

Progress in Allergy

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Progress in Allergy

Vol. 18

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Contents

<i>Introduction</i>	
A. L. DE WECK, Bern	1
<i>Antigen Recognition in Induction of Immunity</i>	
E. DIENER and R. E. LANGMAN, Edmonton, Alta.	6
I. Introduction	6
A. The Genesis of Immunocompetent Cells	7
B. Problem of Self-Recognition	8
II. Antigen Recognition Sites Present on Immunocompetent Cells	10
A. Evidence for Specific Antigen-Binding Receptors on T and B Lymphocytes and some Characteristics of these Receptors	11
1. Studies on Antigen-Binding Cells	11
2. Studies on the Functional Aspects of Antigen-Binding Cells	13
B. The Antigen Recognition Spectrum of T and B Cells	15
1. The Ir-1 Gene Causing a Defect in T Cell Reactivity to Certain Antigens	15
2. Reactivity of T and B Cells for Different Antigenic Determinants	16
3. Receptor Specificity of T and B Cells Revealed in Suicide Experiments	18
III. Early Events in Immune Induction	19
A. Direct Observation of Cell Surface Events	20
B. Stimulation of Lymphocytes by Nonspecific Mitogens	23
IV. Mechanisms of T-B Cell Interaction	24
V. Conclusion	28
A. Antigen Receptors	28
B. The Cell Membrane	30
C. The Cytoplasm	30
References	31

Immunological Tolerance

J. G. HOWARD, Beckenham, Kent and N. A. MITCHISON, London 43

I. Introduction	44
II. Irreversible Tolerance: Clone Elimination	46
A. Kinetics and Dose-Relations in T and B Cells	46
1. Systems for T and B Cell Analysis	46
2. Induction Kinetics	49
3. Dose-Relationships	51
4. Recovery Kinetics	52
5. Overshoot	54
6. Distinct T and B Cell Reactivities	55
B. Forms of Antigen which Favour Tolerance Induction	55
1. Reduction in 'Size' of Antigen	56
2. Chemical Modification of the Antigen	57
C. Conditions of Host which Favour Tolerance Induction	58
1. Possible Mechanisms	58
2. An Example: Cy Treatment	59
D. Affinity and Avidity Changes during Tolerance	60
E. Cellular Mechanisms	61
1. The First Step	61
2. The Second Step: The Relationship between Blocking and Clone Elimination	64
3. Tolerance <i>via</i> Exhaustive Immunisation	66
III. Reversible Tolerance	68
A. Lymphocyte Blockade	68
1. Antigen-Mediated Reversible Suppression of B Cells	68
2. Other Examples of Lymphocyte Blockade	70
B. Active Suppression	72
1. Specific Suppression by T Lymphocytes	72
2. Tolerance of Allogeneic Cells: The Role of Serum Blocking Factors	75

3. Blocking of Lymphocytes by Complexes: An Overview	77
IV. Peripheral Neutralisation	79
V. Self-Tolerance	80
A. In T Cells	80
B. In B Cells	82
References	83

Antigenic Competition

P. LIACOPOULOS, Paris and S. BEN-EFRAIM, Ramat Aviv, Tel Aviv	97
I. Introduction	99
II. Patterns of Antigenic Competition	102
A. Competition during the Primary Response	102
B. Competition during the Secondary Response	108
C. Competition during the Induction of Tolerance	111
III. Competition in the Different Types of Immunological Response	114
A. Antigenic Competition Affecting Production of Various Classes of Antibody	115
B. Effect of Antigenic Competition on Delayed Skin Hypersensitivity	117
C. Competition and Allograft Reactions	120
D. Competition and GVH Reaction	122
E. Effect of Competition on Induction of Autoimmunity	126
F. Nucleic Acid Synthesis during Antigenic Competition	129
IV. Requirements for Occurrence of Interference between Antigenic Stimulations	131
A. Immunogenicity of the Competitor	132
B. Antigenic Strength and Competition	134
C. Antigen-Driven Cell Proliferation and Antigenic Competition	136
D. Antigen-Induced Enhancement of Unrelated Responses	139
E. Cell Co-Operation and Steps of Occurrence of Antigenic Competition	142
V. Mechanism of Antigenic Competition	147
A. Competition for Space or for some Essential Nutrient Factor	148
B. The Role of Phagocytic Cells in the Process of Antigenic Competition	150

