Observations on Blood Viscosity Changes after Acute Myocardial Infarction

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SUMMARY
Serial blood rheologic measurements were made in 25 patients with acute myocardial infarction; measurements included blood and plasma viscosities, hematological data and plasma protein concentrations. The blood viscosity was elevated on admission and for more than 21 days after acute myocardial infarction. However, the cause of the elevated viscosity was changed as a function of time after acute myocardial infarction. During the first three days after admission, the high blood viscosity was mainly attributable to high hematocrit values. Thereafter, the hematocrit fell, but blood viscosity remained high. High blood viscosity after the first three days of acute myocardial infarction can be correlated with increases in plasma viscosity and red cell aggregation, which in turn are explained by elevations of α₂ globulin and fibrinogen concentrations. Patients with higher blood viscosity on admission had a significantly higher incidence of complications, i.e., shock, thromboembolism and left ventricular failure.

Additional Indexing Words:
- Coronary heart disease
- Hematocrit
- Plasma viscosity
- Fibrinogen
- Hemodilution
- Red cell aggregation
- Globulins
- Plasma proteins
- Red cell deformation

IN MYOCARDIAL INFARCTION the acutely injured heart has a reduced contractile performance,¹,² and various hemodynamic consequences occur following such insult.³ In comparison to the large body of information on the effects of acute myocardial infarction on the functions of the heart and blood vessels,¹⁻³ there are relatively few studies concerning the rheological behavior of the blood in this condition.

In 1962, Burch and DePasquale⁴ reported that patients with acute myocardial infarction had elevated red cell concentration, and they suggested that erythrocytosis and high blood viscosity might be predisposing factors in the development of the illness. This observation of erythrocytosis in acute myocardial infarction has been confirmed by some investigators⁵ but not by others.⁶⁻⁸ With the use of capillary viscometer⁹ and rotational viscometers,¹⁰⁻¹² several groups of investigators have found an elevation of blood viscosity in patients with acute myocardial infarction. In most of these studies, however, only single or a few measurements were made on each patient. Furthermore, the rheological determinants of blood viscosity in the patient have not been systematically analyzed. The present investigation was designed to permit a quantitative assessment of the relative roles of each of the following rheological components of blood viscosity: plasma factors, cell concentrations, cell deformability and cell aggregation. These rheological measurements were made serially for one month or longer following the acute episode of myocardial infarction, and the results have been correlated with the clinical course of the illness.

Materials and Methods
The present study was performed on patients with acute myocardial infarction admitted to the Cardiac Intensive Care Unit of the Presbyterian Hospital in the City of New York from November 1971 to February 1972. Only those patients admitted within 24 hours of the initial complaint of chest pain were studied. The diagnosis of acute myocardial infarction was established by a history of chest pain, ECG changes and increased serum levels of cardiac enzymes, i.e., CPK, SGOT, LDH, and HBD.

The first blood sample from each patient was obtained immediately after admission from either the antecubital vein or the femoral vein with the use of a sterile 20 gauge stainless steel needle and a 20 ml heparinized vacutainer tube (Becton, Dickinson & Co). Thereafter, serial samples
were drawn in the morning every other day for one week and then every week for the remainder of the first month. A final sample was obtained at the end of two months. All samples were analyzed as described below, and the results were compared with those obtained from age and sex-matched normal healthy controls.

Hematological analyses

The hematocrit (Hct) of each sample was determined by centrifuging at 15,000 g for 5 min and was corrected for plasma trapping. Red blood cell (RBC) counts were performed in a Coulter counter and hemoglobin (Hb) concentrations were determined by using cyanmethemoglobin reagent. Mean corpuscular volumes (MCV) and mean corpuscular hemoglobin concentrations (MCHC) were calculated from the measured values of Hct, RBC count and Hb.

Plasma Protein Concentrations

The total plasma protein concentration of each sample was determined by a refractometer method (Carl Zeiss, Inc). Plasma fibrinogen concentration was determined by the method of Ratnoff and Menzie, and the plasma protein fractions were analyzed by means of microzone electrophoresis on cellulose-acetate strips.

Viscosity Measurements

Blood is a suspension of cells in plasma, and blood viscosity at a given temperature depends on the cell concentration and plasma viscosity. At given levels of cell concentration and plasma viscosity, blood viscosity varies with cell deformation and cell aggregation, both of which are processes depending on the shearing condition during flow. At high shear rates, e.g., 50 sec\(^{-1}\), red cells are subjected to shear deformation and shear dispersion, resulting in a relatively low blood viscosity. At low shear rates, e.g., below 10 sec\(^{-1}\), however, red cells are less deformed and tend to form rouleaux, leading to an elevation of blood viscosity. In the normal circulation, the shear rate in arteries and capillaries is probably above 200 sec\(^{-1}\) and it is of the order of 20 sec\(^{-1}\) in most venules and small veins. The shear rate can even approach zero in stagnant parts of the circulation such as in some veins of the lower extremities. In pathological conditions, such as shock, the low flow state might result in a generalized reduction of shear rates through the vascular tree. Therefore, in order to evaluate the various factors regulating blood viscosity, viscometric measurements should be made over a full range of controlled shear rates which may be encountered in vivo.

