

PROGRESS in  
CLINICAL and  
BIOLOGICAL RESEARCH  
VOLUME 70

# REPRODUCTIVE IMMUNOLOGY

EDITOR: **Norbert Gleicher**

ALAN R. LISS, INC., NEW YORK

# REPRODUCTIVE IMMUNOLOGY

*Including papers from the First S.B. Gusberg Seminar  
on Reproductive Immunology  
held at The Mount Sinai Medical Center  
New York  
June 26 and 27, 1980*

Editor

**Norbert Gleicher** *ed.*

*Director, Reproductive Immunology  
The Mount Sinai School of Medicine of the  
City University of New York*

**Alan R. Liss, Inc. • New York**

**Address all Inquiries to the Publisher**  
**Alan R. Liss, Inc., 150 Fifth Avenue, New York, NY 10011**

**Copyright © 1981 Alan R. Liss, Inc.**

**Printed in the United States of America.**

Under the conditions stated below the owner of copyright for this book hereby grants permission to users to make photocopy reproductions of any part or all of its contents for personal or internal organizational use, or for personal or internal use of specific clients. This consent is given on the condition that the copier pay the stated per-copy fee through the Copyright Clearance Center, Incorporated, 21 Congress Street, Salem, MA 01970, as listed in the most current issue of "Permissions to Photocopy" (Publisher's Fee List, distributed by CCC, Inc.), for copying beyond that permitted by sections 107 or 108 of the US Copyright Law. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, or for resale.

#### **Library of Congress Cataloging in Publication Data**

Main entry under title:

Reproductive immunology.

(Progress in clinical and biological research;  
v. 70)

Includes bibliographical references and index.

1. Reproduction—Immunological aspects—Congresses.  
2. Human reproduction—Immunological aspects—Congresses. 3. Pregnancy—Immunological aspects—Congresses. I. Gleicher, Norbert. II. S.B. Gusberg  
Seminar on Reproductive Immunology (1st : 1980 :  
Mount Sinai Medical Center (New York, N.Y.))  
III. Series. [DNLM: 1. Fetus—Immunology.

2. Immunity—In pregnancy. 3. Immunological diseases  
—In pregnancy. 4. Fertility. W1 PR668E v. 70 / WQ  
200 R425]

QP251.R44453

612'.6

81-11812

ISBN 0-8451-0070-X

AACR2



## Contributors

**Carlos R. Abramowsky [309]**

Institute of Pathology, Case Western Reserve University, 2085 Adelbert Rd, Cleveland, OH 44106

**Melissa M. Adams [213]**

Bureau of Epidemiology, Center for Disease Control, 1600 Clifton Rd NE, Building 5, Chamblee, Atlanta, GA 30333

**Hugh R.K. Barber [3, 357]**

Department of Obstetrics and Gynecology, New York Medical College and Lenox Hill Hospital, 122 East 76th St, New York, NY 10021

**Philip C. Beers [21]**

Department of Obstetrics and Gynecology, The Mount Sinai School of Medicine of The City University of New York, One Gustave L. Levy Place, New York, NY 10029

**John P. Bennett [269]**

Department of Plastic Surgery, Queen Victoria Hospital, East Grinstead, Sussex RH19 3DZ, England

**Pierluigi E. Bigazzi [461]**

Department of Pathology, University of Connecticut Health Center, Farmington, CT 06032

**Rupert E. Billingham [63]**

Department of Cell Biology, The University of Texas Health Science Center at Dallas, 5323 Harry Hines Blvd, Dallas, TX 75235

**Constantin A. Bona [53]**

Department of Microbiology, The Mount Sinai School of Medicine of the City University of New York, One Gustave L. Levy Place, New York, NY 10029

**Joseph P. Bressler [145]**

Laboratory of Nuclear Medicine and Radiation Biology, Warren Hall, University of California at Los Angeles, Los Angeles, CA 90024

