by complement fixation and neutralization. Arch Virol 53:287-294

Adenovirus Infection, Intestine, Mouse, Rat

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Synonyms. None

Gross Appearance

Gross lesions are absent. Affected mice can be runted, but are usually asymptomatic.

Microscopic Features

The only discernible microscopic lesion in infected mice is the presence of characteristically large, basophilic, intranuclear inclusion bodies in the epithelium of the small intestine and cecum (Hashimoto et al. 1970; Luethans and Wagner 1983; Takeuchi and Hashimoto 1976). The nuclei of affected cells are enlarged and are often atypically situated in the apical position of the cell column, readily permitting visualization at low power (Fig. 352). Inclusions are most numerous in infant mice, but can be found in adults in fewer numbers (S.W. Barthold, unpublished observations). Few to numerous inclusions have been observed in the small intestine of clinically normal athymic nude (nu/nu) mice (Cohen and de Groot 1976). Other organs are not affected.

Ultrastructure

Nuclei of infected mouse intestinal epithelial cells are enlarged and contain viral masses, often embedded in a homogeneous matrix of chromatin material. Infection is confined to columnar and goblet cells on villi and Paneth and goblet cells in crypts. Viral particles occur in aggregates and crystalline arrays (Fig. 353). They are uniform in size, measuring 75 ± 5 nm in diameter. Most particles have dense cores, but some have electronlucent centers. Free and membrane-bound virions are also present in the cytoplasm (Cohen and de Groot 1976; Luethans and Wagner 1983; Takeuchi and Hashimoto 1976).

Differential Diagnosis

Intestinal lesions associated with mouse adenovirus are nearly pathognomonic and can be confirmed by electron microscopy. K virus, a mouse papovavirus, can also induce intranuclear inclusion bodies in the small intestine of young mice, but unlike mouse adenovirus, they are present in the lamina propria and are not as obvious (see p. 171). Nuclei in the apex of villus epithelium must be differentiated from similarly located nuclei in the process of mitosis and from intraepithelial lymphocytes. Several nuclei may have to be scrutinized before convincing evidence of an inclusion is established.

Biologic Features

Natural History

At least two serologically and biologically distinct types of adenovirus are found in the laboratory
Adenovirus FL (AdFL) produces a subclinical multisystemic infection with prolonged viruria in adult mice and fatal disease in neonates. The AdFL strain is transmitted by contact and is excreted from urine and probably nasal secretions, but not feces (Hartley and Rowe 1960; van der Veen and Mes 1973). The lack of AdFL enterotropism needs to be verified, as intestinal lesions and inclusions can be seen in severe combined immunodeficient (scid) mice experimentally inoculated with AdFL (S.W. Barthold, unpublished observations). Intestinal adenovirus infections are due to a second type of adenovirus, which possesses a high degree of tropism for intestine. The intestinal strain that has been isolated and best characterized is the adenovirus K87 (AdK87) strain of mouse adenovirus. This virus infects only intestine, is excreted in feces, and is inefficiently transmitted (Hashimoto et al. 1966; Smith and Barthold 1987; Sugiyama et al. 1967; Takeuchi and Hashimoto 1976). Rats appear to be infected with a serologically related, but distinct intestinal adenovirus (Smith and Barthold 1987).

Pathogenesis

Intestinal mouse adenovirus infects only intestine, regardless of the route of inoculation, underscoring its high degree of enterotropism. Following oral inoculation of 4-week-old mice, virus can be isolated from feces as early as 3 days and may persist for 3 or more weeks, followed by apparent recovery. Maximum infections occur between 7 and 14 days. The course of infection in younger mice is similar (Hashimoto et al. 1970; Sugiyama et al. 1967). Mice of all ages are usually asymptomatic following experimental and natural infection (Luethans and Wagner 1983; Sugiyama et al. 1967), but transient runting has been observed (S.W. Barthold, unpublished observations). Infection appears to be restricted to the small intestine, particularly distal segments, and cecum. Only

Fig. 352. (above) Mucosa, small intestine of a weanling mouse naturally infected with intestinal adenovirus. The nucleus of an atypically aligned enterocyte contains a basophilic inclusion surrounded by a halo (arrow). H&E, ×450

Fig. 353. (below) Adenovirus, nucleus of enterocyte, small intestine, mouse. Crystalline arrays of virus particles and homogeneous viral matrix. From a naturally infected mouse. (Courtesy of Dr. T.N. Luethans and Dr. J.E. Wagner and Laboratory Animal Science.) TEM, ×11000