Anesthesia for Cardiac Surgery:
Principles and Practice

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The brief interval since 1953 covers the entire life-span of open intracardiac surgery with the art and science of whole-body perfusion that makes it possible. No other branch of surgery and anesthesia has been so intensively studied in such a short time; hence, a large volume of knowledge and experience has accumulated. From this has evolved sound principles of cardiovascular anesthesia and supportive care, based on the pathophysiologic and biochemical changes occurring. The purpose of this review is to outline these principles and the reasoning behind them. Our own experience and techniques are presented, primarily, as well as those of others. Included also is a profile of changes taking place in the human body during and after the operative period.

Anesthesia

The aim of any anesthetic technique is to provide a state in which the surgeon can operate with as little physiologic and emotional trauma to the patient as possible. In this respect, cardiovascular anesthesia is not different, but certain other factors are. Our experience is that the impaired circulatory system will tolerate even less depression than in normal patients. Thus, all efforts are directed to maintaining the circulation. The depth of anesthesia needed is less than in robust patients having nonthoracic surgery. Little or no muscle paralysis is required. The need for amnesia is great, to counter the heavy emotional stress, but minimal analgesia is necessary once the incision is made. Vagal reflexes may have to be treated.

It is indeed fortuitous that cardiac patients who tolerate only a minimal anesthetic state require no more than that. Equally comforting is the realization that the patient with an extremely low cardiac output can maintain this narrow balance if given only light anesthesia with ample oxygen. The old dictum that it does not matter what you use, but how well you use it, is ever true. Just about every agent and technique in anesthesia from nitrous oxide-oxygen-ether¹ to neurolept analgesia² has been used for cardiac surgery.³-²⁵ The choice depends on one's preference and experience in relation to local conditions, for example, the use of electrocautery. The methods that have evolved in our large-volume practice have proved best for us; no greater priority than that is claimed for them.

Premedication

Effective doses of sedative drugs are safe and most worthwhile to relieve the great anxiety of the patient facing a cardiac operation. Patients have a smoother induction and anesthetic course, if well premedicated. We use a barbiturate and an opiate drug. Two hours before surgery, pentobarbital, 1 mg/lb, is given orally to a maximum of 100 mg. Children who weigh more than ten pounds receive
2 mg/lb, rectally. Our patients also are given morphine an hour before operation, 1 mg/10 lb, intramuscularly. The usual maximal dose is 10 mg, and no morphine is given to patients who weigh less than 20 lb. Doses are reduced in patients with severe cachexia or cyanosis. Morphine has a calming effect in these patients; it may relieve pulmonary congestion by allowing peripheral pooling and may improve ventricular performance.

Belladonna drugs were not used originally in our premedicating regimen for fear of undesirable tachycardia in patients having closed mitral commissurotomy. This omission should avoid the occasional untoward reactions from atropine, such as cardiac arrhythmia and elevation of temperature in children. Patients without atropine do not have more tracheobronchial secretions than patients who receive it. There is reasonable justification for the use of preoperative belladonna drugs to abolish vagal bradycardia. However, this can be treated effectively by small intravenous doses when indicated.

Other premedicating combinations reported are: meperidine with atropine or scopolamine-morphine with the same drugs, promethazine-meperidine, and trimeprazine-atropine. The decrease in arterial oxygen tension seen with use of meperidine occurs after morphine as well, but is not significant enough to outweigh the advantages of giving opiates.

ANESTHETIC AGENTS AND TECHNIQUE

The principles, briefly, are: (1) maintaining light anesthesia, really amnesia-analgesia, (2) controlling ventilation with adequate oxygenation, and (3) abolishing vagal stimulation.

In our practice, children are coaxed to sleep with nitrous oxide, oxygen, and halothane. In the past we have used cyclopropane-oxygen. As soon as the larynx reflex is gone, succinylcholine, 2 mg/lb, not exceeding 100 mg, is injected intramuscularly. This produces about ten minutes of apnea for intubation and positioning. Neonates are intubated while awake after oxygenation. In adults, induction is accomplished with 200 to 300 mg thiopental in small, well-spaced doses. Intubation is done after 100 mg succinylcholine is given intravenously. Two intravenous routes are established; in children this is done only after intubation, when some venodilatation has occurred. The ankle is preferred in children and the arm in adults. The external jugular is used as one vein, if possible, as a safe route for measurement of venous pressure.

We maintain anesthesia with 50 or 60 per cent nitrous oxide in oxygen, supplemented as needed and tolerated with small concentrations of halothane. In our experience, the more seriously ill the patient, the less halothane needed. If the arterial pressure is less than 90 mm Hg systolic, no halothane is given. However, the most cyanotic patients are anesthetized with halothane and oxygen and may require higher concentrations. The myocardial depressant effect of halothane is well tolerated in light levels of anesthesia. Halothane, 1 per cent, is vaporized initially into the oxygenator during perfusion. When the temperature of the patient is 32 C or less, 0.25 to 0.5 per cent halothane suffices. The well-perfused and oxygenated patient does not need to be paralyzed during perfusion. During this time, in our practice, the lungs are insufflated with equal amounts of helium and oxygen, not ventilated, and statically inflated to a small positive pressure. Other factors that we have found to minimize lung damage are avoidance of pulmonary venous hypertension and not opening the pleural spaces.

With moderate hyperventilation (Paco2 25 to 35 mm), breathing can be controlled without a muscle relaxant. When needed to control breathing in very light anesthesia, succinylcholine is given in divided doses. In patients who are likely to need assisted ventilation via endotracheal tube after the operation, more relaxant can be used, plus intravenous injection of meperidine toward the end of anesthesia. In general, our aim is to give minimal amounts of nonvolatile drugs, since hypothermia prolongs their action.