**Peter J. Brown [77]**

University Department of Immunology, Duncan Building, Royal Liverpool Hospital, University of Liverpool, P.O. Box 147, Liverpool L69 3BX, England

**Lars L. Cederqvist [47]**

Department of Obstetrics and Gynecology, The New York Hospital-Cornell Medical Center, 525 East 68th St, New York, NY 10021

**Gerard Chaouat [137]**

Institut de Recherches sur le Cancer, Centre National de Recherche Scientifique, BP 8, 96800 Villejuif, France

**Sheldon H. Cherry [205]**

Department of Obstetrics and Gynecology, The Mount Sinai School of Medicine of the City University of New York, One Gustave L. Levy Place, New York, NY 10029

**Carmel J. Cohen [371]**

Department of Obstetrics and Gynecology, The Mount Sinai School of Medicine of the City University of New York, One Gustave L. Levy Place, New York, NY 10029

The bold face numbers in brackets following each contributor's name indicate the opening page of that author's paper.

## **xii / Contributors**

### **Liane Deligdisch [323]**

Department of Pathology, The Mount Sinai School of Medicine of the City University of New York, One Gustave L. Levy Place, New York, NY 10029

### **Gunter Deppe [371, 375]**

Department of Obstetrics and Gynecology, The Mount Sinai Hospital Medical Center of Chicago and Rush Medical College, California Ave at 15th St, Chicago, IL 60608

### **Frank J. Dixon [93]**

Department of Immunopathology, Scripps Clinic and Research Foundation, 10666 North Torrey Pines Rd, La Jolla, CA 92037

### **Brent Dorsett [357]**

Department of Obstetrics and Gynecology, Lenox Hill Hospital, 122 East 76th St, New York, NY 10021

### **W. Page Faulk [219, 269]**

Blond McIndoe Centre for Transplantation Biology, East Grinstead, Sussex RH19 3DZ, England

### **Jan Friberg [423]**

Department of Obstetrics and Gynecology, Downstate Medical Center, State University of New York, 450 Clarkson Ave, Brooklyn, NY 11203

### **Robert M. Galbraith [219]**

Department of Basic and Clinical Immunology and Microbiology, Medical University of South Carolina, 171 Ashley Ave, Charleston, SC 29403

### **Norbert Gleicher [xvii, 31, 93, 115, 229, 339]**

Department of Obstetrics and Gynecology, The Mount Sinai Hospital Medical Center of Chicago and Rush Medical College, California Ave at 15th St, Chicago, IL 60608

### **Allan L. Goldstein [145]**

Department of Biochemistry, George Washington University, Washington, DC 20037

### **Susan R.S. Gottesman [121]**

Department of Pathology, Center for Health Sciences, University of California at Los Angeles, School of Medicine, Los Angeles, CA 90024

### **Beatrice Anne Gray [437]**

Sperm Antibody Laboratory, New York Medical College, Metropolitan Hospital, 1900 Second Ave, New York, NY 10029

### **S.K. Gupta [451]**

Department of Biochemistry, All India Institute of Medical Sciences, Ansari Nagar, New Delhi 110029, India

### **Saul B. Gusberg [xv]**

Department of Obstetrics and Gynecology, The Mount Sinai School of Medicine of the City University of New York, One Gustave L. Levy Place, New York, NY 10029

### **Joanne Gustafson [213]**

Office of Maternal and Child Health, Connecticut State Department of Health Services, 79 Elm St, Hartford, CT 06115

### **Gilbert G. Haas, Jr. [413]**

Department of Obstetrics and Gynecology, Hospital of the University of Pennsylvania, 106 Dulles Building, 3400 Spruce St, Philadelphia, PA 19104

### **Kurt Hirschhorn [17]**

Department of Pediatrics, The Mount Sinai School of Medicine of the City University of New York, One Gustave L. Levy Place, New York, NY 10029

### **Christian F. Holinka [151]**

Department of Obstetrics and Gynecology, The Mount Sinai School of Medicine of the City University of New York, One Gustave L. Levy Place, New York, NY 10029

