Effects of dextran-induced hyperviscosity on regional blood flow and hemodynamics in dogs

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CHEN, RICHARD Y. Z., RONALD D. CARLIN, SHLOMOH SIMCHON, KUNG-MING JAN, AND SHU CHIEN. *Effects of dextran-induced hyperviscosity on regional blood flow and hemodynamics in dogs.* Am. J. Physiol. 256 (Heart Circ. Physiol. 25): H898–H905, 1989.—In 10 pentobarbitalized dogs, plasma viscosity (E_p) was raised fourfold while apparent blood viscosity (E_a) increased about twofold by two steps of exchange transfusion of 200 ml of plasma with plasma containing high molecular weight dextran (mol wt 500,000, 20% wt/vol). Elevation of E_a was primarily caused by an increase of E_p but not red cell aggregation. As E_a increased, regional blood flow (by 15-μm microspheres) remained constant in most organs but reduced in the small intestine, spleen, and thyroid gland. Vascular hindrance (Z), which reflects the state of vascular geometry, was calculated as flow resistance per E_a. Among various organs, a reduction in Z was noted in the heart, liver, pancreas, kidney, brain, and adrenal gland. In myocardium, there was a progressive reduction of the endocardial-to-epicardial flow ratio, indicating a less profound vasodilation in endocardium than epicardium. These results indicate that dextran-induced hyperviscosity leads to a compensatory vasodilation in several vital organs thus serving to maintain blood flow and nutrient transport.

plasma viscosity; blood viscosity; regional vascular hindrance

BLOOD RHEOLOGY is the study of flow properties; the flow properties are one of the principal determinants of resistance to flow. Blood is a suspension of cells in plasma, and its viscosity is determined by the rheological behavior of formed elements as well as plasma viscosity. Abnormal blood rheology is found in many disease states. Changes in plasma proteins with an increased fibrinogen-to-albumin ratio result in an increased plasma viscosity and occurrence of red cell aggregation. These changes have been demonstrated after trauma (14) in patients with peripheral arterial occlusive disease and intermittent claudication (20) and in patients with acute myocardial infarction (2, 21). Abnormal rheological behavior with an elevated plasma viscosity and enhanced red cell aggregation are encountered in certain forms of plasma cell dyscrasia due to increased concentration of abnormal macroglobulin (27, 30).

The resistance to blood flow in the body is a function of apparent blood viscosity and vessel geometry. The contribution of vascular geometry to flow resistance is termed vascular hindrance (22). If the vascular hindrance were fixed, as in a rigid tube, the changes in apparent blood viscosity would lead to reciprocal changes in blood flow rate; however, in vivo the autoregulation may change arteriolar hindrance to oppose the flow effects of altered viscosity. The quantitative relationship between changes in blood viscosity and concomitant alterations in regional vascular hindrance, however, has not been fully established.

The present study was designed to examine systematically the hemodynamic adjustments of vascular hindrance in the presence of elevated blood viscosity induced by high molecular weight dextran (HMWD). Because vascular beds in various organs may have regional differences in their responses to HMWD-induced hyperviscosity, we determined regional blood flow in many organs and tissues simultaneously with the use of the microsphere technique.

METHODS

General Preparation

The experiments were performed on 10 mongrel dogs (body wt 10–15 kg) anesthetized with pentobarbital sodium (30 mg/kg iv initially, followed by 50 mg iv per hour). These animals were then immobilized with pancuronium bromide (0.2 mg/kg iv) and mechanically ventilated through an endotracheal tube to maintain arterial CO_2 partial pressure (Pa_{CO_2}) at ~40 mmHg. A low flow of oxygen (~2 l/min) was added to the inspired air to ensure that arterial O_2 partial pressure (Pa_{O_2}) remained above 90 mmHg. Blood gases were determined by the use of a blood gas analyzer system (model 213, Instrumentation Laboratory, Lexington, MA). Esophageal temperature was monitored with a thermistor probe (Yellow Springs Instrument, Yellow Springs, OH) and maintained at 37 ± 1°C with the use of electric heating pads. The left ventricle was catheterized with a pig-tail catheter (US Catheter Instrument, Billerica, MA) through a femoral artery for the injection of microspheres. A flow-directed Swan-Ganz catheter (Edwards Laboratories, Santa Ana, CA) was introduced into the pulmonary artery via a femoral vein for measurements of pulmonary arterial and wedge pressures. The positions of these catheters were confirmed with respective pressure tracings. The lower abdominal aorta and inferior vena cava were cannulated with polyethylene catheters (PE–320) through the other femoral artery and vein, respectively. The animals were then anticoagulated with heparin (500 U/kg). Pressures were continuously recorded by using Statham transducers and a polygraph recorder (model 7, Grass Instrument, Quincy, MA).

