



# Dermatologic Immunology and Allergy

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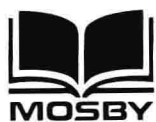
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To

**Dr. Robert A. Good**

educator, scientist, and one of the founders of the modern theory of immunology.

By his brilliant application of theory to clinical disease,  
he made one of the greatest advances in the history of medicine,  
the bone marrow transplant, which has resulted in the  
cure of previously incurable diseases.

# | Foreword

Ralph Waldo Emerson has written that each age must write its own book for the next generation. Books from an older period will not fit, as is the case with speciality books in allergy and immunology.

It is a privilege for me to contribute this foreword to Dr. Stone's excellent book, *Dermatologic Immunology and Allergy*. This book, edited by my long-time associate and friend, has contributions from over 80 clinicians and scientists with expertise in immunology. All of these individuals present not only current data and concepts but also attitudes and philosophies toward these immunologic concepts, as well as clinical diseases with immunologic manifestations.

*Dermatologic Immunology and Allergy* should be especially valuable to all persons in medicine with an interest in dermatologic allergy, particularly residents, postgraduate trainees in allergy, practitioners of dermatology and allergy, and family physicians, who have developed in recent years a great interest in the allergic manifestations in their patients.

This book presents comprehensive reviews of the scientific phase of each of these subjects, in addition to the clinical manifestations. It will help in preparing for board examinations in dermatology and allergy. Individuals who wish to pursue the subject in greater detail may use the comprehensive references, which will be invaluable. This book, with more than 60 subjects covered in depth,

should meet the requirements for information in the field of dermatology, allergy, and immunology for several years to come. It will satisfy those who are interested in basic immunology and pathobiology and those who seek a more practical working solution for everyday problems in allergy and immunology. Many of the contributors have given a great deal of attention to the immunologic manifestations of cutaneous diseases that would not normally be designated to be allergic in origin by many practitioners, such as oral infections, vitiligo, hair loss, acne vulgaris, sexually transmitted diseases, and immunologic granulomas. Excellent chapters are included that describe the use of new drugs and new techniques for managing immunologic problems, such as monoclonal antibodies, the retinoids, the interferon system, and transfer factor in immunotherapy.

There is a heated and significant race in biogenetics. The chapter by Dr. Hollinshead will review this timely subject. The authors in this volume represent a notable group who have communicated skillfully the data on the basic pathobiology of immune processes and the practical aspects of dealing with everyday problems in allergy and immunology.

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# Preface

*There is no darkness, only ignorance.*  
SHAKESPEARE

This textbook is one of those remarkable things that sometimes happen. The story begins in 1972. While reviewing the dermatology and allergy literature on immunology for a paper I was preparing, I became aware of the fact that the revolution in immunology was affecting dermatology, as it was all of medicine and biology, and also that a study of allergy is necessary for a thorough understanding of immunology. Several ideas occurred to me. First, a new dermatology society was necessary for dermatologists to become aware of the new theories and recent advances in immunology and allergy and also to serve as a forum for those in research to discuss and exchange ideas. Second, a new textbook on dermatologic immunology and allergy was needed to bring all of this information together to show how these new theories were changing the way that dermatologists would have to think about cutaneous diseases. A new society and a new textbook—two immense projects that were to occupy me for the next 12 years.

After a great deal of preliminary work and with the help of many wonderful people to whom I will always be indebted, the founding meeting of the American Dermatologic Society for Allergy and Immunology (ADSAI) took place in Chicago at the American Academy of Dermatology meeting in December of 1973. I was elected president and was instructed to proceed with the formation and organization of the society. I invited some of the brightest and best people in dermatology from all parts of the United States to become members of the Board of Directors of ADSAI, the first national dermatologic society devoted to the study of immunology and allergy. We had our first board meeting in Atlantic City, N.J., in the spring of 1974 at the meeting of the Society for Investigative Dermatology. Our first scientific meeting was in New Orleans in September 1975, and we have had nine consecutive yearly meetings since. All of these scientific meetings have been exceptional for the excellent quality of the programs. ADSAI is becoming recognized as the center for research workers in the field of immunology and as an important educational force for clinicians in dermatology.

