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Editorial

Role of blood viscosity in the microcirculation

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Blood fluidity is reported to influence capillary perfusion in healthy subjects and especially in patients with different diseases [6, 10, 29, 31]. Up to now there is no simple way to quantify the influence of the different haemorheological parameters (haematocrit, plasma viscosity, erythrocyte aggregation, erythrocyte deformability) on the velocity of blood cells in human capillaries. In general, only a limited correlation can be shown [18]. One reason is the great variability of the diameter of human capillaries described in healthy subjects, with values between 3 and 15 μm, and in patients – depending on the disease – with values up to 50 μm (e.g. giant capillaries in patients with scleroderma [33]). This is a very large range with respect to the role of the various haemorheological parameters of blood in microcirculation.

The hypothesis of Barras, that plasma viscosity determines the perfusion of microvessels because the absolute capillary haematocrit is about 10–20%, so that blood viscosity in capillaries approaches plasma viscosity seems to be near the truth [4], as long as the capillary diameter is big in relation to the erythrocyte diameter. The work of Lipowsky would seem to confirm this [25]. In the case where the capillary diameter is smaller than the red blood cell diameter, the cells have to be deformed by shear forces before passing through a capillary. In this case the blood flow velocity should additionally depend on the erythrocyte deformability. This fact, which results from a fluid-dynamical point of view, however, is often not seen in patients using capillary microscopy in nailfold capillaries: neighbouring capillaries with different diameters and fed from the same arteriole show the same red blood cell velocity. Therefore we conclude that there is a regulatory mechanism in the capillary network possibly by the microvascular endothelium as described by different groups [8, 15, 26, 34].

In an animal model Driessen showed that rigidified erythrocytes slow down the capillary blood flow (up to stasis) only if the blood pressure was lowered below the normotensive state [9]. On the other hand in extreme cases of sickle cell crisis, a dramatic near zero flow in cutaneous capillaries can occur [21, 24] because of the extremely reduction of the deformability of the sickled erythrocytes [27] together with their adhesiveness [3].

The problem is more complicated in cases of a pathologically elevated erythrocyte aggregation. Under these conditions a massive sludging can be found – firstly described by M.H. Knisely´s group in conjunctival vessels – even in very small cutaneous capillaries [12]. Big erythrocyte aggregates pass very slowly through the capillary while immediately thereafter a single cell perfusion with significantly

higher velocities in the same capillary can occur. In diabetic patients it can be shown that the erythrocyte aggregation correlated well with the mean erythrocyte velocity in nailfold capillaries in diabetic patients in a clinical study with 1256 subjects [18].

In general, rheological phenomena are probably capable of deteriorating microvascular perfusion. However, while the as yet unknown regulatory mechanisms of the perfusion are intact, a direct impact is limited. In most patients microcirculatory disorders are associated with pathologically changed rheological parameters, both processes seemingly in correlation to the extent of the disease. Therefore it can be assumed that in the natural course of arterial diseases endothelial cells, blood cells and the plasma also undergo pathological changes (this can be shown at least in patients with hypertension, diabetes mellitus, and with arterial occlusive disease) [1, 17, 19, 22].

In the case of arterial disease there is a line of events firstly mentioned by A.M. Ehrly [11]: rheological changes could induce and enhance a circulus vitiosus: vessel wall changes (stenosis) – a drop in pressure – a decreased blood flow – an acidosis enhancing the rheological defects – a.s.o.

Sudden increases in blood or in plasma viscosity (in combination with erythrocyte aggregation), lead to a viscosity-dependent drop in capillary perfusion in patients with coronary artery disease. This could be shown in ipsilateral nailfold capillaries by comparison of the effects of injection of high viscous or lower viscous radiographic contrast media into the A. axillaris [32] or in double blind studies in which the injection of high viscous iodinated contrast media were compared with the injection of isotonic sodium chloride solutions [2, 20]. On the other hand, an increase in capillary perfusion could be found after HELP apheresis with a plasma viscosity decrease of more than 20% in patients with macroglobulinaemia [7] or in heart-transplanted patients with transplant vasculopathy [28].

This shows that acute falls in plasma viscosity – though a concomitant decrease in erythrocyte aggregation also occurs because the fibrinogen concentration decreases [23, 30] – induce significant and relevant changes of capillary perfusion in humans. Studies to show the effects of changes of single rheological parameters (erythrocyte deformability, erythrocyte aggregation or platelet aggregation) suffer from serious limitations, because in most cases the drugs or interventional therapies [5, 13, 14, 16] applied, induced a vasodilation or vasoconstriction in addition.

In conclusion it is known that plasma viscosity in acute *in vivo* studies and – but only in the extreme cases of sickle cell crisis – the erythrocyte deformability influences the capillary perfusion. There is evidence that pathologically elevated erythrocyte aggregation slows down the capillary perfusion as long as aggregates perfuse the capillary [18]. In first – unpublished studies – we could see that in cases of increased numbers of circulating platelet aggregates there was a decrease in capillary perfusion which normalised after applying thrombocyte function inhibitors.

There is clearly more work to be done in this area and the role of the leukocyte has not even been mentioned.

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