The Lewis A. Conner Memorial Lecture

Maintenance of Cardiorespiratory Functions by Extracorporeal Circulation

By John H. Gibbon, Jr., M.D.

I AM GREATLY honored to have been selected to give the Lewis A. Conner Lecture before this association. I propose to discuss in this lecture some of the unsolved problems that have arisen from the use of extracorporeal blood circuits, a field in which I have long been interested. Twenty-four years ago at the Massachusetts General Hospital, we constructed an artificial heart-lung apparatus that was capable of maintaining the cardiorespiratory functions of cats for more than 4 hours with the pulmonary artery completely occluded.¹ A few years later, continuing this work at the Harrison Department of Surgical Research at the University of Pennsylvania, we were able to carry the entire cardiorespiratory functions of cats for as long as 26 minutes with prolonged healthy survival of the animals.² World War II interrupted our work in this field, but it was resumed at the conclusion of the war. Six years were then spent in further experimental work in animals, with increasingly long periods of total bypass of the heart and lungs with survival.³⁴ A decreasing mortality rate, and successful experiments in which atrial⁵ and ventricular⁶ septal defects were created and closed. There followed on May 6, 1953, the first successful open-heart operation on a human being in which the entire cardiorespiratory functions were maintained by an extracorporeal circulation.⁷ The heart and lungs were bypassed for 26 minutes while a large atrial septal defect was closed with sutures under direct vision. The patient, an 18-year-old girl, is now, 5 years later, healthy and leading a normal life. Today, as every member of this audience knows, surgical operations on the interior of the heart under direct vision, while the cardiorespiratory functions are maintained by an extracorporeal circulation, are commonplace in many medical centers in this country and abroad. While the mortality in the correction of the simple congenital or acquired cardiac defects now approaches that of other operations of similar magnitude in the hands of experienced surgical teams, much additional knowledge is required to increase the safety of the procedure, especially in the more complicated cases.

This lecture concerns the multitude of physiologic problems that have arisen from the use of a mechanical apparatus to take over temporarily the functions of the heart and lungs. Much virgin territory remains for the competent investigator to explore and conquer.

Blood Flow and Pressure During Extracorporeal Circulation

Very little accurate data exist on cardiac output during operations under general anesthesia.⁸ The flow of blood through the extracorporeal circulation, however, can be easily and accurately measured. There is abundant evidence that low flow rates, 25 to 35 ml. per Kg. body weight per minute, produce harmful effects upon the organs and tissues of the body.⁹¹⁰ It is now generally agreed that flow rates in the neighborhood of 2.3 L. per M.² per minute, or higher, are desirable.¹¹ There is also considerable evidence that the rate of blood flow should be greater in infants and young children than in adults.¹²

Initial Fall in Mean Pressure

The fall in mean blood pressure, which is not infrequently seen on the initiation of total bypass, is generally assumed to be the result

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of a blood flow through the extracorporeal circuit that is less than the cardiac output of the patient immediately preceding total bypass. The addition of blood to the combined system of the subject’s vessels and the extracorporeal circuit is frequently resorted to in order to increase the blood flow and to raise the subject’s blood pressure. Yet if the presumption is correct that the observed fall in blood pressure on initiating total bypass results from a blood flow through the circuit less than the preexisting cardiac output of the subject, it is clear that attention must be directed towards overcoming the technical factors that may contribute to this diminished blood flow. An example of such a technical factor is the decreased internal cross-sectional area of the cannulae in the venae cavae, as compared with the internal cross-sectional area of the cavae themselves. Obviously the nearer these cross-sectional areas approach one another, the easier it will be to obtain the same venous blood flow, and thus the same arterial blood flow and cardiac output, as existed before. Another technical factor that may limit blood flow through the circuit is the resistance offered by the cannula returning the blood to the subject’s arterial system. There is a limit to the pressure which can be employed to overcome this resistance because of (to mention only one facet) the hemolysis resulting from the passage of blood from a high pressure area to a low pressure area through a narrow orifice.\textsuperscript{17}

If, on the other hand, the above-mentioned presumption is inaccurate, and the flow of blood through the extracorporeal circuit is as great, or greater than that which existed immediately prior to initiation of total bypass, then the fall in blood pressure must be related to a decrease in peripheral resistance. Under these circumstances, adding blood to the circuit would compensate for the blood pooled in the area of vascular relaxation. In this case, vasodepressor substances in the blood in the extracorporeal circuit should be sought and if possible eliminated. Other factors, of course, may be responsible for the vasodilatation, such as reflexes arising from baroreceptors in the walls of the atrial,\textsuperscript{18} the venae cavae, or pulmonary vessels.

