ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY

Volume 89

MUCUS IN HEALTH AND DISEASE

Edited by Max Elstein and Dennis V. Parke

MUCUS IN HEALTH AND DISEASE

Edited by

Max Elstein

Southampton General Hospital
Southampton, England

and

Dennis V. Parke

University of Surrey
Guildford, England

With a Foreword by

Sir Francis Avery Jones

PLENUM PRESS • NEW YORK AND LONDON

Library of Congress Cataloging in Publication Data

International Symposium on Mucus in Health and Disease, 1st, University of Surrey, 1976.
Mucus in health and disease.

(Advances in experimental medicine and biology; v. 89)
Includes index.
1. Mucus – Congresses. I. Elstein, Max. II. Parke, Dennis V. III. Surrey, Eng. University. IV. Title. [DNLM: 1. Mucus – Congresses. 2. Gastroenterology – Congresses. 3. Respiratory system – Congresses. 4. Urogenital system – Congresses. 5. Ophthalmology – Congresses. W3 IN91987 1976m / QS532.M5 I62 1976m]
QP215.I57 1976 591.1'858 77-22376
ISBN 0-306-32689-2

Proceedings of the First International Symposium on Mucus in Health and Disease held at the University of Surrey, Guildford, England, September 13–16, 1976

MUCUS IN HEALTH AND DISEASE

ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY

Recent Volumes in this Series

Volume 81
PHOSPHATE METABOLISM
Edited by Shaul G. Massry and Eberhard Ritz • 1977

Volume 82
ATHEROSCLEROSIS: Metabolic, Morphologic, and Clinical Aspects
Edited by George W. Manning and M. Daria Haust • 1977

Volume 83
FUNCTION AND BIOSYNTHESIS OF LIPIDS
Edited by Nicolás G. Bazán, Rodolfo R. Brenner, and Norma M. Giusto • 1977

Volume 84
MEMBRANE TOXICITY
Edited by Morton W. Miller, Adil E. Shamoo, and John S. Brand • 1977

Volume 85A
ALCOHOL INTOXICATION AND WITHDRAWAL – IIIa: Biological Aspects of Ethanol
Edited by Milton M. Gross • 1977

Volume 85B
ALCOHOL INTOXICATION AND WITHDRAWAL – IIIb: Studies in Alcohol Dependence
Edited by Milton M. Gross • 1977

Volume 86A
PROTEIN CROSSLINKING: Biochemical and Molecular Aspects
Edited by Mendel Friedman • 1977

Volume 86B
PROTEIN CROSSLINKING: Nutritional and Medical Consequences
Edited by Mendel Friedman • 1977

Volume 87
HYPOTHALAMIC PEPTIDE HORMONES AND PITUITARY REGULATION
Edited by John C. Porter • 1977

Volume 88
AVIAN IMMUNOLOGY
Edited by Albert A. Benedict • 1977

Volume 89
MUCUS IN HEALTH AND DISEASE
Edited by Max Elstein and Dennis V. Parke • 1977

ORGANIZING COMMITTEE

Organizing Committee

Sir Francis Avery Jones
149 Harley Street
London, W1N 2DE, United Kingdom

Max Elstein
Department of Human Reproduction and Obstetrics
University of Southampton
Southampton General Hospital, South Pathology and Laboratory Block
Tremona Road, Southampton S09 4XY, United Kingdom

Leslie Hough
Department of Chemistry
Queen Elizabeth College, University of London
Atkins Building, Campden Hill Road, London, W.8., United Kingdom

Pierre Masson
International Institute of Cellular & Molecular Pathology
UC1 7430, Avenue Hippocrate 75
B-1200 Brussels, Belgium

Kamran Moghissi
Department of Gynecology-Obstetrics
Wayne State University, Gordon H. Scott Hall of Basic Medical Sciences
540 East Canfield Avenue, Detroit, Michigan 48201, U.S.A.

