Laboratory work preceding the first clinical application of cardiopulmonary bypass

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As a young surgeon tending to a patient who had suffered a massive pulmonary embolism, Dr. John H Gibbon Jr. envisioned the usefulness of an extracorporeal circuit in the surgical management of both pulmonary embolism and in the correction of congenital intracardiac defects during cardiopulmonary bypass (CPB) and under direct vision. Gibbon first demonstrated the feasibility of such an operation in 1937, when he was able to clamp the pulmonary artery of a cat while an extracorporeal circuit maintained the cardiorespiratory function of the animal. The extracorporeal circuit that he used in the original animal experiments contained a rotating cylinder-type oxygenator in which a film of blood coated the internal surface of a rotating cylinder. The blood pumps were of the Dale-Schuster type in which the blood contained within a finger cot was propelled by exerting alternate positive and negative pressure on the outer surface of the finger cot (Figure 1).

In the spring of 1953, Dr John Gibbon Jr. performed for the first time closure of an intratrial septal defect in an 18-year-old female patient while her cardiorespiratory functions were maintained by an extracorporeal circuit containing a mechanical heart and a mechanical lung.

Following the second world war, Mr Thomas J Watson, Chairman of the Board of the International Business Machine (IBM) Corporation, became interested in helping to develop a heart-lung machine, and he assigned the experimental laboratory to the construction of a heart-lung machine. Don Rex was the engineer for the project. The new machine was basically the same as Gibbon’s original device, differing only in the enlarged size of the oxygenator with the expectation that it would be able to maintain the cardiorespiratory function of larger experimental animals. The pumps were now rotating pumps, and the collecting bowl at the bottom of the oxygenator cylinder was gold plated with the purpose of minimizing the effect of the interaction of blood with stainless steel. The control of the arterial pump was photoelectric. The entire machine was contained in two precisely made cabinets of stainless steel and glass (Figure 2).

Experience with this device was disappointing. Very few dogs were survivors of even partial perfusion. It was clearly obvious, as a result of these experiments, that the oxygenation was insufficient for small dogs. To have further enlarged a smooth film oxygenator of this type, using centrifugal force to provide sufficient film for oxygenation for a human patient, would have resulted in an unrealistic geometric design and a huge hold up of blood. There was also an excessive amount of hemolysis in the blood within the circuit, and the photoelectric control, which safeguarded against air embolization, malfunctioned repeatedly, resulting in air embolization to the systemic arteries. Using this device, a small number of experiments were successful in which the vena cavae were occluded and the cardiorespiratory functions of the dog were maintained with the heart-lung machine.

It was decided at this point to use the existing machine only as a structure for further testing of new and advanced components. Animal experiments were suspended. Richards and Drinker introduced turbulence into a film oxygenator of early design and demonstrated that the degree of oxygenation could be vastly enhanced. Accordingly, Stokes and Flick lined the cylinder of the existing oxygenator with a stainless steel screen and were able to show a significant improvement in the degree of oxygenation when turbulence was introduced in this manner. The inadequacy of the photoelectric control was a matter of great importance since a fail-safe system during CPB is required to prevent air embolization. Subsequently, as the ex-
periments proceeded, additional problems became evident — namely that of acidosis during the thoracotomy and during perfusion, the recovery of cardiac venous blood during the open cardiotomy without loss, and the recovery of blood and foam originating in the contracting left ventricle in the presence of interatrial and interventricular septal defects.

Beginning in 1950, I became associated with Dr. Gibbon as a research associate in the surgical research laboratory. All animal experimentation with the first IBM machine was terminated. The apparatus was considered unsuitable for human use and was to be used solely for testing modifications and improvements to an improved extracorporeal circuit. A new machine was to be constructed with the aim of incorporating anticipated improvements and developments. The first priority was to develop an oxygenator capable of supporting the cardiopulmonary function of a large dog. The engineers involved in this project were Alf Malmros, Leo Farr, and John Engstrom. A small test oxygenator was constructed using 2 x 12-in. strips of screens of different wire sizes, mesh sizes, and materials suspended from a weir of 0.015 in. in width. This test device was then suspended in a cylinder containing oxygen (Figure 3). The oxygenation characteristics of each surface were measured as blood flowed down the surface.

