

Measurements of Perfusion Adequacy

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INTRODUCTION:

If one were to survey the many centers performing open-heart surgery in the world and ask the perfusionists, "What do you think is the single most important parameter to monitor during heart-lung bypass to insure adequate perfusion?" I expect a great variety of answers would be forthcoming. Arterial blood pressure, venous pressure, blood flow, urine output, arterial blood gases, venous pO₂, and pH would all surely appear on the list. If we were to compound the question by demanding that the survey respondents also supply the acceptable limits that they feel are required for their chosen parameters, the number of different answers would rise exponentially. The purpose of this presentation is *not* to tell you how to run perfusion but rather to take an indepth look at several monitored parameters. These parameters will be analyzed as to their value in assessing perfusion adequacy and the potential sources of error in using the parameters.

The parameters to be investigated are grouped under three heading; hemodynamic, organ function and chemistry. It should be understood that all of the functions are interrelated so some mixing of categories is inevitable.

HEMODYNAMIC PARAMETERS:

The basic relationships that need to be considered in order to understand the hemodynamics of extracorporeal circulation are expressed in the equations in figure 1.

$$P = Q \times R$$

or $Q = \frac{\Delta P}{R}$

or $Q = \frac{\Delta P}{Q}$

where ΔP = the pressure dropoff across a vascular bed.

Q = the blood flow.

R = the resistance to flow.

Since it is the function of our devices to take over the circulatory function of the heart and lungs, the first of these functions that we will look at is blood flow. In our survey we might well see recommended flow indices ranging from 35 ml/kg/min¹ up to well over 100 ml/kg/min or from 1.4L/m²/min to 4L/m²/min. This wide range of flow indices goes both above and below the physiological cardiac index and probably does have, somewhere within the range, the optimal flow index.

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PRESSURE - FLOW - RESISTANCE RELATIONSHIPS

$$\text{PRESSURE DIFFERENCE} = \text{FLOW} \times \text{RESISTANCE}$$

$$\text{FLOW} = \frac{\text{PRESSURE DIFFERENCE}}{\text{RESISTANCE}}$$

$$\text{RESISTANCE} = \frac{\text{PRESSURE DIFFERENCE}}{\text{FLOW}}$$

Figure 1

NORMAL BLOOD FLOW DISTRIBUTION

ORGAN	FLOW L/MIN	A-V O ₂ DIFFERENCE VOL %	O ₂ UPTAKE ML/MIN
BRAIN	.8	8.0	64
HEART	.3	11.0	33
KIDNEY	1.2	1.7	20
GI TRACT, LIVER, SPLEEN	1.3	2.7	48
MUSCLE, SKIN, BONE	1.4	5.3	75
TOTALS	5.0	4.8	240

Figure 2 AFTER GALLETI AND BRECHER

Figure 2 shows the normal blood flow and its distribution in the resting, average adult human being. There are a number of observations that can be made from these data. The organ mass is not important in determining flow distribution. The kidneys, which constitute approximately one half of one percent of the body weight, receive over 20% of the blood flow.² At the same time it is obvious that oxygen demand is not the key to the high renal fraction because the A-V O₂ difference is very low. The kidneys receive such a high blood flow due to their homeostatic functional requirements.

The heart and brain, on the other hand, though they have high flows for their respective weights, also have large A-VO₂ differences indicating that the high flows are required to deliver adequate substrate supplies to these organs and to remove metabolites as they are produced. The point made by these data is that the body, under normal conditions, takes care of the distribution of flow so that organ systems receive their requirements under a variety of conditions.

PUMP BLOOD FLOW DISTRIBUTION

ORGAN	NORMAL	HIGH	MEDIUM	LOW	AZYGOS
BRAIN	.8	0.7	0.7	0.5	.3
HEART	.3	0.3	0.3	0.2	.15
KIDNEY	1.2	0.7	0.5	0.2	--
GI TRACT	1.3	1.3	0.8	0.5	.25
MUSCLE, SKIN	1.4	1.5	1.0	0.6	.3
TOTALS	5.0	4.5	3.3	2.0	1.0

Figure 3 AFTER GALLETTI AND BRECHER

The next figure (Fig. 3) illustrates flow distribution when the circulation is taken over by heart-lung bypass. From these data, it should be obvious that the bodily regulatory system will continue to perform its function even under extremely low flow conditions. This is accomplished by shunting blood from the systems that can best tolerate ischemia.

