Oxygen transport in hemorrhagic shock as a function of the hematocrit ratio

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The oxygen consumption, arterial and venous oxygen concentration, and the arterial blood pH were measured, and the cardiac output, peripheral resistance and maximum oxygen transport capacity determined in 75 dogs with different hematocrit ratios in which the blood pressure had been maintained at 30 mm Hg for 15 minutes. The O₂ consumption increased as the hematocrit ratio increased until the hematocrit ratio reached 42. However, an increase in the hematocrit ratio above 42 caused a decrease in O₂ consumption. This optimal hematocrit ratio occurs because of the dual role of the hematocrit ratio in determining O₂ content of blood and blood viscosity. A curve obtained by multiplying cardiac output times arterial O₂ showed that when the hematocrit ratio is 42 the O₂ transport is maximal. The oxygen consumed by the animal was determined by the oxygen available. Arterial blood pH was highest in those dogs with the greatest oxygen consumption, but the pH was below limits compatible with life in the anemic animals. Total peripheral resistance increased greatly as the hematocrit ratio increased. Analysis of the data showed that the rate of maximum resistance to hemorrhagic shock coincides with the hematocrit ratio range of maximum O₂ transport. Also, the rate of development of an oxygen debt determines how long the animals can remain hypotensive without developing irreversible shock and indicates that, regardless of the hematocrit ratio, a fixed oxygen deficit must occur before irreversible shock develops.

In the normal animal, the average quantity of oxygen removed as the blood passes through the tissues is only 20–25% of the oxygen available and, if the tissues increase their oxygen consumption, this increase may be accomplished by either an increase in the extraction percentage of oxygen from the blood as it passes through the tissues or by an increase in the rate of blood flow through the tissues. The total O₂ that an animal can obtain is a product of O₂ per unit quantity of blood times the units of blood flow. If, despite circulatory compensations, the available oxygen is less than that required by the tissues, an oxygen deficit develops. In a recent publication it was shown that the hematocrit ratio is an important factor in the resistance of animals to irreversible hemorrhagic shock (1). The resistance of the animal to the development of irreversible shock increased as the initial hematocrit ratio increased from 0 to approximately 37. If the initial hematocrit ratio was increased above 37, the animals were more susceptible to the development of irreversible shock. Since the hematocrit ratio plays a major role, both in the quantity of oxygen per unit of blood and in the units of blood flow, there should be an optimal hematocrit ratio for the transport of oxygen. The present group of experiments was designed to determine if such an optimal ratio exists, what the ratio is, and if it bears any relation to the optimal hematocrit ratio for resistance to hemorrhagic shock.

Methods

Dogs with different hematocrit ratios were obtained by utilizing the natural variation in hematocrit ratio, by infusing saline-washed erythrocytes, and by giving acetyl phenylhydrazine hydrochloride (2). After the hematocrit ratio was in the range desired, the animals were anesthetized with 30 mg/kg of sodium pentobarbital. The trachea was cannulated and attached by tube to a Benedict-Roth basal metabolism machine. A catheter was inserted via the external jugular vein into the right ventricle to obtain mixed venous blood and the femoral artery was cannulated for purposes of bleeding the animal and obtaining arterial blood. The animal was then heparinized with 10 mg/kg of heparin and the arterial pressure lowered to 30 mm Hg by allowing blood from the femoral artery to flow into an external reservoir which was positioned to maintain the 30 mm Hg pressure level. The hematocrit ratio was determined before bleeding. After 15 minutes of hypotension, the O₂ uptake was measured, and arterial and venous samples of blood were taken for purposes of determining arterial and venous oxygen, pH, and hematocrit.

Blood oxygen was determined by analysis with the...
Van Slyke-Neill manometric gas analyzer (3). The cardiac output was determined by the direct Fick principle of dividing the oxygen uptake by the A-V oxygen difference.

Blood pH was determined with a Photo-Volt model 155 pH meter. The changes in the hematocrit ratio following hemorrhage (fig. 7) were obtained from the present experiments and from previous experiments of a similar nature (1).

RESULTS

Oxygen consumption at 30 mm Hg arterial pressure as a function of the hematocrit ratio. Figure 1 shows the O₂ consumed per kilogram per minute as a function of the hematocrit ratio. The oxygen consumption increased greatly as the hematocrit ratio increased from 8 to 42. Increasing the hematocrit ratio above 42 caused a decrease in the oxygen consumption. The maximum O₂ consumption per kilogram per minute occurred at a hematocrit ratio of 42. The curve is a 9-point moving average and the dashed lines are plus or minus 1 standard deviation.

Arterial O₂, venous O₂ and A-V O₂ difference as a function of the hematocrit ratio. As shown by figure 2, increasing the hematocrit ratio increases the arterial oxygen, venous oxygen and A-V oxygen difference. The percentage utilization shown on this graph is defined as the oxygen removed divided by the oxygen available per 100 cc of blood times 100, and is extremely high in these animals.

Cardiac output as a function of the hematocrit ratio. The graph, figure 3, shows that the cardiac output decreases as the hematocrit ratio increases.

