Sendai Virus Infection, Lung, Mouse and Rat

David G. Brownstein

Synonyms. Hemagglutinating virus infection of Japan (HVJ); Japanese hemagglutinating virus infection (JHV); hemagglutinating virus infection of the mouse (HVM); parainfluenza virus infection.

Gross Appearance

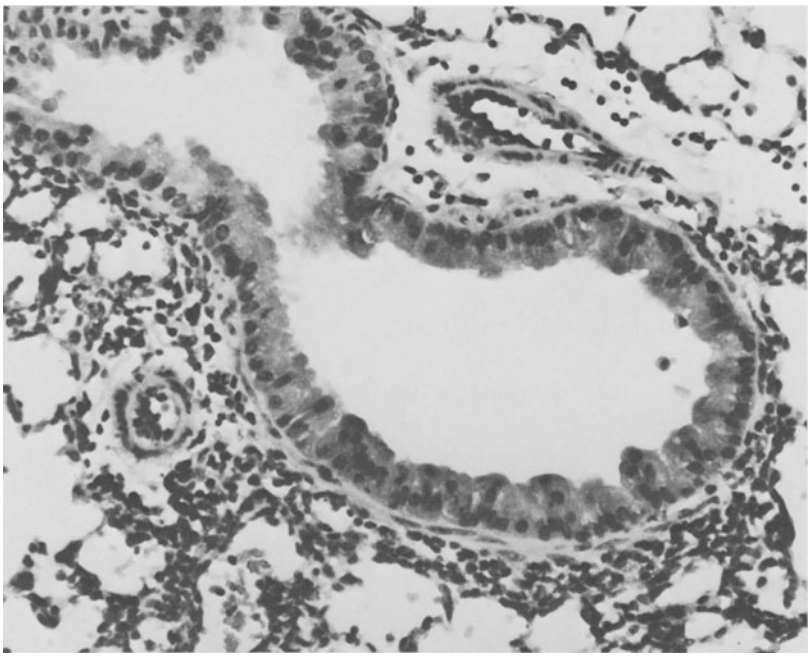
Mice. Asymptomatic or mildly affected mice usually have no gross pulmonary changes other than increased lung weights, although a few mildly affected mice have white lines along the course of bronchi, white foci in lymph nodes, and dual lobes of consolidation. Average increases of 50% have been reported by the 5th day and 100% by the 14th day after experimental infection of Swiss mice (Robinson et al. 1968). Overtly ill and genetically susceptible mice have more dramatic increases in lung weights (200%–300%) (Parker et al. 1978). In these cases, one or more lung lobes are plum-colored or contain sharply demarcated plum-colored foci which exude frothy sanguinous fluid when cut. If these mice survive into the 3rd week, consolidated foci are gray.
Extrapulmonary changes reflect local and systemic activation of the immune system and stress. Regional lymph nodes enlarge during the 2nd week, a change most obvious in the cervical lymph nodes. These nodes may triple or quadruple in weight. Splenic enlargement (20%–50% in weight) also occurs during the 2nd week. Thymic involution is a stress-related change, the degree being roughly porportional to the degree of lung parenchymal injury.

Rats. Asymptomatic infections are the rule and follow a pattern similar to that described for asymptomatic or mildly affected mice.

