The Membrane Lung – Something New

Introduction

For almost a decade, the medical profession has been hearing about the promise of the membrane lung. This device has been heralded as the answer to many of the blood trauma problems associated with attempts to use bubble or disc oxygenators in extended perfusions. Indeed, it has been suggested that the availability of the membrane lung will make possible the treatment of many types of respiratory insufficiency using methods involving perfusions, not for just hours but for days. These treatment methods are now being developed and should become available soon.

The membrane lung, however, has several additional advantages over other oxygenators which recommend its use in the well-established area of total bypass.

1. Better physiological control of blood parameters—therefore improving the patient's postoperative course.
2. Reduced priming volume—thereby reducing the use of banked blood and its hazards.
3. Fixed internal volume—simplifying perfusions by reducing blood volume shift to and from the extracorporeal circuit.

Now the time has arrived when these advantages can be realized—a number of companies have made practical membrane lungs available for clinical evaluation. Already, some of these units are being used routinely, on a limited basis, for open-heart procedures. But in order to use these devices effectively, it is necessary to do more than substitute them for bubble oxygenators in existing circuits.

The unique properties of the membrane lung must be understood in order to realize its potential. The safe and efficient use of the membrane lung requires some understanding of the basic operational differences between it and the bubble oxygenator. The following discussions will focus on describing the fundamentals of gas exchange for these two important classes of gas exchange devices as a step in gaining that understanding.

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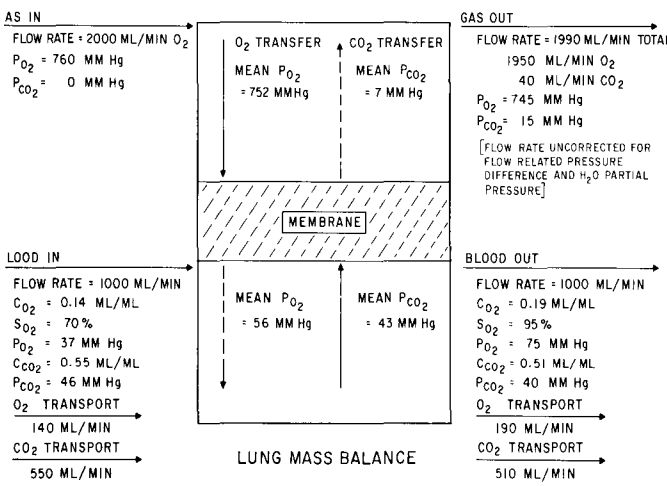


FIGURE 1—Membrane Lung Mass Balance—One Square Meter Membrane Area

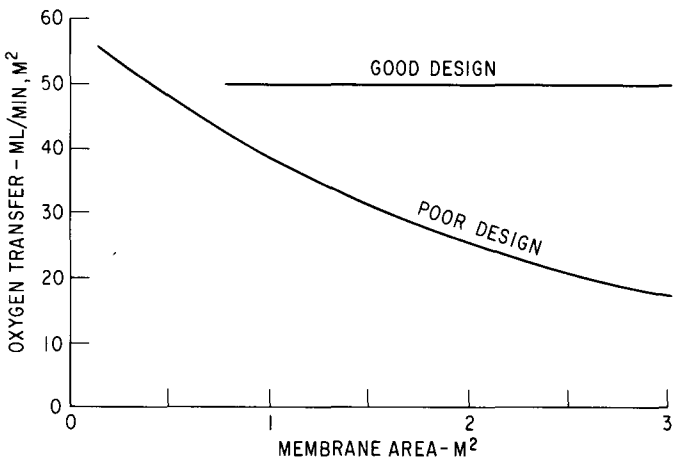


FIGURE 2—Oxygen Transfer as a Function of Lung Size for Good and Poor Designs

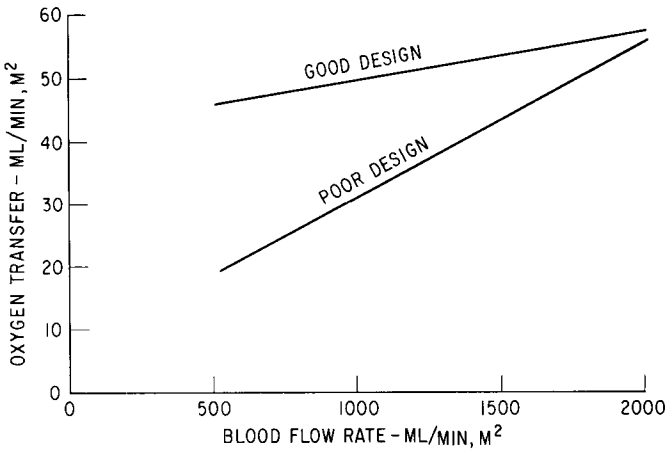


FIGURE 3—Oxygen Transfer as a Function of Blood Flow Rate for Good and Poor Designs

Bubble Oxygenator Operation

In the bubble oxygenator, gas exchange takes place across the interface between oxygen gas within the rising bubble and the surrounding blood. To maximize oxygen transfer in such a device, a stream of very fine bubbles would be used to maximize to total interfacial area. The bubbles must be of sufficient number not only to supply the oxygen requirements of the blood but also to carry off carbon dioxide.

