

Zucker, M. B., *J. Lab. and Clin. Med.*, 1957, v49, 211.

9. Goldstein, R., and Alexander, B. presented be-

fore 1st Internat. Hemophilia Symposium, New York, Aug. 1956.

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Cardiac Retroperfusion with Induced Asystole for Open Surgery upon the Aortic Valve or Coronary Arteries.* (23053)

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The concomitant use of a pump-oxygenator (1,2) for circulatory support during total bypass of the heart together with retrograde perfusion via coronary sinus permits open surgery on the ascending aorta and aortic valves for periods of 15 to 30 minutes. This technic has been tested experimentally and successfully applied subsequently in man (3,4). Retrograde perfusion via coronary sinus of arterial blood supports myocardial activity and prevents coronary air embolism during interval that the ascending aorta remains open. As a rule almost no coronary venous drainage occurs from the right ventricle into the coronary sinus in the dog. Therefore, virtually no retroperfusion of this myocardial area takes place. Despite this fact the canine right ventricle appears to tolerate 15 to 20 minutes of by-pass assisted by retroperfusion, because cardiac workload is almost completely eliminated, and the left ventricular muscle remains oxygenated. In man the anatomical pattern of coronary veins usually permits more adequate retroperfusion of the right heart through the coronary sinus. Previously we reported on retroperfusion technic (4). There were 12 long-term survivals among 16 dogs submitted to this technic, for intervals of 15 to 20 minutes. Only one of 4 deaths was related to cardiac complication.

Four additional animals were submitted to 30 minutes of retroperfusion. Three of them died apparently from irreversible fibrillation appearing at termination of the retroperfusion and presumably induced by intolerable state of right ventricular hypoxia. Blanco *et al.* (5) reported survivals in dogs after retroperfusion of coronary veins up to $7\frac{1}{4}$ minutes.

This duration of retroperfusion, safe for dogs and probably for man, must certainly be extended to 30 minutes or more if we are to realize its full usefulness. Therefore, we have tested the potential advantages of combining retroperfusion of the coronary sinus with asystole induced with potassium citrate, hoping thereby to reduce further myocardial oxygen consumption. Also, the advantages of working in a completely still operative field would be realized. And finally, both experimentally and clinically it has been found dangerous to attempt to re-start a deliberately arrested heart by forward coronary perfusion unless vents into the left ventricle and left atrium have been provided to keep those chambers decompressed. In patients without septal defects it may not be technically feasible to establish these vents; and therefore, a method for restoring the beat (by means of retroperfusion) with the aorta still open becomes valuable. The results of these studies comprise the subject matter of this paper.

Method of study. Forty dogs had their heart and lungs by-passed utilizing a pump oxygenator (1,2). They were subdivided into 4 groups. *Group I* consists of 10 dogs sub-

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mitted to retrograde perfusion of coronary sinus for 30 minutes. *Group II* (10 dogs) had retroperfusion for 30 minutes in combination with asystole induced by potassium citrate. The 10 dogs in *Group III* experienced potassium citrate achieved asystole only, for 15 to 30 minutes. The final 10 dogs in *Group IV*, acute experiments, were studied for metabolic changes and coronary flow distributions during retroperfusion with and without potassium citrate provoked asystole. Two methods for *perfusion of coronary sinus* were tested. In one, arterial blood was tapped off the main arterial limb and carried through a Y connector. In the other, arterial blood from oxygenator reservoir was propelled by separate pump directly into the cardiac venous system. A bifurcating arterial limb (first method) was used for survival experiments. To prevent perfusion of coronary veins at too high pressures, an adjustable clamp was placed on catheter leading into coronary sinus. The tension distal (cardiac) to this clamp was then monitored through a strain gauge and appropriate recording apparatus. We sought to keep it at mean pressure of 30 to 40 mm Hg. Earlier experiments(4) suggested that these pressures were well tolerated by the coronary veins and that they provided for adequate retrograde flow. The coronary sinus was perfused directly from a separate pump in acute metabolic studies so that a more exact coronary flow could be established in each experiment. To cannulate the coronary sinus a #14 polyethylene catheter with a firm plastic adaptor, ridged on end, was placed into the coronary sinus and anchored there either by silk ligature placed around the sinus from outside the heart, or by a purse-string suture about the coronary sinus ostium working from within the right atrium. The latter seems to be the more suitable method and has been utilized for clinical cases. *Cardiac Asystole*: When retroperfusion was combined with potassium citrate asystole, this was induced after the technic of Melrose(6). A 2.5% solution of potassium citrate diluted in the animals' arterial blood was injected rapidly into the ascending aorta until the heart ceased to beat and the aorta cross clamped just above the coronary artery orifices to prevent any

TABLE I. Total Cardiopulmonary By-Pass Procedures with Retroperfusion of Coronary Sinus and K Citrate Asystole.