Eric Odeblad
Department of Medical Physics
University of Umea, Umea, Sweden

Dennis Parke
University of Surrey
Department of Biochemistry, Guildford, Surrey, United Kingdom

Lynne Reid
Brompton Hospital, Cardiothoracic Institute
Department of Experimental Pathology, London, S.W.3., United Kingdom

Stanley Skoryna
McGill University, Donner Building, P.O. Box 6070
Station A, Montreal, Quebec, Canada

Secretaries

Max Elstein
Human Reproduction & Obstetrics
South Laboratory & Pathology Block, Level F
Southampton General Hospital
Tremona Road, Southampton, SO9 4XY, United Kingdom

Dennis Parke
Department of Biochemistry
University of Surrey, Guildford, GU2 5XH, United Kingdom

Local Organizer

Andrew Symons
Department of Biochemistry
University of Surrey, Guildford, GU2 5XH, United Kingdom

FOREWORD

Sir Francis Avery Jones

149 Harley Street, London, W1N 2DE, U.K.

This first international symposium on Mucus in Health and Disease brought together medical scientists, physiologists, pharmacologists, physicians, surgeons, gynaecologists, ophthalmologists, anatomists, biologists, medical engineers and biochemists - a spectrum which indicates the wide field of interest in mucus both in health and in disease. The idea for the meeting came from Dr. S. Gottfried whose researches led to the development of carbenoxolone, a substance which stimulates mucus production and in this way favours the healing of peptic ulcers. The idea was enthusiastically welcomed by Professor Dennis Parke and he, and Mr. Max Elstein, have been the dynamo behind the meeting.

The opening keynote address by Professor Clamp set the scene for the Symposium, painting a broad canvas and highlighting the main features. We cannot do without mucus, irritating though it may be if there is too much or too little, and in so many systems of the body it plays a vital role. For the first time the specialists in different systems of the body have had the opportunity of coming together and discussing their special problems - a cross-fertilisation which proved to be most valuable, not only for one another but also for the medical scientists who had been closely concerned with the chemistry and physical properties of mucus.

Mucus goes far back into evolutionary history and its function has clearly been not only lubrication but also waterproofing, and indeed protecting the organism from sudden changes in osmotic pressure, which it might find difficult or impossible to withstand. Mucus provides a permeable skin for the earthworm, allowing the passage of oxygen and carbon dioxide and the single layer of

goblet cells produces mucus which provides the waterproof protective coat. Eels have a skin made up of layers of goblet cells and if their mucus covering is removed they gain weight by osmosis when placed in distilled water and lose weight when placed in hypertonic saline. In some fish, such as the carp, the olfactory recess is studded with goblet cells and the mucus helps to control the passage of water.

In the alimentary tract mucus is the skin of the gut and serves as effectively, and indeed in a more versatile way than, the skin of the body. In the stomach it has the extra responsibility of protecting the gastric mucosa from the powerful acid and proteolytic secretions. Claud Bernard in 1856 commented that, "the mucus encloses the gastric juice as in a vase, as impermeably as though it were made of porcelain". It does indeed form a coherent protective layer over the living lining of the gastrointestinal tract and its integrity in health prevents both bacterial infection and biochemical damage. At the same time it allows the regulated passage of simple molecules which will pass into the absorbing cells. It is one of Nature's perfections in protection, but even Nature has not anticipated all the noxious influences of western civilization which can reduce the protective powers of the mucus lining.

Secreted, mucus is an elastic gel and its physico-chemical properties are ideal for the task of covering a constantly moving surface. As a clinician I find the physical properties and chemistry of mucus quite fascinating. It consists of strings made up of a protein backbone to which some 600 carbohydrate side chains are attached. This flexible thread-like strand may be likened to coils of cotton with a three-dimensional network due to the presence of cross links by peptide and disulphide bonds. The structure is intensely hydrophilic and sponge-like, containing at least 90-95% water.

The secretion of blood group substances, so important in relation to blood transfusion, by the mucus of the stomach and indeed of some mucus elsewhere has given physicians like myself their first glimpse of the subtle chemistry of these substances. The difference between blood group A and blood group B is merely one sugar at the end of a carbohydrate side chain - a change which makes the difference between life and death in relation to blood transfusion. Here we have a superb bridge between academic biochemistry and clinical practice, and there is a great incentive to learn more about the chemistry and properties of glycoproteins of which mucus is but one subdivision. Today many people see glycoproteins as offering a very valuable line of research in relation to cancer. Normal cells stop growing when they touch each other, but cancer cells grow without restraint, and this

seems to relate to the properties of the cell surface. The subtle stereotaxic three-dimensional shape of these carbohydrate side chains are increasingly suspected of playing an enormously important role in cell surface activity.