### **Peter M. Johnson [77]**

University Department of Immunology, Duncan Building, Royal Liverpool Hospital, University of Liverpool, P.O. Box 147, Liverpool L69 3BX, England

### **Thomas Keane [443]**

Sperm Antibody Laboratory, New York Medical College, Metropolitan Hospital, 1900 Second Ave, New York, NY 10029

**Urszula Krzych [145]**

Department of Bacteriology, University of California at Los Angeles, Los Angeles, CA 90024

**Genevieve A. Losonsky [171, 381]**

Department of Microbiology, The State University of New York at Buffalo, School of Medicine, Buffalo, NY 14226

**Richard N. Matthews [269]**

Blond McIndoe Centre for Transplantation Biology, East Grinstead, Sussex RH19 3DZ, England

**Anthony O. Ogbimi [77]**

University Department of Immunology, Duncan Building, Royal Liverpool Hospital, University of Liverpool, P.O. Box 147, Liverpool L69 3BX, England

**Pearay L. Ogra [171, 381]**

Division of Infectious Disease, Children's Hospital, 219 Bryant St, Buffalo, NY 14222

**Roland A. Pattillo [259]**

Department of Obstetrics and Gynecology, The Medical College of Wisconsin, 8700 West Wisconsin Ave, Milwaukee, WI 53226

**Aparecido B. Pereira [93]**

Department of Immunopathology, Scripps Clinic and Research Foundation, 10666 North Torrey Pines Rd, La Jolla, CA 92037

**William Pollack [185]**

Ortho Diagnostic Systems Inc., Raritan, NJ 08869

**Chandra Prakash [403]**

Department of Medical Microbiology and Immunology, Ohio State University, College of Medicine, 333 West Tenth Ave, Columbus, OH 43210

**J. Victor Reyniak [395]**

Department of Obstetrics and Gynecology, The Mount Sinai School of Medicine of The City University of New York, One Gustave L. Levy Place, New York, NY 10029

**Laxmi C.P. Shah [77]**

University Department of Immunology, Duncan Building, Royal Liverpool Hospital, University of Liverpool, P.O. Box 147, Liverpool L69 3BX, England

**Sidney Shulman [437, 443]**

Sperm Antibody Laboratory, New York Medical College, Metropolitan Hospital, 1900 Second Ave, New York, NY 10029

**Frederick P. Siegal [41]**

Department of Medicine, The Mount Sinai School of Medicine of The City University of New York, One Gustave L. Levy Place, New York, NY 10029

**Israel Siegel [31, 115, 229, 339]**

Department of Obstetrics and Gynecology, The Mount Sinai Hospital Medical Center of Chicago and Rush Medical College, California Ave at 15th St, Chicago, IL 60608

**Josef S. Smolen [283]**

Arthritis and Rheumatism Branch, National Institute of Arthritis, Metabolism, and Digestive Diseases, National Institutes of Health, Bldg. 10, Room 8D19, Bethesda, MD 20205

**Joseph E. Sokolowski [413]**

Department of Obstetrics and Gynecology, Hospital of the University of Pennsylvania, 106 Dulles Building, 3400 Spruce St, Philadelphia, PA 19104

**Harry Spiera [303]**

Department of Medicine, The Mount Sinai School of Medicine of the City University of New York, One Gustave L. Levy Place, New York, NY 10029

**Alfred D. Steinberg [283]**

Arthritis and Rheumatism Branch, National Institute of Arthritis, Metabolism, and Digestive Diseases, National Institutes of Health, Bldg. 10, Room 8D19, Bethesda, MD 20205

**Lorraine Stevens [437]**

Sperm Antibody Laboratory, New York Medical College, Metropolitan Hospital, 1900 Second Ave, New York, NY 10029

