THE INFLUENCE OF ERYTHROCYTE DEFORMABILITY IN THREE TYPES OF FLOW SITUATIONS: CONTINUOUS, CONTINUOUS BUT NON UNIFORM, AND TWO PHASES

M. THAO CHAN, E. FRANZINI
Laboratoire d’Hémorhéologie. Laboratoires Hoechst. 3 avenue du Général de Gaulle. 92080 Paris La Defense.

SUMMARY
The effect of erythrocyte deformability is discussed in three types of flow situation (continuous situation continuous but non uniform situation, and two phases situation), in which the length scale (diameter of the vessels) is similar or not to the diameter of the red cell.

INTRODUCTION
How we deal with vascular disorders is directly related to our increasing understanding of the dynamics of blood flow and the clinical importance of a new branch of medical science known as clinical haemorheology.

The study of the circulatory system has long been limited to the study of the vessels, without any attention being paid to their content: the blood.

The rheological behaviour of blood is dependent both on properties of the individual cells and on the way they interact with each other to influence the overall resistance to flow, that is the whole-blood viscosity.

Blood viscosity is determined by four factors:
1. Plasma viscosity
2. The overall number of cells
3. Red cell aggregation
4. Red cell deformability.

The viscosity of plasma is determined mainly by the concentration of plasma proteins, the most important of which are albumin, the globulins and fibrinogen. In patients with vascular disorders, there is often an increase in the fibrinogen concentration.

The overall number of cells is another important factor in viscosity: white cells and platelets may be present, but the most prevalent components of whole blood are the red cells, which represent approximately 97% of the cellular volume of the blood (5 million/mm3). The amount of red cells in the blood is usually defined by their concentration per unit of volume in the suspension (the haematocrit). In human beings, the average haematocrit is on the order of 40 to 50%. In a disease such as polycythaemia, for example, hyperviscosity is directly attributed to the increase in the number of red cells.

Blood viscosity is also partly dependent on blood flow. In the absence of flow or in circulation with a low flow rate, red cells affect whole-blood viscosity by their tendency to aggregate and form rouleaux. Or, at high flow rates, the cells change their shape and their deformability properties reduce the viscosity. This red blood cell property to deform is particularly important at the microcirculation level. Despite these complexities in the rheological behaviour of blood, a distinction can be made between flow situations in which the range diameter of the vessels is similar or not to the diameter of the red cells. This distinction is a way of quantifying, through macroscopic or microscopic approaches, the rôle of erythrocyte deformability in types of flow situations:

Figure 1: Microscopic structure of the flow.
(From LEHELVEGRE et al. 1)
1. CONTINUOUS SITUATION

For large scale flow situations (where the vessel diameter is up to 50 x that of red cell) it is perfectly acceptable to consider blood as a continuous and uniform medium. In the absence of flow, the red cells aggregate face to face. These aggregates of about 10 red cells are known as rouleaux and these rouleaux also aggregate together.

Four types of flow may be identified at a microscopic level (Fig. 1).1,2

- a) If shearing is very slight, the aggregated structure is organized in networks and, as a result, networks and rouleaux are converted by the flow.
- b) When shearing is slightly greater, but still moderate, the red cells are dispersed, disoriented and move in a pattern of rotation in the direction of the flow.
- c) If shearing is increased further, the red cells remain dispersed, but are progressively oriented in the flow without being deformed, even the membrane makes a tank-treading movement around the intra-erythrocyte contents.
- d) If shearing becomes very marked, the red cells remain dispersed, still oriented in the flow, but are deformed and sometimes take on a biconvex shape.

Under these circumstances, the deformability enables the red cells to orient themselves in the direction of flow and to occupy the smallest space possible. These phenomena thus reduce the friction between the red cells and endow blood, with its low resistance to flow.

2. CONTINUOUS BUT NON UNIFORM SITUATION

The first interesting quantitative findings in the continuous but non uniform situation (20 μm < capillary diameter < 500 μm) for the blood date from 1842, when, in microscopic studies, Poiseuille noted that blood flow in narrow tubes differed from that of water. These phenomena were subsequently studied by Fahraeus and Lindqvist in 1931, using human blood in cylindrical capillaries ranging from 40 to 500 μm. Following these findings, numerous studies have sought to identify the rheological properties in the blood in the so-called continuous but non uniform situation. Mention may be made of the works of Braasch, Chien, Cokelet, Dintenfass, Stoltz. These authors have confirmed the non newtonian nature of the blood (viscosity decreasing when the shear stress is increased), as well as the appearance of anomalous phenomena such as:

- a) The existence of a plasma layer poor in red cells close to the wall.
- b) Flattening of the speed profile (piston flow or plug flow).
- c) The Fahraeus effect (hematocrit in the capillary is lower than the hematocrit at both the point of entry, as well as exit, from the capillary).
- d) The Fahreus Lindqvist effect (apparent viscosity decreases when the diameter of the capillary decreases).