**Volume of Blood in the Lungs**

On the initiation of complete cardiopulmonary bypass, theoretically the volume of blood in the lungs should be markedly reduced, thus increasing the blood volume in the combined system of extracorporeal circuit and the subject’s vascular system. This additional volume should counteract to some extent vascular pooling in the subject’s body, if this is the basis of the observed fall in blood pressure. In the acyanotic patient, the foregoing remarks should be true. On the other hand, in the cyanotic patient who already has a large bronchial artery component entering the pulmonary capillaries, the cessation of blood flow through the pulmonary arterial tree should tend to reduce the resistance in the pulmonary capillaries and to increase the blood flow into the left side of the heart from the bronchial arteries through the pulmonary capillaries and veins. Experience with open-heart operations in the laboratory and in human patients has shown the importance of providing an escape for this blood from the left side of the heart when cardiac arrest is employed.\textsuperscript{19-21} Accurate data on the blood volume and blood flow through the lungs should be obtained before, during, and after bypass, in order to provide for the greatest safety of the patient during the operation.

**Reversal of Flow in Aorta**

In much of the early experimental work on animals, the arterialized blood from the extracorporeal circuit was returned to the subject’s arterial system by way of a centrally directed cannula in a femoral artery. In much of the early human operative work this blood was returned through a centrally directed cannula in the left subelavian artery. In the last few years, however, most surgeons have employed the femoral artery for return of this blood as in the early animal experiments. This shift was made because of the technical difficulty in exposing the left subelavian artery through the usual transverse thoracotomy incision, the inaccessibility of the artery from a
median sternotomy, and also because it shortened the time during which the thorax was open. While many of the aortic branches, i.e., innominate, left carotid, left subclavian, intercostals, and renal arteries, leave the aorta almost at right angles, the mesenteric arteries form an obtuse angle with the normal direction of blood flow. Due to piezometric effects, it is possible that the flow of blood through the mesenteric arteries and celiac axis may be considerably reduced when the direction of blood flow is reversed in the aorta by employing a centrally directed cannula in the femoral artery to return the arterialized blood. If the femoral artery continues to be employed for this purpose, the flow through the superior mesenteric artery as well as the other great branches of the aorta should be measured before and after reversal of the blood flow. The development of an accurate electromagnetic blood flow recorder provides a suitable technical device for obtaining this much-needed information. Dr. John Templeton of our department has recently abandoned the femoral artery, and now returns the arterialized blood through a cannula inserted into the ascending aorta through a stab wound. This method eliminates reversal of flow through the aorta, permits the employment of a cannula with a larger internal lumen than the femoral artery, obviates the possibility of impairment of the blood supply to a lower extremity, and is technically simpler and more rapid than femoral artery cannulation.

Relation of Oxygen Consumption to Blood Flow

Many recent reports have shown that, within limits, the oxygen consumption of the body during extracorporeal bypass of the heart and lungs is directly related to blood flow. A blood flow significantly below basal levels is associated with decreased oxygen consumption. This decrease in oxygen consumption results in a metabolic acidosis that progressively increases in severity throughout the period of low blood flow. Therefore, in human patients maintained at normal, or only slightly reduced body temperature, it is highly desirable to maintain rates of blood flow high enough to avoid tissue hypoxia. Certainly the postoperative period is hazardous enough without imposing the additional burden of metabolic acidosis.

Mean Aortic Blood Pressure During Bypass

In the mammalian vascular system, because of variable peripheral resistance, blood flow and blood pressure will not always vary in the same direction or to the same extent. Recent experimental work with extracorporeal circulations has shown that renal function becomes impaired as the mean aortic pressure declines, and ceases at mean pressures below 50 mm. Hg. Thus, not only should the blood flow be kept at nearly normal basal levels to avoid tissue hypoxia, but also the blood pressure should be kept at a mean level of 80 mm. Hg, or above, in order to ensure normal function of the kidneys and of other bodily organs and tissues. Further work in this area, particularly regarding hepatic function, is required.