The viscometer used in this experiment was an air-bearing co-axial cylinder viscometer with the sensitivity and precision needed for the measurement of blood viscosity over a wide range of shear rates. The essential components and the principle of operations of the viscometer are shown in figure 1. The sample is placed between two concentric cylinders separated by a uniform annular gap and is thermostated by means of a circulating water bath. The inner cylinder is rotated at various speeds (\(\Omega\), in sec\(^{-1}\)) by means of a synchronous motor and gear trains (Sterling) and a servocontrol frequency generator (General Resistance Co). The corresponding shear rates (\(\gamma\), in sec\(^{-1}\)) in the liquid annulus are given by \(\Omega s/(s-1)\), where \(s\) is the ratio of the outer to inner cylinder diameters. The outer cylinder is affixed to an air-bearing rotor shaft. The torque transmitted to the outer cylinder tends to introduce a displacement angle between the rotor shaft and the microsensors which are located at the lower part of the shaft. The resulting signal is transmitted to an electronic feedback system (Dynamics Research Corp), which generates an equal and opposite counter-torque via the magnetic torque generator to hold the rotor shaft from any angular displacement. From the torque reading (T, in dyne-cm) and a geometrical conversion factor (\(\alpha\)) determined with the use of standard Newtonian oils of known viscosities (Cannon Instrument Co), the shear stress \(\sigma\) (in dyne cm\(^{-2}\)) is calculated as \(\alpha T\). The viscosity (\(\eta\), in poise) is obtained as:

\[
\eta = \frac{T}{\alpha \gamma}
\]  

In this study, the viscosity measurements were performed at a temperature of 37°C and over a shear rate range of 416 to 0.01 sec\(^{-1}\). The measurements included: 1) the viscosity of the original blood (\(\eta_o\)); 2) the viscosity of blood with Hct adjusted to 45.0 ± 0.1% by adding either autologous packed cells or plasma (\(\eta_p\)); 3) the viscosity of red cell suspensions in Ringer solution (pH = 7.4, containing 12 mM tris buffer and 0.5 g% human serum albumin) at a Hct of 45.0 ± 0.1% (\(\eta_r\)); and 4) the plasma viscosity (\(\eta_p\)). Since the viscosity of plasma is independent of shear rate, the values obtained at 5.2 and 0.52 sec\(^{-1}\) were averaged. The relative viscosity of blood (\(\eta_r\)), the low shear value of which is an index of the tendency of red cell aggregation, was calculated as:

\[
\eta_r = \frac{\eta_r}{\eta_p}
\]  

Results

Patients

The study was performed on 25 patients with acute myocardial infarction. Eighteen were males and seven females. The mean age was 61.5 years (range 39 to 84). All patients developed characteristic chest pain and elevation of serum cardiac enzymes. The average time between onset of symptoms and first blood sample for viscosity measurement was eight hours (range 2 to 20). The electrocardiographic patterns revealed 14 patients with anterior wall infarction, nine with inferior wall infarction, and two with both anterior and inferior wall infarctions.

![Figure 1](https://circ.ahajournals.org/doi/10.1016/0009-7322(75)90638-3)

The schematic diagram of the essential components and the principle of operation of the viscometer used in the present investigation.
Hematological Data

The initial Hct in patients with acute myocardial infarction ranged from 39.0% to 54.5% upon admission, with an average of 46.4% (fig. 2). The value of Hct fell progressively to an average of 42.5% after four days of hospitalization. Thereafter, it showed only a very gradual decline to an average of 40.9% on the 28th day, and it averaged 41.8% on the 60th day. The initial values of MCV (93.0 ± 7.0 μm², mean ± SD) and MCHC (33.8 ± 1.0 g%) were within normal ranges, and neither value changed significantly during the course of illness.

Plasma Protein Concentrations

The serial observations on plasma protein concentrations in patients with acute myocardial infarction are shown in fig. 3. The initial concentration of total plasma proteins was slightly higher than that of the normal controls, but it fell during the first three days of illness to the normal level (fig. 3). Analyses of plasma protein fractions showed significant changes of albumin, α₂-globulin and fibrinogen. The albumin concentration was normal on admission; it fell progressively during the first three days of illness and rose gradually thereafter. The plasma concentrations of α₂-globulin and fibrinogen were elevated during the first three days and reached peak values between the third and fifth days after the acute episode. Both values gradually fell toward normal levels during the course of observation. The other plasma protein fractions did not show significant changes.

