Leopold Dintenfass

BLOOD MICRORHEOLOGY

VISCOSITY FACTORS IN BLOOD FLOW, ISCHAEMIA AND THROMBOSIS

Blood Microrheology–

Viscosity Factors in Blood Flow, Ischaemia and Thrombosis

Leopold Dintenfass

PH.D., M.SC., F.R.A.C.I., M.I.E. AUST.

Senior Research Fellow, Department of Medicine, University of Sydney, Sydney, Australia; Honorary Senior Research Fellow, Kanematsu Memorial Institute, Sydney Hospital, Sydney, Australia; Honorary Consulting Biorheologist, and Head of Biorheology and Haemorheology Unit, Sydney Hospital, Sydney Australia; Honorary Consulting Rheologist, Children's Medical Research Foundation, Sydney, Australia; Commonwealth Visiting Professor to the University of Strathclyde (1970/71) and Senior Research Fellow, Glasgow Royal Infirmary (1970/71), Glasgow, Scotland

LONDON: BUTTERWORTHS

ENGLAND: BUTTERWORTH & CO. (PUBLISHERS) LTD.
LONDON: 88 Kingsway, WC2B 6AB

AUSTRALIA: BUTTERWORTH & CO. (AUSTRALIA) LTD.
SYDNEY: 586 Pacific Highway, 2067
MELBOURNE: 343 Little Collins Street, 3000
BRISBANE: 240 Queen Street, 4000

CANADA: BUTTERWORTH & CO. (CANADA) LTD.
TORONTO: 14 Curity Avenue, 374

NEW ZEALAND: BUTTERWORTH & CO. (NEW ZEALAND) LTD.
WELLINGTON: 26–28 Waring Taylor Street, 1
AUCKLAND: 35 High Street, 1

SOUTH AFRICA BUTTERWORTH & CO. (SOUTH AFRICA) (PTY.) LTD.
DURBAN: 152–154 Gale Street

Suggested UDC Number: 612·117·2

Suggested Additonal Numbers: 616·151·5
616–005·4
616–005·6

ISBN 0 407 118 50 0

Printed by Redwood Press Ltd., Trowbridge & London.

Preface

My purpose in writing this book has been to bring together information on blood rheology and rheological factors in coagulation and tissue perfusion which would be essential to clinicians and medical workers studying the causes of circulatory diseases – on the one hand – and which would be essential for engineers, physical chemists and rheologists who enter this field and want to apply concepts of the more developed sciences to the so complex problems of medicine, on the other.

In effect, I rather consider medicine more akin to engineering than science. The medical worker and biologist are, as engineers, more concerned with the ways in which things happen than with the more abstract theorems. Systems are studied generally as a whole and isolation of individual fragments of more complex processes is either impossible or very difficult.

Nevertheless an attempt is made to isolate certain rheological processes and then combine them in order to explain the functions of the whole. Neither this attempt, nor the ones which will follow it, can be expected to supply the whole truth.

The field of haemorheology started only after the Second World War, although some of the thoughts, concepts and experiments in this field are centuries old. As in all new fields, this field also had its false starts and cul-de-sacs, but progressed with enormous rapidity. From a handful of investigators in the early 1960s, the number of students and scientists in this field increased to many hundreds in the late 1960s.

But due exactly to the youthfulness of this field, it is difficult to prepare a textbook. By necessity and inclination, this book is woven around the studies in my laboratories at Sydney Hospital and at the Department of Medicine, University of Sydney, Australia.

This book contains an outline of the microrheology of blood and blood cells, an outline of blood coagulation and rheological features in a number of circulatory and haematological disorders. It gives a tentative approach to rheologically based differential diagnosis.

The bibliography is not exhaustive, but includes enough references from the field of rheology, blood coagulation, physiology and pathology of circulatory disorders to serve as a primer.

It was my intention to show haematologists and physicians that the rheological approach permits a better understanding of the mechanisms and aetiologies of the vascular diseases and that it should become of value in preventive and predictive medicine.

Occlusive vascular disease, when considered in terms of total incidence rather than separated according to organ involvement, is the leading health hazard according to S. Sherry (1969). There is no common single pathway. The multiple pathogenetic mechanism of thrombosis might be due in part to the multiple rheological mechanisms of blood viscosity and dynamic blood coagulation.

The rheological approach, based on the viewpoint of molecular physics and colloid chemistry, should not only bring a new insight into the complex aetiologies and symptoms of cardiovascular diseases, but by its inclusion into the methods of clinical medicine, might lead to the enrichment of the rational medicine.

Indications are that the clinical sciences and medicine will become intimately connected with, and crucially dependent on collaboration with scientists and engineers. Indications are that scientists and engineers find more and more challenge and scope in the studies of biology. While the field of surgery might have been first in obtaining the benefits of such collaborations through artificial kidneys, artificial heart or heart valves, or surgical implants of other natures, the field of medicine's turn is now coming.