Experimental Protocol

Isovolemic exchange for dextran-plasma administration. Fresh heparinized blood obtained from a healthy donor dog was centrifuged to separate plasma and packed red cells. The buffy coat was discarded. Dextran with a mean molecular weight of ~500,000 (Dx-500, Pharmacia, Uppsala, Sweden) was dissolved in the plasma to yield a concentration of 20%, wt/vol. This dextran-plasma solution was freshly prepared for each experiment, and its temperature was maintained at 37°C in a water bath. Immediately before infusion, the plasma containing Dx-500 was mixed with packed red cells, and the hematocrit level was adjusted to match that of the experimental dog.

Each experimental dog received two steps of exchange transfusions. In each step of exchange transfusion (200 ml), the dextran-containing blood (mixture of dextran-plasma solution and packed red cells) was infused into the femoral vein, and whole blood was withdrawn simultaneously from the femoral artery at a rate of 40–50 ml/min. Blood volume was measured by simultaneous determinations of red cell volume and plasma volume before and after each step of exchange transfusion. The red cell volume was determined with ^{51}Cr-tagged autologous red blood cells ($Na^{51}CrO_4$, total dose 75–150 μCi, Squibb and Sons, New Brunswick, NJ) and plasma volume with ^{125}I-labeled albumin (total dose 30–60 μCi, Mallinckrodt Nuclear, St. Louis, MO). Detailed procedures of blood volume measurement has been described previously (7).

After surgical preparation and instrumentations, hemodynamic and regional blood flow measurements described below were made first during a control period before any experimental manipulation. All measurements were repeated at 20 and 60 min following the completion of each exchange transfusion. Arterial blood samples were taken immediately before the hemodynamic measurements to determine blood viscosity, arterial blood gases, hematocrit, and the dextran-plasma concentration using the anthrone reagent (10).

Determination of cardiac output and regional blood flow. Microspheres (15 ± 1 μm diam) labeled with radionuclides (^{57}Co, ^{113}Sn, ^{103}Ru, ^{95}Nb, and ^{46}Sc) and suspended in 10% dextran solution (mol wt 78,000) were employed (New England Nuclear, Boston, MA). The use of five radionuclide labels allowed five separate determinations of cardiac output and regional blood flows in each experiment. Before their use each shipment of microspheres was checked for sphere size, status of aggregation, presence of fragmentation, specificity of radionuclide, and specific activity. Radionuclide leaching was tested, and the spheres discarded if the supernatant radioactivity became significant. Microscopic examination was carried out to assure the complete dispersion of spheres and to quantify the number of spheres to be administered during each injection (~1 × 10^5 spheres/kg body wt).

In each measurement, microspheres diluted in 5–10 ml normal saline solution containing 0.05% Tween 80 were injected into the left ventricle over a 30-s interval. Aliquots of the injectate (~0.1–0.3 ml) were taken in triplicate before the injection and their activities per unit weight determined. The total radioactivity of the injectate was then calculated from the averaged value of these aliquots.

Immediately after the injection of microspheres, the left ventricle catheter was flushed with 7 ml of normal saline, which had been warmed to body temperature, over a 10-s period. An arterial reference sample was withdrawn from the abdominal aorta by a syringe pump at a withdrawal rate (Q_{ar}) of 15 ml/min for 2 min. To ensure that arterial reference sampling encompassed completely the injection of microspheres, the pump was started 10 s before the injection. Five measurements were made in each animal according to the experimental protocol outlined in *Isovolemic exchange for dextran-plasma administration.*

At the end of the experiment, the dog was killed by the intravenous injection of an overdose of pentobarbital. The internal organs such as the brain (cerebral cortex, including grey and white matters), liver, spleen, pancreas, diaphragm (muscular portion), small intestine (portion of jejunum), and kidney (coronal sections through renal pelvis, including both cortex and medulla) were removed and dissected into 0.5- to 1.5-g pieces. The heart was exsanguinated, and the myocardium of the left ventricle was separated into two layers (epicardium and endocardium). The radioactivities of the arterial reference blood samples and tissue specimens were determined with a gamma counter (Packard 5130, Auto-Gamma Systems, Downers Grove, IL) coupled with a multichannel analyzer (Tracor Northern, Middleton, WI). The activities attributable to individual radionuclides were resolved from overlapping energy spectra with the use of a previously developed computer program.

The cardiac output (CO, in $ml \cdot min^{-1} \cdot kg^{-1}$) and regional blood flow (RBF, in $ml \cdot min^{-1} \cdot 100\ g^{-1}$) were computed according to the following equations

$$CO = A_i \times Q_{ar}/A_{ar} \qquad (1)$$

$$RBF = C_t \times Q_{ar}/A_{ar} \qquad (2)$$

where A_i is the total radioactivity of a particular radionuclide injected, A_{ar} is the radioactivity of the arterial reference blood sample, and C_t is the radioactivity of that particular radionuclide present in the tissue specimen.

