Effects of polycythemia and anemia on cardiac output and other circulatory factors

Richardson, Travis Q. and Arthur C. Guyton. Effects of polycythemia and anemia on cardiac output and other circulatory factors. Am. J. Physiol. 197(6): 1167-1170, 1959.—Normovolemic anemia and polycythemia were studied in 14 dogs. Cardiac outputs increased with anemia and fell with rises in hematocrit. Although many factors—such as chemical changes—may play an important role in these variations in cardiac output, there was an indication that viscosity alone may have a major effect. There was no significant association between changes in cardiac output and the various pressures—mean arterial, mean right atrial, mean pulmonary and mean circulatory. Although the pressures did not change significantly, there was a significant decrease in total peripheral resistance in anemia and a marked rise in polycythemia. It was also found that the maximum number of red cells present for oxygen transport to the tissues was near the mean normal hematocrit of 40.

Changes in blood viscosity as a result of both increasing and decreasing cell concentration have been studied by various workers (1-3). Other research workers (4-6) have studied the effects of polycythemia on blood flow through certain organs, and still others have examined the effect of various phases of anemia on cardiac output (7-10). In general, it has been found that polycythemia reduces cardiac output while anemia increases the output. Yet, no attempts have been made to keep the animals normovolemic during the studies, and it has not been determined whether the changes in cardiac output were caused by changes in blood viscosity or by other effects of polycythemia or anemia.

Therefore, it was the purpose of these experiments to determine the effects of normovolemic polycythemia and anemia on the cardiovascular system with special emphasis on changes in cardiac output. Also, an attempt has been made to analyze the importance of viscosity itself in causing these effects.

Methods

Fourteen mongrel dogs of various sizes, heparinized with 5 mg/kg of heparin and anesthetized with 30 mg/kg sodium pentobarbital, were first bled and then injected with corresponding amounts of freshly spun red blood cells to make the animal polycythemic, or injected with plasma to produce anemia. Four of these animals were rendered both polycythemic and anemic, two were rendered only anemic, and eight were rendered only polycythemic. The bleeding and reinfusion required only 3 minutes, and there had been no significant change in blood volume after the procedure had been completed as measured by T-1824 in four animals. In six additional animals, the mean circulatory pressure was measured (as described below) before and after rendering the dogs polycythemic or anemic, and this value did not change.

Various measurements were made as follows: mean pulmonary arterial pressure, by catheter through the right external jugular, atrium and ventricle; right atrial pressure, by catheter through left external jugular to the atrium; mean arterial pressure, by catheter in femoral artery; mean circulatory pressure, by fibrillating and defibrillating the heart through the unopened chest while recording arterial and venous pressures using a procedure previously reported (11); hematocrits, by spinning in Wintrobe tubes; and cardiac output, by using the Van Slyke-Neill manometric apparatus.

Results

Effects of Hematocrit

Cardiac output. Fourteen animals were used to plot the points shown in figure 1. The cardiac outputs were run prior to infusion and again 30 minutes after the animals were infused with either cells or plasma. The hematocrits...
Cardiac outputs recorded on 14 dogs with lower, normal and higher hematocrits. The best possible regression line is drawn through the data. Ranged from 20 to 68. From the figure, it is evident that cardiac output per kilogram fell from 154 cc/min. with a hematocrit of 20 down to 29 cc/min. with a hematocrit of 68. The best possible curve is drawn through the data by the least squares method. The coefficient of correlation is .72.

To make further comparisons of the effect of hematocrit on cardiac output, the results in figure 2 were computed. This graph indicates the change in cardiac output which occurred when the hematocrits were changed from the normal. In the anemic animals there was a mean fall in hematocrit of 40.2% with an increase in cardiac output of 26%. In the polycythemic animals the hematocrit was raised to a mean of 47% above normal, and the cardiac output fell 51%. It is obvious from this data that percentage changes in cardiac output are more dramatic in the higher hematocrit ranges than in the lower ones. In this figure, the standard deviation of the mean is represented by the shaded area at the side of each bar. The probability that the difference between the means of the determinations was a chance phenomenon for the polycythemic is almost infinitesimal, the t value being 8.78. The mean difference between the means of the determinations for anemic versus the controls had a t value of 4.204 or a P value of 0.00003.

