

MICROCIRCULATION

Volume 2

**Transport Mechanisms
Disease States**

Edited by

J. Grayson and W. Zingg

MICROCIRCULATION

Transport Mechanisms

Disease States

2

Edited by

John Grayson and Walter Zingg

*University of Toronto
Toronto, Canada*

PLENUM PRESS · NEW YORK AND LONDON

Library of Congress Cataloging in Publication Data

World Congress for the Microcirculation, 1st, University of Toronto, 1975.
Microcirculation.

Sponsored by the Canadian Society for Microcirculation.

Includes bibliographies and index.

CONTENTS: v. 1. Blood-vessel interactions.—v. 2. Transport Mechanisms.

1. Microcirculation—Congresses. I. Grayson, John. II. Zingg, Walter, 1924-
III. Canadian Society for Microcirculation. IV. Title.

QP106.6.W67 1975

599'.01'1

76-26051

ISBN 0-306-37098-0 (v. 2)

Proceedings of the First World Congress for the Microcirculation held at the University of Toronto, Toronto, Canada, June 15-20, 1975 and sponsored by the Canadian Society for the Microcirculation, published in two volumes, of which this is volume two.

© 1976 Plenum Press, New York
A Division of Plenum Publishing Corporation
227 West 17th Street, New York, N.Y. 10011

All rights reserved

No part of this book may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, microfilming, recording, or otherwise, without written permission from the Publisher

Printed in the United States of America

Preface

The recognition of the microcirculation as an ideal interdisciplinary meeting place for the life sciences is really a postwar phenomenon. The European and the American Societies more than any other organizations launched the idea, and the success of the European Society's International Meetings gave impetus to a growth of interest from a handful of specialists to the wide interdisciplinary study which microcirculation now represents. The meeting held in Canada in June 1975 was, however, the first truly international meeting devoted to the microcirculation. It, too, was a success from every point of view, and the exchange of knowledge and new ideas was rewarding. It is our present hope that the tradition of European meetings with their characteristic European flavor will continue, but larded by larger, international congresses conceived on a worldwide basis.

For the present conference we were fortunate in the presence of Dr. B. Zweifach. He was once referred to as the "father of the microcirculation." This claim, unfortunately, I cannot accept. That honor probably belongs to Harvey, who by one of the most brilliant strokes of inductive reasoning in medical history inferred the existence of capillaries though he could not see them. Ben Zweifach's role was rather that of the midwife, presiding at the birth rather than the conception. The baby he delivered long years ago has since thriven lustily and its growth is in no small measure due to the continuing zeal of Zweifach and his associates.

The present volumes are a record of the proceedings of our recent meeting. They consist in part of the main symposium presentations with the exception of the platelet symposium held in Hamilton. The rest of the volumes consists of brief reports based on the free communications. Most of these describe new work, and their number and quality are perhaps the best testimony of all to the appeal of microcirculation in current medical and life sciences research.

Toronto

J. Grayson

FIRST WORLD CONGRESS FOR THE MICROCIRCULATION

Toronto, June 1975

Symposia Chairmen and Section Editors:

David H. Lewis, *Linköping, Sweden*
James B. Bassingthwaite, *Seattle, Washington*
Harry L. Goldsmith, *Montreal, Canada*
Stanley Rowlands, *Calgary, Canada*
Walter Zingg, *Toronto, Canada*

President of the Canadian Society:

Raymond O. Heimbecker, *London, Ontario, Canada*

Organizing and Coordinating Committee:

Secretary General: Glen A. Taylor, *Toronto, Canada*
Members: Glen A. Taylor, *Toronto, Canada*
Irving H. Koven, *Toronto, Canada*
John Grayson, *Toronto, Canada*
Raymond O. Heimbecker, *London, Ontario, Canada*
Walter Zingg, *Toronto, Canada*
James W. Davidson, *Hamilton, Canada*
Sean Moore, *Hamilton, Canada*
Harry L. Goldsmith, *Montreal, Canada*
Eugene M. Renkin, *Davis, California*
James B. Bassingthwaite, *Seattle, Washington*
Harold J. Wayland, *La Jolla, California*
Adolphe Neetens, *Antwerp, Belgium*
David H. Lewis, *Linköping, Sweden*

