A. M. Ehrly

Therapeutic Hemorheology

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For my family
I am pleased to have been asked by Albrecht M. Ehrly to write a foreword for this book. Hemorheology continues to be the most active branch of the science of biorheology. As an organized science, biorheology began in 1948, when I presented, at the First International Congress on Rheology, Scheveningen, Holland, a Plenary Lecture entitled “Rheological Problems in Biology,” in which I introduced the term “biorheology”. Biorheology comprises the study of deformation and flow of biological systems or of materials of biological significance directly derived from living organisms. It deals as well with materials of nonbiological origin, employed in a biological system or setting. Three years later, I introduced the term “hemorheology” at the 25th Anniversary Meeting of the American Institute of Physics, Chicago, in a Plenary Lecture before the Society of Rheology, one of the Institute’s Founding Member Societies.

Ehrly refers to my original definition in the introductory chapter. He also refers to the definition of hemorheology which I gave in 1981 in a Plenary Lecture on the “Future of the Science of Biorheology” at the Fourth International Congress of Biorheology, Tokyo. I postulated that “the blood together with the blood vessels, in which it circulates, constitute two markedly differing but symbiotic portions of a very special organ which is unlike any other organ.” This is emphasized because, in my appraisal, we have to conceive the symbiosis of the vessels and the blood as one single sophisticated organ with its diverse populations of cells and proteins, structures, functions, its vastness, and its diverse rheological behavior.

Hemorheology, in summary, is the study of rheological aspects of the vessel-blood organ. It is the study of the deformation behavior including flow of blood and its constituents and those materials of the blood vessels and surrounding tissues with which blood or its components come into direct contact. In addition, it is also the study of the interaction of blood or its components and the vascular system with added foreign materials, such as drugs, plasma expanders, or prosthetic devices. All in all, hemorheology is the study of how the vessel-blood organ in its two portions, viz., the blood vessel and the blood, can function and interact with other organs which it penetrates, thus playing essential roles in the living organism.

It goes without saying that the above definition gives the science branch of hemorheology and its clinical applications a wider scope which, I am confident, will be dealt with in future studies including clinical hemorheological investigations.

As I emphasized in a plenary lecture of clinical hemorheology last year at the conference in Siena [1], clinical hemorheology, in my appraisal, will become one of the main fields in the practice and teaching of medicine in the not distant future. In the past 100 years many areas in medicine and surgery have developed as special fields of medicine, such as hematology, angiology, dermatology, and ophthalmology, among many others. These highly developed specialties, some of which deal with clinical hemorheology, will profit greatly from the advancement of the latter at present and in the forthcoming years. These advances will include the disciplines of diagnostic, therapeutic, and preventive hemorheology.
As I pointed out in 1981 in Tokyo, in a Plenary Lecture before the International Congress of Biomechanics [2] on the future of biomechanics, this modern life science of merely three decades is the missing link between all life sciences. As far as clinical hemorheology, one of the many branches of the science of biomechanics, is concerned, it appears to be likewise the missing link between the different fields in the practice of medicine and surgery. As this rapidly advancing field concerns the clinical aspects of the rheology of the vessel-blood organ, therapeutic hemorheology will cover not merely what is dealt with in this book, but include such differing areas as hemorrhagic and thrombotic disorders, inflammatory processes, circulatory shock, stroke, edema, embolism – in short any clinical manifestation due to changes in the rheology of the vessel-blood organ. Therapeutic hemorheology will expand by entering most fields and specialties in the practice of medicine and surgery.

Already in 1959, at a conference called “Flow Properties of Blood and Other Biological Systems”, convened jointly by the Faraday Society and the British Society of Rheology and held at the University of Oxford, certain areas in the field of clinical hemorheology were dealt with. “Clinical Hemorheology” was the title of an entire section of the First International Conference on Hemorheology, held at the University of Iceland, Reykjavik, in 1966. It is noteworthy that at that time Ehrly and other clinical investigators reported their studies in the field of clinical hemorheology. He became a charter member of the International Society of Hemorheology, which three years later, at the Second European Conference on Hemorheology, held at the University of Heidelberg, became the International Society of Biomechanics. At subsequent International Congresses of Biomechanics, Ehrly took an active part in presenting studies in clinical hemorheology. Thus, as a clinical investigator and clinician, Albrecht Ehrly became a pioneer in clinical hemorheology.