Determination of blood viscosity. The viscosity of heparinized whole blood and plasma samples were determined at shear rates from 0.05 to 200 s^{-1} in an air-bearing Couette viscometer at 37°C (11). The shear rate of 200 s^{-1} was taken to represent the mean shear rate in the circulation during the control period. When the flow rate was reduced after dextran administration, the effect of low shear rates on apparent blood viscosity was cor-

TABLE 1. *Dextran concentration, red cell volume, plasma volume, and blood volume after exchange transfusion*

	Control	First Exchange 20 min	First Exchange 60 min	Second Exchange 20 min	Second Exchange 60 min
Dextran concn, g/dl	0	1.74±0.29*	1.48±0.22*	3.04±0.50*	2.74±0.44*
Volume, ml/kg					
Red cell	29.86±1.90		27.31±1.87		23.87±1.85*
Plasma	51.20±2.73		54.02±4.11		54.14±2.88
Blood	81.04±4.13		81.29±5.54		78.00±4.12

All values are means ± SE. * Significant difference from control values ($P < 0.05$).

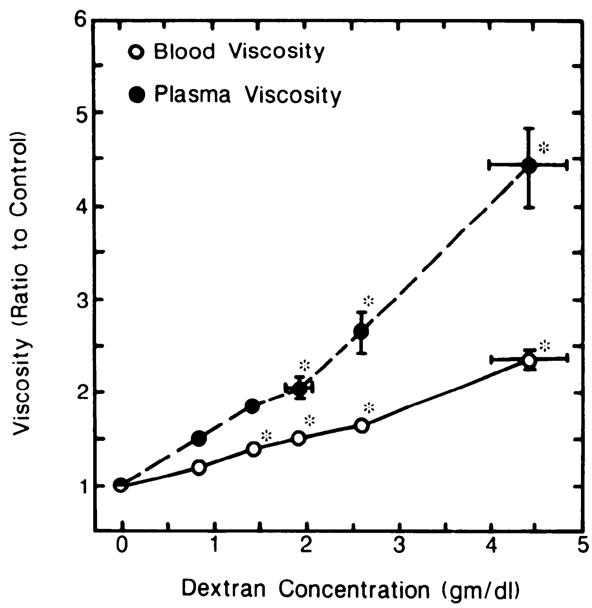

FIG. 1. Effects of isovolemic Dx-500 administration on plasma and apparent blood viscosity. * Significant difference from respective control values ($P < 0.05$).

rected by assuming that the changes of shear rate are proportional to the reduction of cardiac output (8). The apparent viscosity (E_a) of the blood sample was then read from the viscosity-shear rate curve for the appropriate shear rate. The hematocrit value of each blood sample was determined in duplicate after 5 min of centrifugation at 15,000 *g* in a microcentrifuge. The reading was multiplied by a plasma-trapping factor of 0.97 (9) to give the corrected arterial hematocrit. The plasma protein concentration in each sample was determined in duplicate by Lowry method (23).

Calculation of regional flow resistance and vascular hindrance. The flow resistance (R) in the overall systemic circulation and the regional circulations for various organs were calculated from the pressure-to-flow ratios as follows

$$R \text{ (in RU)} = \frac{\text{MAP} - \text{VP (mmHg)}}{\text{RBF (in ml} \cdot \text{min}^{-1} \cdot 100 \text{ g}^{-1})} \quad (3)$$

where MAP is mean arterial pressure recorded from the abdominal aorta; VP is venous pressure recorded from the inferior vena cava; and RU is a resistance unit ($\text{mmHg} \cdot \text{min} \cdot 100 \text{ g} \cdot \text{ml}^{-1}$).

The vascular hindrance (22), which reflects the flow resistance due to vascular geometry, was calculated as follows

$$Z = R/E_a \quad (4)$$

where Z is the vascular hindrance (in $\text{RU} \cdot \text{cP}^{-1}$).

Determination of oxygen transport and utilization. Hemoglobin concentration (Hb) and percent O_2 saturation (S) were determined with the use of a CO oximeter (Instrumentation Laboratory model 182). The P_{O_2}, P_{CO_2}, and pH were determined by means of a blood gas analyzer (Instrumentation Laboratory model 123) at 37°C. The oxygen content (in ml/dl blood) was calculated as the sum of the hemoglobin-bound oxygen (0.0134 × Hb × S) plus the physically dissolved oxygen content (0.003 × P_{O_2}). The oxygen transport rate to each region was the product of regional blood flow and arterial oxygen content.

Data Analysis

The results are presented as absolute values and ratios relative to control values. The statistical significance of changes in various experimental conditions was evaluated with analysis of variance (ANOVA). Multiple comparisons were made with Student-Newman-Keuls test.

RESULTS

The results of plasma dextran concentration and blood volume changes after exchange transfusion of plasma dextran solution are summarized in Table 1. Dextran concentration in plasma increased after each step of exchange transfusion. There was a slight decrease (10–15%) in plasma dextran concentration between 20 min and 60 min after the exchange. After the first step of exchange transfusion, the red cell volume and the plasma volume did not change significantly, and blood volume remained constant. After the second step of exchange transfusion, the red cell volume was reduced but the plasma volume remained unchanged; the slight decrease in blood volume was not statistically significant.