After the fifth meeting of ADSAI in September of 1980, I stated on the second objective, the editing of a

new textbook on dermatologic immunology and allergy. This book would not have been possible without ADSAI. The excellent scientific programs and my association with the brilliant scientists on the board of directors were a necessary part of the preparation for this text. I began this project by writing a table of contents, dividing the book into two sections, the first containing the basic theory of allergy and immunology and the second containing the application of theory to clinical dermatologic diseases. By the spring of 1982 I had a contract with the publisher; it was not until the spring of 1983 that I had contributors for the entire book.

The process of finding contributors for each of the 65 chapters is a long and involved story, but I owe most to the Board of Directors of ADSAI and to my colleagues at Wayne State University Medical School. I am also greatly indebted to Dr. Ariel Hollinshead of the George Washington University for her help in obtaining authors for several difficult chapters and to Dr. Roy Rogers III of the Mayo Clinic for suggesting several excellent authors who have special expertise on certain subjects in immunology.

This book contains subject matter that is new in dermatologic textbooks. "Hemostasis and Blood Coagulation," by Dr. Eberhard F. Mammen, is included because of the intimate relation between factors involved in this subject and immunology. "Biochemistry of the Immune Response," by Dr. Terence M. Phillips, contains a clear and concise explanation of fundamental immune processes. "Psychiatric and Neural Aspects of Allergy and Immunology," by Dr. Michael A. Fauman, is an interesting discussion of the relation between the nervous system and the immune system. The chapter "Dermal Extracellular Matrix," by Dr. Antonio Martinez-Hernandez, makes the suggestion that although the concept of collagen diseases served a useful purpose, these diseases should now be called immunologic diseases because that is what they are and because the collagen in these diseases is normal; Dr. Martinez-Hernandez then discusses the true collagen diseases.

As I stated at the beginning of this preface, a complete understanding of immunology for dermatologists must include a study of allergy. Dermatology textbooks

should have chapters on allergic rhinitis and asthma. All allergy textbooks have chapters on atopic dermatitis, urticaria, and other dermatologic diseases. Allergy as defined by von Pirquet is equivalent to immunology. However, by modern usage as Dr. Stewart Sell explains in his chapter, "Immunopathologic Mechanisms," the term *immunology* implies protection and physiologic reactions, and the terms *allergy* and *hypersensitivity* imply injury and pathologic reactions. The historical foundations of allergy and hypersensitivity are based on skin reactions; thus from the beginning, allergy has always been a part of dermatology. There is a very close relation between respiratory allergy and skin allergy that has never been adequately investigated by dermatologists. The main reason is that dermatologists are not trained in respiratory allergy. Therefore I have included two chapters by an excellent allergist, Dr. Paul A. Greenberger of Northwestern University, the first on basic theory and the second on clinical respiratory allergy, namely, allergic rhinitis and asthma. The time has come for dermatology training programs to include courses in respiratory allergy in addition to courses such as histopathology, mycology, and dermatologic surgery. Dermatologists could then do as much allergy as they believe they are competent to do, just as they now do as much surgery as they believe they are competent to do. This would restore the subject of allergy to its rightful place in dermatology, enlarge the field of dermatology, and bring dermatology into closer contact with the mainstream of medicine.

The editing of this book has been an enormous but rewarding task. The editor alone is responsible for the division of the book into two sections and for all the topics included in each section. The subject matter of immunology is so interrelated that repetition is unavoidable. Thus Chapter 9 and Chapter 26 discuss the same immunologic mechanisms—one from a pathologist's viewpoint and the other from an allergist's viewpoint; it is instructive to note the differences. For a comprehensive new textbook on subjects as important as the current theories and practical applications of immunology and allergy,

repetition is one of the best methods in which to learn a topic so vast and complex. I sincerely hope it will be considered in this light.

This book is dedicated to Dr. Robert A. Good. His class was 2 years ahead of mine at the University of Minnesota Medical School. I followed his inspiring career from the Pediatric Department at the University of Minnesota to the present day. Dr. Robert W. Goltz's excellent biography of Dr. Good tells this remarkable story, and in Chapter 64, Dr. Richard Hong tells the story of how Dr. Good made one of the greatest advances in modern medicine, the bone marrow transplant.