Excessive numbers of fine bubbles, however, are difficult to remove completely from the blood because of their low buoyancy. For this reason, the problem of gas microemboli has remained a matter of concern for users of bubble oxygenators. In usual practice, bubble size distribution and gas flow rate are such that too much carbon dioxide is removed when 100% oxygen is used as the sweep gas. It is necessary to add 2-4% carbon dioxide to the sweep oxygen in order to avoid hypocapnia by establishing a minimum PCO^2 (15-30 mm Hg).

Because of the larger interfacial gas exchange area available in the bubble oxygenator, its ability to fully saturate the blood extends over a wide range of blood inlet conditions and blood flow rates. Indeed, there is often an excess of oxygen dissolved in the plasma. This excess of oxygen, which may result in partial pressures (PO^2) of several hundred, has no physiological advantage.

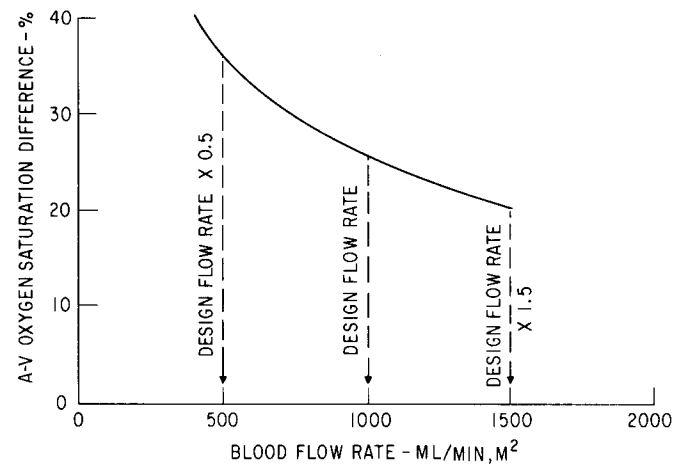
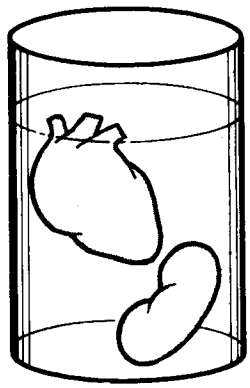


FIGURE 4—A-V Oxygen Saturation Difference as a Function of Blood Flow Rate for Outlet Saturations Below 92%



Membrane Lung Operation and Design

With the membrane lung, we see significantly different oxygen and carbon dioxide transfer characteristics. Interposed between the sweep gas and the blood is an added resistance to gas transfer—the membrane, which protects the blood from the damaging effects of the raw gas interface. In this device, gas exchange takes place because oxygen and carbon dioxide are soluble in the membrane and there exist gas concentration gradients or driving forces between the sweep gas and the blood. These gradients cause gas transfers to take place.

Oxygen is supplised to one membrane surface at one atmospheric pressure, 760 mm Hg, and will move through the membrane into venous blood which has only 44 mm Hg oxygen partial pressure. The driving force is, therefore, 760-40 or 720 mm Hg.

Carbon dioxide in venous blood has a partial pressure of perhaps 45 mm Hg and transfers into the oxygen sweep gas, which has no carbon dioxide in it, as a result of this driving force. Note that as carbon dioxide builds up on the gas side of the membrane, the already small concentration gradient is reduced. This has importance in our later discussion of the influence of sweep gas flow rate on carbon dioxide transfer.

Figure 1 is a mass balance for a typical membrane lung and demonstrates the above diagramatically. The mass balance represents a kind of engineer's accounting sheet of what goes into a system and what comes out. It bears study because it reveals relationships among gas partial pressures (tensions), gas concentrations, oxygen saturation and blood and gas flow rates.