1. Phagocytosis of RES and Antigenic Competition	150
2. Antigen Handling by Macrophages and Competition	153
C. The Function of T Cells in Antigenic Competition	159
1. Relative Cellular Deficit	160
2. Release of a Humoral Inhibitory Factor	160
3. Suppressive Effect of Thymus Cells	165
D. Competition for a Pluripotential Immunocompetent Cell	170
1. Distribution of Specific Antibody Producing Cells after Immunization with two Unrelated Antigens	172
2. Specificity of Precursors of Antibody Producing Cells	174
3. Present Evidence on Double Antibody Production by Single Cells	176
VI. Conclusions	183
Acknowledgments	185
References	186
 <i>The Structure and Metabolism of Lymphocyte Membranes</i>	
CH. T. LADOULIS, T. J. GILL-III, S. H. CHEN and D. N. MISRA, Pittsburgh, Pa.	205
I. Introduction	206
II. Thymus-Derived and Bone Marrow Derived Lymphocytes	207
III. Fractionation of Lymphoid Cells	211
IV. Morphology	214
V. Chemistry and Immunochemistry	216
A. Preparation of Isolated Membranes	216
B. Chemical Composition of Membranes	221
C. Protein Components of Isolated Lymphocyte Membranes	226
D. Lymphocyte Membrane Glycoproteins and Glycolipids	230
E. Enzymatic Analysis	232
F. Normal Lymphocyte Membrane Antigens	235
G. Lymphocyte Surface Immunoglobulins	247
H. Lymphocyte Receptors	251

VI. Membrane Metabolism	253
A. Biosynthesis and Turnover of Membrane Components	253
B. Turnover of Surface Immunoglobulins	254
C. Interaction with Antigens and Mitogens	255
1. Changes in Membrane Phospholipids	256
2. Endocytosis	259
3. The Role of Lysosomes	260
4. Changes in Membrane Permeability	260
5. The Role of Cyclic Nucleotides	261
VII. Structural Models of the Lymphocyte Membrane	262
VIII. Conclusions	264
Addendum	265
References	266

Immunological Aspects of Urinary Tract Infections

J. HOLMGREN, Gothenburg and J. W. SMITH, Dallas, Tex.	289
I. Introduction	290
II. Natural and Experimental UTI	291
A. Natural Infection	291
B. Experimental Infections	295
III. Features of Micro-Organisms which Relate to the Immune Response	296
A. Characteristics of Micro-Organisms Causing UTI	296
B. Antigenic Composition	298
C. Persistence of Antigen	301
IV. Immune Response	302
A. Serum Antibodies	302
1. Antibody Detection Methods	302
2. Antibody Response in Immunized Animals	305
3. Antibody Response in Humans with UTI	309
4. Antibody Response in Experimental UTI	316

B. Local Immune Response	319
1. Methods of Detection	319
2. Features of Local Immune Response	321
C. Urinary Immunoglobulin and Antibody	327
1. Immunoglobulin in Urine	327
2. Immunoglobulin in Urine in Patients with UTI	329
3. Antibody Activity in Urine	330
V. Immunopathological Aspects	332
A. Relationship of Immune Response to the Course of Infection	332
1. Recovery from Infection	332
2. Adverse Local Effects of Immune Response	332
B. Protection against Infection by Immunization	334
Acknowledgement	337
References	337

<i>On a Glycolipid Hapten of Myelin</i>	
B. NIEDIECK, Hamburg	353
I. Introduction	354
A. Development and Structure of the Myelin Sheath	354
B. On the Etiology and Pathogenesis of Demyelinating Diseases	357
C. Aim of the Investigation	361
II. Identification of a Myelin Lipid Hapten in the Agar Diffusion Test	362
A. Introduction: Lipid Haptens Described in the Literature	362
B. Materials and Methods	368
C. Discussion of Results	370
1. Verification of Findings Obtained with the CF Test by Agar Precipitation Test	370
2. Examination of the Ouchterlony Criteria by the Use of Lipid Suspensions as 'Antigens'	372