The most frequently used technique is the semiclosed-circle absorption system. More sensitive control of ventilation is possible by manual means than when a ventilator is used. If only one anesthesiologist is available, a ventilator frees him for other vital tasks.

Different combinations of agents have been used. The use of oxygen with nitrous oxide, ether, or halothane has been reported, as
well as cyclopropane-ether-oxygen. The azeotropic mixture of halothane-ether in oxygen has been tried. Methoxyflurane, meperidine-levorphan, and neurolept analgesia have been advocated. A frequently used combination is nitrous oxide and oxygen with curare. Succinylcholine drip or decamethonium has been used in addition to giving hexafluoridum to prolong the effect of succinylcholine.

**MONITORING**

When a group first begins to operate on patients using whole-body perfusion, as many variables as possible should be measured. When adequate physiologic and biochemical information has been obtained, less monitoring is permissible. Even with considerable monitoring, it would seem unlikely for the team that does open-heart surgery only infrequently to gain enough experience to obtain good results.

At present we monitor central venous pressure, arterial pressure (often only by cuff), temperature, the electrocardiogram, and heart sounds by esophageal stethoscope. Venous pressure is obtained via the external jugular vein until the termination of perfusion. At that time, a small polyvinyl catheter from the right atrium is brought out through the chest wall and used for pressure measurement, for 24 to 48 hours. In patients in whom left ventricular function is critical and in question, a similar catheter is brought out from the left atrium. Bleeding after removal of these catheters has not been encountered. Pressures are sensed by strain-gauge manometers and displayed on a direct-reading dial. The oropharynx is the preferred site of our temperature probe. The esophagus is avoided because it is influenced by aortic blood temperature. A blanket with circulating water is used to maintain normal body temperature after perfusion. This largely avoids vasoconstriction and shivering upon awakening; shivering increases oxygen consumption considerably.

Direct arterial pressure is measured in the most severely ill patients, and probably should always be in most practices. Plastic needles are inserted percutaneously into the radial artery, and few cutdowns are necessary. A small catheter advanced into the femoral or iliac artery is a good means of obtaining arterial pressure. Except in infants or in the presence of brachial arterial spasm, if a pressure by cuff is not obtainable, an inadequate circulation is considered present.

Serial blood analyses for oxygen, acid-base balance, and electrolytes can be omitted as routine measurements when reproducibility of an adequate perfusion has been demonstrated. Their ability to investigate the patient in trouble is a necessity.

**EFFECT OF THE PATHOLOGIC CONDITION ON ANESTHETIC MANAGEMENT**

Congenital defects often produce a decrease or increase in pulmonary blood flow, depending upon the predominance of right-to-left, or left-to-right, shunting. Those defects, with reduced flow to the lungs and cyanosis, include tetralogy of Fallot and tricuspid or pulmonary atresia. Patients with septal defects and patent ductus arteriosus have increased pulmonary blood flow, owing to recirculation of arterial blood, unless pulmonary vascular resistance has increased.

Pulmonary flow may be decreased and pulmonary arterial pressure increased in normal man by an elevated airway pressure, low arterial oxygen tension, or lowered pH. In tetralogy, controlled ventilation may further decrease pulmonary blood flow, thereby shunting more venous blood to the left ventricle and causing further cyanosis. The reduced blood flow to the lungs prolongs an inhalation induction, but agents given intravenously reach the brain rapidly since they essentially bypass the lungs. Patients with increased pulmonary blood flow have more rapid uptake of oxygen and inhaled agents, and they tolerate positive-pressure breathing better than patients with decreased pulmonary flow.

Induction of anesthesia is very slow in patients with transposition of the great vessels because of the extensive recirculation in the lungs and little mixing with the systemic circulation. The arterial oxygen tension is not easily increased by breathing oxygen. A palliative operation creating an atrial septal defect, by the Blalock-Hanlon technique to improve mixing between pulmonary and systemic circulations has one very critical period. The temporary occlusion of the right pulmonary
artery and veins and of the patent foramen ovale may increase hypoxemia, with subsequent bradycardia and cardiac arrest.25

The pathophysiology of acquired valvular disease affects the conduct of anesthesia, as do the electrolyte changes induced by medical treatment. Aortic lesions may produce cardiomegaly, ventricular hypertrophy, and reduced cardiac output. Mitral lesions tend to develop even lower cardiac output, plus left atrial enlargement and atrial arrhythmias. Blood volume is increased, especially within the thorax, until diuretics are given. Pulmonary congestion, alveolar thickening, and subnormal gas exchange are seen more often in the presence of mitral disease. Preoperatively, these patients may have arterial desaturation, cyanosis, and clubbing. The significant changes relating to anesthesia are the increase in blood volume, slowed circulation time, increased alveolar-arterial gradient of oxygen tension, and reduced cardiac output and myocardial contractility. Both intravenous and inhalation agents take longer to reach the brain and myocardial junctions. Longer intervals must be allowed between doses of nonvolatile agents. Inspired oxygen concentration should be 40 to 50 per cent to assure an adequate arterial tension. Myocardial contractility is easily depressed further by potent agents, and concentrations must be kept low. The heart with stenotic valves cannot increase its output to compensate for vasodilatation.

One effect of prolonged treatment with digitals and diuretics is a reduction in total body potassium,42 with or without a low serum level. Total body sodium may be elevated, but the serum concentration is reduced because of water retention.44 The potassium depletion increases sensitivity to digitals and may be accompanied by a metabolic alkalosis.45 At our institution, the use of digitals is stopped 36 hours before operation to avoid possible increased sensitivity after perfusion.47 Undigitized patients are not given digitals before operation unless required for the usual reasons.