Contents

I. Transport Mechanisms in the Microcirculation

1. Capillary Transport and Exchange

1.1.	Introduction	3
	J. B. BASSINGTHWAIGHTE	
1.2.	Endothelia and Epithelia	7
	CHRISTIAN CRONE	
1.3.	Fractional Equilibration of Small Solutes during Transcapillary Passage	11
	EUGENE M. RENKIN	
1.4.	Analytical Approaches to Tracer Exchange	17
	WILLIAM PERL	
1.5.	An Osmotic Weight Transient Model for Estimation of Capillary Transport Parameters in Myocardium	29
	ERIC F. GRABOWSKI and JAMES B. BASSINGTHWAIGHTE	
1.6.	Fluid and Solute Flow across the Walls of Single Capillaries in the Frog Mesentery	51
	C. C. MICHEL, F. E. CURRY, and J. C. MASON	
1.7.	The Extravascular Turnover Rate Constant Estimated from Single Circulation Tracer Dilution Curves as an Index of Cellular Transport	57
	D. L. YUDILEVICH	
1.8.	Effect of the Red Cell Membrane on the Exchange of Materials in the Microcirculation	63
	CARL A. GORESKEY and GLEN G. BACH	
1.9.	Interaction of Aqueous and Lipid Pathways in the Pulmonary Endothelium	71
	FRANCIS P. CHINARD, WILLIAM PERL, and ARTHUR B. RITTER	

1.10.	Capillary Permeability in Some Pathophysiological States JOHN N. DIANA	75
 2. Molecular and Oxygen Transport		
2.1.	Permeability of Arterial Capillary Endothelium . . . PENTTI T. JOKELAINEN, DAVID W. HAACK, and JOHANNES A. G. RHODIN	77
2.2.	Serial Barriers to Blood-Tissue Transport in the Cat Salivary Gland Using Single-Passage Multiple Tracer Dilution D. L. YUDILEVICH and L. H. SMAJE	79
2.3.	A Theoretical Investigation of Fluid Exchange in a Microoccluded Capillary with Axial Variation of Filtration Parameters T. R. BLAKE, J. F. GROSS, and G. P. SCHNEYER	82
2.4.	Effect of Hyaluronidase on Transcapillary Fluid and Solute Exchange in the Isolated Dog Hindlimb . . . JOHN N. DIANA, BERNARD FLEMING, M. HAROLD LAUGHLIN, and MAURICE J. MONTAG	84
2.5.	Transmembrane Ion Transport in Autoperfused Cat Mesentery WALLACE G. FRASHER, JR., and CAROL MARCUS	86
2.6.	Evidence of an Interference in Oxygen Exchange from Erythrocytes to Tissues in Hypertriglyceridemia . . JØRN DITZEL	88
2.7.	O ₂ Transport in the Homogeneous and the Inhomogeneous Microcirculation HERMANN METZGER	90
2.8.	Effect of Elevated Venous Pressure on Intestinal Oxygen Extraction A. P. SHEPHERD	92
2.9.	Effects of Mechanically Increasing Venous Pressure in the Canine Forelimb on Protein Transport during the Local Administration of Histamine and Acetylcholine D. E. DOBBINS, J. B. SCOTT, F. J. HADDY, and G. J. GREGA	94

2.10.	Quantitative Measurement of Macromolecular Transport in Mesenteric Membrane	96
	HAROLD WAYLAND and JAMES R. FOX	
2.11.	Effect of Histamine on Microvascular Macromolecular Transport	98
	JAMES R. FOX, FRANK GALEY, and HAROLD WAYLAND	
2.12.	Regulation of Plasma and Interstitial Albumin: A Theoretical Analysis	100
	D. NEIL GRANGER and AUBREY E. TAYLOR	
2.13.	Transmural Mass Transfer in the Unsteady Microcirculation	104
	JOSEPH F. GROSS and JEROME AROESTY	
2.14.	Transport of Solutes across the Intact Rat Diaphragm .	106
	JEROME S. SCHULTZ	
2.15.	Albumin Permeability of the Renal Peritubular Capillary: The <i>PS</i> Product	109
	J. L. ATKINS, D. R. BELL, J. E. STORK, C. C. C. O'MORCHOE, and G. G. PINTER	

II. Microcirculation in Disease States

3. Effect of Shock on Capillary Transport

3.1.	Transport of Small Molecules	113
	LENNART APPELGREN	
3.2.	Bidirectional Capillary Transport of Small Molecules .	125
	J. B. DAHLBERG and D. H. LEWIS	
3.3.	Oxygen Transport in Shock	133
	K. MESSMER, B. A. KRUMME, and M. KESSLER	
3.4.	The Low Flow State Predisposition of the Venous Microvasculature	143
	G. HAUCK	
3.5.	Tissue-Blood Transport and Metabolism in Canine Adipose Tissue during Hemorrhage and Shock .	152
	SUNE ROSELL	