3. Attempts to Further Characterize the Myelin Lipid Hapten	374
4. Comparative Investigations with Suspensions Containing Cerebrosides	375
5. Immunochemical Examinations of Cerebrosides	384
6. Immunization Experiments with Cerebrosides	387
III. Comparative Quantitative Examinations of Lipid-Antilipid Reactions in the CF Test	391
A. Materials and Methods	391
B. Results	391
C. Discussion	394
D. Epilogue to Parts II and III	396
IV. Characterization of Anticerebroside Antibodies by Ultracentrifugation and Immune Electrophoresis	398
A. Introductory Remarks	398
B. Materials and Methods	398
C. Results	399
1. Examination of Serum Fractions Following Density Gradient Centrifugation with the Precipitation Test and CF Test	399
2. Immune Electrophoretic Examinations of Anti-Spinal Cord Sera and Anticerebroside Sera	401
D. Discussion	403
V. Immunobiological Studies as a Contribution to the Problems of EAE	403
A. Introductory Remarks on EAE	403
B. Materials and Methods	406
C. Discussion of Results	407
1. Examination of the Encephalitogenic Effect of Cerebrosides	407
2. On the Significance of Anticerebroside Antibodies for the Pathogenesis of EAE	407
3. Attempts to Demonstrate a Cellular Immune Response to Cerebrosides	408
4. Effect of Anticerebroside Sera on Myelinated Tissue Culture	409
Acknowledgements	412
References	412

*Immunological Phenomena Associated with Cross-Reactive Antigens of
Micro-Organisms and Mammalian Tissues*

I. M. LYAMPERT and T. A. DANILOVA, MOSCOW	423
I. Introduction	424
II. CR Antigens of Micro-Organisms and Mammalian Tissues	426
III. Mechanism of Induction of Immune Reactions to Microbial CR Antigens ..	428
IV. Immunological Phenomena Associated with CR Antigens of Micro-Organisms	435
V. Immunologic Unresponsiveness to CR Antigens and Mimicry of Micro- Organisms	437
VI. CR Antigens and Autoimmunity	439
A. CR Antigens of Group A Streptococcus and the Myocardium	442
B. Streptococcal and Myocardial CR Antigens in the Myocardium	444
C. CR Antigens of the Staphylococcus, other Micro-Organisms and the Myo- cardium	445
D. The Study of CR Antigens of Group A Streptococcus and the Myocardium by Immunodiffusion Methods	446
E. CR Antigens of Group A Streptococcus and Connective Tissue	447
F. CR Antigens of Micro-Organisms and Renal Tissue	451
G. CR Antigens of Micro-Organisms and Intestinal Wall Tissue	451
H. CR Antigens of Micro-Organisms and Brain	451
I. CR Antigens and the Induction of Autoimmune Reactions	452
J. CR Antigens and Human Autoimmune Processes	454
VII. Immunopathological Disorders Associated with CR Antigens and the Problem of Vaccination	458
VIII. CR Antigens and Transplantation Immunity	459
IX. CR Antigens and Genetic Control of the Immune Response	462
X. Conclusion	465
References	466

Introduction

A. L. DE WÉCK

When 35 years ago the first volume of the present series appeared under the editorship of PAUL KALLÓS, it was a first attempt to mate in a sequence of continuing reviews the clinical aspects of problems caused by allergic diseases and the new possibilities opened by quantitative experimental procedures in serology and immunology. It also inaugurated a trend which has now become quite popular, namely the serial publication of detailed review articles by knowledgeable experts in the field. In this volume again, some of the most important immunological phenomena are critically reviewed at a basic level, whereas other contributions deal with more practical aspects of immunological diseases.

The central problem of antigen recognition by antigen-sensitive T and B lymphocytes is reviewed in a lucid manner by DIENER and LANGMAN. These authors expose most of the currently accepted views on differences in the nature of T and B cell receptors and on different modes of antigen recognition by these cells. A considerable effort is made at the present time in the investigation of early events in immune induction and in the mechanisms of 'triggering' of antigen-sensitive cells. DIENER and LANGMAN give a very clear picture not only for the established findings but also of the still numerous unsolved problems. This review completes and extends a precedent review on antigen recognition by immune receptors from SINGAL and WIGZELL in this series (vol. 15) and those by CLAMAN and MOSIER on cellular interactions in the immune response (vol. 16) and by MÄKELÄ and CROSS on the diversity and specialization of immunocytes (vol. 14).

