Blood viscosity responses to maximal exercise in endurance-trained and sedentary female subjects

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MARTIN, DALE G., EARL W. FERGUSON, SUSAN WIGUTOFF, TIMOTHY GAWNE, AND ERIC B. SCHOOMAKER. Blood viscosity responses to maximal exercise in endurance-trained and sedentary female subjects. J. Appl. Physiol. 59(2): 348-353, 1985.—To assess whether the rheological properties of blood might be altered by exercise, we measured whole blood viscosity, plasma viscosity, and its components in healthy female subjects before, immediately after, and 1 h after maximal upright exercise using the Bruce graded exercise protocol. Forty-seven female subjects (15 sedentary, 14 who ran 5-15 miles/wk, and 18 who ran >50 miles/wk), ages 18-43 yr, were evaluated. Whole blood viscosity, measured with a cone and plate viscometer, increased an average of 12.6% with exercise. The increase was greater than can be attributed to the observed 8.9% increase in hematocrit alone due to a coincident increase in plasma protein concentration. However, plasma viscosity did not rise to the degree expected, likely due to a disproportionate observed loss of fibrinogen from the protein pool. These changes were independent of conditioning level or aerobic capacity. In this cross-sectional study, there appears to be no adaptive adjustment in females to physical conditioning that results in changes in blood viscosity.

plasma viscosity; exercise; aerobic capacity; fibrinogen; hematocrit

MULTIPLE BIOCHEMICAL, hematological, and hemodynamic adjustments occur with aerobic conditioning (1). These changes account for the improved endurance and performance capacities that characterize physically fit individuals (20). The cardiovascular system figures prominently in these adaptations. This system is the limiting factor in determining blood flow to the tissues. Blood flow is, in turn, determined by arterial pressure, arteriolar geometry, and blood viscosity (2, 23).

Viscosity of blood varies with the hematocrit, concentrations of certain key plasma proteins, and erythrocyte deformability (2). Many of these variables change with maximal upright treadmill exercise (24) and may be altered by aerobic conditioning (15). For example, maximal exercise may result in plasma volume losses as great as 20% (25). Since it is believed that both erythrocyte (18) and plasma protein content (21) remain relatively stable during maximal treadmill exercise, this loss in plasma volume causes concurrent increases in hematocrit, hemoglobin concentration, and the concentrations of plasma proteins.

Most previous studies that have evaluated blood viscosity and its relationship to physical fitness have made vague definitions of fitness or have compared healthy populations with patients with disease (8, 11, 15). Whether blood viscosity is significantly altered during aerobic conditioning in a healthy population is unclear. This study focuses on a population of healthy female subjects in well-defined fitness categories in order to characterize blood viscosity responses to maximal treadmill exercise.

MATERIALS AND METHODS

Subjects

Forty-seven healthy nonsmoking premenopausal adult female subjects were evaluated. Fifteen were on no regular exercise program and were categorized as sedentary. Fourteen were running 5-15 miles/wk and were considered moderately conditioned. Eighteen who ran >50 miles/wk were classified as highly conditioned. The three groups were matched as closely as possible for age and body habitus. All subjects participated with informed consent and completed a medical history questionnaire.

All subjects were free of detectable cardiovascular diseases as determined by a medical examination, including a 12-lead electrocardiogram. Potential subjects with a clinical history or other evidence of medical problems that could limit maximal exercise performance were excluded from the study. Attempts were made to find lesser conditioned subjects who were lean.

The subjects were free from any medication for at least 1 wk prior to the study. Subjects who had taken oral contraceptives in the previous 3 mo were excluded from the study. This study had the approval of the Human Use Committee of the Uniformed Services University.

Body density was determined by hydrostatic weighing (19). Percent body fat was calculated from this density measurement. Lean body mass was calculated from body weight and total body fat.

