Physiologic Studies during Cardiopulmonary Bypass Eliminating Heparinized Blood

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Many adverse physiological changes associated with temporary cardiopulmonary bypass recently have been attributed to use of large quantities of homologous blood to prime various types of pump oxygenator. Several technics of open heart surgery have been suggested as a means of eliminating the need for a pool of homologous blood. Both Panico and Neptune and Long and associates reported use of blood substitutes for extracorporeal circulation. Greer, Carey, and Zuhdi demonstrated that 5 per cent dextrose in distilled water could be used clinically to prime the pump oxygenator, combining this approach with hypothermia. DeWall and colleagues elaborated upon a similar technic of open heart surgery.

Approximately two and one-half years ago, our experience with emergency pulmonary embolectomy emphasized to us the need for blood substitutes. At that time, animal investigations demonstrated the feasibility of using 5 per cent dextrose in distilled water to prime the pump oxygenator, and we recommended this technic for emergency situations. Further laboratory experience, description of the homologous blood syndrome, and demonstration of the clinical practicality of hemodilution perfusion, prompted us to use such a method of open heart surgery.

In April, 1962 we adopted a technic of cardiopulmonary bypass employing disposable plastic oxygenators, primed with 5 per cent dextrose in distilled water, under normothermic conditions. Results in 601 consecutive clinical cases have been most gratifying (Table 1). This report summarizes various physiologic changes associated with our technic of cardiopulmonary bypass, particularly in comparison to those which occur when a homologous blood prime is used.

Technic of Bypass

Table 1—Diagnosis and Result in Patients Undergoing Open Heart Surgery Without Homologous Blood Prime

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. of Cases</th>
<th>Deaths</th>
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<tbody>
<tr>
<td>Congenital</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventricular septal defect</td>
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<td>3</td>
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<tr>
<td>Atrial septal defect</td>
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<td></td>
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<td>0</td>
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<td>Ostium primum</td>
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<td>1</td>
</tr>
<tr>
<td>A-V canal</td>
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<td>3</td>
</tr>
<tr>
<td>Tetralogy of Fallot</td>
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<td>10</td>
</tr>
<tr>
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<td>2</td>
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<tr>
<td>Aortic stenosis</td>
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<td></td>
</tr>
<tr>
<td>Aortic stenosis</td>
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<td>12</td>
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<tr>
<td>Aortic insufficiency</td>
<td>44</td>
<td>12</td>
</tr>
<tr>
<td>Mitral stenosis</td>
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<td>6</td>
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<tr>
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<tr>
<td>Coronary endarterectomy</td>
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<td>1</td>
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<tr>
<td>Sinus of Valsalva fistula</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>3</td>
<td>2</td>
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<tr>
<td></td>
<td>204</td>
<td>46</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>601</strong></td>
<td><strong>81</strong></td>
</tr>
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</table>

*From the Cora and Webb Mading Department of Surgery, Baylor University College of Medicine, and the St. Luke's Episcopal, Texas Children's and Ben Taub General Hospitals. Supported in part by the Houston Heart Association and the U. S. Public Health Service (HE-03137) and (HE-5387). Presented at the Interim Clinical Meeting, American College of Chest Physicians, Portland, Oregon, November 3-December 1, 1963.

pumps and a motor-driven frame to hold the oxygenator bag (Fig. 1). Blood from the venae cavae flows by gravity to the base of the oxygenating column and is driven up into the defoaming chamber by the oxygen dispersion system (Fig. 2). In the defoaming chamber, oxygenated blood passes over stainless steel sponges coated with antifoam. Blood then flows through a filter into an angulated reservoir, from which it is returned to the patient via the common femoral artery using a roller pump. Coronary venous return and bronchial flow is aspirated from the heart by two roller pumps and passes through a defoaming, collecting reservoir into the base of the oxygenating column.

