eally into rats receiving calcium ethylene diamine tetra acetic acid subcutaneously did not produce the usual polycythemic response.

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Total Cardiac By-pass Utilizing Continuous Perfusion from Reservoir of Oxygenated Blood.* (21997)

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The goal of our cardiac research efforts has been the development of simple, safe, and effective technics for direct vision intracardiac surgical procedures. The demonstration that total cardiac by-pass with right ventricular cardiotomy and septal suture can be successfully performed even in seriously ill patients by utilizing controlled cross circulation(1-4) doubtless will stimulate further rapid developments in this field.

This experimental study has been carried out on dogs to evaluate a method of substituting arterial and venous reservoirs of blood for the donor in the cross circulation set-up. By such a plan, it would be possible to perform intracardiac operations in a dry heart without the need of a donor in the operating room. Such a scheme immediately poses problems of procurement and storage of blood to supply the arterial reservoir. In this present experimental study intended to develop a feasible technic for total cardiac by-pass utilizing the reservoir method of perfusion, the arterial blood was obtained prior to the intended perfusion from a donor used as an oxygenator entirely independent of the perfusion set-up. The use of arterialized venous blood to supply the arterial reservoir has been described elsewhere(5).

Method. Collection. Ordinary 1,000 cc plasma vac§ bottles were used as reservoirs. These containers were readied for use by instilling in each 100 cc 5% dextrose and water solution containing heparin (25 to 32 mg) and at the same time exhausting the vacuum completely. Arterial blood was collected into these bottles (while in the inverted position) by gravity using a commercially available plastic collection set§ connected to a plastic cannula‖

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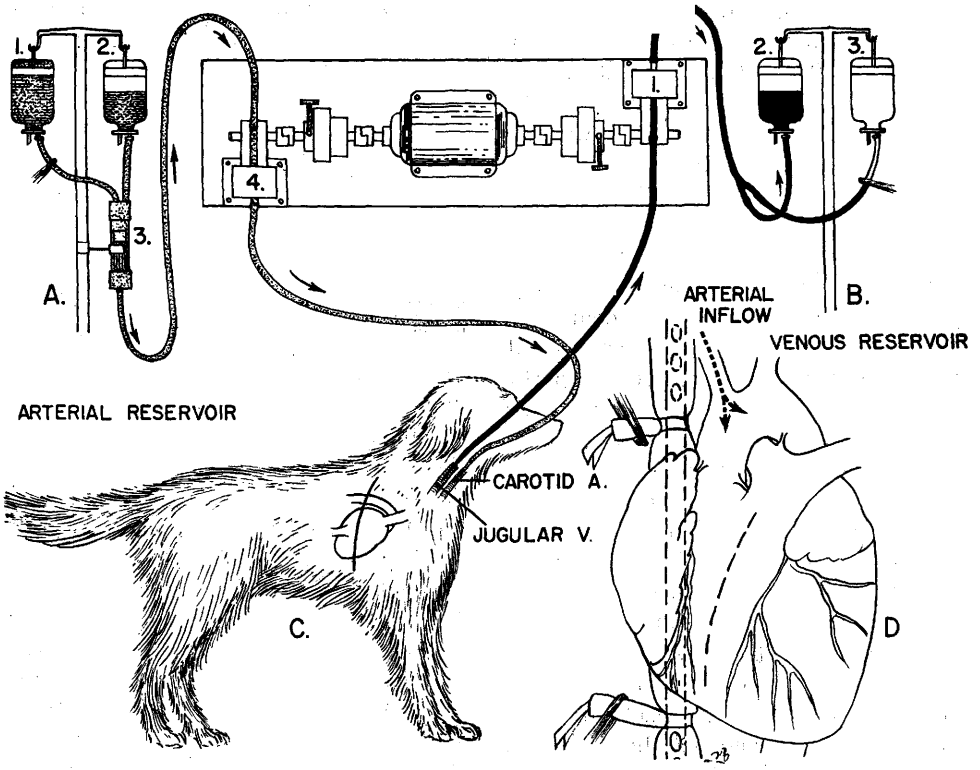

FIG. 1. Arterial reservoir perfusion. A. Arterial reservoir showing bottles of arterial bloo (1 & 2), blood filter (3), and arterial pump (4). B. Venous portion of perfusion circuit wit venous pump (1) and bottles (2 & 3) for collection of venous blood withdrawn from the patient's caval system. C. Recipient's relationship to the system is depicted in center of diagram and site of cannulations of right carotid artery and jugular vein are shown. Arterial cannula is inserted 3-4 cm down the carotid artery and ligated in place. Venous cannula with holes at tip and along shaft (the distance between these 2 sets of holes is determined by the space between the vena caval occluding tapes of the animal concerned) is passed down the jugular vein into the venae cavae until the holes are in the proper relation to the occluding tapes as indicated in D. At top center is pumping assembly which consists of separate pumps at each end driven by a single motor (center) and separate speed changers which are interposed between the motor and each pump head.

