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Compaction stasis due to gravitational red cell migration and floatational plasma skimming

Reversal of the fahraeus effect due to pathological RCA-formation in plastic tubes and mesenteric venules

W. Göbel, J. Perkkiö, and H. Schmid-Schönbein
Department of Physiology, RWTH-Klinikum, D-5100 Aachen, Federal Republic of Germany

Summary. A horizontally aimed microscope was directed at isolated rat mesentery preparations as well as artificial microchannels cast in polyester blocks. They were perfused with aggregating red cell suspensions containing about 7 g/l of bovine fibrinogen at various perfusion pressures. The effects induced by gravitational influences were monitored by measuring the local red cell concentration (video-densitometry) and velocity profiles (IPM-dual slit velocimetry). At low perfusion pressures, sedimentation during maintained flow occurs, leading to a relative red cell slowing compared with plasma. Consequently, a progressive deposition of red cells at the bottom of vessels occurs and finally, blocking of the vessel by aggregated red cells is seen. Thus, the well-known phenomenon of compaction stasis must be attributed not merely to a transmural plasma loss but also to gravitationally induced haemoconcentration.

Key words: Erythrocytes – Velocity profiles – Aggregation – Gravitation – Sedimentation – Stasis

Introduction

Ever since intravital microscopy was performed on transparent tissues of mammalian species, a characteristic mode of microvascular occlusion has been observed, based on the stuffing of microvascular segments (primarily venular but also capillary and arteriolar) by red cells (Cohnheim 1867). In ordinary incident light microscopy, they appear to be filled with a completely transparent mass, whereas interference contrast microscopy in vivo as well as transmission electron microscopy reveals that the individual red cells, known to be highly flexible, are being deformed into irregular polyhedra and thus become closely packed to a volume fraction of almost 1.0 (100% haematocrit value). Provided that preparations of the mesenteric membrane are carefully prepared and well rinsed, the stasis phenomenon occurs exclusively under low flow conditions and when the red cells of experimental animals are aggregating strongly (Driessen et al.: Arbeit über Dissertationsschriften mit Fibrinogen). The phenomenon is fully reversible in principle whenever normal arterial pressure is restored (Krogh 1929). In fact however, the majority of sites of "compaction stasis" are quite refractory to reperfusion after normalization of the arterial pressure and may give rise to permanent microvascular occlusion. In summary, compaction stasis is based on the local increase in the haematocrit value to almost 100%, under conditions of generalized arterial hypotension and on low local flow velocity (and thence shear stresses). Highly aggregating red cell suspensions and a certain positioning of the vessel in the topology of complex microvascular networks are also important.

Classically, compaction stasis was explained by assuming local haemoconcentration due to transmural plasma exudation. Recently, haemorheological factors have also been invoked: in earlier attempts to explain the occurrence of microvascular no-flow states on the basis of the well known non-Newtonian flow properties of the blood, our group has proposed the concept of "collateral blood viscidation" (Schmid-Schönbein 1975). It was assumed that due to the existence of a finite yield shear stress of whole blood as a "Casson-fluid" (Merrill 1969), the shear stress in vessels with lower than average hydraulic conductivity might fall below the yield shear stress of blood, resulting in a standstill of blood flow in the particular segment. Radtke tested this concept experimentally (Radtke

Offprint requests to: W. Göbel

et al. 1984) in simplified artificial networks in vitro and calculated the yield shear stresses at which blood flow comes to a standstill. The values obtained are in the order of 0.01 dyn/cm^2, (1 mPa): while these data were consistent in order of magnitude with those extrapolated from low shear rotational viscometry measurements (Merrill 1969, Charm and Kurland 1974), these threshold pressures for the solid-fluid transition of blood samples with normal haematocrit values were extremely low in comparison with measured pressure gradients and thence physiological shear stresses in microvessels in vivo (10^3 Pa/mm and 1–10 Pa, respectively). Since Radtke's work, the phenomenon of intravascular stasis was systematically investigated by Hoymann (1986) in entire networks of microvessels in the intact and in the haemodynamically isolated mesenteric microcirculation; he applied a network scanning technique that allowed him to assess not only each individual vessel, but also to attribute the stasis phenomenon to the position of the affected vessel in the network (the topological order). These studies proved beyond reasonable doubt that under low flow conditions abnormal aggregation in combination with normal haematocrit values did cause the stasis phenomenon and thus non-homogeneous microvascular perfusion. However, when checking the validity of the concept of a finite yield shear stress of blood in glass tubes of microscopic dimensions (5–25 μm diameter), Gaehtgens (1987) failed to find evidence for it and therefore refuted the suggestion that the non-Newtonian properties of the blood, so prominent in rotational viscometers, had any pathophysiological significance.