We will attempt to quantify "optimal blood flow rate" later in this discussion. We do know that pump oxygenator systems are traumatic so, for the present, "optimal flow rate" will be defined as the lowest flow rate that will maintain homeostasis.

Blood pressure is the next function that we need to investigate. It is quite convenient to consider the arterial and venous pressures separately. However, one should not forget that the two systems are interconnected via the capillary bed and hemodynamically we must consider pressure differences. It is pressure differences that cause blood to flow.

There is as much controversy concerning optimal arterial pressure as there is regarding blood flow rates. Reed and Clark³ state that as the pressure approaches 90, hypotensive drugs should be used. A perfusionist who works across the parking lot from Reed and Clark is instructed to start the Neo-synepherine if the pressure is as low as 90 mm Hg.

Going back to the pressure, flow, resistance formula, it should be apparent that if the flow rate is adequate, the arterial pressure is essentially a function of the total vascular resistance. The effect of venous pressure on the arterial pressure during heart lung bypass is usually minimal whereas in the intact individual venous pressure is important because it provides the primary filling pressure for the right ventricle and thus affects cardiac output. The venous system is also the capacitance system where almost half of the total blood volume is to be found.⁴ In the intact individual the venous pressure then gives us important information concerning blood volume and right ventricular filling pressure.

For the moment neglecting venous pressure, we can analyze the resistance factors controlling arterial blood pressure under optimal flow conditions by using the familiar Poiseuille's formula describing resistance. (Fig. 4) The two variables that are important are viscosity and vessel radius. Viscosity varies with temperature and dilution.⁵ As we hemodilute, if the flow is kept constant, the pressure should be lowered. If hypothermia is induced, the viscosity increases causing a rise in blood pressure. Plasma protein denaturation, a function of pump-oxygenator trauma, may also significantly increase viscosity.⁶

POISEUILLE'S LAW

$$R = \frac{8 \eta L}{\pi r^4}$$

R = RESISTANCE

$$\frac{8}{\pi} = \text{CONSTANT}$$

η = VISCOSITY

L = LENGTH

r = RADIUS

Figure 4

By far the most potent control over total vascular resistance is described in the r^4 factor. As the arterioles constrict and dilate to control the flow of metabolic substrates and metabolites to and from the various capillary beds, they exert approximately 41% of the total vascular resistance.⁷

So, what does high or low pressure mean? Does high arterial pressure insure good perfusion? No, it only signifies high arteriolar tone. Does low arterial blood pressure indicate poor perfusion? The answer must again be no. Low pressure may simply mean that the total resistance is down and capillary perfusion is occurring as usual. As a generality, it is probably safe to assume that as long as the arterial pressure exceeds the critical closing pressure of the organ system with the highest critical closing pressure, perfusate is reaching all vascular beds. Experience tells us that, when we deliver adequate blood flow to our patients with our essentially pulseless pumps, we will see blood pressures ranging between 50 and 90 mmHg. Deviations from this "normal range" do not necessarily indicate perfusion problems but rather variances from the normal vascular resistance patterns. These changes *may* forecast problems but, by themselves, are of little value in predicting perfusion adequacy.

I would be totally remiss if I did not modify the above discussion when faced with a patient with vascular disease that may impair the normal blood flow distribution functions. If a patient has a partial obstruction of the carotid artery that will not allow the normal selective shunting to the brain in the event of hypotension, it is probably wise to insure perfusion of this bed by maintaining the blood pressure at approximately the patient's normal level.