Microscopic Features

Mice. Histopathologic changes in experimental and natural disease can be divided into: acute phase, characterized by degeneration and necrosis of target epithelium and exudative inflammation; reparative phase, characterized by regeneration of damaged target cells and interstitial inflammation; and resolution phase, characterized by a rapid subsidence of inflammation and repair.
During the acute phase, which lasts from 8 to 12 days, there is a descending infection of conducting airway epithelium. This frequently extends to proximal type II and, to a lesser degree, type I alveolar epithelium (Brownstein et al. 1981; Parker and Richter 1982; Richter 1970, 1973; Zurcher et al. 1977). The result is an acute endobronchitis-bronchiolitis and bronchogenic alveolitis. The earliest airway changes are segmental. Infected bronchiolar epithelial cells are hypertrophied with eosinophilic foamy, granular, or homogeneous cytoplasm. The nuclei of infected cells are poorly polarized and may be enlarged and vesicular. Inflammatory infiltrates appear shortly after these initial cytological changes (Fig. 241). The lamina propria and adventitia are expanded by edema, dilated lymphatics, and cellular infiltrates. Initially, these infiltrates are a mixture of polymorphonuclear leukocytes, reactive lymphoid cells with moderate amounts of homogeneous amphophilic or eosinophilic cytoplasm, and large round or fusiform lymphoreticular cells. The relative number of each type depends on the age and genetic composition of the host and the dose and route (intranasal versus aerosol) of viral exposure. In genetically susceptible or immature mice, neutrophils often predominate as they do after exposure to large doses of virus. Peribronchiolar pulmonary arterioles and venules have increased intimal cellularity. The endothelium is hypertrophied and elevated by asymmetric accumulations of leukocytes in the

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



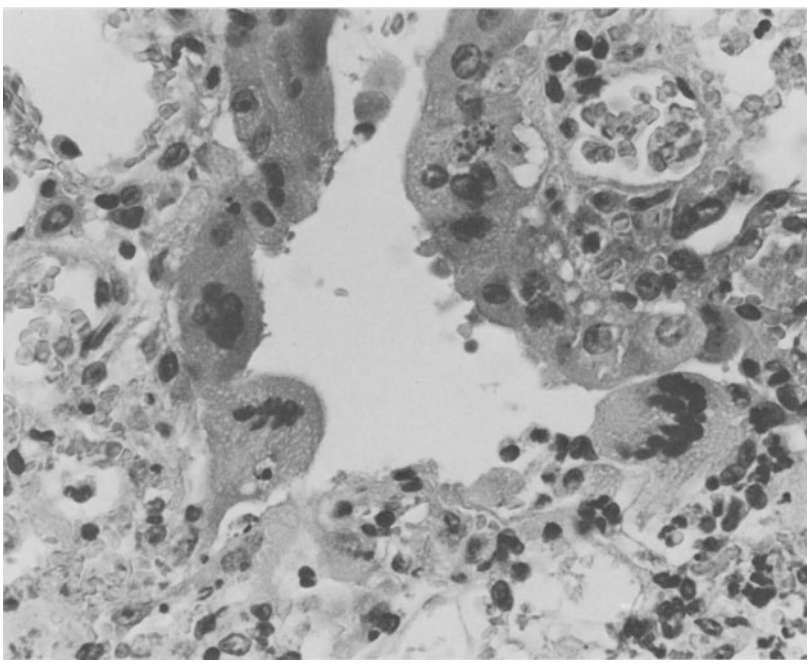
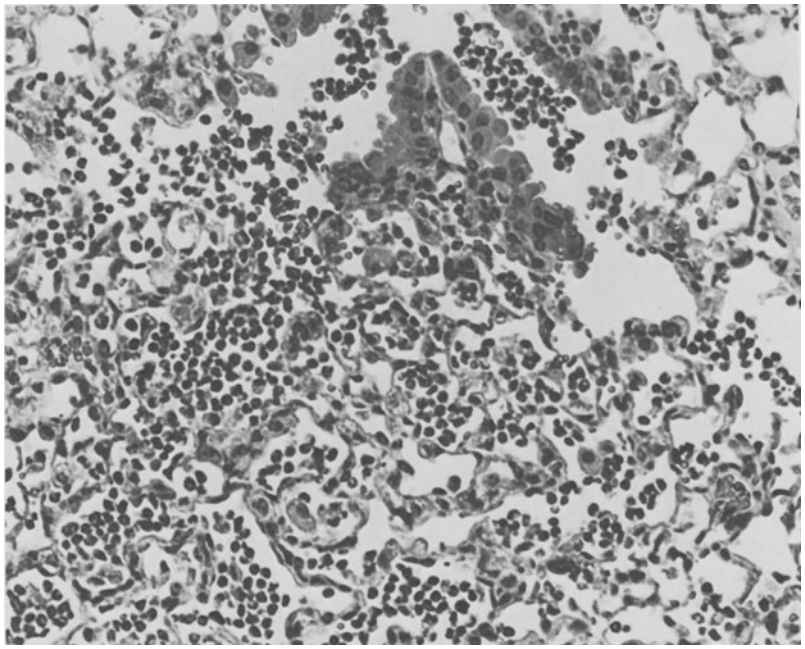


