250, 739; 1974), and other protease inhibitors had no selective effect on tumour cell growth (McIlhinney and Hogan, *Biochem. biophys. Res. Commun.*, **60,** 348; 1974). Furthermore those that did arrested cells in the G_2 phase of the cell cycle (Collard and Smets, *Expl Cell Res.*, **86,** 75; 1974) and the cells continued to make DNA at their saturation densities (Schnebli and Haemmerli, *Nature*, **248,** 150; 1974). But these results only show that normal cell properties cannot be restored by certain protease inhibitors; they cannot rule out the possibility that some proteases are involved in maintaining the transformed state.

More antigens in hepatitis B

from Arie J. Zuckerman

AUSTRALIA ANTIGEN, now referred to as hepatitis B surface antigen in view of its close association with hepatitis B virus, was discovered as a lipoprotein which was immunologically distinct from normal low density lipoproteins. Examination of this antigen in the electron microscope revealed a remarkable morphological heterogeneity consisting of three principal virus-like particles (see Fig. 1). The main antigenic constituent is a small pleomorphic particle, 16–25 nm in diameter. A characteristic feature is the presence of tubular forms which vary greatly in length but with a constant diameter of 20 nm except for the bulbous swelling at one or both ends of the tubules. The third type of particle, the Dane particle, is also spheroidal measuring about 42 mm in diameter, with a 27 nm core, a 2 nm shell and an outer coat about 7 nm in thickness. There is now substantial evidence that the 42 nm particle is the human hepatitis B virus, the core being the nucleocapsid and the outer protein coat representing hepatitis B surface antigen. Immune electron microscopy and more recently various serological tests revealed the existence of two distinct antigen–antibody systems associated with the Dane particle; antibody to the core has a specificity entirely different from antibody against the outer protein coat. The morphological complexity of the particles associated with hepatitis B is matched by the complex antigenic reactivities of the outer coat. The antigenic constitution of the core is still under investigation.

The antigenic activity of the coat protein is associated with the small spherical particles, the tubular forms and the coat of the Dane particles. All these structures share a common group specific antigen (a) and the particles generally carry at least two subdeterminants: either d or y, which usually behave in a mutually exclusive manner although carried on the same antigen particle, and either w or r. There is evidence that the subtypes are the phenotypic expressions of distinct genotype variants of hepatitis B virus. Four principal phenotypes are currently recognised: adw, adr, ayw and ayr, but others are not precluded. Indeed complex permutations of these subdeterminants and new variants have been described, all apparently on the surface of the same physical particles. A remarkable geographical pattern of distribution of hepatitis B subtypes has emerged with four global zones, where there is an excess of one subtype, and regions where a mixture of subtypes is common (*Nature*, **247,** 2; 1974). These subtypes provide valuable epidemiological markers and offer a method for distinguishing one of several sources of infection. The surface antigenic reactivities do not seem to be associated with particular clinical forms of liver disease.

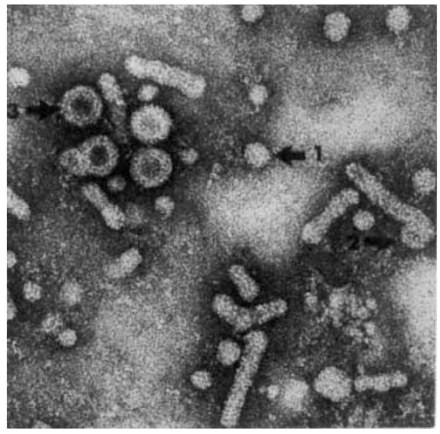

Fig. 1 Morphological appearance of hepatitis B antigen in serum showing three distinct entities: (1) Small pleomorphic spherical particles with a diameter of 16–25 nm. (2) Tubular forms. A terminal bulbous swelling is shown. (3) Double-shelled 42 nm Dane particles with a core and an outer coat. ×252,000. (Electron micrograph reproduced with permission from A. J. Zuckerman *Hepatitis-Associated Antigen and Viruses;* North-Holland, 1972.)

The above summary serves as an introduction to another antigen–antibody complex which is associated with molecules distinct from particles of hepatitis B antigen. Magnius and Espmark (*Acta path. microbiol. Scand.*, **B80,** 335; 1972) described a new disinct precipitating antigen, which they termed e, in sera containing hepatitis B surface antigen. This antigen differed markedly from the previously described determinants of the surface antigen. Paradoxically, antibody against e was found in serum specimens from healthy carriers of the surface antigen. The e antigen seemed to be somehow intimately associated with the pathogenesis of liver damage. Recently, Nielsen and colleagues (*Lancet*, **ii,** 913; 1974) reported their interesting observations on the e determinant. The e antigen was found by the simple immunodiffusion technique to be significantly more common in patients with chronic liver disease (chronic hepatitis and cirrhosis) with persistent hepatitis B antigenaemia than in patients with acute viral hepatitis. Furthermore, the e antigen seemed to be a valuable and important prognosic marker since progression to chronic liver disease was recorded by serial liver biopsies in 11 out of 19 consecutive patients with surface antigen-positive acute hepatitis associated with the e antigen. The clinical significance of the e antigen was supported by differences in the clinical, biochemical and histological findings between the patients with the e antigen and those without this antigen during the initial phase of viral hepatitis.

The exact nature of the e antigen is uncertain; it might be a host antigen produced by virus-infected liver cells or it might be related to another antigenic constituent of the infecting virus, perhaps the core of the Dane particle. Preliminary results from Nielsen's laboratory showed a large number of Dane particles in serum samples containing the e antigen, whereas e antibodies have previously been found in healthy carriers of the surface antigen in whom Dane particles had not been demonstrated. Though the precise relationship of e to hepatitis B virus is yet to be established, it is evident that the antigenic complexity of this unique infectious agent will continue to unravel.

Position effects in gene inactivation

from Benjamin Lewin

GENES translocated to positions close to heterochromatin seem in many species to become inactivated. Among the earlier observations were those made in *Drosophila* where, for example, some of the facets of the eye are white instead of red in heterozygotes in which the dominant gene has been transferred to a site adjacent to heterochromatin (see Lewis, *Adv. Genet.*, **3,** 75–115; 1950). It has since become apparent that this position effect variegation takes place in *Drosophila* when a wild type allele is placed in *cis* alignment with heterochromatin, with a recessive allele carried on the normal homologue; the wild type allele is inactivated in some cells, thus causing the variegation. The probability that a locus will be subject to this effect depends upon its relationship to the site of translocation; the closer it lies to heterochromatin, the more likely it is to be inactivated. Inactivation is de-