10 F. catheter was placed in the left atrium through a convenient pulmonary vein so that bronchial return was deflected into the oxygenator. Some bronchial drainage gains access to the pulmonary artery, but in the absence of a septal defect the pulmonary artery does not effectively decompress the left atrium. The ascending aorta was dissected to permit its occlusion independent of the pulmonary artery. The femoral artery was used to direct blood from the

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TABLE I.—PRELIMINARY GROUP (NO CARDIAC HYPOTHERMIA)

No.	Weight, kgm.	Flow rate, ml./min.	Duration of cardiac anoxia, mins.	Duration of machine support, mins.	Total bypass time, mins.	Ventricular fibrillation	Fate
	18.6	1200	8	22	35	None	Long term survivor
	14.1	1500	10	25	40	With release of aortic occlusion	Long term survivor
	13.7	1200	15	20	38	After 6.5 mins. aortic occlusion	Long term survivor
	18	1800	15	25	42	Induced	Long term survivor
	16	1500	15	25	45	Induced	Long term survivor
	16.3	1400	15	17	35	Induced	Long term survivor
	18.2	1400	15	55	72	Induced	Long term survivor
	19	1400	20	30	55	Induced	Long term survivor

TABLE 11.—THIRTY MINUTES OF CARDIAC ANOXIA WITH HYPOTHERMIA OF THE HEART

No.	Weight, kgm.	Flow rate, ml./min.	Duration of machine support, mins.	Total bypass time, mins.	Ventricular fibrillation	Fate	Temperature C. °		
							R.V.	L.V.	Body
	22	1400	30	62	Induced	Long term survivor	—	—	—
	19	1400	25	60	Induced	Long term survivor	—	—	—
	17.3	1400	20	55	Induced	Long term survivor	—	—	—
	13.7	1000	22	55	Induced	Long term survivor	—	—	—
5	13.6	1400	15	50	Induced	Long term survivor	24	28	34

oxygenator into the systemic arterial circulation. A rotating disc oxygenator was utilized in all experiments. The contralateral femoral artery was cannulated for continuous registration of pressure.

A 4 to 6 centimeter right ventriculotomy was performed in each animal so that recovery from the period of anoxia would be comparable to the clinical situation. Functional inefficiencies of right ventricle after ventriculotomy were noted by Stirling.

Since ventricular fibrillation was inevitable because of the cardiomy in an anoxic heart further stimulated by local cold, fibrillation was induced in some experiments immediately after occlusion of the aorta. A weak shock of 20 to 30 milliamperes in strength and 0.1 second in duration was delivered to the heart surface by means of bipolar electrodes. An S-4-D Grass stimulator generated the stimulus. Duration of the stimulus was intentionally long to project into the vulnerable period. No signal synchronization circuit was utilized. Defibrillation was routinely and uniformly effected by

a countershock of approximately 1.5 amperes and 0.01 second. No effort was made to defibrillate until coronary circulation was established for at least 5 minutes after disocclusion of the aorta. Simultaneously with removal of the aortic clamp both caval chokers were released to prevent heart dilatation on the right side. The left atrial catheter was not withdrawn until defibrillation was accomplished. In some animals in which the vigor of fibrillation did not increase rapidly with restitution of coronary flow, 0.1 milliliter of 1: 1,000 epinephrine was injected into the left ventricle before massage and electric shock restored regular rhythm to the heart. The need for epinephrine did not correlate with the duration of anoxia or the degree of myocardial hypothermia.

The ventriculotomy was made before cross-clamping the aorta and repaired a few minutes before its release. The heart assumed full responsibility for the circulation by increments while pump-oxygenator support was gradually diminished.

The experimental design was established

after a preliminary series of dogs was submitted to from 8 to 20 minutes of cardiac anoxia during bypass with the heart-lung machine, but selective cooling of the heart was not used. After this pilot group, 3 series of dogs were subjected to 30, 45, and 60 minutes respectively of cardiac anoxia; selective cardiac hypothermia was induced in all by irrigating the myocardial surface with normal saline at from 0 to 5 degrees C. Myocardial temperatures were recorded at intervals in some animals by means of a thermistor on the tip of a 22 gauge hypodermic needle. Body temperature was maintained by the heating element on the oxygenator. Three infrared bulbs under the oxygenator provided an efficient heat source.

