The practical advent of the intensive care unit has markedly improved the salvage rate in acute respiratory insufficiency of all types. There have been important improvements in the handling of the airway, in the use of respirators and the management of humidification, in means of decreasing respiratory effort and combating infection, and in the treatment of cardiac, fluid, and acid-base abnormalities. Nevertheless, on occasion arterial PO2 may decrease and compliance increase inexorably as portions of the lung become atelectatic or consolidated, and right-to-left shunting occurs.

Under such circumstances, because of the need for an increasing inspiratory oxygen concentration with the attendant danger of oxygen toxicity, and high inflation pressures which may produce pneumothorax, pulmonary dysfunction cannot be reversed. Patients with potentially reversible pulmonary lesions thus still die because the means of safely augmenting their respiratory function is lacking.

A few patients may be effectively handled by judicious use of hyperbaric oxygenation, although this increases the danger of oxygen toxicity. Other patients may benefit from hypothermia, but this requires expert suppression of the homeostatic heat regulatory mechanisms and has not been well explored. A current promising approach is the temporary use of an artificial extracorporeal lung.

In most centers, this therapeutic modality is best applied in the intensive care unit. The artificial lung may be used as a pure respiratory supplement or for combined cardiac and respiratory support. Acute respiratory insufficiency is marked by increasing demands on the heart and lungs, and standard methods of therapy often not only fail to lighten these demands, but may even augment cardiac and respiratory work. Therapeutic measures, such as high inspired oxygen concentrations, cardiac drugs with positive inotropic action, etc., are accompanied by deleterious side effects which may outweigh their advantages. A temporary artificial lung reduces cardiac and pulmonary work and, therefore, can provide rest for both these important organs.

The purpose of this article is to review the current state of the art in reference to the temporary artificial lung and to make some limited future projections. An attempt will be made to answer questions related to availability, characteristics, associated morbidity, and special problems of the artificial lung. The discussion will be limited primarily to acute, potentially reversible respiratory insufficiency, but will also be pertinent to acute respiratory problems superimposed on chronic respiratory insufficiency. Indications for initiating and discontinuing perfusion are discussed.

The Temporary Lung

Most currently employed extracorporeal gas exchange devices have a direct blood gas interface and have been shown repeatedly to produce serious blood damage.6-8 In recent years a variety of devices with membrane interposed between the blood and the gas have been developed.12,17-23 These cause much less blood damage and may be used for relatively prolonged periods of time for cardiorespiratory support. Perfusions for as long as ten days have already been performed in patients with membrane lungs.3,8,24
Table 1—Membrane Lungs in Clinical Use for Long-Term Perfusion

<table>
<thead>
<tr>
<th>Principal Developer</th>
<th>Type</th>
<th>Size and Use</th>
<th>Longest Clinical Use</th>
<th>Availability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bramson²²</td>
<td>Round Sandwich</td>
<td>Large</td>
<td>9½ days</td>
<td>Hallikainen Inst. and</td>
</tr>
<tr>
<td></td>
<td>semi-disposable</td>
<td>Up to full flow in adults</td>
<td>(3)</td>
<td>Cutter Labs</td>
</tr>
<tr>
<td>Kolobow¹¹,²⁴</td>
<td>Flat spiral (coil)</td>
<td>Small</td>
<td>10 days</td>
<td>Not known to be in</td>
</tr>
<tr>
<td></td>
<td>Disposable</td>
<td>Newborn infants</td>
<td>(8)</td>
<td>general production</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Large</td>
<td>10 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Adults, partial bypass</td>
<td>(24)</td>
<td></td>
</tr>
<tr>
<td>Land²¹</td>
<td>Square Sandwich</td>
<td>1 and 3 meters²</td>
<td>8½ days</td>
<td>Edwards Laboratories</td>
</tr>
<tr>
<td></td>
<td>Disposable</td>
<td>with multiples of 3M², to full flow</td>
<td>(26)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>in adults (25)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peirce¹⁰,²⁷</td>
<td>Rectangular Sandwich</td>
<td>0.5 to 3 meters²</td>
<td>6 days*</td>
<td>General Electric Co.</td>
</tr>
<tr>
<td></td>
<td>Disposable</td>
<td>(four sizes)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Full flow in infants (28) with multiples</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>to full flow in adults (29)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Kahn, et al.: Personal communication.