Peripheral resistance in hypotension as a function of the hematocrit ratio. Figure 4 shows the peripheral resistance expressed in PR units as a function of the hematocrit ratio. The peripheral resistance increased greatly as the hematocrit ratio increased from 10 to 30, increased slowly between hematocrit ratio values of 30 to 40, and showed an extreme increase for hematocrit ratio values above 40.

Total O₂ available and total O₂ utilized during hypotension. Figure 5 shows the O₂ consumption per kilogram per minute as a function of the hematocrit ratio, a curve (obtained by multiplying the cardiac output times the arterial oxygen) representing the total amount of oxygen available to the animal, and a curve (the product of the cardiac output times the venous oxygen) representing the oxygen not utilized by the animal. If one subtracts the oxygen not utilized from the oxygen available, the oxygen utilized is obtained which is, of course, identical with the oxygen uptake as shown in figure 1. These curves show that the utilization of oxygen is dependent on the oxygen available. The percentage utilization on this graph represents the percentage of total oxygen available rather than the percentage of oxygen per 100 cc of blood. It shows that the animal is utilizing 80-90% of the O₂ available and utilizing a higher percentage in anemic and polycythemic ranges of hematocrit ratio than in the normal range.

Arterial blood pH as a function of the hematocrit ratio. Figure 6 shows the arterial blood pH of animals with different hematocrit ratios after 15 minutes of hypotension. The pH of the animals with hematocrit ratios between 40 and 50 is in the normal range. However, as the hematocrit ratio changes either higher or lower, the arterial blood pH decreases, and those animals with hematocrit ratios below 30 have pH values that are considered to be incompatible with life.

Correlation between optimal resistance to hemorrhagic shock and optimal O₂ transport. Figure 7 shows the initial hematocrit ratio of the animals, the hematocrit ratio 15 minutes after initial bleeding, and in some cases the hematocrit ratio over a period up to the development of irreversible shock by the animal. The dashed line is the average period of time required for animals with initial hematocrit ratios shown on the ordinate to develop irreversible shock (1). The average oxygen consumption of the animals as a function of the hematocrit ratio is also shown. Maximal resistance to hemorrhagic shock occurs if the initial hematocrit ratio is approximately 37.
However, the maximal oxygen transport occurs if the hematocrit ratio is 42. Those animals with initial hematocrit ratios below 30 usually show a decrease in their hematocrit ratio following bleeding, indicating that they have changed their hematocrit ratio away from the point of maximum oxygen transport. Those animals with initial hematocrit ratios of 40 or higher also tended to shift away from the point of maximum oxygen transport. Some of the animals, however, particularly those with initial hematocrit ratios of approximately 37, tend to increase the hematocrit ratio with bleeding and actually shift toward the hematocrit ratio of maximum O₂ transport, and furthermore, the hematocrit ratio remains in the general region of maximum oxygen transport for much longer periods of time than the hematocrit ratio of other animals. This provides the correlation between resistance to hemorrhagic shock with initial hematocrit ratio of 37 and maximum oxygen transport with hematocrit ratio of 42, for the graph shows that animals exhibiting maximal resistance to hemorrhagic shock shift their hematocrit ratios to the range of maximum oxygen transport during the process of bleeding.

Rate of anaerobic metabolism and estimated O₂ deficit. The normal oxygen consumption of the dogs with hematocrit ratios in the range of 20–55 was 4.61 cc/kg/min., and the oxygen consumption did not vary with the hematocrit ratio, as shown in figure 8. If the oxygen need remains normal even though the pressure has decreased and the oxygen consumption at 30 mm Hg arterial pressure is subtracted from the oxygen needed, the rate of oxygen deficit is obtained. The error in this assumption will be discussed later. The rate of oxygen deficit in the anemic dogs at 30 mm Hg arterial pressure is actually greater than the oxygen consumption, but as the hematocrit ratio increases to 40, the rate of oxygen deficit decreases. However, as the hematocrit ratio increases above 42, the rate of oxygen deficit increases and again becomes greater than the oxygen consumption if the hematocrit ratio is above 55.

The hypotensive oxygen consumption shown in figure 8 is the average oxygen consumption during the period of hypotension required to produce irreversible shock and was obtained as follows: the oxygen consumption for the first 15 minutes of hypotension for a given hematocrit ratio was determined from figure 1. The oxygen consumption after the first 15 minutes of hypotension was estimated by assuming that the oxygen consumption varied as the hematocrit ratio varied (fig. 7). The total oxygen consumed was divided by the total time required for irreversible shock to develop to obtain an estimated rate of oxygen consumption during the hypotensive period. If the rate of oxygen deficit is multiplied by the average time required for the development of irreversible shock (as shown in fig. 7), an estimation of the total oxygen deficit at the time irreversible shock developed is obtained. The total O₂ deficit for animals with hematocrit ratios of 15 was very low; however, in the hematocrit ratio range of 20–55, the estimated oxygen deficit ranges from 100 to 60 cc O₂/kg of animal
DISCUSSION

