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Rat Coronavirus Infection, Lung, Rat

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Synonym. Parker's rat coronavirus infection.

Gross Appearance

Naturally infected adult rats rarely have grossly observable changes. Experimentally infected 9–10 week old axenic rats develop gross lesions in the lung on postinoculation 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 rat coronavirus 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).

Microscopic Features

Lung changes in young adult rats are mild and short-lived (Bhatt and Jacoby 1977). Bronchus-associated lymphoid tissue is hyperplastic (Fig. 248), some pulmonary veins and venules are cuffed by lymphocytes (Fig. 249), and there is patchy interstitial pneumonia (Fig. 250). Septa of affected alveoli are thickened by mononuclear cells and neutrophils. Adjacent alveolar spaces contain desquamated pneumocytes, foamy macrophages, lymphocytes, and neutrophils.

Transient rhinotracheitis also occurs and may lead to segmental erosion of the respiratory epithelium covering nasal turbinates. The lamina propria is edematous and infiltrated with lymphocytes and neutrophils. Some nasal respiratory surfaces are covered with exudate consisting of mucus, neutrophils, desquamated epithelium, and detritus. Tracheal epithelium is rarely eroded but large numbers of transepithelial neutrophils may be present. The lamina propria is mildly edematous, congested, and infiltrated with lymphocytes and neutrophils.

Lesions of salivary glands are uncommon but may help distinguish rat coronavirus infections from other rat respiratory infections. Mild parotitis and submaxillary sialoadenitis have been reported and are identical to, but less severe than, those caused by sialodacryoadenitis virus (Bhatt and Jacoby 1977). There is necrosis of salivary ducts with periductular and interstitial inflammatory edema. Lesions apparently do not occur in lacrimal glands. Infected neonatal rats develop diffuse interstitial pneumonia, focal atelectasis, and compensatory emphysema (Parker et al. 1970).

Ultrastructure

Infected epithelial cells have focally dilated cisternae of endoplasmic reticulum and cytoplasmic vacuoles which contain spherical dense cores, 60–70 nm, in diameter, surrounded by an envelope 80–120 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. Morphologically, rat coronavirus is indistinguishable from sialodacryoadenitis virus.

Differential Diagnosis

Respiratory tract lesions must be differentiated from those caused by sialodacryoadenitis virus, Sendai virus, pneumonia virus, *Mycoplasma pulmonis*, and pathogenic bacteria. Lesions in salivary glands, when present, are generally milder than those caused by sialodacryoadenitis virus.

Biologic Features

Natural History. Rat coronavirus causes acute limited infections of the respiratory tract. The epizootiologic characteristic of this infection has not been reported. No evidence for a carrier state has been reported and host range studies have been limited to the rat. The virus is highly infectious and is presumably transmitted by aerosol or direct contact. The infection is subclinical in rats shortly following weaning. Infected neonatal rats may die with severe respiratory distress.

Pathogenesis. Rat coronavirus is epitheliotropic and replicates at all levels of the respiratory tract during the 1st week of infection. The highest titers

are reached in the nasal cavity and trachea. Limited replication occurs in salivary tissues. Neutralizing antibodies to rat coronavirus and sialodacryoadenitis virus are detectable on day 6 or 7. Complement-fixing antibodies appear later and cross-react with sialodacryoadenitis and mouse hepatitis viral antigens (Bhatt and Jacoby 1977; Parker et al. 1970; Jacoby et al. 1979).

Etiology. Rat coronavirus is a typical member of the Coronaviridae: a pleomorphic, enveloped RNA virus with plump, pedunculated surface projections (corona). It measures 76–98 nm in diameter in negatively stained preparations with 12–25 nm surface projections (Parker et al. 1970). Virions are formed in cytoplasmic vesicles and cisternae of endoplasmic reticulum. The virus is closely related antigenically to sialodacryoadenitis virus (Bhatt et al. 1972).