Finally, it is useful to consider the pressure dynamics acting on the capillaries. These forces are summed up in figure 5. The pressure entering the capillary is

CAPILLARY DYNAMICS

INTERSTITIAL PRESSURE - 5 mmHg ONCOTIC PRESSURE - 4 mmHg	INTERSTITIAL PRESSURE - 5 ONCOTIC PRESSURE - 4																				
<u>ARTERIOLAR</u>	<u>VENULAR</u>																				
HYDROSTATIC PRESSURE - 28 mmHg ONCOTIC PRESSURE - 28 mmHg	HYDROSTATIC PRESSURE - 15 ONCOTIC PRESSURE - 28																				
END	END																				
SUMMATION OF FORCES	SUMMATION OF FORCES																				
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Figure 5

controlled by the arteriole. The amount of arteriolar tone is, under most perfusion conditions, controlled by the concentration of metabolites leaving the capillary. So with adequate perfusion this pressure stays relatively constant. The venular pressure however, is subject to drastic elevation during heart-lung bypass. If the venous cannulation is inadequate, the venous pressure may be elevated. This is communicated to the capillary and may impede the take up of water resulting in tissue edema. This is especially true if a non-colloid hemodilution has lowered the plasma oncotic pressure to any degree. The lower the venous pressure, as long as return is not impeded, the better for capillary bed drainage.

ORGAN FUNCTION

Many organ systems have been studied during ECC in an effort to ascertain the adequacy of perfusion to that organ system. Since the central nervous system is that system with the least hypoxic tolerance, it has been subjected to intense study. In the early days of ECC, it was common to attach electroencephalographic leads to all patients and to run continuous EEG traces in at least one lead during the entirety of heart-lung bypass. The normal pattern of EEG behavior was established in this fashion. Most patients show gross disturbances in the EEG patterns upon the initiation of bypass, disturbances that revert to the normal anesthetized pattern within five to ten minutes. As a result of the thousands of EEGs performed in those early days of heart-lung bypass, confidence was gained in the ability of the circulation to protect the brain from hypoxia under a wide range of conditions. The EEG is not routinely monitored during bypass in most centers today.

The major hazard that exists relative to the CNS today is that of embolization. These hazards are being reduced by the use of filters in the extracorporeal circuit. The exact type of filter and the filtration size is still being debated and studied. Regardless of this debate, there is an overwhelming body of evidence that filtration is desirable to insure adequacy of brain perfusion.⁸⁻⁹⁻¹⁰

The effect of perfusion on the heart has been extensively studied also. The studies have generated the same conclusions as in the brain perfusion studies. In the patient

with normal coronary blood vessels, who is provided with an adequate total blood flow, the autoregulatory system will insure adequate coronary perfusion through the normal routes. The problem that does arise in insuring perfusion adequacy to the heart is that in many operations, one can not provide normal coronary distribution. Quite often the aorta must be cross clamped. Often the heart is arrested or fibrillated. The patient population undergoing heart-lung bypass has changed also. The number of patients with maldistribution of coronary blood supply has risen sharply as surgical procedures for correcting these problems have been developed. The debate on the best way to protect the myocardium during periods of ischemia is still in progress. It appears that ultimately some combination of hypothermic cardioplegia supplemented by the addition of an anaerobic substrate to the myocardium may prove to be the best method of protecting the heart when we cannot insure adequate perfusion.

The organ system that provides the best monitoring capability for assessing total body perfusion is the renal system. The kidneys in the average patient have the highest critical closing pressure. Thus, if there is urine being produced, we are assured that the kidneys are being perfused and we can assume that perfusate is reaching the other capillary beds.

The problem in depending on urine output as an indicator of perfusion is in determining what is "normal" output, what the reasons for decreased output may be, and how to treat real renal perfusion problems.

Figure 6 lists a number of factors that alter urine output. If these factors are remembered in assessing renal function, a number of conditions that might appear to be indicative of poor perfusion may turn out to be physiologic.