Earlier observations in our own lab had given strong indication that compaction stasis in mesenteric microvessels might not just be associated with plasma evasion, but with intravascular sedimentation: using high resolution interference contrast optics (30 × 12.5 LEITZ) during intravital microscopy of horizontally placed specimens, we frequently observed that when the aggregated and progressively compacted red cell rouleaux had come to a stop, there was a residual flow of plasma as evidenced by a distinct motion of blood platelets. Furthermore, we frequently noticed that in apparently stationary red cell aggregates the apparent haematocrit continued to increase (often within less than 60 s) until the compaction stasis described above became fully developed. The pronounced local haemoconcentration did not appear to be associated with severe oedema and/or exudation, since the mesentery remained quite normal in its translucency. These observations, as well as the accidental observation of compaction stasis in Radtke's artificial capillary system with impermeable walls suggested that the sedimentation processes (the consequences of the reduced suspension stability of the blood) might play a more prominent role in inducing rheological flow impediments than hitherto assumed. To test this hypothesis, we developed a horizontally aimed intravital microscope in order to observe the microvessels in a vertically placed mesenteric membrane and artificial systems of microtubes. As will be detailed in this report, under these conditions the effects of red blood cell sedimentation can be observed and measured: as was to be expected, sedimentation not only affects local haematocrit, but even more the velocity profile in a slowly perfused microvessel.

Methods and materials

The experiments were carried out on an isolated preparation of rat mesentery, perfused at various hydrostatic perfusion pressures from reservoirs containing human RBC suspensions in various colloidal solutions (v.i.). The mesenteric artery and vein of 200–250 g Sprague-Dawley rats were cannulated with PE-tubes drawn to outer tip diameters of 0.5 mm. After ligation of arteries and veins leading to neighboring modules, segments of 4–5 cm width (and enclosed by 2–3 radial arteries and veins) were sectioned free. The dissected intestine was cannulated and drained by PE-tubes of about 4 mm outer diameter. The isolated mesentery preparation was fixed by glueing the intestine onto a vertically placed transparent foil, using polyacryl adhesive designed for medical purposes ("Bucrylat", Ethicon). It was wetted by a drip of isotonic saline (pH 7.4). The transparent foil was attached to a perspex microscope stage that could be moved in X-Z-directions. A special horizontally aimed microscope was constructed from commercially available optical parts in our workshop (Fig. 1) and placed into a thermostatic chamber allowing to maintain the preparation at any desired temperature: in all experiments using high concentrations of fibrinogen, we set the temperature at 37° C. Most experiments were done with low or intermediate magnification (4×, 10× and 20× objectives, 10× ocular). The microscope was attached to a closed circuit TV-system and videorecorder described in detail elsewhere (Driessen 1979). The videotapes were replayed for measurements of optical density and of velocity profiles using standard equipment (video densitometer, IPM-dual-slit-correlator).

The isolated mesentery was either perfused with isotonic, buffered saline (containing 0.1% bovine albumine) or with suspensions of human RBC in colloidal solutions. These were heparinized (2000 I.U./ml), albuminated (0.1% bovine albumin) and contained either FICOLL (M.W. 400000, Serva), in the majority of experiments at a concentration of 4% (w/v) or bovine fibrinogen (0.7%, w/v, Sigma). When washed human RBC were added, the former produced a typical kind of "clump aggregation" (described earlier as occurring with high molecular weight Dextrans and α2-macroglobulin: Schmid-Schönbein et al. 1973), whereas the bovine fibrinogen produced the typical "network aggregation" described earlier for human fibrinogen. The haematocrit values were set at 20, 30 and 40%. In order to avoid sedimentation prior to perfusion, these suspensions

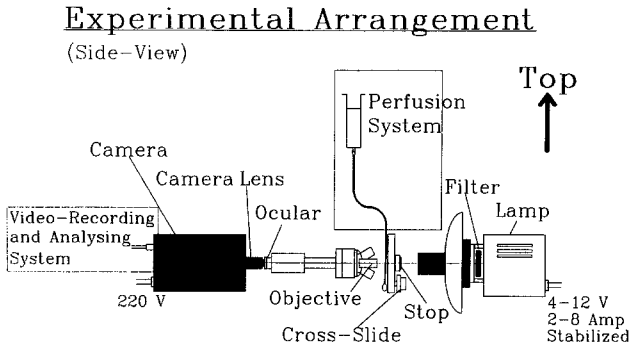


Fig. 1. Experimental setup: vertical microscope table and horizontally aimed optical pathway; perfusion of isolated mesentery and microtube network through a mixing chamber at variable arterial pressure

were sheared (about 100/s) in a reservoir constructed as a closed coaxial cylinder viscometer (described in detail in: Hoymann 1986). The reservoir was also placed in the thermostatic housing and pressurized by an adjustable reservoir containing isotonic saline solution.

In parallel experiments, we used an in vitro network of microchannels: as described in detail by Radtke, these were produced by embedding non-tensilized nylon threads of 80 and 100 μm diameter into unpolymerized polystyrene. To produce a microscopic bifurcation, the 100 μm filament was perforated by a precision microdrill, and a 80 μm filament was threaded into the hole. For other experiments, the 100 μm filament was bent sharply at a right angle.

