## news and views

## Receptor maps for viruses

from Arie J. Zuckerman

VIRUSES are not motile and they rely on such processes as diffusion and transport within body fluids to bring them into contact with susceptible cells. The critical step in successful viral infection is the susceptibility of cells, and the means by which viruses are incorporated into host cells has been the subject of much research. The susceptibility of cells is usually determined by early steps in virus-cell interactions which include the attachment and penetration of the virions and the release of the viral nucleic acid in the cells. With some animal viruses such as the influenza viruses and some of the picornaviruses such as Coxsackie virus and poliovirus, attachment is associated with the presence of specific receptors for viral adsorption on the cell surface, but whether receptors are required for all viruses is not known. The presence or absence of receptors on the cell surface depends on several factors which include the particular type of tissue or organ, stage of maturity, changes in the physiological environment such as culture in vitro, and genetic factors involving cellular rather than immunological mechanisms.

On the other hand, there are also viruses, including arboviruses, poxviruses and herpes viruses, which will grow in a variety of cell types, and therefore there appears to be little specificity about the adsorption process of such viruses. In these instances a mechanism such as phagocytosis or viropexis may be important in the incorporation of virus into susceptible cells. Another mode of viral entry entails fusion of the viral envelope with the plasma cell membrane. Fusion takes place by a process of alignment of the two membrane structures, followed by the formation of a channel between virus and the cytoplasm through which the nucleocapsid passes into the cell. A more recently described mode of entry of virus into the cell is by a process of membrane fission rather than by viropexis.

Lonberg-Holm and his colleagues point out on page 679 of this issue of

Nature that the specific receptors for several nonenveloped viruses are present on cells in limited number and therefore these can be saturated with excess virus. They report results of experiments in which the attachment to HeLa cells of highly purified virus particles radiolabelled with carbon, sulphur and phosphorus was measured. Four receptor families were found. The first family contains receptors to human rhinovirus types 2, 1A and 1B. The second family contains receptors to human rhinovirus type 14 and Coxsackie A21 and a number of other rhinovirus serotypes. The third family contains poliovirus, and the fourth contains Coxsackie B3 and probably the other Coxsackie B serotypes as well as several serotypes of adenovirus. It is reasonable to consider that receptor specificity influences virus tropism in the tissues thereby contributing to the patterns of pathogenesis of virus infections. An example is the finding that Coxsackie A21 shares receptors with a large number of human rhinoviruses and this may be related to the ability of Coxsackie A21 to cause coryza. Another example is that both Coxsackie B viruses and adenoviruses produce persistent infections in HeLa cells cultured in the presence of human serum.

Burrows pointed out, however, (Microbial Pathogenicity in Man and Animals, 303-332, Cambridge University Press, 1972) that many investigators have attempted to associate characteristics of virus growth and behaviour in vitro with virus behaviour in the intact host. Characteristics such as tissue receptor activity, the production of or susceptibility to interferon, growth and cytopathogenicity in cultured cells and virulence for laboratory animals have all been linked to differences in virulence for the normal host. The determinants of virulence, although clearly related to those of virus growth, differ markedly between viruses and indeed between strains of the same virus. It was Chaproniere and Andrewes (Virology, 4, 351; 1957) who

stressed that the ability of many viruses to grow in monolayer cell cultures derived from tissues or hosts which are not susceptible to the virus, limits the usefulness of such cultures for basic studies of susceptibility as they relate to the intact host.

It is generally considered that the morphological and functional capacity of cells maintained in organ culture may offer a system for cultivating viruses which closely simulates conditions in the intact host. Examples of the specificity of the effect on the target organ and differential susceptibility of different hosts are found within each class of viruses and organ cultures have reproduced many, but not all, of the phenomena of specificity observed in the intact animal. Extension of the studies reported by Lonberg-Holm and his colleagues and the precise identification of the properties of the specific virus receptors may provide a key to the understanding of viral pathogenesis and perhaps also to the prophylaxis and even therapy of virus infections.



## A hundred years ago

After discussing the results obtained by Stoney, Thompson, and Clerk-Maxwell, mainly derived from the properties of gases, I come to the conclusion that in the present state of our knowledge the best approximation that we can make to the size of the ultimate atoms of matter is the mean of their determinations. I adopt for simplicity  $\frac{1}{1000}$ th of an inch as the unit of length, and  $\frac{1}{1000}$ th of an inch cube, or 10000000000th of a cubic inch, as the unit of volume. In the case of a true gas the number of atoms in the length of  $\frac{1}{1000}$ th of an inch at 0 °C, and a pressure of one atmosphere, would be 21,770, and hence,  $\frac{1}{1000}$ th of an inch cube, about 10,320,000,000,000.

From Nature, 13 (February 24), 332; 1876.