Tension of Gases in Blood

Excessive Oxygen Tension

Pendido et al. have shown that with a bubble-type oxygenator, the tension of oxygen in the blood may reach or exceed 700 mm. Hg. There is, of course, no advantage to oxygen tensions of this magnitude in blood of normal hemoglobin content, as the hemoglobin will be normally saturated with oxygen at a tension in the neighborhood of 100 mm. Hg. Theoretically, there might be a slight advantage to oxygen tensions approaching 700 mm. Hg during extracorporeal bypass if the blood flow were inadequate. Every 100 ml. of blood under these circumstances would then carry 2.1 ml. of oxygen in physical solution in the plasma in addition to the 20 ml. carried in the form of oxyhemoglobin, whereas normally with 100 mm. Hg oxygen tension, only 0.3 ml. of oxygen is carried in the plasma of each 100 ml. of blood. This approximately 10 per cent increase in oxygen-carrying capacity per unit of blood theoretically could compensate
for a 10 per cent decrease in the rate of blood flow to the tissues. On the other hand, high tensions of oxygen in the blood introduce the hazard of oxygen emboli in the vascular system if the patient’s body temperature is above the temperature of the blood as it leaves the artificial oxygenator.

Oxygen poisoning from the prolonged inhalation of 100 per cent oxygen is well documented in both animals and man. A tension of oxygen in the neighborhood of 700 mm. Hg for 1 hour is not toxic in man, and no ill effects have been noted in dogs during cardiopulmonary bypass for 45 to 60 minutes with oxygen tensions of 600 mm. Hg in the arterial blood. It will obviously not be easy to obtain accurate data on this matter because of the difficulty of controlling other parameters during the period of perfusion. Measurements of myocardial oxygen tension, by the methods which have been so admirably developed by Montgomery, have already been reported during hypotension. Studies during cardiac bypass should provide much useful data in this field.

**Carbon Dioxide Tension before, during, and after Bypass**

Some surgeons have recommended hyperventilation prior to bypass in order to reduce the carbon dioxide tension below normal. This has been particularly advocated during the use of hypothermia alone for open cardiopulmonary bypass. However, Bigelow has shown a subsequent increase in metabolic acidosis in patients subjected to respiratory alkalosis during the induction of hypothermia, and mild degrees of hypothermia are commonly used in association with extracorporeal circulation. Vigorous hyperventilation by the anesthesiologist rarely reduces the carbon dioxide tension below 20 mm. Hg. In conscious man, very little impairment of mental acuity has been demonstrated until the carbon dioxide tension of arterial blood is reduced below 25 mm. Hg. Nevertheless, lowering of carbon dioxide tension is known to produce cerebral vasodilatation. Creech, however, in a recent report observed no increase in cerebral blood flow in animals on extracorporeal circulation when 5 per cent carbon dioxide and 95 per cent oxygen were substituted for 100 per cent oxygen in the extracorporeal lung. If these observations can be substantiated, there would appear to be no advantage in raising the carbon dioxide tension during extracorporeal circulation in order to increase cerebral blood flow.

**Relation between Respiratory and Metabolic Acidosis**

Holaday has reported that respiratory acidosis tends to produce metabolic acidosis. Recent observations in our laboratory have not confirmed this. Dogs rebreathing carbon dioxide for a period of 2 hours, but with a normal arterial oxygen saturation, exhibited a lowering of lactic acid in the blood. There was the expected marked elevation of lactic acid in the blood in another group of animals breathing diminished concentrations of oxygen, but with normal carbon dioxide tension.

We, and others, have adopted the practice, when using extracorporeal circulation in patients, of maintaining a carbon dioxide tension of about 40 mm. Hg prior to and during bypass. Under these circumstances, any fall in the pH of the blood at the termination of the extracorporeal circulation is indicative of metabolic acidosis. This, fortunately, is usually of a degree not greater than that seen following most operations of similar magnitude. Its occurrence is obviously due to some degree of tissue hypoxia. Measures directed toward the avoidance of such metabolic acidosis should, therefore, be concerned with maintenance of adequate blood flow and pressure and the carrying of a normal volume of oxygen per unit volume of blood during the extracorporeal bypass.