Dr. Good gives us a history of modern immunology in which he played so important a part, followed by the first section of the book, which contains a series of chapters explaining the basic theory of modern immunology beginning with the wonderful introductory chapter, "Origins of the Immune Response," by Dr. Noel R. Rose, and continuing with "Thymus and Regulatory Factors," "Genetics and HLA," "Arachidonic Acid Cascade," "Autoimmunity," "Direct and Indirect Immunofluorescence," and other chapters pertaining to theory. The second section contains the application of basic theory to a comprehensive list of specific clinical dermatologic diseases, including genetic diseases, bullous diseases, collagen-vascular diseases, infectious diseases, oral mucous membrane diseases, granulomas, tumors, papulosquamous diseases, and allergic diseases. The last six chapters comprise subjects of special interest for immunology. These include the retinoids, monoclonal antibodies, transfer factor, the human interferon system, immunotherapy, and finally, genetic engineering. After reading this second section of the book one can appreciate how these new theories in immunology and allergy are modifying and changing the theoretical foundations of dermatology and how important it is for physicians to understand these theories and their application to clinical disease. I hope this book will appeal to residents, clinicians, and investigators.

Julius Stone, M.D.

# Biography of Robert A. Good

Robert W. Goltz

Into each generation of physicians are born only a few who have that rare combination of energy, originality of thinking, and organizational ability that enables them to make monumental contributions to biomedical science and thus to have a fundamental impact on the practice of medicine. In our generation there is Dr. Robert Alan Good. The innovations he has made and new directions he has set in immunobiology have already been of incalculable benefit to humanity. The final impact of his conceptions cannot even now be fully assessed. It has been said that consequences of the French Revolution of 1790 are not yet known. The same is true of the revolutionary contributions of Good.

Good was born on May 21, 1922, in the small northern town of Crosby, Minn., where his father was a school principal and his mother was a schoolteacher. When he was only 5 years old, his father died of cancer. This may have had a subconscious if not conscious influence on his later interest in controlling this dread ailment. After his father's death, the family found itself in severely straitened financial circumstances, and he was forced to contribute to the family's finances by doing odd jobs. At age 11 years he began working summers on a farm. This may have been the seed for his interest in a farm that he now owns and operates outside of Minneapolis.

Later the family moved to Minneapolis, where Good finished public high school, graduating in 1940. He enrolled in the premedical course at the University of Minnesota, receiving his bachelor's degree with cum laude honors in 1944 and election to Phi Beta Kappa. In the summer of 1944 he was stricken with a febrile illness, perhaps poliomyelitis. From this he recovered after many months, being left with some weakness in his legs, which has led to a characteristic way of walking. In spite of this crippling illness, he entered the University of Minnesota Medical School on schedule in 1943, received his M.D. in 1947, ranked first in his class, and was elected to Alpha Omega Alpha honorary medical society. Simultaneously he carried out research in anatomy and bacteriology as a teaching assistant in the Department of Anatomy and received his Ph.D. in anatomy in 1947. His doctoral dissertation bore the title, *Morphological Mech-*



*anisms of Hyperergic Inflammation in the Brain, with Special Reference to the Significance of Local Plasma Cell Formation.* In this work he demonstrated that the plasma cell is responsible for antibody production.

While doing his residency in pediatrics at the University of Minnesota Hospital in 1947 and 1948, he was honored by being named Fellow of the National Foundation of Infantile Paralysis. The following year he was named the Helen Hay Whitney Foundation Fellow in Rheumatic Fever Research. Part of this fellowship was served doing research at the Rockefeller Institute in New York. He returned to the University of Minnesota in 1950, where he held a Markle Foundation Scholarship in Medical Science. He was appointed to the faculty of the University of Minnesota Medical School as an instructor but rose quickly to the ranks of Assistant Professor of Pediatrics in 1951 and associate professor in 1953. In 1954 he was named the American Legion Memorial Heart

Research Professor of Pediatrics at the university. This position he held until leaving to accept the position of director and head of the Rockefeller Institute in 1973. In 1962 Good was named professor of microbiology at the University of Minnesota Medical School, and in 1965 he was named distinguished service professor. In 1969 he was elevated to the prestigious rank of Regents Professor of Pediatrics and Microbiology at the University of Minnesota Medical School. In 1970 he assumed the additional responsibility of being professor and head of the Department of Pathology.