FACTORS AFFECTING URINE OUTPUT	
<u>GFR FACTORS</u>	<u>OTHER FACTORS</u>
ARTERIAL BLOOD PRESSURE	ADH LEVELS
PRECAPILLARY SHUNTING	HYPER-OSMOLARITY
PULSATILE BLOOD FLOW	HYPO-OSMOLARITY
RETROGRADE PRESSURE	DRUGS
GLOMERULAR STATUS	DIURETIC DRUGS
PLASMA PROTEIN CONCENTRATION	MUST BE FILTERED

Figure 6

CHEMISTRY:

The body consumes many substrates. Among these are water, amino acids, sugars, fats and oxygen. For most of these substrates, the body has a built in reserve allowing for periods of noningestion of the substrates. The one vital substrate with the least amount of reserve, and thus the one in most constant demand, is oxygen. Four or five minutes deprivation of oxygen can irreversibly damage certain tissues and the

ANAEROBIC AND AEROBIC ENERGY PRODUCTION

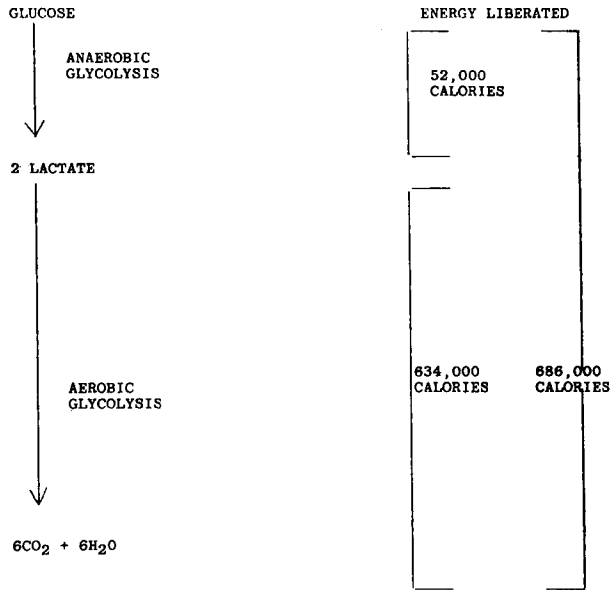


Figure 7

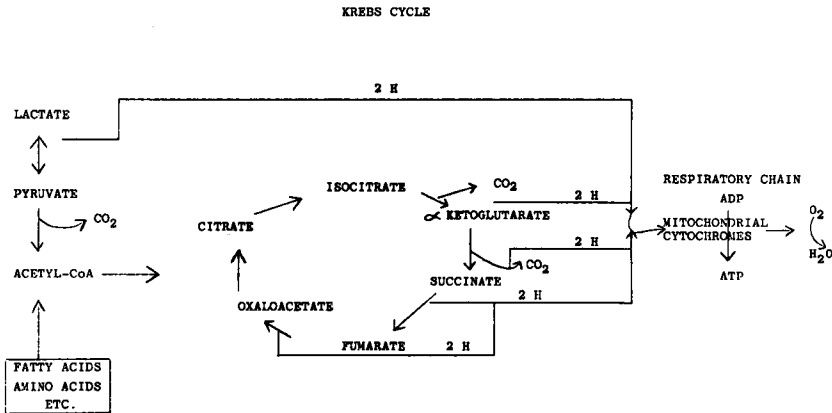


Figure 8

entire organism will die within ten minutes after the onset of anoxia. How and why is oxygen utilized and what are the results of oxygen lack?

Figure 7 shows the amount of energy released through the metabolic breakdown of glucose in the body. Of the total 686,000 calories available, it should be noted that only 52,000 or less than 1/10 of the total is released through anaerobic metabolism. The remaining 90% of the energy is only released through the aerobic pathway in the mitochondria. This is the major production pathway for the large amounts of energy required to maintain cellular integrity in the mammalian organism. (Fig. 8)

AVERAGE NORMAL VALUES

ARTERIAL pO ₂	100 Torr	Venous pO ₂	40 Torr	
ARTERIAL Saturation	98%	Venous Saturation	70%	
ARTERIAL Content	20Vol%	Venous Content	15Vol%	
Hemoglobin	15gm%			
HEMATOCRIT	40%	A-V O ₂ Difference	5Vol%	Figure 9

FICK PRINCIPLE

$$\text{CARDIAC OUTPUT} = \frac{\text{OXYGEN CONSUMPTION}}{\text{A-V O}_2 \text{ DIFFERENCE}}$$

$$\text{A-V O}_2 \text{ DIFFERENCE} = \frac{\text{OXYGEN CONSUMPTION}}{\text{CARDIAC OUTPUT}}$$