Viscosity Studies

The results of serial measurements on the viscosity of original whole blood (η₀) in patients with acute myocardial infarction are illustrated in figure 4. Values at three shear rates, i.e., 52, 5.2, and 0.52 sec⁻¹, represent blood viscosities at high, medium, and low shear rates, respectively. At all shear rates, the initial

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Figure 2

Serial hematocrit (Hct) changes in myocardial infarction (MI) patients after admission to hospital. The vertical bars denote SEM and the closed dot indicates normal controls.

Figure 3

Serial measurements of plasma concentrations of total protein, albumin, α₂ globulin and fibrinogen (β) in MI patients after admission to hospital. The vertical bars denote SEM and the closed dots indicate normal controls. The α₁ globulin, β globulin, and γ globulin were essentially unchanged during the course of MI and were not shown in the figure.

Figure 4

Serial changes in viscosity of original blood (η₀) at different shear rates in MI patients after admission to hospital. The vertical bars denote SEM and the closed dots indicate normal controls.

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months after the episode, the $\eta_r$ values at all shear rates were still slightly higher than those of normal controls. The initial value of plasma viscosity in patients with acute myocardial infarction was higher than that of normal controls (fig. 5). The value reached a peak on approximately the third day of illness and fell gradually throughout the remaining period of observation. The low-shear $\eta_r$ of blood with Hct adjusted to 45%, which is an index of the tendency of red cell aggregation, was elevated in patients with acute myocardial infarction upon admission (fig. 6). The peak values of low shear $\eta_r$ developed on approximately the fourth day of illness. Throughout the remaining period of observation, the values of low shear $\eta_r$ of the patients were still higher than those of normal controls. The viscosity of 45% red cell suspensions in Ringer solution ($\eta_m$, which is an index of red cell deformability, was normal at all shear rates during the entire course of observation.

Discussion

It has long been recognized that in a steady, laminar flow of a homogeneous fluid through a straight, cylindrical tube the flow resistance ($R$), or the pressure-flow ratio ($\Delta P/\dot{Q}$), is primarily determined by the geometry of the tube and the viscosity ($\eta$) of the fluid in the form of Poiseuille-Hagen equation:

$$R = \Delta P/\dot{Q} = 8\eta L/\pi r^4$$

where $L$ and $r$ are the length and radius of the tube, respectively. The application of this equation to human circulation has several limitations. First, the circulatory system consists of a complicated network of vessels both in series and in parallel, with considerable branching, tapering and curvature. Second, blood is a non-Newtonian fluid, the viscosity of which is not a constant value but varies with the rate of shear. Third, the pulsatile nature of blood flow in vivo changes the vascular geometry and the blood viscosity with time in each cardiac cycle. Although equation 3 cannot be applied quantitatively to the hemodynamics of the circulation in vivo, the qualitative interrelation of the factors in this equation is still valid. Thus, the over-all flow resistance in the circulatory system is a function of 1) the degree of vasoconstriction of the resistance vessels and 2) the viscosity of blood. For a given perfusion pressure and a given degree of vascular hindrance, the flow through an organ is inversely related to the blood viscosity.

The present investigation has demonstrated a significant increase of blood viscosity in patients suffering from acute myocardial infarction. A higher than normal viscosity of blood could indicate an abnormality in one or more of the following rheological factors: 1) hematocrit, 2) plasma viscosity, 3) red cell aggregation, and 4) deformability of red cells. The design of the present study allowed an assessment of each of these rheological factors.

The initial blood viscosity ($\eta_r$) of the patients was elevated at all shear rates (fig. 4). The major contributory factor was probably the high initial Hct values in these patients (fig. 2). In seven of the 25 patients, the initial Hct exceeded 50%. The high Hct values in the patients were associated with elevations in the total plasma protein concentration (fig. 3).

![Figure 5](image1.png)

Figure 5

Serial changes in plasma viscosity ($\eta_m$) in MI patients after admission to hospital. The vertical bars denote SEM and the closed dot indicates normal controls.

