

EDITORIAL

RED CELL RIGIDITY, "Tk", AND FILTRATION

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Rheological properties of the red blood cell remain the cornerstone of blood flow characteristics and tissue perfusion. The very fact that red cell is fluid has been advocated by Bidloo in 1685 (1) against great opposition. For a long time afterwards red cell was considered a rigid particle. In 1962, I stated (2) that blood must behave as a nearly ideal emulsion, otherwise the packed red cells (used commonly for transfusion) would exhibit consistency of concrete. The fluid concept of red cell requires, in order to satisfy Oldroyd (3) and Taylor (4) criteria, a fluid interior and a fluid membrane. The first point is more easy to visualize: haemoglobin being either in solution or in suspension, both would allow fluidity. The red cell membrane presented a problem: it must be fluid, otherwise - even in the interior of the cell were fluid - the cell would behave as a rigid particle.

According to the Danielli model (5), the red cell membrane was to be a bilayer of lipids, in a continuous mode. This was rheologically impossible, as it was showed indeed that a membrane must consist of heterogenous structures of fluid characteristics (6). However, at the time of submission of this hypothesis, which included a multi-phase and thixotropic-dilatant structure of the membrane, it was much opposed.

Few years later, I submitted an equation for the viscosity of blood which included a term for the internal viscosity of the red cell (7). In its first form,

$$\eta_r = (1 - kTC)^{-2.5}$$

in which T was the Taylor's factor, k was plasma trapping factor, C was volume fraction of cells, and η_r was the relative viscosity of blood (viscosity of blood divided by viscosity of plasma). To calculate term "Tk" which is a measure of rigidity of the red cell, one has to transform the equation in a following manner:

$$CTk = (\eta_r^{0.4} - 1) / \eta_r^{0.4}$$

which is easy to apply by the means of a calculator which allows to use exponent 0.4.

One could ask the question: where are the potential sources of error? The first, and obvious, point is that blood viscosity should be measured at shear rates high enough for the red cells to be dispersed, otherwise the structural viscosity will be present and will elevate the value of Tk. We used a shear rate of 180 rec. sec. At the time, it was considered to be high enough for disaggregation of red cells. This is not always true, and fractionally higher shear rates would be advocated at the present time. The second point is the shape of the

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red cell, and whether it is permissible to apply Einstein's exponent 2.5 (of which exponent 0.4 is an inverse value) intended for ideal spheres (8), to the red cells which show discoidal characteristics. This problem has been discussed in detail by me (9). I applied various exponents, with a final conclusion that the error due to coefficient is only of marginal importance, especially in the area of clinical haemorheology. Then still another query emerged.

It would have been logical to study plasma viscosity at the same shear rate as blood, in a rotational viscometer. However, plasma exhibits flow instability (seen as an apparent increase in the viscosity, of up to 50 per cent), and thus a capillary viscometer is definitely required. Flow instability may be induced by the presence of rigid red cells, as shown by Liao Fu-lung and Dintenfass (10). One can treat flow instability as a new viscosity factor, and utilize it to define abnormality of pathological blood.

Notwithstanding the above, the concept of calculated rigidity of the red cell (the cell itself not being touched or manipulated) appears to have an advantage, as artefacts due to direct manipulation are absent. Many years ago, Ponder (1) warned that a direct manipulation of red cell affects its property; while experience of the work on the cell membrane suggested that a direct manipulation increases membrane viscoelasticity and rigidity.

Can indeed term "Tk" supply an information of value in diagnosis and prognosis in diseases? My answer is unequivocal 'yes'. Various disorders can be characterized by "Tk"; survival and prognosis of patients show statistically significant correlations with "Tk". Not only the juvenile onset diabetes and hypertension exhibit high "Tk", but most anaemias do also.

This brought the rigidity of red cell, and term "Tk", into the centre of my hypothesis for autoregulation of blood viscosity. In the open systems, as our bodies represent, any physiological value must be controlled in order to remain constant (Cannon (11)). In human, especially in male, the value of blood viscosity in health remains constant for a period of 60 to 80 years. It is not likely that such constancy of value could exist without a direct regulatory mechanism. This led to my hypothesis that viscosity receptors exist and form the basis of viscosity regulation.

The most important portion in the circulation is the microcirculation. This is the true interface between nutrients and cells. But the microcirculation acts also as sewage collector and heat exchanger; as well as the highway for cellular or chemical messengers and immunological defense systems.

As noted first by Fahraeus and Lindqvist (12), the apparent viscosity of blood decreases as the tube diameter decreases. This is a very convenient architectural design to reduce resistance. However, there is a critical vessel radius below which there is a pronounced increase in resistance, and/or a pronounced increase in apparent viscosity. This is directly related to rheology of blood cells and of blood (rigidity, crowding, dilatancy) and was described first by me (13, 14) as 'inversion phenomenon'. Extensive work in this area was carried out recently by Gaetgens (15).

Nearly ten years ago, the idea that a cell must pass through a capillary or a pore, and that this should be used in measurements relevant to clinical haemorheology, received great attention, especially in France, mainly due to the efforts of Marcel (16). Filtration as such has been used by Teitel (17) for decades, although he used (by necessity) paper filters and not modern Nucleopore or other filters. This idea was attractive since the method was simple.

It appeared at that time that filtration of blood would be the answer to red cell rigidity measurement. However, the apparent simplicity of the concept

of filtration run into complications of theoretical and practical nature. Thus, Lingard (18) clearly warned that filtration of blood has very little to do with red cells, but nearly all with white cells. After some years, many other investigators confirmed that filtration time is affected by white cells and platelets (inter aelia, Stuart et al (19)). 'Purification' of blood from white cells and platelets appeared to founder on the fact, noted early by Ponder (1), that such prepared red cells bear little relationship to the red cells in human blood. Only the originator of filtration, Teitel (20) was always aware that filtration is a complex process, and that while it can be used as microviscometer, its theory is difficult.

Finally, filtration of blood led to development of single cell filtration apparatus (21), and thus to another way of determination of cell rigidity which, however, still involves a more direct manipulation of the red cell. That is not to say that filtration methods do not supply information of clinical importance.

However, for determination of rigidity of red cell I propose 'Tk'. (22).

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