

HEMODILUTION & RENAL FUNCTION - A Review

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Continuing experience with extracorporeal circulation has resulted in an increased understanding of the physiology of perfusion. Four and five hour perfusions can now be conducted with safety equivalent to that of one hour perfusions performed five years ago. Much of this safety is attributable to the use of diluents as partial or total substitutes for blood prime in the pump oxygenator. Severe, progressive hypotensive and hypovolemic reactions have been mitigated and postoperative management of critically ill patients has become simplified. Nevertheless, several problems still remain. Perfusions lasting longer than five or six hours are still attended by substantial mortality and much of this mortality is related to the perfusion itself.

Homologous Blood Reactions:

Early experience with cardiopulmonary bypass in dogs revealed the consistent development of a syndrome characterized by hypotension, acidosis, effective circulating hypovolemia, and frequent demise. A similar syndrome was encountered in patients. Comparison of pre- and postoperative blood volumes, as measured by isotopic techniques, disclosed substantial postperfusion deficits in both the plasma and erythrocyte compartments. Those patients suffering the most severe volume changes were also the ones whose immediate and early postoperative courses were most stormy. Investigation of the phenomenon in the experimental animal permitted exclusion of many possible variables. It became evident that many of the difficulties encountered could be reproduced by simple exchange infusion of large volumes of homologous donor blood. The results were not substantially altered by typing and cross matching the blood by available techniques. Employment of any one of a number of diluents to replace blood was accompanied by striking amelioration of many of these adverse sequelae.

Hemodilution:

Hemodilution, as introduced by Gollan and further developed by other investigators, has now achieved widespread acceptance. However, critical information about the nature of an optimal diluent is still being accumulated. Currently available diluents include isotonic solutions which have no colloid osmotic pressure effect such as saline, Ringer's solution, and 5% dextrose in water. Another group of diluents widely employed is characterized by hyperosmolality. Principle examples of this group are 5% dextrose in Ringer's solution and 5% dextrose in saline. A third group of diluents partially duplicates the colloid osmotic effect of plasma. High and low molecular weight dextrans and serum albumin have been employed to this end. The fourth type of diluent employed is plasma, either autologous or homologous. Exchange infusion of each of these groups of diluents in experimental animals reveals specific problems attributable to each: (Fig. 1)

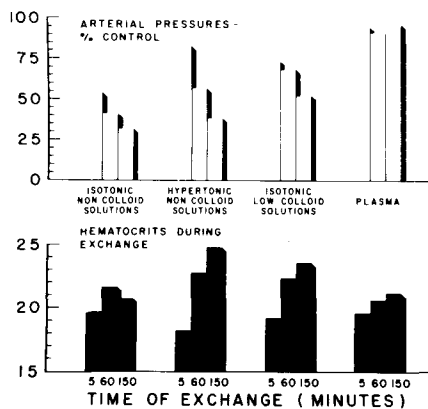


Figure 1: Correlation of arterial pressure and hematocrit changes during exchange infusion of four different types of diluents. Sharp rise of hematocrits in the hypertonic and low colloid groups is indicative of loss of intravascular fluid volume.

1. Isotonic, non colloid solutions - constant volume exchange of large volumes (100 ml./Kg.) of these fluids results in rapid production of severe hypotension. Cardiac output is well maintained and calculated total peripheral vascular resistance drops precipitously. An initial dilutional acidosis appears which is followed by the development of severe

metabolic acidosis. Approximately 50% of animals so exchanged will expire during the operative procedure. The reactions are not materially influenced by addition of large amounts of buffer or by having the animal inspire high concentrations of carbon dioxide to inhibit lactic acid production at the cellular level. The reaction is not dependent on the electrolyte make-up of the diluent being used. In a sense a type of low peripheral vascular resistance shock is produced. (Fig. 2) Meas-