Exercise Blood Sampling

Subjects rested 15-20 min in a reclining chair before measurements of O2 consumption at rest were made and
the first blood sample obtained. Subjects then exercised on a treadmill according to the multistaged Bruce protocol. Electrocardiograms were monitored on each subject before, during, and after exercise (model 633, Quinton Instruments, Seattle, WA). A metabolic measurement cart (Beckman Instruments, Sidler Park, IL) was used to analyze and record O₂ consumption, respiratory quotient, and other cardiorespiratory variables every 30-60 s at rest, during exercise, and during recovery.

All subjects were encouraged to remain on the treadmill to exhaustion. Objective criteria for maximal effort included >3-fold increase in blood lactate concentrations, a plateau in heart rate or O₂ consumption, and a respiratory quotient of >1.0. Data on subjects who failed to exert themselves to a maximal degree, as defined by these criteria, were excluded from the analysis.

Forty-five-milliliter blood samples were drawn by separate venipunctures during the rest period, immediately after exercise, and after 1 h of recovery by use of a two-syringe technique drawing from an antecubital vein. Subjects were in a reclining chair for all venipunctures and remained in the chair throughout the recovery phase. Microhematocrits were obtained by using a centrifuge (model MC, Damon International Equipment, Needham Heights, MA). At least three measurements were taken; these were averaged for each sample and recorded to the nearest 0.1%. Hemoglobin (Hb) concentration was measured in duplicate by the cyanomethemoglobin method. Erythrocyte counts were determined with a particle counter (Coulter Electronics, Hialeah, FL). From these measurements [hematocrit (Hct), Hb, and erythrocyte], mean corpuscular volumes and mean corpuscular Hb concentrations were calculated.

Total plasma proteins were measured with a handheld refractometer (AO TS Goldberg Meter, American Optical Scientific Instruments, Buffalo, NY). Fifty microliters plasma were placed on the clean surface of the refractometer and read to the nearest 0.1 g/dl. Albumin and total serum protein concentrations were measured using a Centrifichem System 500 (Baker Instrument, Allentown, PA) and standard procedures. Fibrinogen concentration was assayed by using values for Hct and Hb (6). The percent change in plasma volumes was calculated by using Microhematocrits adjusted to 45 t 0.2%, the 15.1% increase in Hct adjusted to 45.0 t 0.2%, the 15.1% increase in Hct and presumably a 9.8% increase in Hb), a 10.6% increase in WBV resulted (Fig. 1). Similarly, a 10.6% increase in WBV was distinctly different among the three conditioning groups. Duration of exercise on the treadmill was also different among the groups and strongly correlated with the measured VO₂max (r = 0.950, P < 0.001).

**Determinants of Blood Viscosity with Maximal Exercise**

**Hematocrit.** Mean Hct values during rest, exercise, and recovery from exercise were similar among the three groups. With exercise, Hct increased an average of 8.9% (Table 2). The percentage increase in Hct among the groups was not statistically different. Within 1 h of the completion of exercise, the Hct fell to a level below that before exercise. If we assume a restoration of the preexercise whole blood volume, the total mean decrease of -4.6% in Hct is consistent with the calculated erythrocyte loss from phlebotomy.

In the range of Hct studied, a linear 1:1 relationship between Hct and WBV was observed. The mean Hct for control samples was 41.0%. When the Hct were adjusted to 45.0 ± 0.2% with autologous plasma (a mean increase of 9.8% in Hct and presumably a 9.8% increase in Hb), a 10.6% increase in WBV resulted (Fig. 1). Similarly, when the Hct (mean 39.1%) of the recovery samples were adjusted to 45.0 ± 0.2%, the 15.1% increase in Hct was accepted with P ≤ 0.05 or better. Correlations were used where the underlying hypothesis suggested meaningful relationships might exist. Multiple linear regression was used to rate the variables in order of importance in influencing the independent variable (22).

**RESULTS**

**General Anthropometric Data**

General anthropometric data are given in Table 1. Mean age, mean total body weight, and mean lean body weight were similar in the three groups. Percent body fat was distinctly different among the three groups.

