Letter to the Editor

A PROPOS OF THE 'PRESENCE OF VIRUS-LIKE BODIES IN LIVER CELLS OF PATIENTS WITH INFECTIOUS HEPATITIS'

In a recent study of liver biopsies of patients with hepatitis, Babudieri *et al.* (*J. clin. Path.*, 1966, 19, 577) have described 'virus-like' particles, 200 Å in diameter, in cytoplasmic 'sacculles' of hepatocytes and endothelial cells. The authors distinguish these particles from ribosomes, polysomes, and glycogen on the basis of their morphology and of their resistance to enzymatic extraction by diastase. However, the last paragraph casts a doubt on the validity of these criteria since it says that these virus-like particles could be 'the endothelial type of particulate glycogen . . . not yet observed in the human liver'.

It would have been interesting to see this assumption supported by some morphological evidence and by the effects of enzymatic extraction upon these particles using the same technique as for hepatitis biopsies, in normal liver or another tissue. Before submitting their paper, Babudieri *et al.* received a communication of our comments about their findings, and of the pictures published with this letter. We have had the opportunity to examine several biopsies of normal human liver and we found that glycogen is frequently present in endothelial cells and almost constantly in subendothelial cells (Fig. 1). In both these types of cells, the glycogen is in monoparticulate form and the particles are about 200 Å in diameter. Some fragments of endothelial cells are occasionally seen, apparently free in the sinusoidal lumen in the plane of section, and are similar to the 'sacculles' described by Babudieri *et al.* (Fig. 2). In hepatocytes, the glycogen has the 'rosette-like' appearance in the cytoplasm and the monoparticulate form occurs in the nucleus (intranuclear aggregates of glycogen are not unusual in livers of healthy individuals).

These findings should be taken into consideration when examining human livers in pathological conditions. They strongly support our belief that the particles described by Babudieri *et al.* are actually glycogen particles.

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Book reviews

INTERNATIONAL REVIEW OF EXPERIMENTAL PATHOLOGY
VOL. 5. Edited by G. W. Richter and M. A. Epstein.
(Pp. x + 374; illustrated. 132s.) New York: Academic
Press. 1967.

This, the fifth volume of the series, maintains the high standard set by previous volumes. Each of the seven chapters is a comprehensive review of some topic of current interest and importance. All are first rate and they cover a wide range.

Gowans deals concisely with the lymphocyte. Mellors describes the autoimmune and immunoproliferative diseases that afflict NZB/BC mice and hybrids and shows how this spontaneous 'experiment of nature' is shedding light on many important human diseases. The chapter by Moor on freeze-etching contains a host of valuable technical hints and a series of beautiful illustrations which reveal the potential, and the limitations, of this method for investigating biological ultrastructure. Technique is also an important part of Rose's chapter on culturing tissues under cellophane membranes but the author also provides ample evidence of how the method, by maintaining cell differentiation and restraining mitosis and cell migration, has a great deal to offer the biologist and pathologist.

Svoboda writes with clarity on the difficult topic of the interaction of oncogenic viruses with heterologous cells. Less readable but equally interesting is Godman's review of the cytopathology of the human enteroviruses (polio, ECHO, and Coxsackie viruses). The longest chapter, however, and perhaps the best, is French's review of the structural changes, as visualized by electron microscopy, that comprise the atherosclerotic lesion. Anyone studying arterial disease cannot fail to benefit from reading it.

The volume will probably be of interest primarily to those working in one or other of the fields reviewed but pathologists too will read it with pleasure and benefit, though they may find the going rather heavy in places.

R. C. CURRAN

BIOCHEMICAL VALUES IN CLINICAL MEDICINE, 3RD ED.
By R. D. Eastham. (Pp. iv + 162. 15s.) Bristol:
John Wright and Sons. 1967.

Three editions of this book have appeared since 1960 and it has been translated into Italian, Spanish, and Greek. This testifies to the demand for it and to the author's energy in revising it. Nevertheless, it is difficult to know the purpose of this type of book unless it is the answering of multichoice examination questions.

Factual errors mentioned in a review of the first edition in this Journal remain unaltered and there are additional defects. The paragraph on lactic acid dehydrogenase, for instance, contains contradictory statements listing pulmonary infarction amongst the causes of raised values, and of unaltered values without any qualification. The normal range of activity given for this enzyme is much wider than that reported by most laboratories.

Biopsy of normal human liver. Fixation = 1% osmium tetroxide in 0.1 M phosphate buffer. Embedding in Epon-Araldite. Staining = lead hydroxide, according to Karnovsky (method A).