Availability

Table 1 shows the current availability and a general description of all of the devices now known to be in clinical trial for longterm perfusion. All of these utilize a dimethylsilicone membrane or a copolymer of this material since these are the best currently available gas exchange membranes that are also relatively atraumatic to blood. The Landé-Edwards and the General Electric-Peirce (G.E.-Peirce) lungs are available as disposable units and will work with almost all existing pump equipment. The actual membrane unit of the Bramson lung is semidisposable, but it requires its own unique and relatively complicated perfusion apparatus. The Kolobow device is not yet generally available. A device manufactured by the Waters Company requires its own pumps and some additional unique equipment.¹⁸ It is not known to have been used for longterm bypass. A machine described by Katsu-hara et al¹⁹ is potentially suitable, but is not known to be available. Machines of advanced design, including capillary types²²,²⁸ and toroidal flow types²³,³⁰ are under study, but not yet available for clinical use. Descriptions of other membrane lungs may be found in previous publications.⁵,¹²

Principal Characteristics

Membrane devices currently available for clinical longterm bypass have more similarities than differences. Three are sandwich devices,⁵,²⁰,²¹ and one is made of coiled flattened tubes.¹⁷ When properly operating, all of these devices offer the possibility of careful control of the extracorporeal blood volume. The discussion will be simplified by giving data on the G.E.-Peirce lung, whose general operating characteristics are seen in Table 2.

Blood trauma. A tolerable level of red blood cell damage is considered to be approximately 0.1

Table 2—Operating Characteristics of a 1M² G.E.-Peirce Lung

<table>
<thead>
<tr>
<th>Blood Flow ml/min</th>
<th>500</th>
<th>1000*</th>
<th>1500</th>
</tr>
</thead>
<tbody>
<tr>
<td>A-V O₂ difference % (at outlet sat. 90%)</td>
<td>40 ± 10</td>
<td>25 ± 6</td>
<td>20 ± 5</td>
</tr>
<tr>
<td>Outlet Saturation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At inlet sat. 40%</td>
<td>85</td>
<td>74</td>
<td>64</td>
</tr>
<tr>
<td>At inlet sat. 55%</td>
<td>92</td>
<td>84</td>
<td>77</td>
</tr>
<tr>
<td>At inlet sat. 70%</td>
<td>97</td>
<td>95</td>
<td>90</td>
</tr>
<tr>
<td>Oxygen exchange ml/min. **</td>
<td>40 ± 6</td>
<td>46 ± 8</td>
<td>50 ± 9</td>
</tr>
<tr>
<td>CO₂ exchange ml/min.</td>
<td>35</td>
<td>38</td>
<td>40</td>
</tr>
<tr>
<td>Perfusion pressure mmHg</td>
<td>40-55</td>
<td>75-110</td>
<td>110-160</td>
</tr>
<tr>
<td>Priming volume ml</td>
<td>190</td>
<td>200</td>
<td>210</td>
</tr>
</tbody>
</table>

*Flow rate for which lung is designed.
**For hematocrit of 45% at outlet saturation of 90%.
***At O₂ flow of 2 liters per minute.

Values for A-V O₂ difference and O₂ exchange are ±S.D.
The artificial lung in respiratory insufficiency

**Figure 1.** Hemolysis data from controlled six-hour *in vitro* perfusions are shown. Blood was recirculated approximately 500 times through comparable circuits with and without a membrane lung. The red cell destruction represents about 0.5 percent of all the red cells, an amount less than the usual retirement rate for cells under normal circumstances. The control values are for uncirculated blood kept at the same temperature (25°C). Figures 1, 4, and 5 are reproduced by permission of Appleton-Century-Crofts, New York, Surgery Annual 1972, P. Cooper and L. Nyhus (editors).