**Helen R. Strausser [145]**

Department of Zoology, Rutgers University, 195 University Ave, Newark, NJ 07012

## **xiv / Contributors**

### **Osias Stutman [121]**

Memorial Sloan-Kettering Cancer Center, New York, NY 10021

### **Shoshichi Takeuchi [245]**

Department of Obstetrics and Gynecology, Niigata University, School of Medicine, 1 Asahimachi-Dori, Niigata, Japan

### **G.P. Talwar [451]**

Department of Biochemistry, All India Institute of Medical Sciences, Ansari Nagar, New Delhi 110029, India

### **A.K. Tandon [451]**

Department of Biochemistry, All India Institute of Medical Sciences, Ansari Nagar, New Delhi 110029, India

### **Argyrios N. Theofilopoulos [93]**

Department of Immunopathology, Scripps Clinic and Research Foundation, 10666 North Torrey Pines Rd, La Jolla, CA 92037

### **Don P. Wolf [413]**

Department of Obstetrics and Gynecology, Hospital of the University of Pennsylvania, 106 Dulles Building, 3400 Spruce St, Philadelphia, PA 19104

### **Tatsuru Yamanaka [381]**

Division of Infectious Diseases, Children's Hospital, 219 Bryant St, Buffalo, NY 14222

## Foreword

The science of immunology, starting as a tool of microbiology, which was then called bacteriology, has now touched almost every discipline of biomedical science—and it has enriched them all. Although not all the phenomena of immune competence have as yet yielded to investigation, the cascade of the host's immunologic defenses in health is increasingly understood, and its relevance and translation to the problems of disease are beginning to come under analysis.

The so-called "biologic revolution" of the 1960s and 1970s might more properly be called a revolution in molecular biology, based upon the emergence of microbial genetics, the introduction of the biochemical insights into the field of genetics as most of the biologic sciences began to fuse, and thereafter the concept of molecular information transfer, which has so enriched immunology and the other biologic disciplines through its studies of gene expression. Expression of abnormal lymphocyte function, especially of T cells, and serum factors, especially complement, affect the immune process, as does the immunogenetic variation of the HLA antigen.

Reproductive science appears particularly attractive to immunologic study, from the onset of conception and the attendant problems of fertility and infertility control, to pregnancy wastage and other unresolved disorders of pregnancy related to the fetal-host relationship, to the similar problem of the alien growth of cancer in an unwilling host. Indeed, the questions concerning immune competence in pregnancy and cancer have invited speculation and hypothesis for some time, and evidence is beginning to accumulate that similarities do exist. Of course, in the case of the latter dread disorder, there is a clear invitation to the study of antigenicity to aid early diagnosis, and to the study of antibody response to aid in treatment.

The study of these basic and applied immunologic problems has barely started, for the science itself, in modern technologic terms, is really in its infancy; but there seems little reason to doubt its increasing importance. The high scientific merit brought together for this symposium should focus attention on the immunologic problems of reproductive science and stimulate investigation into this critical area. I believe this volume represents a milestone, for it will establish the identity of reproductive immunology as a significant area of basic immunology and as a significant division of the discipline of reproductive medicine.

**Saul B. Gusberg**

*Distinguished Service Professor  
Mount Sinai School of Medicine of the  
City University of New York*



## Preface

The field of reproductive immunology has seen very extensive growth and development in recent years. The volume presented here represents an outgrowth of this development. Its publication was first considered during the early planning stages for the First S. B. Gusberg Seminar on Reproductive Immunology, which took place at the Mount Sinai Medical Center in New York in June 1980 and was meant to achieve two main purposes: First, to honor Saul B. Gusberg, then president of the *American Cancer Society* and one of the most eminent gynecologic oncologists in the country, and second, to unite reproductive immunologists both from within the United States and from overseas in a meeting dedicated solely to this exciting field. As the number of announced participants in that meeting grew, it became apparent that the Festschrift in honor of Dr Gusberg that had been planned by the *Mount Sinai Journal of Medicine* could not include all of the material presented; at that stage, the decision was made to publish a "proceedings" volume to contain all of the material. In addition, other contributors have since been invited to cover certain areas felt to be essential in a book to be entitled "Reproductive Immunology." Thus, the product presented here represents a compendium of material largely based on papers presented at the First S. B. Gusberg Seminar on Reproductive Immunology, but also includes material that has never before been presented. Most of the contributions included here, if they ever appeared before in print, have been completely restructured.