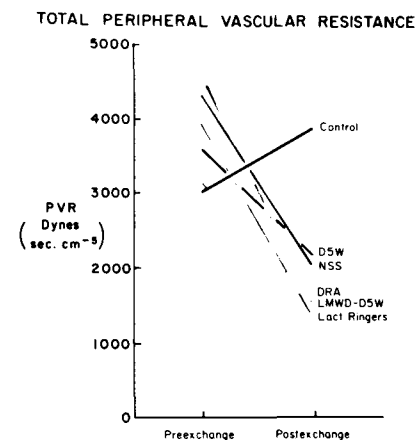


Figure 2: Precipitous fall of total peripheral vascular resistance occurring with exchange of diluents.

ured blood volumes and hematocrits remain the same after the initial dilution indicating no significant changes of intravascular volume.

2. Hypertonic solutions - immediately after onset of constant volume exchange, the systemic arterial pressure is maintained. Volumetric studies reveal a transient augmentation of intravascular compartment by the hyperosmolar solution. Shortly thereafter, however, the intravascular volume begins to decline and there is a significant increase in the hematocrit. As intravascular water loss proceeds, the animal becomes hypotensive and substantial hypovolemia is demonstrable.

3. Isotonic low colloid solutions - the response to this group is similar in most respects to the reactions to hyperosmolar diluents. After a brief period of stability, there is evidence of intravascular water loss, hypovolemia, and progressive hypotension and acidosis.

4. Plasma - unlike the other groups of diluents utilized for constant volume exchange, the oncotic effect of plasma appears to protect the animal from most of the changes observed. Arterial pressures are well maintained throughout the exchange infusion and acidosis does not develop despite elimination of additional buffering under these normothermic conditions. The degree of dilution is identical to the other groups indicating that acute anemic anoxia is not the cause of the problem. Dialysis of autologous plasma against Ringer's solution removes all catecholamines and trace elements. This plasma behaves favorably under the conditions of these experiments. All animals subjected to this type of exchange were long term survivors. It should be pointed out that in this type of exchange infusion there is no oxygenator in the system and one does not therefore deal with problems of denaturation of plasma proteins by an oxygenating system. This factor would appear to be a limiting one in the use of plasma as a diluent. In addition, homologous plasma produces specific anaphylactoid reactions which limit its usefulness.

At present, it is necessary to understand and accept the limitations of all diluents during hemodilution perfusion and make appropriate corrections. The dilutional and meta-

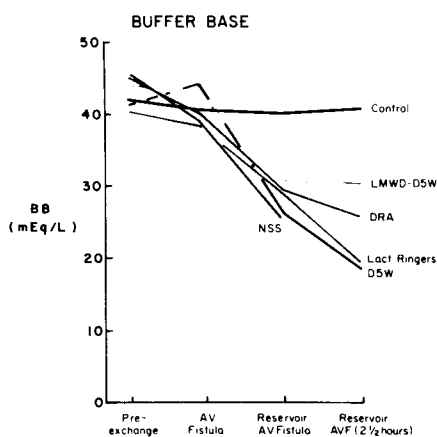


Figure 3: Dilutional and metabolic acidosis appearing with constant volume.

bolic acidosis (Fig. 3) occurring during hemodilution perfusion re-

quires adjunctive buffering with either organic buffers such as THAM or inorganic buffers such as sodium bicarbonate. The hypotensive reaction and hypovolemic states must be counteracted by substantial degrees of over infusion both during and immediately after perfusion. Further protection can be offered by mild hypothermia during the period of exchange. Considerable safety has been attainable by these methods, however it should be realized that perfusions lasting longer than five or six hours are still attended by substantial morbidity and mortality. An ideal diluent would probably consist of a colloid substance of approximately the same osmotic concentration as plasma proteins but which will not produce allergic reactions and will not undergo substantial changes during oxygenation.