But the impact of science and engineering on medicine is not, and is not going to be, a one-way street. On the contrary, the challenge presented by the complexity of the living matter results in a development of new scientific concepts, and requires, indeed, an elaboration of old and a formation of new theories and techniques in physics, rheology, and colloid chemistry.

In a similar manner, as the study of pathological states promotes an understanding of the normal states in medicine, so perhaps a study of the living matter will promote new developments in many aspects of the non-biological rheology and engineering.

L.D.

Foresight

At the time I started my studies in blood rheology, in 1961, and in some years to follow, I was told repeatedly by Australian and American experts that blood viscosity cannot be studied, that blood viscosity has nothing to do with blood flow or blood circulation, and that viscosity has nothing to do with disease. During one of my travels in the United States of America I came across various mottos pinned to the laboratory blackboard. These two illustrate well the mood and the spirit of things:

'As far as sinking a ship with a bomb is
concerned, you just can't do it.'

Rear-admiral Clark Woodward, 1939

'That is the biggest fool thing we have ever
done. The (atomic) bomb will never go off, and
I speak as an expert in explosives.'

Admiral William Leahy, 1945

Acknowledgements

This work was a result of a series of more or less accidental events in my life: earlier, study of rheology of suspensions, and later, in 1961, an enticement to the Surgical Research Unit of Sydney Hospital by Mr. B. Bloch, Honorary Surgeon. Very shortly I moved (as a Senior Research Fellow) to the Department of Medicine, University of Sydney, where the Chairman of the Department, Professor C.R.B. Blackburn, gave me an entirely free hand in the organization of a haemorheological laboratory, for which I am most grateful. I am indebted for his most helpful support to Professor J. Loewenthal, Professor of Surgery and Dean of the Faculty of Medicine, University of Sydney.

The Board of Sydney Hospital took an important step in 1963 in appointing me the Honorary Consulting Biorheologist, with all its rights and privileges, and especially the access to hospital wards. I appreciated greatly being accepted to the Honorary Medical Officers body, the Medical Board, and the help, assistance and advice of its members, which followed.

I am greatly indebted to my medical collaborators who, each in his own field, and over different time periods of my study, enlightened me and helped to expand my horizons. In chronological order, from 1962 until today, my thanks go to Dr. Desmond Julian, Cardiologist (now at Edinburgh Royal Infirmary); Dr. G. Miller, at the time a Research Fellow in Cardiology (Sydney Hospital); Dr. M. Rozenberg, at the time a Research Fellow in thrombosis at the Clinical Research Unit of the Royal Prince Alfred Hospital, and now Chief of Haematology at Prince Henry Hospital, Sydney; Dr. Peter Castaldi, then the Head of the Haemophilia Clinic at the Royal Prince Alfred Hospital and now at Austen Hospital, Heidelberg, Victoria; Dr. Eric Burnard, paediatrician and Senior Research Fellow at the Women's Hospital (Crown Street, Sydney); Dr. John Yu, at the time a Research Fellow.

However, my special thanks go to Dr. Alan Sharp, Honorary Surgeon and senior member of the Peripheral Vascular Clinic, Sydney Hospital; to Dr. Gaston E. Bauer, Honorary Cardiologist, Cardiovascular Clinic, Sydney Hospital; to Dr. John Stewart, Renal Physician, Kanematsu

Institute; and to Professor John Read, Respiratory Physician and Professor of Medicine, Sydney Hospital and the University of Sydney.

My thanks go to Dr. A.A. Palmer, earlier a Senior Research Fellow, and now the Deputy Director of Kanematsu Memorial Institute, for his advice and assistance, specially during the first, formative years of this study; and to a number of residents, sisters, nurses and technicians of Sydney Hospital who assisted in different ways.

I was fortunate to have support in establishing, in 1965, the first ever Biorheology and Haemorheology Unit at the Sydney Hospital (on the premises of the Kanematsu Institute), and my thanks go to the Chief Executive Officer, Mr. H.R. Beer, and to the Superintendents of the Hospital, as well as to the Sydney Hospital Research Fund. Support of the two Directors of the Kanematsu Institute, Dr. Malcolm Whyte (who left in 1967 for the Australian National University) and Dr. Fred Gunz, was most appreciated.

I was very fortunate to have the support of the National Heart Foundation of Australia, and I am especially grateful to Dr. Ralph Reader, Medical Director of this Foundation, for his steadfast support in face of much opposition.

I am grateful for the trust shown to me by such appointments as Honorary Senior Research Fellow of the Kanematsu Institute, Honorary Rheologist of the Children's Medical Research Foundation, and election to the Cardiac Society of Australia and New Zealand, and for the membership to a number of other societies in medical research.