**The Heart during and after Bypass Induced Cardiac Arrest**

Probably the most interesting development in open cardiac surgery since the initiation of extracorporeal circulation is the concept of elective cardiac arrest. Cessation of myo-
cardiac contractions and elimination of cardiac venous blood from the operative field allows the intracardiac surgical procedure to be performed with greater dispatch and accuracy. Elective arrest was first suggested by Melrose, who induced cardiac arrest in dogs by injecting a solution of potassium citrate into the ascending aorta proximal to an occlusive clamp after the establishment of extracorporeal circulation. Effler was the first to induce arrest by this means in human patients. Lam employed acetylcholine for the same purpose in patients. Potassium citrate has been used more generally than acetylcholine, probably because potassium salts produce more complete relaxation of the heart. When acetylcholine is used, it is more difficult to produce complete arrest and the operative manipulations occasionally initiate contractions that may prove troublesome to the surgeon. Combinations of potassium and magnesium salts and other substances have also been used to produce cardiac arrest.

Another method of inducing cardiac arrest during extracorporeal circulation consists in merely cross-clamping the aorta distal to the coronary ostia. This "anoxic" arrest has been employed successfully in patients by a number of surgeons, who prefer it to the use of potassium or acetylcholine. Some surgeons who formerly employed potassium arrest now use it rarely because of the increased incidence of heart block in patients with myocardial damage and coronary insufficiency and because of the conviction that the heart does not function as well during the immediate postoperative period following such arrest. This conviction is widely held despite the demonstration that no deleterious effect upon the capacity of the heart to do work can be demonstrated following potassium citrate arrest. Induced cardiac arrest is usually not employed for the simpler lesions, such as incomplete atrial septal defects and pure pulmonary stenosis. It is generally employed in patients with the tetralogy of Fallot or ventricular septal defects.

The whole problem needs further investigation and clarification. The proponents of "anoxic" arrest produced by merely cross-clamping the aorta, state that all cardiac arrest is anoxic. This is true because the metabolism of the myocardium continues even when it is not contracting. Nevertheless, there is a marked difference in the degree of hypoxia of the myocardium resulting from potassium or acetylcholine arrest which occurs promptly, and that produced in "anoxic" arrest which occurs more slowly with progressively weaker contractions of the hypoxic left ventricle. The question to be answered may be stated simply. Which method is least harmful to the heart as measured by the ability of the heart to contract at a normal rate, rhythm, and force following the period of arrest?

Cardiac Hypothermia

Induced cardiac arrest has given rise to many other physiologic problems. We do not know whether some of the observed cardiac arrhythmias in the postoperative period are due to some special sensitivity of the sinoatrial node, the atrioventricular node, or the bundle of His to hypoxia and the accumulation of acid metabolites. With the ascending aorta cross-clamped and no blood flowing through the coronary vessels, the temperature of the heart will eventually fall to the ambient room temperature. The rate at which this drop in temperature occurs should be measured. It would appear obvious that the temperature of the thick-walled ventricles, and particularly of the left ventricle, which is unopened and contains blood, should fall less rapidly than the thin-walled atria. The effect such temperature differences may have on the spread of the electrical excitation waves, or the coordinated muscular contraction of the entire organ, is unknown and merits investigation. If differential cooling should prove to be responsible for any of the cardiac difficulties in the postoperative period, then the results of uniform perfusion of the organ with a cold fluid should be explored. The cold would then be uniform and the heart could be rapidly cooled and rapidly rewarmed. The local hypothermia during bypass could be of any desired degree and might increase the safe duration of arrest by decreasing metab-
olism and the production of acid metabolites. The fluid used to perfuse the coronary arteries might be cold blood with a sufficient concentration of potassium salt or acetylcholine to maintain the arrest, or it could consist of cold plasma to maintain anoxic arrest. Paradoxically Kaplan and Fisher, working with hypothermic dogs, found better tolerance of the heart to caval occlusion when the pericardium was perfused with warm saline. Much remains to be explored in this field.

Postoperative Pulmonary Dysfunction

Rather unexpectedly, postoperative pulmonary dysfunction has probably contributed more than other complications to the morbidity of open cardiac operations with an extracorporeal circulation. The usual postoperative pulmonary difficulties, such as retention of tracheobronchial secretions, or inadequate depth of respiration, appear to be enhanced after operations employing an extracorporeal circulation. Over and above these common difficulties, there not infrequently occurs in the immediate postoperative period some impairment of the gas exchange function of the lungs. This pulmonary dysfunction is manifested by both hypoxemia and hypcapnia, and is apparently unrelated to left heart failure.

