Microrheology and Light Transmission of Blood

IV. The Kinetics of Artificial Red Cell Aggregation Induced by Dextran


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Summary. Employing both microscopic and photometric methods the rheology of pathological red cell aggregation was studied in model experiments. Suspensions of washed human red blood cells in dextran solutions containing rising concentrations of dextrans (M.W. 40000, 70000, 110000, 250000, 500000) were used. At low concentrations (<500 mg.\text{g}^{-1}) of high molecular weight dextrans (>70000) red cell suspensions formed aggregates similar to the ones found in normal human blood. At higher concentrations, the aggregates were similar to those observed in pathological human blood. The aggregates were studied under the condition of stasis, slow flow and at shear rate of their hydrodynamic dispersion. Besides, the flow behavior of the dispersed cells at high shear rates was studied. We found:

1. In all samples the rate of spontaneous aggregate re-formation in stasis (following hydrodynamic desaggregation) rose with rising dextran concentration up to 5.0 g.\text{g}^{-1}.

2. The shear resistance of the aggregates, as measured by the shear stress necessary to keep them dispersed, rose up to concentrations of 2.5 g.\text{g}^{-1}, but fell at higher concentrations.

3. Only with dextran of a molecular weight above 110000 coarse agglomerates could be produced at high concentrations. Loose elastic meshes were rapidly produced at high concentrations of Dx 70.

4. When subjected to steady state low shear (7 sec\textsuperscript{-1}) only the agglomerates, but not the meshes rapidly grew in size.

Most of the aggregation kinetics recorded by photometry and microscopy evaded detection by viscometry.

Key words: Red Cell Aggregation — Rouleaux — Photometry of Blood — Viscometry of Blood — High Molecular Weight Dextrans — Low Molecular Weight Dextrans.

The recording of the flow dependent changes of light transmission of blood has recently been introduced as a new method to quantify the microrheological behavior of red blood cell suspensions in viscometric flow (e.g. [17.39]). In concert with traditional viscometry, this method has supplied not only information about steady state behavior of the red cells, i.e. their aggregation in flow and their deformation in rapid flow,

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but also about the kinetics of transitory behavior in response to quick changes of the flow velocity. These kinetics have lately been monitored by simultaneous microcinematography and photometry in viscometric flow [33]. Consequently, the photometric method lends itself for quantifying rapidly occurring instabilities of the flow behavior i.e. the progressive deformation or aggregation of red blood cells (RBC) in spite of constant shear rates [32].

Pathologically increased aggregation of red blood cells [13], the most common abnormality of clinical hemorheology, is accompanied by such instabilities [18]. The reduced suspension stability in stasis is the cause of the increased sedimentation of such samples; its hemodynamic significance, however, has so far evaded quantification. The enhanced tendency to aggregation in these cases indeed prevents accurate measurements of its viscous effect in flow, due to pronounced phase separation [9, 24, 37] in Couette and due to settling in capillary and cone plate viscometers [29]. Settling and phase separation in the vessels of the human microcirculation in vivo have also been described by Knisely and coworkers [18,19] in patients exhibiting pronounced intravascular aggregation of RBC in the microvessels of the bulbar conjunctiva.

Microrheological studies on patients' blood have shown, however, that aggregation occurring in disease appears to be merely an intensification of physiological red cell aggregation (RCA) in the form of rouleaux. In either case, the binding between the cells is reversible, brought about by plasma proteins, the aggregates are highly shear dependent and can be dispersed hydrodynamically. Furthermore, the actual size of the aggregates is primarily dependent on the ambient shear conditions. However, the aggregates in many pathological states were shown to be more shear resistant [31], and, while "physiological" rouleaux formed secondary networks due to end-to-side attachment (reticulated suspensions), the pathological rouleaux were attached side by side and frequently formed irregular clumps (agglomerated suspension) that were rotating and tumbling in flow [32]. High molecular weight dextrans have traditionally been used as models of plasma proteins causing pathological RCA [38]. The present report, therefore, deals with the influence of the molecular weight and the concentration of these molecules on the kinetics of aggregation and desaggregation in viscometric flow.

Materials and Methods

A) Aggregometry. The transparent chamber used to monitor flow dependent changes in light transmission of blood has been described in detail in three previous publications [19,33,35]. In addition, the details of the microrheology of cells and cell aggregates were studied in a counterrotating rheoscope chamber [32]. In this chamber, pictures of flowing blood under quantified shear forces can be taken at