This is a subject which will justify further symposia, both local and international. The editors are to be congratulated on achieving such rapid publication - a publication which is likely to stimulate great interest around the world.

ACKNOWLEDGMENTS

The organisers wish to express their thanks for financial support of the Symposium to the following:

Sir F. Avery Jones
Barclays International
Beecham Research Laboratories
Berk Pharmaceuticals
Biorex (Marketing) Limited
Boehringer (Ingelheim) Limited
Bournonville Pharma B.V.
Bowater Scott Corporation
Brocades (G.B.) Limited
Chemiwerk, Homborg
Dr. De Vitre
Fisons (Pharmaceuticals) Limited
Glaxo Laboratories
Imperial Chemical Industries Charity Trust
Merrell International
Ortho Pharmaceuticals Limited
Parke-Davis & Company
Pfizer Limited
Roche Products Limited
A.H. Robins Incorporated
Royal Society
Schering Chemicals Limited
Smith, Kline and French Laboratories Limited
Syntex Limited
Tobacco Research Council
University of Surrey
USV Australia Pty Limited
Wellcome Trust

PREFACE

Max Elstein and Dennis Parke

There has long been a need for a multidisciplinary approach to the study of mucus, a unique biological material found throughout the animal kingdom at many levels of organisation. Although mucus of different origins is collectively recognised by its distinctive physical properties, the functions of mucus have specific characteristics suited to its particular location. The biophysical properties of mucus are related to these functions and although similar in some aspects, differ according to the rôle played by the organ concerned. To a major extent these physical properties depend on the biochemistry of the mucus and on the biosynthetic processes involved in its production. It is now well apparent that mucus from a particular site has certain features in common with mucus obtained from different sites, yet in other ways it is specific to its particular anatomical tract and physiological functions. Advances in technology for the study of high molecular weight biological polymers have facilitated the study of the physical properties and biochemical structure of mucus glycoprotein. This together with the increased awareness of the clinical importance of mucus has provided the impetus for this conference. It seemed appropriate therefore, to bring together basic scientists and clinicians working in the three major fields of investigation of human mucus, namely, the gastrointestinal, respiratory and genito-urinary tracts, and thereby to encourage the exchange of ideas and expertise.

Important and novel aspects of mucus structure and function were raised during the symposium; one particular area, perhaps originally neglected by the programme organizers, being that of the human eye. The wide ranging discussion revealed exciting new developments in the relationship between the glycoproteins of mucus

and those of the cell surface and the possible relationship of these latter to carcinogenesis. The rate and form of mucus secretion were found to be a reflection of both cell turn-over and cell-life. The mature cell produces abundant mucus with its particular protective, lubricant and transportation rôles in the tissues, whilst the rapidly growing cell in hyperplastic conditions produces less mucus, perhaps of a different type, possibly related to cell transformation and the development of malignancy. The rôle of the glycosyl transferases in the synthesis of specific glycoproteins, that confer particular physical properties on cervical mucus which thus prevents or facilitates sperm transport, is an exciting concept. The release of enzyme inhibitors into the cervical canal has interesting possible application in the development of contraceptives which would act by altering the cervical mucus, and thereby preventing sperm migration. Means of measuring cilial function remain elusive and are urgently required, particularly for investigation in the respiratory tract.

This Symposium has been a valuable and fruitful meeting of concepts and ideas concerning a difficult and fascinating biological material, which is not without its frustrations. The objectives of bringing together investigators from the various fields of mucus have been amply fulfilled. The general enthusiasm, and the duration of the discussions, throughout this meeting reflected the vital nature of this subject and was felt by all those involved at each level. The value of this interchange of ideas was evident from the widely expressed desire for a similar meeting in a few years to evaluate new discoveries in this rapidly evolving and dynamic area of medical research.

KEYNOTE ADDRESS

CONTENTS

KEYNOTE ADDRESS

MUCUS PRODUCTION AND ITS REGULATION