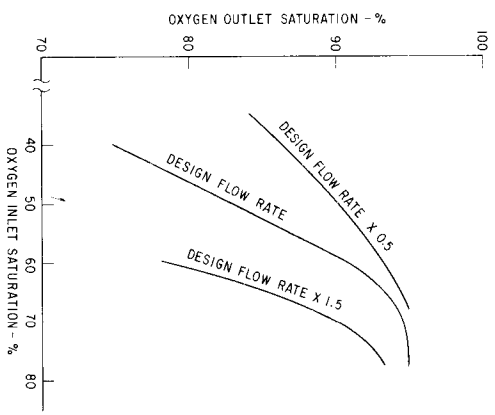


FIGURE 5—Oxygen Inlet Saturation Verus Outlet Saturation

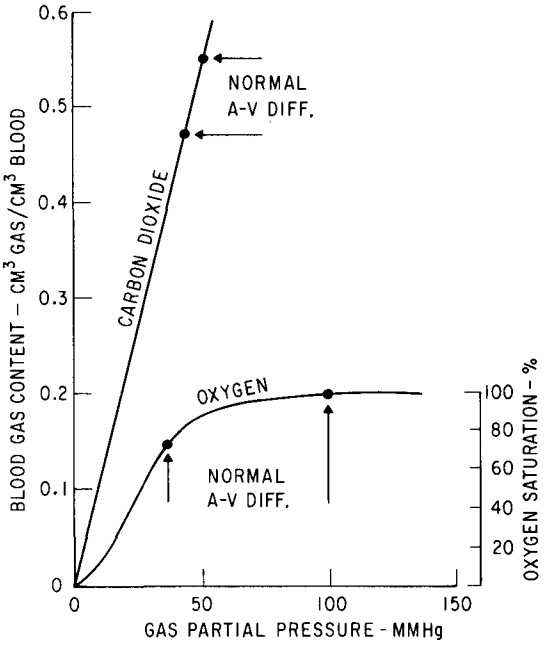


FIGURE 6—Oxygen and Carbon Dioxide Dissociation Curves

The gas transfer values shown in Figure 1 describe the performance of a particular membrane lung having one square meter of membrane area. Naturally, the total gas transfer capability of a device will depend upon the membrane area exposed to the blood. Performance specifications, therefore, are often expressed in units which include the membrane area, usually in square meters, e.g. milliliters O^2 transfer/minute, square meter, and blood flow in liters/minute, square meter.

Evaluation

One of the first considerations in the evaluation of membrane lung designs is the oxygen transfer efficiency as a function of the exposed area. As shown in Figure 2, the oxygen transfer on a unit area basis should be independent of size. However, in a poor design, there is often a *decrease in efficiency* as the unit size increases, usually because of poor blood distribution, Thus, it is dangerous to extrapolate performance of small laboratory size units to larger clinical units without knowing the effect of size. Indeed, this has been one of the major obstacles with many design concepts.

An extremely important part of good membrane lung design is the control of the blood film which is spread over the active exchange area of the membrane. For efficient oxygenation, this film must be both thin and uniform. A non-uniform film will result in "shunts" in which preferential flow through the thicker portions of the film causes poor utilization of the available membrane area and compromises performance. If the film is too thick, contained blood volume within the device will be excessive and only the small amount of blood that comes into close proximity to the membrane becomes saturated. The remainder of the blood in the center of the film remains relatively unsaturated.

One way to reduce the effect of thick blood films is to increase the velocity of the blood flowing past the membrane. With fixed dimensions, this can be done by increasing the blood flow rate. In the well designed lung where the blood film is minimal to begin with, there will be only a modest increase in oxygen transfer with increasing blood flow rate. In the poorly designed lung in which a thicker blood film exists, increasing the blood flow rate yields considerably greater oxygen transfer rates. This marked dependence of oxygen transfer on blood flow rate is shown in Figure 3.

These facts suggest that, particularly for a poorly designed lung, one would want to use high blood flow rates to improve oxygen transfer. Indeed, this is sometimes done through the use of high rates of recirculation around the lung. Such recirculation, however, carried with it the risk of increasing blood trauma, the very thing one uses the membrane lung to avoid. Single pass operation, therefore, is to be preferred.

However, in such single pass operations, there is an upper limit imposed on blood flow rate by certain physiological considerations. As flow rate is increased, even though there may be an improvement in oxygen transfer, the contact time of a unit volume of blood with the membrane decreases. This results in a decrease in the volume of oxygen added to this unit of blood.

Such a decrease reduces the outlet saturation of the blood. It is unlikely that an arteriovenous saturation difference of less than 25%—the normal value achieved by the human lung—would be adequate in most perfusions.

Design Flow Rate

In Figure 4, the flow which corresponds to thia A-V saturation difference is designated Design Flow Rate and is the maximum flow at which this minimum physiological saturation difference can be maintained. This is the single most important factor in choosing an appropriate size lung are mechanically possible, it must be recognized that this will be at the expense of outlet saturation, even though the oxygen transfer per unit area may well be somewhat increased.

In Figure 5, outlet saturation is plotted versus inlet saturation for a typical membrane lung. For a given blood flow rate this should be a straight line relationship. Indeed, this is true up to an outlet saturation of about 92%. Above this, there is a significant change in the slope of the oxyhemoglobin dissociation curve. The leveling off of the inlet-outlet saturation curve is, then, a result of the character of the blood and not of the membrane lung.

