SERONEGATIVE POLYARTHRITIS

V. Wright, M.D., F.R.C.P.

J.M.H. Moll, B.Sc., D.M., M.R.C.P.

SERONEGATIVE POLYARTHRITIS

V. Wright, M.D., F.R.C.P.

Professor of Rheumatology, University of Leeds; Consultant Physician in Rheumatology, The General Infirmary at Leeds and Royal Bath Hospital, Harrogate (Great Britain)

and

J.M.H. Moll, B.Sc., D.M., M.R.C.P.

Consultant Physician in Rheumatology, Sheffield Centre for the Investigation and Treatment of Rheumatic Diseases, Nether Edge Hospital, Sheffield; Honorary Lecturer in Rheumatic Diseases, University of Sheffield, Sheffield (Great Britain)

1976

NORTH-HOLLAND PUBLISHING COMPANY
AMSTERDAM · NEW YORK · OXFORD

Published by:
Elsevier/North-Holland Biomedical Press
335 Jan van Galenstraat, P. O. Box 211
Amsterdam, The Netherlands

Sole distributors for the U.S.A. and Canada:
Elsevier/North-Holland Inc.
52 Vanderbilt Avenue
New York, N.Y. 10017

Library of Congress Cataloging in Publication Data

Wright, Verna.
Seronegative polyarthritis.

Bibliography: p.
Includes index.
1. Arthritis deformans. 2. Arthritis. 3. Rheumatoid factor. 4. Serum diagnosis. I. Moll, John Michael Henderson, joint author. II. Title.
[DNLM: 1. Arthritis. WE344 W953s]
RC933. W74 616.7'2 76-28213
ISBN 0-7204-0591-2

xix + 488 pages, 185 illustrations, 152 tables

PRINTED IN GERMANY

Acknowledgements

We are grateful to our colleagues Dr I. F. Macrae, Dr D. I. Haslock, and Dr M. A. Chamberlain for invaluable discussions, and also for their help in contributing data collected in the course of their family studies of ulcerative colitis, Crohn's disease, and Behçet's syndrome respectively. Dr A. G. S. Hill (Director of the Regional Rheumatic Research Centre at Stoke Mandeville Hospital) initiated these familial investigations some years ago by sparking an interest in psoriatic arthritis. From the General Infirmary at Leeds we thank Professor J. C. Goligher, who contributed many patients with bowel disease, the late Dr J. A. H. Hancock who contributed patients with Reiter's disease, and Dr J. R. Lambert who provided data on hyperuricaemia in psoriatic arthritis. Invaluable clinical help has also been rendered by Dr G. R. Newns and Dr M. S. Derini (Nether Edge Hospital, Sheffield), and Dr R. S. Morton (The Royal Infirmary, Sheffield). Dr L. A. D. Tovey and Dr S. M. Rajah (Regional Blood Transfusion Centre, Leeds), and Dr D. Lee (Regional Blood Transfusion Centre, Sheffield) kindly undertook histocompatibility antigen investigations. Biochemical data on psoriatic nail tissue were kindly provided by Miss M. S. Greaves (Rheumatism Research Unit, Sheffield). We would also like to thank Mr J. M. Williamson (Northern General Hospital, Sheffield) who did the half-tone drawings and many of the line illustrations; the pen portraits, summary diagrams, and line illustrations for Chapters 1, 3 and 4 were done by J. M. H. M. We have appreciated photographic assistance from Mr R. Brooks, Mrs R. Gregory, Mr F. Knowles, Mr A. K. Tunstill, Miss B. Walsh, Mrs B. A. Watson, Mrs J. White, and Mr M. Williams. Secretarial and technical assistance was rendered by Mrs E. Dawson, Mrs P. Drake, Miss A. Greaghan, Mrs A. Helliwell, Miss M. Lampard, Mr A. Moreton, and Mrs M. Walker. In acquiring photographic material outside Leeds and Sheffield, we are indebted to Dr C. Wells (Palaeopathologist, Hapton, Norfolk), Dr T. R. Hendrix and Dr A. Gonzalez-Licea (Johns Hopkins Hospital), Dr M. G. Cook (The London Hospital), Mr L. M. Payne (Librarian, Royal College of Physicians, London), and Mr H. C. Buckwell (Stanley Cox Medical Equipment, Rank Precision Industries, Herts). We are grateful to the Editors of the *Annals of the Rheumatic Diseases*, *Rheumatology and Rehabilitation*, *Nursing Times*, *Medicine* (*Baltimore*), and *British Journal of Hospital Medicine* for permission to reproduce certain diagrams and tables. Dr J. S. Keates (Elsevier/Excerpta Medica/North-Holland) and Mr G. R. Schrager (formerly of North-Holland Publishing Co.) have cooperated with courtesy and enthusiasm in the production of this book.