Bronchial Artery Component of Pulmonary Blood Flow

It seems reasonable to assume that this pulmonary dysfunction arises during the period of bypass from some change in the milieu interieur of the pulmonary capillaries, the alveolar membranes, or the lining of the bronchioles. During bypass with cessation of blood flow through the pulmonary artery, there continues to be a small circulation of blood through at least some of the pulmonary capillaries by way of the bronchial arteries. As mentioned earlier, this flow of blood probably increases, because of decreased pressure in the pulmonary capillaries, when the flow through the pulmonary artery ceases. In cyanotic patients, the blood flow through the bronchial arteries may reach huge proportions. In the cyanotic patient without a septal defect, and without cardiac arrest, a vent need not be provided for the blood entering the left heart, because this blood will be ejected into the aorta by the left ventricle which is being perfused with oxygenated blood. If cardiac arrest is employed under these circumstances, a vent should be supplied for the escape of blood from the left atrium to prevent a gradual rise in pulmonary venous and capillary pressure with resultant pulmonary edema. Of course, cardiac arrest is rarely employed in such patients.

In the acyanotic patient with an atrial septal defect, cardiac arrest is also rarely employed, and even if it were, there would be an adequate vent for the blood in the left atrium through the septal defect when the right atrium is open. In the usual case without cardiac arrest, the presence of blood in the left atrium helps to avoid air embolism, and after the defect is closed, there is no danger of increased venous pressure with a resultant pulmonary edema, as the left side of the heart is able to eject any blood which reaches it because it is being perfused with oxygenated blood.

In the acyanotic patient with a ventricular septal defect and a left-to-right shunt, cardiac arrest may or may not be employed. If cardiac arrest is not employed, there is no danger of increased pulmonary venous pressure either before or after closure of the defect. If cardiac arrest is induced in these patients, a vent for the escape of blood from the left side of the heart should be provided after the defect is closed, unless the aortic clamp is promptly removed and vigorous cardiac contractions begin at once.

In the cyanotic patient with a septal defect and pulmonic stenosis, cardiac arrest likewise may or may not be employed. In any case, the flow of blood into the left atrium contributed by the bronchial arteries can be expected to be quite large. In such cases, when cardiac arrest is employed, it is always advisable to provide a vent in the left side of the heart for the escape of blood after closure of the septal defect.

The vents in the left side of the heart can be provided by a catheter inserted in the left ventricle near the apex of the heart or, more
simply and easily, by a catheter inserted into the left atrium through the left atrial appendage. Blood draining from such a catheter is, of course, returned to the extracorporeal circuit. By providing such vents in the left side of the heart when they are indicated, pulmonary edema from elevated pulmonary capillary pressure can be avoided.

**Pulmonary Ventilation during Bypass**

It is evident that during total bypass of the heart and lungs, ventilation of the lungs to provide oxygen and to eliminate carbon dioxide is not necessary. In the cyanotic patient with a large bronchial arterial flow of blood through the pulmonary capillaries, ventilation of the lungs during bypass is probably not harmful, although it could be expected to reduce carbon dioxide tension and raise the pH of the blood. In the cyanotic patient with a small bronchial arterial flow, pulmonary ventilation is obviously not necessary, and conceivably might be deleterious if it produced significant changes in the composition of the alveolar gases. Vigorous ventilation of the lungs in an acyanotic patient during bypass, with only a small flow of blood through some of the pulmonary capillaries from the bronchial arteries, would certainly reduce the normal carbon dioxide tension of the alveolar gas from 40 mm Hg to almost zero, unless carbon dioxide were added to the ventilating gas. If, as is frequently the case, the ventilating gas is oxygen, ventilation during the period of bypass would raise the tension of oxygen in the alveolar gas from its normal level of 90 or 100 mm Hg to the neighborhood of 700 mm Hg. Finally, if a high gas flow, nonrebreathing technic were employed, harmful drying effects might be produced on the mucous membrane lining the tracheobronchial tree, as well as on the extremely thin cells of the alveoli themselves.

