The importance of disease in immunodeficient mice and rats

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INTRODUCTION

The very features that make the immunodeficient animal so valuable in research also present those responsible for breeding and maintaining it with the greatest problems.

Diseases are much more common in these animals than in those with an intact immune system, in fact, if one accepts a common definition of disease, 'a specific state of malfunction of an animal body' (Dorland, 1959) then one must accept that immunodeficient animals are in a permanent diseased state.

This paper will be confined, however, to the more specific aspects of naturally occurring disease with particular emphasis on infectious agents.

VIRAL DISEASE

Mouse Hepatitis Virus

Although it is in the nude mouse (nu nu) that the wasting syndrome has attracted most attention, a very similar condition was first described in neonatally thymectomised mice (East et al., 1963). In that outbreak mouse hepatitis virus (MHV) was shown to be involved, causing necrotic foci in the liver.

The pathogenesis of MHV infection is very complex as there are a number of different strains of the virus which may produce quite different pathological effects. Moreover, responses vary with age and strain of mouse.

The first strain of virus identified has since been called MHV-1 (Dick et al., 1956). It produces little evidence of disease in normal adult mice; although there may be a transient interstitial pneumonia after infection via the respiratory route in weanling mice (P. Carthew and S. Sparrow, unpublished observations). In the thymus-deprived mouse, the naturally athymic nude mouse, the mouse made immunodeficient by treatment with antilymphocyte serum or cortisone and in the mouse with intercurrent disease such as Eperythrozoon coccoides infection or murine leukaemia it can produce extensive liver lesions as shown in figure 3.1
MHV-1 infection in the nude mouse. Extensive liver necrosis and some cellular infiltration. Haematoxylin and eosin, × 240.

(East et al., 1963; Pantelouris, 1968; Allison, 1970; Gallily et al., 1964; Gledhill et al., 1955; Nelson, 1952). In the first two cases, thymus-deprived and nude mice, chronic disease from infection with MHV-1 results in the characteristic 'wasting syndrome'.

A very similar picture of wasting has been described by Fujiwara and his co-workers (1977) with a strain of virus he designated as MHV-U. This virus causes 100 per cent mortality in nude mice but only produces disease in heterozygous litter mates after the injection of cortisone.

Four strains of virus that produce overt disease in normal mice (JHM, MHV-S, MHV-2, MHV-3) produce rapid death in nude mice, as distinct from the wasting syndrome. The pathogenesis of the infection may be different in the immunodeficient animal. In the nude mouse death is invariably associated with extensive liver necrosis, but in euthymic mice the target organ of JHM infection is the brain and spinal cord where it causes demyelination (Cheever, 1949), and MHV-3 is now thought to be responsible for the disease previously known as lethal intestinal virus of infant mice (LIVIM) which is manifest by a fatal diarrhoea in preweaning mice (Broderson et al., 1976; Carthew, 1977).

Another strain, MHV-A59, which can cause acute liver necrosis in normal mice (Manaker et al., 1961) appears from initial investigations to be more chronic in nude mice leading again to a wasting syndrome (P. Carthew and S. Sparrow, unpublished observations).