The raw data of blood and plasma viscosities after the exchange transfusion were assorted into five groups according to the ascending order of plasma dextran concentrations. The viscosities of plasma and blood increased progressively as plasma-dextran concentration was elevated (Fig. 1). There was a fourfold increase in plasma viscosity and a twofold increase in the apparent viscosity of whole blood when the plasma dextran concentration was raised to ~4.5 g/dl. The increase of blood apparent viscosity was less than that of plasma viscosity and was accompanied by decreases in hematocrit and plasma protein concentration (Fig. 2).

The control values of hemodynamic variables obtained before the exchange transfusion of plasma with dextran plasma solution are summarized in Table 2. The experimental data obtained after the exchange transfusion were plotted as a function of the blood viscosity. The cardiac output, heart rate, mean arterial blood pressure, and systemic and pulmonary flow resistances remained relatively constant at different levels of blood viscosity (Figs. 3 and 4). As the blood viscosity was elevated, the central venous pressure and mean pulmonary arterial pressure increased significantly by 30–50% above their respective control values. The pulmonary wedge pressure showed a trend of increase, but the change was not statistically significant due to the relatively large scatter in data. The flow resistance in both systemic and pulmonary circulations remained relatively constant when the blood viscosity increased. The systemic and pulmonary vascular hindrances decreased as the blood viscosity rose, indicating the occurrence of compensatory vasodilation at high blood viscosity (Fig. 4). The systemic oxygen transport and consumption rates, as well as the oxygen ex-

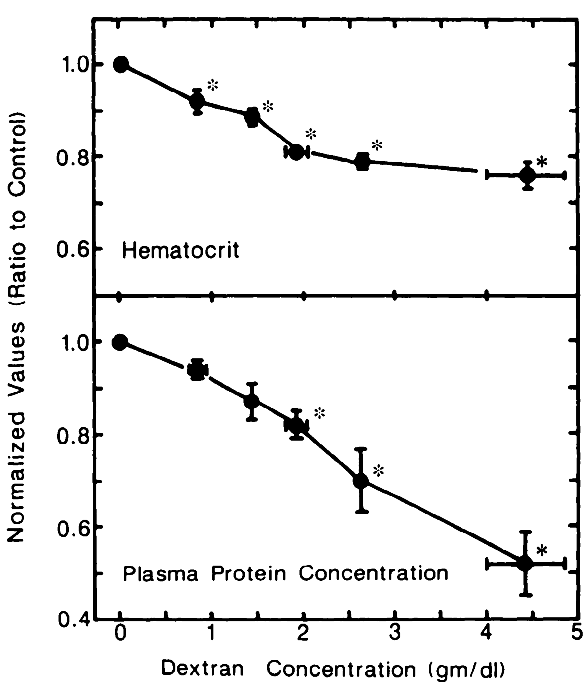

FIG. 2. Effects of isovolemic Dx-500 administration on hematocrit and plasma protein concentration. * Significant difference from control values ($P < 0.05$).

TABLE 2. *Control values of hemodynamic variables*

Parameter	Means ± SE
Mean arterial pressure, mmHg	139.2±2.1
Inferior vena caval pressure, mmHg	6.4±0.2
Mean pulmonary arterial pressure, mmHg	16.8±0.5
Pulmonary wedge pressure, mmHg	6.0±0.2
Cardiac output, $ml \cdot min^{-1} \cdot kg^{-1}$	92.3±4.8
Heart rate, beats/min	168.1±2.6
Stroke volume, ml	8.3±0.3
Hematocrit, %	43.3±0.6
Plasma protein concentration, g/dl	6.3±0.1
Blood viscosity ($200\ s^{-1}$), cP	4.1±0.2
Plasma viscosity, cP	1.3±0.04

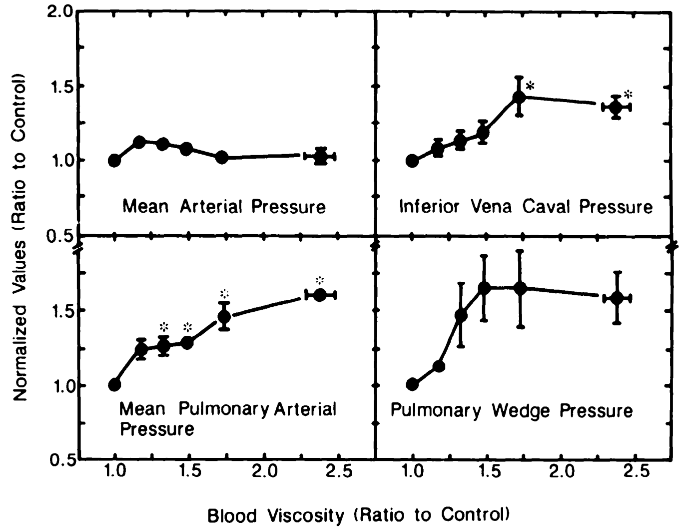

FIG. 3. Effects of changes of apparent blood viscosity on mean arterial pressure, inferior vena caval pressure, mean pulmonary arterial pressure, and pulmonary wedge pressure. * Significant difference from control values ($P < 0.05$).