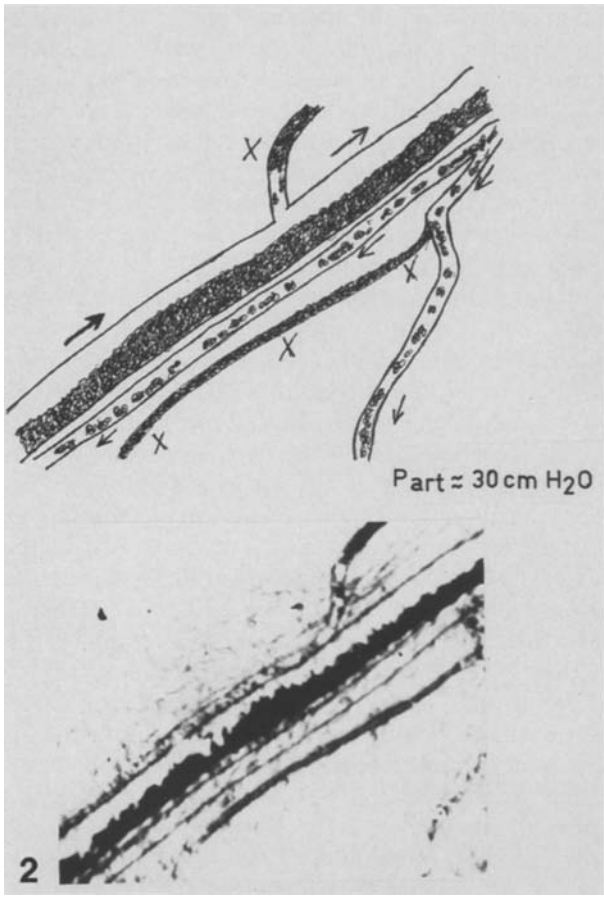
After chemical polymerization, curing and hardening, the filaments were extended and pulled out of the transparent polyester block. To produce the bifurcation, the 80 μm filament was stretched and completely drawn out of the transparent block, and the 100 μm filament was carefully set back until its end had just passed the crossing of the 80 μm channel. Subsequently, polyethylene tubing were adjusted to luer-locks previously attached to the filaments, care being taken that the inner diameter of the tubing did not exceed 150 μm (to avoid local sedimentation). Flow visualization studies were performed by attaching these artificial channel systems to the vertical microscope described above; the channels were perfused with the red cell suspensions described above. For these experiments, we designed a U-shaped perfusion system allowing to set the pressure differential to very low values (2–5 cm H_2O), the feeding reservoir containing a small magnetic stirrer.