that had been placed in the donor's femoral artery. This cannulation in the donor animal was ordinarily done under pentothal sodium anesthesia or curare paralysis to permit endotracheal intubation for artificial respiration with 100% oxygen during the period of collection. However, in an occasional trained or cooperative animal cannulation was possible with only local procaine anesthesia. Synchronously with the withdrawal of arterial blood from the donor animal stored venous blood was infused into the donor's femoral vein by means of a cannula similar to that in the artery. To avoid any undesirable alterations in the donor's blood volume this venous infusion was maintained at a rate equal to the removal of arterial blood. The quantity of arterial blood withdrawn from the donor animal was dictated by the desired rate and duration of perfusion and usually ranged between 2000 to 3500 cc. After collection, the arterial blood was ordinarily placed in a water bath maintained at 39°C where it remained until needed for the perfusion. However, when there was to be a longer time interval between collection and perfusion the blood was kept refrigerated (at 4°C). In such instances it was rewarmed to 39°C before it was used for perfusion. *Operative method.* Mongrel dogs weighing from 4.4 to 11.5 kg were used as re-

cipient animals. All were premedicated with morphine 3-4 mg/kg of body weight and atropine gr. 1-100, and then anesthetized with 2½% solution of pentothal sodium injected intravenously. Endotracheal tubes were inserted, and except for the period of perfusion the animals were artificially respired throughout the operative procedure. Details of the methods of arterial and venous cannulations. vena cava occlusion, connections to the pump[¶] are depicted in Fig. 1 and were identical in every respect to those of the recipient animals in the cross circulation study group reported in detail elsewhere(1). The rates of perfusion were calculated on the basis of the reduced flow principle(6) and ranged between 25 to 30 cc/kg of recipient body weight/min. The length of perfusion was arbitrarily set at 20 minutes, during which time total cardiac and pulmonary by-pass was in effect. *Reservoir perfusion* (Fig. 1). As indicated above, the patient's (or recipient's) relationship to the extracorporeal circuit (C & D) is unchanged from that employed for cross circulation. The donor, on the other hand, has been replaced by containers of arterial blood (A 1 & 2) and empty venous receptacles (B 2 & 3) respectively. The 2 bottles of arterial blood were connected by means of a Y to a blood filter (A3) similar to those used for infusions of blood on the hospital wards. Blood was allowed to fill the filter system with the latter inverted so that all air was displaced from the chamber. The outflow of the filter chamber was then connected to the plastic tubing leading to the arterial pump (A4). After these connections were made, the pump was turned on for a few moments to completely fill the arterial circuit before the arterial outflow limb of the pump was connected to the arterial cannula (C & D) of the recipient. With this done, the arterial circuit was complete and after the recipient's caval cannula was connected to the tubing leading to the venous pump (B) perfusion was begun. Blood was withdrawn from the recipient's vena cavae via the cannula (C & D) connected to the plastic tubing by the venous pump (B1) and was collected into either venous receptacle (B2 or 3). In practice the arterial pump drew blood from only one bottle at a time and was replaced by another full one so that at all times there was an uninterrupted perfusion. Similarly when the venous reservoir (B2) was full, the venous outflow was diverted into the empty reservoir (B3) and (B2) was replaced by another empty bottle. The output from each pump was preset before the perfusion at the rate desired. Usually for the study animals these were set equal. However, occasionally when blood loss from a cardiotomy was anticipated an imbalance was intentionally created by reducing the venous pump rate below that of the arterial.

[¶] Sigmamotor Inc., Middleport, N. Y.

TABLE I. Changes in Donor Hemoglobin and Platelets.*

Hemoglobin	
Control	13.6 g %
Final	12.8
Platelets	
Control	512,000
Final	365,000

* Avg figures for 10 donors, 3000 cc arterial blood was withdrawn from the femoral artery of each synchronously with infusion of equal amount of venous blood into femoral vein over a 1-2 hr period.

Observations. A total of 34 animals was used in this study (17 as recipients and 17 as oxygenators) to evaluate and develop this method of reservoir perfusion. Certain physiologic determinations were made on both the recipient and blood donor animals in an attempt to assess the alterations imposed by the method.

Hemoglobin and platelet alteration in the donor. Blood samples were taken from the donor's femoral vein cannula for hemoglobin and platelet determinations just before and after the collection of the arterial blood. The changes in 10 donors are tabulated in Table I. In these animals 3,000 cc of arterial blood was withdrawn from the femoral arteries while a like amount of citrated dog blood was administered into the femoral vein over a period of approximately one to 2 hours. The infused blood had been obtained from several dogs at sacrifice or as the by-product of a previous perfusion and had been stored for periods up to 5 days. Despite the varying quality and age of this infused venous blood the altera-

TABLE II. Hematologic and Metabolic Changes* Produced in Recipient after Reservoir Perfusion for 20 Min.

Recipient	pH	O_2 (vol %)	CO_2 (vol %)	Hgb. (g)	Platelets per mm^3
Control					
Artery	7.48	15.33	34.16	—	—
Vein	—	10.93	41.94	11.2	317428
Final					
Artery	7.26	18.53	30.67	—	—
Vein	—	12.03	38.96	13.4	182000

* The above are mean figures for 8 animals. The apparently low control arterial O_2 content is consistent with the avg control hemoglobin level (see text).

tions noted were relatively insignificant. In most of the donors the hemoglobin drop was approximately one-third of their normal level.

