

87-11488

Gastro-intestinal Mucosal Blood Flow

Editor

L. Peter Fielding

Foreword by Eugene D. Jacobson



Churchill Livingstone

Gastro-intestinal Mucosal Blood Flow

Edited by

L.P. Fielding MB FRCS

*Assistant Director, Academic Surgical Unit,
St. Mary's Hospital Medical School, London*

Foreword by

Eugene D. Jacobson MD

*Associate Dean, College of Medicine,
University of Cincinnati, Ohio*



CHURCHILL LIVINGSTONE

EDINBURGH LONDON AND NEW YORK 1980

CHURCHILL LIVINGSTONE

Medical Division of the Longman Group Limited

Distributed in the United States of America by
Churchill Livingstone Inc., 19 West 44th Street, New York,
N.Y. 10036, and by associated companies,
branches and representatives throughout
the world.

© Longman Group Limited 1980

All rights reserved. No part of this publication
may be reproduced, stored in a retrieval system,
or transmitted in any form or by any means,
electronic, mechanical, photocopying, recording
or otherwise, without the prior permission of the
publishers (Churchill Livingstone, Robert Stevenson
House, 1 – 3 Baxter's Place, Leith Walk,
Edinburgh, EH1 3AF).

First published 1980

ISBN 0 443 02119 8

British Library Cataloguing in Publication Data

Workshop on Gastro-intestinal Mucosal Blood Flow

Gastro-intestinal mucosal blood flow.

1. Digestive organs – Blood-vessels – Congresses

2. Mucous membrane – Congresses

3. Regional blood flow – Congresses

I. Title II. Fielding, L Peter

612'.33 QP108.5.D/ 79.41820

Printed in Great Britain by Bell and Bain Ltd., Glasgow

Gastro-intestinal Mucosal Blood Flow



*The Late Dr Pamela Holton, BA. D.Phil.
Reader in Physiology, St Mary's
Hospital Medical School
(13.8.23 to 19.3.77)*

Foreword

Advances in our understanding of physiological processes depend mostly upon the emergence of unique ideas which can be tested by conventional methods or upon the development of new techniques to test established ideas. The major bottleneck to better comprehension of the mucosal circulation of stomach and gut two decades ago was the lack of quantifiable methods for estimating that blood flow. In the mid-sixties new methods were applied successfully to the measurement of gastrointestinal mucosal blood flow under a variety of circumstances. These included determination of the clearance of weak bases such as aminopyrine and aniline in the stomach, the clearance of radiolabelled noble gases and other elements in the intestine, and the clearance of microspheres in the gut and stomach. Questions of physiological and pathophysiological import which could then be addressed more meaningfully included:

Are gastric secretion and mucosal blood flow interrelated?

If so, in what ways?

Is there a role of this circulation in protecting the mucosa of either stomach or gut against topical or systemic stresses which destroy the integrity of the enteric lining?

What mechanisms connect absorptive, motor and secretory events in the intestine to its circulation?

Does the circulation play an aetiological role in mucosal ulceration and in non-occlusive ischaemia of the gut?

Explorations of the past decade also uncovered limitations in the aforementioned techniques which have prompted more sceptical interpretations of results and have stimulated development of more discreet methods. Use of clearance alone has not elucidated much about the mucosal microcirculation or the passage of oxygen from capillary to cell. Nor have these techniques allowed much localisation of vulnerable sites in the mucosa to ulceration, shock or ischaemic necrosis. It will require more sophisticated approaches than we currently possess to link the circulation to such exciting mysteries about the mucosa as 'cytoprotection' and the 'barrier', let alone more established electrophysiological and metabolic mechanisms of the mucosa. Understanding control of the mucosal microcirculation by endogenous vasoactive materials such as histamine, cyclic nucleotides, prostaglandins, and polypeptides will require a new generation of techniques.

The last great international meeting which concerned itself with the gastrointestinal circulation occurred in the mid-sixties in the middle of a new flurry of

research into the subject. The current proceedings constitute another mile-stone to mark the record of accelerating investigation into that circulation.