The dissociation curve, which is presented in Figure 6, acts to limit the increase in oxygen saturation achievable through addition of more oxygen gas. Addition of sufficient oxygen to overwhelm even this natural barrier—as can be done in the bubble oxygenator—would, with current membrane lung designs, require the use of inordinate amounts of membrane material and, thereby, significantly compromise the priming volume of the device—as well as its

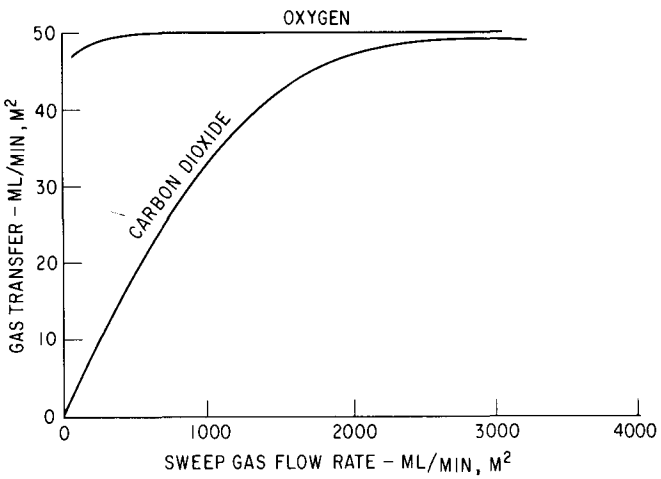


FIGURE 7—Gas Transfer as a Function of Sweep Gas Flow Rate

cost. The designer of the membrane lung, therefore, seeks to mimic the function of the natural lungs and not that of the bubble oxygenator.

Gas Flow Rate

Another factor in membrane lung operation is the sweep gas flow rate. As shown in Figure 7, the sweep gas flow rate influences oxygen transfer very little. Carbon dioxide, on the other hand, is affected to a considerable extent. This is so because, as noted above, at low sweep gas flow rates, the partial pressure of carbon dioxide in the sweep gas becomes significant.

Thus, the already small carbon dioxide concentration gradient is reduced still further and the transfer is reduced. This phenomenon may offer to the perfusionist a method of control of blood PCO^2 which is unavailable with the bubble oxygenator. By varying gas flow rates, the patient's PCO^2 and acid-base balance may be influenced.

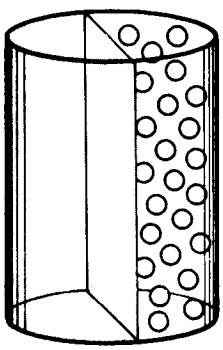
This method assumes, of course, that adequate carbon dioxide transfer capability is available. This will only be so if the lung size chosen is adequate. Here lies the second important point about lung sizing—a lung should be chosen with a knowledge of the carbon dioxide removal requirements of the subject in mind.

From the foregoing, it is clear that unlike the bubble oxygenator, where blood flow rate is often the basis for choosing a device size, the membrane lung size must be chosen with a full understanding of gas transfer requirements of the case—both for oxygen and carbon dioxide. This understanding, coupled with a knowledge of the underlying principles of membrane lung function and suitable circuit designs, will provide tools for successful perfusions of *both* short *and* extended term.

Summary

In order to take advantage of the oft described advantages of the membrane lung, one must understand some of the basics of its design and function. These differ markedly from those of the bubble oxygenator. Membrane lung performance depends upon the area of membrane available for gas transfer, the blood and gas flow rates, and the gas partial pressure gradients between the blood and sweep gas. The choice of a membrane lung must be based first upon the oxygen delivery and carbon dioxide removal requirements of the patient, and only secondarily on the blood flow rate anticipated. This paper will demonstrate why this is so and also offer guidelines for distinguishing between good and poor membrane lung designs.

Dialysis



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PHAGOCYTOSIS BY POLYMORPHONUCLEAR LEUKOCYTES IN PATIENTS WITH RENAL FAILURE ON CHRONIC HEMODIALYSIS

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ABSTRACT

Polymorphonuclear leukocytes (PMN) and plasma were obtained from patients with chronic renal failure (CRF) to determine in vitro phagocytic and bactericidal capabilities. Patients who were maintained on chronic maintenance hemodialysis and comparable CRF patients not on hemodialysis maintained normal PMN bactericidal activity. Plasma from these patients demonstrated normal opsonic activity. Intracellular PMN cathespin D was increased in both dialysis and CRF patients.

Phagocytosis and bactericidal activities in PMN's from dialysis and CRF patients were, therefore, normal. It is apparent then that those patients who develop infections while on hemodialysis do so not because of impaired PMN phagocytic capacity but because of multiple other factors.