Furthermore, the possibility must be accepted of the existence of lifts of hydrodynamic origin, which can propel the red cells far from the wall. In 1962, Segre and Silberberg, using very dilute suspensions of spheres, showed that the particles emigrate towards the position of equilibrium characterized by the capillary radius of approximately 0.6 R, implying the presence of both centrifugal and centripetal lifts. Several theoretical analyses predict centripetal lift acting on a single sphere placed in a shearing flow, but the existence of a centrifugal lift remains very uncertain.

Despite the complexity of flow flow in its non uniform situation, a number of studies (10, 11, 12, 7) have attempted to correlate the phenomena. The Fahraeus Lindqvist effect may be explained in part by the Fahraeus effect,13 which, in its turn, is explained by the existence of a plasma layer due to red cell migration phenomena.

For in vitro experiments, this migration effect may also be quantified by the ratio between the haematocrit of the central nucleus (Hc) and that of alimentation (Ho) which can give a migration index of these red cells (Fig. 2). This ratio (Fig. 3a, 3b, 3c) is slightly greater at high haematocrit than at low haematocrit levels.

As a result, at both high and low shearing, deformability favoursizes the formation of a thicker parietal layer and amplifies the Fahraeus and Fahraeus-Lindqvist effects. Therefore, these phenomena cause a decrease in the resistance to flow.

3. TWO PHASE SITUATION

When the diameter of the microvessels becomes similar to that of the red cells, the problem becomes very complex and it is no longer possible to retain the hypothesis of a continuous medium.
THE INFLUENCE OF ERYTHROCYTE DEFORMABILITY

Figure 3: Migration effect of different types of suspensions as a function of channel thickness.

However, it remains valid to treat the plasma as a continuous fluid, since the diameter of the smallest capillary is still 2,500 times greater than that of one molecule of water. By contrast, red cells are large bodies which, in certain capillary lumen. The problem of rheology in these vessels must thus be studied as a two phase flow problem.

Expressed in mechanical terms, it consists of the flow of a non compressible and Newtonian continuous fluid (the plasma) in a cylindrical conduit (the microvessel), loaded with deformable free particles (red cells). In such capillaries, shear stress is relatively high, which results in marked red cell deformation. As a result, there is a second problem (coupled with the first) which is that of the deformation of red cells which are also continuous bodies. At the time of transit of the particle, independently of the flow effects in the inlet region of a circular pore, which are not negligible, the link of the particle with the wall or with other particles have equally to be investigated in the study. The nature of these links is very complex: hydration phenomenon, electrostatic and electrolytic phenomena, Van der Waals's bond.

From a theoretical standpoint, two major types of approach may be envisaged for the study of this phenomenon:

- a macroscopic type of approach, which has given rise to phenomenological laws (Darcy law in porous medium, Poiseuille law in Newtonian fluid). This approach results in concepts of permeability, porosity, friction coefficient, apparent viscosity, etc.

- a microscopic or microstructural approach, which takes into account respectively the three variables of the red cell, which are the rheology of the particle, the surface properties of the particle, which may be linked together on the capillary walls, and, finally, local hydromechanical conditions of measurement.

In the two phase situation, deformability plays a particularly important role in local hemodynamic consequences:

- an increase in red cell rigidity decreases the local velocity of the particle. This phenomenon thus results in disturbances in mass exchange (O₂, lactate, potassium) between the blood and tissues.

- rigidification of the red cells is also reflected by traffic-jam in the microcirculation. If rigid red cells are included only in a proportion of 1% in the particularly fluid medium, local haematocrit levels are disturbed distally in all of the branches. This hemodynamic disturbance may result in three situations of fundamental pathological importance: blood stasis, intravascular red cell aggregation and the use of arte- riovenous anastomoses.

CONCLUSION

It would seem that discovery of erythrocyte deformability is as old as that of the red cell itself. However, it was only at the beginning of the 20th century that the physiological importance of red cell deformability was fully realized.

It is now known that the property of deformability enables red cells in the complex conditions of the circulation to ensure optimal irrigation of the capillary network and endows the blood with its low resistance to flow. From an hemorheological standpoint, its reduction, in other circumstances than in certain hematological disorders is the common denominator between the various cardiovascular risk factors. As a result, the physiopathological interest of red cell deformability still offers enormous possibilities of exploitation and wide research studies.

REFERENCES