In 1973 Good was appointed president and director of the Sloan-Kettering Institute for Cancer Research, with the additional rank of director of research at the Memorial Hospital for Cancer and Allied Diseases. He was also director of research at the Memorial Sloan-Kettering Cancer Center in New York. He was director of the Graduate School of Medical Sciences at the Sloan-Kettering Division of Cornell University in New York and adjunct professor and visiting physician at Rockefeller University. He was professor of pathology at Sloan-Kettering Division, the Graduate School of Medical Sciences, Cornell University, and attending physician in the Departments of Medicine and Pediatrics, Memorial Hospital for Cancer and Allied Diseases. He was also attending pediatrician at the New York Hospital, and professor of medicine and professor of pediatrics at Cornell University Medical College. In 1980 he was named head of the Laboratory of Developmental Immunobiology, Cellular Engineering and Cancer Immunotherapy of the Sloan-Kettering Institute for Cancer Research.

In 1982 Good struck off in a new direction when he became professor of pediatrics and research professor of medicine at the University of Oklahoma Health Sciences Center, Oklahoma City. There he is head of the cancer program of the Oklahoma Medical Research Foundation and attending pediatrician and head of Pediatric Clinical Immunology at Oklahoma Children's Memorial Hospital, Oklahoma City.

Good's contributions to biomedical knowledge are extraordinary. Perhaps more than anyone else, he was responsible for developing concepts underlying the modern science of immunology. This field, undoubtedly the most exciting and productive area in current biomedical science, is to a large extent based on the discoveries he made in the 1950s and 1960s. His concepts form the basis for the cellular theory of immune mechanisms.

Early in the 1950s, Good's studies on agammaglobulinemia led him to a reevaluation of the role of the thymus. Up to that time this organ had been considered unimportant, even vestigial. But Good's studies convinced him that the thymus played a key role in the establishment of immune competence. Laboratory studies showed that ablation of the thymus in experimental animals immediately after birth led to profound crippling

of the immune mechanisms. Thymic abnormalities were then demonstrated in cases of congenital immunologic deficiency in humans. Further studies by Good led to definition of the thymus-dependent lymphocyte, or T cell, as the primary cell mediator of cellular and tissue immunity and the B lymphocyte as the factory for the production of circulating immunoglobulins. T lymphocytes were named for their derivation from or at least processing by the thymus gland, whereas B lymphocytes received their name from their relationship to the bursa of Fabricius of chickens, an organ "rediscovered" by Good that had an apparent counterpart in lymphoid tissues of the human gastrointestinal tract.

Development of this basic theory of divergence of lymphocyte function eventually led to development of that currently crucial area of biomedical progress, transplantation immunology. Good and his coworkers in the 1960s were the first to apply human bone marrow transplantation to restore immune function to children congenitally deficient in it. Bone marrow transplantation has since become the prime method of dealing with hematologic malignancy, particularly in children, and in the treatment of aplastic anemia and the congenital immunologic deficiency states. All of this has derived from the fundamental theories developed by Good and his coworkers more than a decade ago.

Recently Good has been interested in nutritional influences on immune mechanisms, particularly as they apply to cancer. This interest was engendered in the early 1970s when Good and his coworkers observed that they were able to foster resistance to certain blood and breast cancers in rodents by alteration of their protein intake. He has traveled widely in the Far East in an effort to determine why certain forms of cancer are more prevalent in one district than in another and any influence of diet in those areas on these differences.

### Honors and awards

One of the results of Good's pioneering contributions to biomedical science is the huge number of significant honors and awards that he has received. The first of these was the Borden Undergraduate Research Award at the University of Minnesota Medical School while he was still a student in 1946. Later he was the Fellow for the National Foundation for Infantile Paralysis in 1947, the Helen Hay Whitney Foundation Fellow in Rheumatic Fever Research from 1948 to 1950, Markle Foundation Scholar in Medical Science from 1950 to 1955, recipient of the E. Mead Johnson Award for Outstanding Research Contributions to Pediatrics presented by the American Academy of Pediatrics in 1955, recipient of the Theobald Smith Award for Outstanding Research Contributions to Medical Science presented by Eli Lilly and Company in 1955, recipient of the Sixth Annual Parke Davis Award for Excellence of Research in Experimental Pathology