It seems reasonable to avoid these possibly deleterious changes in the water vapor and other gas concentrations of alveolar air by omitting pulmonary ventilation during bypass in the acyanotic patient. Suggestive evidence that such changes are deleterious to the function of the lungs in the postoperative period was obtained in our laboratory several years ago in experiments on normal dogs. The right and left lungs were ventilated separately, but equally, by appropriate endobronchial technics, and the oxygen consumption of each lung was measured with the thorax open. The pulmonary artery of 1 lung was then occluded for a period of 1 hour, while the lungs were ventilated as before. Following release of the occlusion, the oxygen consumption of each lung was again measured. In the majority of experiments, the oxygen consumption of the lung in which the pulmonary artery had been occluded fell below the preoclusion measurement. After a period of 2 to 4 hours, the oxygen consumption of this lung tended to return to its previous level. On the other hand, when the lung with the occluded pulmonary artery was held stationary in an inflated position, the decline in oxygen consumption was not observed in the postocclusion period. These experiments suggest that ventilation of a lung without blood flow through the pulmonary artery may produce at least temporary impairment of pulmonary function. Therefore, while ventilation of the lungs of cyanotic patients during bypass may not be harmful, in the acyanotic patient, such ventilation may contribute to postoperative pulmonary dysfunction.

**Atelectasis and Pulmonary Inflation**

It is generally considered advisable to avoid prolonged complete collapse of the lungs during thoracic operations because, among other reasons, it becomes difficult to reinflate fully the lungs, and to do so excessively high inflationary pressures must be employed. If, then, the lungs are not ventilated during bypass, it is probably advisable to keep them inflated, though stationary. The degree of inflation probably need not be more than that existing in the normal position of expiration. The lungs then will not be tense and will not interfere with surgical exposure of the heart.

**Postoperative Aids to Pulmonary Function**

If all the precautions outlined above are taken, the patient's pulmonary function dur-
ing the first few hours, or even the first day or 2 after operation, may still not be ade-
quate to avoid hypoxemia and hypercapnia. 
This may be true, even though the usual post-
operative measures to aid pulmonary function 
are employed. These measures include the 
breathing of a moist atmosphere enriched 
with oxygen, a tracheostomy to decrease re-
spiratory dead space, and the encouragement 
of deep breathing by the alleviation of pain 
by drugs. The use, where possible, of median 
sternotomy and unilateral thoracotomy, which 
are less painful with respiration than the 
usual transverse thoracotomy, results in less 
impairment of respiratory excursions. In the 
experience of our group, the most important 
single means of aiding pulmonary function 
in the postoperative period is the use of in-
termittent positive pressure breathing. Not 
only is ventilation immediately improved, but 
secretions in the tracheobronchial tree are 
cleared by the great velocity of gas flow during 
the early part of expiration. Further study of 
this interesting field of postoperative 
pulmonary function is indicated.

LENGTH OF PERFUSION

If an extracorporeal blood circuit exactly 
duplicated the functions of the heart and 
lungs, then, theoretically, there would be no 
limit to the period of time that such an ap-
paratus could be used to substitute for these 
natural functions. Unfortunately such is not 
the case. Harmful phenomena occur in the 
extracorporeal blood circuit, or arise from the 
method of connecting the vascular system of 
the subject to the extracorporeal circuit, so 
that there is a limit to the time during which 
an extracorporeal circulation can be used 
safely. Much remains to be learned concerning 
these phenomena and their prevention.

Partial bypass of the heart and lungs can 
be tolerated by animals for periods of 4 and 
5 hours with low mortality, whereas total by-
pass with open cardiotomy for a period of 2 
hours in dogs results in a 50 per cent mor-
tality.47 Undoubtedly with both partial and 
total bypass, the harmful phenomena that 
occur in the extracorporeal circuit are cumu-
lative, and finally reach such a degree that 
they can no longer be tolerated by the organ-
ism. When the same connections to the vas-
cular system of the subject are used, there 
are 2 major differences between partial and 
complete bypass of the heart and lungs. The 
first is that in partial perfusion, only a part 
of the blood reaching the arterial system has 
passed through the extracorporeal circuit, and 
thus it will take a longer time for the harmful 
phenomena to become lethal. The second 
major difference is that in total bypass, blood 
no longer flows through the pulmonary capil-
laries except for the small component entering 
them by way of the bronchial arteries.

The measurable harmful phenomena that 
occur in the extracorporeal circuit are sur-
prisingly few. They consist almost entirely 
in damage to the corpuscular elements of the 
blood. In brief, these phenomena consist of 
a gradually progressive hemolysis, a drop in 
the number of white blood cells to perhaps a 
fifth of their former concentration, and a 
sharp and profound thrombocytopenia. The 
2 latter phenomena occur rapidly with only 
a very slow further decline. The hemolysis 
is less rapid, but exhibits the same general 
type of curve. The observed phenomena 
may be related to the age of the individual 
corpuscular elements, especially as regards 
resistance to trauma of the erythrocytes. How-
ever, no adequate data exist to support this 
hypothesis. It might well be studied by tag-
ging the corpuscular elements with radioac-
tive isotopes.