The data presented show why the hematocrit ratio plays an important part in the resistance of an animal to the development of irreversible shock. First, increasing the number of cells in the blood increases its oxygen carrying capacity, and, therefore, on the basis of this fact alone, blood composed entirely of erythrocytes would have the maximum oxygen transport capacity. Yet, because of the effect of the hematocrit ratio on the apparent viscosity of blood, increasing the hematocrit ratio decreases blood flow, and the maximal flow of blood would occur if there were no erythrocytes, or, in other words, if the blood were pure plasma. If both oxygen per unit quantity of blood and the units of blood flow are considered, an intermediate value for the hematocrit ratio is found at which the oxygen carrying capacity of the blood is the highest possible without markedly increasing the viscosity to such an extent that the decrease in blood flow offsets the increase in oxygen carrying capacity. The data presented indicate an optimal hematocrit ratio of 42, and this is approximately the hematocrit ratio of a normal dog. It is also obvious that determinations of cardiac output alone are in themselves useless criteria for the evaluation of irreversible shock, because, in the extreme anemic range, the cardiac output at 30 mm Hg arterial pressure may actually exceed that of a normal dog at 120 mm Hg arterial pressure. It may also be shown that studies of A-V O₂ differences are in themselves not good criteria of oxygen utilization as the A-V O₂ difference varies from 3 to over 20 cc O₂/100 cc blood as one varies the
FIG. 7. Changes in hematocrit ratio of dogs with various initial hematocrit ratios and O₂ consumption at various hematocrit ratios after 15 min. of hypotension.

FIG. 8. Normal O₂ consumption, estimated average O₂ consumption during hypotension, rate of O₂ deficit and total O₂ deficit of dogs subjected to hypotension.

The arterial blood pH is accumulatively affected by the quantity of anaerobic metabolites present, especially by the lactic acid produced in the anaerobic metabolism of pyruvate (7). The role of the pH in shock has not been clearly elucidated. However, reexamination of figure 6 shows that after 15 minutes, the extremely anemic animals are already at pH levels which would in themselves be lethal. Also, the rapid decline in pH with hematocrit ratios below 30 appears to be a factor in the quantity of oxygen in the arterial blood because projection of the linear portion of the arterial oxygen curve of figure 2 toward zero shows that there is less oxygen than one would expect on a basis of the projection. Presumably the acidity causes a shift in the hemoglobin dissociation curve such that more oxygen is delivered to the tissues, but less oxygen is absorbed from the lungs.

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blood is replaced with tissue fluid from the animal plus a
moderate quantity of stored erythrocytes, causing a
slight rise in hematocrit ratio. Since the data show that
the maximum oxygen transport occurs at a hematocrit
ratio of 42, it appears that if the hematocrit ratio were
maintained at this point, the time required for the
development of irreversible shock would be prolonged.
The hematocrit ratio was not controlled in these animals;
however, (from fig. 7) those animals with hematocrit
ratios that on an average were near the hematocrit ratio
of maximum oxygen transport actually required a
longer period of time to develop irreversible shock. It
might also be noted at this point that the oxygen con-
sumption is asymmetric around the optimal level and
that an increase in the hematocrit ratio tends to de-
crease the available oxygen by a much larger amount
than the same percentage decrease in the hematocrit
ratio.

Figure 8 shows the average rate of oxygen deficit as a
function of the hematocrit ratio. The sharp peak in
oxygen consumption shown in figure 1 is not present
because of the averaging effect of changes in the hematocrit
ratio. The average oxygen consumption was sub-
tracted from the normal rate of oxygen consumption,
and the difference is shown as the oxygen deficit ex-
pressed in centimeters of oxygen per kilogram per min-
ute, which represents the energy that the animal must
supply from anaerobic glycolysis. Figure 8 shows that
those animals with the lowest rate of anaerobic glycolysis
require the longest time to develop irreversible shock.
Furthermore, if this rate of oxygen deficit is multiplied
by the average time for animals with a given initial
hematocrit ratio to develop irreversible shock (fig. 7),
an estimation of the total oxygen deficit (expressed in
cc of O₂/kg of animal) developed by the time the animal
goes into shock is obtained. This curve shows a decrease
in oxygen deficit as the hematocrit ratio increases,
although one value in the anemic range is low. The oxy-
gen contained in the blood at the beginning of the experi-
ment is not shown on the curve, and this reserve oxygen
increases as the hematocrit ratio increases, a factor which
would tend to offset the decrease in oxygen debt as the
hematocrit ratio is increased. Furthermore, the exact
oxygen need of an animal in hypotension varies from
that of the normal animal because of changes in cardiac
and ventilatory work. However, of the various parame-
ters determined by this study of irreversible hemorrhagic
shock, the total oxygen deficit is the only one that shows
some degree of constancy. Whether this implies that
exhaustion of the reserve energy of some organ is con-
cerned or whether a quantitative amount of anaerobic
glycolysis produces some toxic factor is unknown.

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