YEAR BOOK®

YEAR BOOK OF ALLERGY, ASTHMA, AND CLINICAL IMMUNOLOGY™ 2001

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YEAR BOOK
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2001

The Year Book of ALLERGY, ASTHMA, AND CLINICAL IMMUNOLOGY™

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Statement of Purpose

The YEAR BOOK Series

The YEAR BOOK series was devised in 1901 by health professionals who observed that the literature of medicine and related disciplines had become so voluminous that no one individual could read and place in perspective every potential advance in a major specialty. That has never been more true than it is today.

More than merely a series of books, YEAR BOOK volumes are the tangible results of a unique service designed to accomplish the following:

- to *survey* a wide range of journals
- to *select* from those journals papers representing significant advances and statements of important clinical principles
- to provide *abstracts* of those articles that are readable, convenient summaries of their key points
- to provide *informed commentary* about their relevance

These publications grow out of a unique process that draws on the talents of outstanding authorities in clinical and fundamental disciplines, trained literature specialists, and professional writers—all supported by the resources of Mosby, the world's preeminent publisher for the health professions.

The Literature Base

Mosby and its editors survey approximately 500 journals published worldwide, covering the full range of the health professions. On an annual basis, the publisher examines usage patterns and polls its expert authorities to add new journals to the literature base and to delete journals that are no longer useful as potential YEAR BOOK sources.

The Literature Survey

More than 250,000 peer-reviewed articles per year are scanned systematically—including title, text, illustrations, tables, and references—by the publisher's team of literature specialists. Each scan is compared, article by article, to the search strategies that the publisher has developed in consultation with the nearly 200 outside experts who form the pool of YEAR BOOK editors. A given article with broad scientific or clinical implications may be reviewed by any number of YEAR BOOK editors, from one to a dozen or more, regardless of the discipline for which the paper was originally published. In turn, each editor who receives the article reviews it to determine whether it should be included in his or her volume. This decision is based on the article's inherent quality, its relevance to readers of that YEAR BOOK, and the editor's goal to represent a comprehensive picture of a given field in each volume of the YEAR BOOK. In addition, the editor indicates when to include figures and tables from the article to help the YEAR BOOK reader better understand the information.

Of the quarter million articles scanned each year, only 5% are selected for publication within the YEAR BOOK series, thereby assuring readers of the high value of every selection.

The Abstract

The publisher's abstracting staff is headed by a seasoned medical editing professional and includes individuals with extensive experience in writing for the health professions. When an article is selected for inclusion in a YEAR BOOK, it is assigned to a member of the abstracting staff. The abstractor, guided in many cases by notations supplied by the physician editor, writes a structured, condensed summary designed to rapidly communicate to the reader the essential information contained in the article.

The Commentary

The YEAR BOOK editorial boards, sometimes assisted by guest contributors, write comments that place each article in perspective. This provides the reader with insights from authorities in each discipline that point out the value of the article and that often reflect the authority's thought processes in assessing the article.

Additional Editorial Features

The editorial boards of each YEAR BOOK organize the abstracts and comments to provide a logical and satisfying sequence of information. To enhance the organization, editors also provide introductions to sections or individual chapters, comments linking a number of abstracts, citations to additional literature, and other features.

The published YEAR BOOK contains enhanced bibliographic citations for each selected article, including extended listings of multiple authors and identification of author affiliations. Each YEAR BOOK contains a Table of Contents specific to that year's volume. From year to year, the Table of Contents for a given YEAR BOOK may vary, depending on developments within the field.

Every YEAR BOOK contains a list of the journals from which articles have been selected. This list represents a subset of approximately 500 journals surveyed by the publisher and occasionally reflects a particularly pertinent article from a journal that is not surveyed routinely.

Finally, each volume contains a comprehensive subject index and an index to authors of each selected article.

