sensitivity of counter-immunoelectrophoresis is now recommended as a desired minimum for use throughout the world. The terminology of hepatitis has been a confusing and contentious subject for many years and the views expressed on terminology will undoubtedly be welcomed by many.

The present status of efforts to propagate the viruses of hepatitis A and B in tissue and organ cultures and in nonhuman primates is recorded. The immunopathogenesis and the possible influence of genetic factors are reviewed. The association between hepatitis B antigen and primary liver cancer is also discussed and attention is drawn to the many factors that may be of significance in the pathogenesis of liver cell cancer. The problems of hepatitis in blood transfusion services, special groups of patients and hospital staff are discussed and detailed recommendations are made on the use of tests and on the application of control measures.

Several other important recommendations are made. The question of availability of suitable standardized reference reagents is given priority so as to provide more reliable comparison of results. WHO should support the training of scientific and technical personnel as well as the establishment of international and regional reference centres. The free exchange of information and collaboration crossing national boundaries is an urgent need and WHO could and indeed does play a leading part in developing such cooperation.

Three more specific practical recommendations are made. First, blood containing hepatitis B antigen should not be used for transfusion and the method used for detecting the antigen must be simple, rapid, sensitive and specific. Second, the vexed issue of carriers of hepatitis B antigen belonging to medical or other professions coming into close contact with the general population is considered. It should not be assumed that a staff member who is a chronic antigen carrier is necessarily a hazard. Nevertheless, such individuals should use precautions in their professional activities, and studies of the professional and other contacts of these carriers should be made to detect whether transmission of infection occurs. The value of specific human hepatitis B immunoglobulin in passive protection should be determined.

This report is an authoritative account of the current state of knowledge of hepatitis and, together with the recommended codes of practice in renal dialysis units, blood banks and laboratories, this monograph is an invaluable document which will, no doubt, be consulted by all concerned.

CHOLINERGIC RECEPTORS

Molecular Basis

from a Correspondent

THE molecular basis of cholinergic receptors was the topic of a symposium organized by the American Society for Neurochemistry in Columbus, Ohio, on March 12 to 15. Techniques of assay are still subject to much discussion, though elapid snake venom toxins are clearly the reagent of choice. Both Dr E. Reich (Rockefeller University) and Dr M. A. Raftery (California Institute of Technology) use absorption of a solubilized snake venom toxin-receptor complex on DEAE paper to separate bound and unbound toxin; this is apparently a quick and sensitive assay dependent on the mildly acidic isoelectric point of the complex. Preparations of purified receptor were reported using "affinity" chromatography with resins coupled to quaternary ammonium analogues of acetylcholine or venom toxins.

The number, size and chemical nature of the purified materials varied greatly from source to source and author to author. Estimates for the total size based on Stokes's radius from gel filtration are obviously dependent on the degree of detergent binding (see Meunier *et al.*, *FEBS Lett.*, **24**, 63; 1972); figures reported ranged from 200,000 to 600,000 daltons. Some agreement was reached on the range of subunit weights (40,000–60,000 daltons). Dr A. Karlin (Columbia University) demonstrated an apparently homogenous subunit, by affinity labelling of the binding site of purified receptor, with a similar molecular weight to the labelled site in whole cells (see Reiter *et al.*, *Proc. US Nat. Acad. Sci.*, **69**, 1168; 1972). By contrast to this material from *Electricus*, *Torpedo* receptor has a somewhat heterogenous protein population (Schmidt and Raftery, *Biochemistry*, **12**, 852; 1973), and Dr Raftery proposed that the material might be a microheterogenous glycoprotein, on the basis of the presence of sugar residues in the purified preparation. Dr Reich also reported that his preparation from *Electricus* contained about one glucosamine residue per 45,000 daltons.

Dr L. T. Potter (University of Miami) showed electron micrographs of purified membranes from *Torpedo*, and interpreted them as containing rings of approximately 60 Å diameter, with six subunits in a hexagon. The great popularity of *Torpedo* is presumably because its electroplaques contain a higher content of receptors.

Two models for the interaction of the reception site and the ionophore have been proposed. In the first, the ionophore is formed within a specific subunit by being activated by the reception subunit. Alternatively, the ionophore could be formed between subunits by their relative motion after activator binding, and reception subunits alone would be sufficient. Various intermediate structural possibilities obviously exist. In the first case, the purification of the reception subunit might unwittingly involve the separation of the two kinds of protein chain—reception and ionophore. This possibility lends some urgency to the issue of the reconstitution of the ion flux induced by acetylcholine, either in "excitable microsacs" or in thin lipid films, apart from its own inherent importance. Dr G. Hazelbauer (Institut Pasteur, Paris) and Dr L. T. Potter both reported experiments of microsac reconstitution. Dr Hazelbauer found that his preparations only "resealed" about half the time, and two-thirds of those were excitable. Using thin films, Dr E. De Robertis (University of Buenos Aires) reported reconstitution of receptor and ionophore (*J. Gen. Physiol.*, **60**, 454; 1972). Dr E. A. Barnard (State University, Buffalo) has found acetylcholine-induced changes in potassium ion permeability in films from partially purified skeletal muscle receptors.

The organization of receptors during development, when a uniform distribution gradually changes to one specifically at end-plates (and the reverse of this phenomenon after denervation), is an aspect of differentiation becoming more and more amenable to current methods. Using iodine-labelled α-bungarotoxin, Dr D. Famborough (Carnegie Institution of Washington, Baltimore) has measured the synthesis and incorporation into membranes of skeletal muscle fibres, of new toxin binding sites, not apparently induced by toxin, but whose synthesis is reduced by cycloheximide.

The pharmacological effects of histrionicotoxin (2,7 - (cis - 1 - buten - 3 - ynyl) - 8 - hydroxy - 2 - (cis - 2 - penten - 4 - ynyl) - 1 - azaspiro (5.5) undecane), reported by Dr E. X. Albuquerque (State University, Buffalo) suggests that a toxicological probe may be on hand for the ionophore. He concluded that α-bungarotoxin and *d*-tubocurarine both bind to the reception site, and bungarotoxin irreversibly blocks neuromuscular transmission when at this site. A second site, possibly the ionophore, is also blocked by bungarotoxin and by histrionicotoxin, but in this case both are reversible. Histrionicotoxin is not effective at the reception site (see *Proc. US Nat. Acad. Sci.*, **70**, 949; 1973).

Although it may still be some years before cholinergic receptor can be bought from biochemical companies, there has been very substantial progress, with the promise of much more to come, in the chemical aspect, and this has laid a solid base for studies of mechanism and organization and differentiation.