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Editors:
PAUL. KALLUS, Helsingborg and BYRON H. WAXSMIN, New Haven, Conn

Contributors:

GEORGE M. BERIER, Washington, D.C.
L. BEEEMENS, Utrecht
Aiia M. CROSS, Helsinki
A.A. GOTTLIEB, New Brunswick, N.J.
R. LAISON, Jerusalem

O. MAKELA, Helsinki
R.J.W. RYDER, Dublin
M.D. SCHARFF, Bronx, N.Y.
R.S. SCHWARRZ, Boston, Mass.
R.N. TAUS, New York, N.Y.

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In introducing a new volume of Progress in Allergy, it is worth noting that any one volume can cover at best a few of the currently active fields of immunology. The increasing pace of laboratory and clinical research in this subject is reflected in the recent or projected appearance of several new journals, notably Infection and Immunity, Cellular Immunology, Transplantation Proceedings, and European Review of Immunology, and such new review journals as Transplantation Reviews and Current Topics in Microbiology and Immunology.

Some aspects of the intense recent effort to work out antibody structure, whether by studies of paraproteins [1] or of unusually homogenous specific antibody preparations [2], are brought up to date in BERNIER’S review in the present volume. Interest is focussed on the physical-chemical basis for the specificity and combining affinity of antibody combining sites as well as on the genetic implications of the amino acid sequences actually identified. Enough polypeptide chains have now been partially or fully analyzed to permit reasonable estimates of the frequency with which a given polypeptide is observed and of the diversity of the total pool of such chains in a single individual. Earlier reviews in Progress in Allergy which deal with this general topic were those of GELL and KELUS in volume 11 and WALDIAN in volume 13. SCHARFF reviews recent work which establishes that synthesis of the light and heavy chains is like other forms of protein synthesis, requiring translation of a conventional messenger RNA on polysomes whose size is related to the size of the message and of the polypeptide product.

The role of different cell populations and their interaction in the immune response, which continues to be one of the most exciting areas of study at the present time [3], is the subject of two reviews in the present volume. MÄkELÄ and CROSS discuss the known lymphocyte populations and their reactivity with antigen.
(This subject was most recently reviewed by NASPITZ and RICHTER and SELL and AsOFSKY in volume 12.) As RoITT and his colleagues have suggested, they replace the terms `thymus-derived' and 'bone marrow-derived' lymphocytes with the noncommittal designations `T-lymphocytes' and `B-lymphocytes'. SCHWARTZ, RYDER, and GOTTLIEB review evidence that the macrophage participates in immune responses as well. The nature of cooperation among two or all three of these cell types in various forms of immunity (i.e. primary or secondary antibody responses, elicitation of `cell-mediated' reactions, tolerance) remains obscure, as does their relation to the as yet poorly defined determinant, carrier, and adjuvanticity functions of the antigen molecule [4].

Of the various more or less specific regulatory mechanisms recognized at present (tolerance, desensitization, feedback inhibition by specific antibody, blockade, the Liacopoulos phenomenon, and competition of antigens), only inhibition by antibody is discussed in the present volume. SCHWARTZ et al. mention evidence that it may be mediated at the surface (or in the interior) of the macrophage. This topic will be treated at greater length in a forthcoming review by VolsIN and his colleagues. The use and study of nonspecific immunosuppressive agents is exemplified in TAUB's paper on antilymphocyte serum, one of the most interesting. Like most of the other topics treated here, this one now exceeds the bounds of a single review. The specific problem of antilymphocyte serum in infectious disease will be discussed by ALLISON and CALLOW in volume 15.

Finally we continue our tradition of reviewing the status of research on problems of atopic allergy With BERRENS' paper on housedust allergens. SHULMAN'S review of insect allergens and PATTERsON's discussion of animal atopy in volumes 12 and 13, respectively, were earlier contributions in this field.