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Year Book of Sports Medicine®: Drs Shephard, Alexander, Kohrt, Nieman, Torg, and Mr George

Year Book of Surgery®: Drs Copeland, Bland, Cerfolio, Deitch, Eberlein, Howard, Luce, Seeger, and Souba

Year Book of Urology®: Drs Andriole and Coplen

Year Book of Vascular Surgery®: Dr Porter

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Journals Represented

Mosby and its Editors survey approximately 500 journals for its abstract and commentary publications. From these journals, the Editors select the articles to be abstracted. Journals represented in this YEAR BOOK are listed below.

Allergy
American Journal of Human Genetics
American Journal of Physiology
American Journal of Respiratory and Critical Care Medicine
Annals of Allergy, Asthma, & Immunology
Annals of Internal Medicine
Archives of Dermatology
Archives of Disease in Childhood
Archives of Family Medicine
Archives of Internal Medicine
Blood
British Journal of Dermatology
British Medical Journal
Cell
Chest
Clinical Immunology and Immunopathology
Clinical and Experimental Allergy
European Respiratory Journal
International Journal of Epidemiology
Journal of Allergy and Clinical Immunology
Journal of Applied Physiology
Journal of Clinical Investigation
Journal of Immunology
Journal of Investigative Dermatology
Journal of Manipulative and Physiological Therapeutics
Journal of Pediatrics
Journal of the American Academy of Dermatology
Journal of the American Medical Association
Lancet
Nature
New England Journal of Medicine
Pediatrics
Proceedings of the National Academy of Sciences
Respiratory Medicine
Science
Thorax

STANDARD ABBREVIATIONS

The following terms are abbreviated in this edition: acquired immunodeficiency syndrome (AIDS), cardiopulmonary resuscitation (CPR), central nervous system (CNS), cerebrospinal fluid (CSF), computed tomography (CT), deoxyribonucleic acid (DNA), electrocardiography (ECG), health maintenance organization (HMO), human immunodeficiency virus (HIV), intensive care unit (ICU), intramuscular (IM), intravenous (IV), magnetic resonance (MR) imaging (MRI), ribonucleic acid (RNA), ultrasound (US), and ultraviolet (UV).

NOTE

The YEAR BOOK OF ALLERGY, ASTHMA, AND CLINICAL IMMUNOLOGY™ is a literature survey service providing abstracts of articles published in the professional literature. Every effort is made to ensure the accuracy of the information presented in these pages. Neither the editors nor the publisher of the YEAR BOOK OF ALLERGY, ASTHMA, AND CLINICAL IMMUNOLOGY™ can be responsible for errors in the original materials. The editors' comments are their own opinions. Mention of specific products within this publication does not constitute endorsement.

To facilitate the use of the YEAR BOOK OF ALLERGY, ASTHMA, AND CLINICAL IMMUNOLOGY™ as a reference tool, all illustrations and tables included in this publication are now identified as they appear in the original article. This change is meant to help the reader recognize that any illustration or table appearing in the YEAR BOOK OF ALLERGY, ASTHMA, AND CLINICAL IMMUNOLOGY™ may be only one of many in the original article. For this reason, figure and table numbers will often appear to be out of sequence within the YEAR BOOK OF ALLERGY, ASTHMA, AND CLINICAL IMMUNOLOGY™.

Publisher's Preface

The publication of the 2001 YEAR BOOK series marks the 100th anniversary of the original Practical Medicine Series of Year Books. To commemorate this milestone, each 2001 Year Book includes an anniversary seal on the cover. The content and format of the Year Books remain unchanged from the beginning of the last century—each volume consists of abstracts of the best scholarly articles of the year, accompanied by expert critical commentaries.

The first Year Book appeared in 1900 when Gustavus P. Head, MD, produced the first *Year Book of the Nose, Throat and Ear*, a volume consisting of highlights from the previous year's best literature, enhanced by expert observations. Dr Head assembled a small group of distinguished physicians to serve as editors, and the first series of Year Books was published in 1901. The first volumes of the Year Book series—*General Medicine, General Surgery, The Eye, Gynecology, Obstetrics, Materia Medica and Therapeutics, Pediatrics, Physiology,* and *Skin and Venereal Diseases*—appeared at monthly intervals, with 10 volumes published in 1 year. The entire series was met with critical enthusiasm.