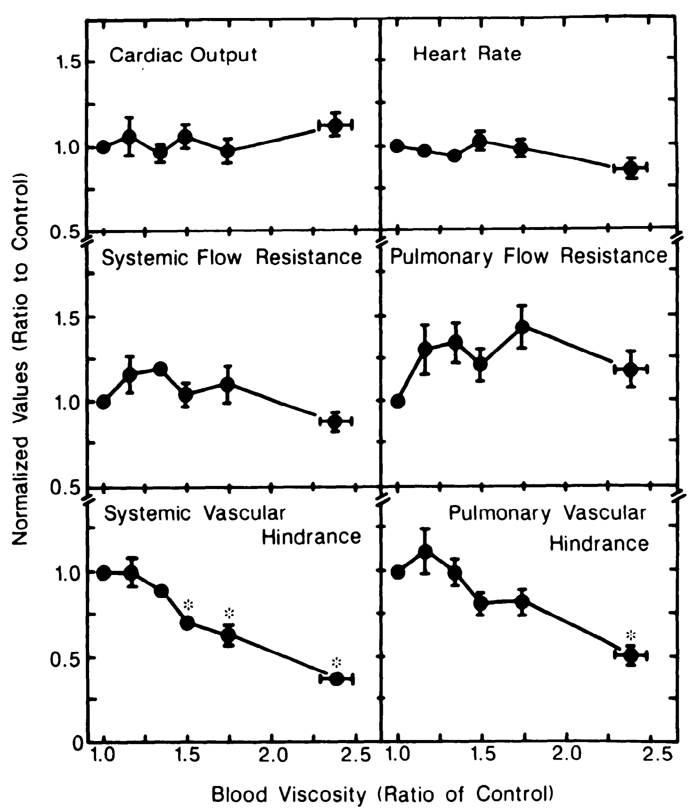

FIG. 4. Effects of changes of apparent blood viscosity on cardiac output, heart rate, systemic flow resistance, pulmonary flow resistance, systemic vascular hindrance, and pulmonary vascular hindrance. * Significant difference from respective control values ($P < 0.05$).

traction ratio, did not show any significant difference from their respective control values (Fig. 5). The arterial blood pH values were stable in all experiments.

The values of regional blood flow for various organs obtained at the control measurements before the exchange transfusion procedure are summarized in Table 3. The myocardial blood flow revealed a trend of increase with the dextran-induced elevation of blood viscosity,

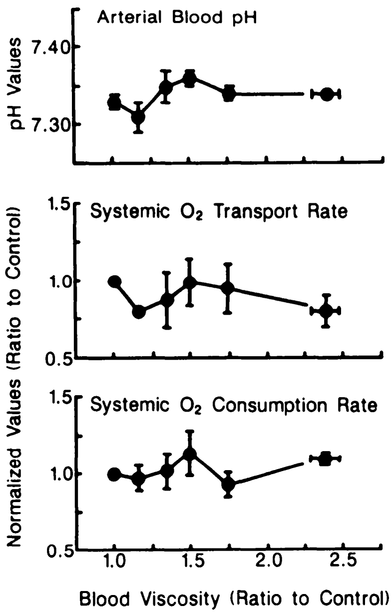

FIG. 5. Effect of changes of apparent blood viscosity on arterial blood pH (actual values), systemic oxygen transport rate (ratio to control), and systemic oxygen consumption rate (ratio to control). None of the experimental results was significantly different from control values.

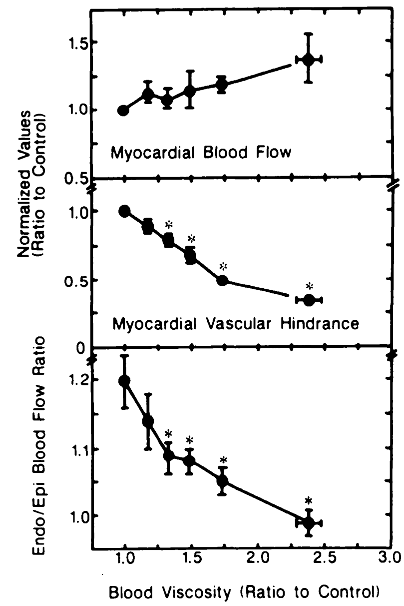

FIG. 6. Effects of changes of apparent blood viscosity on myocardial blood flow (ratio to control), myocardial vascular hindrance (ratio to control), and endocardial-to-epicardial (endo/epi) blood flow ratio (actual values). * Significant difference from respective control values ($P < 0.05$).

TABLE 3. *Control values of regional blood flow*

Parameter	Means ± SE
Endocardium	141.5±7.6
Epicardium	115.8±5.6
Myocardium	128.6±6.7
Diaphragm	10.0±0.5
Liver (hepatic artery)	38.0±2.1
Kidney	371.5±15.7
Brain	36.8±1.1
Adrenal gland	260.2±6.1
Pancreas	34.1±1.2
Small intestine	51.1±2.7
Spleen	151.1±7.2
Thyroid gland	74.8±4.3

Values are measured in $ml \cdot min^{-1} \cdot 100\ g^{-1}$.

but the changes were not statistically significant (Fig. 6). The myocardial vascular hindrance showed progressive and significant reduction (Fig. 6), indicating a marked compensatory coronary vasodilation as the blood viscosity increased. This vasodilation is less prominent in the endocardial layer than in the epicardial layer; the endocardial-to-epicardial (endo/epi) blood flow ratio showed a significant and progressive reduction as the blood viscosity was raised (Fig. 6).