The lung has long been known to be an effi-
cient filter for the blood. Undoubtedly other 
capillary beds act in a similar fashion, but no 
other capillary bed in the body filters all of 
the blood. Some of the destroyed leukocytes 
and thrombocytes very likely remain attached 
to the internal lining of the extracorporeal 
circuit. The free hemoglobin is removed 
largely by the reticuloendothelial system.

In partial bypass, no detectable alteration 
of the blood occurs consistently, aside from 
destruction of the cellular elements. With 
total bypass, as mentioned earlier, inadequate 
oxgenation of the tissues may result in 
metabolic acidosis if the blood flow and blood
pressure fall below a certain minimum level. No other changes are consistently detectable in the blood. For example, there is no significant alteration in the level of fibrinogen during 2 hours of total bypass in animals, and only 2 of 16 animals exhibited measurable degrees of fibrinolysis.  

**Summary**

The experimental use of extracorporeal blood circuits during the past 24 years, and the clinical experience of the past 5 years, have posed many interesting physiologic problems. A few of these have been solved for practical purposes by much excellent recent investigation. Among those remaining to be solved the following might be listed:

On the initiation of total bypass of the heart and lungs by an extracorporeal circulation, is the blood flow to the body increased or decreased in relation to the cardiac output before bypass? Available technical methods exist to answer this question.

The volume of blood in the lungs before, during, and after total bypass should be determined. Technics are available to accomplish this.

The rate of blood flow through the major branches of the aorta should be measured before and during bypass with a normal direction of flow in the aorta, as well as with reversal of flow. The recent perfection of square-wave electromagnetic blood flow recorders makes this a relatively simple task.

Adequate studies have been performed to indicate the importance of maintaining a nearly normal blood flow and pressure during perfusion. Further investigation is needed to determine how long high oxygen tensions may be maintained in the blood without toxicity. The conflicting evidence concerning the relation of metabolic to respiratory acidosis should be resolved.

Induced cardiac arrest requires a great deal of further study. What is the best method of producing arrest, and how long and under what circumstances can it be safely maintained?

Finally, the subject of postoperative pulmonary dysfunction needs much further study. The results of such study may well lead to a reduced morbidity and mortality following operations involving open cardiectomy with the extracorporeal circulation.

**Summario in Interlingua**

Le uso experimental de circuitos extracorporal de sanguine durante le passate 24 annos e le experiencia clinic del passate 5 annos ha sublevate multe interessantae problemas physiologic. Plures inter illos esseva resolvite, in tanto que lor signification practic es concernite, per multe excellentae investigationes in le recente passato. Quanto al problemas que remane a solver, le sequentes merita esser listate:

Post le transferimento completo del funciones cardiorespiratori al circulation extracorporal, es le fluxo de sanguine a in le corporo augmentate o reduite in comparation con le rendimento cardiace ante le institution de ille transferimento? Le methodos technic pro resolver iste question es jam disponibile.

Le volumine de sanguine in le pulmones ante, durante, e post le transferimento completo debea esser determinate. Le technicas pro effectuar tal determinationes existe.

Le intensitate del fluxo sanguinee a transverso le major brancae del aorta debe esser mesurate ante e durante le transferimento, con fluxo normal in le aorta e etiam con fluxo revertite. Le recente perfection de electromagnetic fluxometros a undas quadrato pro le mesuration de fluxos sanguinee rende iste problema relativamente simple.

Studioes adequate ha essite effectuate, demonstrante le importanza de mantenir un quasi normal fluxo e tension de sanguine durante perfusiones. Investigationes additional es requirite pro determinar durante quante tempore alte tensiones de oxygeno pote esser mantenite in le sanguine sin effectuar toxicitate. Le contradictiones in le datos concernente le relation inter acidosis metabolic e acidosis respiratori debe esser resolvite.

Induce arresto cardiac require un grande concentration de studios additional. Qual methodo es le melior pro effectuar arresto cardiac, e durante quante tempore e sub qual conditiones pote illo esser mantenite sin risco?
Finalmente, le tema del post-operatori dysfunction pulmonar require multe studio additional. Le resultatoes de tal studios va forsan caur un reduction del morbiditate e mortalitate post operationes in que cardiotomi aperte es interprede con le adjuta de un circulation extracorporee.

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