Procedure	Vent. fib., %	Card. mort., %	Comments
A Retroperfusion, 30 min.	40	40	All 4 fatalities had irreversible fibrillation at end of retroperfusion
B <i>Idem</i> with K citrate asystole, 10-30 min.	40	20	2 fatalities 2 hr postoperative
C K citrate asystole alone, 15-30 min.	80	90	1 dog had irreversible fibrillation; remaining deaths within 12 hr postoperative

perfusion via this route.

In recent experiments (not herein reported) it has been found technically feasible to arrest the heart retrogradely by slowly injecting 25% potassium citrate solution into the arterial blood in the retroperfusion catheter. When arrest occurs, this injection is stopped and the retroperfusion catheter is cross-clamped. The heart is restarted by re-initiating the retroperfusion.

Results. The results for 10 dogs retroperfused for 30 minutes are presented in Table I. Four animals fibrillated at end of retroperfusion, and it was not possible to defibrillate any.

The data in 10 experiments wherein asystole was achieved and in which there was standstill varying from 6 min. to 30 min. with concomitant retrograde perfusion of the coronary sinus of 30 min. duration in all are presented in Table I(B). We noted that when the hearts did resume their beat at the end of the experiments, that this was solely a left ventricular contraction. The poorly perfused right ventricles usually remained quiescent at first, and then gradually and progressively acquired a satisfactory beat. Two of these 10 dogs died from cardiac causes during the immediate experiment. In these animals the period of induced asystole was 15 min. and 25 min., respectively. Four additional dogs succumbed several days postoperative from non-cardiac complications.

TABLE II. Comparison of Distribution of Retroperfusate. Dog #1855 had retroperfusion alone and dog #1494 had retroperfusion in combination with K citrate asystole.

Mean pressure in cor. sinus, mm Hg	Dog No. and procedure	Flow in cc/min.		
		Cor. sinus input	L. cor. artery outflow	Right thebesian outflow
20	1855, retro. alone	16	5	8
	1494, retro. with K citrate	30	14	15
30	1855	32	9	20
	1494	33	16	16
40	1855	42	12	28
	1494	35	16	18
50	1855	64	18	42
	1494	44	17	24

These deaths are probably ascribable to use of clean but not sterile technic. The late incidence of severe infections was substantial. Of 10 dogs (with cardiopulmonary by-pass) submitted to potassium citrate induced asystole for 15 to 30 minutes (Group III, Table I(C)) only one survived for a long term. All of the deaths in this group occurred within 14 hours postoperative.

Table II lists distribution of retrograde flow at different coronary sinus pressures. A representative study of retroperfusion alone has been compared with a comparable study utilizing both retroperfusion and cardiac asystole. The retrograde flow from the left coronary ostia was approximately the same in both experiments. A high volume flow from the coronary sinus into right ventricle via thebesian veins was revealed in both animals.

Certain aspects of cardiac metabolism were studied in 5 dogs subjected to retroperfusion alone, and in a similar number of dogs submitted to combination of retroperfusion and potassium citrate induced asystole. Mean values of these data are presented in Table III. In all cases coronary sinus pressure was monitored at 40 mm Hg. Representative blood samples were drawn after 15 minutes of retroperfusion. Apparently retroperfused hearts utilized oxygen, glucose, and lactate in a manner similar to that of normally perfused hearts but in substantially lower amounts. The oxygen consumption of retroperfused left

ventricle was approximately one-third that of normally perfused left ventricle in a by-passed state. This is probably a reflection of the diminished amount of retrograde flow, which is approximately one-third the volume of normal forward coronary blood flow. It was of interest to note that only a slight reduction in consumption of oxygen and glucose occurred in the retroperfused hearts, asystolic from an injection of potassium citrate.

Discussion. The canine heart is not anatomically well adapted to retrograde perfusion through the coronary sinus because the right ventricle receives little flow under these circumstances. Nevertheless, these canine hearts are capable of tolerating this predicament for periods up to 20 minutes. However, when the canine heart is subjected to 30 minutes of retrograde flow it is likely to fibrillate on termination of the run with a great likelihood of death then ensuing.

