Still another category of fluctuations in superfluids is critical-point fluctuations. Although these can be observed in helium, as Tyson showed, critical-point fluctuations in superconductors appear to be of theoretical importance only, because the temperature must be within about 10^{-8} °K of the transition temperature in order for one to observe these fluctuations in superconductors.

Fluctuations and the behavior of small systems, such as whiskers or microbridges, were discussed by James Langer (Carnegie-Mellon University), Ronald Parks (University of Rochester), and Watt Webb (Cornell University). Small systems offer more opportunity for observing fluctuations, since the fluctuations are approximately inversely proportional to length. An interesting debate resulted over the question of how closely one could determine the depression in the critical temperature ΔT_c by measuring resistance. Parks analyzed some simulated data which indicates an error of a factor of from 2 to ∞. Webb cited evidence that the error was probably of the order of tens of percent, although he conceded that considerable care in sample preparation and measurement techniques would be necessary for such precision.

Michael Fisher and John Reppy (Cornell) described an analog to flux flow resistivity in superconductors—the decay of superflow in helium. The time dependence of this decay is logarithmic in the same way as for flux creep in superconductors.

As with many "first" conferences in a newly developing area of research, one is struck most by what is not known rather than by what is understood. Fluctuations in superconductors appear to be sometimes much larger than fluctuations in normal systems, but they also are often much smaller. However, the types of noise which occur in superconductors appear to be similar to those in normal systems. Thermal, shot, and flicker noise all occur in superconductors, and no noise source has yet been shown to be unclassifiable in terms of noise mechanisms of normal systems.

The proceedings of the conference have been published. Copies are available from the authors and from the U.S. Defense Documentation Center, Building 5, Cameron Station, Alexandria, Virginia 22314.

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Immunological Tolerance

An international conference on immunological tolerance, sponsored by the Extramural Programs of the National Institute of Allergy and Infectious Diseases and arranged by Maurice Landy, was held at Augusta, Michigan, 18–20 September 1968. The topic of each of the six half-day sessions of the meeting was outlined by a designated speaker, whose presentation was followed by an open discussion period averaging about 3 hours. As the number of participants was limited to 42, a very free and rapid exchange of ideas and information was possible.

One theme permeating each session was that a unifying mechanism which explains satisfactorily both immunological tolerance and antibody synthesis will be found. The participants seemed convinced that tolerance can be understood only in terms of immunogenicity, and that the process of antigen recognition is central to the induction of immunological tolerance. Yet how the same substance can induce both tolerance and antibody synthesis—even simultaneously—is not understood. It may be that antigens that are freely diffusible in body fluids are tolerogens, whereas those that are phagocytosed are immunogens. But, as was brought out by several discussants, this interpretation cannot account for immunological tolerance induced by particulate antigens, such as erythrocytes or polymerized flagellin.

The long-held idea that tolerance is the result of antigen-overloading has been shattered by the discovery of "low-dose" tolerance—the induction of tolerance by repeated injections of minute amounts of antigen. According to Nossal, extremely small amounts of flagellin, 10^{-14} molar, when given to rats repeatedly, readily induces immunological tolerance. An interesting difference between the low- and high-dose forms of tolerance is that the immunochemical specificity of the former is greater than that of the latter.

At least two kinds of lymphocytes were implicated in the immune response by several participants. Although antibody-synthesizing cells seem to originate from marrow lymphocytes, mice lacking lymphocytes derived from the thymus form antibodies poorly. However, when both marrow and thymic lymphocytes are present, antibody synthesis proceeds normally. It is unknown how these two kinds of lymphocytes "cooperate." Mitchison postulated that thymic lymphocytes trap antigen by means of a hypothetical immunoglobulin, "IgX," but no physical evidence of an antigen-concentrating mechanism in these cells has yet been obtained.

Another two-cell system, lymphocytes and macrophages, was discussed intensely. The immunogenic material contained in RNA-antigen complexes extracted from the macrophages of immunized rats was found by Gottlieb to be a peptide that contained only 15 amino acids. How this finding will affect the notion that the tertiary structure of an antigen is required for its immunogenicity remains to be determined. Since the immunizing antigen was the T-2 phage, it is evident that considerable processing is carried out by macrophages. Braun presented his theory that an RNA, derived from macrophages and acting as a nonspecific depressor, may activate lymphocytes; antigen bound to the RNA "guides" it into the appropriate stem cell of antibody-forming clones. Whatever "processing" may be ultimately, there was no general agreement that it is essential for antibody synthesis, and until more direct evidence has been obtained, disagreement on the role of the macrophage in the immune response is likely to continue.

Two interesting experiments dealt with the role of carriers in immunity. In the first, it was found that strain-13 guinea pigs, ordinarily unresponsive to dinitrophenol-polylysine, formed antibodies to that antigen when it was coupled to a carrier, bovine serum albumin. However, when strain-13 guinea pigs were rendered tolerant of that carrier, they failed to respond to dinitrophenol-polylysine-bovine serum albumin. In the other example, it was found that cells primed only to the carrier moiety of a hapten-protein conjugate increased the responses of irradiated mice to challenge with the complete conjugate. These experiments imply a role for carriers beyond that of a simple *schlepper*; but how they function in the immune response remains unclear.

Considerable efforts are now under way to induce tolerance in vitro. Several experimental systems were described, all of them dependent upon repopulation of heavily irradiated syngeneic "test" animals with lymphoid cells supposedly rendered tolerant in vitro. All of these models suffer the major drawback of antigen carry-over to the irradiated host. Unless this technical difficulty is eliminated, most of the participants were unwilling to accept

fully the evidence for the induction of tolerance in vitro.

A long-standing problem, the mechanism of immunological paralysis following administration of large amounts of pneumococcal polysaccharides to mice, now appears solved. Mice given "paralyzing" amounts of pneumococcal polysaccharide lack specific antibodies in their serums, but Howard found that their spleens contain numerous cells that are able to form antibodies. It appears that this slowly catabolized antigen persists in tissues, neutralizing antibody as it is produced. Thus, this form of paralysis represents an immunological treadmill.

The last session of the conference was largely devoted to an attempt by Melvin Cohn to provide a molecular model of tolerance based entirely on the evidence he had heard in the preceding 3 days. He began with four assumptions: (i) the only recognition element is antibody itself; (ii) there is constant birth of antigen-sensitive cells throughout life; (iii) antigen-sensitive cells express but one antibody-response and will produce it as secretable antibody on induction; (iv) depending on the signal received, an antigen-sensitive cell may go on to either paralysis or to antibody formation. Assuming that a signal could be a conformational change in an antibody, he sketched a model in which paralysis represented a "half-open" position of an antibody molecule on a cell surface achieved by combination with a single antigenic determinant. For antibody formation the model required a "wide-open" antibody, resulting from a combination of two separate antigenic determinants held on the cell surface in an extended configuration by a factor he designated "carrier antibody."

The discussions were transcribed, are now being edited, and the proceedings will be published by March 1969.

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Calendar of Events

National Meetings

April

1. Arkansas Acad. of Science, Fayetteville, Ark. (G. E. Templeton, Dept. of Plant Pathology, Univ. of Arkansas, Fayetteville 72701)