Arterial pressure seldom dropped below 80 millimeters of mercury except for the few moments after release of aortic occlusion when the diminution in resistance was reflected immediately by a transient fall in blood pressure. Flow rates were held in the area of 60 to 100 milliliters per kilogram per minute. No change in arterial flow was made during the course of the perfusion except when the animal was weaned from his extracorporeal source of support. Blood from the cavae and left atrium was returned to a reservoir by gravity and pumped from the reservoir into the oxygenator.

The liter or 2 of cold saline was aspirated and discarded. The amount of blood also discarded was minimal even when occlusion was maintained for 1 hour. Bronchial flow reaching the right ventricle from the pulmonary artery constituted the only source of blood in the operating field. Most of the bronchial return was picked up by the left atrial catheter.

In the preliminary group, no left atrial catheter was used, and in 1 of the hour-long occlusive experiments the left atrial catheter was purposely omitted. This resulted in the only death in any group. The left side of the heart and pulmonary venous system were distended, and the additional mass detracted from the efficiency of the cooling.

No untoward effect could be attributed to

the use of a long-acting barbiturate in patient animals. Blood for priming the oxygenator was drawn by gravity from the carotid arteries of dogs anesthetized with pentothal sodium. Twenty milligrams of heparin per 500 milliliters of blood sufficed to prevent clotting. Siliconed glass containers, 2,000 milliliters each, were used to collect blood from donor animals. Each experiment required 3 liters of blood to prime the reservoir, oxygenator, and tubing and to provide a reserve of 300 to 500 milliliters.

## RESULTS

Table I shows results of the preliminary series. Hypothermia was not used in any of these experiments. Ventricular fibrillation was not induced in the first 3 dogs but developed regardless if the duration of cardiac anoxia was 10 minutes or longer. Because ventricular fibrillation was apparently inevitable and because defibrillation was no problem, deliberate use of the arrhythmia was instituted. The heart was arrested immediately without the period of contractions of diminishing amplitude which heralds anoxic arrest. The defibrillatory effort was delayed for 5 to 8 minutes after aortic disocclusion and consisted of massage and electric countershock with or without a minute dose of epinephrine. No other drugs or chemicals were used in any experiment.

The uniformity of flow rates reflects the constant use of Nos. 22 F. and 24 F. catheters in the superior and inferior venae cavae respectively. Duration of support generally exceeded the period of anoxia and approached 1 hour in dog 7. All dogs survived and were sacrificed for blood 1 to 2 weeks later.

It was clear from data in the early group that periods of anoxia longer than 20 minutes would require inordinately long support with the heart-lung apparatus. Selective cardiac hypothermia was adopted with a view to prolonging the safe period of cardiac anoxia without a concomitant increase in the duration of pump-oxygenator support. The least complicated method for inducing

TABLE III.—FORTY-FIVE MINUTES OF CARDIAC ANOXIA WITH HYPOTHERMIA OF THE HEART

No.	Weight, kgm.	Flow rate, ml. /min.	Duration of machine support, mins.	Total bypass time, mins.	Ventricular fibrillation	Fate	Temperature C. °		
							R.V.	L.V.	Body
1	13.6	1400	25	72	Induced	Long term survivor	22	25	36
2	19	1400	13	60	Induced	Long term survivor	—	—	—
3	15	1400	15	62	Induced	Long term survivor	25	28	35

TABLE IV.—ONE HOUR OF CARDIAC ANOXIA WITH HYPOTHERMIA OF THE HEART

No.	Weight, kgm.	Flow rate, ml. /min.	Duration of machine support, mins.	Total bypass time, mins.	Ventricular fibrillation	Fate	Temperature C. °		
							R. V.	L. V.	B o d y
1	19	1400	30	92	Induced	Long term survivor	22	29	36
2	23	1500	90	152	Induced	Died	28	31	36
3	26	1800	30	95	After 3 mins. aortic occlusion	Long term survivor	16	20	35
4	24	2000	20	85	After 5.5 mins. aortic occlusion	Long term survivor	20	28	36
5	14	1400	20	82	After 7 mins. aortic occlusion	Long term survivor	16	22	35

hypothermia of the heart seemed to be simple perfusion of the suspended pericardial sac. The following groups were submitted to varying limits of cardiac anoxia under protection of selective cooling of the heart.