**Figure 2.** In 24-hour perfusions in dogs the plasma hemoglobin rises to a peak at 12 to 18 hours and then falls indicating probable passivation of the membrane. White blood cell levels fall initially and then rebound. Platelets average about half the normal level at the end of 24 hours. Redrawn from.

**Figure 3.** Oxygen exchange and arteriovenous oxygen difference values are shown for varying blood flow rates with no recirculation. The oxygen exchange confidence band is the equivalent of a standard deviation. Data are for eight oxygenators manufactured during 1971. (Data corrected to hematocrit of 45 percent and outlet saturation of 90 percent.) In one 36-hour human perfusion, using a two square meter lung and blood flows up to 2400 ml/min, the maximum plasma hemoglobin level was 29 mg percent.

**Figure 4.** As in a normal mammalian lung, CO₂ exchange varies directly with minute volume. Venous and arterial Pco₂ data were obtained in a total cardiopulmonary bypass experiment. As oxygen exchange is little influenced by gas flow rate until it is very low, low arterial Pco₂ values may be readily corrected by reducing gas flow. A change from oxygen to an oxygen-carbon dioxide mixture is not necessary. From data presented in ref 46.
percent and no problems have been ascribable to this (Fig 2). The use of platelet deaggregators has not been reported in prolonged assisted circulation, but would appear to have potential value.

White blood counts fall initially and cells are quickly replaced by an adequate number of juvenile types (Fig 2). No problems from this appear likely.

Protein damage has been demonstrated to be small in membrane lung. Lipoproteins are not greatly affected. There has been no evidence of prohibitive alteration of any of the major clotting factors.

Gas exchange potential. Single G.E.-Peirce lungs of 3 meters square have a potential oxygen exchange up to 150 ml/min and a carbon dioxide exchange about 80 percent as great (Fig 3). Used in parallel pairs, exchange of approximately 300 ml/min is possible. Oxygen exchange is limited by the blood flow rate and the oxygen capacity of the in flowing venous blood. It is only slightly affected by pH, temperature, and gas flow through the lung. On the other hand, carbon dioxide exchange varies primarily with gas flow through the lung and is little influenced by other factors. This offers the opportunity to control carbon dioxide tension by gas flow rate (Fig 4).

Table 3—Known Assisted Circulation for Acute Pulmonary Insufficiency in Large Children and Adults as of January 1972