1980

Eugene D Jacobson

Preface

Clinicians, physiologists, pharmacologists, an anatomist and even a 'pure' mathematician joined for two days to take part in this Workshop on Gastro-intestinal Mucosal Blood Flow. To closet forty people from ten countries, of such widely different professional expertise in a quiet backwater of the English countryside to present data and to discuss and generate new ideas was, for the St Mary's Group, an experiment in itself. Like most experiments the results can be interpreted in a number of ways. From the point of view of the organising group (Stephen Knight, Richard McIsaac and myself) it was a success in that we learned much about our subject and also about the organisation of such a meeting. From the delegates' point of view, the exercise seemed to be of value in that they spent so freely of their time, concentrated during prolonged and detailed debates, and provided their contributions for publication.

However, it is to Pamela Holton, the late Reader in Physiology at St Mary's Hospital Medical School, London, that our gratitude must be directed. It was Pamela's insight and understanding of the subject which laid the foundations for our current work which in turn led us to arrange the Symposium. At the opening of the meeting, Pamela Holton's contribution to her profession and family was described; eloquent and sensitive, Dr Harold Edwards, Dean of St Mary's Medical School, paid her tribute and for this I thank him. Professor Hugh Dudley introduced the Workshop, with characteristic clarity, hoping that it would be a 'benchmark' setting the background for future experiments and clinical study into the nature of Gastro-intestinal Mucosal Blood Flow and its relationship to other physiological processes in health and disease.

As always, there are many people to thank: Rosemary Hittinger and Mark Flannery, for their help in running the meeting; Christine Terry, for expert secretarial assistance in the preparation of the volume; my wife, Jennifer, for tolerating the absentmindedness of her husband; the agencies which gave financial support so generously; and the publishers who have been courteous and helpful at all times.

However, my greatest thanks are to the delegates, particularly the Chairmen and Speakers, whose efforts have made possible the publication of this volume.

Acknowledgements

We are grateful for the generous financial support received from:

BLAT - Centre for Health and Education, BMA House, London

British Journal of Surgery Society Ltd., The Royal College of Surgeons, 35–43
Lincoln's Inn Fields, London

Cambmac Instruments Ltd., Cambridge Road, Milton, Cambridge

Department of Health and Social Security, Alexander Fleming House, Elephant
and Castle, London

Downs Surgical Ltd., Church Path, Mitcham, Surrey

Duphar Laboratories Ltd., West End, Southampton

Glaxo-Allenbury's Research, Ware, Hertfordshire

Lipha (UK) Ltd., Old Farm Road, West Drayton, Middlesex

St Mary's Hospital Special Trustees, St Mary's Hospital, Praed Street, London

Smith, Kline and French Institute and Smith, Kline and French Research, Welwyn
Garden City, Hertfordshire

Tillot's Laboratory, Henlow Trading Estate, Henlow, Bedfordshire

The Wellcome Foundation Ltd., 183 Euston Road, London

Contributors and chairmen

J. Hugh Baron, Department of Surgery, Royal Postgraduate Medical School, Hammersmith Hospital, London

Alan Bennett, Surgical Unit, King's College Hospital, Denmark Hill, London

John G. Bowen III, Department of General Surgery, Ochsner Clinic, New Orleans, Louisiana

David C. Carter, Department of Surgery, Royal Infirmary, Glasgow

Laurence Y. Cheung, Department of Surgery, Barnes and Wohl Hospitals, St Louis, Missouri

Michael J. Daly, Department of Pharmacology, Glaxo-Allenburys Research, Hertfordshire

Marcus C. Dugas, Department of Medicine, University of Pittsburgh School of Medicine, Pennsylvania

Douglas G. Gilmour, Department of Peripheral Vascular Surgery, Royal Infirmary, Glasgow

Paul H. Guth, Department of Gastroenterology, Cure, Veterans Administration, Wadsworth Hospital, Los Angeles, California

Lars E. Ivarsson, Department of Surgery, University of Goteborg, Ostra Sjukhuset, Goteborg

Gordon Kauffman, VA Wadsworth Hospital Centre, Los Angeles, California

Stephen E. Knight, Academic Surgical Unit, St Mary's Hospital Medical School, London

Stanislav J. Konturek, Institute of Physiology, Nicolaus Copernicus Academy of Medicine, Krakow

H.J. Lewi, Department of Surgery, Royal Infirmary, Glasgow

Ove Lundgren, Department of Physiology, University of Gothenburg, Gothenburg

Richard L. McIsaac, Department of Physiology, St Mary's Hospital Medical School, London