Cell flow. The term cell flow is defined here as the quantity of red cells available each minute for carrying oxygen to the tissues. It is evident that when the cardiac output per kilogram is multiplied by the hematocrit the number of cubic centimeters of red cells per kilogram available each minute for oxygen transport is determined.

Figure 3 shows the effect of changes in hematocrit on cell flow. An interesting point is that the maximum number of cells available to the tissues occurred at a hematocrit of 49, which was within 0.6% of the mean control hematocrit in these dogs. These results are similar to Crowell’s observations on dogs in shock (12). That is, if an animal's hematocrit is either raised or lowered from the usual normal value, then the number of cells transporting oxygen each minute decreases.

Total peripheral resistance. Figure 4 illustrates the effect of red cell concentration on the total peripheral resistance. It is evident from this graph that the total peripheral resistance changed considerably with increased hematocrit. With an average drop of 40.2% in hematocrit in six animals, the resistance decreased an average of 25.6%. The TPR rose an average of 50.1% in 11 animals which had hematocrit increases averaging 47.5%. The tremendous rise in resistance was attributed to a great increase in viscosity at the higher hematocrits. In this figure the standard deviation of the means are also represented by small shaded areas at the sides of the bars. This information, too, is extremely significant, the
FIG. 3. Effect of varying hematocrits on the number of cells available for transporting oxygen.

Mean circulatory pressure, mean arterial pressure, mean pulmonary arterial pressure and mean right atrial pressure. The mean circulatory pressure was measured in six animals. Four of these animals were rendered both polycythemic and anemic. The average mean circulatory pressures in millimeters of mercury were as follows: normal 6.2, anemic 6.1 and polycythemic 6.1. This information indicates that hematocrit has no effect on the mean circulatory pressure. The mean arterial pressure for 14 normal animals was 111.2 mm Hg, while that of the six anemic animals was 117 and that of the polycythemic animals was 97. There was a fall in the mean arterial pressure following the injection of red cells in every animal tested. This pressure drop occurred approximately 15 minutes after the red cells were infused. After the introduction of plasma into the animal, there was a slight fall in blood pressure which lasted for 15 minutes. Following this initial fall the blood pressure rose to a level above the normal control.

The mean pulmonary arterial pressure and mean right atrial pressures remained practically normal. The mean pulmonary arterial pressures for the animals were as follows: normal 9.15 mm Hg, anemic 9.3, and polycythemic 9. Since cardiac output fell greatly in the polycythemic animals and rose in the anemic, these pressures indicate that there is a great increase in pulmonary resistance for the polycythemic animal, and a decrease in pulmonary resistance in the anemic animal.

In the four animals rendered both anemic and polycythemic the procedure of injecting the cells or plasma was reversed in two animals without any change in results. There was practically no change in the right atrial pressures under the tested conditions.

DISCUSSION

Cause of Effects on Cardiac Output When Hematocrit is Changed

The principal objective of this study has been to examine the effects of varying hematocrits on cardiac output and various circulatory pressures under controlled conditions. The blood volumes were maintained as near to normal as possible with only changes in hematocrit.

An increase in hematocrit to polycythemic levels had a much greater effect on cardiac output in this study than a similar decrease in hematocrit. This is the effect that one would expect if the decreased cardiac output in polycythemia is caused primarily by an increase in viscosity, because previous studies have shown that changes in hematocrits in the low range have little effect on viscosity while changes in the high hematocrit range have a much greater effect (1-3). Unfortunately, though, measurements of viscosity and its effect on blood flow have been performed on either inelastic tubes or small portions of the circulatory system. Therefore, considerable confusion could result from extrapolating the results to the intact animal.