<table>
<thead>
<tr>
<th>Reference</th>
<th>No. Patients</th>
<th>Device</th>
<th>Condition</th>
<th>Perfusion</th>
<th>Patients Improved*</th>
<th>Lived after bypass</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hill et al</td>
<td>4</td>
<td>Bramson</td>
<td>Viral pneumonia</td>
<td>26-60 hrs</td>
<td>2</td>
<td>3, 9 days</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Bramson</td>
<td>Aspiration pneumonia</td>
<td>30 hrs-91½ days</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Bramson</td>
<td>“Shock” lung</td>
<td>75 hrs-6½ days</td>
<td>2</td>
<td>6 days, recovered</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Bramson</td>
<td>Fat embolism</td>
<td>23 hrs</td>
<td>1</td>
<td>1 day</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Bramson</td>
<td>Respiratory burn</td>
<td>12 hrs</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td>Landé et al</td>
<td>2</td>
<td>Landé</td>
<td>“Shock” lung</td>
<td>to 8½ days</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td>Weinreich and Lipton</td>
<td>1</td>
<td>Landé</td>
<td>Aspiration pneumonia</td>
<td>oxygen toxicity</td>
<td>36 hrs</td>
<td>0</td>
</tr>
<tr>
<td>Kennedy</td>
<td>1</td>
<td>Landé</td>
<td>Fat embolism</td>
<td>4 days</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td>Martini</td>
<td>1</td>
<td>Landé</td>
<td>Fat embolism</td>
<td>70 hrs</td>
<td>1</td>
<td>2 days</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Landé</td>
<td>Pulmonary vein</td>
<td>60 hrs</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Landé</td>
<td>oclusions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peirce et al</td>
<td>1</td>
<td>G.E.-Peirce</td>
<td>“Shock” lung</td>
<td>36 hrs</td>
<td>1</td>
<td>3 days**</td>
</tr>
<tr>
<td>Kahn et al</td>
<td>1</td>
<td>G.E.-Peirce</td>
<td>Viral pneumonia</td>
<td>6 days</td>
<td>1</td>
<td>7 days</td>
</tr>
<tr>
<td>Bernhard</td>
<td>1</td>
<td>G.E.-Peirce</td>
<td>“Shock” lung</td>
<td>2 days</td>
<td>—</td>
<td>3 days</td>
</tr>
<tr>
<td>Joseph et al</td>
<td>1</td>
<td>G.E.-Peirce</td>
<td>P. carinii pneumonia</td>
<td>4 days</td>
<td>1</td>
<td>30 days****</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Kolobow</td>
<td>P. carinii pneumonia</td>
<td>?</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td>Zapoli</td>
<td>1</td>
<td>Kolobow</td>
<td>“Shock” lung</td>
<td>10 days</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>oxygen toxicity</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Sufficiently for perfusion to be discontinued. **Kidneys used for transplants. ***Personal communication. ****Recovered from pneumonia, died of renal transplant rejection.
the efficacy of the pulmonary support. White et al\textsuperscript{8} reported veno-venous perfusion in three newborn infants for two, three, and ten days using the Kolobow lung.\textsuperscript{7} The efficacy of the respiratory support was suggested by the fact that infants tended not to make any respiratory effort on perfusion. The principal cause of death has been hemorrhage and this is found in a high percentage of infants who die of hyaline membrane disease. An earlier decision for support may be indicated. The special problems have been ably discussed by White et al.\textsuperscript{8}

**Acute Respiratory Insufficiency in Adults**

At least 22 patients have had prolonged temporary lung support for acute pulmonary insufficiency.\textsuperscript{4,6,24,26,30,34,35,36} Although there is only one known longterm survivor, earlier perfusion will undoubtedly improve the salvage rate. Known cases to January, 1972, are summarized in Table 3. Since many groups are now interested in this mode of therapy,\textsuperscript{22,33,39} additional cases are being added fairly rapidly and devices may well have been used without the author's knowledge.

**Viral pneumonia.** Although the survival rate has been improved by modern respiratory therapy, severe fulminating viral pneumonia has a high mortality.\textsuperscript{14,46} Reversal of pulmonary dysfunction during temporary lung support was demonstrated by Hill et al\textsuperscript{3} in four adults. One patient lived nine days after perfusion. A decrease in pulmonary shunt flow and in the alveolar arterial oxygen gradient coincided with improvement in oxygenation when the lung support was successful (Fig 5).\textsuperscript{3} Unfortunately, viral infections affect other vital organs as well. After successful temporary lung support, two of Hill's cases died of cardiac failure due to myocarditis, and one may have had cerebral viral involvement. In 13 cases of influenzal pneumonia successfully treated with hyperbaric oxygenation, four later died of hepatorenal failure.\textsuperscript{1} The overall salvage rate will, therefore, depend not only on the reversibility of the pulmonary lesions, but also on the involvement of other organs. A patient recently treated with perfusion by Kahn et al\textsuperscript{30} for seven days using the G.E.-Peirce lung had residual brainstem damage and was found to have underlying leukemia. The prognosis may thus be expected to be greatly affected by other coexisting diseases.