This was first time ever that a rheologist *cum* physical chemist *cum* chemical engineer achieved such support in medical circles and this support was freely given by way of understanding the requirement, if not the necessity, for the development of a new branch of medicine – Clinical Haemorheology.

And last, but not least, my thanks go to Irene, my wife – not only for her help in preparation of this manuscript, but for her patience over so many years when all my efforts were concentrated on studies and research, and for her trust, assurance and moral support.

Acknowledgements are due to Drs. Robert Haynes, S.G. Mason, H. Goldsmith, and G. Farrer-Brown for permission to use their figures (respectively, two, one, and two), and to the respective publishers or editors of the Journal of Applied Physiology, Rheology and Cardiovascular Research. Acknowledgements are due to Drs. Dennis Halmagyi, Allan Palmer and Joe Still for permission to use their figures (one, two and two, respectively). I have utilized a number of my figures published previously, although many of them were redrawn, and also many entirely new figures.

Assistance of the Photography Departments of the University of Sydney, and of the Sydney Hospital, is here acknowledged.

L. D.

Contents

1. Introduction

AIMS, QUESTIONS, POSSIBILITIES: WHY RHEOLOGY?

Our life depends on the flow of blood. As long as blood circulates, the natural defence of our bodies can take care of a number of types of injuries; but once blood flow becomes sluggish, once the flow stops, the natural defence is breached and only external help – even if available – might reverse the deadly process.

In our circulation blood flows through a series of vessels, first of diminishing and then of increasing diameters. In the enormous network of capillaries, blood flows through the tissues bringing nourishment and taking away metabolites. Water, electrolytes, oxygen, proteins, lipids and so on are continuously exchanged between the blood and the tissues. The vascular system serves for the irrigation and collection of refuse. It serves also as a highway for the transit of cells and chemical agents required for the defence of integrity of the circulation.

But something can go wrong; and today, in the western world, nearly half of the adult male population dies from ischaemia, infarction and thrombosis. The studies of the pathogenesis of cardiovascular diseases attracted many able investigators; the biochemistry and histology have been studied; great attention was paid to the blood driving pressures and to the nature and bore of the vessels. Yet at the same time, the role of the fluid which this pressure has to drive through the vessels was neglected. It has been assumed by many – in such a convenient way – that blood flows like water. Even in some 'haemodynamic' experiments workers used water; it was cleaner to work with than blood.

These studies continued in this manner, notwithstanding the directions given by Virchow (1856) more than a century ago, that a triad of factors responsible for thrombosis includes (1) alteration in blood content, (2) alteration in blood flow, and (3) alteration in the vessel wall. Only during the most recent years have such aspects as the viscosity of blood, aggregation of blood cells, or effect of flow velocity on blood viscosity and blood coagulation been seriously considered.

Blood is not like water. It is more like a gel-paint which, when standing, is rather like a blob of solid gel, but when stirred becomes fluid like water. The effect of deformability and internal fluidity of the single blood cell is paramount in the flow through narrow capillaries. The role of the single red cell in the control of the microcirculation has been overlooked and the main attention given to capillary 'collapse', vasodilatation or vasoconstriction. This attitude was understandable as long as one could presume that capillaries can collapse or open depending on the pressure drop existing in the particular areas of the microcirculation. This attitude is not so secure now as it has been shown that capillary walls are relatively rigid, they might behave as 'tunnels' in a rigid matrix and that, on theoretical grounds, capillary collapse is unlikely.

The action of some drugs, purporting a vasodilator action, might be also operative via the effect on the rheology of the red cell, and not so much on the bore of the vessel. The rheology of blood might be thus the most important feature of the stability of circulation. Thus, the tissue perfusion, and not necessarily the blood pressure, might be the criterion of circulation efficiency.

Even greater neglect of rheology is in the field of blood coagulation and actual thrombosis formation. It is rather amazing to review the field of blood coagulation and note that, with few exceptions, the bulk of the studies is carried out in test-tubes, under static conditions. This is amazing, as the obvious point that blood flows and that intravasal coagulation processes must take place under the conditions of flow (even if of very slow flow) is somehow lost or disregarded.

Surely a question could be asked – do the coagulation processes proceed in a similar manner under conditions of flow as under static conditions? Or is the role of coagulation factors or pro-factors affected by the flow of blood and by the velocity and nature of this flow? Or is the significance of the levels of factors or pro-factors found in the test-tube similar or even relevant to the levels of these factors in the flowing blood?

It would appear that the answer, in each case, is yes, and that flow, blood rheology, and dynamic (flow-controlled) blood coagulation are intimately related.

Finally, what is rheology? Rheology is a science of flow and deformation of all matter. It weaves as a common thread through various branches of sciences and technologies, be they of industrial or biological nature. Thus, the basic properties of flow and deformation are common to blood and paint, synovial fluid and polymeric solutions, protoplasm and ink, drilling muds and lubricants, cream and rocket fuel, napalm and bronchial mucus, and so on.