Data derived from these experiments provided the basis for the design of a new oxygenator using a turbulent film. The first geometric configuration

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**Figure 1** Photograph of the Gibbon heart-lung machine used during experimental surgery in the 1930s. The oxygenator was a rotating cylinder film-type and the pumps were of the Dale-Schuster-type. (Reprinted from Miller BJ. *Surg Gynecol Obst* 1982; 154: 404, with permission.)

**Figure 2** Photograph of the IBM-Gibbon heart-lung machine model I, circa 1950. The pumps (right-hand cabinet) were of the DeBakey roller-type. (Reprinted from Miller BJ. *Surg Gynecol Obst* 1982; 154: 405, with permission.)
consisted of a screen cylinder with a superimposed cone upon which blood was deposited from a rotating jet. Filming of the blood was not uniform, and the blood tended to descend on the screen surface in rivulets, producing a thick film of small surface area. Only after painting the screen with a protein solution, such as a dilute solution of blood, could a complete film be established. The final design of the oxygenator consisted of six stainless steel screens, measuring $30.5 \times 45$ cm in size, suspended from individual weirs or a series of slots, each measuring 0.015 in. in width.

It was expected that blood pumped through the weir, which was located in the floor of the distribution chamber and at the top of each screen, would be uniformly distributed along the entire width of the screen. Again, filming was incomplete and erratic. A uniform film of blood was able to be established by flooding the oxygenator case with saline solution and then, as blood was being pumped into the distribution chamber, the mixture of saline solution and blood was rapidly emptied. The falling layer of blood located at the top of the saline solution painted the screen, and the film was then maintained by the continuous recirculation of blood from the bottom of the oxygenator case to the distribution chamber. To reduce the volume of blood contained within the oxygenator assembly, the pool at the bottom was replaced, in part, by a block of plastic material, which also served to maintain the position of the screens. The rate of flow through the recirculating pump was maintained at the maximum rate for which the oxygenator was designed. With six screens, this oxygenator could raise the saturation of blood with oxygen from 65% to 95% at a flow rate of 2500 mL/min (Figure 4).

The original photoelectric level control device used for controlling the rate of evacuation of the oxygenator and control of the arterial pump functioned erratically. Proper control of this pump was extremely critical lest air be pumped into the arterial

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**Figure 3** Drawing of the model trough oxygenator used to test various wire screens or other surfaces to obtain adequate blood mixing and optimal gas exchange. (Reprinted from Miller BJ et al. *Ann Surg* 1951; 134: 696, with permission.)

**Figure 4** Photograph of the six-screen film oxygenator (two views). Side view is shown on left and top view on right. (Reprinted from Miller BJ et al. *Ann Surg* 1951; 134: 698, with permission.)
Figure 5 Drawing of the capacitor servo-regulated system. The venous pump (D) was servo-regulated by a pressure sensor (B) located before the roller pump linked to an electronic control (C) to automatically reduce venous pump speed in the event of caval collapse. The arterial pump (P) was also servo-regulated by a level sensor (N) located at the bottom of the stationary 6-screen (J) film oxygenator. Oxygen gas was added at the top (F) of the oxygenator case and exhausted at (H); venous blood flow was distributed by a series of weirs (I and I') located at the top of the oxygenator case. The recirculation pump (E) was set to operate at a higher flow rate than the sum of flow rates from the venous and arterial pumps to maintain blood filming on the screens regardless of arterial pump flow rate. A vent (G) was used during priming. The reverse flow arterial filter (Q) is shown located after the arterial pump for removal of air. (Reprinted from Miller BJ et al. Ann Surg 1951; 134: 699, with permission.)