**Exercise Performance**

Cardiopulmonary performance data are shown in Table 1. As expected, mean maximal O₂ uptakes (VO₂max) were distinctly different among the three conditioning groups. Duration of exercise on the treadmill was also significantly different among the groups and strongly correlated with the measured VO₂max (r = 0.950, P < 0.001).

**TABLE 1. Anthropometric and performance data**

<table>
<thead>
<tr>
<th></th>
<th>Sedentary</th>
<th>Moderately Conditioned</th>
<th>Highly Conditioned</th>
<th>Significant Differences</th>
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<td>n</td>
<td>15</td>
<td>14</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Age, yr</td>
<td>33.3</td>
<td>33.4</td>
<td>32.1</td>
<td></td>
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<tr>
<td>+6.0</td>
<td>+5.5</td>
<td>+7.3</td>
<td></td>
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<tr>
<td>Ht, cm</td>
<td>165.0</td>
<td>164.0</td>
<td>166.5</td>
<td></td>
</tr>
<tr>
<td>±11.0</td>
<td>±6.2</td>
<td>±4.3</td>
<td></td>
<td></td>
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<tr>
<td>Wt, kg</td>
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<td>55.8</td>
<td>55.1</td>
<td></td>
</tr>
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<td>±10.4</td>
<td>±4.1</td>
<td>±4.9</td>
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<td></td>
</tr>
<tr>
<td>Body fat, %</td>
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<td>21.4</td>
<td>16.4</td>
<td>M &lt; S*, H &lt; M*</td>
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<tr>
<td>±6.6</td>
<td>±4.0</td>
<td>±4.7</td>
<td>4.7</td>
<td>H &lt; S†</td>
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<tr>
<td>Lean wt, kg</td>
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<td>43.9</td>
<td>46.0</td>
<td></td>
</tr>
<tr>
<td>±7.7</td>
<td>±4.4</td>
<td>±4.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VO₂max ml·kg⁻¹·min⁻¹</td>
<td>34.1</td>
<td>44.8</td>
<td>51.0</td>
<td>M &gt; S*, H &gt; M*</td>
</tr>
<tr>
<td>±5.5</td>
<td>±4.4</td>
<td>±5.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time on treadmill, min</td>
<td>±1.1</td>
<td>±0.9</td>
<td>±1.1</td>
<td>H &gt; S†</td>
</tr>
</tbody>
</table>

Values are means ± SD. S, sedentary; M, moderately conditioned; H, highly conditioned. * P < 0.05 significant difference among groups. † P < 0.01 significant difference among groups.
FIG. 1. Whole blood viscosity at native hematocrit (WBVn) (open triangles) and WBV when hematocrit (Hct) was 45% (WBVa) (closed circles) vs. Hct for control (C), exercise (E), and recovery (R). This figure demonstrates a 1:1 relationship between WBV and Hct for range of Hct samples studied. Control WBVn 41.0% is shown as open triangle. Increasing Hct by 9.8-45% results in increase in WBV of 10.6%. Similarly, a 15.1% increase in Hct in R increases WBV 15.3%. Arrow represents increase in WBV from C to E above that expected from increase in Hct alone. Increase in WBVa between C and E correlated to increase in plasma protein concentration and plasma viscosity. paralleled the 15.3% increase in WBV.

When the exercise blood samples are compared with controls, an 8.9% increase in Hct and a 6.8% increase in Hb were accompanied by a 12.6% increase in WBV. The arrow in Fig. 1 represents the increase in WBV, which is greater than can be attributed to the increase in Hct alone.

For the entire study group the increase in erythrocyte count (6.1%) and Hb (6.8%) with exercise was less than the 8.9% increase in Hct. Thus the calculated values for mean corpuscular volume increased and mean corpuscular hemoglobin concentration decreased with maximal exercise. During recovery, the small drop in Hct (-4.6%) paralleled the loss in erythrocyte (-6.0%) and Hb concentration (-4.3%), indicating a return to the control values for the mean corpuscular volume and hemoglobin concentration.

