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Rat Coronavirus Infection, Lung, Rat

David G. Brownstein

Synonym. Parker's rat coronavirus, rat submaxillary gland virus, sialodacryoadenitis virus

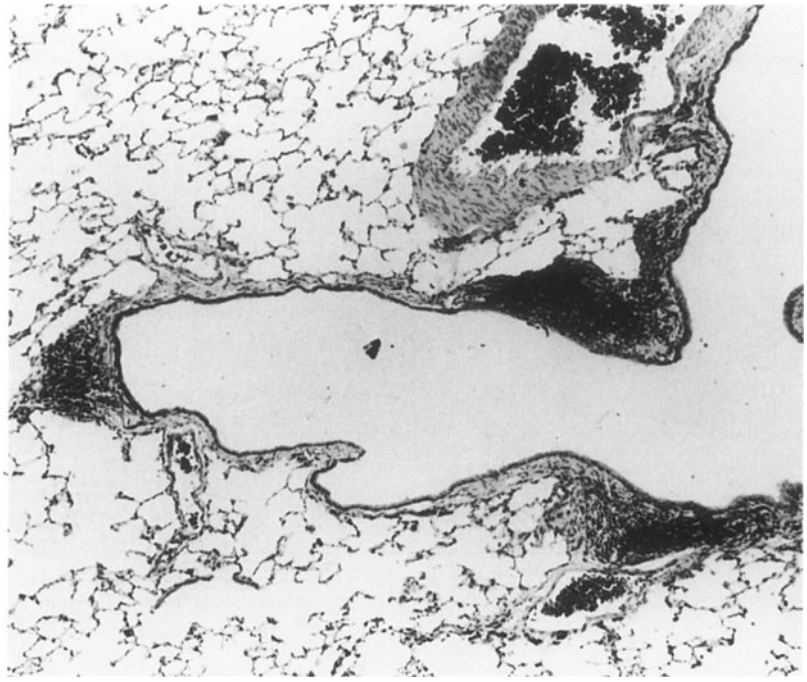
Gross Appearance

Naturally infected adult rats rarely have grossly observable lung changes. Elsewhere macroscopic lesions are absent or confined to salivary glands and periglandular tissue. Ocular changes may also occur as a consequence of keratitis sicca. Axenic rats experimentally infected with Parker's rat coronavirus (PRC) develop gross lesions in the lung on postinnoculation days 6 and 7, which consist of randomly dispersed red-brown to gray foci less than 1 mm in diameter (Bhatt and Jacoby 1977). Although PRC may cause fatal pneumonia in a high percentage of newborn and day-old rats, gross pulmonary lesions have not been described (Parker et al. 1970). Outbred young adult SPF Wistar rats experimentally infected with sialodacryoadenitis virus (SDAV) develop mild randomly dispersed red foci 5–7 days after intranasal inoculation (Wojcinski and Percy 1986).

Microscopic Features

Lung changes in young adult rats are mild and short-lived irrespective of the infecting strain. Nonsialotropic strains such as PRC produce hyperplasia of bronchusassociated lymphoid tissue (Fig. 356), perivenular lymphoid infiltrates (Fig. 357), and patchy interstitial pneumonia (Fig. 358; Bhatt and Jacoby 1977). Sialotropic strains such as SDAV produce more severe acute inflammatory changes in bronchioles and lung parenchyma (Wojcinski and Percy 1986). Random patches of bronchiolar epithelium undergo necrosis in conjunction with infiltration and exudation by neutrophils. Acute inflammation may extend from terminal bronchioles into adjacent alveoli. Affected alveolar septa are edematous, infiltrated by leukocytes, and alveolar spaces contain desquamated pneumocytes, macrophages,