Figure 6 Schematic drawing of the complete extracorporeal circuit. Note two venous pumps (C and D) servo-regulated by sensors (A) to permit uninterrupted flow in the event one venous cannula became obstructed. A burette (B) permitted the addition of volume to the circuit. The oxygenator, or recirculation pump (F), maintained blood filming on the screens by constantly drawing blood from the bottom of the oxygenator (H) via shunt tubing (J) and was servo-regulated by a pressure transducer (G). The pH of the blood leaving the oxygenator was monitored by an electrode (I), which was servo-regulated to adjust gas flow. The arterial pump (K) was also servo-regulated by a transducer (G) not to exceed a pressure of 300 mmHg. A monel metal screen filter (L) was located on the systemic blood flow tubing after the arterial pump. Temperature of venous and arterial blood was monitored by thermocouples (E and E'). (Reprinted from Miller BJ et al. Med Clin North Am 1953; 37: 1607, with permission.)
tree of the subject being perfused. A new device was conceived (Figure 5). The blood level in the bottom of the oxygenator was considered one element of a capacitor. The other element of the capacitor was a fixed electrode separated by a dielectric, which, in this case, was the plastic of the oxygenator case. Accordingly, a small metal plate was incorporated within the case and completely sealed. The capacity between the blood level and the fixed plate, in conjunction with an inductance, formed a tuned circuit operating at 10.7 megacycles. Changes in the blood level altered the frequency of the tuned circuit and provided the error signal for the control of the arterial pump. The arterial pump was then controlled completely by the blood level in the bottom of the oxygenator case. The variable capacitor circuit functioned well and appeared to be completely reliable providing control of the arterial pump at a maximal flow within 0.1% and safeguarding against air embolization through the systemic arteries. The accurate and instantaneous control of the capacitor system maintained the blood volume control in both machine and subject being perfused. A filter of new design based upon the reverse flow of blood was then included in the arterial line. This filter provided for the removal of air or fibrin from the chamber during the initial filling.

With this modified machine, a number of dogs were perfused successfully during total bypass. At this time, the venous pumps were placed at a higher level than the heart of the subject being perfused. It was necessary to withdraw the blood from the vena cava with a moderate degree of suction. Since the venous DeBakey pumps were pulsatile, the moment the roller contacted the tube, there was a marked increase in velocity with a concurrent decrease in the lateral pressure and, therefore, at a high flow rate, the caval wall would be drawn into the orifice of the cannula, interrupting vena caval blood flow. When this occurred, blood could not be withdrawn through the occluded cannula despite the fact that the venous blood continued to flow into the cava. In order to control this phenomenon, a small segment of easily collapsible rubber tubing was placed within the venous line and used as a pressure sensor. In the final design, a linear variable differential transformer sensed the intermittent collapse or change in diameter of the rubber tube in the venous line circuit (Figure 6). A spring-loaded lever rested against the segment of rubber tubing, which was linked to the core of a variable differential transformer. Minute changes in the diameter of the tube as a result of variations in pressure during the pumping cycle produced the necessary control signal to effect reliable automatic control. At the moment of occlusion of the vena cava, the rubber tubing collapse was sensed by the device and the venous pump motors were instantaneously stopped. Intermittent erratic pressure changes preceding complete occlusion were indicated by a loud audio signal and visual fluctuation of a meter, known as a flutter meter. The perfusionist was then alerted to reduce the speed of the venous pump to prevent repeated occlusion of the cava and a cessation of flow in the system.

At this point, the new machine arrived in the laboratory (Figure 7). An intense program of animal experimentation was undertaken. The motors of the venous pump in the first IBM machine were direct current (DC) motors, operating directly from rectifiers. The low torque at reduced speed of direct current motors made them unsuitable for this purpose. Accordingly, in the new machine, alternat-
ing current motors replaced the direct current motors of the venous pumps. Variable speed control was effected by Graham mechanical transmissions. Quick braking of alternating current motors was achieved by instantaneously applying a direct current to the motor.

The early phases of animal experimentation with the new machine took place early in 1951. The new machine was only moderately successful. The mortality was unduly high despite the apparently satisfactory condition of the animals during perfusion. Attention was now focused upon this problem. Gasometric studies during anesthesia with a laboratory respirator revealed marked hypoxia and acidosis. The notion of assisting respiration by increasing tidal volume of expired gas at the expense of the reserve gas volume without increasing intratracheal pressure by the use of suction was investigated. Accordingly, a laboratory model of a respirator containing a timing circuit that alternately operated solenoid valves on both the inspiratory and the expiratory lines of the respirator was constructed.\(^6\)

Expiration was assisted by suction produced with a Venturi jet. The respirator operated at 5 lb line pressure of room air (Figure 8). With the new device, it was possible to saturate arterial blood with oxygen using room air. Carbon dioxide could be removed from the circulating blood to the point where the animal would remain apneic at the conclusion of anesthesia for a number of minutes (Figure 9). This device was used in all subsequent experiments, and hypoxia and acidosis were no longer problems.

Nearly all animals survived total CPB for as long as 100 minutes.