Reproductive immunology represents a field of basic and applied research that is being entered from various directions by increasing numbers of investigators. These multiple points of view resulted initially in a rather diffuse definition of the field; but with its increasing sophistication, reproductive immunology has been more clearly defined. The recent creation of two specialty journals in the field, the *Journal of Reproductive Immunology* and the *American Journal of Reproductive Immunology*, has led to the recognition that reproductive immunology may be considered a well established subentity within general immunology.

No claim of completeness is made for the volume presented here. An attempt was made, however, to give a representative overview of the variety of activities at present in this rapidly growing field. It is hoped that this volume will, on the one hand, give reproductive immunologists an authoritative review of current active research in the field and, on the other hand, allow the bystander — whether clinician or general immunologist — to gain interest and insight into the field.

None of this work would have been possible without the dedicated collaboration of many friends and coworkers; it would be impossible to list them all. Let me therefore concentrate on those few who made some direct contribution to the development of this book. It was Saul B. Gusberg, chairman of the Department of Obstetrics and Gynecology at the Mount Sinai School of Medicine, who, as a gynecologic oncologist, very early recognized the importance of reproductive immunology. His early support encouraged the development of reproductive immunology at Mount Sinai. John P. Gusdon, Jr's, untiring efforts over many years finally led to the foundation of the *American Society for the Immunology of Reproduction*, which Dr Gusdon so deservedly chairs as its first president. It was Dr Gusdon's effort that was so essential in clearly defining reproductive immunology as a separate entity within the United States. Last

and most deservingly, I have to thank all those investigators who worked to define and develop the field during the early years; they were the forerunners who allowed us later to earn part of their glory. Again, it seems impossible to note them all; but no one deserves mention more than Rupert E. Billingham and William Pollack, who so graciously contributed to this volume, and whom we all admire as "fathers" of reproductive immunology. Let it be hoped that this volume will be of some value to those who will follow in the footsteps of these great scientists.

**Norbert Gleicher**

*Editor*

# Contents

Contributors	xi
Foreword	
<i>Saul B. Gusberg</i>	xv
Preface	
<i>Norbert Gleicher</i>	xvii
<b>General Aspects of Immunology</b>	
1 Introduction to Immunology	
<i>Hugh R.K. Barber</i>	3
2 Genetic Control of the Immune System	
<i>Kurt Hirschhorn</i>	17
3 Immunoassay in Reproductive Medicine	
<i>Philip C. Beers</i>	21
<b>Developmental Immunology</b>	
4 Development of the Fetal Immune System	
<i>Israel Siegel and Norbert Gleicher</i>	31
5 Functional Ontogeny of Human Lymphoid Cells as a Factor in Maternal-Fetal Tolerance	
<i>Frederick P. Siegal</i>	41
6 Fetal Synthesis of Immunoglobulins	
<i>Lars L. Cederqvist</i>	47
7 Sequential Activation of V Genes During Postnatal Life	
<i>Constantin A. Bona</i>	53
<b>Pregnancy Immunology</b>	
8 Immunobiology of the Maternal-Fetal Relationship	
<i>Rupert E. Billingham</i>	63
9 The Human Syncytiotrophoblast Microvillous Plasma Membrane	
<i>Peter M. Johnson, Peter J. Brown, Anthony O. Ogbimi, and Laxmi C.P. Shah</i>	77
10 The Biology of Immune Complexes and Their Possible Role in Pregnancy	
<i>Argyrios N. Theofilopoulos, Norbert Gleicher, Aparecido B. Pereira, and Frank J. Dixon</i>	93

