immunology series volume 15

Immunological Aspects of Aging

edited by
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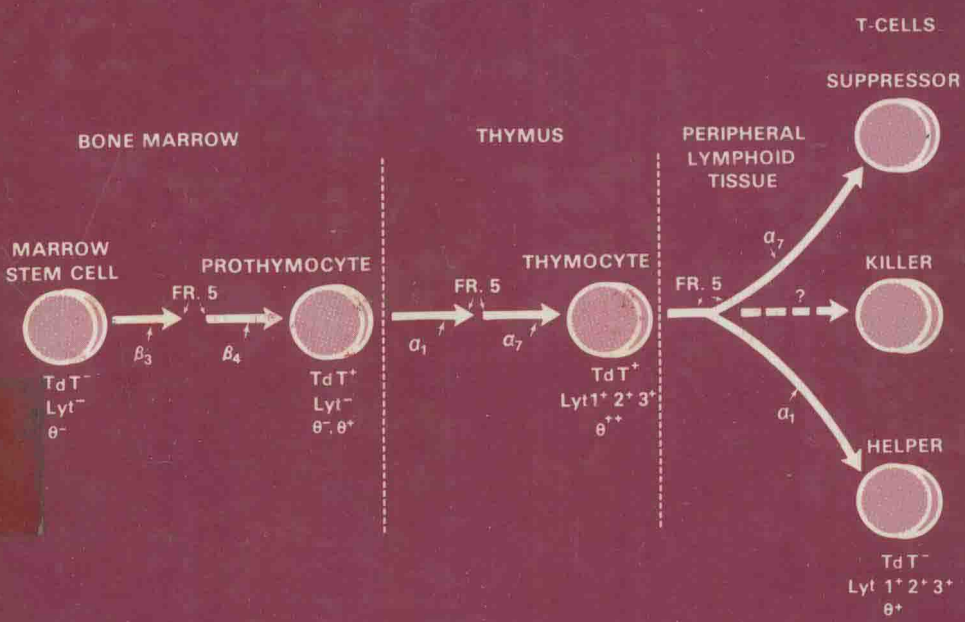

Immunological Aspects of Aging

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MARCEL DEKKER, INC. New York and Basel

Library of Congress Cataloging in Publication Data
Main entry under title:

Immunological aspects of aging.

(Immunology series ; 15)
Includes index.
1. Aging--Immunological aspects--Congresses.
2. Immunologic diseases--Age factors--Congresses.
I. Segre, Diego, [date]. II. Smith, L. (Lester),
[date]. III. Series. [DNLM: 1. Aging--Congresses.
2. Immunity, Cellular--In old age--Congresses.
3. Autoimmune diseases--In old age--Congresses. W1
IM53K v.15 / WT 104 I325 1979]
QP86.I48 616.07'9 81-15254
ISBN 0-8247-1349-4 AACR2

MARCEL DEKKER, INC.

270 Madison Avenue, New York, New York 10016

Current printing (last digit):

10 9 8 7 6 5 4 3 2 1

PRINTED IN THE UNITED STATES OF AMERICA

FOREWORD

Much progress has been made over the last 20 years with regard to our immunological interpretation of aging. We once thought that only vertebrate systems possessed true immunological systems. We now know that specific immunocompetence is also possessed by echinoderms, annelids, and coelenterates. This knowledge would seem to present exciting possibilities for immunogenetic investigations of aging, but unfortunately only a few invertebrates have been studied immunologically and even fewer investigated genetically. We hope this volume and the chapter on invertebrate immunology will serve to stimulate additional research.

The bulk of our knowledge regarding immune function has come from research on higher animals subjected to laboratory experimentation or clinical observation. All vertebrate species so far investigated, including birds and amphibia as well as mammals, possess a major histocompatibility complex (MHC) (e.g., the H-2 system in the mouse and the HLA system in man) which appears to be the master gene system for controlling or influencing the immune response, particularly as it involves thymus-dependent functions. It has been suggested that the MHC might be fundamentally involved in the aging process.

