PRINCIPLES OF BLOOD RHEOLOGY

J. MARTINS e SILVA
Depart. of Biochemistry, Fac. Med. Lisbon, Portugal.

Blood rheology, that embraces the study of the deformation and flow of the blood, is an outbursting science. There are reasons to think that the development of blood rheology (or Hemorheology) will imply deep changes in medical thought concerning the diagnosis, prognosis or therapy of several clinical disorders.

Hemorheology is not a specific field of medicine or of any of the classic specialties. Likewise, it is not also foreseeable that it will assume the form of an independent speciality in the future. In fact, several scholars pertaining to different academic sciences, particularly biochemists, biophysicists, physiologists, hematologists and cardiologists, are involved in the investigations concerning hemorheology. Most of the works that have beem so far published on this subject sprang out from a multidisciplinar cooperation and it is plausible that this characteristic be maintained in the near future.

Hemorheology studies circulatory phenomena and their implications from an original point of view; while the investigations so far performed were almost exclusively confined to the study of bloodvessels'wall, rheology is mostly concerned with the study of bloodvessels'content. In fact, the circulation may not be considered apart from the vascular content since the rheologic behaviour of the blood, depending on the properties of its components (cells and plasma), will ultimately influence the blood viscosity, peripheral resistance and, finally the relationships between blood pressure and volume.

The utmost importance of erythrocyte deformability in blood viscosity is due to two main reasons: a) the pressure of the intravascular bloodflow induces alterations of globular shape (usually discoid), compromising the fluency of bloodstream; b) In the microvessels and capillaries with a diameter inferior to the size of the erythrocyte, the ability of globular deformation assures nutrient exchange and tissue oxigenation to be carried out under conditions of maximum efficacy. The erythrocyte deformability in any territory of the circulation, though mainly in the microcirculation, may be viewed as an undoubtedly vital phenomenon influencing the rheologic properties of the blood and also as being the main determinant of globular half-life.

Erythrocyte deformability is affected by factors intrinsic to the globule and by exogenous forces applied to its surface. In the latter case, the change of shape is mostly dependent from the distribution of the exogenous forces into the cell surface and from geometric factors such as the vascular morphology.

The intrinsic deformability of the erythrocyte is ruled by three main factors (viscoelastic properties of the membrane, viscosity of the globular contents, erythrocyte geometry), which are dependent on several influences namely the concentration of ATP and Ca^{2+} on the spectrin-action cellular frame that coats the internal face of the erythrocytes.

Erythrocyte deformability does not connote by itself that the circulation be perfect or oxygen delivery and tissue perfusion be adequate.

In a normal bloodstream the erythrocytes easily cross narrowest arteries and capillaries without modifying their disc-like shape; in crotched points the erythrocytes take peculiar shapes e. g. drop-like, of circumflex accent-like, etc.; in venules, though the erythrocytes keep their discoid shape, they tend to clump together forming temporary rouleaux that may persist under conditions of retarded bloodflow; when normal drainage is hampered erythrocytes frequently adhere to the endothelium clogging perhaps perma-

nently the bloodflow. Likewise, the presence of abnormal proteins or their high plasma concentration contributes to erythrocyte aggregation and therefore to increased blood viscosity.

Leucocytes and platelets, a lot thougher, are a natural obstacle to erythrocyte transit in the microcirculation; when normaly deformable the erythrocytes cross without dificulty the free spaces between the leucocytes and the wall of the microvessels. However, if there is reduction of erythrocyte deformability or of bloodflow pressure, if vascular walls are injured and leucocytes are abnormally stiff or present in great number, temporary or permanent occlusions of local circulation may befall.

Unrelated to the important physiologic role it may play for the transference of recently formed cells from the marrow to the general circulation or as a determinant of globular half-life, several abnormalities of erythrocyte deformability have been noticed in several pathologic conditions, whether or not coexistent with hypoxia.

Those pathologic conditions may be classified in two subgroups, one encompassing hematologic abnormabilities second to alterations of the physical properties of the erythrocyte, the other including more frequent situations that course with tissue ischemia but the reason of erythrocyte stiffness is still debatable.

Among the hematologic conditions stand out those characterized by shape abnormabilities (e.g., spherocytosis, macrocytosis), membrane abnormalities (e.g. due to antibodies, Heinz bodies, globular age) or abnormabilities of erythrocyte contents (e.g., hemoglobinopathies, thalassemias, enzyme deficiencies). Generally speaking, the reduction of erythrocyte deformability in the group of hematologic disorders seems to be the main cause of early globular sequestration by spleen and attendant hemolysis.

