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Workshop Red Cell Aggregation, Lisbon, July 1, 1997

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Chairmen:

- Max R. Hardeman, Amsterdam, The Netherlands,
  on behalf of the ISCH Expert Panel for Standardization in Blood Rheology Laboratory Techniques, with special reference to Red Cell Rheology
- Mike Rampling, London, UK,
  on behalf of the ISCH Expert Panel for Standardization in Blood Rheology Laboratory Techniques, with special reference to Acute Phase Reaction

Participants:

- Lajos Bogar, Pécs, Hungary
- Jean-Fréderic Brun, Montpellier, France
- Fu-Iong Liao, Beijing, China
- George Mchedlishvili, Tbilisi, Georgia
- Pavel Riha, Nancy, France
- Megha Singh, Madras, India
- Xiong Wang, Nancy, France

Introduction

In these days, the field of clinical hemorheology is struggling for its existence as a separate specialism among other clinical specialisms. One of the reasons that we are losing ground is the lack of standardisation in hemorheological laboratory determinations as well as the lack of causality of these laboratory results with clinical symptoms. It may be easy to establish a significant difference in a laboratory parameter between normal individuals and a patient group. It is extremely difficult, however, to establish whether these *in vitro* significances also reflect clinical significances. After that, we still have to deal with the question of cause, consequence or coincidence. In other words: does a disease improving treatment lead to hemorheological normalisation and/or does correction of the hemorheological deviation lead to

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clinical improvement? The latter question is even more difficult to answer because of the lack of active, sensitive and specific medication directed to alleviation of a hemorheological disturbance, except of course hemodilution.

Due to the fact that the rheological potential of blood is so important for life, nature has supplied the organism with either compensatory mechanisms against sudden rheological disturbances (e.g., vasodilation, hemodilution in the blood–brain barrier) or with other defense mechanisms like the narrow range in which, e.g., red cell deformability may move before the cells are removed from the circulation. In the latter situation it can be understood that also *in vitro* (i.e., in blood taken from the circulation) only small changes can be found, emphasizing the need for sensitive and highly reproducible laboratory techniques. Another reason why many practisizing clinicians remain wary of clinical hemorheology is undoubtedly the discrepancy or variability seen in the outcome of hemorheological variables analysed in clinical studies. An example is the presence (or not!) of less deformable RBC in Diabetes Mellitus. The majority of these conflicting results can simply be explained by differences in methodology and the lack of knowledge about what (aspects of) determinants these techniques really measure. Therefore, concensus among hemorheologists about the relative values of different techniques purporting to measure the same variable is of primary importance. To this end, standardisation and a quality control protocol for the various measurements is indispensable. For that purpose Expert Panels for Standardization in Hemorheological Laboratory Techniques were formed during the ISCH–Biorheology meeting (Big Sky, 1995).

One of the most widely studied parameters determining whole blood viscosity is the red cell's aggregation behavior (rouleaux formation, in the normal situation). This has led to a rather large number of instruments and/or techniques, each with its own defined Aggregation Index and/or kinetic indices. Therefore, it seems that this parameter should be the first to be investigated in relation to the problems cited before.

In France, a working group (Houbouyan, Stoltz) started a national trial on standardisation of RBC aggregation by sending blood samples to different laboratories all over the country, but analysed with the same technique. Recently, in Germany a similar national Task Force was founded (Kiesewetter, Schuff-Werner).

During the Xth European Conference on Clinical Hemorheology, Lisbon, Portugal (1997), hemorheologists from various countries discussed this subject at an informal meeting. The aim of this meeting was to gather information about the various techniques reported in the literature with respect to RBC aggregation measurement and to initiate further meetings for direct practical comparison of these techniques.

How to achieve this?

1. *Listing of all relevant techniques*

   Key reference + short (1 A4) description of measuring principle + practical details like amount of blood needed, etc. With the acquainted information, (anonimous) evaluation of a certain technique/instrument is possible by members of the Expert Panel or any other interested colleague, which can be a basis for further discussion.

   In order to get a more or less complete list a call for sending information was published in the journals *Clinical Hemorheology* and *Biorheology*. Among other reactions, there was a report by Prof. N. Maeda on Hemorheology Laboratory instruments, constructed in Japan and either commercially available or only in use at the laboratory level.

   What is a "relevant" technique?

   – well described in general accessible journal/book;

- easily available, commercialisation in principle possible;
- ability to measure both static and kinetic aspects of aggregation and preferably also the tendency for (or force to prevent) aggregation.

2. *Simultaneous comparative testing* (unfortunately a reliable and stable standard is lacking)

   (A) under identical laboratory conditions. The presence of a hospital has the advantage that also pathological samples can be measured in the comparative trial. Best place in this respect seems to be a laborarory which already has a number of techniques and apparatus in routine use, e.g., Nancy, Los Angeles, Amsterdam.

   (B) parallel to conferences, etc. This has the advantage that the workshop can be organised in cooperation with the commercial exhibition (sponsoring?). Next meetings are scheduled in Antalya, Turkey (RBC Aggregation, October 1998), Pécs, Hungary (ISCH/Biorheology, 1999), and Reims, France (ECCH, 2000).

Concensus about working protocol

All techniques should be characterised by one and the same protocol for establishing at least reproducibility and sensitivity.

It was suggested by M. Singh to use whole blood viscosity (at what shear rate?) as a standard. M. Rampling suggested an easy to standardise washed cell system with dextran, leaving the question to what extent such artificial system reflects that of RBC-aggregation in whole (anticoagulated) blood unanswered.

Conclusion

All participants unanimously agreed about the need for further activities in this respect. Suggestions for this are welcome and can be sent to Max R. Hardeman, Ph.D., Department of Internal Medicine, Academic Medical Center, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands; Fax: 00 31 20 5664440; E-mail: M.R.Hardeman@amc.uva.nl.