Table II lists 5 dogs with cardiac anoxia of 30 minutes. Ventricular fibrillation was induced and abolished in each animal. All hearts were cooled by direct contact with saline at 0 to 5 degrees C. Pump-oxygenator support did not exceed the period of cardiac anoxia in any animal and in fact corresponded to the requirement for lesser limits of anoxia at normal heart temperature.

Again survival was routine, and since the endpoint was clearly not in the immediate area of 30 minutes of aortic occlusion, the period of anoxia was increased to 45 minutes.

Table III shows the results obtained in 3 animals with 45 minutes of cardiac anoxia. With the right ventricle uppermost in the right thoracotomy approach, myocardial temperature was predictably less diminished in the left ventricle. Fibrillation was induced in all dogs, and all survived. The period of support was no greater than in dogs with 30 minutes of cardiac anoxia. Dogs 2 and 3 required no epinephrine, but the first animal

was not successfully defibrillate until 15 minutes after restoration of coronary flow: 0.5 milliliter of 1: 1,000 epinephrine was used to enhance coronary arterial blood flow prior to electrical countershock.

The ease with which the last 2 dogs assumed the burden of the circulation suggested that myocardial anoxia could be extended to a full hour with expected survival.

Table IV shows the validity of this suggestion. All hearts were cooled by the local application of saline. The only dog failing to survive did not have the benefit of a left atrial catheter to prevent distention of the heart with bronchial return. Fibrillation was not induced in 3 dogs but developed shortly after occlusion of the aorta. No good evidence was found to indicate that the limits of cardiac anoxia had been reached under the conditions of this experiment. The last 2 dogs required only 20 minutes of support with the heart-lung machine, the same interval administered to dogs undergoing 15 minutes of anoxia at normal temperature.

#### DISCUSSION

Anoxic arrest was utilized initially by Lillehei who placed a choker around the

supravalvular aorta. The coronary circulation was intermittently suspended for the placement of a crucial stitch. Melrose adapted Sidney Ringer's original observations for elective cardiac arrest with potassium. Potassium arrest was widely used, but the uncertainty of resuscitation after more than 30 minutes of cardioplegia and the increased incidence of postoperative heart block directed attention again to simple anoxia of the heart with or without hypothermia.

Selective cooling of the heart is an attractive adjunct for anoxic arrest because of the need for abolishing coronary flow for a considerable interval of time in the surgical correction of many cardiac lesions. Surface cooling is effective and adds little to the inherent complexity of the bypass procedure. Pericardial irrigation with cold saline or other isotonic solution during anoxic arrest avoids the disadvantages of potassium arrest or coronary infusion with cold blood, yet it provides a dry, quiet heart for prolonged periods.

Of interest is the fact that the only death in any group was of an animal whose bronchial return was not removed during the perfusion by a left atrial catheter. The heart was distended but defibrillate uneventfully at the conclusion of the prescribed period of anoxia. Despite 1 ½ hours of extracorporeal heart-lung support, a satisfactory arterial pressure could not be maintained in the systemic circulation.

Consistent survival in the animals of this study attests to the efficiency of local hypothermia of the heart when prolonged periods of cardiac anoxia are desired. Experiments are now under way in which the duration of cardiac anoxia is necessarily protracted, and

results thus far confirm the findings of this study.

#### SUMMARY

Selective, local hypothermia of the heart permits at least 1 hour of cardiac anoxia in the dog during cardiopulmonary bypass with blood at normal body temperature. The usual duration of pump-oxygenator support is 20 minutes after release of aortic occlusion. Decompression of the left atrium is essential to prevent cardiac distention and to provide for maximal cooling of the heart.

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