In contrast to hematologic disorders, always unfavorable to globular survival, there are other situations compromising several body organs and systems that secondarily interfere with the blood rheologic behaviour, particularly with erythrocyte deformability. Among these non-hematologic pathologies stand out acute events (e.g., myocardial infarction, stroke) or chronic situations (e.g., peripheral arterial vasculopathy, myocardial disease, diabetes mellitus hypertension). In any of these conditions, tissue hypoxia is a potential constant and the reduction of deformability may result from different mechanisms. It is currently admitted that erythrocyte stiffness observed in the acute disorders be essencially mediated by plasmatic factors, considering the alterations of erythrocyte intrinsic properties in chronic conditions.

Paralleling the reduction of erythrocyte deformability, and sometimes as a direct consequence, noteworthy alterations of blood viscosity are observed that, altogether, affect bloodflow through the macro- and, particularly, microcirculation. Obviously, these changes of blood fluidity tend to reduce tissue oxygenation and nutrition, further aggravating the prognosis and/or triggering the development of associated complications.

Among the main causes of blood hyperviscosity stand out those resulting from abnormalities of the cellular components of the blood (e.g., polycythemia, leukemia, erythrocyte hyperaggregation, erythrocyte stiffness) or from plasma disorders (e.g., multiple myeloma, Waldenstrom's macroglobulinemia).

Blood hyperviscosity and attendant ischemic and thromboembolic episodes frequently observed in cardiovascular disorders and in diabetes mellitus, seem to result from the disturbance of one or several factors mainly from the rise of erythrocyte stiffness.

Concluding, erythrocyte deformability plays a rather important role in the determination of the rheologic behaviour of the blood, affecting bloodflow through the microvessels and greatly influencing blood viscosity mainly in low caliber vascular segments. It is still a moot question whether the loss of erythrocyte deformability is the cause and/or the consequence of the disorder associated with it. The mechanism of erythrocyte stiffness is also still unclarified. However, it is generally assumed that the reduction of erythrocyte deformability be attibuted to several causes depending on the coexistent disorder. According to the experiments performed, the changes of globular deformability seem to affect the prognosis of the disease, being noticeable the clinical improvement that follows the use of drugs consecrated to the adjustment of this globular property.

The ever increasing important role played by hemorheology in human clinical disorders is being evidecend by the number of Congresses and Symposia held recently on this subject. Accordingly the 1st International Symposium on Erythrocyte Deformability, Microcirculation and Vascular Pathology, is the first public session held in Portugal to present and debate the theoretic concepts and pratical application concerning blood rheology.

For the event, it was our great privilege to assemble in Portugal several distinguished scientists who lead hemorheologic research in their respective countries. Therefore, it is our pleasure to emphasize the collaboration of Professor Branemark, represented by Dr. Braide, who, in the first part of the symposium, stresses the microscopic relationship between the microvessels and their contents particularly underlining the adaptation of the erythrocytes to narrowing and segmentation of the vessels. In his lecture, Prof. Boivin emphasizes the role of erythrocyte membrane for this globular adaptation to microcirculation, presenting a complete description of the biochemical pro-

perties of intrinsic membrane proteins and particularly of the contractile ability of spectrin. Professor Boisseau, after describing the most common techniques of erythrocyte filtration, concentrates his exposition on clinical subjects stressing some vascular disorders that course with known abnormality of globular deformability. Dr. Dormandy, after presenting the relationship between erythrocyte filtrability and other rheologic blood factors, emphasizes, by way outstanting clinical examples, the importance of blood viscosity in macro- and microcirculation. Finally, among the foreign speakers, Dr. Marcel discusses the presently available therapies that, acting on erythrocyte deformability, make possible normalization of circulatory conditions.

The 2nd part of the Symposium, a round table moderated by Professor Paulo Ramalho, includes the works of several portuguese scientists pertaining to microcirculation and erythrocyte filtrability. A co-worker of Professor Cunha-Vaz, Dr. Faria de Abreu reports on several aspects of retinal circulation emphasizing the most modern methodology developed for this purpose.

Finally, some of the works performed by the «Grupo Português de Trabalho sobre Filtração Eritrocitária» are presented pertaining to each of the four themes: tobacco intoxication, hypertension, diabetes mellitus and stable angina. The themes are introduced by Dr. J. Freitas, Eng.ª Carlota Proença, Dr. Levy Cruz e Dr. Lúcio Botas.

Professor Nogueira da Costa closes the meeting making a global appraisal of the works and summarizing the main conclusions.

This meeting, that may definitely have contributed to the development of the rheology in Portugal, was made possible thanks to the collaboration of the «Hoechst Portuguesa» and the sponsorship of the «Junta Nacional de Investigação Científica e Tecnológica».

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Address for reprints: J. Martins e Silva
Department of Biochemistry
Fac. of Medicine of Lisbon
Lisbon. Portugal