Closed Cardiac Operations

Almost all intracardiac procedures are now accomplished by the open method, but closed operations are done without a pump oxygenator. The extracardiac anomalies such as patent ductus arteriosus and coarctation fall in this group. The patient having resection of a constrictive pericardium requires careful management until the heart can increase its stroke volume. Even after removal of the constriction, the weakened myocardium may dilate. Closed mitral commissurotomy is being done less often now. This is one of the most critical operations, because the patient’s low cardiac output is further depressed during the intracardiac manipulation. The circulation during this time is improved by giving a positively acting inotropic agent such as ephedrine before the heart is entered. This reduces the duration of hypotension and the resultant poor coronary perfusion. Adequate vagal blocking will often accomplish the same result by increasing heart rate and contractility. A critical point in the operation for myocardial revascularization occurs when the tunnels are being made through the myocardium. This is particularly true when the heart is displaced to visualize the posterior wall.

Another group of closed operations consists of palliative shunting procedures in the desperately ill infant.39 The objective is to supply more blood to the lungs for oxygenation, regardless of whether the vena cava or an artery is anastomosed to the pulmonary artery. Risk of these operations is increased by their critical condition and management is difficult. Body temperature should be maintained with a warming blanket, since hypothermia decreases cardiac output and makes it difficult to monitor the constricted arterial system. Atropine will usually abolish bradycardia and allow time to complete the shunt.

The era of using surface cooling for intracardiac surgery is fortunately past. Working on the hypothermic, hyperirritable heart without a pump oxygenator carries a risk that is best avoided. Even the resection of a coarctation in a patient without sufficient collateral vessels, as evident from palpable femoral arterial pulses, is better done with a temporary bypass graft.

Whole-body Perfusion

Although survival after three to four hours of whole-body perfusion is common today,48 the incidence of complications is directly re-
lated to duration.\textsuperscript{49} Perfusion is still a highly abnormal state, causing both frank and subtle physiologic changes. The best likelihood of success after prolonged perfusion may come with the use of a membrane oxygenator.\textsuperscript{50, 61} This avoids the direct gas–blood interface, which in all other oxygenators is damaging to blood.\textsuperscript{25}

Descriptions and comparisons of oxygenators are not pertinent here,\textsuperscript{63} nor are we concerned with surgical aspects of the subject. The pump-oxygenator most frequently used in the past has been some form of rotating disk, but the disposable bubble oxygenator has become widely accepted, mainly for shorter perfusions. Great differences of surgical practices and techniques of perfusion exist and many successful variations are in use. Critical to success is that a pump team knows the extracorporeal system thoroughly (how it works, its capabilities and limitations) and what is occurring within the patient during and after perfusion. Our experience has been gained with the Mayo–Gibbon vertical-sheet oxygenator.\textsuperscript{54} The following information is related to it, but should be transferable to other perfusing systems that oxygenate satisfactorily and perfuse with similar flows and priming solutions.

**TECHNIQUES OF PERFUSION**

Many changes in technique have evolved to improve perfusion and its safety. Major points include the following six factors: (1) Lowering body temperature by a heat exchanger\textsuperscript{55} to 28 to 30°C reduces oxygen consumption by 25 to 40 per cent.\textsuperscript{56} Our patients are cooled to 30°C and perfused with the same flows used at 37°C. Others reduce flow after cooling. (2) Flows of 2.0 to 2.4 l/min/m² appear to provide satisfactory tissue homeostasis and survival of several hours’ perfusion.\textsuperscript{57} There need be little concern about the blood pressure if flows of this magnitude are retained. (3) Priming with acid-citrate-dextrose (ACD) blood\textsuperscript{58, 69} has lessened demands on blood banks and made the technique more available on short notice. The ACD blood we use may be as old as 48 hours and is buffered with tris(hydroxymethyl)amino methane (THAM).\textsuperscript{60, 61} (4) Dilution of the blood in the oxygenator\textsuperscript{62} or priming the latter with non-blood fluid\textsuperscript{63–66} has several advantages: saving of blood, lowering viscosity for better peripheral blood flow during hypothermia, and better renal function as a result of the water and solute load. (5) Direct perfusion of the coronary arteries for aortic-valve replacement provides good oxygenation of the myocardium. We use total flows for the left and right coronaries of approximately one tenth the whole-body flow. We accept pressure up to 250 mm Hg in the coronary flow lines since much of this pressure is due to the cannula itself. (6) Periods of aortic clamping of 15 to 20 minutes, at 30°C, are well tolerated in patients with congenital heart disease and allow a nonbeating heart in which to work.

The data on the prime for our pump oxygenator are shown in table 1. The diluent, about 40 per cent of the total, is 5 per cent dextrose in 0.5N NaCl, plus THAM. Others add mannitol, low-molecular-weight dextran, lactated Ringer’s solution, or 5 per cent dextrose.

**EFFECTS OF PERFUSION**

Certain changes take place in the body during and after perfusion. One can be sure that many more deviations from normal, as yet undocumented, are occurring in the complex biochemical systems which keep us alive. In the discovery of the more subtle changes that occur during whole-body perfusion and in cardiac failure lies our best hope of helping more of these people to survive.

**Oxygenation** (fig. 1). Many severely ill cardiac patients have arterial hypoxemia and pulmonary dysfunction before operation.\textsuperscript{67, 68} However, the mean Pa\textsubscript{O\textsubscript{2}}, on air in these six patients with mitral and aortic valve disease was 77 mm Hg. The inhalation of 40 per

<table>
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<tr>
<td>Dextrose (5 per cent) and sodium chloride (0.45 per cent)</td>
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<td>Heparin (1,000 units/ml)</td>
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<tr>
<td>Acid-citrate-dextrose blood</td>
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<tr>
<td>THAM (0.3M)</td>
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<td>20 mEq</td>
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<td>Calcium chloride (100 mg/ml)</td>
<td>25 ml</td>
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* In order of addition to the pump-oxygenator.
cent oxygen with nitrous oxide before and after perfusion gave mean levels of 171 and 156 mm Hg, indicating the widened alveolar-arterial gradient of oxygen tension due to intrapulmonary shunting or ventilation-perfusion abnormalities. The efficiency of the oxygenator determines arterial tension during perfusion. Arterial tension in the oxygenator decreases when re-warming the patients to 36 C, since there is greater desaturation of the venous blood presented to the oxygenating surface. The lowered oxygen content throughout perfusion imposed by hemodilution is also seen. After surgery, the lowered hemoglobin may be a major factor in tissue oxygenation, in addition to cardiac output and respiratory function. Oxygen uptake has been found to decrease by 15 per cent during anesthesia for open-heart surgery and to increase immediately after surgery. During perfusion at 30 C, oxygen uptake is about 60 to 75 per cent of that at normal temperature.