Frank G. Moody, Department of Surgery, College of Medicine, The University of Utah, Salt Lake City, Utah

David A.A. Owen, The Research Institute, Smith, Kline and French Laboratories Limited, Welwyn Garden City, Hertfordshire

Kristopher Piasecki, Department of Anatomy, The Royal Free Hospital School of Medicine, London

William Silen, Beth Israel Hospital, Boston, Massachusetts

Amnon Sonnenberg, Department of Gastroenterology, Statshospital Tremli 8063, Zurich

Brendan J.R. Whittle, Department of Prostaglandin Research, The Wellcome Research Laboratories, Beckenham, Kent

Participants

- Lynn W. Baker, Department of Surgery, Faculty of Medicine, University of Natal,
P.O. Box 17039, Congella, Durban, Republic of South Africa
- Jim W. Black, Therapeutic Research Dept., Wellcome Research Laboratories,
Langley Court, Beckenham, Kent
- Andre L. Blum, Medizinische Klinik, Birmensdorferstrasse 497, 8063 Zurich,
Switzerland
- Richard Creese, Department of Physiology, St Mary's Hospital Medical School,
London
- Brian P. Curwain, Department of Physiology, St Mary's Hospital Medical School,
London
- L. Peter Fielding, Academic Surgical Unit, St Mary's Hospital Medical School,
London
- Mark C. Flannery, Academic Surgical Unit, St Mary's Hospital Medical School,
London
- Rosemary A. Hittinger, Academic Surgical Unit, St Mary's Hospital Medical School,
London
- Hugh Lafferty, Department of Applied Mathematics, Sheffield University, Sheffield
- Richard Langford, The Middlesex Hospital, Mortimer Street, London
- Louis J. Levien, Department of Surgery, University of Witwatersrand Medical
School, Hospital Street, Johannesburg 2001, Republic of South Africa
- Jacob Lindhagen, Department of Surgery, Central Hospital of Norrkoping, S-601
82 Norrkoping, Sweden
- Mike E. Parsons, Department of Pharmacology, The Research Institute, Smith,
Kline and French Laboratories Ltd., Welwyn Garden City, Hertfordshire
- Christopher D. Rennie, Academic Surgical Unit, St Mary's Hospital Medical School,
London
- R. Christopher G. Russell, The Middlesex Hospital, Mortimer Street, London
- Karl-Friedrick Sewing, Institute of Pharmacology, University of Tübingen,
Wilhelmstrasse 56, D-7400 Tübingen 1, Federal Republic of Germany
- Roger Stables, Department of Pharmacology, Glaxo-Allenbury's Research, Ware,
Hertfordshire
- Michael Starlinger, The General Hospital of Vienna, Clinical Surgery, Alserstrasse 4,
1090 Vienna IX, Austria

Collaborators

Poland

*Institute of Physiology, Nicolaus Copernicus Academy of Medicine, Krakow,
UL Grzegorzewska 16*
P. Gustaw and K.M. Walus

Sweden

*Department of Surgery, University of Goteborg, Ostra Sjukhuset, S-416 85,
Goteborg*
N. Darle, L. Hulten, J. Lindhagen, O. Lundgren

United Kingdom

Department of Peripheral Vascular Surgery, Royal Infirmary, Glasgow
A.R. Aitkenhead and I. McA. Ledingham
Department of Pharmacology, Glaxo-Allenbury's Research, Ware, Hertfordshire
J. Bell and G.R. Manchee
*The Research Institute, Smith, Kline and French Laboratories Limited, Welwyn
Garden City, Hertfordshire*
Carol A. Harvey, Barbara M. Johnston, K.D. Shaw

United States of America

Beth Israel Hospital, 330 Brookline Avenue, Boston, Massachusetts
A. Barzilai, E. Kivilaasko, R. Schiessel
*Department of Gastroenterology, Cure, Veterans Administration, Wadsworth
Hospital, Wiltshire and Sowtelle Boulevards, Los Angeles, California*
T. Moler and H. Wayland
*Department of General Surgery, Ochsner Clinic, 1514 Jefferson Highway, New
Orleans, Louisiana*
J.G. Payne
*Department of Medicine, University of Pittsburgh School of Medicine,
Pittsburgh, Pennsylvania*
R.L. Weschler
VA Wadsworth Hospital Centre, Los Angeles, California
D. Aures and M.I. Grossman