The blood flow changes in other regions of the body are summarized in Fig. 7. The blood flow to the diaphragm and liver showed a trend of increase as the blood viscosity was elevated, but these changes were not statistically significant. The blood flow to the kidney, brain, and adrenal gland remained relatively constant, whereas the blood flow to the pancreas decreased at the highest level of blood viscosity attained. There were significant reductions of blood flow to the small intestine, spleen, and thyroid gland, which began with only a slight increase in blood viscosity and remained at that level when the blood viscosity was further elevated.

The changes of vascular hindrance in various organs are shown in Fig. 8. A significant reduction of vascular hindrance in the diaphragm, liver, kidney, brain, and adrenal gland was noted as the blood viscosity increased, indicating that a compensatory vasodilation occurred in these organs. A similar pattern was seen in pancreas, but the changes were not statistically significant. The vascular hindrance in the small intestine, spleen, and thyroid gland showed an initial increase but reduced toward control values as the blood viscosity was further increased.

DISCUSSION

In the present study, we modified blood viscosity with the use of HMWD and analyzed the response in vascular hindrances from the measured changes in blood flow and blood viscosity. Although it is difficult to simulate the clinical hyperviscosity states, it has been suggested that infusion of HMWD causes hyperviscosity of blood to an extent similar to the hyperviscous state after extensive trauma (14). It has been used in model experiments to evaluate the role of red cell aggregation in vitro (6, 26) and to induce hyperviscosity of blood in vivo (12, 17–19). It should be emphasized, however, that the effects of HMWD are not necessarily equal to those of excessive concentrations of normal or abnormal plasma proteins.

Although rheological alteration induces physiological adjustments, high concentrations of HMWD may exert direct and indirect actions on the vascular smooth muscle. It may interact with the blood-borne vasoactive substances present and involved in the regulation of vascular tone. Furthermore, since shearing forces developed during blood flow may involve in the release of endothelial-vasodilating substances and since wall-shear stresses are altered in these experiments, there may be

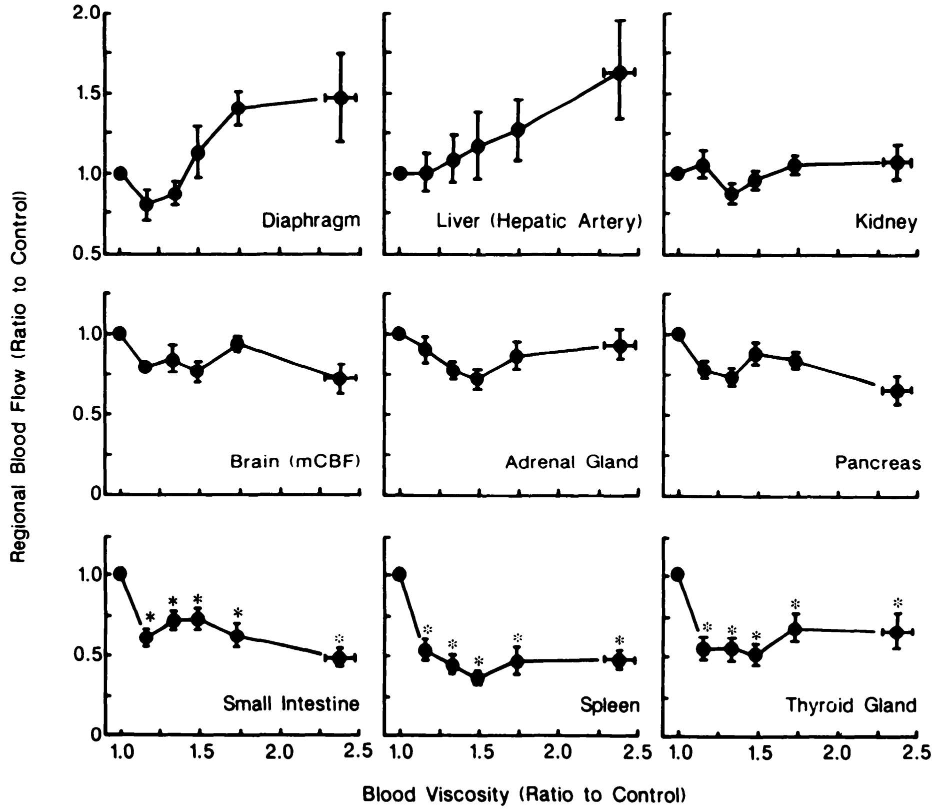

FIG. 7. Effects of changes of apparent blood viscosity on regional blood flow to various organs. * Significant difference from respective control values ($P < 0.05$).