Arterial flow to the patient is adjusted to equal the volume of blood returned to the oxygenator from the venae cavae and from the collecting reservoir. With the base of the oxygenating column approximately 45 cm. below heart level, flow rate usually establishes itself at 60-80 ml. per minute per kilogram of body weight. Body temperature is maintained above 36°C. by passing a coil of plastic tubing in the arterial line through a warm water bath.

In most instances, the extracorporeal unit is primed with 20 ml. of 5 per cent dextrose in distilled water per kilogram of body weight. In small patients, a slightly larger volume is required, and in very small infants one unit of fresh, heparinized blood is added due to the relatively large size of the unit and tubings in comparison to the blood volume of the patient. Extracardiac blood loss is replaced intravenously with stored acid-citrate-dextrose blood. Upon completion of bypass, all blood remaining in the reservoir and in the tubings is returned slowly to the patient.

**Renal Function**

During bypass marked diuresis occurs and usually persists for several hours following operation. Thereafter, urine flow generally returns to normal levels. In this way, most of the dextrose solution used to prime the pump oxygenator is eliminated relatively rapidly.

In order to compare renal hemodynamic effects of using 5 per cent dextrose in distilled water with the effects of using fresh, heparinized blood as the priming agent for extracorporeal circulation, mongrel dogs were subjected to 30 minutes of total cardiopulmonary bypass by each technic. Discrete renal function studies were performed before and after bypass. In the group in which homologous blood was used to prime the pump oxygenator, glomerular filtration rate (Fig. 3) and renal blood flow (Fig. 4) were depressed to approximately two-thirds of control values. Renal vascular resistance was significantly elevated (Fig. 5). In contrast, when 5 per cent dextrose in distilled water was used as the priming
agent little or no change in renal function was noted following operation (Figs. 3, 4, 5), indicating more optimal maintenance of renal function by this technic.

**Blood Volume and Formed Elements of Blood**

Twelve patients undergoing temporary cardiopulmonary bypass by this technic for correction of congenital or acquired cardiac lesions were studied for changes in blood volume and formed elements of the blood. Total blood volume was measured by dilution of radiiodinated human serum albumin. Immediately following bypass and return of all fluid remaining in the pump oxygenator to the patient, total blood volume averages were somewhat lower than control values (Fig. 6). Determinations within the first 24 hours after operation demonstrated a further slight fall in total blood volume, followed by a return toward normal at 48 hours. Seven days later, total blood volume values were similar to those present before operation.

Changes in hemoglobin and hematocrit approximated each other and were not significant during the first 24 hours following surgery (Fig. 6). Forty-eight hours after operation, a slight decrease in hemoglobin and hematocrit values was noted.

**Figure 2:** Drawing illustrating technic of total cardiopulmonary bypass. Blood from venae cavae drained by gravity to base of oxygenating column. Blood aspirated from heart passes through defoaming, collecting reservoir on left into base of oxygenating column. Oxygen-dispersion system forces blood up oxygenating column into defoaming chamber, where blood passes over stainless steel sponges coated with antifoam. Blood flows from defoaming chamber through filter into angulated reservoir. Roller pumps return blood from reservoir outlet to patient via common femoral artery.

**Figure 3:** Diagrammatic comparison of average changes in glomerular filtration rate following 30 minutes of cardiopulmonary bypass in animals by technics indicated.
Seven days later hemoglobin and hematocrit determinations averaged 10.9 grams and 33.3 volumes per cent, respectively. These changes apparently reflected our efforts to curtail transfusion with acid-citrate-dextrose blood to replace extracardiac blood loss in order to avoid the possibility of overloading the vascular system and to reduce the incidence of post-transfusion hepatitis.

Efficiency of the blood coagulation mechanism in these patients was truly impressive as compared with bleeding tendencies often present in patients following open heart surgery by technics in which the pump oxygenator is primed with pooled homologous blood. Blood replacement by acid-citrate-dextrose blood averaged 390 ml. in children and 1,200 ml. in adults, amounts similar to those required for any major thoracotomy. These figures include blood replacement not only during operation, but during the entire period of hospitalization.