presented by the American Society of Experimental Pathologists in 1962, and recipient of the Rector's Medal of the University of Helsinki for Outstanding Contributions to Medicine and Microbiology in 1963. He received the Distinguished Service Award of the University of Minnesota in 1965, the Pemberton Lectureship Award for Outstanding Contributions to the Study of Rheumatic Disease presented by the Philadelphia Rheumatism Society in October of 1966, the R.E. Dyer Lectureship Award for Outstanding Achievement in Research Important to Medical Science presented by the National Institutes of Health in 1967, the Gordon Wilson Lectureship Award and Medal for Outstanding Research in Medicine presented by the American Clinical and Climatological Association in 1967, the Robert A. Cooke Memorial Lectureship and Gold Medal for Outstanding Contribution to Immunology presented by the American Academy of Immunology in 1968, the Clemens von Pirquet Gold Medal for Outstanding Contribution to Allergy presented at the Ninth Annual Forum on Allergy in May of 1968, the President's Medal of the University of Padua for Outstanding Contributions to Immunopathology in 1968, the first Squibb Award for Excellence of Achievement presented by the Infectious Disease Society of America in 1968, the McGraw Medal for Outstanding Contribution to Transplantation Surgery presented by the Detroit Surgical Association in 1969, the John Stewart Memorial Award of Dalhousie University for Outstanding Contribution to Medicine in 1969, the Howard Taylor Ricketts Award of the University of Chicago for Outstanding Contribution to Understanding Resistance to Infection, the Gold Plate Award of the American Academy of Achievement for the first successful marrow transplantation to correct inborn errors of metabolism in 1970, the Gairdner Foundation Award, Toronto, in recognition of his many contributions to the understanding of host defense mechanisms in 1970, the Borden Award for Outstanding Contribution to Developmental Biology presented by the Association of American Medical Colleges in 1970, the Annual Salute to Medical Research of the City of Hope, Chicago, for outstanding contribution to cancer research in 1970, the Albert Lasker Lectureship Award for Outstanding Contribution to Immunology presented by the Salk Institute in 1971, the Third Annual Award for Service to Humanity presented by the Greater New York Chapter of the National Foundation in 1971, and the American College of Physicians Award for distinguished contribution to sciences related to medicine.

As noted above, Good was appointed to the rank of Regents Professor at the University of Minnesota in 1969. In 1970 he received the single most prestigious American award, the Albert Lasker Award for Clinical Medical Research presented by the Albert and Mary Lasker Foundation, in which he was cited for his exciting and lifesaving new procedures in cellular engineering,

which led to a new era in the control and treatment of disease. In 1971 he was a Harvey Lecturer of the Harvey Society in New York. He received the Silver Medal of Honor of the Swedish Medical Society, Lucy Wortham James Award of the James Ewing Society, and the David A. Karnofsky Memorial Medal of the American Society of Clinical Oncology.

In addition to these honors, Good has been named recipient of the Dr. Chaim Yassky Award of the New York Chapter of Hadassah, visiting professor of the Royal Postgraduate Medical School, University of London in 1973, and College Medalist for Meritorious Service in Diseases of the Chest presented by the American College of Chest Physicians in 1974. He received the Guest Lectureship Award for Basic Science Research in Cytology presented by the American Society of Cytology in 1974, the Lila Gruber Memorial Award for Cancer Research presented by the American Academy of Dermatology in 1974, and the Award in Cancer Immunology for Pioneering Research on the Immunodeficiencies of Cancer Patients and the Increased Incidence of Certain Tumors in Immunologically Deficient Patients presented by the Cancer Research Institute in 1975. He was named to the first Daniel Y.E. Perey Research Lectureship of McMaster University in 1976, the second annual Myron Karon Memorial Lectureship Award of Children's Hospital in Los Angeles and the first Honorary Charter Membership of the Wright State University Academy of Medicine in 1978. Also, in 1978 the American Dermatologic Society for Allergy and Immunology presented him their Medal of Honor in recognition of meritorious contribution to immunology and immunodermatology. In 1978 he was given the Outstanding Achievement Award of his alma mater, the University of Minnesota, in recognition of noted professional attainment. More recently he has received other honors, including the Man of the Year Award of the Chapter of the Leukemia Society of America and honorific recognition in India, Korea, and the People's Republic of China.