**Aspiration pneumonia.** Patients with major pulmonary aspirations who survive the initial insult frequently develop severe respiratory insufficiency. They demonstrate major problems in compliance, diffusion, and shunting. The mortality rate has been reported to be as high as 40 percent.\textsuperscript{41} Death may follow prolonged respirator care as a result of oxygen toxicity or be hastened by alveolar rupture secondary to high inflation pressures. Weinrich et al performed a 36 hour perfusion in a young man suffering from both pneumothorax secondary to artificial ventilation and oxygen toxicity.\textsuperscript{28} He responded favorably to the temporary pulmonary support, which was given in conjunction with hyperbaric oxygenation, only to succumb to massive intrathoracic bleeding. In one instance of aspiration pneumonia, where the process was aggravated by oxygen toxicity, Hill et al\textsuperscript{3} noted no improvement during 30 hours of perfusion. In a second instance, perfused for nine and one-half days, improvement in respiratory function reached a plateau and then declined. This case was marked by severe pulmonary edema and massive bilateral pneumothorax. Respiratory function was inadequate for survival on completion of the perfusion. Evidence is thus incomplete, but aspiration pneumonia is certainly potentially salvageable by use of extracorporeal pulmonary support used in a timely manner.

**Bacterial pneumonia.** Severe bacterial pneumonia may offer some problems of potential sepsis at sites of cannulation, but temporary pulmonary support should certainly be considered when salvage does not appear possible by conventional means.

**Pneumocystis carinii pneumonia.** This formidable
opportunistic protozoan infection is seen in patients being treated with immunosuppressive agents. Loss of pulmonary function is very great and the mortality rate is high. Pentamidine appears to be the best current chemotherapeutic agent. Joseph et al$^8$ have recently reported two patients with severe respiratory insufficiency who were treated with membrane oxygenators. In one case, the treatment was not successful while in the other there was reversal of pulmonary pathology and at least temporary recovery after four days of perfusion. This was a 14-year-old with a $Po_2$ of 32 mm Hg on 100 percent oxygen prior to treatment. The G.E.-Peirce lung was used.

**Shock lung and related conditions.** Severe hemorrhagic and septic shock, crush injuries to the chest, prolonged conventional perfusion, multiple transfusions, and protracted respirator therapy may all be associated with severe pulmonary insufficiency. These conditions are characterized by a decreased compliance, diffusion defects, and massive right to left lung shunts. The mortality is very high. Mechanical damage, infection, oxygen toxicity, and embolic occlusions may be underlying problems. Two such cases treated by Hill et al$^3$ for three days and six and one-half days showed clear-cut reversal of the pathophysiology. In both patients adequate lung function was restored and one patient recovered fully. One patient in this category treated by Peirce et al$^6$ showed reversal of the severe pulmonary dysfunction in 36 hours, but unfortunately, died as a result of brain damage which began prior to the perfusion. Nevertheless, organ recovery was sufficient so that the kidneys were suitable for transplantation. Landé, et al$^{38}$ briefly reported two patients who showed improved respiratory function initially on perfusion. Temporary lung support thus seems to be a rational mode of therapy for severe shock lung not responsive to conventional treatment.

**Fat embolism.** Cerebral involvement is a major factor in this condition and led to the death of a patient treated by Hill et al with a 23-hour bypass.$^3$ Patients have also been reported by Kennedy$^{24}$ and by Martini.$^{34}$ The lung lesions appear to be reversible and some patients should certainly be salvageable.

**Respiratory burn.** In a severe respiratory burn case treated by Hill et al,$^3$ autopsy indicated that the lung had been destroyed and that perfusion would not be expected to be effective. With less severe burns, perfusion support with a temporary lung might well be satisfactory.