**Total Body Water and Compartmentalization**

Eleven patients undergoing open heart surgery for complicated acquired cardiac defects were studied for changes in total body water and compartmentalization.

Five had total replacement of aortic valve, three had total replacement of the mitral valve, and three underwent mitral annuloplasty. Total body water was determined by dilution of tritium labeled water, and extracellular fluid volume was estimated by measurement of the radioactive sodium sulphate space. Intracellular fluid volume was calculated by subtracting extracellular fluid volume from total body water.

Determinations of extracellular fluid volume and total body water and calculations of intracellular fluid volume prior to operation closely approximated calculated normal values (Fig. 7). Immediately after bypass, mean extracellular fluid volume increased to 115 per cent of calculated normal values. Mean values for total body water were 104 per cent of calculated normal values, and those for intracellular fluid volume were 97 per cent of calculated normal values. However, neither of these latter changes was statistically significant. Seven to ten days following operation, mean extravascular volume and total body water remained slightly elevated, while mean intracellular fluid volume was 99 per cent of calculated normal values.

The close approximation of control determinations to calculated normal values in these patients with far advanced, acquired heart disease probably was related to the
fact that all had been hospitalized on intensive medical management for varying periods of time prior to surgery. In many instances parenteral mercurial diuretics were used freely before operation. The slight, although statistically significant, increase in extracellular fluid volume following return of all fluid in the pump oxygenator to the patient in spite of marked diuresis at that time, suggested that it probably is advisable to limit amounts of intravenous fluid therapy given during and following operations in which hemodilution technics of extracorporeal circulation are employed.

**Serum Electrolytes**

Changes in serum electrolytes following open heart surgery by this technic of cardiopulmonary bypass usually followed a similar pattern. Immediately after bypass and return of all fluid in the pump oxy-
genator to the patient, values for serum sodium, potassium, carbon dioxide and chloride were depressed somewhat (Fig. 8). However, these values rapidly returned toward control levels without specific therapy as early as four hours later. Twenty-four and 48 hours following operation serum electrolyte concentrations usually were within the range of normal. As the extracellular fluid volume generally was somewhat elevated at the time serum electrolyte values were depressed, these changes would appear to be primarily a dilutional phenomenon rather than actual electrolyte loss, particularly in regard to sodium concentration. Studies of urinary sodium excretion before and after cardiopulmonary bypass by the hemodilution technic demonstrated insignificant changes.

Hemolysis

In order to determine the degree of hemolysis produced by this technic of cardiopulmonary bypass, determinations of plasma hemoglobin were made prior to operation, during operation, but before onset of bypass, at ten-minute intervals during bypass, following completion of bypass, and after operation (Fig. 9). Short operations for correction of simpler congenital anomalies were associated with insignificant changes in plasma hemoglobin levels. Following one hour of cardiopulmonary bypass serum hemoglobin levels averaged 46.9 mg. per cent. In no instance was hemolysis of sufficient magnitude to produce a serum hemoglobin concentration as high as 100 mg. per cent.

Microcirculation and Blood Viscosity

Microcirculation in small vessels of the omentum in dogs was studied before, during, and after perfusion and recorded cinematographically. Immediately following onset of cardiopulmonary bypass using pooled homologous blood, there was aggregation and sludging of erythrocytes with plugging of many small vascular radicals. Although this tended to diminish somewhat as the perfusion progressed, significant sludging remained following completion of bypass. In contrast, this phenomenon of aggregation of erythrocytes with sludging was almost entirely absent when 5 per cent dextrose in distilled water was used to prime the pump oxygenator.

In order to compare the relationship of this aggregation and sludging of erythrocytes to changes in blood viscosity, blood viscosity was studied using an Ultra-viscosen. In those animals in which pooled homologous blood was used to prime the pump oxygenator, minimal changes in blood viscosity occurred throughout perfusion, although hematocrit values tended to rise somewhat (Fig. 10). In contrast, when 5 per cent dextrose in distilled water was used, there was marked decrease in blood viscosity immediately following on-

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*Bendix Corporation, Cincinnati, Ohio.