4. Shock and Microcirculation

- 4.1. Special Features of Disorders of Microcirculation and Transcapillary Exchange during Experimental Shock 163
A. M. CHERNUKH and Y. M. SHTYKHNO
- 4.2. Regional Blood Flow following Traumatic Shock . . . 164
ASRAR B. MALIK, DANIEL J. LOEGERING, JOHN E. KAPLAN, and THOMAS M. SABA
- 4.3. Hemodynamic Response of the Terminal Vasculature in Different Species during Reversible and Irreversible Hemorrhagic Shock 167
ARNOST FRONEK
- 4.4. Energy Factors and Insulin Resistance in Hemorrhagic Shock 169
IRSHAD H. CHAUDRY, MOHAMMED M. SAYEED, and ARTHUR E. BAUE
- 4.5. Quantitation of White Cell Sticking in Hemorrhagic Shock 171
E. ERIKSSON, S. A. WALDMAN, and R. L. REPLOGLE
- 4.6. Microvascular Response to Hemorrhage in the Rat during Nitrous Oxide (N_2O) Relaxant Anesthesia 173
DAVID E. LONGNECKER and NAN M. ROGIER
- 4.7. Microcirculation in the Pathophysiology of Endotoxin Shock 175
HERBERT J. ROBB and CLARENCE M. JABS
- 4.8. Endotoxin-Induced Microcirculatory Disturbances 176
B. URBASCHEK, W. G. FORSSMÄNN, and R. URBASCHEK
- 4.9. Role of Skeletal Muscle Venules in the Response to Endotoxin Shock 179
J. GOLDSTONE and N. H. SANDOW
- 4.10. The Microcirculatory Response to Shock Lung Factor . 182
MORRIS D. KERSTEIN and CHAU VAN DANG
- 4.11. The Microcirculation in Cardiopulmonary Resuscitation 184
HUGH E. STEPHENSON, JR., and HOWARD L. MUSSELL
- 4.12. Effects of Prostaglandins in Endotoxin Shock . . . 191
CLAYTON H. SHATNEY and RICHARD G. LILLEHEI

4.13.	Microcirculatory Approach to the Treatment of Shock Using a New Analogue of Vasopressin	193
	BURTON M. ALTURA	
4.14.	Effects of Synthetic Glucocorticoids on Shock-Induced Alterations in Cyclic Nucleotide Metabolism and Lysosomal Enzyme Release	195
	ROY D. GOLDFARB and THOMAS M. GLENN	
 5. Hypoperfusion, Ischemia, and Graft Rejection		
5.1.	Interstitial Tissue Barrier during Low Flow: Its Correction by Hyaluronidase	197
	IRVING H. KOVEN, KENNETH P. H. PRITZKER, AMY LISWOOD, ROBERT H. STUBBS, and SUE F. LO	
5.2.	Endonasal Granulomata and Hypoperfusion	200
	M. W. KANAN and T. J. RYAN	
5.3.	Factors Influencing Responses of Single Arterioles to Occlusion	202
	JULIAN H. LOMBARD and BRIAN R. DULING	
5.4.	Redistribution of Blood Flow during Cooling and after Total Circulatory Arrest with Profound Hypothermia	204
	L. V. KOCK, A. H. FLASTERSTEIN, M. AOYAGI, and J. H. KENNEDY	
5.5.	Blood Gas Analysis as an Aid in Assessing the Microcirculation in the Ischemic Limb	206
	K. S. CHATTERJEE and D. W. B. JOHNSTON	
5.6.	Microcirculatory Reactions to Controlled Ischemia: A Vital Microscopic Study of Hamster Cheek Pouch . . .	208
	E. MICKAEL ROMANUS	
5.7.	Microvascular Elements of Xenograft Lung Rejection .	210
	K. RICHARDS, J. HAGSTROM, E. J. NAGY, and F. J. VEITH	
5.8.	Microangiography of Rejected Human Kidney Transplants	213
	M. KORMAMO and B. KOCK	
5.9.	The Role of Vasospasm in Experimental Renal Xenograft Rejection	216
	E. J. NAGY, D. H. OSMOND, and G. A. TAYLOR	

- 5.10. Progressive Microvascular Obliteration during Canine Renal Allograft Rejection 219
R. L. CLARK, E. V. STAAB, S. R. MANDEL, and W. P. WEBSTER