Fig. 241 *(Above).* Sendai virus infection, acute phase. Bronchiolar epithelium is hypertrophied with some loss of nuclear polarity. The adventitia is edematous and infiltrated with lymphoid cells. H and E, × 354 (reduced by 15%)

Fig. 242 *(Below).* Sendai virus infection, acute phase. Bronchiole with multiple epithelial syncytia. H and E, × 791 (reduced by 15%)

subendothelial layer of the intima. There is striking leukocyte pavementing. The adventitia of these vessels is also hypercellular due to leukocytic infiltrates similar to those infiltrating airways. The adventitia is also expanded by edema. Cytopathic changes in bronchiolar epithelium are afforded some specificity if syncytia, cytoplasmic inclusions, or intranuclear inclusions are present. The lesions may depend, in part, on virus and mouse strain.

These changes are usually not seen or are equivocal, since infected cells tend to slough prior to their development. Syncytia usually appear as central clusters of condensed or pyknotic epithe-



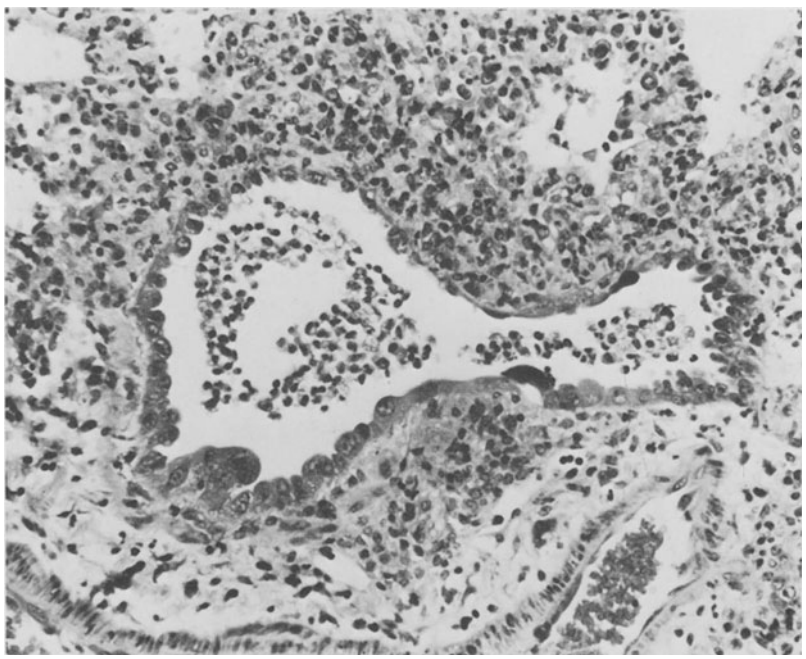


Fig. 243 *(Above).* Sendai virus infection, acute phase. Alveoli radiating from an infected terminal bronchiole contain a mixed inflammatory exudate. Alveolar septa are edematous and infiltrated with mononuclear cells. H and E, × 345 (reduced by 15%)

Fig. 244 *(Below).* Sendai virus infection, reparative phase. Bronchiole with disorganized regenerating epithelium. Nuclei are pleomorphic and vesicular with prominent nucleoli. H and E, × 245 (reduced by 15%)

lial nuclei surrounded by foamy eosinophilic cytoplasm that crowds adjacent cells (Fig. 242). Cytoplasmic inclusions represent aggregates of redundant nucleocapsids within the cytoplasmic matrix (see Ultrastructure). They are most obvious as homogeneous spherical or irregular eosinophilic cytoplasmic bodies surrounded by a narrow halo. This halo is a fixation shrinkage artifact. Intranuclear inclusions are rare in Sendai virus infections but intranuclear viral particles have been described in DBA/2 mice (Richter 1970) and intranuclear inclusions have been

reported in athymic nude mice (Ward et al. 1976).