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**Figure 8:** Graphic demonstration of average changes in serum electrolytes associated with described technic of cardiopulmonary bypass.
set of bypass with return toward control values at the completion of bypass (Fig. 11). Although these changes tended to follow changes in hematocrit, blood viscosity in this latter group remained somewhat decreased even after hematocrit values had returned almost to control levels. Determinations of plasma viscosity suggested that these changes in blood viscosity were related to both hemodilution and a decrease in plasma viscosity. Studies in patients undergoing open heart surgery by the described technic closely approximated findings in animals in which dextrose solution was used to prime the pump oxygenator.

**DISCUSSION**

These studies indicate that this technic of open heart surgery employing plastic disposable oxygenators, primed with 5 per cent dextrose in distilled water, under normothermic conditions is well tolerated by the patient. The priming solution is quickly excreted following the procedure with little or no tendency to overload the circulation, although amounts of intravenous fluids used during and immediately follow-

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**Figure 9:** Diagrammatic illustration of average magnitude of hemolysis associated with described technic of cardiopulmonary bypass.

**Figure 10:** Graphic demonstration of average changes in hematocrit and blood viscosity associated with standard 30-minute period of cardiopulmonary bypass in animals, priming pump oxygenator with homologous blood.
ing operation should be limited. The coagulation mechanism of the blood is far less altered than when pooled homologous blood is used to prime the pump oxygenator. As less stored, acid-citrate-dextrose blood is required during and after operation by this technic, the incidence of transfusion reaction and development of hepatitis is reduced significantly. Perfusion appears more adequate as indicated by more satisfactory maintenance of renal function and by relative absence of aggregation of erythrocytes and sludging at the capillary level. Furthermore, it has been demonstrated that oxygen availability is as great or greater during hemodilution perfusion than when whole blood is used to prime the pump oxygenator, in spite of a diminished oxygen carrying capacity of diluted blood.13

Clinical results employing this technic of open heart surgery also are impressive. Table 1 summarizes results in 601 consecutive patients undergoing operation by this technic since April, 1962. These patients tended to be alert mentally immediately following operation, much sooner than when homologous blood was used to prime the pump oxygenator. There was a total of 70 deaths in this group of patients, none of which could be attributed to the technic of cardiopulmonary bypass. For the most part, deaths in patients with congenital anomalies were associated with incorrectible lesions and this outcome would have been expected regardless of the method of operation. Deaths in patients with acquired heart disease occurred predominantly in those suffering from far-advanced valve lesions prior to our use of Starr-Edwards prostheses. Recently, with the use of Starr-Edwards valves, our mortality rate for total aortic valve replacement in 88 consecutive patients was only 14.7 per cent. In every instance, this technic of cardiopulmonary bypass provided adequate support of circulatory status during even the most complicated operations.

Two previous successful cases of pulmonary embolectomy by technics requiring fresh, heparinized blood to prime the pump oxygenator were difficult to organize and valuable time was lost obtaining the necessary amounts of fresh blood. Usefulness of this method for such emergency surgery recently was demonstrated by successful pulmonary embolectomy in a 54-year-old patient.14 Preparations by the described technic were completed in approximately 15 minutes, less time than required to anesthetize the patient and make a thoracotomy incision.

![Figure 11: Graphic demonstration of average changes in hematocrit and blood viscosity associated with standard 30-minute period of cardiopulmonary bypass in animals, priming pump oxygenator with 5 per cent dextrose and distilled water.](image)
PHYSIOLOGIC STUDIES DURING CARDIOPULMONARY BYPASS

This technic of cardiopulmonary bypass also has been employed in seven patients of the religious sect known as Jehovah’s Witnesses. Based on their interpretation of the scriptures, this group will not accept blood transfusion under any circumstances. In six of the seven patients open heart surgery was successful. Operations included such procedures as aortic commissurotomy and mitral annuloplasty and the only death was in a patient who bled following operation from a transected internal mammary artery. No transfusions were administered to any of these patients during operation or throughout the entire period of hospitalization.