![Figure 6](image2.png)

Figure 6

Serial changes in relative viscosity of blood with Hct adjusted to 45% ($\eta_r$) at different shear rates in MI patients after admission to hospital. The value of $\eta_r$ at low shear rates is an index of the tendency of red cell aggregation in blood. The vertical bars denote SEM and the closed dots indicate normal controls.
These findings indicate a development of hemoconcentration in the initial phase of acute myocardial infarction. Twenty out of 25 patients gave a history of decreased fluid intake after the acute episode of chest pain. Dehydration due to such fluid restriction might be one of the causes of hemoconcentration. Altered cardiovascular state following acute infarction might also play a significant role in the development of the hemoconcentration by causing transcapillary fluid efflux. It is noteworthy that 18 of the 25 patients showed evidence of congestive heart failure on admission, as evidenced by the presence of S₃ gallop, pulmonary rales or X-ray finding of interstitial pulmonary edema. A recent study by Sedziewz et al.²⁹ has demonstrated a fall in plasma volume as pulmonary edema occurs in patients with acute myocardial infarction. Besides the decrease in fluid intake and the development of myocardial failure, other factors may also play a role in the development of hemoconcentration in the patients. Administration of epinephrine has been shown to cause a decrease in plasma volume in human subjects.²³ Hence, the increased sympathetic activity and circulating catecholamines seen in some patients in the acute phase of myocardial infarction²⁴ might also contribute to the fluid shift from the intravascular space to the tissue. It should be pointed out that the present data were obtained only in the postinfarction period. It would be interesting to learn those changes in blood viscosity that occur before and at the time of infarction. Such data would shed further light on the mechanism of the postinfarction elevation of blood viscosity found in the present study.

The progressive fall of Hct during the first week of hospitalization (fig. 2) indicates an alleviation of the factors which caused the hemoconcentration. Although a part of the decrease in Hct may be explained by diagnostic blood sampling during hospitalization,⁸ the amount of diagnostic phlebotomy in our patients was not sufficient to account for the total change.

During the third to fifth days of illness in patients with acute myocardial infarction, the viscosity of whole blood remained high at all shear rates (fig. 4), despite the fall of Hct (fig. 2). Were it not for this decrease in Hct, the viscosity values would have been much higher at all shear rates. The high viscosity of the whole blood found during this period is explained by the high plasma viscosity (fig. 5) and the increased tendency of red cell aggregation, as reflected by the low-shear relative viscosity data (fig. 6). These increases in plasma viscosity and red cell aggregation resulted primarily from elevations of α₂-globulin and fibrinogen concentrations (fig. 3), which probably represented a response of the body to acute tissue injury,⁸ ²⁵ ²⁸ rather than changes specific for myocardial infarction. Albumin concentration has only a minor influence on plasma viscosity²⁷ ²⁸ and red cell aggregation,²⁹ so that its decrease during the first week of illness can be neglected.

In the present investigation, the significant increase in blood viscosities in patients with acute myocardial infarction were thus due to: 1) an initial increase in Hct value, and 2) more sustained changes in plasma protein concentrations with resultant increases in plasma viscosity and the tendency of red cell aggregation. The increased blood viscosity might result in an increase of flow resistance in the microcirculation of acutely injured heart as well as in the remainder of the body. In this series of 25 patients, three patients developed shock, eight patients had S₃ gallop, and one patient developed pulmonary embolism, during the first week of illness. Figure 7 shows the scatter diagram of the levels of blood viscosity and Hct on admission. It is noteworthy that high initial values of blood viscosity and Hct were generally found in

![Figure 7](http://circ.ahajournals.org/content/51/6/1083)  
Distribution of initial values of hematocrit and blood viscosity in MI patients. Closed circles indicate patients developing complications (shock, S₃ gallop, or pulmonary embolism) during the course of observation, open circles indicate patients without the complications, and open triangles indicate patients who developed shock and died. The viscosity data were determined at a shear rate of 0.52 sec⁻¹. The shaded area indicates so of normal controls.
patients who developed these complications (closed circles in fig. 7). We also studied three other patients whose acute myocardial infarction was complicated by cardiogenic shock (open triangles in fig. 7). They died within 72 hours after admission and, therefore, were not included in the other figures of this paper. They all had initial high values of blood viscosity and Hct: $\eta_b$ at shear rate of 0.52 sec$^{-1}$ ranged from 58 to 103 centipoises and Hct ranged from 50 to 58%.

In recent years the mortality rate from arrhythmias during hospitalization for acute myocardial infarction has been reduced, but mortality from the complications of hemodynamic deterioration, especially shock, has not been significantly altered.$^{20, 31}$ A better understanding of the serial changes of the rheological components affecting blood viscosity in acute myocardial infarction might permit the development of a therapeutic program to lower the increased blood viscosity and improve the microcirculation. The present study suggests that hemodilution therapy might be more beneficial in patients with high blood viscosity and that evaluation of hemodilution treatment in such therapeutic trials would be materially aided by rheologic and hemodynamic measurements.

References
Observations on blood viscosity changes after acute myocardial infarction.
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