6. Trauma and Inflammation

- 6.1. A Model of Peripheral Vascular Disease and Assessment of Wound Healing by Angiographic and Nuclear Medicine Techniques 223
S. M. FISHER, N. D. GREYSON, and E. N. C. MILNE
- 6.2. Pathology of the Capillary Wall: Diagnosis and Therapy 225
F. E. BIRCHER
- 6.3. Potential Role of Prostaglandins in Modulating Vascular Permeability Changes during Inflammation through Local Alterations in Blood Flow (Hyperemia) 227
MILES G. JOHNSTON, JOHN B. HAY, and HENRY Z. MOVAT
- 6.4. An *in Vivo* Quantitative Evaluation of Radiation Damage and Repair to Microcirculation 230
G. S. DIMITRIEVICH, S. L. HAUSLADEN, F. T. KUCHNIR, and M. L. GRIEM
- 6.5. Electron Microscopic Findings in the Microvessel Wall Affected by Venom of the Snake *Trimeresurus flavoviridis* 232
M. TSUCHIYA, Y. FUJISHIRO, C. OHSHIO, M. OHASSHI, and A. OHSAKA
- 6.6. *In Vivo* Skin Capillary Abnormalities in Vinyl Chloride Workers 235
H. R. MARICQ, M. N. JOHNSON, C. L. WHETSTONE, and E. C. LEROY
- 6.7. Vascular Function in a Hamster Cervical Carcinoma following X-Irradiation 238
HUBERT A. EDDY
- 6.8. Role of Tissue Fluid Hyperosmolality: The Pathogenesis of Posttraumatic Fluid Loss 240
R. A. LITTLE
- 6.9. Albumin Compartmental Changes Secondary to Sepsis 241
MAXIMO DEYSINE, NEIL LIEBLICH, SAUNDERS STEIN, RICHARD SHANNON, MARCUS ROTHSCHILD, and ARTHUR H. AUFSES, JR.

6.10.	Elevation of Plasma Lysosomal Enzyme Levels after Trauma in Association with Impairment of Hepatic Reticuloendothelial Function	242
	DANIEL J. LOEGERING, JOHN E. KAPLAN, and THOMAS M. SABA	
6.11.	Fibrinolytic Activity in the Lungs following Trauma	244
	B. RISBERG and H.-I. PETERSON	
6.12.	Platelet Function and Severe Head Injury	246
	C. J. VECHT and C. T. SMIT SIBINGA	
6.13.	Disseminated Intravascular Coagulation and Head Injury	249
	C. T. SMIT SIBINGA and C. J. VECHT	

7. Diabetic Angiopathy

7.1.	Diabetic Nephropathy: Form and Function	253
	KNUD LUNDBAEK	
7.2.	The Problem of Tissue Oxygenation in Diabetes Mellitus as Related to the Development of Diabetic Angiopathy	263
	JØRN DITZEL	
7.3.	The Morphology of Angiopathy	275
	JOSEPH R. WILLIAMSON and CHARLES KILO	
7.4.	The Chemistry of Angiopathy	281
	W. CARL BRECKENRIDGE	
7.5.	Comments	291
	ROBERT F. BRADLEY	

8. Diabetes and Microcirculation

8.1.	Hemorheological Changes in Diabetes Mellitus	295
	E. VOLGER, H. SCHMID-SCHÖNBEIN, and H. MEHNERT	
8.2.	Quantitative Studies of von Willebrand Factor (VWF) in Normal and Diabetic Subjects: Role of VWF in Second-Phase Platelet Aggregation	296
	K. E. SARJI, H. B. SCHRAIBMAN, A. L. CHAMBERS, R. M. G. NAIR, and J. A. COLWELL	
8.3.	Capillaries of Israeli Diabetics: I	298
	R. E. YODAIKEN, L. YANKO, H. B. HERMAN, and E. DAVIS	

8.4.	Cutaneous Microangiopathy in Prediabetes, Chemical Diabetes, and Overt Diabetes	300
	L. R. ROUEN, R. A. CAMERINI-DAVALOS, E. N. TERRY, and W. REDISCH	
8.5.	Microscars: A Manifestation of Diabetic Microangiopathy	302
	E. N. TERRY, R. CAMERINI-DAVALOS, R. CLAUSS, L. ROUEN, and W. REDISCH	
8.6.	Quantitative Studies of the Retinal Circulation in Juvenile Diabetic Retinopathy	304
	IAIN STUART BEGG and WAH JUN TZE	
8.7.	Abnormal Red Cell Aggregation in Diabetic Retinopathy	306
	ALVIN H. SACKS and HUNTER L. LITTLE	
8.8.	Insulin Response in Patients on Intravenous Hyperalimentation	309
	MERVYN DEITEL and IAN SANDERSON	
8.9.	Osmolality of Hyperalimentation Solution in Superior Vena Cava	311
	MERVYN DEITEL, VICTOR KAMINSKY, and PARVESH ANAND	
8.10.	Effect of Aprotinin on the Pancreas of the Rat after Temporary Ischemia: Light and Electron Microscopic Investigations	313
	G. SCHNELLS, H. FLENKER, and W.-H. VOIGT	
8.11.	Diabetic Retinopathy: A Challenge to Treatment	316
	A. NEETENS and D. BADANIOVA	
 9. Tumors, Cancer, and Muscular Dystrophy		
9.1.	Laser-Induced Microvascular Injury and Tumor-Cell Lodgement	321
	A. M. CHERNUKH and V. S. SHINKARENKO	
9.2.	Effects of Epinephrine on Increasing Arterial Perfusion of Experimental Liver Metastases	323
	NORMAN B. ACKERMAN	
9.3.	Changes in Intrahepatic Tumor Circulation Due to Increasing Tumor Growth	325
	NORMAN B. ACKERMAN	