**Pulmonary embolism.** Since more than 75 percent of deaths from pulmonary embolism occur within a few hours,$^{44}$ partial cardiopulmonary bypass with support of both heart and lung would appear to be the initial treatment of choice. The condition has been shown to be reversible,$^{44}$ and a test of fibrinolytic enzymes$^{45}$ could be carried out safely even when severe cardiorespiratory failure was present. Perfusion support should facilitate definitive diagnosis and would not be contraindicated in most conditions simulating pulmonary embolism. The perfusion would, of course, simplify surgical embolectomy.

**Pulmonary oxygen toxicity.** This is almost always a complication of therapy for some other primary condition$^{42}$ and is believed to be reversible if the inspiratory oxygen concentration can safely be reduced below 60 percent.$^{43}$ Earlier perfusion would limit this complication.

**Respiratory failure in conjunction with cardiac failure.** In the "low output" syndrome following open heart surgery, respiratory dysfunction may be severe. In myocardial infarction, respiratory failure, including frank pulmonary edema, may be a prominent feature. Use of temporary cardiopulmonary support might be efficacious in such circumstances providing major hemorrhagic complications can be avoided and central pressures are adequately monitored to avoid left ventricular overload.

**Decisions to be Made**

**Criteria for initiating temporary pulmonary support.** Hill et al$^3$ have suggested that perfusion with a temporary lung should be considered whenever there is evidence of cerebral or cardiac hypoxia, the arterial $Po_2$ falls below 35 mm Hg on 100 percent oxygen, and the condition under consideration is potentially reversible. We feel that these criteria are probably too conservative. A potential complication of cerebral hypoxia is hemorrhage, and its gravity is likely to be compounded by the use of heparin with the perfusion. It is probably imperative, if salvage is to be significant, to start perfusion before there is any clearcut evidence of hypoxic myocardial or cerebral failure. If the arterial $Po_2$ progressively falls to 45 mm Hg on 100 percent oxygen, the inflation pressure progressively increases to 45 cm of water or more, or the inspiratory oxygen concentration exceeds 60 percent for several days or 100 percent for 24 hours, perfusion support should be seriously entertained. It should not be necessary to have a bilateral pneumothorax, severe oxygen toxicity, or brain damage from hypoxia before standard respirator therapy is considered to have failed. Intracranial bleeding or unmanageable bleeding elsewhere probably contraindicates perfusion with our present knowledge of heparinization.
Moderate degrees of bleeding, however, may be controlled by reduction of the heparin level as explained below.

When to discontinue the use of the temporary lung. When the patient can be supported adequately with a respirator employing a reasonable inflation pressure and inspiratory oxygen concentration, a test of discontinuing the perfusion is indicated. The lung should be operated at stand-by for at least several hours before the perfusion is dismantled. Hill et al.24 have indicated that patients responding favorably will exhibit a distinct decrease in the degree of right to left shunting (Fig 5) as manifested by a progressive drop in the alveolar arterial gradient on 100 percent oxygen. In addition, there should be a favorable change in the pulmonary compliance. In situations where a return of pulmonary function is satisfactory, perfusions have varied from perhaps 24 hours to six and one-half days. It might be anticipated that if sufficient improvement is to occur, it will do so within ten days, although this is only an approximate estimate.

It may be advisable to discontinue perfusion when there is conclusive evidence of brain death and it may be necessary to discontinue when hemorrhage develops and cannot be controlled.

Mode of Perfusion

Arteriovenous perfusion, in which the patient pumps the blood through the artificial lung, may eventually be a most useful mode, but it is still in the stage of experimentation.46

Veno-venous perfusion. Most workers have favored this method for frank acute respiratory insufficiency, and it has been shown to be effective by Hill et al.,2 Kahn et al.,46 Joseph et al.,35 and White et al.8 Properly carried out, it produces no hemodynamic disturbance. Similarly, it produces no hemodynamic benefit, and many patients with respiratory insufficiency may have some degree of cardiac failure also. The blood perfusing the artificial lung is freely mixed with the prelung blood and the function of the artificial lung is usefully added to that of the natural lung. The better oxygenated blood is distributed throughout the body. A potential disadvantage of veno-venous perfusion is that any embolic material (fibrin, platelet clots, etc) will lodge in the lung and augment damage already present. Veno-venous perfusion with a disc oxygenator was used by Schramel et al.49 to produce lesions of "perfusion lung." Although the various membrane lungs are probably much less traumatic, some embolic material almost certainly results from the extracorporeal perfusion.48 Significant pulmonary lesions were not demonstrated, however, in the lungs of dogs one week after 24-hour veno-venous perfusion using a membrane lung.7