Renal Function:

The presence of a large urine volume during and after perfusion is not in itself indication of optimal renal function. Excretion of urine is the sum of total of many complex physiological occurrences including excretion, reabsorption, extra renal hormonal control, and other specific aspects such as counter current multiplier exchange. It is possible, for example, by blocking reabsorption to have a large volume of urine produced in the face of severely impaired renal function. This is perhaps best illustrated by some numerical data. In the normal man approximately 650 milliliters of plasma per minute pass through the kidneys. Approximately 120 milliliters per minute or urine is filtered at the glomerular level. If none of this urine were absorbed this would result in a urine flow of approximately 7 liters per hour or over 160 liters of urine in a 24 hour period. Obviously then reabsorption occupies a significant role in total urine production. The use of solutes such as glucose or mannitol in the perfusate results in a high concentration of these particles in the urine. Reabsorption of these particles is limited by the kidneys. Consequently, most of the particles pass out into the urine and pull water with them. (Fig. 4) It is

therefore possible to have substantial volume of urine produced in the presence of diminished renal plasma

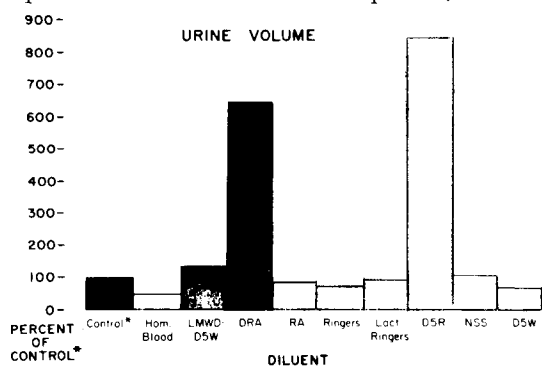


Figure 4: Urine flows during exchange infusion of various diluents. Note high urine volumes with hyperosmolar solutions DRA and D5R.

flow (occurring secondary to diminished cardiac output) and diminished glomerular filtration rate. Physiological studies during experimental and clinical cardiopulmonary bypass have demonstrated that both renal plasma flow and glomerular filtration rate are in actuality diminished throughout the period of perfusion irrespective of the diluent utilized. The total response may represent only 50% of normal function. Urine flow may also be enhanced by the use of such non reabsorbable solutes as THAM. However, once again the effect is to pull water out by preventing its reabsorption rather than to specifically improve renal function. Some beneficial effects may result from this wash out mechanism. It is extremely important to understand the pattern of renal function and urine flow for whatever diluent is being utilized. Urine osmolality is of substantial help in determining whether oliguria late after perfusion is a result of return to normal reabsorptive mechanisms or is secondary to renal disease. Most renal problems occurring after perfusion are the result of poor renal perfusion due to inadequate cardiac output. Primary renal abnormalities after hemodilution perfusion are relatively rare.

Summary:

Considerable improvement in perfusion and postperfusion mortality and morbidity have resulted from

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Monitoring Blood Gases & pH During Open-Heart Operations

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Tensions of oxygen and carbon dioxide, and pH, in blood may be considered indicators of adequacy of lung (and oxygenator) function and tissue perfusion. The cardiologist draws such inferences during preoperative study, and anesthesiologist, surgeon, and extra-corporeal apparatus technician make similar assessments before, during, and after cardiopulmonary bypass.

Malfunction of myocardium or hypovolemia are implied when there are wide arteriovenous differences of oxygen, CO₂, or pH. During bypass the implication is inadequate rate of flow. Postoperatively one infers improper blood volume, excess vasoconstriction for which "dilators" or blocking agents are indicated, or poor myocardial contractility requiring stimulation or control of rhythm.

Normally there are 20 cc. of oxygen in 100 cc. of arterial blood (20 volumes percent) and 15 cc. in 100 cc. of venous blood (15 volumes percent). Percent oxygen saturation is approximately 100 percent in arterial blood, 75 percent in

venous blood of patients with normal circulation. Thus, 5 cc. oxygen difference (5 volumes percent difference) is equivalent to 25 percent oxygen saturation difference between arterial and venous blood. For practical considerations, 5 percent saturation is approximately 1 volume percent.