Acid-Base Balance (fig. 2). In the early days of open intracardiac surgery, metabolic acidosis occurred commonly, as a result of poor perfusion and, after the operation, owing to low cardiac output. Deficient tissue oxygenation, anaerobic metabolism, susceptibility to ventricular fibrillation, and stimulation of catecholamine production inevitably followed. As seen in figure 2, alkalosis rather than acidosis is now the common finding. This pattern occurs in noncardiac patients as well. A respiratory alkalosis is imposed during surgery by hyperventilation and by controlling the concentration of carbon dioxide added to the oxygenator. The THAM used in the prime not only corrects the acidosis of the ACD blood but also maintains buffer base in these cases in a normal range for two hours of perfusion. A dangerous time for development of arrhythmias is at the end of surgery, when pH decreases rapidly as carbon dioxide increases with resumption of spontaneous breathing.
After the operation, a metabolic alkalosis occurs, at least partly from metabolism of the sodium citrate given in ACD blood.

Electrolytes (figs. 3 and 4). The cations most essential to myocardial function are sodium, potassium, and calcium. Chloride and bicarbonate constitute most of the anion concentration of the body. Osmolality expresses the molecular concentration of a solution and reflects its solute and water content. The hypo-osmotic state of cardiac failure has an increase in extracellular water, with sodium dilution in spite of an absolute increase in extracellular sodium. Serum sodium is low during surgery because of the hemodiluted prime. Osmolality is elevated as a result of the glucose and THAM load. After perfusion, the volume of extracellular fluid increases, with no change in total body water. There must be redistribution of fluid as well as the prime being eliminated by the kidneys. The chloride level remains in the normal range throughout. Because the measurement of serum potassium samples only the 2 per cent that is extracellular, it is a poor indicator of the total body potassium. Patients who have had intensive treatment with digitalis and diuretics have reduced total body potassium in the presence of normal serum potassium levels. We add 20 mEq of KCl to the prime. Nevertheless, as seen in figure 3, the serum level decreases to low normal at the end of surgery and shortly afterwards. The recalcification of the ACD blood in the prime causes an elevated serum calcium concentration which lasts through surgery. This may be a level with significant positive inotropic effects, unless the ionized portion is reduced. The decrease of total calcium concentration correlates with a decrease in cardiac output, which is regularly seen on the evening of surgery. After the operation, serum osmolality decreases markedly, as expected from the hyponatremia, because sodium ions account for one half of osmolality. None of these patients were in cardiac failure in spite of the apparent water retention.

Metabolites (figs. 5 and 6). After fasting, most body tissues, including the heart, metabolize predominantly nonesterified fatty acids (NEFA) for energy. Other fuels extracted by the heart, depending on their arterial con-
centration, are glucose, lactate, pyruvate, and ketone bodies. All these are readily available to the myocardium during open-heart surgery.

The concentrations of fatty acids rise steeply before perfusion under the stimulus of catecholamines and heparin. In normal man these acids are cleared from the blood quickly after a large infusion of glucose. During perfusion only a slow reduction in NEFA occurs after the glucose load. The abnormally high amounts of NEFA after the operation can be accounted for by the continued stress, the fasting state, or deficient utilization of sugar.

The glucose level rises before perfusion, as seen in other studies and after epinephrine release. The prime contains a large glucose load, which the body and the myocardium do not appear to utilize. The rate of oxidation of both NEFA and glucose has been found to be decreased by the elevated levels of lactate (fig. 6).

The concentration of ketone bodies also rises before perfusion and remains above normal throughout the operative and postoperative periods. Ketones usually clear from the blood quickly after insulin or a glucose load. That ketones do not follow this course in this situation implicates inadequate carbohydrate utilization. The postoperative ketosis is greatest in children and on the second day after surgery in all types of cases.

Pyruvate concentration does not rise above the normal range, except for a brief period after perfusion (fig. 6). In striking contrast,
the lactate level rises before perfusion, usually in the presence of a low cardiac output. The arterial concentration continues to rise during perfusion and reaches a peak at the end of surgery. Both the glucose load and the hyperventilation present could add to the high blood levels, but the ratio of lactate to pyruvate also rises, pointing to anaerobic metabolism and lactate production in the body. No difference in lactate and pyruvate levels between whole-blood prime or hemodiluted prime has been seen.

Renal Performance. With the Mayo–Gibson oxygenator, there is no urinary output during perfusion if mean arterial pressure is below 60 mm Hg. When blood pressure rises above 70 mm Hg, a diuresis of several hours' duration occurs. Glomerular filtration rate and renal plasma flow are decreased under anesthesia but return to normal by the day after surgery. Much of the diluent from the prime is eliminated by the osmotic diuretic effects of glucose and THAM. Since using hemodilution we have had no cases of primary renal failure after open-heart surgery. Potassium is steadily lost after the operation, and sodium is maximally retained. Renal afferent arteriolar vasoconstriction during perfusion has been suggested as causing reduced glomerular filtration rate. Although elevated concentrations of catecholamines have been correlated with efferent arteriolar constriction and phenoxybenzamine (dibenzyline) has been advocated to block the effect, this drug has not been used in our practice.