Good holds a number of honorary degrees as well as honorary memberships in American and foreign scientific societies. These include Doctor of Medicine (Honorary) of the University of Uppsala, Sweden; Doctor of Science of New York Medical College; Doctor of Science, Medical College of Ohio at Toledo; Doctor of Science of the College of Medicine and Dentistry of New Jersey; Doctor of Science, Hahnemann Medical College, Philadelphia; Doctor of Science, University of Chicago; Doctor of Science, St. John's University, New York; Doctor of Science, University of the Health Sciences of the Chicago Medical School; and Professor Emeritus of the Catholic Medical College, Seoul, South Korea. He holds full membership in a large number of societies related to immunology, experimental pathology, pediatrics, rheu-

matology, allergy, and dermatology. He has served on the editorial boards of no less than 30 scientific journals covering a wide variety of fields, including immunology, nephrology, cancer biology, transplantation, immunopharmacology, and experimental pathology.

Good has lent his talents to a number of philanthropic bodies, including service on the World Health Organization Expert Advisory Panel on Immunology in 1967, the World Health Organization Experimental Animal Model for Human Disease in 1970, and the Ad Hoc Committee to the President's Scientific Advisory Council on Biological Medical Sciences in 1970. In addition, he has served on U.S. Public Health Service panels, and as a special program planning consultant to the National Institute of Child Health and Human Development. In 1972 he was asked by the President to serve on the panel to advise on the Conquest of Cancer program.

Throughout his career, Good has been a prolific writer. His bibliography numbers well over 1500 publications, and he has been author or editor of 26 books. The depth and breadth of the studies covered in these publications is truly astounding and includes some of the pioneering works in modern immunology and immunopathology.

### **Personal qualifications**

Good, in addition to being a giant of an intellect, is also a large man physically, standing over 6 feet 2 inches. In spite of somewhat impaired walking because of his paralytic illness of 1946, he presents an aura of tremendous vigor and vitality. Any difficulty in locomotion has certainly never slowed him down. His capacity for work is truly awe inspiring. He is famous for calling together his colleagues and staff at 3 or 4 AM for an impromptu meeting to discuss ideas that have come to him during the wee hours when everyone else was asleep. His workday often begins at that hour and goes on until well after dark in the evening. The demands he makes on his fellow workers and students are enormous, but because of the excitement he generates, none of Good's colleagues believes that he or she has been put upon or overworked. Throughout his career Good has been unusually successful in attracting to his side a large number of exceedingly able students. He has inspired them to achieve their greatest potential, many becoming the leaders of academic immunology of the present generation. Over a hundred of his former students are now professors. Fellows who worked with him and whose careers he shaped include Paul Quie, Henry Gewurz, Richard Hong, Alfred Michael, Robert Jordon, Richard O'Reilly, Max Cooper, Robert Vermer, and Dorothy Windhorst. Many others might also be mentioned.

One of Good's most endearing characteristics has

been his optimism and faith in the ability of young people to do creative work, given the opportunity and a little encouragement. He has always been willing to give anyone who showed interest and inclination a chance to prove himself or herself in the laboratory. As might be expected, not all lived up to their promise, but in this culture medium of freedom and encouragement grew an imposing number of new careers in biomedical investigation.

A visit to Good's office shows him involved in a tremendous number of projects, writing, inspiring, and overseeing research of younger investigators, and carrying on his own many current projects. He has always maintained a lively personal involvement in clinical medicine and daily makes his appearance on the wards and in the clinics to visit his patients, usually children, who love him dearly. Good's almost unbelievable work schedule has left him little time for personal pursuits, but he and his wife do maintain as a retreat a farm outside Minneapolis, where Bob has shown a special interest in organic farming. Perhaps this ties in with his current interest in the relationship between diet and immunity and susceptibility to cancer.

In sum, Robert Alan Good, M.D., Ph.D., is truly one of the towering figures of biomedical science of the second half of the twentieth century. His ideas and his research have led to the development of the single most important area of biomedical science of this generation: understanding of immune mechanisms and transplantation biology. His current studies give promise of leading to further understanding of the biology, prevention, and cure of cancer. His laboratory plays a leading role in the study of cell-cell interaction in immunologic reactivity, cell proliferation, and cell differentiation and control. Good remains, as he has always been, an inspiring leader and teacher of young persons. Many of his past and present students are the leaders of the science of immunobiology of today and tomorrow.