In 1904, Dr Head's brother, Cloyd, assumed responsibility for the management of the Year Books. In 1905, the volumes began to appear at regular intervals during the calendar year instead of on a monthly basis. By World War I, the Year Books had been established as an authority on medical and surgical progress.

The postwar period brought about a significant change in the practice of medicine: specialization. To accommodate the rise of specialization in medicine, the Year Books were now sold as individual volumes rather than only as a complete set. This change brought about a tremendous response and sales of the books increased. In 1922, the Year Books became even more specialized, as the books now had different editors for the different medical specialties covered in each volume. Later, in 1933, the title of the series changed from the Practical Medicine Series of Year Books to the Practical Medicine Year Books to reflect these new designs.

The Year Books have grown significantly from the first 10-volume series in 1901 to a diversified series of 32 volumes in 2001. That the Year Book series is the only series of their kind to have survived is a testament to the vision and commitment of its founders. Some minor changes in format and design have occurred throughout the years, but the mission of the Year Book series—to provide a record of exceptional medical achievements distinguished by the reflections of many of the great names in medicine today—has remained constant.

Introduction

The publication of the 2001 YEAR BOOK OF ALLERGY, ASTHMA, AND CLINICAL IMMUNOLOGY has proved to be a very rewarding and challenging experience, as it has been for a number of years.

This year, I would like to recognize the contributions of Gabriele Cheatham, who has replaced Mary Peterson as the YEAR BOOK coordinator and who has worked very hard at coordinating the papers, comments, abstracts, and finally putting together the final manuscript.

As usual, we have another fine set of work put together by the editorial board, including Drs John Routes, Joseph Spahn, Mark Boguniewicz, and Henry Milgrom. This year, our book is divided into 6 major chapters that have been utilized for a number of years.

The first chapter involves basic mechanisms in genetic molecular biology related to allergy and immunology. The second chapter looks at both basic and clinical studies in asthma and upper and lower biology mechanisms. The third chapter looks at allergic reactions including drug, food, insect sting, anaphylaxis, and allergic rhinitis. The fourth chapter examines immunologic skin disorders and atopic dermatitis. The fifth examines autoimmunity, immunodeficiency, and vasculitis, and the sixth chapter, unique pharmacologic and biological therapies and factors that control therapy in allergic and immunologic diseases.

Once again, more than 37 journals were represented in the selection of the literature. The first chapter has 32 articles, the second has 72 articles, the third has 17 articles, the fourth has 24 articles, the fifth has 9 articles, and the sixth has 34 articles for a total of 188 articles.

The field of allergy and immunology has continued to advance. We are beginning now to see therapies emerge that will have profound effects on the armamentarium of treatment of allergic diseases in the next decade, as the new millennium advances. Some of the treatments have been effective and look promising, some have been less intriguing, but all of them have had their start—and many of the articles cited in this YEAR BOOK attest to these new treatments—based on our concepts of mechanisms of disease.

In addition to thanking Gabriele Cheatham for her outstanding work in compiling this edition of the YEAR BOOK, I also thank Victoria Cernich and Cheryl Smart at Mosby, who have supported this effort for the past year.

Lanny J. Rosenwasser, MD
Editor-in-Chief

Table of Contents

THE NATIONAL JEWISH MEDICAL AND RESEARCH CENTER ASSOCIATE EDITORIAL BOARD ix

JOURNALS REPRESENTED xiii

PUBLISHER'S PREFACE xv

INTRODUCTION xvii

1. Basic Mechanisms of Allergy and Immunology 1

2. Asthma and Lower Airway Biology 41

3. Allergic Reactions: Drug, Food, Insect, Anaphylaxis, and Allergic Rhinitis 159

4. Atopic Dermatitis and Immunologic Skin Disorders 191

5. Autoimmunity, Immunodeficiency, and Vasculitis 237

6. Pharmacologic and Biological Therapy for Allergy and Immunologic Diseases 249

SUBJECT INDEX 315

AUTHOR INDEX 339

1 Basic Mechanisms of Allergy and Immunology

Fetal and Neonatal IL-13 Production During Pregnancy and at Birth and Subsequent Development of Atopic Symptoms