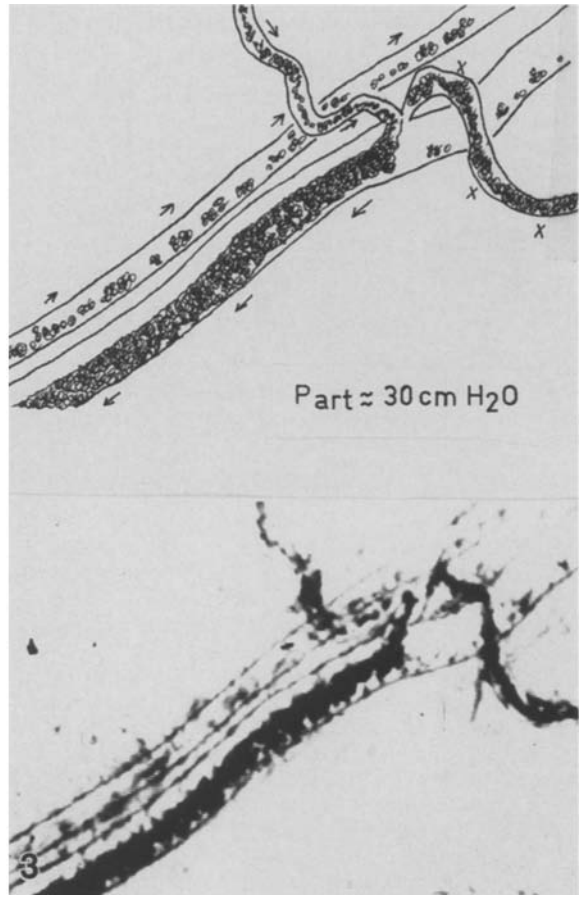
Results

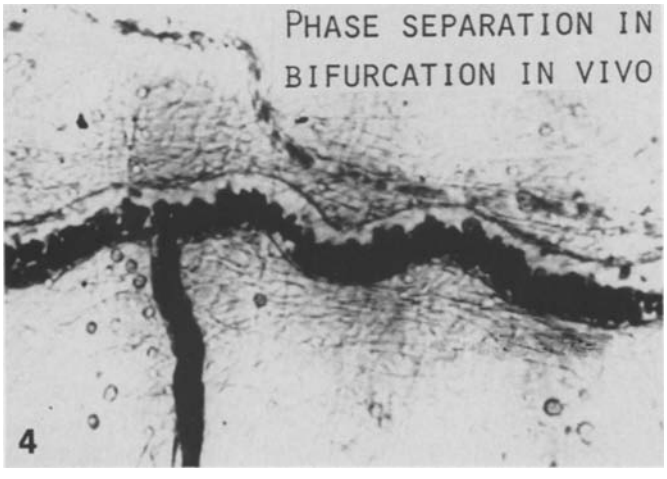
When examining the microcirculation from the side, pronounced sedimentation effects can be observed in all venules, their magnitude and haemodynamic effect depending on the presence or absence of red cell aggregates. At very low perfusion pressures (15–20 cm H_2O), sedimentation can be detected even without such aggregates. When slowly perfusing our isolated mesentery preparation with human RBC in an isotonic albuminated solution without added macromolecules, we could see a distinct layer of cell-free suspension medium in the majority of venules, sometimes even in arteriolar vessels. This shows that while travelling through the terminal vasculature, even individual red cells sediment under gravitational forces, to an extent producing a visible phase separation. However, even at the lowest perfusion pressures, the extent of this phase separation is limited and not progressive, leading only to a small vertical gradient in red cell volume fraction.

The sedimentation distances covered during passage through the venular parts of the microcirculation are much higher whenever an aggregating RBC suspension is used as a perfusate: characteristic examples are given in Figs. 2 and 3, taken from the video screen during the perfusion with a 0.7% fibrinogen solution as a suspension medium. Even the arteriole (A) shows a clear-cut accumulation of the small aggregates on the bottom side of the vessel. In capillaries proper, very little sedimentation is seen, however, the small venule (SV) feeding vertically into the larger venules (LV) conveys immediately the erythrocytes into the dependent part of the latter. There is a wide variety of sedimentation patterns in the venular network, with obvious dependencies upon such factors as vessel diameter, orientation in space and within the network and most of all flow velocity. The lower the arterial pressure (here produced by the hydrostatic pressure in the perfusion system) and the stronger the tendency to aggregate, the more pronounced are the phase separation effects. As a consequence of these, one can observe an extreme variation in red cell volume fraction in the individual segments of the venular network, ranging between two extreme situations, namely almost complete perfusion with apparently packed red cells in those segments that drain from the dependent part of an upstream venule (Fig. 4) or almost zero haematocrit in those draining from the upper part (a type of skimming phenomenon caused by plasma floatation). Accordingly, the flow velocities in the different parts of the venular network differed. Frequent changes in flow direction could be observed during our experiments due to the multiple interconnections in the rat mesentery (Hoymann 1986).

In the present initial stage of investigating the hydrodynamic consequences of phase separation processes in both individual venules and in the venular network, we chose the situation in more or less horizontally running venules of the 3rd to 4th order (using the Horton-classification) with characteristic diameters between 70 and 90 μm. We have to stress that the phenomena to be described below could also be observed in venules of smaller diameter and lower order; in these, however, the







Figs. 2, 3. Photographs and schematic drawings of intravascular sedimentation in a vertically placed mesentery at low perfusion pressure

Fig. 4. Consequences of layered flow: feeding of packed red cells from the depending part of a venule

fluid-dynamic situation was so unstable that there was usually not enough time to record and analyse the very pronounced phase separation culminating in the full development of compaction stasis.

The most important determinant of the phenomenon of intravascular sedimentation is the perfusion pressure and/or the flow velocity in all observed microvessels including the larger venules. If the perfusion pressure was maintained at 100 cm H_2O, no detectable sedimentation occurred in aggregating samples with haematocrit levels of 20–40%: if, however, an even lower haematocrit perfusate was given, a slight sedimentation (revealed by slightly higher transparency of the upper part) occurred, which was barely detectable by a minute change in the velocity profile. Whenever the perfusion pressure was lowered, intravascular sedimentation became noticeable: for