Ehrly’s activities in clinical hemorheology alone give him exceptional credentials for his writing of the first book on therapeutic hemorheology. These high qualifications are further augmented by his leadership in introducing new therapeutic approaches and drugs in the treatment of circulatory disorders due to pathological conditions affecting the vessel-blood organ. His clinical hemorheological findings on defibrinogenation, which are of particular importance, invite further detailed clinical investigation. Recent advances in experimental hemorheology, including surface hemorheology, have led to new facts and insights pertaining to the vessel-blood organ [3–7]. Thus, for instance, endoendothelial fibrin lining (EEFL) as well as in vivo fibrinogen formation, i.e., the aggregation of fibrinogen molecules and subsequent gelation without thrombin action, are expected to have a great impact on the practice of medicine and surgery. The interface between the two portions of the vessel-blood organ is EEFL, which serves as the crucial filtration barrier for transcapillary transport between the blood and tissues. Moreover, the EEFL plays highly significant roles in the circulation of the blood. It acts as a physical anticoagulant and an antithrombotic agent, and, in the microcirculation, it aids the action of the heart by decreasing markedly the apparent viscosity of blood, known as the Copley-Scott Blair phenomenon. These roles provide the basis for new approaches in hemorheological therapy, including the selection of prosthetic devices. It should also be noted that the recent biomicroscopic investigations pertaining to thrombogenesis by S. Witte [4, 6] (1980) and earlier findings pertaining to the initiation of hemostasis by B. W. Zweifach [4, 6] (1954) show clearly that their findings of in vivo fibrinogen formation open up new vistas in hemorheological therapy. Our recent studies suggest the antithrombogenic action of a number of substances, such as low molecular weight heparins, chondroitins A, B and C, among others [4, 5, 8]. These new advances in experimental surface hemorheology are expected to be developed within the next
decade for clinical application. What likewise may be expected is the development of in vivo hemorheological testing, as well as hemorheological tests, which come as close as possible to the in vivo situation.

In 1982 it was pointed out by Witte [9] that the processes involved in capillary (or vascular) permeability included those which occur within the interstitial space, across the parenchymal cell membrane in the lymph. Witte proposed to call these processes the "inner circulation." I fully concur with Witte that the field of clinical hemorheology must also deal with this inner circulation. Modern clinical hemorheology will, therefore, need to be extended to include the rheology of the interstitial spaces, their contents, parenchymal cell membranes, the lymph, lymphatics, and its walls. "Perihemorheology" was introduced by me, at the Siena Conference, as a new term to designate the above extension of clinical hemorheology. As I emphasized, perihemorheology has already a long history in medicine and, as in the case of modern clinical hemorheology, modern clinical perihemorheology will play a significant role in the future. One of its important practices will be perihemorheological therapy [10, 11].

This book is a courageous effort by the author to acquaint the physician and surgeon with many drugs in the management of circulatory disorders and diseases. As a first book on the subject, it cannot yet deal with a number of aspects of clinical hemorheology pertaining to the vessel wall, referred to above. This is in great part also due to the paucity of clinical investigations and of reliable methods of testing, thus far available, of the vascular portion of the vessel-blood organ.

*Therapeutic Hemorheology* will be greatly appreciated by clinicians and surgeons as a guide for further exploration of the growing field of clinical hemorheology. I applaud Albrecht Ehrly in presenting his book to the practitioners and specialists in the different branches of medicine and surgery. I feel confident that the book will prove as a stimulus to continued clinical investigation and to clinical evaluations of drugs in the management of the diseases and pathological conditions affecting the vessel-blood organ.

**References**


New York, NY (USA)  

Alfred L. Copley
As one of the co-founders of clinical hemorheology at an international level, especially with regard to its therapeutic aspects, Albrecht Ehrly has undertaken the enormous and very successful task of bringing intellectual and factual order into this clinical area which is steadily increasing in significance. It is even more to his credit since especially the therapy of hemorheologic diseases is in a complex state of development. There are still great gaps between its theoretic basis and its practical application, even though the material available both on the research and clinical levels is immense.

It is easy to deal with terminology and facts that are already backed by a historic development of their own. However, especially in clinical hemorheology, the relationship between the clinical and therapeutic aspects is undergoing a highly active exchange. The trends are very evident but the final product cannot as yet be foreseen.

The principle of organization chosen by the author of *Therapeutic Hemorheology* was based on the fact that, with growing clinical experience, the clinicians are confronted on the one hand with a constantly increasing number of pathologic hemorheologic cases requiring therapy, yet on the other hand therapeutic measures in general and treatment with medications in particular often only indirectly show a certain logic of procedure. For here neither the understanding of pathogenesis and the cause of disease can be easily brought to a common denominator, nor can an immediate conclusion be drawn from this constellation as to the necessary medicinal effect. The declarations of drug manufacturers as to the rheologic efficacy of medications as well as to the cause of this efficacy often have only a very indirect relationship to the therapeutic effect achieved. In the extreme case, nothing of what is said to be the mode of action of a drug holds true, despite the fact that the positive effect is, as expected, perhaps even better.