The extent of our knowledge on actual defects within the immune system is limited and subject to different interpretations. We know from anatomical studies that lymphoid tissues undergo involutional changes with advancing age. The thymus reaches maximum size in early childhood and begins to involute rapidly during puberty. Precisely how this involution affects T-cell function (which is apparently decreased with age) is not known, and thus, several

chapters within this book will examine the influence of age on T-cell function. There is some evidence indicating that the level of thymic hormone decreases with age during the course of thymic involution.

The B-cell system, with regard to its role in the primary immune response, shows an age-associated decline, especially in the response to those antigens requiring a T-cell interaction with a B cell. The situation with regard to the secondary response is different. There is not an age-associated decline, as demonstrated by the well-known clinical observation that childhood diseases are rarely seen in adults. It has been proposed that aging could be due to autoimmune phenomena within and against the body's own tissues. In general, the incidence of diseases which are regarded as being caused by autoimmune reactions (e.g., rheumatoid arthritis) increases with age. The incidence of autoantibodies in clinically asymptomatic individuals (e.g., antithyroid and antinuclear autoantibodies) increases with age. In general, there is a considerable amount of circumstantial evidence linking autoimmunity with aging, but the definitive experiments have yet to be performed to establish a clear interrelationship.

The National Institute on Aging has responded to the need to understand how and why the immune system is altered during aging by establishing a program in immunology. Studies at various universities and medical schools are exploring the effects of aging on antibody synthesis, T and B cells, and other recently discovered cell populations. Some studies are directed toward clarification of extrinsic and intrinsic factors, while others are attempting to understand what happens when the immune system is perturbed by artificial means. It is apparent from the contributions which follow that more emphasis must be placed on species other than the mouse.

Robert N. Butler, M.D.
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PREFACE

In 1971, the year one of us (Lester Smith) joined the scientific staff of the extramural aging program, then a part of the National Institute of Child Health and Human Development, National Institutes of Health (Bethesda, Maryland), very few immunologists were being supported for the conduct of age-related research. This was a reflection not so much on budget as it was on the state of the art of immunology and aging. As a means of stimulating the interest of immunologists in aging research, intensive workshops on various aspects of immunology were held throughout the country. These workshops covered such topics as cellular immunology, autoimmunity, nutrition and immunity, and other current themes. The Five Year Plan required by the Congressional Act which created the National Institute on Aging (NIA) (Public Law 93-296, Section 461, May 31, 1974) gave immunology very high priority for further development. The program is now represented by over 35 grants. The chapters in this volume were contributed by many of the investigators involved in the research and training programs supported by NIA.

In keeping with policy, investigator-initiated research is encouraged, although not infrequently NIA chooses to announce specific topic areas of interest to the Immunology Program. The choice of laboratory model is that of the investigator; some have availed themselves of the mice strains available from the NIA contract colony. Those areas still receiving attention as of this writing are studies on:

The influence of age on B-cell activity to anti-immunoglobulins and T-cell reactivity to contact sensitizers

The nature of serum precursor for amyloid (SAA) protein

The relationship of autoimmunity to aging

The effects of aging on tolerance induction

The role of decline in thymic function as related to immunological capacity

The role of suppressor cells in the pathogenesis of immunologic perturbations associated with aging

The influence of nutrition and cellular engineering on longevity and immunity

It appeared timely to convene a major conference of international status to reflect on the early but significant and interesting research results from representative laboratories. We met some 75 strong in Bethesda, Maryland on May 7 and 8 of 1979. The conference was a tremendous success. Hopefully, readers will find the resulting book of value and up to date with current research directions.

Special thanks to the chairmen, Drs. M. Weksler, R. Walford, and E. Yunis, who devoted their precious time to conference organizing and moderating the deliberations and to those of the NIA staff, Ms. Susan Cantor, and Ms. Tracy Spellmans, who assisted in the draft preparation of the manuscript. Our appreciation is also due to the staff at the University of Illinois, Ms. Marjorie M. Hildreth and Ms. Joyce A. Amacher, who so painstakingly prepared the manuscript in camera-ready form.

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