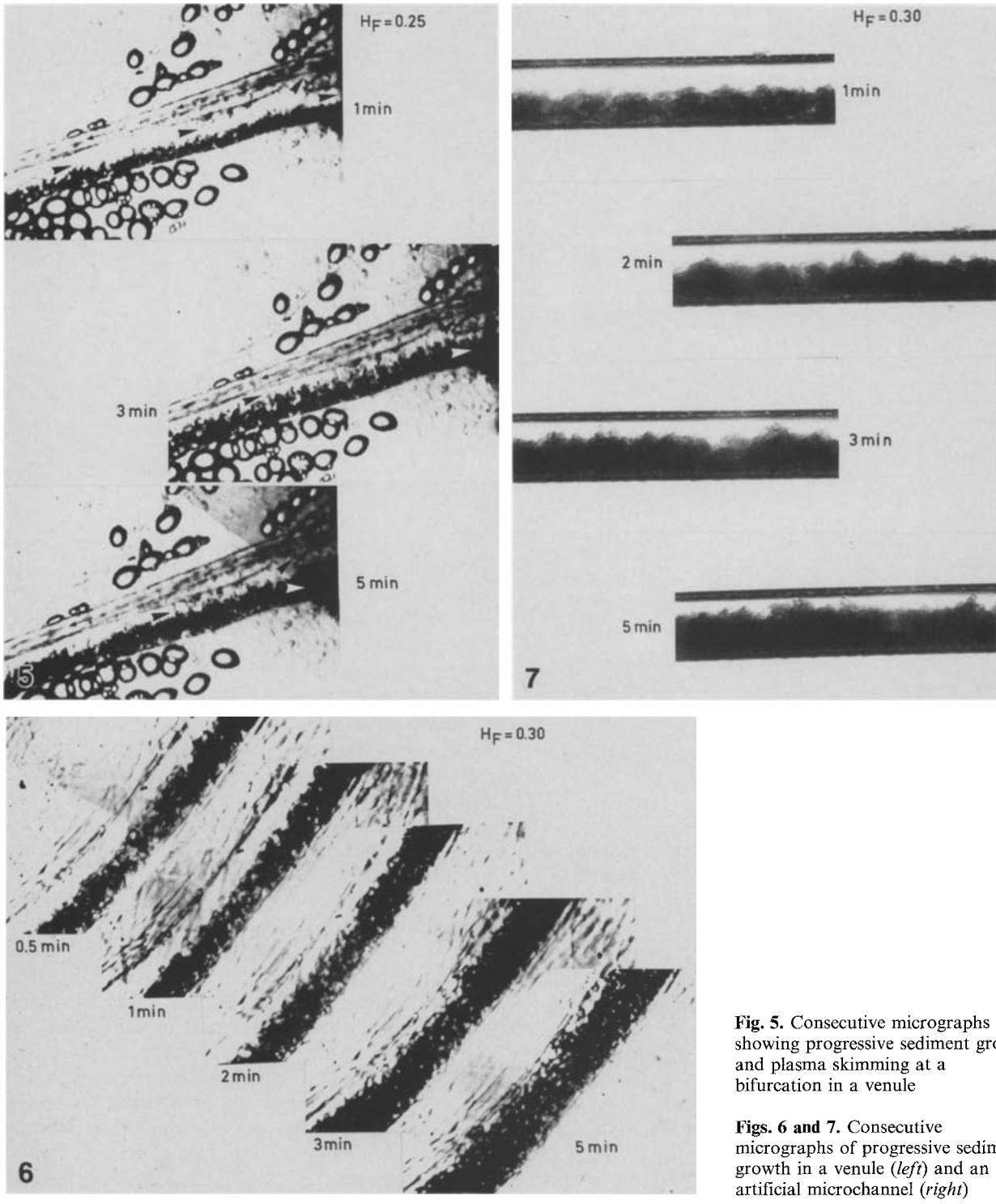
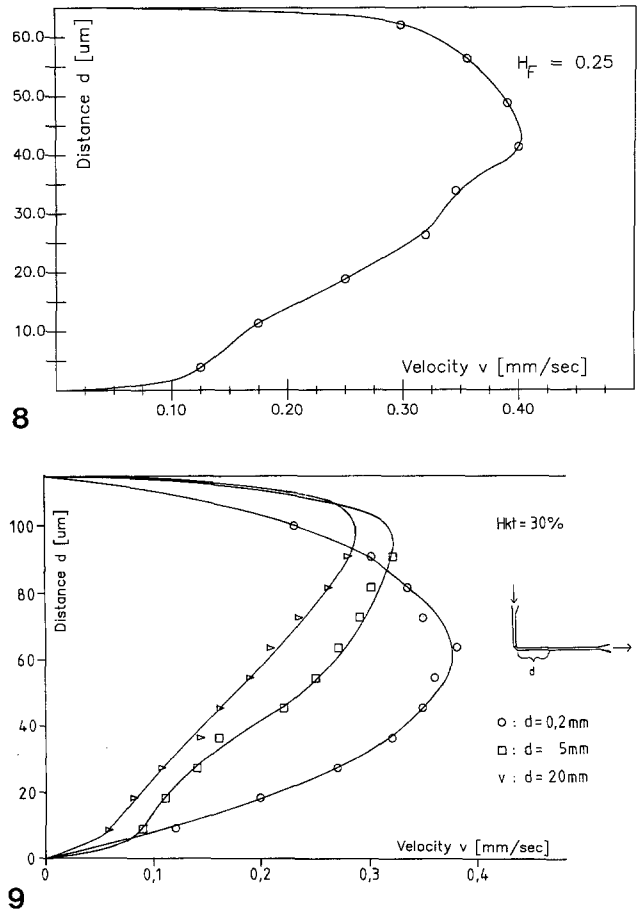


Fig. 5. Consecutive micrographs showing progressive sediment growth and plasma skimming at a bifurcation in a venule