Contents

Session 1: The basis of methods used to estimate mucosal blood flow

Chairman: Hugh Baron

1. Patterns of blood supply to human gastro-duodenal mucosa: a basis for local ischaemia 3
Kristopher Piasecki
2. Study of the gastric microcirculation by in vivo fluorescence microscopy 17
Paul H. Guth, T.L. Moler and H. Wayland
3. The use of microspheres to measure gastric mucosal blood flow 27
Laurence Y. Cheung and F.G. Moody
4. Analysis of aminopyrine clearance to measure gastric mucosal blood flow: insight derived from mathematical models 35
Marcus C. Dugas and R.L. Weschler
5. Limitations to measurement of gastric mucosal blood flow by ^{14}C -aminopyrine clearance 43
Amnon Sonnenberg and A.L. Blum
6. Determination of blood flow distribution in the gastro-intestinal tract with inert gases 59
Ove Lundgren
7. Measurement of colon blood flow in greyhounds 66
Douglas C. Gilmour, A.R. Aitkenhead and I. McA. Ledingham
8. Measurement of oxygen tension in the canine gastric mucosa: use of an ultramicroelectrode 77
John C. Bowen
9. The basis of the methods to estimate mucosal blood flow 83
Frank G. Moody

Session 2: Mucosal blood flow in gastric physiology

Chairman: Ove Lundgren

10. Gastric blood flow in man: ^{85}Kr elimination technique 89
Lars E. Ivarsson, N. Darle, L. Hulten, J. Lindhagen and O. Lundgren

11. Simultaneous measurement of gastric mucosal blood flow by the ^3H -aniline and ^{14}C -aminopyrine clearance methods in the conscious Heidenhain pouch dog <i>M. Daly, R. Stables, J.A. Bell and G.R. Manchee</i>	94
12. Studies of gastric mucosal blood flow: neutral red clearance and dose-response curve analysis <i>Stephen E. Knight, R.L. McIsaac, C.D. Rennie, M.C. Flannery and L.P. Fielding</i>	105
13. Histamine-induced increase in gastric blood flow in cats: comparison of findings with different experimental techniques <i>David A.A. Owen, Carol A. Harvey, Barbara M. Johnston and K.D. Shaw</i>	125
14. The effect of sepsis on canine gastric mucosa <i>John C. Bowen and J.G. Payne</i>	132
15. Gastric blood flow: comparison of venous outflow, gamma labelled microspheres and aminopyrine clearance methods <i>L.Y. Cheung and F.G. Moody</i>	138
16. Mucosal blood flow in gastric physiology <i>Richard L. McIsaac</i>	147

Session 3: Gastric mucosal blood flow, prostaglandins and cytoprotection
Chairman: William Silen

17. Ulceration of rabbit antral mucosa <i>William Silen, A. Barzilai, E. Kivilaakso and R. Schiessel</i>	159
18. Effect of indomethacin and aspirin on basal gastric mucosal blood flow in conscious dogs <i>G.L. Kauffman, D. Aures and M.I. Grossman</i>	162
19. Comparison of arachidonic acid, prostacyclin and prostaglandin E_2 on gastric secretion and gastric blood flow <i>Stanislav J. Konturek, K.M. Walus and P. Gustaw</i>	170
20. Actions of prostaglandins on gastric mucosal blood flow <i>B.J.R. Whittle</i>	180
21. Intravenous prostaglandin synthetase inhibitors potentiate the effect of topical taurochocholate on transmucosal ion flux <i>H.J. Lewi and D.C. Carter</i>	192
22. Mechanisms of gastric mucosal protection <i>Alan Bennett</i>	202
23. Gastric mucosal barrier and mucosal blood flow <i>David C. Carter</i>	206

Session 4: Measurement of intestinal blood flow
Chairman: L. Peter Fielding

24. Results of $^{133}\text{Xenon}$ clearance studies in the greyhound colon <i>Douglas G. Gilmour, A.R. Aitkenhead and I. McA. Ledingham</i>	219
--	-----

25. Intestinal blood flow in man studied by an isotope washout technique	230
<i>Jacob Lindhagen, L. Hulten and O. Lundgren</i>	

Index	237
-------	-----

SESSION 1: The basis of methods used to estimate mucosal blood flow.