Jaundice. One group has found a 13 per cent incidence of jaundice in 232 patients after open-heart surgery. Of their patients with mitral valve disease, 17 of 31 patients developed jaundice. The incidence decreased greatly after accepting, as standard, lower venous pressure and blood volume after operation than in the previous group. Hemolysis, heart failure, and infection were implicated, but not drugs or viral infection. In another series there was a 9 per cent rate of jaundice in 736 operations, with halothane and shock believed to be the most relevant causes. Although halothane has not been shown to be responsible for hepatic necrosis, prudence would seem to dictate not using this anesthetic in patients with previous histories of jaundice.
Hormones. Blood levels of catecholamines and serotonin are reported to be elevated during surgery with whole-body perfusion.\textsuperscript{112} Similarly, the plasma 17-hydroxycorticosteroid level rises during cardiac surgery, and there is no evident inability to increase blood levels even after the severe stress of operation.\textsuperscript{113} Giving massive doses of corticosteroids has been suggested to stabilize the membrane properties of intracellular lysosomes.\textsuperscript{114} The study suggested that the lysosome membrane is damaged by perfusion, with possible fibrinolysis activation and decrease in pulmonary surfactant. After open-heart surgery the levels of certain enzymes have been found to be somewhat greater than after closed procedures.\textsuperscript{115} Glutamic oxaloacetic transaminase, creatine phosphokinase, alpha-hydroxybutyrate dehydrogenase, and lactate dehydrogenase are all increased. This pattern probably reflects the effects of elevated catecholamines during surgery and perfusion.

Damage to the Blood. Patient survival after perfusions of more than three to five hours has been thwarted by damage to blood in the extracorporeal circuit. Hemolysis of erythrocytes is of major concern in the design and operation of a pump-oxygenator.\textsuperscript{116,117} Turbulent flow in the circuit,\textsuperscript{118} subjecting the blood to line pressures that are high and drawing too much air through the intracardiac suction, is destructive to erythrocytes.\textsuperscript{117} Much of the plasma hemoglobin\textsuperscript{119} is handled in the body, but that remaining is a criterion of overall damage to erythrocytes. Platelets decrease markedly during perfusion and disappear dur-
Fig. 6. Mean values of lactate and pyruvate and ratio of lactate to pyruvate in the six patients. Lactate level rises steadily throughout surgery, without a comparable increase in pyruvate level.

Storage of blood, by exposure to plastics and to heparin, and by protamine. Decreases in leukocytes, fibrinogen, and factor V, with an increase in factor VIII, also have been found. Coagulation problems after perfusion are due to a general deficiency of clotting factors, rather than to any specific defect.

A bleeding diathesis is a rare complication now after perfusions up to three hours. Meticulous hemostasis must be practiced. Important also is not only the initial degree of heparinization but the maintenance of high circulating levels. We give 90 mg/m² initially, half that dose after one hour of perfusion, and one quarter the dose each subsequent hour. The aim is to avoid fibrin formation which depletes clotting factors in both the patient’s circulation and the pump-oxygenator. Intravascular clotting and increased clottability of blood enhance fibrinolytic activity.

Elevated blood levels of the fibrinolysin are found during open-heart surgery. In fact, the main clotting defect has been attributed to this. Epsilon-aminocaproic acid (Amicar) is an effective antifibrinolytic agent by preventing activation of fibrinolysin, but routine use during surgery has not, in our hands, significantly reduced the incidence or degree of postoperative bleeding. One report attributes an increase in myocardial contractility to Amicar. Trasylol also seems to be of value in preventing fibrinolysis.

Continued oozing as a result of inadequate neutralization of heparin is possible. Giving protamine sulfate, 1.3 times the total dose of heparin, has, in our experience, resulted in complete neutralization of heparin when blood clotting is tested one half an hour later. Protamine given too rapidly will cause severe hypotension. Fresh whole blood is the best treatment for a bleeding diathesis. Postoperative bleeding which does not diminish in several hours almost always is due to leakage from an artery, vein, or the heart, necessitating reopening the chest.
The Circulation during Surgery. A minimally adequate circulation can be maintained routinely until perfusion begins, even though flow cardiac output exists. The pattern of arterial and venous pressures during perfusion, seen in figure 7, is typical. The initial period of severe hypotension, due to vasodilatation and shift of blood volume to the oxygenator, is largely innocuous. The gradual increase in arterial pressure due to vasocostriction also occurs in the absence of hypothermia. The rate of blood pressure rise is related to the arterial flow and the state of preoperative peripheral resistance. Patients with mitral valve disease, for instance, may have high peripheral resistance before surgery. We do not use vasoconstrictors or dilators to alter arterial pressure or peripheral flow.

The basic principle in reestablishing a satisfactory circulation in order to terminate perfusion is to regain that blood volume which provides ventricular filling pressures slightly above normal. By then stroke volume should have increased, by Starling's law. The appropriate blood volume at that time is governed by the adequacy of myocardial contractility and the state of peripheral vascular tone, bearing no direct relation to blood volume previously. The regulation of the circulation is so dynamic at this time that watching atrial and arterial pressures is the most rational approach to a satisfactory end point.