Lewis et al. (13) found that polycythemic patients have near normal cardiac outputs but lacked the ability to increase cardiac output adequately after exercise. Mack and Snider (14) found that secondary polycythemia promoted an increase in viscosity with a concomitant rise in blood volume. The normal cardiac outputs found in these two studies, however, must not be confused with the situation of normovolemic animals. As stated previously, the present study was conducted under controlled conditions that allowed only changes in hematocrit to occur. Under these conditions, there was a tremendous
fall in cardiac output with high hematocrits. The cardiac output fell from a normal of 107 cc/min. at a normal hematocrit of 40.6 down to a mean of 29 cc/min. when the cell concentration was raised to 68. These results indicate that changes in blood viscosity may have a tremendous effect on cardiac output.

Where in the cardiovascular system does the change in viscosity have its greatest influence on cardiac output? Several theories may be conjectured, but for this study it is suggested that the high hematocrits produce a sluggishness in venous return. Previous studies in this laboratory have shown that increased venous resistance decreases cardiac output tremendously while increased arterial resistance has very little effect on cardiac output but a very marked effect on arterial pressure. From this it is concluded that a high arterial resistance caused by high viscosity would have little effect on cardiac output. Then the primary site of high viscosity action was probably in the venous system, for cardiac outputs decreased without any compensatory rise in mean arterial pressure; instead, the pressure fell, which is an effect also noted previously when the venous resistance is increased.

The reason for the increased cardiac output in anemia is much more difficult to analyze than the decrease output in polycythemia, because two separate effects occur that are known in other situations to decrease total peripheral resistance. These are, first, the decrease viscosity of the blood that is associated with anemia and, second, the decreased oxygen content of the blood. Previous studies by Sunahara and Beck (7) and Brannon et al. (8) have indicated that it is mainly the decrease in oxygen content that causes the increased cardiac output. However, it is doubtful that such a firm conclusion as this can yet be made. In the present experiments, for instance, the increase in cardiac output was not very great in anemia and the total increase could possibly be explained strictly on the basis of viscosity changes alone. Yet, there are many reasons for believing that this, too, is not true. First, other studies from this laboratory have shown that a decrease in hemoglobin saturation, without any changes in blood viscosity, will cause progressive increases in blood flow almost in proportion to the diminishment of blood oxygen content (16). Therefore, an oxygen deficiency in anemia could quite readily explain the increased cardiac output. Second, in very severe anemia the cardiac output can sometimes rise to as high as several times normal, and it is hard to believe that this could be caused entirely by viscosity changes because measurements of viscosity in the hind leg of the dog indicate that this changes very little below a hematocrit of 30 (3). Therefore, one would again suspect changes in oxygen content or some other changes in hemodynamics, such as blood volume, vasomotor tone, or so forth, as the cause of the increased cardiac output. Thus, for the present one can probably assume that both decreased viscosity as well as decreased oxygen content of the blood play major roles in causing the increased cardiac output of anemia.

Effects of Hematocrit Changes on Other Circulatory Factors

An interesting finding in this study was the failure of the pressures—mean right atrial, mean pulmonary and mean circulatory—to deviate significantly from the normal in anemia and polycythemia. The mean arterial pressure dropped in every animal immediately following transfusion with either plasma or red blood cells, but it reached a stable point within 15 minutes. The pressure after stabilization had changed from the normal mean of 111 to a mean of 97 in the polycythemic animals and to 117 in the anemic animals. Sunahara and Beck (7) noted that the initial response to hemodilution was a fall in cardiac output followed by a secondary rise. This is what happened to the mean arterial pressures in the animals studied here.

Cell flow decreased from normal in both polycythemia and anemia. This information indicates that normovolemic animals have the capacity to transport the maximum amount of oxygen at normal hematocrits. The benefits of this can easily be appreciated.

REFERENCES