11	Fetal and Maternal Red Cell Immune Adherence (RCIA) Receptors <i>Israel Siegel and Norbert Gleicher</i>	115
12	Comparison of Cellular Immune Changes in the Draining Paraaortic Lymph Nodes in Syngeneic and Allogeneic Pregnancies <i>Susan R.S. Gottesman and Osias Stutman</i>	121
13	Regulation of Cellular Immune Response From the Mother to the Paternal Antigens of the Conceptus <i>Gerard Chaouat</i>	137
14	Effects of Sex Hormones on Some T and B Cell Functions as Evidenced by Differential Immune Expression Between Male and Female Mice and Cyclic Pattern of Immune Responsiveness During the Estrous Cycle <i>Urszula Krzych, Helen R. Strausser, Joseph P. Bressler, and Allan L. Goldstein</i>	145
15	Age-Related Impairments in Rodent Pregnancy Functions in Relation to the Maternal Immune System <i>Christian F. Holinka</i>	151
16	Maternal-Neonatal Interactions and Human Breast Milk <i>Genevieve A. Losonsky and Pearay L. Ogra</i>	171

### Clinical Aspects of Pregnancy Immunology

17	Rh Hemolytic Disease of the Newborn: Its Cause and Prevention <i>William Pollack</i>	185
18	Current Clinical Concepts in Hemolytic Disease and Blood Group Incompatibility <i>Sheldon H. Cherry</i>	205
19	Epidemiology of Rh Hemolytic Disease of the Newborn, United States, 1960-1979 <i>Melissa M. Adams and Joanne Gustafson</i>	213
20	Some Immunological Similarities and Differences Between Normal and Diabetic Pregnancies <i>Robert M. Galbraith and W. Page Faulk</i>	219
21	The Immunologic Concept of EPH-Gestosis <i>Norbert Gleicher and Israel Siegel</i>	229
22	An Immune Dependency of Trophoblastic Growth Implied by the Antithetic Difference in Immunology Between Spontaneous Abortion and Hydatidiform Mole <i>Shoshichi Takeuchi</i>	245
23	Histocompatibility Antigens in Pregnancy, Abortions, Infertility, Preeclampsia, and Trophoblast Neoplasms <i>Roland A. Pattillo</i>	259
24	Amnion on Wounds: A Perspective <i>Richard N. Matthews, John P. Bennett, and W. Page Faulk</i>	269

**Immunologic Disease in Pregnancy**

- 25 Systemic Lupus Erythematosus and Pregnancy: Clinical, Immunological, and Theoretical Aspects  
*Josef S. Smolen and Alfred D. Steinberg* 283
- 26 The Clinical Picture of Connective Tissue Diseases in Pregnancy  
*Harry Spiera* 303
- 27 Lupus Erythematosus, the Placenta, and Pregnancy: A Natural Experiment in Immunologically Mediated Reproductive Failure  
*Carlos R. Abramowsky* 309

**Common Aspects of Pregnancy and Malignancy**

- 28 Trophoblastic Disease: A Bridge Between Pregnancy and Malignancy  
*Liane Deligdisch* 323
- 29 Common Denominators of Pregnancy and Malignancy  
*Norbert Gleicher and Israel Siegel* 339

**Reproductive Tumor Immunology**

- 30 The Immune System in Gynecologic Malignancies  
*Hugh R.K. Barber and Brent Dorsett* 357
- 31 Immunotherapy for Gynecologic Malignancies  
*Carmel J. Cohen and Gunter Deppe* 371
- 32 Gynecologic Aspects of Malignancies Following Immunosuppressive or Cytotoxic Therapy  
*Gunter Deppe* 375