Good, perhaps more than anyone else, has been responsible for the creation of the modern science of immunobiology. New understanding of immune mechanisms, inflammation, and the whole gamut of cell-cell interaction have already made a profound contribution to the understanding of the pathogenesis of many diseases, not the least of which are disorders of the skin, and already to the practice of clinical dermatology. And the end is not yet in sight. Indeed, because of immunobiology, we are only at the beginning of a whole new and exciting era in allergy and dermatology. This we owe in large measure to the seminal ideas of Good. It is altogether fitting therefore that he should be again honored by having this book of the allergy and immunology of the skin dedicated to him.



# Some reflections on key historical events in development of a science of allergy

Robert A. Good

Discoveries in modern immunology promise at long last to lift the cloak of black magic from the clinical discipline of allergy. The history of allergy is deeply intertwined, however, with that of immunology. Indeed, this has to be true, since understanding of allergic disease is based on progress in analysis of cellular and molecular aspects of immunology. Thus the most important steps in development of modern allergy have been the definition of reagins, like other antibodies, in molecular terms<sup>23</sup>; definition of the biologic function of the thymus<sup>13,43</sup> and discovery that two major systems of cells subserve immune reactions<sup>6,8</sup>; elucidation of the genetic controls of production of antibodies of the IgE immunoglobulin class<sup>41</sup>; elucidation of the influence of the major histocompatibility complex on cell-cell interactions in production of antibodies<sup>60</sup>; definition of the rearrangement of jumping genes to account for almost unlimited numbers of antibody specificities<sup>39,40,53</sup>; definition of chemistry of the receptors on surfaces of antibody-producing cells<sup>32</sup>; identification and analysis of the receptor molecules and growth factors that address them and thus that are involved in expansion of specific cellular populations involved in immune reactions<sup>7,51</sup>; understanding of the nature of receptors on mast cells and the biochemistry of the antigen-antibody triggering reactions<sup>17,44</sup> that underlie degranulation of these elements in allergic response; and understanding the biochemistry of specific, class-specific, and nonspecific regulation of immunologic events and effector phenomena.<sup>31</sup> Thus for allergy there is an obligatory parallel with the surging development of immunology. The basic sciences are inseparable.

Pursuit of knowledge in each of these directions I believe makes it certain that a truly basic scientific approach to allergy will generate a powerful immunopharmacology and even provide the basis for scientific immunoprophylaxis that will control allergic disease. With the scientific enterprise going so well, success is inevitable.

Although much progress has been made, some of it quite recently, in understanding each of these issues, the hope that the patient with allergy can be put at ease regularly, completely, and safely remains an aspiration and goal of modern medicine, immunology, and allergy. Realization of these great promises, however, is largely a subject for the future rather than a story of the past. Nonetheless, as is revealed in the pages of the present volume, progress in the science underpinning allergic disease, and progress that permits understanding of the nature and management of allergic disease has been so great in recent years that it seems certain that these goals will soon be achieved. Thus it is quite pertinent to consider briefly the historical perspective on how it is that allergy has come to its present state and from these considerations to try to project the future of the fascinating discipline of clinical allergy.

As with all of modern immunology, development of our understanding of allergy has involved an extraordinary interplay between experiments of nature in the clinics on the one hand, and on the other, the surging advances in chemistry and technology to yield progressive understanding of crucial relationships in allergy that surely will underlie effective prevention and treatment of allergic diseases.<sup>9-11</sup>

It all began with Jenner's interpretation<sup>28</sup> of that extraordinary experiment of nature represented by the clear-skinned milkmaids at a time when the disfiguring plague—smallpox—was rampant. Jenner's contributions from interpretation of the immunity of milkmaids to smallpox yielded a four-component legacy: (1) it introduced the initial example of an effective, safe, and widely distributable immunization against disease; (2) it was the first use of an attenuated virus in prophylaxis; (3) it gave the first clear evidence that protection against disease could be associated with increased rather than decreased reactivity of the host against a potential pathogen (allergy); and (4) it provided the first glimpse of interference of