9.4.	Unusual Localization of Kaposi's Sarcoma with Histological and Electron Microscopic Findings	327
	HERBERT F. HABERMAN and ANDREW PAWLOWSKI	
9.5.	Alterations in the Microvasculature of Various Tissues in Murine Muscular Dystrophy	330
	HEATHER R. STEPHENS and EDMUND B. SANDBORN	
10. Blood Pressure and Hypertension		
10.1.	Ultrastructure of Arteriolar Nephropathy in Hypertension	333
	ANIL KUMAR MANDAL, EDWARD DAVID FROHLICH, KATERINA CHRYSAANT, JOHN AUGUST NORDQUIST, and ROBERT CARL MUEHRCKE	
10.2.	Microvascular Characteristics in the Renovascular Hypertensive Rat	335
	DAVID L. WIEGMAN, PATRICK D. HARRIS, FREDERICK N. MILLER, and MICHAEL J. DEVANEY	
10.3.	Elastosis of Renal Arterioles in Hypertension	338
	ANIL KUMAR MANDAL, EDWARD DAVID FROHLICH, KATERINA CHRYSAANT, STEVEN CHRYSAANT, and JOHN AUGUST NORDQUIST	
10.4.	On the Nature of Human Activatable Renin	340
	G. E. MURRAY and D. H. OSMOND	
10.5.	Effects of Acute Hypertension on Pial Microcirculation in Rats	343
	TOSHIMI SUZUKI, SHIRO TOMINAGA, and TAKASHI NAKAMURA	
10.6.	Microvascular Effects of Propranolol in the Spontaneously Hypertensive Rat	344
	P. M. HUTCHINS and A. W. GREENE	
10.7.	Inhibition of Actions of the Fungal Protease Brinolase on the Vasopeptide (Kinin) System	346
	HARVEY J. FREEDMAN, HANS J. WILKENS, and NATHAN BACK	
10.8.	Kininogen and Kininase Activity in Patients with Acute Myocardial Infarction	349
	KEIICHI HASHIMOTO, JOSEPH WANKA, ROBERT M. KOHN, HANS J. WILKENS, ROBERT STEGER, and NATHAN BACK	
	Index	353

I

Transport Mechanisms in the Microcirculation

Capillary Transport and Exchange

1.1. Introduction

J. B. BASSINGTHWAIGHTE

This symposium represents one of several rapidly developing areas of research concerning the microcirculation. The particular topic, "Capillary Transport and Exchange," is certainly not at all new, as can be seen from Professor Crone's fine review (Crone, 1974), written 100 years after August Krogh's birth. At the 1969 Benzon Foundation Symposium (Crone and Lassen, 1970) held at the Royal Danish Academy of Sciences and Letters, much of the groundwork for today's session was laid, and deep discussion of the quantitative aspects of capillary-tissue exchange was the order of the day. Now, in the papers to be presented, we attempt to review the work of the intervening years.

The symposium is focused on two approaches to the estimation of the permeability of capillaries to small hydrophilic solute molecules, the extraction of tracer-labeled solutes and the induction of water shifts by changing of the osmolarity of a perfusate. In theory, both osmotic and tracer techniques should provide the same estimates for the permeability and reflection coefficient of a given solute for a given capillary membrane. The conundrum posed by the published data is that the osmotic techniques have given higher estimates of permeability *and* higher estimates of reflection coefficients, implying smaller pores or slits, than estimates obtained by tracer techniques. Clearly, modifications of the techniques of experimentation or analysis are required to resolve the disparity, and although some explicit attempts have been made using the two techniques

J. B. BASSINGTHWAIGHTE · Department of Physiology and Biophysics, Mayo Graduate School of Medicine, Rochester, Minnesota 55901. Present address: Center for Bioengineering, University of Washington School of Medicine, Seattle, Washington 98105.