Four recording potentiometers were included in the front panel of the machine as a means of providing permanent records of physiologic data. The pH recorder indicated the pH of arterialized blood and, in addition, maintained a pH of 7.2 by automatically adding carbon dioxide when the pH rose above this value. Another recorder indicated the degree of oxygen saturation of the arterialized blood from a cuvette in the arterial line that measured light transmission at 540 and 620 Å. Another recorder indicated subject temperature and also controlled the temperature of blood in the machine. There was excessive hemolysis because of the required high temperature gradient and the small mass of the heater. The use of this feature was discontinued. The remaining recorder measured flow rate by means of a square wave flow meter.

Because cyclopropane and ether were anesthetics frequently used at that time, the machine was pressurized with nitrogen because of sparks originating in the DC motor, and the large number of open relays within the machine cabinet made explosion a real possibility. There was, in addition, a battery-operated emergency supply in the event of failure of the hospital’s electrical supply.

The ultimate goal of this work was to achieve a bloodless cardiac chamber during total bypass, providing a means for the performance of precise surgical operations in the human patients under

![Figure 8 Drawing of an improved laboratory respirator. During inspiration the solenoid valve (G) opened, introducing room air into the animal's lungs, and the solenoid valve (C) closed. Gas flow through the circuit was regulated by manually controlling pressure valves (A and H). The maximum intrapulmonary air pressure during inspiration was controlled by the spring-loaded valve (D). During expiration the solenoid valve (C) closed and the solenoid valve (G) opened. Full line pressure was then diverted to the Venturi jet (B), producing suction, which rapidly exhausted respiratory gases from the lungs. The rate with which the expired gas was withdrawn was regulated by the pressure control valve (A). The final degree of vacuum attained within the trachea and lungs at the end of expiration was again limited by the spring-loaded valve (D). The water manometer (E) indicated pressure gradients during the respiratory cycle. Spring-loaded valve (F) was for positive pressure relief. (Reprinted from Miller BJ. Surgery 1957; 42: 723, with permission.)](image-url)
The next logical step was to create defects within the septa and then to attempt to repair them while the cardiorespiratory function was maintained by the heart-lung machine. As we had hoped, the new machine functioned surprisingly well with most animals surviving. The blood volumes of both the subject and the machine were precisely maintained, the pH was maintained within normal range, and the servocontrol systems protected completely against air embolization.

Therefore, the next logical step was to create defects within the septa under direct vision during total bypass and then to attempt to repair them while the cardiorespiratory function of the subject was maintained by the heart-lung machine. The magnitude of cardiac venous blood entering the right atrium was not fully anticipated before the first atriotomy was performed during bypass. The first experiment was a complete failure because the large volume of blood returning to the right atrium could not be coped with by simple means.

An additional and unforeseen complication appeared when experimental atrial defects were produced during bypass. Air entered the left atrium as soon as the interatrial septal defect was produced. Blood and air trapped beneath the mitral leaflets were then pumped by the pulsating left ventricle into the systemic circulation, thus embolizing the coronary circulation and other systemic arteries. This was indeed a profound complication, but the solution was actually simple. A tube was introduced into the left ventricle of the beating heart by ventriculotomy at the apex and, secured with a purse string suture, provided a low impedance path for the escape of the air from the contracting left ventricle. This procedure was assisted by mild suction. Both the returning cardiac venous blood from the open atrium and the blood aspirated from the left intraventricular catheter were directed into a collecting chamber. Because a certain amount of air was always mixed with the blood returning from the atrium, the bubbles formed in this manner were dissipated during their gradual descent onto the inner surface of the tall cylinder. The negative pressure within the collecting chamber also assisted in dispersing the bubbles. As the blood accumulated in a pool at the bottom of the collecting chamber, the elevation of the blood level was then sensed by the same variable capacitor circuit used in the control of the arterial pump. This circuit energized an additional pump, which returned both the cardiac venous blood and the left ventricular blood and bubbles to the extracorporeal circuit (Figure 10).

A number of atrial septal defects were produced in dogs during total bypass and repaired by suturing a pericardial patch to the edges of the defect. In some situations, the patch was introduced into the right atrium through a stab wound onto the medial surface of the atrium and left connected to its base with the aim of providing circulatory support to the graft. This procedure was found to be unnecessary. In another group of animals, intraventricular septal defects were produced under direct vision by the use of a sharp cork bore and suction. These defects were then repaired by direct suture. Ninety per cent of these animals survived.