We increase the patient's blood volume, without altering pump flow, until left atrial pressure is about 15 mm Hg. The latter is always monitored when the patient is coming off perfusion. At that time right atrial pressure is usually a little less than the left. Arterial pressure is usually normal at this blood volume and filling pressure, unless myocardial contractility is poor. Perfusion can be discontinued and the heart takes over. If arterial pressure and atrial pressures decrease upon ending perfusion, more blood is transfused. If arterial pressure decreases and atrial pressures increase to more than 20 mm Hg, myocardial contractility is poor. Perfusion must be restarted while certain measures are taken: further surgical repair to allow the myocardium to improve or air bubbles to escape from the coronary vessels, or contractility is improved by drugs. Figure 7 graphically shows the effect of increasing blood volume in elevating cardiac output and pulsatile pressure. Measurement of left as well as right atrial pressures is important to avoid causing pulmonary
edema. The usual response is for left atrial pressure to rise higher than the right as blood volume increases. If right atrial pressure is higher, right coronary air embolism must be suspected.

After perfusion, further arterial transfusions are given in increments, to supply the highest safe blood volume. At this time we force the mean left atrial pressure up to about 20 mm Hg to obtain the highest cardiac output of any time in the postperfusion period. This maneuver is meant to reverse peripheral vasoconstriction and reestablish complete perfusion of the tissues. We tend to stop transfusion at lower atrial pressures in patients with poor myocardiums. They seem more easily tipped onto the failure side of ventricular function. The abnormally high atrial pressures decrease within minutes owing to loss and redistribution of blood. Myocardial contractility also appears to improve significantly in the half hour after perfusion.

Postoperative Management

Optimal care after surgery is best accomplished by integration of the knowledge and experience of all related medical specialties. There should be free interchange of views, with one service having primary responsibility for writing orders and carrying them out. At our institution, this one service is the cardiac surgical service.

Many events that affect ultimate survival have already occurred by the end of surgery. Factors involved include the severity of the illness necessitating operation, degree of success in correcting the anatomic lesion, adequacy of the perfusion, preservation of the myocardium, and the excellence of anesthetic management and supportive care. The repair must improve hemodynamics significantly or the patient is not likely to survive the operation. Other than elimination of the anesthetic and termination of operation, little else changes as the patient enters the intensive-care area. Monitoring of the same vital signs must continue, plus assessment of consciousness. Concern over the state of gas exchange and adequacy of the circulation goes on; the latter includes treatment of rhythm disturbances and blood loss. Fluids and analgesia are provided cautiously. The first postsurgical days are those of careful watching to detect trends early. Close observation should lead to treatment of a preventive rather than therapeutic nature.

Monitoring

Our patients are monitored by electrocardiogram (five days), atrial pressure (24 to 48 hours), and occasionally, direct arterial pressure (24 to 48 hours). These techniques are in addition to the usual measures of checking blood pressure by cuff and recording pulse, temperature, and blood loss from drainage tubes. An indwelling urinary catheter is used to determine urinary volume only when cardiac output is suspected to be low. The setup in our intensive-care area is seen in figure 8.

Circulation

The principles used at the end of perfusion to establish the best possible cardiac output and tissue perfusion are the bases for keeping that circulation satisfactory. Ventricular filling pressures are primary determinants of cardiac output. Knowledge of these pressures, as inferred from the atrial pressures, allows optimal control of cardiac output by adjusting blood volume. Right atrial pressure is measured after all perfusions. Left atrial pressure gives more precise information of left ventricular function and is used especially after mitral valve surgery. It must be remembered that with the chest closed, the filling pressure is the difference between atrial pressure and intrapericardial pressure. The latter ranges from 4 to 15 mm Hg.

Left atrial pressure maintained at 10 to 15 mm Hg and right atrial pressure at 5 to 10 mm Hg generally result in a stable circulation. As during anesthesia, low cardiac output is treated by transfusion of blood until left atrial pressure reaches 20 to 25 mm Hg or right atrial pressure reaches 15 to 20 mm Hg. Blood transfusion may not increase cardiac output in the presence of severe disturbances of rate or rhythm.

Cardiac output has been found to be lowest a few hours after surgery, rising higher on the next two days, but still not normal. Cardiac output is lower after mitral and multivalvular replacement than after aortic valve replacement.
Increasing the blood volume when left atrial pressure is more than 25 mm Hg or right atrial pressure more than 20 mm Hg may cause myocardial failure with cardiac distention and development of pulmonary edema, in which case either myocardial contractility or distensibility, or both, is impaired. If cardiac tamponade (decreased distensibility) can be ruled out, the low cardiac output is most likely to be due to reduced contractility or valvular dysfunction.

Other signs of tamponade include distant heart tones by auscultation, decreased drainage from the chest tubes after initial excessive drainage, and widening of the mediastinum on roentgenograms of the chest. In operating to relieve tamponade, the surgeon (and the patient) must be ready before induction of anesthesia for immediate opening of the chest. The vasodilating and myocardial depressant effects of anesthetic induction usually will cause blood pressure to fall acutely. The blood pressure will return to a satisfactory level soon after the tamponade is relieved. In addition to improved myocardial distensibility, another reason for improvement is that blood previously held peripherally by the high intrapericardial pressure can now enter the heart.

Several studies have examined blood volume and cardiac output after open-heart surgery. In one study of patients having one to three valves replaced, early postoperative blood volume was decreased. Increase in blood volume enhanced cardiac output, except in the presence of residual valvular lesions or myocardial disease. Another study found a 6 to 14 per cent decrease in blood volume shortly after surgery. Erythrocyte mass decreased more than plasma volume. Extracellular, extracellular fluid was increased, being directly related to length of perfusion and degree of preoperative cardiac failure. Deficits averaging 25 per cent of blood volume an hour after surgery are also reported, with a rise in 48 hours accompanied by a decreasing hematocrit.

The Failing Myocardium

The term “low-output syndrome” has been used when signs of deficient peripheral perfusion, cyanosis, decreased urinary output, low arterial and narrow pulse pressures, anxiety, and venostasis are present, with or without high atrial pressures. Several conditions must be ruled out before the low cardiac output can be ascribed to a deficient myocardium. These include tamponade, rhythm disturbances, and the presence of a residual defect, such as an incompetent valve or a residual septal defect. Only after the atrial pressures have been elevated close to “failure” level, in the absence of tamponade, residual defect, or arrhythmia, can we say that the myocardium is failing. The causes of impaired myocardial function at this time include intractable preoperative congestive failure, myocardial fibrosis or infarction, poor preservation of the myocardium during perfusion, residual pulmonary hypertension, and acidosis. Metabolic acidosis can both cause and aggravate the syndrome.

