antibody production after immunization with basic myelin protein. It looks as if, whatever the role of cell-mediated immunity in adjuvant arthritis, T-cell depletion by thymectomy enhances the likelihood of arthritis on this immunizing schedule through an effect on humoral responses. Incorporation of another antigen blocks the effectiveness of mycobacteria emulsions in inducing adjuvant arthritis, so Lennon and Byrd's explanation of their chance finding is that when T-cell numbers or function are depleted, the resulting impairment of capacity to form antibody to thymus-dependent antigens favours continuing antigen excess over antibody with consequent formation of soluble circulating immune complexes capable of mediating tissue damage.

There are several gaps in the argument, but it is at least possible to test the entailed hypothesis that the presence of complement-binding immune complex deposits in rheumatoid synovial membrane and in rheumatoid synovial fluid cells should correlate significantly with indices of diminished T-cell function. E. J. H.

ENZYMES

Open and Shut Case

from our Molecular Biology Correspondent

VOLUMES could by now be written about the conformation of NADH, both free and on proteins. Broadly speaking there are two possible states—open, with the two rings splayed out, and shut, with the rings folded on each other. Now two states are one too many, and much of the heavy artillery available to physically minded biochemists has consequently been brought to bear on the modest endeavour to establish which state prevails. Well before high-resolution nuclear magnetic resonance had begun to make its impact on biochemical problems, it was largely agreed that free NADH in solution must be in the closed configuration. This in any case best conforms with the tenets of nucleotide chemistry, which lay it down that nucleotides are adhesive molecules with a strong tendency to stack on each other (as in helical polynucleotides).

This conclusion was further strengthened by the observations of ring-current shifts, arising from the perturbation by the π system of an aromatic ring of the signals from protons lying close to it. This far then there was total accord. As to the state of the NADH (or NAD^+) in its cofactor role on a dehydrogenase, there are spectroscopic arguments to favour an open configuration, but the NMR results of Sarma and Kaplan, based on what looked again like ring-current shifts, persuaded them that the opposite was the case, and that on lactate dehydrogenase at least, the NADH was in the closed configuration. At this point, however, and not for the first time, the crystallographer irrupted tactlessly onto the scene with a 5 Å structure from Rossmann and his group of dogfish muscle lactate dehydrogenase, which showed all too plainly the cofactor in the open form.

Rossmann and his colleagues have now refined their structure further, and at a resolution of 2.8 Å they are able to make more detailed inferences about the state of the cofactor, and of its analogues, on the enzyme. At the same time Lee, Eichner and Kaplan (*Proc. natn. Acad. Sci. U.S.A.*, **70**, 1593; 1973) have had a new look at the NMR of NADH and NAD^+ in the presence of a number of dehydrogenases, and have brought their interpretation into line with crystallographic fact. Lactate dehydrogenase from chicken and lobster, and the structurally related malate dehydrogenase, all induced similar shifts and broadening of the lines in the NADH spectrum. Very small downfield shifts are observed in the adenine ring protons. In yeast alcohol dehydrogenase, by contrast, these signals move upfield. The pyridine ring protons exhibit large broadening in both cases. The oxidized cofactor has been examined in the same way, and here a series of dehydrogenases induce downfield shifts in everything. These binding-induced shifts, moreover, are sensitive to temperature and diminish in magnitude as the temperature is raised, that is to say as the conformational equilibrium in the free cofactor is progressively displaced in favour of the unstacked, open form. This indicates that it is the open form which corresponds to the state of the molecule when bound. NADH is more strongly bound than NAD^+, so that the sticking time of the ligand is large, and only small shifts and large broadening are observed. The reason for the small perturbation of the adenine proton resonances is the absence of ring currents in the nonaromatic dihydropyridine ring. The observed shifts are pre-

Adhesiveness of T and B Cells

THE notion that T cells (of thymic origin) and B cells (derived from the bursa of Fabricius or its mammalian equivalent) can cooperate in the course of humoral antibody production is widely accepted. Quite plausible mechanisms have been advanced to explain how everything works—*in vitro* that is. Furthermore, it is reasonable to suppose that the various analytical experiments *in vitro* are not complete artefacts and that they give results which relate somehow to real life. But the technical difficulties in the way of ascertaining for sure what happens in the lymphoid system of an intact animal are formidable and many cellular immunologists have shied away from them. Curtis and de Sousa, however, more resolutely in *Nature New Biology* next Wednesday (July 11) present evidence which perhaps gets a little further to understanding the many factors likely to be involved in cooperation between T and B lymphocytes.

Curtis and de Sousa measure the adhesiveness of T cells, derived from the thymus by teasing, or B cells from mice which have previously been treated with antilymphocyte antiserum to remove some of the T cells, and artificial mixtures of such T and B cells. They find that each cell type has a characteristic adhesiveness with its own kind but that when the two sorts of cell are mixed a marked drop in overall adhesiveness occurs. Curtis and de Sousa favour the explanation that some soluble product of one or other or both of the two cell species affects the surface properties of the cells in the mixture in such a manner as to facilitate their dispersion. This phenomenon they liken imaginatively to a similar drop in adhesiveness following mixing of cells from different strains of the sponge *Ephydatia fluviatilis*.

Curtis and de Sousa go on to show that supernatants from cultures of T cells reduce the adhesiveness of B cells in culture and *vice versa*. They also find that cells from unstimulated mouse lymph nodes have low adhesiveness—a result predictable from their artificial mixtures. Furthermore, cells from lymph nodes draining the site of application of the skin-sensitizing agent oxazolone have even lower adhesiveness. It would be fascinating if the authors were to apply their methods to other kinds of reacting lymph nodes in which the phenomenon of interaction between lymphocytes is better established—the response to sheep red cells is less spectacular than that to oxazolone but it is better analysed in terms of cooperating cells.

The authors feel that they may have stumbled upon a phenomenon by which systematization of cells during an immune response can be brought about. The results should be of interest to those who harvest efferent lymph in order to study reactive changes during a response to antigenic stimulus. Aside, however, from this, the communication perhaps marks the beginning of a swing back to a more physiological mode of investigation of the lymphoid system, away from the resolutely academic approach of immunologists.