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The present volume of Progress in Allergy illustrates three distinct facets of current immunologic research. Shulman’s review of Insect Allergy shows how a classical problem, the analysis of insect allergens, responsible for atopic allergic responses in human subjects, has entered upon a new and rapid phase of development with the application of modern biochemical and immunochemical techniques. A second review, that of Levine and Stollar on Nucleic Acid Immune Systems, is concerned with the question, by now equally classic, of antigenic specificity in a well recognized example of autoimmunization in man, the formation of antinuclear factors by patients suffering from systemic lupus erythematosus. In both cases, the authors are themselves major contributors to the fields under consideration. An entirely different problem has been
to identify the cause of autoimmunization in specific, well-recognized disease constellations. Asherson, in his review of The Role of Microorganisms in Autoimmune Responses, has brought together an impressive body of information to show how microbial, and in particular bacterial, antigens which cross react with mammalian tissue elements are common causes of autoantibody formation and possibly of autoimmune disease. In this instance, a hypothesis widely held for over 20 years is only now receiving substantial experimental support. Again advances in the sensitivity and discriminative power of techniques of immunochemical analysis have permitted demonstration and characterization of the cross-reacting systems. The remaining reviews, those of Naspitz and Richter on The Action of Phytohemagglutinin in vivo and in vitro and Sell and Asofsky on Lymphocytes and Immunoglobulins deal with what has recently been the most active field of immunobiological investigation, namely the central role of lymphocytes in immune responses, both as precursors of antibody-forming cells and as effectors of immunological memory and/or delayed allergy (See Gowans’ reviews in Volume IX and in [1].

The problem of autoimmunization, which is the subject of two of the present reviews, has been repeatedly discussed in earlier volumes of this series, most recently by Isacson in connection with the possible role of viruses in inducing autoimmunization (Volume X). Developments of the last 2 years, which appear to relate viral neoplasia of lymphoid cells to certain types of autoimmunization have opened a Pandora’s box of new possibilities not even considered at the time of Isacson’s review. Most murine lymphocytic leukemias, including those induced by the well-known Gross virus and the Friend-Rauscher-Moloney group of viruses, have been shown to begin as thymus neoplasms [2-4]. The fowl leukoses, on the other hand, begin as viral neoplasms of the bursa of Fabricius and affect the follicles and germinal centers of spleen and lymph nodes [5]. A similar viral neoplasm of the follicle-germinal center system may occur in mammals as well [6]. These are RNA viruses, whose oncogenic potential is realized in the central lymphoid organs. The abnormal lymphocytes, like those in human lymphomas, show a loss of their usual reactivity [7-9], and the diseased animals (or human subjects) express a corresponding diminution of immunologic responsiveness [10-15]. It now appears that the NZB mouse and

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related strains are hosts for a similar virus and develop lymphomas [16-19]. However these animals characteristically produce autoantibodies, e.g. against erythrocytes and nuclear antigens, and develop disease resembling human lupus erythematosus [19, 20]. In human subjects, the common association of lymphoma with immunologic deficiency on the one hand and autoimmunization on the other is well recognized [14, 15, 21-23]. It appears probable that the neoplastic lymphocytes in these cases retain the ability to respond to antigen with formation of antibody and at the same time have an abnormality of the tolerance function. Indeed a striking deficiency in the ability of NZB mice to develop tolerance against foreign protein antigens has now been clearly shown [24]. The mechanism of this abnormality remains to be elucidated. A possible clue is the persistence of the characteristic TL antigen of the thymus in peripheral lymphocytes of murine leukemias [25-27]. A persistence of thymus function in peripheral cells may imply that these continue to develop new specificity characteristics in a location where they are as likely to become immunized as to develop tolerance. Recently a herpes-like (DNA) virus infecting peripheral lymphocytes has been shown to cause infectious mononucleosis [28, 29] and related DNA viruses may produce other lymphocytic neoplasms such as Marek’s neurolymphomatosis of fowl. The frequent occurrence following infectious mononucleosis of secondary diseases such as thrombocytopenic purpura or polyneuritis [30-32], which resemble diseases produced by autoimmunization, may again reflect a partial functional abnormality of the infected lymphoid cells with failure of the tolerance function. This Pandora’s box may yet provide further insights related to the theme of neoplasia affecting lymphoreticular organs and autoimmunity. Reticulum cell sarcomas develop in mice which survive the acute phase of graft-versus-host disease [33-35]. These occasionally slow features reminiscent of Hodgkin’s disease in man. They may be of viral origin and perhaps owe their initial growth and persistence to the profound reduction in immunologic reactivity characteristic of homologous disease. Whether the neoplastic cells of this class can participate in normal (or abnormal) immune responses remains to be investigated.

References

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