T. C. Jones et al. (eds.), *Respiratory System*



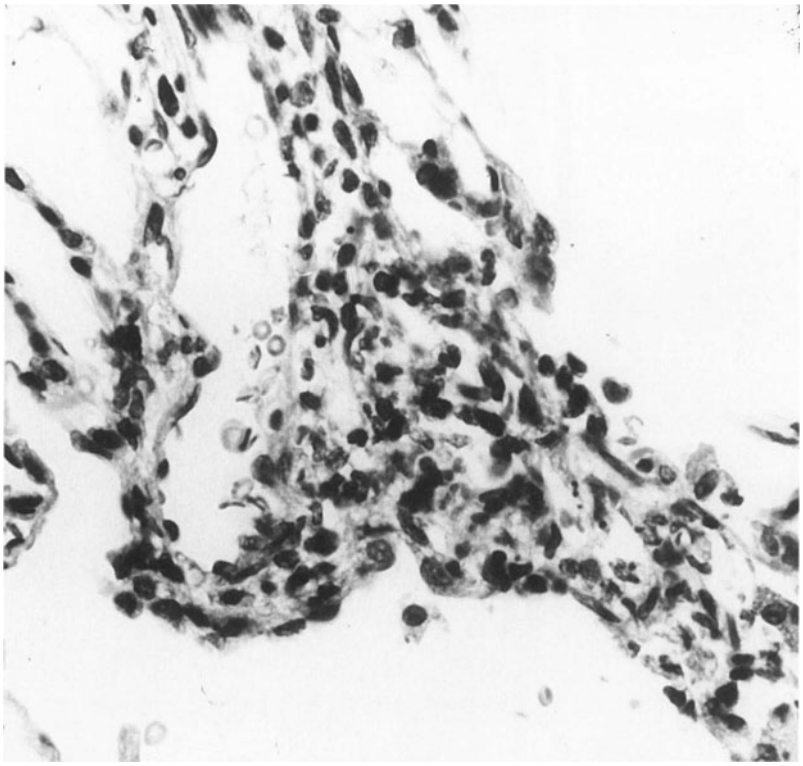


Fig. 356. (*above*) Rat coronavirus infection, lung. Bronchiole with mildly hyperplastic lymphoid nodules following experimental infection. H&E, ×58

Fig. 357. (*below*) Rat coronavirus infection, lung. Perivenular lymphoid cells in an experimentally infected rat. H&E, ×536

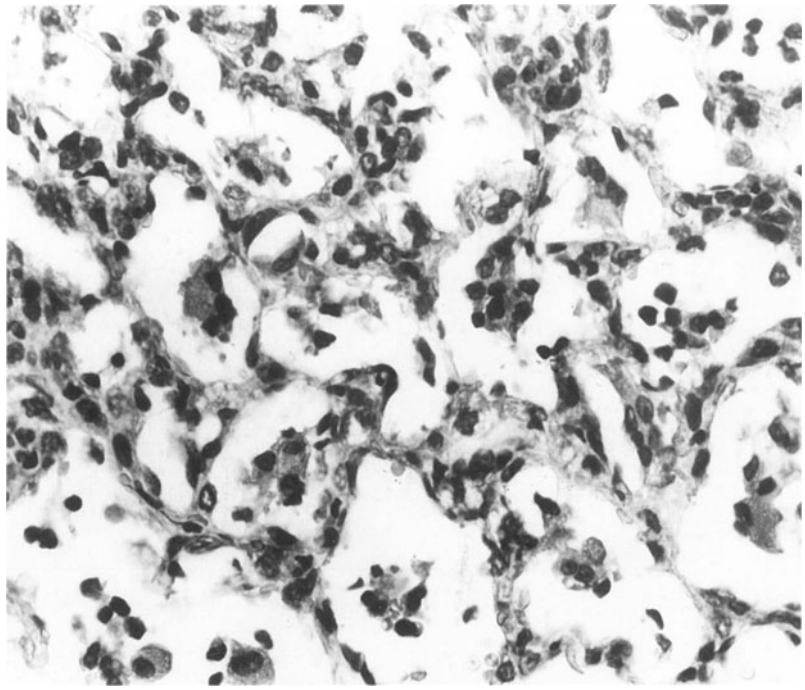


Fig. 358. Interstital pneumonia following experimental infection with rat coronavirus.Alveoli contain foamy macrophages and lymphoid cells. Septa are inflitrated with mononuclear cells. H&E, ×536

and neutrophils. The reparative phase is characterized by hyperplasia of bronchiolar epithelium and pneumocytes, infiltration by lymphoid cells, hyperplasia of bronchus-associated lymphoid tissue, and perivenular lymphoid infiltrates (Wojcinski and Percy 1986).