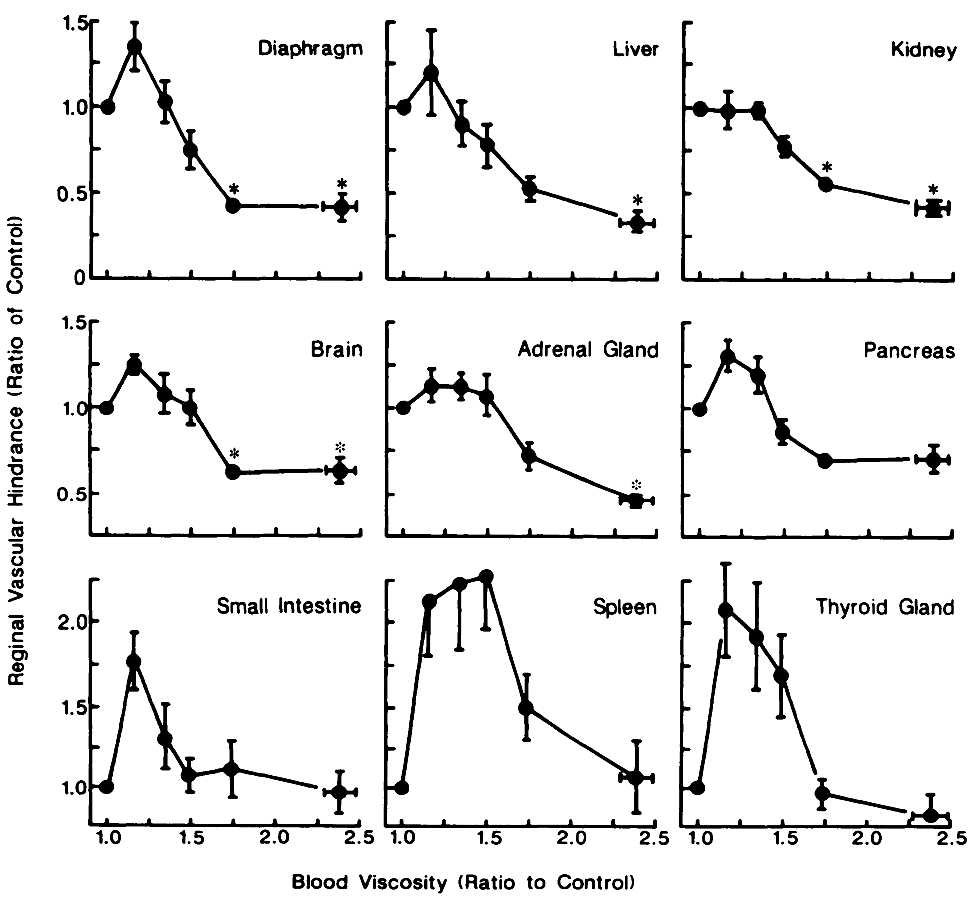

FIG. 8. Effects of changes of blood viscosity on regional vascular hindrance in various organs. * Significant difference from respective control values ($P < 0.05$).

other complex explanations offered for the observed phenomenon.

The rheological behavior of blood is governed primarily by cell concentration, plasma viscosity, red cell aggregation, and cell deformability. Experiments in vitro have shown that HMWD can alter the fluidity of blood by enhancing red cell aggregation and elevating plasma viscosity (6). The synergistic effects of these two factors would greatly increase the apparent blood viscosity. In the present experiments, however, the plasma viscosity was elevated more than fourfold but with only twofold increase in apparent blood viscosity of the circulating blood. This result supports the notion that the elevation of apparent blood viscosity following HMWD infusion in vivo is mediated primarily through the increase in plasma viscosity rather than an enhanced red cell aggregation (17). At least three mechanisms are involved. *1*) The red cell aggregates are likely to be trapped in the microcirculation in certain vascular beds and thus be excluded from the circulation. The reduction of red cell volume found in the present investigation may reflect sequestration of these red cell aggregates. The exact location of the sequestered red cell aggregates is not known. In cat skeletal muscle, Djojosugito et al. (12) have found evidence of microvessel plugging by red cell aggregates after HMWD infusion.

2) At high concentrations of HMWD, red cell aggregation is decreased because of enhanced electrostatic repulsion between cells (6). The tendency of HMWD-induced red cell aggregation in vivo was also counteracted by the decreased plasma protein concentration, particularly the plasma fibrinogen level and the decreased hematocrit.

3) The shear rates in the general circulation is sufficiently high to disperse the red cell aggregation. In the present experiments, extensive red cell aggregation was observed on microscopic examination of blood samples after HMWD infusion at zero shear rate in vitro. Observations with intravital microscopy on the conjunctival microvessels of our experimental animals (unpublished observations) revealed that sluggish flow with red cell aggregation was only transiently present in venules during the diastolic phase, but red cells dispersed and move forward during the systolic phase. The shear rate is lowest in the venules at the end of diastole, but during the systolic phase the shear rate is generally high enough to disperse the red cell aggregate (6, 25, 29).