Figs. 6 and 7. Consecutive micrographs of progressive sediment growth in a venule (*left*) and an artificial microchannel (*right*)

the reasons given above, we select for detailed description the phenomena seen at 15–20 cm H_2O and reservoir haematocrit values between 20 and 30%. A characteristic example is given in Fig. 5, showing photomicrographs of a venule bifurcating into two daughter vessels and accompanied by a much smaller arteriole. One minute after lowering the perfusion pressure from 100 to 20 cm H_2O, the venule shows clear-cut phase separation: the aggregated red cells travel in the dependent parts, the plasma in the upper ones. There is a clearly visible separation line between plasma and sedimented



Figs. 8 and 9. Vertical velocity profile in a venule (*upper half*) and a synthetic microtube (*lower half*)

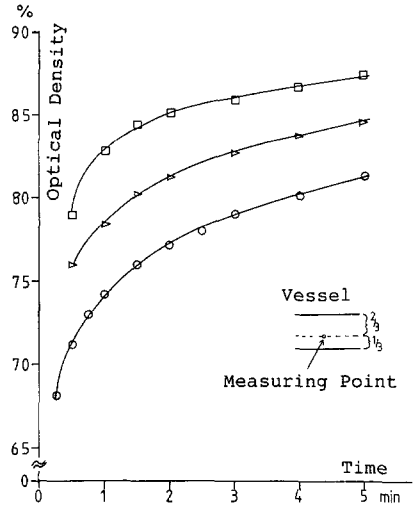


Fig. 10. Time dependence of optical density measured at a fixed point in the dependent part of a synthetic microvessel; comparison of different haematocrit levels in the reservoir: o = 20%; ▷ = 30%; □ = 40%

RBC. This results in the skimming of almost pure plasma into the branch leading in the upward direction and the perfusion of the branch leading downwards by densely packed red cells. Respectively, two and four min later, the separation line has moved towards the top of the vessel, while the number of erythrocytes flowing along the bottom of venule has progressively increased.

A further example of clear-cut progressive accumulation of RCA is given in Fig. 6. Thirty seconds after lowering arterial pressure, about one half of the vessel segment (diameter about 80 μm) is filled with RCA. After five min, the separation line between the suspension fluid and the RBCs has nearly reached the top of the venule, the vessel now being nearly blocked by RCA.

The single micro-channel, the construction of which has been described above, gives a good opportunity of studying velocity profiles and optical density variations under fairly constant conditions, allowing to vary easily the perfusion speed and the haematocrit in the channel segment under observation. We used feed haematocrits of 20% to 40% and applied differential pressures of 2–5 cm H_2O. As we were mainly interested in those velocity ranges that produce progressive sedimentation, we limited detailed studies to maximum perfusion speeds of 0.3 to 0.6 mm/s.

Profile measurements were performed at 3 distances from the entrance of the horizontal part of the microchannel. A single profile was obtained by measuring RBC velocities at 9–11 points of the vessel diameter. Figure 9 shows such profile recordings for a feed haematocrit of 30% and a maximum speed of 0.4 mm/s. (Similar profiles were recorded in mesenterial venules, an example being given in Fig. 8). Shortly after the entrance (d = 0.2 mm), the profile is still nearly symmetric and no clear separation line between suspension medium and RCA can be detected. After travelling 5 mm along the horizontal part of the vessel, the RCA have sedimented to the bottom of the channel, leading to a deformation of the velocity profile, the RBC layer moving at a distinctly lower speed than the suspension medium. This effect is even more noticable after 20 mm of travel.

We also recorded the optical densities 35 μm from the bottom of the vessel over 5–10 min, using the video analysing system described above, the output of which was recorded. The curves thereby obtained revealed a significant increase in the concentration of RBC in the dependent parts of the channel (Fig. 10).

The bifurcation network described above was most suitable to examine the skimming effect of

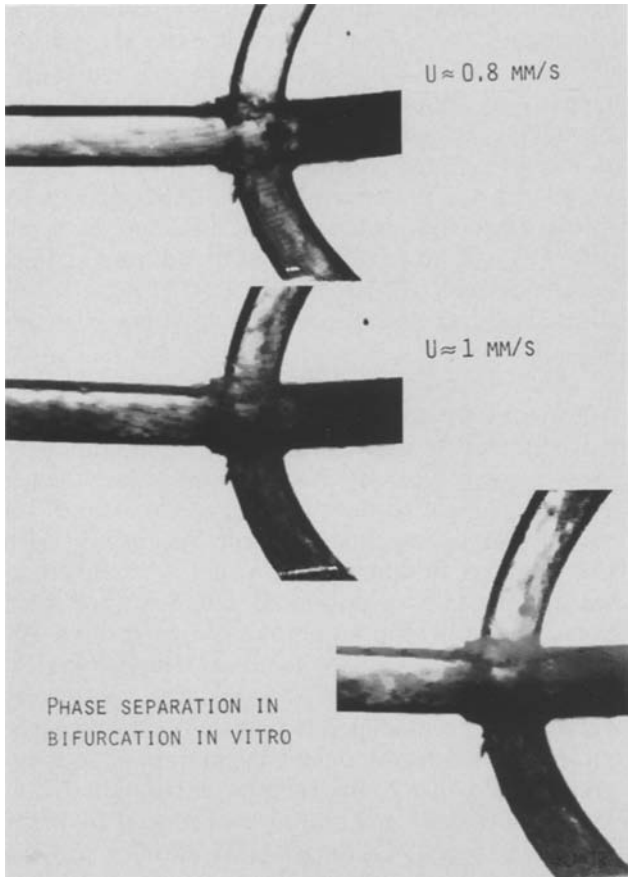


Fig. 11. Plasma skimming at an artificial bifurcation: note the dark staining of the daughter branch facing downward in comparison to the light staining of the daughter branch facing upward