While the clinical impression of a therapeutic effect is of primary importance, particular significance must be attached to a therapeutic control such as measuring the blood flow properties. This has always been a special concern on the part of the author which, especially in the Federal Republic of Germany, has given him the reputation of a critical therapist of the first order. At a time when this science is only in its adolescence, it takes creative courage to present the reader not only with informative but also with a constructive insight on the clinical aspect in particular. The incoherence still existing between theory and practice allowed Albrecht Ehrly to formulate the idea that, contrary to the customary way up to then, practice should not be primarily led by theory. He has accepted the principle of the ex juvantibus therapy deliberately. With the change-over from the inductive to the deductive mode of knowledge, he utilizes the facts of pharmacology in this science by not starting out from the effects which can be theoretically expected, but rather proceeding in a critical and comparative manner from the effects experienced in practice. This is a method that leads to a modus vivendi, i.e., a concrete therapeutic tool for the practitioner. Without this, the urgently needed expansion of an aspect of medicine that up to now has been under-represented cannot be achieved.
This book is primarily directed at an extensive target group of clinicians and practitioners. Its niveau, which is beyond that achieved within this framework up to now, also addresses the relevant specialists, the angiologists, the intensive care clinicians, the hematologists and anesthesiologists, as well as pharmacologists and pathophysiologists. They are offered a critical evaluation of all the therapeutic possibilities known within the rheologic frame up to now. In addition, each section is presented with a well-founded commentary that also makes the study of this realistic guide to hemorheologic therapeutic activity a useful and lasting enjoyment for all readers.

Kaiserslautern

Hellmut Hartert
Preface

Therapeutic measures to improve the flow properties of blood (hemorheologic therapy) have become increasingly important since their tentative beginnings about 80 years ago. Nowadays, drugs which have or should have a beneficial effect on the flow properties of blood are being used more and more and are being administered in a large number of diseases and groups of diseases, in particular vascular disorders. Accordingly, in the last few years reports on the research and application of such therapeutic measures have been increasing in the relevant literature and at congresses on clinical hemorheology. This book was written because, on the one hand, a detailed study of this aspect of clinical hemorheology had not existed before and, on the other hand, the interest of clinicians and general practitioners in this field has increased considerably. The author feels competent to present this study not only because of his extensive experimental research in the field of hemorheology, but also more importantly, because he is a therapist.

During the time when I was taking my first steps in the field of hemorheology in 1962 — supported by my colleagues F. Gramlich and H. E. Müller in Mainz — there was neither a “school” nor a “teacher” of hemorheology or clinical hemorheology in Germany. So I had to rely on publications by Bayliss, Copley, Dintenfass, Fahraeus, Gelin, Gregersen, Merrill, Scott-Blair, Wells, etc. — scientists whom, for the most part, I did not get to know until 1966 at the first International Congress on Biorheology at Reykjavik, Iceland and for whose fundamental studies I am greatly indebted. At about this time, I also became acquainted with two German physiologists, Peter Gaethgens und Holger Schmid-Schönbein, who were beginning to do work on experimental hemorheology. As an angiologist I greatly profited from the, in part, controversial discussions to add impetus to my more pathophysiologic and clinically oriented research. The same applies to many other colleagues of that time, such as J. P. Barras, D. Braasch, A. L. Copley, S. Chien, J. Ditzel, H. Meiselman, Y. Isogai, G. V. F. Seaman, and T. Somer, to mention only a few.

In the following years, clinical hemorheology and, as a result, hemorheologic therapy continued to develop, especially after clinical practitioners also increasingly discussed the significance of hemorheologic factors with regard to prevention, diagnosis, pathogenesis, pathophysiology, and therapy of diseases. The increasing significance of the hemorheologic therapy of diseases must, therefore, be seen as a logical consequence based on the knowledge already acquired in the fields of hemorheology, biorheology, and especially clinical hemorheology. It must be pointed out that it is not the goal of this book to compile or comment on clinical studies or individual studies on the question of the clinical efficacy of hemorheologic therapy in patients (see Sect. 2.2.1).

In this book on therapeutic hemorheology, the attempt was made to collect and comment on as high a percentage as possible of the literature of those publications in which hemorheologic changes were found within the framework of therapeutic measures and in which a connection with the therapeutic goal was assumed. I am nevertheless aware
that owing to the wide distribution of scientific contributions to Therapeutic Hemorheology, I have inevitably left out some thematically relevant publications. I would be very grateful if these authors or the readers of this book would point out such missing contributions to me.

I would also like to take this opportunity to thank all my co-workers for their assistance with this book. Special thanks are due to Dr. Winfried Volkmann who, for the purposes of his dissertation, accomplished the great task of compiling the literature, as well as to Dr. J. Schenk and Dr. R. Dehn.

Prof. A. L. Copley and Prof. H. Hartert, both pioneers in biorheology and hemorheology, have both agreed to write a foreword to this book. I would like to take this opportunity to express my sincere gratitude to my friends Alfred and Hellmut for performing this task.

Frankfurt, September 1991

A. M. Ehrly
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