A considerable evolution in our understanding of the phenomenon of immunological tolerance has taken place during the past 5 years. It has now

been clearly recognized that several completely different mechanisms at the molecular and cellular levels may lead to the specific absence of an immune response towards a large variety of antigens. The present review on immunological tolerance by HOWARD and MITCHISON gives a timely and stimulating account of the current conceptions about immunological tolerance. Recent acquisitions such as the establishment of distinct tolerance events between T and B cells, the increasing understanding of the nature of antigen interactions with B cells leading to tolerance and the analysis of active suppression systems are emphasized. Among the main mechanisms possibly leading to an absence of immune response, the irreversible tolerance by selective elimination of lymphocyte clones, the enhancement phenomenon produced by antibodies interfering with access of antigen to lymphocytes, the reversible tolerance *via* blockade of lymphocyte receptors by antigen alone or by antigen-antibody complexes and the identification of suppressor lymphocyte populations are thoroughly discussed. In cases where tolerance appears to rest on clone elimination, the authors favor the possibility that tolerance results from receptor blocking (by antigen) followed by elimination of blocked cells, instead of postulating two different triggering signals at the cellular level, e.g. an immunogenic and a tolerogenic signal. Reviews on similar topics in recent volumes include the extensive discussion on the facilitation-enhancement phenomenon by VOISIN (Vol. 15), on the cellular basis of immunological memory by CELADA (Vol. 15), and on the proliferative and differentiation manifestations of cellular immune potentials by MAKINODAN and ALBRIGHT (vol. 10).

Intimately bound to the phenomena of antigen recognition and induction of immunological tolerance is also the phenomenon of antigenic competition. The present state of affairs as well as their personal experience are extensively reviewed by LIACOPOULOS and BEN-EFRAIM. Three main mechanisms seem worth discussion for explaining the phenomenon of antigen competition: an obliteration of the handling of antigen by macrophages, an inhibition of antigen-sensitive T or B cells after stimulation of other cells (i.e., following release of inhibitory factors) or by interference with cell-to-cell contact, finally the still controversial issue of competition for limited numbers of pluripotential immunocompetent cells. This review usefully extends the previous discussion of that topic by ADLER (vol. 18) which was one of the first comprehensive reviews on the phenomenon of antigenic competition.

The interest of molecular immunology is increasingly focused on the structural elements and dynamic interactions taking place on the lympho-

cyte cell membrane. It has become evident that one of the clues in effective manipulation of the immune response will probably lay in a better understanding of molecular interactions between antigen and receptors occurring on the cell membrane of lymphocytes and macrophages. Whereas only a few years ago membranologists and biochemists involved in the isolation and identification of structural elements from cell membranes on the one hand and classical immunologists on the other hand had apparently little to say in common, this situation is rapidly changing. In recent years, numerous new tools have become available for studying the structure of cell membranes and molecular interactions occurring at their surface. Furthermore, immunobiological models defining with precision some of the critical phenomena in the immune response may now be used for this kind of investigation. Accordingly, time seems ripe for a combination of these two approaches into an integrated investigation of the lymphocyte membrane at various stages of immunologically induced stimulation. The review by LADOULIS, GILL, CHEN and MISRA represents, therefore, not only a welcome evaluation of a still relatively crude knowledge but also a declaration of intent and an opening of perspectives in a field which will certainly manifest a great deal of activity within the next years.

The next review of this volume deals with a more directly clinical problem, namely the immunological aspects of urinary tract infections, which are reviewed by HOLMGREN and SMITH. The extent, development and evolution of urinary tract infections, especially of chronic pyelonephritis, appear to be dependent on the one hand on the antigenic composition and persistence of the micro-organisms causing such infections and on the immune response they cause on the other. Whereas extensive data have accumulated on the presence and possible role of serum antibodies, another important aspect is also discussed here, namely the possible role of the local immune response in the infectious process and in the development of chronic inflammatory lesions. On the other hand, the role of cellular immune responses in urinary tract infections, as measured by the activity of either circulating or local lymphocytes, has not yet been extensively investigated.

Studies on the chemical structure and on the immunological properties of natural substances susceptible to function as antigens in immunological diseases continue to be of prime importance as well for the understanding of the disease as for the establishment of diagnostic and therapeutic procedures. Among the antigens involved in the production of experimental allergic encephalomyelitis and possibly associated with the pathogenesis of

multiple sclerosis and other demyelinating diseases, basic myelin protein and corresponding encephalitogenic peptides have attracted the greatest attention. However, as demonstrated by NIEDIECK in a review of her own work during the past years, lipid antigens and haptens should not be neglected in the immunological evaluation of the demyelinating diseases. NIEDIECK demonstrates convincingly the possibility to raise and establish the presence of anticerebroside antisera, which may apparently also be myelinotoxic, although their pathogenic role in experimental allergic encephalomyelitis is not yet established. Lipids are too frequently considered as 'poor relatives' in the large family of natural antigens, a picture which was already somewhat modified by the authoritative review on lipid antigens by RAPPORT and GRAF (vol. 13).