When the myocardium itself is failing, positively-acting inotropic drugs are indicated. Peripheral vasoconstrictors including norepinephrine are not indicated, since they only increase the burden for the myocardium. Cardiac-stimulating agents are available either for short-term or long-term use. For the patient who cannot maintain a satisfactory arterial pressure, a drip of isoproterenol is probably best. Producing only beta-receptor stimulation, this drug seems to provide a satisfactory increase in cardiac output with better peripheral perfusion, less ventricular irritability, and less stimulation of the central nervous system than epinephrine. A carefully adjusted drip of 0.8 mg in 250 ml is our choice. Epinephrine has similar effects but also stimulates alpha-receptors, causing vasoconstriction in the kidney and skin. In addition, these patients are given digitalis if they have not been receiving this drug previously. Depression of contractility from rapid transfusion of large volumes of acidotic, hyperkalemic, nonwarmed ACD blood is best treated by repeated 100-mg doses of calcium chloride intravenously.

Patients with the less severe states of inadequate circulation also should be treated with digitalis. The criteria for its use are the usual ones: rapid ventricular rates of supraventricular origin or evidence of cardiac failure. Digitalis has a positive inotropic and constri-
Fig. 8. Postoperative cardiac intensive-care setup.

Rate and Rhythm Problems

Rapid ventricular rates of atrial or nodal origin may require treatment with digitalis. Conversely, sinus bradycardia or the excessively slow rate of digitalis toxicity may be reversed by atropine sulfate. Counteracting the vagal effect increases myocardial contractility as well as heart rate, with improvement of cardiac output.

Ventricular ectopic beats and rhythms are ominous and should be treated immediately. A sequence may occur of increasing frequency of ventricular extrasystoles, bigemini, ventricular tachycardia, or sudden fibrillation. In patients who have been receiving prolonged digitalis and diuretic therapy, total body potassium is reduced and serum levels decrease initially after surgery. A significant reduction of intracellular potassium can be present without change in serum potassium. A rational treat-
ment of the hyperirritable myocardium is to give potassium chloride.\textsuperscript{159, 160} A solution containing 40 mEq is started by drip, with close attention to the rate of administration. Combining KCl with isoproterenol is reported to be successful,\textsuperscript{161} with the potassium eliminating the tendency to ectopic beats.

Hyperirritability may be a consequence of such factors as ventriculotomy, prolonged periods of aortic clamping, and development of metabolic acidosis. Another approach to treatment is to depress the ectopic foci with lidocaine,\textsuperscript{162} diphenhydantoin (Dilantin),\textsuperscript{163} quinidine,\textsuperscript{164} or procainamide.\textsuperscript{165} The disadvantage of these drugs is that they also depress contractility and peripheral vascular tone to some extent. Lidocaine\textsuperscript{166, 167} is effective and is used often because it appears to have fewer adverse side effects.\textsuperscript{168} An initial dose of 1 to 2 mg/kg intravenously of 1 per cent lidocaine is followed by a drip of 2 to 4 mg/min until the desired effect takes place. Diphenhydantoin has been commonly used,\textsuperscript{172, 173} but development of arrest or fibrillation has been reported \textsuperscript{174, 175}; the dose used is 50 to 250 mg intravenously, given over one to three minutes. Beta-adrenergic blockade also has been advocated for treatment of arrhythmias. Propranolol\textsuperscript{176, 177} is reported to be effective in atrial and ventricular tachycardia but less successful in atrial fibrillation or flutter. It appears to be useful in both the digitalis-induced and digitalis-resistant tachycardias.\textsuperscript{178} Propranolol decreases cardiac output and heart rate while pulmonary artery pressure rises.\textsuperscript{179} The drug has been found to counteract arrhythmias during certain types of anesthesia\textsuperscript{180} but it is an additional myocardial depressant and may cause bronchoconstriction. The recommended dose is 0.5 to 1.0 mg given intravenously every two to three minutes while arterial and venous pressure and pulse are monitored.\textsuperscript{176}

In our practice, both ventricular tachycardia and fibrillation are converted by direct-current electroshock.\textsuperscript{183} Patients who have had episodes of complete heart block during operation undergo temporary pacing via epicardial wires. PACing can be done by an intravenously placed catheter when block, as from digitalis, occurs after the operation. The heart having severe intractable ventricular arrhythmias or recurring ventricular fibrillation can sometimes be kept regular by pacing via a right ventricular electrode.

**FLUIDS AND RENAL FUNCTION**

After the operation, fluids are restricted to 500 ml/m\textsuperscript{2} from the end of surgery until midnight. The daily allowance is 750 ml/m\textsuperscript{2} on the next two days, some of it orally. The reason for restriction of fluids is the possibility of water retention with reduced osmolality and sodium dilution (fig. 3), which is correlated with the finding of an increase in extracellular fluid\textsuperscript{181} and is related to length of perfusion and degree of persisting congestive failure.

The diuresis induced by the hemodilution and solute load lasts until several hours after surgery. From then on the urine output is directly related to the cardiac output. If the output falls below 15 ml/hr, mannitol (12.5 g) is given by intravenous drip, in addition to the measures to increase cardiac output.