Perhaps addition of potassium induced citrate asystole to prolonged period of retroperfusion may offer some improvement in this death rate by placing the cyanotic right heart at greater rest. This is supported by the fact that the cardiac mortality after 30 minutes of retroperfusion alone was 40%; whereas, after 30 minutes of retroperfusion plus potassium citrate arrest, it was 20%.

Recently in a few experiments we have injected the sinoauricular node with xylocaine, instituted retroperfusion of the coronary sinus for one hour, and have maintained an excel-

TABLE III. Average Metabolic Values for Dogs Submitted to Retroperfusion Alone and Retroperfusion in Combination with Potassium Citrate Asystole.

Calculated per 100 g left ventricular wt/min.	By-passed heart with normal coronary flow 10 animals*	By-passed heart with retroperfusion of coronary sinus and potassium citrate asystole	
		5 animals	5 animals
Flow	54.9 cc	19.0 cc	14.2 cc
Oxygen C†	7.18 "	2.62 "	2.03 "
Glucose C	3.7 mg	3.2 mg	2.4 mg
Lactate C	2.5 "	.66 "	.01 "

* Metabolic values in Column I were obtained as initial studies in the 2 groups.

† C = Consumption.

lent beat without fibrillation or other signs of cardiac arrhythmia.

To date the technic of total cardiopulmonary by-pass with retroperfusion of the coronary sinus has been applied to 8 patients(4). The first case was done over a year ago(3) and the patient is well at this time. The clinical lesions for which we have used retroperfusion were instances of aortic stenosis, and regurgitation, aortic-pulmonary window, ruptured sinus of Valsalva, and complete transposition of the great vessels. The longest clinical retroperfusion was 32 minutes, and in every patient a strong beat was maintained throughout the procedure with no instance of fibrillation during or after the retroperfusion. These clinical observations substantiate the anatomical fact that the human heart is more completely perfused than the dog's by a retrograde flow through the coronary sinus. On the basis of these experimental studies and the clinical observations mentioned above, the combination of retroperfusion and potassium asystole appears valuable for precise, direct vision reparative procedures upon the aortic valve or coronary arteries in a quiescent operative field.

Conclusions. 1. Only one of 10 dogs submitted to 15 to 30 minutes of potassium citrate produced asystole was a long-term sur-

vival (90% mortality). 2. Ten dogs were submitted to 30 minutes of retroperfusion of the coronary sinus, and 4 died from cardiac causes, a 40% mortality. 3. Ten additional dogs were subjected to combination of 30 minutes retroperfusion and potassium citrate provoked asystole. Two of the 10 died from cardiac complications, mortality 20%. 4. Certain aspects of cardiac metabolism in the retroperfused heart with and without potassium citrate induced asystole have been studied in 10 dogs. There appears to be an additionally reduced degree of metabolism under these latter circumstances.

1. Lillehei, C. W., DeWall, R. A., Read, R. C., Warden, H. E., and Varco, R. L., *Diseases of the Chest*, 1956, v29, 1.

2. DeWall, R. A., Warden, H. E., Read, R. C., Gott, V. L., Ziegler, N., Varco, R. L., and Lillehei, C. W., *Surgery Clinics N. Am.*, 1956, v36, 1.

3. Lillehei, C. W., DeWall, R. A., Gott, V. L., and Varco, R. L., *Diseases of the Chest*, 1956, v30, 123.

4. Gott, V. L., Gonzalez, J. L., Zudhi, M. N., Varco, R. L., and Lillehei, C. W., *Surg., Gynecol., and Obstet.*, 104: 319-328, March, 1957.

5. Blanco, G., Adams, A., and Ferrandez, A., *J. Thor. Surg.*, 1956, v32, 171.

6. Melrose, D. G., Dreyer, B., Bertoll, H. H., and Baker, J. B. E., *Lancet*, 1955, v269, 21.

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Failure to Transmit Human Nonbacterial Gastroenteritis to Cats.* (23054)

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Existence of acute infectious nonbacterial gastroenteritis of presumed virus etiology has been documented by epidemiologic observations(1-3) and by transmission of the disease to human volunteers(1,4,5) although no eti-

ologic agent has been established in tissue culture or laboratory animals. Studies in collaboration with Gordon and Dorrance(4) demonstrated, by feeding stool supernates to volunteers, that there are at least 2 different types of such gastroenteritis. Because Yamamoto *et al.*(6) had reported transmission of human diarrheal disease to cats by feeding 2 to 5 ml of filtered supernatant of aqueous stool, aliquots of the same inocula used in human experiments with Gordon and Dorrance(4) were given to cats. The present re-

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