RBC sedimentation, because it provided two exactly identical branches, one leading upwards, the other leading downwards at the same angle. When perfusing the artificial network at velocities below 1.5 mm/s, a difference in optical density at corresponding points of the two branches departing from the main vessel could be detected (Fig. 11). The difference grew when slowing down the perfusion velocity up to a point where all the RBC departed into the dependent branch, whereas the upward leading branch was only perfused by suspension media. Naturally, the appearance of this phenomenon depended predominantly on the feed haematocrit and the blood flow velocity. There was no detectable separation at 2 mm/s (irrespective of haematocrit), separation increasing as flow was retarded. The separation was complete at 0.6 mm/s for a haematocrit of 20% and 0.4 mm/s for a haematocrit of 30%.

Discussion

In our experiments on the vertically oriented, haemodynamically isolated rat mesentery we observed: rapid and pronounced intravascular red cell aggregate sedimentation, especially in the venules, leading to: progressive deformation of the velocity profile with retardation of the dependent and acceleration of the superfluent layer, which in turn leads to progressive increase of haematocrit value in the gravitationally lower parts of the venules and outflow of more or less cell-free plasma. This culminates in the well-known phenomenon of "compaction stasis". Basically the same phenomena were observed in artificial microtube networks, cast in polyester and possessing walls impermeable to plasma. Thence, we feel justified to conclude that – contrary to conventional concepts – compaction stasis can also result from pure haemorheological phenomena and not only from transmural exudation and/or transsudation of plasma.

In textbooks of general pathology (Letterer, Anderson) the stasis phenomenon is clearly separated from mere standstill of normal blood. Phenomenologically, the dense packing of red cells and the resulting changes in the light diffraction properties is discussed. The reversible nature of the phenomenon is stressed; since it is discussed in the context of inflammatory reactions, it is tacitly assumed that the dense packing of erythrocytes is caused by excessive transmural efflux of plasma. The haemodynamic consequences of static blood are clearly appreciated. While we cannot exclude the possibility that the stasis phenomenon is in part caused by filtrative haemoconcentration, we submit as an alternative explanation that the local haemoconcentration is caused by a novel type of plasma skimming. Skimming simply means that the two phases of the blood are separated. So far only skimming due to axial drift of red cells in the rapidly perfused microvessels was considered in physiology and pathology. We submit that the local haemoconcentration is caused by floatation of plasma that occurs in association with sedimentation of red cells. The observations we report offer an explanation for the rapid occurrence of stasis; the mechanism we propose justifies the use of the word "compaction stasis" that was originally used by Cohnheim and was reintroduced into the haemorheological literature by Copley (1986).

To the best of our knowledge, Harding and Knisely (1960, 1965) are the only previous investigators who have systematically studied sedimentation effects in microvascular networks. They not

only directed a horizontally aimed microscope onto the conjunctival vessels of human subjects afflicted with various diseases, but also studied the microcirculation in a mesenteric preparation of the frog that was fixed in vertical position extensively. Their primary aim was to stress that the phenomenon of "intravascular settling" occurs not only after death – a well-known post-mortem event – but also in living bodies. While they clearly illustrate both intravital settling of erythrocytes, "gravitationally layered flow" and "decanting of clear plasma" into venules fed from the superfluent layer, they seemed to have been unaware of the fluid-dynamic consequences of this "heterophase effect" as far as the phenomenon of compaction stasis is concerned. Not only numerous experimental pathologists but also eminent microcirculation physiologists such as A. Krogh (Krogh 1929) and E. Landis (Landis 1934) had described "compaction stasis" as a central pathogenetic event in low flow states of various aetiology. According to Knisely's concepts (last summarized in his article in the 1965 edition of the Handbook of physiology), aggregated red cells were thought to cause microvascular disturbance by obstructing converging arteriolar (pre-capillary) vessels. Experimental pathologists, in turn, generally agree that "compaction stasis" regularly seen in venules, occurs in conjunction with signs of tissue oedema; it is therefore generally assumed to be caused by transmural plasma loss (filtrational haemoconcentration). While we are not trying to dismiss this concept, we clearly showed that compaction can occur without transmural fluid evasion. Since, however, compaction stasis creates a substantial outflow impediment for the microcirculation, it will give rise to an increase in effective filtration pressure in all upstream vessels and may thus be the cause (rather than the consequence) of tissue oedema.