Figure 10 $\text{OXYGEN CONSUMPTION} = \text{CARDIAC OUTPUT} \times \text{A-V O}_2 \text{ DIFFERENCE}$

FICK PRINCIPLE

$$\text{OXYGEN CONSUMPTION} = 5\text{LPM} \times .05 \text{ liter/liter}$$

$$\text{OXYGEN CONSUMPTION} = .25\text{liters/minute}$$

$$\text{OXYGEN CONSUMPTION} = 250 \text{ ml/minute}$$

Figure 11

As can be seen from the figure, no CO₂ is produced until the aerobic cycle begins, and O₂ is not available at the end of the sequence, the whole system backs up and pyruvate will be converted to lactate, causing an accumulation of acidic by-products. The body can survive only a very short time on the energy released by anaerobic glycolysis. Without oxygen, not enough energy is available to maintain cellular function and cells die. To paraphrase Haldane: Anoxia not only stops the cells, it destroys them.

Of great significance in this scheme is the fact that tissue hypoxia announces itself by the production of nonrespiratory acids, the so called lactic acidemia of poor tissue perfusion. The rapid appearance of this metabolic acidosis makes acid base balance a most sensitive indicator of the adequacy of perfusion.

Now that we have reviewed the site of utilization of oxygen and the results of not having the oxygen available, let us turn our attention to quantification of oxygen requirements. I am going to limit these remarks to the average adult patient for simplicity's sake. We should all be aware, however, that children and infants have higher oxygen requirement indices than adults.

Figure 9 gives typical blood gas data for the average adult individual. Measuring the arterial and venous pO₂ or oxygen saturation, and the hemoglobin concentration allows us to calculate the arteriovenous oxygen content difference. In the average, normal individual this approximates 5 volumes percent. Solving the Fick formula (Fig. 10) for oxygen consumption and (Fig. 11) plugging in the A-V O₂ difference and