Williams TJ, Jones CA, Miles EA, et al (Univ of Southampton, England)
J Allergy Clin Immunol 105:951-959, 2000 1–1

Background.—In several studies, the results have suggested that the priming of cells of the fetal immune system to antigen occurs in utero. It has also been demonstrated that the development of atopic eczema in children is more strongly associated with the mother's atopic status than with the atopic status of the father; thus, the prenatal environment is an important influence on the child's immune response to antigen. The production of cytokines at the maternofetal interface may be a factor in the development of atopy-predisposing immune responses. IL-13 has demonstrated IL-4–like activity and thus may have a role in the regulation of the immune response seen in atopy. If so, then IL-13 may be a contributing factor in the expression of the atopic phenotype initiated in utero. The expression of IL-13 by fetal and neonatal cells and the placenta was examined in term infants of parents with and without a history of atopy.

Methods.—Production of IL-13 by fetal and neonatal T cells was investigated by culturing the cells in the presence or absence of PHA. Infants were considered to be at high risk of atopy if 1 or both parents were atopic, whereas infants of parents with no history of atopy were placed in a low-risk control group. The production of IL-13 at term was investigated in the context of subsequent development of atopic disease in the child. Immunohistochemistry was used in the assessment of IL-13 expression in the placenta.

Results.—Immunoreactivity of IL-13 within the placenta occurred only between 16 and 27 weeks' gestation, whereas release of IL-13 by fetal mononuclear cells was first observed from 27 weeks' gestation but was not detectable after 37 weeks' gestation. IL-13 levels were increased in 80% of the samples of PHA-stimulated mononuclear cells. Significantly lower

concentrations of PHA-induced IL-13 were found in term babies with a parental history of atopy, with atopic symptoms by the age of 3 years compared with infants with no parental history of atopy.

Conclusions.—A defect in the production of IL-13 at birth was observed in babies at risk of atopic disease in infancy. This inhibited IL-13 production in these infants may be an indication of an inherent immaturity in the development of T cell–cytokine responses in infants at genetic risk of atopy, or it could be a consequence of the downregulation of responses by other factors. A normal pregnancy is associated with the production of significant amounts of IL-13 first by the placenta and then by the fetus, regardless of atopic status. It is unclear how this production is regulated and what the consequences of its regulation are for the mother and fetus.

► This article examines the production of IL-13 in the antenatal, fetal, and neonatal periods. This group has been very prominent in studying the T_{H2}-like atmosphere of the placenta and uterus during pregnancy. The skewing of immune response toward T_{H2} responses during this period is thought to potentially predispose to later development of atopy. There are many difficulties with interpretation of these experiments on IL-13 because it is clearly shown to be produced during pregnancy, and in the neonatal period IL-13 is an important cytokine to be evaluated in this light. Rather than interpret the potential role of IL-4 and IL-13 during pregnancy and in the neonatal period as being necessarily skewed toward T_{H2} responses, one can also interpret this information as overproduction of IL-4, IL-13, and IL-10 as a mechanism to enhance fetal survival by moderating proinflammatory cytokine production within the placenta and during pregnancy. It is clear that the placenta produces large amounts of potentially proinflammatory cytokines such as IL-1, IL-6, and TNF during pregnancy. The clear demonstration that IL-13 is normally regulated and produced in the antenatal and postnatal periods, both in the placenta and by cord blood, indicates that this important cytokine may potentially be immune regulated during these critical periods of development.

L. J. Rosenwasser, MD

A Cluster of Seven Tightly Linked Polymorphisms in the IL-13 Gene Is Associated With Total Serum IgE Levels in Three Populations of White Children

Graves PE, Kabesch M, Halonen M, et al (Univ of Arizona, Tucson; Univ Children's Hosp, Munich, Germany; Univ Children's Hosp, Leipzig, Germany; et al)

J Allergy Clin Immunol 105:506-513, 2000 1–2

Background.—A significant risk factor for the development of asthma is increased levels of total serum IgE. IgE has also been found to be involved in host defenses against parasites and fungi. There have been reports of a link between total serum IgE and markers located close to the 3 Mb cluster

of cytokine genes in chromosome 5q31. It is also known that IL-4 and IL-13 are essential factors in IgE synthesis. The role of polymorphisms in the IL-13 gene in the linkage between chromosome 5q31 and total serum IgE levels was investigated.