Recently, Driessen and especially Hoymann (Driessen et al., Hoymann 1986) have studied the occurrence of intravascular stasis systematically by changing the aggregation tendency and the haematocrit value on the one side, and the arterial pressure on the other. In these studies, pronounced standstill – primarily in venules, but also in capillaries and even arterioles – was found consistently when the arterial pressure was lowered. These studies further showed that – provided venular obstruction in mesentery preparations was avoided as carefully as possible – there was no stasis unless there was aggregation in conjunction with arterial hypotension. However, stasis persisted frequently if, after having been produced, the arterial pressure was normalized. More detailed observation of stasis then revealed three additional features that prompted the present experiments (Hoymann 1986). Small (primarily venular) microvascular segments were found completely filled with red cells, producing a local haematocrit much higher than that of the animal and the remainder of the microvessels. In the presence of stasis, there were many microvessels that were stagnant, filled not with red cells but with low haematocrit blood, and at high magnifications, the residual motion of platelets indicated plasma flow above the completely stagnant red cells.

The observation of the microcirculation with a horizontally aimed microscope clearly corroborated the latter observations, and the quantitative assessment of velocity distribution in the affected venules brought to light a novel mechanism of intravascular haemoconcentration. In keeping with the previous findings by Hoymann, we failed to see any stasis or pronounced sedimentation with non-aggregating blood samples. When strongly aggregating blood samples were used, the rheological and microhaemodynamic events were extremely variable and even depended on the kind of macromolecule chosen to induce aggregation. Clump aggregates induced by high-molecular-weight Ficoll (MW 400000, 40 g/l) and also produced by high-molecular-weight Dextran (MW 500000) and the high-molecular weight plasma protein α_2-macroglobulin (MW 920000), while sedimenting and displacing the velocity profile downward, glided over the endothelium, producing neither progressive sedimentation nor progressive haematocrit increase. Despite the fact that the velocity profile is asymmetric (displaced to the bottom) it is not skewed; therefore the net outflows of plasma and of red cells are equal to the corresponding net inflows. Quite in contrast, fibrinogen induced so-called "network aggregates" consistently led to instabilities of local haematocrit and flow velocity, ranging from total compaction of a vessel by RBC and flow stagnation on the one hand to pure plasma flow and rapid flow velocities on the other. Only after concentrating on more or less horizontally positioned larger venules and after repeated analysis of the videotapes, could an underlying coherent pattern be recognized.

Under low arterial perfusion pressures, some venules displayed the phenomenon of immediate sedimentation at the inflow site from an upstream vessel (vertical venule or capillaries) with continuing sedimentation from the superfluent red cell plasma mixture and outflow of almost cell-free plasma. Consequently, in these venules the interface between the sediment and the superfluent plas-

ma gradually rose in vertical direction. As this occurred, the flow velocity (and therefore obviously the flow rate) gradually decreased: a residual flow could be observed to deliver more or less individual cells that were deposited immediately upon the already layered aggregates so that eventually the whole segment was occluded. As time went on, secondary compaction could be seen. In vessels which were fed from a venule with "horizontally layered flow" (an expression introduced by Knisely and based on Einstein's description of a particular flow pattern of suspended sediment in natural rivers (Einstein 1941)), the haematocrit could be either very high or zero, depending solely on their position in space. Those draining the bottom and leading downwards received densely packed red cells; those venules departing from the top of the vessel received virtually cell-free plasma. For this phenomenon, Knisely used the very descriptive term "plasma decanting" in analogy to chemical decanting procedures. Our experiments in the artificial microchannels, featuring a bifurcation with an upward and a downward branch revealed the same phenomenon, namely virtually pure plasma flow into the upper branch, associated with delivery of compacted sediment into the lower one. As a consistent observation we found a marked tendency of intravascular sediment growth in the individual vessels and appearance of compaction stasis in more and more venules: unless the arterial pressure was elevated, the overall circulation tended to deteriorate progressively, a finding also regularly observed in experiments with conventionally positioned (horizontally oriented) microvessels (Hoymann 1986). These observations in the rat mesentery were strongly corroborated by our experiments in the artificial microchannel which equally showed progressive sediment growth and increase in tube haematocrit.

From our measurements of the velocity profile as well as of those of the time dependence of optical density changes at a fixed point of a venule, we can deduce the microfluid-dynamics of the sedimentation process (as shown by the growth rate of the deposit or time dependent increase in local haematocrit). The result of gravitational viscidation and floatational plasma skimming is a dramatic shift in local residence times of the continuous and suspended phase respectively, and thence a fundamental change in the red cell flow fraction ("discharge haematocrit") and the red cell volume fraction ("tube haematocrit") (See Schmid-Schönbein 1988 for a detailed theory of the sedimentation process and its fluid-dynamic consequences). As a result, the well-known phenomenon of "compaction stasis" may occur: more or less complete filling of the venules by densely packed red blood cells.

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