Contents

Chapter 2. The "Seronegative Spondarthritides" — A New Concept

Chapter 3. Ankylosing Spondylitis

Chapter 4. Psoriatic Arthritis

Chapter 5. Reiter's Disease

Chapter 6. The Arthritis of Ulcerative Colitis

Chapter 7. The Arthritis of Crohn's Disease

Chapter 8. Whipple's Disease

Chapter 9. Behcet's Syndrome

Chapter 10. Still's Disease

Chapter 11. Uncomplicated Seronegative Polyarthritis

Chapter 12. Management and Treatment

Chapter 13. Seronegative Spondarthritides and Histocompatibility Antigens

CHAPTER 1

The Meaning of Seronegativity and Seropositivity

1.1 Historical background

Until recently medical writers were barely able tc distinguish different types of chronic arthritis and observers up till the turn of the century considered them all to be variants of gout.

It is probable, however, that both Hippocrates and Soranus of Ephesus (second century A.D.) were aware of the difference between "chronic rheumatoid arthritis" and "chronic podagra". In more modern times, H. W. Fuller in 1854 (cited by Copeman 1964) provided a good description of rheumatoid arthritis, calling it "rheumatoid gout".

Further strength was added to the distinction between true gout and other forms of arthritis by Sir Alfred Garrod's discovery of an excess of uric acid in the blood of gouty subjects. Garrod in 1859 was the first to give rheumatoid arthritis its present name.

In 1857, osteoarthritis (or osteoarthrosis as it is now called) became separated from rheumatoid arthritis by Robert Adams in his *Treatise on the Rheumatic Gout*. Ankylosing spondylitis also became widely known as a separate entity at about this time, not only due to the classical reports by Bechterev and Strümpell from Germany and Marie from France, but also in the United Kingdom from the work of C. Hilton Fagge in 1877. For further historical details the reader is referred to the excellent monograph by Copeman (1964).

The next significant advance in rheumatological classification was made by Waaler in 1940, and again by Rose et al. in 1948, when rheumatoid factor, a gamma-M immunoglobulin, was discovered. This finding made possible a division of inflammatory arthritis into two main groups, i.e. those in which rheumatoid factor was present (seropositive and usually typical rheumatoid arthritis), and those in which the factor was consistently absent throughout the natural history of the disease (seronegative arthritis). It is with this second group, the seronegative arthritides, that we have been particularly concerned, and in order to study this subject in further detail it is clearly important to examine in some depth the immunological background to rheumatoid factor.

1.2 Rheumatoid factors

1.2.1 Physicochemical features of rheumatoid factors

Rheumatoid factors are antibodies mainly of the IgM class with a molecular weight of about 1,000,000 and an ultracentrifugal sedimentation coefficient of 19S (Franklin et al. 1957). These macro-gamma globulins constitute a class of proteins which contain, in addition to rheumatoid factors, many other types of antibody such as cold agglutinins, the Wassermann and heterophil antibodies, and typhoid "O" agglutinin.

The evidence for the antibody nature of rheumatoid factors has been summarised by Anderson and Buchanan (1966):

(1) Rheumatoid factors are immunoglobulins (usually IgM, sometimes IgG) which react only with IgG and with no other protein or tissue antigen.

(2) Rheumatoid factors demonstrate, with few exceptions, primary specificity for human IgG and cross-reactivity with other mammalian IgG (Butler and Vaughan 1964), which is consistent with the behaviour of classical antibody.

(3) Rheumatoid factors frequently demonstrate specific reactivity with certain genetically determined groupings (Gm Groups) (Grubb 1961; Fudenberg and Kunkel 1961) which suggests the specificity characteristic of antibodies.

(4) Rheumatoid factors have been shown by immunofluorescent techniques to be located in, and hence presumably produced by, cells capable of producing antibodies. These cells include plasma cells and germinal centre cells of lymph nodes, and also plasma cells in affected synovia and around subcutaneous nodules (Mellors et al. 1959; Mellors et al. 1961; McCormick 1963).

(5) Rheumatoid factor-like serum factors, albeit of IgG class, have been produced in animals by immunization with autologous denatured IgG incorporated in Freund's adjuvant (Milgrom and Witebsky 1960; McCluskey et al. 1962).

Although it is now reasonably clear that rheumatoid factors are antibodies to IgG, it is still not fully understood whether they are antibodies to native IgG or IgG denatured by immune complex formation or by physical aggregation. There is equally good evidence to support both the "native" (Grubb 1961; Fudenberg and Kunkel 1961) and "denatured" (Christian 1958; Edelman et al. 1958) hypotheses.

There is also controversy as to whether rheumatoid factors should be regarded as auto-antibodies or iso-antibodies (Milgrom and Witebsky 1960). However, as McCormick (1963) has pointed out, rheumatoid factors probably represent a heterogeneous collection of immunoglobulins, some behaving as auto-antibodies, some as iso-antibodies, and some as hetero-antibodies to IgG. It is also apparent that the reactant (IgG antigen) of normal human serum and other mammalian sera is complex in its antigenicity, and it is likely that different rheumatoid factors react with different parts of the IgG reactant molecules.