

the position of the break introduced into the chain, the difference between  $\pi$ - and  $\delta$ -chymotrypsins being also at this site. At the same time the peptide (residues 1-15) appears to coil back on itself. The remaining important difference occurs in another part of the molecule, in which a short segment of the chain is displaced, with consequent unmasking of a cavity. In this are located two out of the three inhibitor molecules which have been introduced into the crystals. This is evidently the basis of the "uncorking" process. It may be recalled that the chymotrypsin structure described by Matthews *et al.* (*Nature*, **214**, 652; 1967) reveals that the new N-terminal group which appears on activation forms an ion-pair with a residue at the active site, and this may be supposed to stabilize the native conformation.

Kraut *et al.* have also calculated difference-Fourier maps between the different chymotrypsin forms, and variously inhibited states. Apart from the removal of the dipeptides, the differences between the successive enzyme forms are very small and localized. Between active and inhibited  $\gamma$ -chymotrypsin one observes, in addition to the differences due to the inhibitor itself, only one local change, which it is suggested would arise from a movement, involving a displacement of some 6 Å, of one or two side chains only. This is evidently the extent of the "induced fit" effect, and it is interesting that it should be so small. It may well prove possible to define these details more precisely in terms of the 2 Å maps of Matthews *et al.* It will also, of course, be of great interest to have a precise description of the differences between enzyme and zymogen, and to reconcile the small structural differences between the four forms of the enzyme with reported variations in activity.

## Teaching Immunology

It is often difficult for people who have finished their formal education to obtain systematic instruction in a new subject. This is particularly true when the subject is changing rapidly, or is of general interest to specialists in other disciplines. Although the lectures given in technical colleges do something to meet the need, few people can find time to attend weekly lectures. In many subjects, indeed, the general point can be made that there is a need for intensive courses in which people could rapidly acquire knowledge of a subject after their periods of formal education.

The British Society of Immunology and the World Health Organization have recently attempted to provide something of the sort. With organization supplied by Professor Leslie Brent, they held a five day summer school in immunology at the University of Southampton. The object was to provide a summary of the present state of immunology for those who have to teach medical students, and for others who wished to know about the clinical and fundamental aspects of immunology. It was not intended primarily for professional immunologists. The course was attended by about fifty people, including some from Europe sponsored by WHO, and seems to have been hard work. Lectures during the day by invited lecturers were followed by demonstrations and discussion, and the broader aspects of the subject were covered by symposia in the evenings.

The intensive nature of the course and the fact that the participants were accommodated together in a Hall of Residence contrived to give participants the impression of going back to university, and it was possible to provide a reasonably balanced picture of the present state of immunology. Particularly valuable was the arrangement for making copies of the slides used by speakers, for distribution to people concerned with the teaching of immunology. Preparing slides on a range of topics is beyond the scope of any one department. The principles behind this symposium could well be applied in other disciplines, in an attempt to come to terms with the problems of further education in adult life.

## Metabolic Roles of Citrate

THE Biochemical Society held a symposium in honour of Sir Hans Krebs, FRS, at Oxford on July 14. Appropriately enough the topic for discussion was the metabolic roles of citrate. The many different disciplines represented illustrated the diverse ramifications that resulted from the original formulation of the tricarboxylic acid cycle some thirty years ago. Not even the imagination needed for such a discovery could have foreseen the widespread biochemical significance of the cycle.

The first two speakers described studies of purified enzymes of citrate metabolism; Dr P. A. Srere (Dallas) discussed whether kinetic studies on isolated enzymes at concentrations of  $10^{-10}$  molar or less gave a true picture of intracellular enzyme behaviour, since the concentrations of some enzymes at their intracellular sites were calculated to be as high as  $10^{-4}$  molar. Dr D. E. Atkinson stressed the importance of intracellular energy conservation for the control of the tricarboxylic acid cycle, and this was also the theme of Dr P. B. Garland's talk. Whereas Dr Atkinson in Los Angeles had studied purified enzymes and then extended the implications to more complex situations, Dr Garland in Bristol had proceeded in the reverse manner—it was gratifying that both approaches led to the same general conclusions. Dr J. Lowenstein (Brandeis) gave an account of the manner in which citrate linked the extramitochondrial synthesis of acetyl-CoA to the cytoplasmic synthesis of fat, a study which emphasized the significance of permeability barriers and membranes in the organization of cell metabolism. The same theme was continued by both Professor P. J. Randle (Bristol) in his description of the manner in which citrate formed in the mitochondria could control glycolysis occurring in the cytoplasm, and by Dr J. B. Chappell (Bristol) in describing the di- and tricarboxylic acid permeases of mitochondrial membranes. Professor M. Klingenberg from Munich gave an account of the adenine nucleotide translocase of the mitochondrial membrane which has extensive implications for the organization of intracellular metabolism.

The occasion marked the retirement of Sir Hans Krebs from the Whitney Chair of Biochemistry at the University of Oxford. At the conclusion of the symposium, Sir Hans modestly thanked the members of the Biochemical Society for the honour they had bestowed on him. It could not have been better deserved.