A light microscopic marker of non-A, non-B viral hepatitis

As Grimaud and coworkers¹ pointed out in their letter of 2 October 1980, there is still a need for markers of non-A, non-B viral hepatitis. At present the diagnosis is made in those patients who present with histological and biochemical evidence of viral hepatitis, by exclusion of demonstrable HA, HB, cytomegalovirus or Epstein Barr virus infections. Electron microscopy may be of value^{1,2} but in routine diagnostic pathology, supplementary simple markers of non-A, non-B viral infection would be welcome so long as specific serological tests are not available.

As part of a multidisciplinary study, we have made a morphological examination with light and electron microscopy of liver biopsies in five chimpanzees. Specimens were taken at weekly intervals after inoculation with non-A, non-B infectious material. In parallel a large number of liver biopsies, obtained from patients with presumptive non-A, non-B acute or chronic hepatitis were studied. We observed in liver biopsies of chimpanzees and humans a common striking histopathological feature. This consists characteristically of many small foci of single cell necrosis which resemble but are not identical to Councilman's bodies. The viral hepatocytotoxic effect produces small groups of irregular cell fragments localised in the space of Disse. These fragments are amphophilic and show coarse granularity (Fig. 1). Analogous

Fig. 1 Light microscopy. Fragmented Councilman-like body with coarse granularity (→) surrounded by unaltered hepatocytes in human liver biopsy. Haematoxylin and eosin $\times 1600$.

alterations can be recognised in the cytoplasm of some non-necrotic liver cells and transitional forms between this and the complete lesion may be found.

In tissue prepared for electron microscopy similar cell fragments may be identified. They are a mixture of membranous or microtubular structures or both surrounded by electron-dense flocculent material. In liver biopsies from chimpanzees a variable number of those cytoplasmic structures characteristic² of non-A, non-B viral hepatitis, were found in addition in these fragments (Fig. 2).

Fig. 2 Electron microscopy. Detail of a Councilman-like body showing disintegrating cytoplasmic structures (→) characteristic for non-A, non-B hepatitis in chimpanzee liver biopsy. Scale marker denotes 0.2 μm .

We suggest that the accumulations of fragmented "Councilman-like" bodies can be used as a light microscopic marker for the non-A, non-B viral aetiology of a hepatitis, just as ground-glass hepatocytes may point to viral hepatitis type B.

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Clinical significance of an ultrafast alkaline phosphatase isoenzyme

We have recently detected a technical error in our paper "Clinical significance of an ultrafast alkaline phosphatase isoenzyme."¹ The error was in Fig. 11 and random specimens Table 2. It resulted from either an inadvertent misalignment or a miscoring of the cellulose plate. The small band displaced anodally relative to the ultrafast isoenzyme or band in the bottom tracing should coalign with the ultrafast band. Additionally, in Table 1, case 5 and 6 should have a positive sign in the ultrafast column corresponding to the tracings in Fig. 5 and Fig. 6.

Our initial preliminary observation on three random cases (retrospectively, all of which had evidence of liver disease) were based on the comparisons of densitometric recordings. This was considered to be an objective means of assessing differences in staining intensity rather than by subjective visual interpretation. However, when we recently assessed our original experimental and control plate containing the random cases, by transillumination, although the plates had probably faded somewhat, we observed faint blue and/or blue-violet bands, and in most of the terminal experimental band locations in the former, but not in the latter plate. We now appreciated a tinctural difference in staining quality of some of these bands when compared to the more cathodic liver isoenzyme. This finding needs to be further investigated. We have also occasionally seen this type of tinctural coloration of the terminal region in some of our more recent studies.

In general we have tried to elucidate the terminal apparent isoenzyme of alkaline phosphatase, and have found evidence which is suggestive of its presence on prolonged comparing of subtle differences in the intensity of staining of the terminal anodal region between the experimental and control plate. However we have found it difficult to reproduce our data consistently on repetitive testing of the