**PULMONARY DYSFUNCTION**

The respiratory function of the lungs likewise is affected adversely by whole-body perfusion.\textsuperscript{182, 184, 185} The syndrome is well recognized, but why it occurs is less clear.\textsuperscript{186} Hypoxia of the pulmonary parenchyma\textsuperscript{187} and a toxic factor produced during perfusion\textsuperscript{188} have been implicated. Patients with severe cardiac disease have been found to have subnormal vital capacity and arterial oxygen tension, the latter due to a high alveolar–arterial difference of oxygen tension on air.\textsuperscript{189} The clinical picture is described\textsuperscript{189, 190} as one of rapid shallow breathing with cyanosis and tachycardia, with or without obvious secretions. Decreased compliance and increased work of breathing elevate oxygen consumption and fatigue the patient.\textsuperscript{191} Differentiating the respiratory from the cardiac causes of dyspnea, cyanosis, and arterial hypotension is essential to proper management.\textsuperscript{192} Diffuse collapse of alveoli rather than lobular atelectasis, is accepted as the main lesion.\textsuperscript{193} Auscultation and the roentgenogram of the chest often do not reveal much until the severe form is present.\textsuperscript{190} There is arterial hypoxemia without difficulty in removing carbon dioxide.\textsuperscript{194, 195} Arterial pH may be elevated owing to the hyperventilation of tachypnea. Cardiac output may not be severely decreased. The amount of intrapulmonary
shunting is related to severity of preexisting lung disease as well as the length of perfusion.

Various detrimental effects of perfusion have been documented. Diffusing capacity has been reported to be decreased after mitral surgery and is attributed to altered ventilation-perfusion ratios. The microscopic lesions found include alveolar collapse, intrapulmonary hemorrhage, pulmonary congestion, erythrocytes in alveoli, and leukocyte infiltration. Changes in surfactant are probably not major factors in pulmonary dysfunction, but may occur secondary to atelectasis and lung damage. In another study, low tension of carbon dioxide in the airway during perfusion caused decreased compliance plus increased work of breathing and resistance to air flow. Compliance has been found to be decreased by continuing ventilation with oxygen during perfusion and by complete deflation of the lungs during this time. Two papers reported an increase in pulmonary vascular resistance after perfusion, with circulating histamine or serotonin suggested as causative.

Most patients can maintain a satisfactory arterial oxygen tension when breathing 40 to 50 per cent oxygen, which is needed for several days. The PaO₂ decreases to 50 to 70 mm Hg when air is breathed. Of primary importance is intensive chest physiotherapy: the forced deep breathing and coughing and the frequent changes of position to raise secretions. The patients who have the severest hypoxemia are those who will not cough. Opiate drugs which depress the respiratory center must be used sparingly. Our maximal dose of morphine is usually 5 gm every four hours for the largest patients. Intermittent positive-pressure breathing with nebulized acetylcysteine or isoproterenol, to break up mucus and to relax bronchial muscle, is helpful for patients who have more severe pulmonary dysfunction.

Approximately 10 to 15 per cent of patients in our practice have the endotracheal tube left in after surgery, for assisted ventilation. They are the most severely ill patients before and after operation, especially those with mitral or multivalvular disease. Other factors influencing this practice are the state of the circulation and how well the patient breathes at the end of surgery. We supply assisted ventilation via endotracheal tube for 48 hours before doing a tracheostomy. The critically ill patient tolerates the tube well; minimal sedation is needed in the more robust ones. The benefits include reduced oxygen needs from diminished work of breathing, plus improved gas exchange and ability to re-expand collapsed alveoli. Extubation is done on the basis of satisfactory PaO₂ while the patient is breathing oxygen spontaneously via the endotracheal tube. The inspired concentration of oxygen must be adjusted to produce a PaO₂ of no more than 150 mm Hg; this level avoids pulmonary changes due to oxygen toxicity. Saline solution (5 to 10 ml) instilled down the endotracheal tube will help to loosen secretions, induce coughing, and facilitate suctioning when the lungs have low compliance from retained secretions.

Disadvantages of assisted or controlled ventilation include an incidence of arrhythmias and possible reduction of cerebral blood flow from respiratory alkalosis. Increased pulmonary arterial and right ventricular pressures, impaired venous return, and decreased cardiac output are some of the adverse effects, plus the technical and nursing problems of ventilator care. In general, the practice should be reserved for the patient who really needs it—then it well may be life-saving.

PSYCHIATRIC AND NEUROLOGIC PROBLEMS

A significant number of patients have varied degrees of dream states, hallucinations, paranoid reactions, or depression. Probably there is an emotional component as well as an undefined biochemical change. The typical time of appearance is on the third to the fifth day. The emotional implications of cardiac surgery are enormous. The realization by the patient that he has survived to face a new kind of life may be involved. However, the picture is also seen in children too young to comprehend the significance of the event. The similarity of the syndrome to sleep deprivation has been suggested. The loss of concept of time, the frequency of events which awaken the patient in an intensive-care unit, and the sensory deprivation are contributory factors.

At least one effort to find a biochemical basis has been reported. A large increase in lactate concentration of the internal jugular
Hemodiluted perfusion with moderate hypothermia is adequate for two to three hours of open-heart surgery. Survival after longer perfusions is jeopardized by excessive damage to blood.

Many biochemical changes that must be minimized or reversed to ensure survival take place during perfusion. Miliary atelectasis causes pulmonary shunting and arterial oxygen desaturation when air is breathed. Electrolyte and water imbalances are more frequent in patients with acquired heart disease. There is a heavy dependence on fat metabolism for energy needs, with ketosis and inadequate utilization of sugar by the body.

Both during surgery and afterward, the circulation is maintained as guided by atrial and arterial pressures. Blood volume is adjusted to retain optimal ventricular filling pressures, hence optimal cardiac output and arterial pressure. The patient with a failing myocardium is treated with digitalis or isoproterenol to increase contractility. Careful application of accepted principles makes it possible for critically ill patients to survive operation if cardiac defects are properly corrected.

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