Because the venous pumps were at a slightly higher level than the heart, a moderate degree of suction by the pump was needed to ensure a maximum flow from the vena cavae. To further minimize the problem of pulsatile blood flow from the DeBakey pump, a further modification to the circuit was made. Using mild negative pressure, caval blood was directed into a separate collecting chamber. As the blood accumulated in the bottom of the chamber, the level was sensed by the electronic circuit used to automatically control the arterial pump (Figure 11).

Under normal operating conditions, all that was needed to initiate bypass and perfusion was the removal of the hemostats from the venous and the arterial lines. As blood from the subject entered the extracorporeal circuit, the heart-lung machine then functioned completely automatically, requiring only occasional adjustments of the negative pressure to the collecting chamber and small addition of blood as needed to maintain blood pressure. A large and
Figure 10  Drawing of the cardiac venous and left ventricular blood collecting apparatus. Note use of negative pressure (≈ 40 cmH₂O) applied to chamber to effect blood aspiration, which then descended along the sides to the bottom of the chamber by gravity. Most of the air aspirated was rapidly dissipated from the film of blood. A DeBakey roller pump returned blood to the venous side of the extracorporeal circuit and was servo-regulated to maintain a constant minimum level in the bottom of the chamber. (Reprinted from Miller BJ et al. Med Clin North Am 1953; 37: 1615, with permission.)

Figure 11  Schematic drawing of final modification to extracorporeal circuit. This configuration differs from that shown in figure 6 by the addition of two venous blood-collecting chambers (A and C) to minimize pulsating negative pressure effects from the roller pumps that frequently collapsed the vena cavae. The venous (E) and cardiac venous blood (D) pumps were also servo-regulated to maintain constant blood levels in the collecting chambers. The negative pressure required to empty the vena cavae was rarely greater than −10 mmHg. (Reprinted from Miller BJ et al. J Thorac Surg 1953; 26: 601, with permission.)
successful experimental experience had been achieved by this time. The apparatus functioned splendidly. Oxygenation with a new oxygenator of greater capacity than the previous one was sufficient for perfusion of a human patient of average size.

Dr Gibbon and this author, together with the laboratory group (Figure 12), had every confidence that the next phase, the use of the apparatus in operations upon humans, would also be successful. Accordingly, Dr Gibbon initiated the use of this device in human applications. The heart-lung machine was sterilized by first filling the machine with zephiran solution the evening before the contemplated operation, followed by repeated flushes with saline prior to filling the machine with five units of blood. The first patients were two small children who failed to survive for reasons other than the failure of perfusion.

In May of 1953, Dr Gibbon performed an open cardiotomy during bypass under direct vision at Jefferson and repaired an interatrial septal defect in a teenage girl (Figure 13). Unfortunately, because of the duration of the thoracotomy and a marginal dose of heparin to the patient, blood clotting on the oxygenator screens took place during the closure of the defect. Automatic controls in the heart-lung

Figure 12 Photograph of author (third from the left) and Jefferson Medical College laboratory group in 1953. Miss Joann Corothers, who operated the heart-lung machine for the animal experiments, is shown to the right of Dr Miller.

Figure 13 Photograph taken during first successful cardiopulmonary bypass case for closure of an interatrial septal defect, 6 May 1953. Dr Gibbon is seen at center right, Dr Frank H Allbritton Jr. is assisting and opposite Dr Gibbon, and Dr Miller is on far right with his back to the camera. (Reprinted from Gibbon JH Jr. Rev Surg 1970; 27: 239, with permission.)
machine sensed the problem and stopped all pumps. It was then necessary to make an emergency reconnection of the blood circuit and, while operating the pumps under manual control, maintain the patient’s blood volume with fluids and what blood was available at the time. At this point, ventricular fibrillation occurred, but a normal rhythm was established immediately with an electric shock. This patient had an uncomplicated postoperative course, recovered completely, and has remained well with normal cardiac function for many years postoperatively.

References

9 Miller BJ, Gibbon JH Jr., Greco VF, Cohn CH, Allbritten FF Jr. The use of a vent for the left ventricle as a means of avoiding air embolism to the systemic circulation during open cardiotomy with the maintenance of the cardiorespiratory functions of animals by a pump oxygenator. Surg Forum 1953; 4: 29–33.