FIG. 1. From right to left are seen the sinusoidal lumen (S), the thin cytoplasmic processes of endothelial cells (E), a finely fibrillar material (f), but no definite basement membrane, a subendothelial cell (SE) with a prominent nucleus (N) and part of the cytoplasm of a hepatocyte (H). Glycogen particles are in rosette-like form (g_1) in the hepatocyte and the size of the aggregates ranges from 300 to 800 Å. In the subendothelial cell, glycogen is in monoparticulate form (g_2) and the size of the particles is about 200 Å. They are distinct from membrane-bound ribosomal particles (r) measuring about 150 Å in diameter. $\times 32,000$.

FIG. 2. Cellular fragment, free in the sinusoidal lumen in the plane of section. It contains monoparticulate glycogen (g_2) distinct from the extracellular rosette-like aggregates (g_1) presumably originating from hepatocytes. The various incidences of section probably partly account for the variation in size and density of glycogen particles. $\times 41,000$.

moreover the units used are not defined; they are certainly not International Units. Reference to 'cortisol in plasma' directs us to '17-hydroxycorticosteroids' but should read '11-hydroxycorticosteroids'. The causes of elevated serum vitamin B₁₂ levels are recorded but those of decreased values are not. Although a list relating levels of alcohol to symptoms is given, we are not told whether blood or urine figures are being used and the legally important blood level of 80 mg./100 ml. is not mentioned. Whilst a number of sections have been deleted from this edition as not being useful, the retention of the Kepler, Power Robinson test is difficult to justify.

In the preface to the first edition, the author is careful to emphasize the limitations of the approach to clinical chemistry characterized by this book. It is to be feared that most of those who buy will not heed his good advice.

B. W. MEADE

SYMPOSIUM UBER DEN LIQUOR CEREBROSPINALIS. VIENNA, 16th January, 1965. *Wiener Zeitschrift für Neuroheilkunde*, suppl. 1. Edited by Prof. Dr. F. Seitelberger. (Pp. 224; 132 figures. \$19.25.) Vienna and New York: Springer Verlag, 1966.

A symposium concerning various aspects relating to the cerebrospinal fluid was held early in 1965 in Vienna and this volume records some two dozen communications together with the ensuing discussion of each.

Appropriately an excellent pathological and anatomical survey by Professor Seitelberger is recorded first for he was largely responsible for the volume. It is difficult to single out particular papers for the excellence of so many is obvious. These range from aspects of pharmacology, detailed electron microscopic appearances of the choroid plexus and the glia, the cytology of the cerebrospinal fluid itself illustrated by some beautiful photographs, the electrophoretic pattern of proteins and the results of amino acid examinations, especially in Parkinson's disease, Huntington's chorea, and polyneuritis. There are also valuable papers on immunoelectrophoresis, the results of which are well illustrated.

The volume is well produced but is entirely in German; however, all symposia have the failing of not producing abstracts in another language. To those interested in the cerebrospinal fluid it can be well recommended.

J. N. CUMINGS

PRINCIPLES OF MEDICAL STATISTICS 8th ed. By Sir Austin Bradford Hill. (Pp. ix + 381; illustrated. 15s.) London: Lancet Limited, 1966.

Since it was first published before the war, this book has guided several generations of medical research workers. This edition is largely based on the successful seventh edition, but has been expanded in two important sections. With the great increase recently in clinical trials, the chapter dealing with the ethics of these situations has been enlarged; the important statements of the Medical Research Council and the Helsinki declaration are included as an appendix.

The other main change is a last chapter on statistical evidence and inference. This is now a non-mathematical

discussion of the meaning of significance tests and the inferences which can be drawn from differences which are unlikely to be due to chance. The issues are clearly stated and the logical conclusions drawn. This chapter now forms an important guide for anyone interested in medical research, whether or not he intends to employ the numerical methods described in the earlier parts. Written especially for the doctor, this book continues to be one of the best introductions available to the non-mathematician.

I. D. P. WOOTTON

LES TRAITEMENTS ANTICOAGULANTS. Table Ronde des V^e Journées de Thérapeutique de la Faculté de Médecine de Nancy, 26th Mars, 1966. By G. Arnould and others. (Pp. 164; 20 figures. 20F.) Paris: Expansion Scientifique Française, 1966.

This slim publication contains nine papers on heparin and oral anticoagulants given at a meeting held by the medical faculty at Nancy. The participants were all from French universities with a strong local representation.

The introduction by Dr. Soulier, which lays down some important guiding principles governing anticoagulant administration, is excellent. The remaining papers are on the pharmacology of anticoagulant drugs, the principles of laboratory control, and the clinical applications and dangers of therapy.

It would probably have been more helpful at the publication stage to expand the papers to cover their subject more comprehensively and to include adequate references to the published literature. Most of the chapters contain no references at all, and some, *e.g.*, the paper on side effects, do not adequately cover the subject. The international nomenclature for clotting factors was not always used and there was overlap between contribution, *e.g.*, heparin therapy, with differing opinions. Those conversant with the English language literature on anticoagulants will probably find little to change their views or opinions on this controversial subject.

L. POLLER

Symposia

THE THYROID GLAND

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