It is difficult to foresee in what area the most exciting work of the next few years will be accomplished. The task of identifying distinct cell populations, whether by morphological or by biological and immunological criteria, is far from complete. When the problems of specificity, posed incisively in the review of MIKLÄ and CROsS, have been solved, we shall know a good deal concerning the nature of specific combining sites present in or on the surface of T and B-lymphocytes, their number and diversity, their combining
affinities, and even perhaps the makeup of their constituent polypeptide
chains. Yet we must still identify the properties of the
cell surface responsible for immunocompetence. These may have
nothing to do with the combining site itself but rather with other
essential attributes of the cell such as its ability to pass through
the endothelium of the postcapillary venule during recirculation
[5].

Effective answers to questions of this nature will require detailed
topographic mapping of the cell surface, such as that recently
undertaken by Bonse, OLD, and their colleagues [6, 7], and mapping
on the chromosomes of genes corresponding to surface components
of interest [8]. For topographic mapping of the lymphocyte
surface, investigations are in progress along 3 lines: study of combining
sites for antigen (antibody-like receptors) [9, 10], study of
cell membrane components which can be identified by their distinctive
antigenic specificities [6, 7], and use of plant lectins such
as phytohemagglutinin, pokeweed mitogen, and concanavalin A
to identify additional membrane constituents with which they combine
specifically [11]. The second and third approaches are comparable
to the well-known mapping of the erythrocyte surface by
the use of isoantisera and of lectins. The nature of the differentiation
undergone by T-lymphocytes within the thymus or of other
lymphocytes in the bone marrow will have to be reinvestigated by
such mapping techniques. The ability of each cell type to be rendered
tolerant, its ability to follow normal physiologic pathways in
recirculation, and its ability to participate in an immune response
must be related to specific elements of its surface. The controls affecting
thymic differentiation, which may include both exogenous
hormonal influences exerted by the pituitary-adrenal system [12]
or the thyroid [13] and local determinants, possibly in the form of
a thymus hormone [14], are yet to be fully identified. Similar controls
affecting lymphocytic differentiation in the bone marrow must
also be uncovered.

At the same time, any mechanism of thymic differentiation
which is proposed must make sense in genetic terms. OLD and Bonse,
in their study of antigenic modulation [15], appear to be coming
to grips with the problem of gene expression in T-lymphocytes and

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the possible masking of some surface components by others. The
differentiation of T-lymphocytes within the thymus appears to be
a differentiation of lymphocytic precursors, coming from the bone marrow, in the presence of epithelial cells, derived from branchial cleft epithelium, under the influence of the mesenchyme [16, 17]. This is a 3-cell system comparable to that involved in differentiation of the vertebrate lens, and its mechanisms pose a problem in modern embryology [8].

Study of lymphocyte differentiation and its regulation within central lymphoid organs such as the thymus must be paralleled by study of the transformation of the same cells when they react with antigen. This is the focus of the many recent studies of blast transformation [19]. The mechanism whereby combination of antigen, antibody, or lectin with a constituent of the cell membrane leads promptly to the chain of biochemical and morphologic changes involved in blastogenesis and mitogenesis is comparable to such classic problems in developmental biology as the nature of the events which initiate hepatic cell replication following partial hepatectomy. The triggering of lymphocyte transformation has been shown to require reaction either of a sufficient number of sites at the cell surface [20, 21] or of individual sites with sufficiently large reactants, GELL's `piggy-back' effect [22]. Evidence also exists to show that reaction of a number of sites in excess of the optimum may suppress rather than stimulate the cell's reaction [20, 23]. The relationship of these phenomena to the more familiar relationships between antigen size or dose and the induction of an immune response or of tolerance has not so far been established. Again, the events in question may involve cooperative effects between several cells and are subject to the regulatory mechanisms mentioned earlier. AUERBACH [18] has offered a challenging comparison between the development, and function of immunocompetent cells and the development, and function of germ cells.

In both cases, cells which originate in the yolk sac undergo differentiation in intermediate organs as a result of `specific inductive tissue interactions'. Their `release and relocation permits new interactions to occur between the now diversified cell types'. The immediate future appears, therefore, to pose problems in embryology and cell biology closely similar to those in fields unrelated to immunology.

Introduction XV

References


Author’s address: Dr. BYRON H. WAKSMAN, Department of Microbiology, Yale University, 310 Cedar Street, New Haven, CT 06510 (USA)