Whole blood viscosity at native hematocrit. Whole blood viscosity at native hematocrit (WBVn), measured at 450 s⁻¹, increased in all subjects with exercise and returned to or below control levels after 1 h of recovery (Table 2). The mean WBVn before, immediately after, and 1 h after exercise were not different among the groups. The increase in WBVn with exercise did not correlate with VO₂max (Fig. 2) time on the treadmill, or postexercise lactate concentrations. The Hct values strongly correlated with WBVn ($r = 0.835$, $P < 0.05$) at 450 s⁻¹. In multiple linear regression analysis in which WBVn was the dependent variable, most of the variability in WBVn ($r² = 0.88$) was due to the Hct and total plasma protein concentration.
Whole blood viscosity corrected to 45% with autologous plasma. When Hct was standardized to 45% with autologous plasma, mean whole blood viscosity (WBV45) during control, exercise, and recovery periods were similar among the groups. For all subject groups, a significant increase in WBV45 was recorded with exercise. A positive correlation existed between the increase in WBV45 and the increase in total plasma protein concentration \((r = 0.781, P < 0.05)\) and plasma viscosity with exercise. The increase in WBV45 after exercise varied from 2.8 to 3.9% among the groups. Decreases in WBV45 with parallel decreases in plasma viscosity and total plasma proteins were observed with recovery.

**Changes in Plasma Protein Concentration and Content with Exercise**

Marked changes in the concentrations of the major plasma proteins occurred with exercise and recovery from exercise. The mean increase of 10.2% in plasma protein concentration was independent of conditioning (Table 2). The entire study group underwent a calculated loss of plasma volume averaging 11.1%. From these data the percent loss in total intravascular protein content was calculated to be 1.9% for all subjects. However, the loss of fibrinogen content was much greater (−7.5%). The 45 ml of blood sampled prior to exercise contained an average of 1.3% of circulating plasma proteins. Therefore, a computed loss of only 0.6% of the total plasma proteins occurred as a consequence of maximal exercise stress compared with a 6.2% loss of fibrinogen (Table 3).

**Plasma Viscosity**

Plasma viscosity and plasma protein concentrations before and after exercise are shown in Table 2. At rest, plasma viscosity, total plasma proteins, total serum proteins, globulins, and albumin were similar among the groups. However, fibrinogen concentration was greater \((P < 0.05)\) in the highly conditioned female subjects (Table 2). Among all subjects the plasma viscosity before exercise correlated most closely with total plasma protein concentration \((r = 0.804, P < 0.05)\). Weaker correlations were observed with fibrinogen concentration \((r = 0.576, P < 0.05)\), globulin concentration \((r = 0.459, P < 0.05)\), and albumin concentration \((r = 0.525, P < 0.05)\).

Multiple linear regression analyses performed on these data, in which plasma viscosity was the dependent variable and fibrinogen, globulin, and albumin were independent variables, demonstrated that fibrinogen exerted the greatest relative effect on plasma viscosity. When compared per unit of protein weight, globulin and albumin also had a statistically significant yet much smaller influence on the plasma viscosity, as represented by the following equation: plasma viscosity = 0.585 + 0.816[F] + 0.076[G] + 0.060[A], where [F] is fibrinogen concentration, [G] is globulin concentration, and [A] is albumin concentration.

As expected, given the aforementioned changes in plasma protein concentrations with exercise, plasma viscosity increased significantly in all groups with exercise.

**Effect of Sampling**

Removal of a total of 90 ml of blood for control and exercise samples affected measurements of WBV in exercise and recovery samples. In the average 55-kg subject with a 4-liter blood volume, this represented a 2.2% loss of erythrocytes. The initial 45 ml of blood removed for control measurements affected the exercise measurements. Thus it is likely that the WBV, Hct, and plasma protein concentrations after exercise were underestimated. This would affect the magnitude but not the direction of the changes in these variables with exercise. If we assume that the entire loss of erythrocyte mass and plasma was replaced by interstitial water, we would expect a 4% decrease in Hct in the recovery sample and a 6% decrease in plasma protein concentration. Our recovery sample data agreed closely with these calculations; an overall 4.6% decrease in Hct coupled with a 5.2% loss in total plasma proteins was observed.