Oxygen tension in arterial blood refers to the gas which has diffused through walls of alveoli and capillaries of lung. A human being with normal function of lungs and heart, breathing room air at sea level, has tension (capital P is the symbol for tension; partial pressure is a synonym for tension) of oxygen of approximately 100 mm. Hg in arterial blood, and 35 in venous blood. Fortunately, for ease of remembrance and usefulness of application, there are numerical relationships between percent oxygen saturation and PO₂. These may be seen in the oxyhemoglobin dissociation curve.

concerned with perfusion and oxygenation of blood of patients.

What is the importance of knowing percent oxygen saturation of venous blood? Spencer, et. al noted that prediction of survival correlated closely with percent oxygen saturation of venous blood, since the latter corresponds with adequacy of tissue perfusion.

When venous saturation is 70 percent, the team may be confident of supplying tissues with their oxygen requirements. Venous saturations below 60 percent demand correction of causes, for brain function may be depressed if blood flow to the brain is so low that percent oxygen saturation of blood draining from the brain is below 60 percent. Death may be imminent if saturation is below 40 percent. Metabolic acidosis will occur rapidly and progressively at this low saturation.

Arterial blood PO₂ normally is 100 mm. Hg. It seems unreasonable to allow patients with heart disease undergoing heart surgery and cardiopulmonary bypass to have lower PO₂. There is an exception which is tolerated during cardiopulmonary bypass, where 70 mm. Hg is the lowest value permissible in blood leaving the oxygenator. This corresponds to saturation of 90 percent, the level frequently observed in pediatric and adult patients with heart or lung diseases, and in most normal patients following anesthesia. It is rare that PO₂ falls to this level and the drop unusually is transient, using a disc oxygenator. Attempts to raise PO₂ from levels below 100 mm. Hg involves increased flow rate of gases or increased disc speeds, both of which lower PCO₂. In the interest of physiologic perfusion, it is preferred to maintain near-normal PCO₂. In the interest of simplicity, it is preferred to omit the addition of gasses containing carbon dioxide.

Partial pressure of carbon dioxide (PCO₂) normally is 38 mm. Hg in arterial blood, 44 mm. Hg in venous blood. The commonest deviation is low PCO₂ readily induced with a few deep breaths. Hyperventilation may be due to

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the use of diluents to replace blood primes in large volume pump oxygenating systems. The various diluents presently available are not in themselves inherently without dangers. Perfusion and postperfusion management must take cognizance of the specific deficits of each of the diluents of appropriate protective measures to be taken. These include overinfusion and buffering. Moreover, the mere presence of a large volume of urine during and immediately after perfusion does not signify excellent renal function. In fact renal function during perfusion, even with optimal hemodilution, is invariably depressed. However, primary renal failure following hemodilution perfusion is rare. Most difficulties with renal function are the result of inadequate cardiac output immediately after cardiopulmonary bypass.

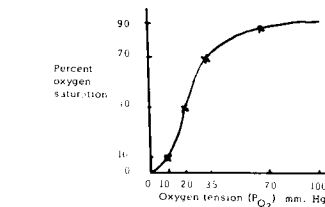


Figure 1. Oxyhemoglobin dissociation curve.

Percent Oxygen Saturation	Oxygen Tension	Ratio
1 - 10%	1 - 10 mm. Hg	1:1
40 - 70%	20 - 35 mm. Hg	2:1
90 - 100%	70 - 100 mm. Hg	Slowing toward 1:1

Figure 2. Normogram of relationships between oxygen saturation and tension.

The oxyhemoglobin dissociation curve shows the relation between percent oxygen saturation and PO₂ (partial pressure; oxygen tension). It may be noted there is a ratio of 1:1 up to 10 (10 percent saturation, 10 mm. Hg); 2:1 between PO₂ of 20 mm. Hg, equivalent to 40 percent to 70 percent saturation; tapering toward 1:1 again at 90. Thus, PO₂ 20 mm. Hg is equivalent to 40 percent saturation; 25 mm. Hg is 50 percent saturation; 30 mm. Hg is 60 percent saturation; and 35 mm. Hg is 70 percent saturation: These approximate conversions are helpful to all personnel