Veno-arterial perfusion. This mode of perfusion is clearly valuable when some degree of cardiac failure is present. Landé et al.28 have demonstrated the hemodynamic efficacy of this method although they have not had any longterm survivors.28 Recently, Hill et al. have used this mode in preference to veno-venous perfusion and have reported one longterm survivor in four patients so treated. Our limited experience also indicates this mode of perfusion offers advantages.6 The patient's cardiac output is reduced which minimizes the chance of pulmonary edema. If hypotension is present, the bypass will raise the systemic blood pressure and produce improved coronary perfusion. There are certain problems, however, related to potential left ventricular overload and to poor distribution of the oxygenated arterial blood.

In the case of a failing heart, veno-arterial bypass must be instituted with great care. Since the central venous pressure may not accurately reflect the left atrial pressure, the patient should be monitored, if possible, with the pulmonary wedge pressure, and the rate of perfusion carefully gauged to prevent an excessive left atrial pressure. In patients with "low output" syndrome, relatively small extracorporeal flow rates may be very supportive to the circulation and return patients from low blood pressure and anuria to normotensive levels with good urinary

![Graph](https://example.com/graph.png)

Figure 6. The administration of ethacrynic acid made it possible to maintain a stable weight, packed cell volume, central venous pressure, and arterial pressure in a dog perfused for 24 hours. Urine volume may be expected to lag non-colloid fluid administration when a diuretic is not administered. This occurred during the final hours of the perfusion. Redrawn from ref 7.

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A high left atrial pressure precluded initial extracorporeal perfusion and the square meter area of lung required for this type of regional perfusion has, in most instances, resulted in satisfactory improvement in central arterial saturation. Nevertheless, arterial blood should be sampled from the upper part of the body and where sufficient improvement is not produced, the use of a subclavian artery cannula to return blood to the root of the aorta should be considered. An alternative possibility, suggested by Hill et al, is to return some of the blood by the venous route.

**Sizing the Lung**

Figure 8 illustrates the estimated normothermic oxygen consumption of patients of different size on partial cardiopulmonary bypass. Hill et al have emphasized that the oxygen consumption of patients with severe acute respiratory insufficiency may be considerably larger than expected. To reduce respiratory work, muscle paralysis should be considered when the respiratory support appears inadequate. My limited experience with partial bypass indicates that a two square meter lung with a nominal oxygen exchange capacity of 100 ml/min is suitable for an adult with acute respiratory insufficiency, and that smaller units should be suitable for children and infants. In general, one should aim to put about half the basal calculated cardiac output about half the basal calculated cardiac output through the extracorporeal circuit. Under these circumstances, a lung of about half the size required for total cardiopulmonary bypass should be satisfactory.

**Cannulation**

A special feature of prolonged extracorporeal circulation is the need to cannulate each artery and vein both proximally and distally to avoid ischemia and venous congestion. When arteries are not doubly cannulated, the patient may experience severe and unremitting pain even though there is no actual danger of limb loss from ischemia. The cannulation is not difficult and can best be done with flexible cannulas of suitable size. The double cannulas for each vessel are joined at the main perfusion line with a Y connector.

**Perfusate and Fluid Balance**

Although blood substitutes are very satisfactory for short-term perfusion, these materials do not sustain the blood volume permanently. Dilution may be used to start the perfusion, but then an effort should be made to return the packed cell volume to a normal range and to replace all blood loss with whole blood. Even when this is done, there is a tendency for fluid retention in the extravascular-extracellular compartment with attendant progressive edema. For this reason, fluid balance must be followed with great care. Satisfactory urinary output will generally require cautious use of ethacrynic acid.