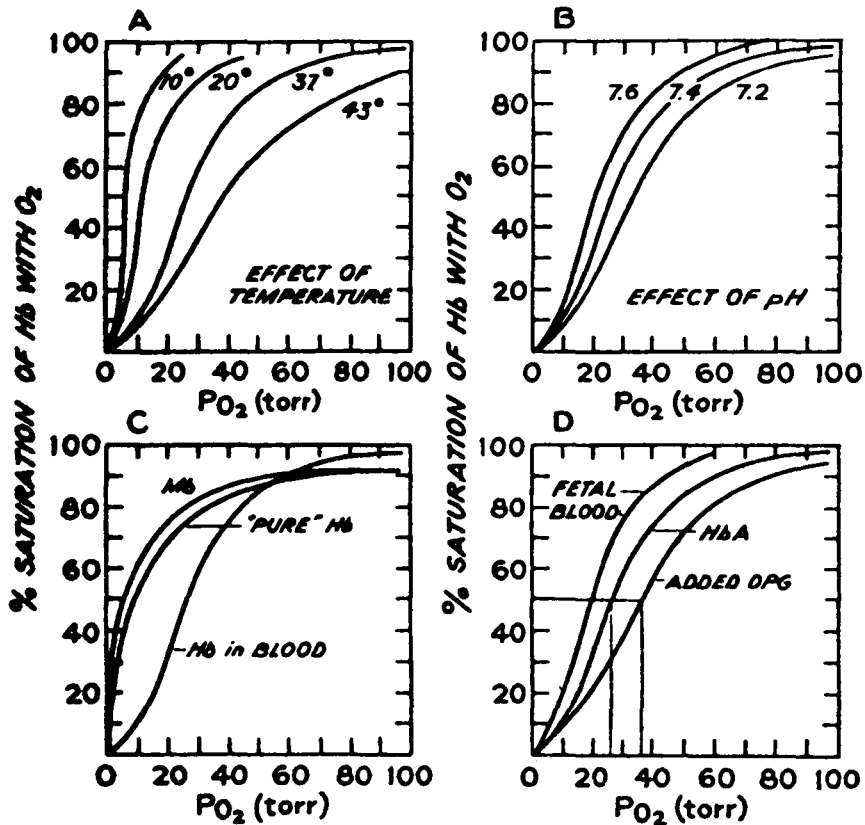


Figure 12

UNDESIREABLE SIDE EFFECTS OF HYPOTHERMIA

- INCREASED BLOOD VISCOSITY
- INCREASED VISCOSITY OF NONBLOOD PERFUSATE
- INCREASED SLUDGING WITH INTRAVASCULAR AGGREGATION
- INCREASED HEMOCONCENTRATION
- ARTERIOVENOUS SHUNTING
- PRECIPITATION OF FAT EMBOLI
- MYOGENIC VASOCONSTRICTION
- CELLULAR EDEMA

Figure 13

the average resting cardiac output of 5 liters per minute, the average oxygen consumption in the adult can be calculated and is determined to be 250 ml/min. This calculated rate gives us an oxygen consumption index of approximately 150 ml/min/m² of body surface area. The perfusionist's challenge is to deliver enough oxygen to meet the patient's demand.

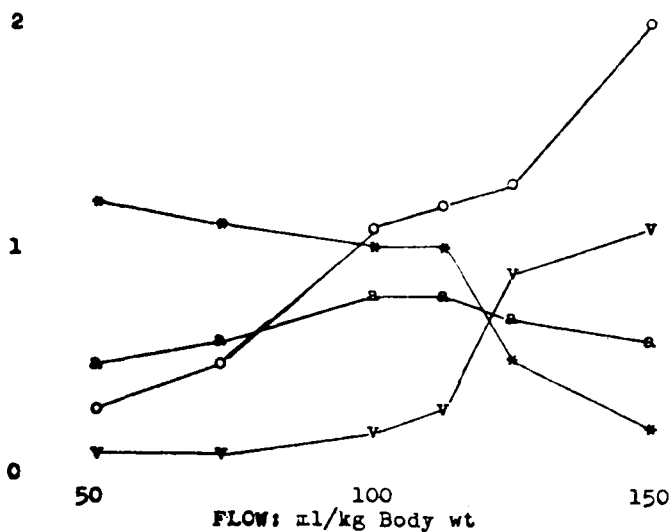
There are a number of factors we must consider in meeting this challenge. First, hemodilution is used virtually nationwide. So, we are starting out with a reduced oxygen carrying capacity in the perfusate. The amount of hemodilution is varied but pump hematocrits of 20 to 30% are common. This hemodilution corresponds to a reduction in oxygen capacity between 25% and 50%. The advantages of hemodilution are well known, but this leaves the perfusionist with the problem of delivering adequate oxygen with a reduced transport capability. If the patient is maintained in a resting state, i.e., with a normal O₂ consumption, and we attempt to maintain a normal venous pO₂, we must increase the pump output to levels as high as twice the normal cardiac output.

The way we resolve this problem, of course, is to reduce the oxygen requirement. A number of mechanisms are available to us to achieve this reduction. Anesthesia, skeletal muscle paralysis and mechanical ventilation are three of our major allies in this effort. At rest, the work of respiration alone accounts for 1/3 of our total oxygen consumption. If we do this work mechanically, we reduce O₂ demand by this magnitude. Add to this the loss of even normal muscle tone due to the use of neuromuscular blocking agents and the depressant effect of the anesthetic, and the open-heart patient's O₂ requirement is reduced to the point where, instead of doubling the cardiac (pump) output due to hemodilution, we can run the pump at rates below the cardiac index. Pump flow rates of 2.0 to 2.5 liters/min/m² have been repeatedly demonstrated to provide sufficient oxygen delivery to prevent metabolic acidosis for the routine open-heart patient.

The other ace up the perfusionist's sleeve is that we can further reduce oxygen demand by inducing hypothermia. The relationship between oxygen consumption and temperature is well understood and has led to the concept of Q-10 which describes the relationship of chemical activity to temperature change. Arrhenius discovered that for various chemical reactions, since they need energy input to begin, the rate of reaction is temperature dependent. For many biological reactions, the magnitude of this change in rate is approximately two for each 10 degree change in temperature. The average of all changes in the system, per 10 degree change is the Q-10. In humans this has reported to be between 2 and 2.4. This means that for a 10 degree decrease in temperature, one can expect to reduce the oxygen consumption in half. It is important to keep in mind, however, that this is a gross oversimplification using *average* changes in reaction rate. Some reactions may well stop with a 10 degree drop in temperature while others continue at near normal rates. This means that there will be depletion of some biological chemical species and an accumulation of others. This inequality in reaction rate change is probably at least partially responsible for the mild metabolic acidosis that is so often reported as attendant with the use of hypothermia.