Cross-reactions between antigens from mammalian tissues and antigen from bacteria or other micro-organisms continue to be a topic of prime importance for basic and clinical immunology. Such cross-reactions may play an important role in clinical medicine in a positive (autoimmune diseases and lesions consecutive to immunization with cross-reacting antigens) as well as in a negative sense (insufficient response to infections). The Soviet immunologists, LYAMPERT and DANILOVA, review this aspect of their work and also give to our readers access to an experience and immunological literature which is not readily available to most. This topic has consistently been a preoccupation of the editors of 'Progress in Allergy' and the review by LYAMPERT and DANILOVA usefully completes the previous extensive reviews of SPRINGER on the structure of microbial antigens related to mammalian antigens (vol. 15), of KAPLAN (vol. 13) on autoimmune reactions to heart antigens and of ISACSON (vol. 10) on the role of myxoviruses in autoimmunity.

There used to be a time where the pace of medical, biological and immunological research permitted the scientist to meditate quietly in his armchair on the evolution of his field, to survey effectively the various new findings and research trends emerging from year to year and to place them in a proper long-range perspective. The emergence of immunology and allergy, as one of the most active fields of medical and biological research, makes this kind of general survey increasingly difficult. To illustrate the present evolution, it may be recalled that the number of registered members from national immunological societies throughout the world has increased within 3 years (1971-1974) by more than 50%! This increase in active membership of course reflects the explosive increase of immunological journals and literature. In this context, we feel that the publication of

review articles on topics of basic and clinical immunology will remain a rewarding and important endeavor. We thank the contributors of this volume and the publisher for their most effective co-operation.

I. Immunological Basis of Inflammation	1
A. The Immune System	1
B. The Immune Response	1
C. The Immune System and the Immune Response	1
D. The Immune System and the Immune Response	1
E. The Immune System and the Immune Response	1
F. The Immune System and the Immune Response	1
G. The Immune System and the Immune Response	1
H. The Immune System and the Immune Response	1
I. The Immune System and the Immune Response	1
J. The Immune System and the Immune Response	1
K. The Immune System and the Immune Response	1
L. The Immune System and the Immune Response	1
M. The Immune System and the Immune Response	1
N. The Immune System and the Immune Response	1
O. The Immune System and the Immune Response	1
P. The Immune System and the Immune Response	1
Q. The Immune System and the Immune Response	1
R. The Immune System and the Immune Response	1
S. The Immune System and the Immune Response	1
T. The Immune System and the Immune Response	1
U. The Immune System and the Immune Response	1
V. The Immune System and the Immune Response	1
W. The Immune System and the Immune Response	1
X. The Immune System and the Immune Response	1
Y. The Immune System and the Immune Response	1
Z. The Immune System and the Immune Response	1

A. Introduction

The immune system is unique in its capacity to recognize and react to an almost limitless array of antigens. This considerable degree of diversity

Since this manuscript was submitted for publication in February 1987, some of the contents may not therefore accurately reflect the current state of knowledge.

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Antigen Recognition in Induction of Immunity¹

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Contents

I. Introduction	6
A. The Genesis of Immunocompetent Cells	7
B. Problem of Self-Recognition	8
II. Antigen Recognition Sites Present on Immunocompetent Cells	10
A. Evidence for Specific Antigen-Binding Receptors on T and B Lymphocytes and some Characteristics of these Receptors	11
1. Studies on Antigen-Binding Cells	11
2. Studies on the Functional Aspects of Antigen-Binding Cells	13
B. The Antigen Recognition Spectrum of T and B Cells	15
1. The Ir-1 Gene Causing a Defect in T Cell Reactivity to Certain Antigens	15
2. Reactivity of T and B Cells for Different Antigenic Determinants	16
3. Receptor Specificity of T and B Cells Revealed in Suicide Experiments	18
III. Early Events in Immune Induction	19
A. Direct Observation of Cell Surface Events	20
B. Stimulation of Lymphocytes by Nonspecific Mitogens	23
IV. Mechanisms of T-B Cell Interaction	24
V. Conclusion	28
A. Antigen Receptors	28
B. The Cell Membrane	30
C. The Cytoplasm	30
References	31

I. Introduction

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