Methods.—The study involved 3 groups of children in the United States and Germany. The first group of children were participants in the Tucson Children's Respiratory Study, which was a large, longitudinal study of asthma and allergies in an unselected population enrolled at birth. The second group comprised children in a cross-sectional study in Munich, and the third group consisted of children from a similar study in the former East Germany. The German groups were unselected for asthma and allergies. The total study population was 1399 children. Total serum IgE levels were assayed, and allergy skin tests were conducted on 8 local aeroaller-

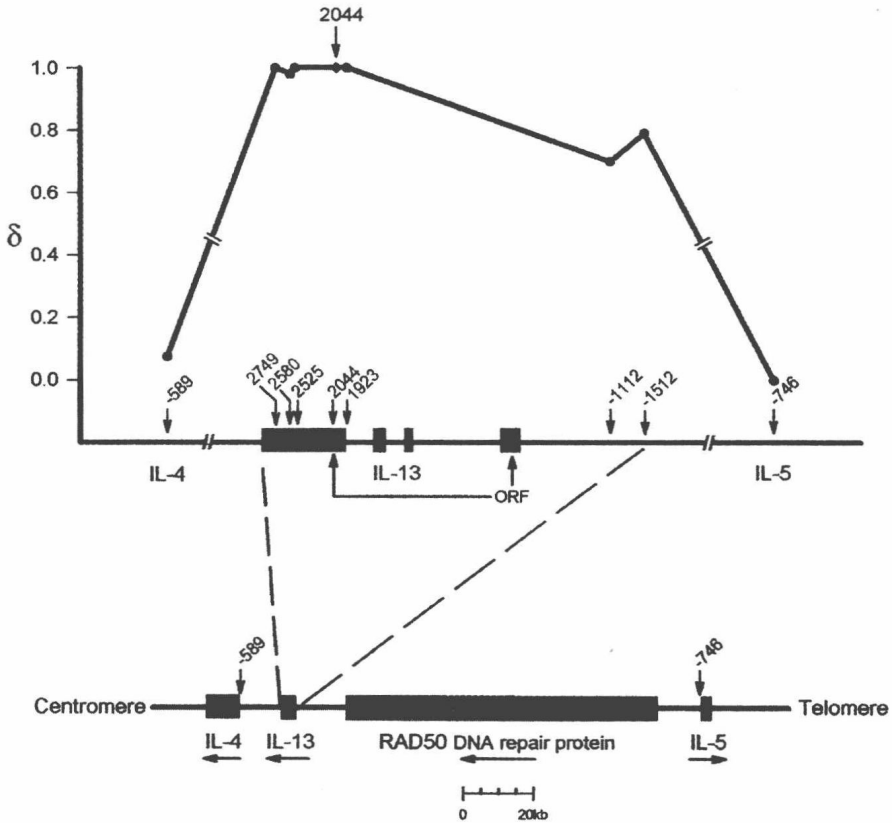

FIGURE 1.—Chromosome location of IL-13 gene relative to 3 adjacent genes in chromosome 5. *Lower panel*, Arrows below each gene represent direction of transcription. Numbers above genes indicate location of relevant polymorphisms relative to first nucleotide of open reading frame of each gene. *Upper panel*, Linkage disequilibrium map of 7 novel polymorphisms in IL-13, 1 in IL-14, and 1 in IL-15 in Tucson population. The δ was calculated relative to Arg130Gln (2044) polymorphism. IL-13 exons are indicated by boxes and coding region by lighter shade. (Courtesy of Graves PE, Kabesch M, Halonen M, et al: A cluster of seven tightly linked polymorphisms in the IL-13 gene is associated with total serum IgE levels in three populations of white children. *J Allergy Clin Immunol* 105:506-513, 2000.)