Changes in the recipients. In Table II are summarized the results of pH, O_2, CO_2, hemoglobin and platelet determinations made on 8 of the recipients just before and immediately after reservoir perfusion during which total cardiac by-pass was in effect. The most pronounced effect noted was the reduction in pH which in this instance fell from an average preperfusion level of 7.48 to 7.26 immediately postperfusion. This acidosis was similar to the observations made in total cardiac by-pass by other methods in studies previously reported(1,7,8) and probably was also due to the accumulation of acid metabolites during the perfusion period. The blood oxygen and carbon dioxide content determinations showed very little change. On first inspection the average control arterial O_2 content would appear to be low. However, this figure is consistent with the low control hemoglobin levels. The finding of an anemia in new stock animals admitted to the colony has not been unusual especially during the winter months. The rise in hemoglobin and its resultant increase in arterial O_2 content at the end of the perfusion was comparable to the hemoconcentration noted in previous perfusion experiments(7,8). The average blood platelet count fell to approximately one-half of its control level. The greatest drop in platelets demonstrated by any of the recipient animals was one-third of the control figure and ordinarily the recovery was relatively prompt so that the postoperative count was usually doubled by the following day and was back to its control level within 2 to 3 days.

There was no donor mortality in this study. During the early phases before the optimum heparin dosage had been established postoperative bleeding in the recipients was a frequent complication, and 6 of the first 7 recipients succumbed to this complication. However, of the last 10 recipients who received blood collected in less heparin (25-32 mg/liter) this complication has not occurred and 8 were long term survivors. The 2 deaths resulted from avoidable errors; one from avulsion of a carotid artery during decannulation and one from pulmonary edema caused by the inadvertent rapid infusion of a large amount of saline in the early postoperative phase.

Discussion. The results herein reported indicate that the use of the described method of continuous arterial perfusion from a reservoir of oxygenated blood is a feasible means for totally by-passing the heart and lungs for a time interval sufficient to perform intracardiac operations under direct vision. By the removal of the donor from the operating theater the treatment of patients with intracardiac abnormalities would be further simplified by a reduction in the number of personnel and the amount of equipment necessary. This method of collection of arterial blood from the donor with synchronous replacement by an equal quantity of compatible venous blood into the same body region would appear to be a simple and safe procedure for the donor associated with about the same risk as a conventional blood transfusion. If the blood is collected within a short time of its intended use the recipient (or patient) would appear to derive almost the same physiological benefits as when the donor is interposed directly into the extracorporeal circulation.

An obvious limiting factor inherent in this reservoir type of perfusion for clinical use is the fact that the length of the perfusion is limited by the amount of arterial blood collected for the reservoir. In practice several factors would appear to minimize this objection. First, clinical experience has confirmed the safety and practicability of total body perfusions at normal temperature utilizing re-

duced flow rates (25 to 40 cc of blood/kg body weight/minute). Secondly, experience gained in the corrective surgical treatment of intracardiac defects by the use of controlled cross circulation has indicated that, with direct vision, the majority of ventricular defects required well under 20 minutes of intracardiac operating time. These two factors coupled with the obvious fact that many of the urgent candidates for intracardiac operations are infants or small children make the technic herein described attractive for further investigation and clinical application.

In the present study the donor animal was used as an oxygenator for the procurement of arterial blood with which to supply the arterial reservoir. It is interesting to note that there was a relatively small depreciation in the donor's hemoglobin and platelets even though he "processed" a volume of blood which was usually greater than his total blood volume over a relatively short period of time. Also, this occurred in spite of the somewhat dubious quality of the stored venous blood infused into the donor dogs. This observation attests to the efficacy of the dog's hematopoietic regenerative powers and it would be reasonable to anticipate even less depreciation in these factors clinically with the use of a better quality of bank blood for the replacement.

Experimentally it was usually necessary to anesthetize the donor animal for the collection of arterial blood, but this would not be required in the clinical application of the method. Under these conditions, the collection could be performed via an arterial puncture of several compatible donors or from a single donor using local procaine infiltration of the puncture sites.

Summary. 1. A simple method permitting total by-pass of the heart and lungs for the performance of intracardiac surgical operations is described. 2. This method utilizes continuous perfusion of the recipient's (patient's) arterial system from a reservoir of oxygenated blood. An equivalent quantity of venous blood is removed from the recipient's superior and inferior cavae. 3. A pump is utilized to control this exchange between the recipient and the arterial and venous reservoirs. 4. Arterial blood for the reservoir was obtained from a donor animal used as an oxygenator independent of the perfusion system. This was done by collecting arterial blood from the donor's femoral artery into a heparin glucose solution while stored venous blood was infused into his femoral vein at an equal rate. Ordinarily 2,000 to 3,500 cc of arterial blood was collected from a single donor dog in this fashion. 5. The optimum dose of heparin to prevent clotting in the arterial blood collected for this purpose was 25 to 32 mg/liter of blood. 6. The simplifications of the clinical application of this method are briefly discussed.

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