**DISCUSSION**

**Study Population**

A common failing of previous studies that examined blood viscosity changes with fitness levels was the characterization of the study population. Previous studies employed arbitrary measurements of fitness level, indirect measurements of \(\dot{V}O_{2\text{max}}\), or failed to report objective data \((7, 8, 15)\). In this study, the subject population was carefully chosen and well characterized for fitness level and aerobic capacity. In addition, subjects were sampled under strictly controlled conditions to limit other temporal (diurnal, menstrual, seasonal) variations in blood viscosity \((2)\).

The viscosity of blood at higher shear rates \((\geq 30 \text{ s}^{-1})\) is a function of cell concentration (Hct), plasma viscosity, and cell deformability \((2, 23)\). The WBV increase of 12.6% in this study with maximal upright treadmill exercise was due to an 11% loss of plasma volume unaccompanied by a loss of erythrocytes or plasma protein. The intensity and duration, as well as the mode of exercise, greatly influences the fluid shifts and the size of erythrocytes \((5, 16, 21, 25)\). In this study, maximal upright treadmill exercise resulted in increased Hct \((8.9\%)\), Hb \((6.8\%)\), plasma protein concentrations \((10.2\%)\), and mean corpuscular volume \((8\%)\) of the erythrocytes. This
degrees of hemoconcentration and erythrocyte swelling is consistent with previous studies in humans under similar conditions (25). Our data suggest the extent of hemoconcentration is a function of the relative intensity rather than the absolute work load and is not influenced by aerobic capacity or endurance training in females. Hemoconcentration with exercise causes multiple perturbations in Hct, plasma protein concentrations, and erythrocyte cell size, which can affect the rheological properties of blood in a complex manner (2, 17).

A suspension of erythrocytes of the same size in plasma of the same viscosity should produce equivalent increases in Hct, Hb, and WBV in the range of Hct studied. Thus a 9% increase in Hct and Hb should elicit a 9% increase in WBV. In the maximally exercise-stressed subject, the increase in WBV of 12.6% was much greater than the 6.8% increase in Hb or 8.9% increase in Hct. This greater than expected rise in WBV suggests an increase in viscosity without concurrent improvement in O2 carrying capacity in large vessels during maximal upright exercise stress.

In this study, WBV was not different in the three groups nor did it correlate with aerobic capacity (Fig. 2). Dintenfass and Lake (8) have suggested a correlation between fitness levels and decreased blood viscosity; however, their study compared data from healthy individuals with those with a variety of diseases. Multiple rheological abnormalities have been reported in patients with various cardiovascular diseases (3, 7). These include increased blood viscosity in hypertensive subjects and postmyocardial infarction due to increases in plasma viscosity, fibrinogen concentration, and Hct (3, 7, 14). Rheological measurements in patient evaluation have become a useful diagnostic indicator of impending circulatory problems and as a prognostic tool (3). Therefore, it is not surprising to see significant differences in blood viscosity factors in a group of fit subjects and a group of less-fit subjects, when many of the latter have concurrent medical conditions.

### Plasma Viscosity Changes with Exercise

The contribution of plasma viscosity to WBV was small but significant. After exercise, WBV averaged 3.9% higher than control samples. The vast majority of this increase in WBV was due to the 6.3% increase in plasma viscosity. Therefore, due to the elevated plasma viscosity, the increase in WBV was greater than would be expected from the increase in Hct alone. However, the increase in plasma viscosity is less than would be expected from the degree of hemoconcentration of plasma proteins due to exercise-induced loss of fibrinogen from the vascular pool. With maximal exercise, the increase in plasma viscosity was smaller among the groups and averaged 6.3%, whereas the concentration of total plasma proteins increased >10%. Most of this increase was due to albumin and globulin fractions, whereas the rise in fibrinogen concentration was relatively small. Thus the slight increase (3.7%) in fibrinogen concentration, in fact, suggests a loss of 6.2% of the fibrinogen content in the plasma during exercise, whereas total plasma protein content remained rather constant (0.6% change).

