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CLINICAL HEMORHEOLOGY, QUO VADIS?
ROUND TABLE DISCUSSION
(On behalf of the Benelux Society for Microcirculation)

guest editor Max R. Hardeman

Participants: Michel Boisseau (Bordeaux)*, Sandro Forconi (Siena),
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HEMORHEOLOGICAL LABORATORY DETERMINATIONS DO NOT
BEAR ANY CLINICAL RELEVANCE

(Introduction to the Round Table Discussion at the 9th European Conference on
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Problem recognition

1. Unlike "static" clinical chemistry values of blood, as plasma sodium
content or RBC hemoglobin concentration, the viscosity of whole blood is
inherent to its nature, a dynamic property. It is well known that blood is a
non-Newtonian suspension which means that we can not speak about the
 viscosity of blood but should always associate this parameter with the corre­
sponding shear rate used in its measurement. In literature, however, this has
frequently been omitted. Furthermore, two different blood samples may quite
well have an almost equal high shear viscosity value, but appear to diverge
significantly at low shear rates due to a difference in RBC aggregation
behaviour. The confusion can be avoided if we start to define the viscosity
behaviour as the laboratory parameter for a particular blood sample, i.e.
always state viscosity values for at least two shear rates (one low, one high)

* during the discussion Gerard Potron (Reims) represented Michel Boisseau.
2. It is still far from certain, however, what the relevance is of the laboratory assessment of blood viscosity behaviour with respect to the prediction of pathophysiological flow behaviour: the Fahreus-Lindquist effect and the morphological constraints imposed on the RBC in the microcirculatory bed can not be mimicked in the rotational viscometer.

3. The viscosity behaviour of blood is determined by intrinsic factors (hematocrit, plasmaviscosity, red blood cell deformability, red blood cell aggregation) which on their turn can be influenced by various extrinsic factors (shear rate, osmolality, pH, pO₂, PGI, etc.) Both intrinsic and extrinsic factors can vary in different parts of the body. In other words: the flow and composition of the suspension called blood is not constant throughout the body, e.g. hemorheological parameters are found to differ in arterial versus venous blood, in patients (1,2,3), in healthy subjects (4), in an animal model (5) and within an organ (6). Even within a blood vessel there exists no homogeniety: RBC are concentrated in the center while plasma and platelets are found mainly in the near vesselwall region (Fahreus-Lindquist).

4. Hemorheological measurements are usually performed on blood obtained from the antecubital vein (forearm), a region, however, where rheological problems not often occur. It is conceivable, therefore, that reversible changes in blood viscosity or its determinants are missed by studying blood taken from the antecubital vein, although local factors elsewhere in the body might cause serious hemorheological problems, leading to severe pathology.

5. The viscosity behaviour of "whole blood" is considered to be an overall property of this suspension. It should be taken into account, however, that measurable changes in the viscosity determinants should not necessarily lead to measurable changes in a particular whole blood viscosity value e.g. a slight rigidification of RBC will not influence significantly whole blood viscosity values as measured in the LS-30 viscosimeter at a large range of shear rates (7).

6. In the clinical setting, differences in bloodviscosity parameters can be extremely small and yet be significant, resulting in (micro) circulatory disturbances. In order to be of clinical relevance an in vitro technique should be sensitive enough to detect such small differences, e.g. the range of variations in deformability of circulating RBC is limited, the extend of which is dictated by the sensitivity of the spleen for sequestrating old and/or rigid RBC.

7. An increasing number of methods, instruments and techniques exist for the laboratory determination of hemorheological parameters (8,9). Until now there is only one instrument described which can measure multiple hemorheological parameters (10). A consensus for the methods and mutual comparison as well as standardization of the techniques is very important.
Possible approaches to tackle some of these problems

A: the definition, assessment and use of viscosity behaviour in order to indicate the flow property of a blood sample. Chien and coworkers suggested already in 1970 to use the parameter "shear dependence ", calculated as:

\[
\frac{\eta_{\text{low shear}} - \eta_{\text{high shear}}}{\eta_{\text{high shear}}}
\]

This may be a solution for the wish of some clinicians to have a number in stead of a curve, reflecting blood viscosity behaviour.

