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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), Max Hardeman (Amsterdam, Chairman), Michael Rampling (London), Amparo Vaya (Valencia)

HEMORHEOLOGICAL LABORATORY DETERMINATIONS DO NOT BEAR ANY CLINICAL RELEVANCE

(Introduction to the Round Table Discussion at the 9th European Conference on Clinical Hemorheology, Siena June 29-July 1, 1995)

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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 corresponding 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)

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* 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, pO_2, 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 necessarilly 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:

$$(\eta_{\text{low shear}} - \eta_{\text{high shear}}) / \eta_{\text{high shear}} \quad (11).$$

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. Whereever 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. pO_2-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 accompanied 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 hemorheological 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).

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