We have now discussed oxygen consumption and alterations that we can induce in oxygen demand. Let us now turn our attention to the delivery of oxygenated perfusate to the patient's cells. I am going to assume that we all have at our disposal devices that can oxygenate that perfusate to the point of hemoglobin saturation. The fact that we have oxygen in the blood and a normal pO₂ or oxygen saturation does not insure that

EFFECT OF HIGH FLOW



- * = PRU in mmHg/ml CO/sec
- a = Art pressure in 100 mmHg
- v = Ven pressure in 10 mmHg
- o = Ven pO₂ in 40 Torr

Data from 20 dog experiments using bubble oxygenators, roller pumps, primed with Lactated Ringers with 1.5% colloid to achieve hemodilution to 30%

Figure 14

the oxygen will get to the cells and be released. Figure 12¹¹ demonstrates the effect of several factors on the oxygen-hemoglobin dissociation curve. Decreasing temperature shifts the curve to the left allowing for saturation at lower pO₂. However, it should also be noted that the tissue pO₂ must decrease in order to get the normal amount of oxygen released at the cellular level. Decreasing the H⁺ ion concentration (increasing the pH) or lowering the pCO₂ have the same effect on oxygen delivery. For this reason it is especially important to get accurate temperature corrected blood gas and acid-base data in order to assure the adequate delivery of oxygen to the tissues during hypothermic perfusions. Figure 13 shows a number of additional undesirable features of hypothermia that should be considered in evaluating the efficiency of the perfusion technique.

We have now assured ourselves that we have enough oxygen delivery capability to meet the oxygen requirements of the patient. The only thing left to us is to make sure that the blood entering the patient gets to the right places. We have come full circle and to the hemodynamic considerations.

Figure 14 will serve as an example of perfusion data that might be misleading. This illustrates the effect of increasing flow on several other parameters. As the flow

approaches 120ml/kg several drastic changes occur. If one were to look at just one datum, the correct interpretation of these events might well be missed. For example, if one were dependent on the venous pO₂ as their main adequacy index, the might well think that a good perfusion has gotten better when in actuality, the proper interpretation of these data would probably lead one to the conclusion that A-V shunting has occurred and that, in spite of the venous blood gas, the perfusion is deteriorating. And in fact, metabolic acidosis invariably followed in these animals.

Figure 15 summarizes our assessment of the various parameters commonly used as monitors of perfusion adequacy. Acid-base balance is the most reliable and most sensitive index of adequacy. Oxygen consumption and organ function follow. The hemodynamic parameters are of less value although normal values should be strived for.

INDICES OF PERFUSION ADEQUACY

1. ACID-BASE BALANCE

UNDERSTAND POTENTIAL ERRORS IN MEASUREMENT

2. OXYGEN CONSUMPTION

UNDERSTAND POTENTIAL ERRORS IN MEASUREMENT

3. ORGAN FUNCTION

PRIMARILY RENAL

4. FLOW RATE

UNDERSTAND FLOW REQUIREMENTS

5. BLOOD PRESSURE

UNDERSTAND FACTORS THAT CAUSE ALTERATION

SPECIAL IMPORTANCE IN VASCULAR DISEASE

Figure 15

In conclusion, if we could predict with 95% accuracy the requirements for the adequate perfusion, we would all be out of jobs. A computer could be programmed to do our job better with less chance for error. At present, the best way to insure adequacy of perfusion is to have a competent perfusionist behind the pump, one who can receive a mass of information, sort the data and form a composite picture of the patient's status. The perfusionist then must recall the basic physiological demands, integrate all of this information with the surgical problem and then make intelligent decisions on the control of the perfusion.

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