Frequency. The frequency of rat coronavirus infection within rat colonies is difficult to ascertain because of the close relationship of this virus to sialodacryoadenitis virus. Serological evidence of infection with coronaviruses is common in commercial and institutional rat colonies. In one survey of 4 germ-free, 5 specific-pathogen-free (SPF), and 11 conventional rat colonies, 3 of the SPF and 11 of the conventional colonies were infected while the germ-free colonies were not (Parker et al. 1970). In another report, all retired breeders from six vendors were positive (Jacoby et al. 1979).

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; systemic infections in cats 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, bursa, and oviducts, producing inflammatory disease at these sites. Human respiratory coronaviruses are apparently restricted to the upper respiratory tract, causing rhinotracheitis and pharyngitis.

◁ **Fig. 248 (Above).** Rat coronavirus infection, lung. Bronchiole with mildly hyperplastic lymphoid nodules following experimental infection. H and E, $\times 59$ (reduced by 15%)

Fig. 249 (Middle). Rat coronavirus infection, lung. Perivascular lymphoid cells in an experimentally infected rat. H and E, $\times 536$ (reduced by 15%)

Fig. 250 (Below). Interstitial pneumonia following experimental infection with rat coronavirus. Alveoli contain foamy macrophages and lymphoid cells. Septa are infiltrated with mononuclear cells. H and E, $\times 536$ (reduced by 15%)

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Pneumonia Virus of Mice Infection, Lung, Mouse and Rat

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Synonyms. Mouse pneumonia virus; pneumonia virus.

Gross Appearance

Mice. Gross lung changes are not seen in mice naturally infected with pneumonia virus of mice (PVM). Pulmonary consolidation has been produced experimentally using tissue-culture-adapted virus (Harter and Choppin 1967; Tennant et al. 1965) or serially blind-passed PVM-infected lung tissue (Horsfall and Hahn 1940; Curnen and Horsfall 1947). Initially, consolidation is hilar in distribution with subsequent radiation along bronchioles. Consolidated foci are dark red and exude sanguinous fluid when cut. Later these foci become gray.

Rats. Naturally infected adult rats usually have no gross lung changes but may have focal or multifocal plum-colored to gray foci less than 2 mm in diameter. These may occur in any lobe.

Microscopic Features

Mice. Histopathologic lung changes are rare in naturally infected mice. Lesions produced experimentally with tissue-culture-adapted (Carthew and Sparrow 1980a; Vogtsberger et al. 1982) or serially blind-passed infected lung tissue (Horsfall and Hahn 1940) include both airway and parenchymal changes. PVM adapted to BHK-21 cells and inoculated at high doses (10^4 – 10^5 TCID₅₀) in-

tranasally causes a mild erosive bronchiolitis and interstitial pneumonia. Bronchiolar epithelium first develops granular eosinophilic cytoplasm followed by lifting from the basal lamina. Desquamated epithelium and neutrophils may plug affected airways. Alveolar changes generally lag behind those in the airways. Alveolar septa are edematous, congested, and infiltrated with neutrophils and macrophages. There is some necrosis within alveolar walls. By the time bronchiolar epithelium has regenerated and returned to a normal appearance, alveolar septa are thickened by dense infiltrates of lymphocytes, macrophages, and scattered neutrophils. Alveolar spaces may contain an exudate with a similar inflammatory cell composition. Inflammatory changes in the parenchyma peak near the end of the 2nd week of experimental infection and are usually resolved by the end of the 3rd week.

Lower doses ($<10^3$ TCID₅₀) of tissue-culture-adapted PVM cause vascular-oriented inflammation and interstitial pneumonia (Vogtsberger et al. 1982). The vascular component has been described as an acute vasculitis with infiltrates of neutrophils and lymphocytes followed by a mild nonsuppurative vasculitis, which persists to the end of the 3rd week of infection. The interstitial pneumonia is acute, but its duration and histological features have not been reported.

Mild rhinitis is a constant feature in mice infected intranasally with tissue-culture-adapted PVM, even at doses that fail to produce pulmonary histopathology. The nasal mucosa is edematous with multifocal erosions. Neutrophils and lymphoid cells infiltrate the lamina propria. A sparse ex-