Transient rhinotracheitis also occurs which is more severe with SDAV than with PRC. In the former there is epithelial erosion and necrosis of perilaryngeal glands and ducts (Wojcinski and Percy 1986). In the latter there may be segmental erosion of epithelium covering nasal turbinates. In both cases lamina propria of the nasal cavity is edematous and infiltrated by lymphocytes and neutrophils. Some nasal respiratory surfaces are covered with exudate consisting of mucus, neutrophils, desquamated epithelium, and detritus.

Lesions of salivary glands are common with SDAV and uncommon or mild with PRC. With SDAV severe inflammatory changes occur in mixed or serous salivary glands, exorbital glands, and harderian glands. Mild parotitis and submaxillary sialoadenitis may occur with PRC. Description of these changes is beyond the scope of this chapter. The reader is referred to several excellent studies of sequential changes in these tissues (Innes and Stanton 1961; Jacoby et al. 1975, 1979; Bhatt and Jacoby 1977).

Ultrastructure

Infected epithelial cells have focally dilated cisternae of endoplasmic reticulum and cytoplasmic vacuoles which contain spherical dense cores 60–70 nm in diameter (Parker et al. 1970; Jonas et al. 1969). The characteristic corona, seen in negatively stained preparations, is not seen by transmission ultramicroscopy.

Differential Diagnosis

Respiratory tract lesions must be differentiated from those caused by Sendai virus, pneumonia virus, *Mycoplasma pulmonis*, and pathogenic bacteria. Identification of the infecting agent is necessary for definitive diagnosis.

Biological Features

Etiology. Rat coronaviruses are typical members of the Coronaviridae; pleomorphic, enveloped RNA viruses with plump, pedunculated surface projections (corona) measure 76–98 nm in diameter in negatively stained preparations 12–25 nm surface projections (Parker et al. 1970). Viruses are formed in cytoplasmic vesicles and cisternae of

endoplasmic reticulum. The viruses are closely related to mouse hepatitis virus (Bhatt and Jacoby 1977).

Natural History. Rat coronaviruses cause acute limited infections except in immunologically disabled individuals such as athymic rats. They are highly contagious and are transmitted by aerosol, by direct contact, and transiently by fomites. There are two patterns of infection. Enzootic infections occur primarily in breeding colonies, where sucklings are passively immune, adults are actively immune, and weanlings are a continuous source of susceptible individuals due to waning passive immunity. It is therefore weanlings that generally exhibit clinical signs. Epizootics occur in nonimmune colonies, where morbidity is most likely to occur in young or aged animals. With SDAV the signs are usually transient and consist of intermandibular and cervical edema, swelling of submaxillary glands, sneezing, nasal and ocular discharges which are often red-tinged due to a high content of porphyrin, photophobia, and keratoconjunctivitis and its sequelae. Some complications of keratoconjunctivitis, such as glaucoma and phthisis, cause permanent disfigurement (Jacoby et al. 1979). Subclinical infections are the rule for PRC and are common for SDAV. Extensive host range studies have not been carried out but SDAV can be used to infect mice by the respiratory route (Bhatt et al. 1977).

Pathogenesis. Rat coronaviruses are epitheliotropic and replicate at all levels of the respiratory tract during the 1st week of infection. The highest respiratory titers are reached in the nasal cavity and trachea. SDAV but not PRC replicates extensively in certain exocrine tissues of the head. Neutralizing antibodies are detectable on day 6 or 7. Complement-fixing antibodies appear later and cross react with mouse hepatitis viral antigens (Bhatt and Jacoby 1977; Parker et al. 1970; Jacoby et al. 1979).

Frequency. Coronavirus infections are common in institutional rat colonies and in some commercial colonies. Different strains of rat coronavirus cannot be distinguished serologically.

Comparison with Other Species

Coronaviruses are ubiquitous in humans, animals, and birds (Bohl 1981). They cause enteritis in swine, cattle, dogs, mice, turkeys, and humans; encephalomyelitis in swine and mice; sialodacryoadenitis in rats; and respiratory infections in chickens, rats, and humans. Avian infectious bronchitis virus infects the trachea and lungs of chickens, causing respiratory distress, especially in young chicks. The virus also replicates in kidneys, bursae, and oviducts, producing inflammatory disease at these sites. Human respiratory coronaviruses are apparently restricted to the upper respiratory tract, causing rhinotracheitis and pharyngitis.

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