This study confirms that fibrinogen concentration has the greatest relative influence on plasma viscosity (2, 23). This smaller than expected rise in fibrinogen concentration has several rheological consequences that are advantageous in the exercising subject. If fibrinogen concentrations had increased as much as Hct, even more marked increases in plasma viscosity would have occurred. As Hct increases, O2 transport is augmented. However, increases in plasma viscosity elevate WBV and decrease flow, without enhancing O2 transport (23). This blunting of the increase in plasma viscosity with exercise is likely due to a relatively large removal of fibrinogen (Table 3).

Increased fibrinolytic activity has been suggested as the mechanism for fibrinogen removal, thus maintaining the fibrinogen concentration at near preexercise levels during exercise-induced hemoconcentration (15). It is well documented that fibrinolytic activity is markedly accelerated with exercise (0, 10). However, whether or not accelerated fibrinogenolysis occurs with exercise is controversial (4, 9, 12). If fibrinogenolysis does not occur, fibrinogen content must decrease by another mechanism. Hypotheses include removal of fibrinogen from the plasma by transudation into the interstitial spaces and increased fibrin clot formation with exercise. Increased deposition of fibrin clots during exercise is most likely (10). Regardless of the mechanism for attenuation of the decrease in fibrinogen, the result would subsequently lower plasma viscosity.

Letcher et al. (15) proposed that a decrease in plasma viscosity in endurance-trained individuals at rest and exercise would increase efficiency of O2 delivery. He found significantly lower plasma viscosities in a group of 13 subjects (12 males, 1 female) who ran 20-70 miles/wk when compared with 12 sedentary subjects (11 males, 1 female) (15). The difference was primarily due to a lower fibrinogen concentration in the runners. In the present study of 47 female subjects, there were no differences in

![Whole Blood Viscosity vs. Maximal Oxygen Uptake (VO2max)](image)

<table>
<thead>
<tr>
<th>VO2max (ml kg^-1 min^-1)</th>
<th>Whole Blood Viscosity (CP)</th>
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</thead>
<tbody>
<tr>
<td>25</td>
<td>2.5</td>
</tr>
<tr>
<td>30</td>
<td>3.0</td>
</tr>
<tr>
<td>35</td>
<td>3.5</td>
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<tr>
<td>40</td>
<td>4.0</td>
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</table>

FIG. 2. Whole blood viscosity vs. maximal O2 uptake (VO2max). There was no correlation between whole blood viscosity (CP, at 400 s^-1) and aerobic capacities (ml kg^-1 min^-1) for 15 sedentary subjects (S), 14 moderately conditioned (M), or 18 highly conditioned (H).
plasma viscosity among the three conditioning groups (Table 2). In contrast, female subjects running higher mileages in our study had increased fibrinogen concentrations. Similarities in the plasma viscosities among the three groups are likely due to the equivalent total plasma protein concentrations. In this cross-sectional study of females, aerobic conditioning was not associated with differences in plasma viscosity, and long-distance running did not have a favorable effect on resting fibrinogen concentration.

The WBV decreased 6.0% during recovery. These results are difficult to interpret due to the large amount of blood withdrawn in control and exercise samples (90 ml). The calculated loss of plasma proteins and drop in Hct are consistent with the rapid restoration of the total blood volume with interstitial fluids. Subsequent decreases in WBV (6.0%), WBVA5 (−2.1%), and plasma viscosity (−3.7%) are due to restitution of blood volume without recovery of plasma protein or erythrocyte content lost from venipuncture.

Results of this study demonstrate that 1) whole blood viscosity increases with maximal exercise more than could be attributed to the hematocrit alone, due to a coincident increase in plasma protein concentrations; 2) plasma viscosity did not rise to the degree expected due to loss of fibrinogen content; and 3) these changes were independent of conditioning level, aerobic capacity, or time on the treadmill.

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