A significant finding of the present study is that there is a remarkable compensatory vasodilation reflected by the progressive reduction of both systemic and pulmonary vascular hindrances in response to the increase in blood viscosity. The mechanism of this vascular adjustment following dextran-induced hyperviscosity is not fully understood. In the pulmonary circulation, the increase in blood viscosity resulted in an elevation of pulmonary arterial pressure (Fig. 3). The rise in transmural pressure would increase the number of open capillaries and thus decrease the pulmonary vascular hindrance. In the systemic circulation, however, the decrease in vascular hindrance is most likely related to an autoregulatory function serving to maintain blood flow and nutrient transport.

The present results on the systemic circulation were different from those of a previous study in which the cardiac output was found to be progressively reduced and the systemic vascular hindrance remained unchanged when the apparent blood viscosity was raised threefold by isovolemic increase of red cell volume (13). This discrepancy may be related to the fact that the arterial oxygen content varies directly with hematocrit; the rate of oxygen delivery actually remains relatively constant in polycythemic hyperviscosity. HMWD infusion, however, is accompanied with a reduction of hematocrit and oxygen-carrying capacity (18). Tissue perfusion is maintained through a more marked compensatory vasodilation to meet the metabolic needs in face of HMWD-induced hyperviscosity.

The present investigation on regional hemodynamics through a large number of organs and tissues demonstrates that there are significant regional variations following HMWD administration. The findings on the overall systemic circulation represent the integrated changes of these variables in individual organs, and the interpretations require considerations of regional responses. In this regard, the results of the present experiments are in general agreement with those of our previous study on hematocrit-induced hyperviscosity (13). In hemoconcentration, vasodilation reflected by decreased regional vascular hindrance occurred in several vital organs including the myocardium and the brain to maintain constant oxygen supply. Similar findings are observed in several vascular beds in the present investigation. Thus the myocardium, liver, diaphragm, kidney, brain, adrenal gland, and pancreas, exhibited a reduction of their vascular hindrances as the apparent blood viscosity elevated with the increased HMWD concentration. The regional variations in the magnitude of compensatory vasodilation are attributable to the differences in the sensitivity of hypoxic response of tissues to the decreased oxygen availability when blood flow is impeded by the elevated viscosity.

The oxygen utilization of the tissues is not completely governed by the oxygen transport rate. Most tissues, with the exception of myocardium, respond to a reduction in oxygen transport readily by increasing oxygen extraction, and compensatory vasodilation does not become significant until blood viscosity is markedly elevated. The myocardial oxygen extraction is near maximum under normal conditions, and myocardial oxygen utilization is mostly dictated by oxygen transport. Compensatory coronary vasodilation occurs with even mildly elevated blood viscosity to ensure adequate nutrient transport. The reduction of endocardial-to-epicardial flow ratio indicated that the vasodilating effect is more profound in the epicardial layer than in the endocardial layer. This is probably attributable to the fact that endocardial vessels are normally more dilated than those of the epicardium at control state (3, 28), thus having a lesser vasodilating reserve in face of increased blood viscosity.

The small intestine, spleen, and thyroid gland were found to increase their flow resistance and vascular hindrance leading to a reduction of blood flow even when the blood viscosity was only moderately elevated. The increase of vascular hindrance in these organs may be attributable to vasoconstriction secondary to sympathetic activation. The splanchnic vascular bed as a blood reservoir is well known to respond to sympathetic activation in a variety of stressful situations (4, 5, 15). The vasoconstricting response of the spleen is greater than that of liver and intestine (4). A similar pattern of vasoconstricting response was found in response to blood hyperviscosity induced either by elevating the plasma viscosity with HMWD infusion or by increased red cell concentration (13). The thyroid gland is among the most fertilely vascularized and innervated tissues of the body. Sympathetic activities cause vasoconstriction and strongly affect thyroid blood flow especially when their effect is combined with thyroid-stimulating hormone (24). Infusion of epinephrine also resulted in a prompt and substantial diminution of thyroid blood flow (1). The present results indicate that the initial vasoconstricting response of thyroid gland to HMWD-induced hyperviscosity is as prominent as that of the spleen. As the blood viscosity is further elevated and oxygen delivery is compromised; however, these organs also exhibit compensatory vasodilation as their vascular hindrances decrease and return toward the control values.

The liver receives two sources of blood supply. The hepatic artery normally provides about two-thirds to three-quarters of the hepatic oxygen supply and the remainder from the portal vein (15). The decrease of blood flow to intestine and spleen may lead to a greater oxygen extraction by these organs and a lower oxygen saturation of portal venous blood. As a result, the relative contribution of hepatic arterial blood flow to the hepatic oxygen supply would be increased as the lowering of portal venous oxygen saturation is compounded by the decrease in portal blood flow and red cell concentration.

In summary, the present investigation indicates that hyperviscosity of blood induced by HMWD infusion is primarily dependent on the increase in plasma viscosity. The results show that there were considerable regional variations in hemodynamic response to the HMWD-induced hyperviscosity. A concomitant compensatory vasodilation reflected by a reduction of vascular hindrance associated with the increase in blood viscosity occurred in several vital organs, thus serving to maintain blood flow and nutrient transport.

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