SUMMARY

Many adverse physiologic changes following temporary cardiopulmonary bypass recently have been attributed to the use of large quantities of homologous blood to prime various types of pump oxygenators. We have adopted a technic of open heart surgery employing plastic disposable oxygenators, primed with 5 per cent dextrose in distilled water, under normothermic conditions. Results of this technic in 601 clinical cases have demonstrated its superiority to technics employing pooled homologous blood in almost every respect. In order to determine physiologic changes associated with this technic of open heart surgery, several investigations were performed and included determinations of changes in renal hemodynamics, changes in blood volume and formed elements of the blood, changes in body water and compartmentalization, changes in serum electrolytes, and changes in blood viscosity. The magnitude of hemolysis during and following this technic of cardiopulmonary bypass also was studied. Results of these studies would appear to offer additional evidence that this technic of open heart surgery is superior to those employing pooled homologous blood.

RESUMÈ

De nombreuses modifications physiologiques défavorables suivant une circulation extracorporelle temporaire ont récemment été attribuées à l’utilisation de larges quantités de sang homologue, avec d’excellents types divers d’oxygérateurs à pompe. Nous avons adopté la technique de chirurgie au cœur ouvert qui utilise des oxygérateurs en matière plastique, préparés avec 5% de dextrose dans l’eau distillée, dans les conditions de normothermie. Les résultats de cette technique dans 601 cas ont montré la supériorité de cette technique, à pratiquement tous les points de vue, aux techniques employant du sang homologue conservé. Dans le but de déterminer des modifications physiologiques associées avec cette technique de chirurgie au cœur ouvert, plusieurs investigations ont été faites et ont inclus des déterminations de modifications dans l’hémodynamique rénale, des modifications dans le volume sanguin et les éléments figurés du sang, des modifications dans l’eau corporelle et sa réparation, des modifications dans les électrolytes du sérum et dans la viscosité du sang. L’importance de l’hémolyse pendant et après cette technique de circulation extracorporelle a également été étudiée. Les résultats de ces études semblent amener des preuves supplémentaires que cette technique de chirurgie au cœur ouvert est supérieure à celles qui emploient du sang homologue conservé.

RESUMEN

Muchos cambios fisiológicos adversos después de la desviación circulatoria temporal cardiopulmonar se han atribuido recientemente al uso de grandes cantidades de sangre homóloga para purgar los diversos oxigenadores de bomba. Hemos adoptado una técnica de cirugía de corazón abierto empleando oxigenadores de plástico, descartables, purgados con 5 por ciento de dextrosa en agua destilada bajo condiciones normotérmicas. Los resultados de esta técnica en 601 casos clínicos han demostrado su superioridad sobre la que emplea sangre homóloga, en casi todos respectos. Para determinar los cambios fisiológicos que ocurren con esta técnica de corazón abierto se llevaron a cabo varias investigaciones e incluyeron determinación de los cambios en la hemodinámica renal, en el volumen sanguíneo y en los elementos formados de la sangre, en el volumen de agua y en compartimentalización; cambios en electrolitos séricos y en la viscosidad sanguínea. La magnitud de la hemólisis durante y después de esta técnica de desviación cardiopulmonar se estudió también. Los resultados de estos estudios parecerían ofrecer una evidencia adicional de que esta técnica es superior a la que usa sangre colectada homológica.

ZUSAMMENFASSUNG

Viele der ungünstigen physiologischen Veränderungen in Zusammenhang mit temporären car-

References

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CARDIOPULMONALY FUNCTION IN YOUNG SMOKERS

In a group of young subjects, comparable in most respects except for smoking history, some physiology abnormalities are present in smokers. The alterations in function include: 1) greater oxygen debt accumulation during exercise; 2) decreased diffusing capacity at rest and with exercise, and 3) decreased total lung capacity, inspiratory capacity, and vital capacity. The underlying bases for these abnormalities have not been elucidated. These differences may not be interrelated, but instead may be multiple different effects of the same stimuli.