**Figure 6**

![Cardiovascular Support from Veno-Arterial Perfusion](image)

**Figure 7**

A patient had both "low output" syndrome and severe respiratory insufficiency following a three valve replacement operation. Preperfusion respiratory insufficiency prevented removing the patient from a hyperbaric environment. In addition, she was in shock with poor urinary output and a blood pressure at times below 70 mm Hg systolic. A high left atrial pressure precluded initial extracorporeal flows above 1 liter per minute. Nevertheless, the patient was returned to normotensive levels and began to have a satisfactory diuresis. The relationship between blood pressure and extracorporeal flow is illustrated. In the first hour on perfusion the patient gave up about 1 liter of blood to the circuit indicating extensive preperfusion venous pooling.

**Figure 8**

One-half the estimated normothermic oxygen consumption and the square meter area of lung required for partial cardiopulmonary bypass are shown together with confidence limits of plus and minus 25 percent. Requirements may be reduced by both hypothermia and respiratory paralysis. Example: A 30 kg subject would be expected to need a 2M² lung for a partial cardiopulmonary bypass at 37°C.
Acid or furosemide. Where possible, monitoring the patient's weight will greatly assist in managing the fluid balance (Fig 6).7

Anticoagulation

The management of anticoagulation has generally been a very difficult problem in long-term perfusions because of the risk and extreme gravity of internal bleeding. It is probable that standard anticoagulating levels of heparin predispose to intracranial bleeding when there is prior vascular damage from hypoxia. The heparin levels used for open heart surgery are not satisfactory. Since the rate of clearance of heparin from the blood varies quite a bit from patient to patient, being influenced by urinary output8 and other less well understood factors, no standard heparin dose suffices. The Lee-White clotting time takes too long and heparin titration tests are not only time-consuming, but fail to provide information on the actual state of anticoagulation. Recently, the activated partial thromboplastin time (APTT) has been used by several investigators.8,9,10 Levels two to four times normal appear to give generally satisfactory anticoagulation with a reduced risk of bleeding. Unfortunately, only a very limited heparin range may be followed with the APTT (Fig 9), because the relationship between the APTT and the heparin level is nonlinear. An activated clotting time has been utilized by Hill et al.3,5,3 Recently, we have compared a test of recalcification time to the APTT.5 Limited experience would suggest that the recalcification time shows a much more linear relationship to the heparin level and should thus prove to be a more satisfactory clinical test (Fig 9). The half clearance time for heparin is about one to two hours.5 Consequently, a test of anticoagulation effect should be carried out about once an hour and appropriate small doses of heparin should be administered. If this is done, there should be a considerably reduced risk of bleeding (Fig 10).

Circuitry and Equipment

This subject has been dealt with in some detail elsewhere. The reader is referred to recent papers by Hill et al.,3,5 Landé et al.,10 and Peirce et al.5,7,14

Artificial Lung Support for Chronic Respiratory Disease

Use of a paracorporeal lung placed in a chronic arteriovenous fistula is under investigation.46 Such a device would be somewhat analogous to the artificial kidney now used for chronic dialysis. Patients with severe chronic respiratory distress might have considerable improvement in their gas exchange capabilities with limited risk. For those with cor pulmonale or incipient cor pulmonale, the use of a small pump with reversal of the flow in the arteriovenous fistula would provide effective venoarterial support. It should be quite possible to devise a portable lung, pump, and oxygen scrubber to permit useful ambulatory chronic respiratory augmentation.
An implantable artificial lung may eventually be possible. Some work has been carried out already and the problems do not seem insurmountable. The degree of reliability necessary for an implantable lung is, however, several orders of magnitude greater than for a paracorporeal lung since the latter could be replaced periodically.

REFERENCES


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