DO HAEMORHEOLOGICAL LABORATORY ASSAYS BEAR ANY CLINICAL RELEVANCE?

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If the title of this workshop were to be taken literally there would be little argument that the answer is undoubtedly "yes". The literature is replete with papers showing disturbances of haemorheological factors in many clinical conditions. Thus blood and plasma viscosity are generally recognised as being raised in association with, for example, hypertension, diabetes and hypercholesterolaemia, almost any condition associated with a high fibrinogen level exhibits exaggerated rouleaux formation, and red cell deformability is known to be reduced in, for example, sickle cell anaemia (1).

It is clear, therefore, that there is clinical relevance--so perhaps a more provocative question should be addressed, ie "are the haemorheological changes simply markers of the clinical conditions in which they are found or do they have a direct role to play in their clinical progress?" and, in the context of this workshop, answered provocatively. If the answer is that they are only markers, then haemorheology is only of real clinical relevance if these haemorheological parameters can give better diagnostic and prognostic information, or are easier and cheaper to measure, than existing clinical indicators. Some progress has been made in this direction, particularly in respect of plasma viscosity. It can now be measured easily and relatively cheaply, but more important it gives better information than the Erythrocyte Sedimentation Rate Test that it replaces (2). The result is that it is increasingly being used in routine haematology departments. Unfortunately, progress elsewhere has been less significant, for example several instruments are now available for quantitating rouleaux formation but they appear rarely, if ever, in routine departments. This is presumably because it is not yet clear that they produce an improvement in diagnostics. The measurement of blood viscosity (at low as well as high shear rates) and cellular deformability are still too technically demanding, and again need to be shown to offer improvements over other clinical techniques.

What would revolutionise the situation would be a convincingly affirmative answer to the second part of the question posed above, that is to say that haemorheology is influential on the course of clinical conditions in which it is disturbed. This would convince the general clinician of the

necessity to monitor haemorheology directly, and that it does offer more than just another set of "markers". Here much needs still to be done. To take whole blood viscosity, our "core" measurement, as an example; this is usually measured at a haematocrit to be found in large vessels, yet the bulk of the resistance to flow in vivo is in the microcirculation where the haematocrit is generally much lower and where the vessels have a remarkable capacity to regulate their size and patency to compensate for inadequate flow. It is now common to make blood viscosity measurements at low as well as high shear rates as both obtain in any vessel. However, they are almost invariably done in a constant shear and cell concentration regime across the measuring vessel. Yet in the circulation there is a continuously changing shear field across any blood vessel and, usually, a varying cell concentration. In reality, the situation is even more complex since on the arterial side of the circulation a pulsatile pressure field obtains. So what do our current blood viscosity measurements tell us of the situation in vivo? Such experimental evidence as does exist on the influence of blood viscosity on haemodynamics in vivo is frequently ambiguous, for example it is clear that haemodilution can lead to improved flow, but how much of this is due to reduced viscosity and how much to the altered oxygen carriage leading and hypoxia-driven vasodilatation (3)?

Continuing in a similar fashion, it is intuitively obvious that if plasma viscosity is reduced it will improve microvascular flow but how much will the haemorheological advantage be overridden by vascular autoregulation (4)? Similar arguments obtain with respect to the effects of alterations in red cell deformability and rouleaux formation.

We haemorheologists have in the past tended to be too narrow in our view. We have delicate techniques capable of accurate measurements, can find small statistically significant differences in our haemorheological parameters in many clinical conditions and often extrapolate wildly as to their haemodynamic and physiological influence. The result is that people outside the field, with no rheological axe to grind, frequently cast scorn on our extrapolations. There are papers, indeed books, which suggest a major role for haemorheology on the course of everything from thrombosis to deafness! The time has come for a concerted effort to look for more firm and quantitative evidence for real rheological effects. Some work of this nature has already been done of course. As long ago as 1933 Whittaker and Winton (5) showed flow rate changes in the isolated hind limb of dogs as the haematocrit and viscosity of the blood was altered. Thomas et al (6) showed the same sort of phenomena in the human cerebral circulation and that this was due to both autoregulatory and rheological effects (3). Then, of course, there is the work of Lipowski (7) on the effects of systemic haematocrit variation on microvascular haemodynamics. More recent examples are the work of Vicaut (8) looking directly at the effects of altering rouleaux formation on microvascular flow in animal models and of Baskurt (9) studying the effect of fibrinogen, as a haemorheologically active agent, on cardiac haemodynamics. However, much more is needed in this direction in order to quantitate the degree to which haemorheological alteration can affect in vivo haemodynamics and in what circumstances.

The message of this paper is that we should be unsatisfied in finding statistically significant changes in our haemorheological parameters until we have experimental evidence that they produce physiologically significant changes in vivo as well. When we have, the field will have come of age and then we can insist that we have machinery of clinical relevance that has to be brought into the over-all armoury of the clinician.

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