**Fertility Immunology**

- 33 Local Immunologic Defenses in the Genital Tract  
*Pearay L. Ogra, Tatsuru Yamanaka, and Genevieve A. Losonsky* 381
- 34 Immunology of Infertility  
*J. Victor Reyniak* 395
- 35 Etiology of Immune Infertility  
*Chandra Prakash* 403
- 36 Interfering Effect of Human IgG Antisperm Antibodies on Human Sperm Penetration of Zona-Free Hamster Eggs  
*Gilbert G. Haas, Jr., Joseph E. Sokoloski, and Don P. Wolf* 413
- 37 Seminal Immunoglobulins, Autoagglutination in Ejaculates, and Infertility in Men  
*Jan Friberg* 423
- 38 Local Immunity to Sperm as Shown in the Cervical Mucus: Use of Bromelin as a Dissolving Agent and the Retention of Antibody Activity  
*Sidney Shulman, Beatrice Anne Gray, and Lorraine Stevens* 437



**x / Contents**

<b>39</b>	Human Soluble Antigens: Their Isolation and Use in Sperm Antibody Testing <i>Sidney Shulman and Thomas Keane</i>	443
<b>40</b>	Immunologic Interruption of Pregnancy <i>G.P. Talwar, S.K. Gupta, and A.K. Tandon</i>	451
<b>41</b>	Immunologic Effects of Vasectomy in Men and Experimental Animals <i>Pierluigi E. Bigazzi</i>	461
	Index	477

## **General Aspects of Immunology**



# Introduction to Immunology

HUGH R. K. BARBER

*New York Medical College and Lenox Hill Hospital, New York*

## INTRODUCTION

The medical world has turned over many times since I was a medical student. Some specialties have come into their own while others have faded in importance. Today immunology is the glamor specialty of medicine cutting across all specialties.

Modern immunology started when Jenner discovered that inoculation with cowpox protected man against smallpox. The next great advancement in immunology was made by Louis Pasteur. Many contributions followed in the field of infectious diseases. Attempts to convert these contributions towards earlier diagnoses and therapy in oncology met with little success.<sup>1,2</sup>

The medical scientists of that time concluded that tumor-specific antigens logically should be present. Proof of this concept was not forthcoming for another half-century. Numerous attempts at cancer immunotherapy have been undertaken since the turn of the century when studies with outbred laboratory animals demonstrated that strong immunity could be induced against transplantable rodent neoplasms. There followed a period of intense laboratory and clinical investigation of tumor immunotherapy with the anticipation of subsequent control of malignant disease. However, it soon became evident that the immunity demonstrable against normal alloantigens (histocompatibility antigens [HL-A]) was carried in tumor cells rather than against tumor-specific antigens. Although an occasional striking regression occurred, the clinical use of autologous vaccines as immunoadjuvants was equally disappointing. Thus, clinical interest in immunotherapies declined as rapid advances in the fields of surgery, ra-

diation therapy, and chemotherapy provided more promising modalities for cancer therapy.

It is difficult to realize that, during my student days at Columbia College of Physicians and Surgeons, I had the opportunity to be taught by Michael Heidelberger, one of the modern day pioneers of immunology. Alphonse Raymond Dochez was phasing out as chairman of the Department of Bacteriology at that time. They had been preceded by Philip H. Hiss, Frederick Parker Gay, and Hans Zinsser. These scientists represented notable figures in Columbia College of Physicians and Surgeons' great tradition of immunology. Although it all seemed so esoteric, impractical, and far away it obviously stimulated and challenged the minds of the students who studied during that era. The school has continued its leadership in the science of immunology.

Three difficulties face the student of any rapidly developing and expanding subject. It has been difficult to establish a common vocabulary. However, this has now been fairly well achieved. The advancing frontiers always seem very complicated until they are understood and placed in their right perspective. Last in this list is the task of incorporating these advances into the clinical care of the patient. It gives relevance to the subject and permits the physician to accumulate his own experience. Immunology is the subject of the future and, although it is changing almost daily, a sound background in the basic principles of the subject will allow the practitioner to grow with the subject.<sup>3-5</sup>

Immunology is a relatively new medical discipline, the basic concepts of which are fundamental to understanding the prin-