B: determination of relevant blood viscosity determinants, e.g. plasma viscosity, RBC deformability, RBC aggregation, hematocrit, fibrinogen etc.

C: a consensus about all clinically relevant hematological factors which have a direct influence on blood viscosity behaviour and/or its determinants.

D: establishment of physiological and pathological values of such factors in different parts of the body. Probably, a lot of information can be found in this respect in the literature. The problem is, however, that this is usually cited in another than hemorheological context. Wherever there is a possibility, however, to have blood taken from local body sites, other than the large veins, e.g. during operations, it is worthwhile that the relevant hematological factors are meticulously analysed in the clinical and hematological laboratory, followed by publication of the results and preferably a report to the Expert Panel on Blood Rheology (see under H).

E: direct measurement of rheological parameters of blood obtained from various sites of the body (as in D).

F: laboratory simulation of the circumstances expected to prevail in the particular body part of interest, imposed on antecubital vein blood, e.g. pO2-changes in sickle cell studies, osmotic changes in kidney failure studies, pH changes in ischemic situations, hematocrit changes in edemic regions, etc.

G: before we can generally accept that an in vitro parameter truly reflects a valid physiological and pathological variable, three criteria have been proposed by Dormandy et al (12) which have to be fulfilled:

1. abnormal levels of the variable should be present in most patients with expected circulatory diseases and the degree of abnormality should be related to the severity of the disease;
2. the measurements should be directly related to in vivo macro- or microcirculation;
3. therapy which abolish the abnormal measurement should be accompa­
nied by parallel improvement in disease.

H: In order to achieve general consensus about methods and laboratory
determinations, an Expert Panel on Blood Rheology (chairman J. Stuart)
produced a triad of papers containing recommendations for hemor­
heological laboratory measurements (13 - 15). Due to the expansion of
the field and the retirement of prof. Stuart, four new specialists panels
are formed (16):

- acute phase response (chairman Michael Rampling, London)
- clinical trials (chairman Wolfgang Koenig, Ulm)
- red cell rheology (chairman Max Hardeman, Amsterdam)
- white cell rheology (chairman Jean-Luc Wautier, Paris).

REFERENCES

1. FORCONI, S., GUERRINI, M., RAVELLI, P., ROSSI, C., FERROZZI, C.,
PECCHI, S., BIASI, G. Arterial and venous blood viscosity in ischemic lower
limbs in patients affected by peripheral obliterative arterial disease. J. Car­

2. TSUCHIDA, H., YAMAGUCHI H., ISCHIMARU S., FURUKAWA K. Local
changes in red cell deformability in peripheral arterial disease. In: Microcircu­
ation, an update, vol.1 Tsuchiya, M. et al. eds., Elsevier Science Publ.,

3. MOKKEN, F.Ch., van der WAART, F.J.M., HENNY Ch.P. Differences in
peripheral arterial and venous hemorheologic parameters. Submitted for
publication.

4. DAAE, L.N.W., HALVORSEN, S., MATHISEN, P.M., MIRONSKA, K. A
comparison between haematological parameters in "capillary" and venous blood

5. LIPOWSKI, H.H., USAMI, S., CHIEN, S. In vivo measurements of "apparent
viscosity" and microvessel hematocrit in the mesentery of the cat. Microvasc.

6. PAPPENHEIMER, J.R., KINTER, WB. Hematocrit ratio of blood within
mamalian kidney and its significance for renal hemodynamics. Am. J.
Physiol. 185, 377-390, 1956.

7. SCHUT, N.H., HARDEMAN, M.R., GOEDHART, P.T., BILO, H.J.G.,
WILMINK, J.M. Blood viscosity measurements are not sensitive enough to
detect changes in erythrocyte deformability in cyclosporin-treated patients and
its subsequent reversal with fish and corn oil. Clin. Hemorheol. 13, 465-472,
1993.
8. FORCONI, S. see table II of his contribution to this Round Table.

9. BOISSEAU, M. see table 1 of his contribution to this Round Table.