Near the end of the acute phase, infected epithelium has sloughed in sheets or as individual cells which lie within the lumen along with an inflammatory exudate. Because of the segmental nature of the infection, some airways may be devoid of lining cells while others are lined by intact, hypertrophied epithelium. Airways with desquamating epithelium frequently have focally dense lymphoid aggregates within the lamina propria, which cause overlying epithelium to bulge into the lumen.

The alveolar component of the acute phase is characterized by accumulations of polymorphonuclear leukocytes, macrophages, lymphoid cells, and desquamated pneumocytes within alveolar spaces. Alveolar septa are thickened by edema, congested capillaries, and hypertrophied alveolar corner cells. These changes are multifocal, being oriented around infected terminal bronchioles. In severe cases foci of parenchymal inflammation may become confluent, resulting in lobar pneumonia. Alveolar spaces may fill with fibrin or extravasated blood. Foci of emphysema may occur where septal integrity has been destroyed. Near the end of the acute phase fibrin deposits have condensed along denuded alveolar surfaces or as discrete deposits in alveolar spaces. Increased cellularity of thickened alveolar septa is due to accumulating mononuclear cells (Fig. 243). Inflamed alveoli may be partially atelectatic.

The reparative phase is heralded by the appearance of regenerating epithelium. This may be seen as early as the 3rd day, but does not predominate over degenerative airway changes until days 8–12. Initially, partially denuded airways contain continuous or interrupted patches of low cuboidal, polygonal, or squamous cells with basophilic cytoplasm and large pleomorphic vesicular nuclei which are poorly polarized and contain prominent nucleoli (Fig. 244). Mitotic figures are common in these cells. Once denuded airways are reepithelialized, lining cells become columnar and rapidly assume a normal mucociliary appearance. Sessile or pedunculated airway excrescences are extremely common during the reparative phase. These may be composed solely of epithelium or have cores of lymphoreticular cells or fibroblasts. These are ephemeral structures and are rarely seen after the 3rd week. It is common during this phase for terminal bronchioles to be lined by nonkeratinizing stratified squamous epithelium. The metaplastic epithelial cells most closely resemble spinous cells, although intercellular bridges are usually difficult to identify. The adventitia and lamina propria of segments undergoing repair are less edematous than in the acute phase, and are densely infiltrated with lymphocytes and plasma cells. The intimal cellularity of pulmonary arterioles and venules seen during the acute phase in usually absent in the reparative phase, but adventitial infiltrates of lymphocytes and plasma cells are prominent.

During the reparative phase, alveolar inflammation has shifted from the airspaces to the interstitium. Two forms of alveolar repair are recognized. In the first, septa are lined by cuboidal epithelium (adenomatous hyperplasia, alveolar bronchiolization, alveolar epithelialization) (Fig. 245). These epithelial cells are initially undifferentiated, but soon differentiate into pneumocytes or ciliated, mucous or Clara cells. In the second form of repair, sheets and nests of metaplastic squamous epithelium fill alveolar spaces (Fig. 246). There is partial or total atelectasis of affected alveoli during this phase. If fibrin has been deposited it undergoes lysis or organization. Macrophages surround and infiltrate large fibrin deposits. Plump fibroblasts may also traverse these deposits. During the 3rd week collagen bundles can be identified in organizing fibrin depositis. The reparative phase is usually complete by the end of the 3rd week.

The resolution phase may be as short as 1 week, so that by the end of the 4th week residual lesions are difficult to identify. There are, however, several changes which may persist for long periods. The most severe sequela, and one that may persist for the life of the animal, is organizing alveolitis with or without bronchiolitis fibrosa obliterans (Fig. 247). This change is the end result of the organization of extensive fibrin deposits in denuded alveoli and terminal airways. Sheets of haphazardly arranged collagen bundles and fibroblasts in natural infections may obliterate parenchymal architecture or may fill alveolar spaces, leaving parenchymal architecture intact. Other residual lesions include foci of emphysema containing inspissated secretions, cholesterol crystals, and macrophages; focal aggregates of foamy, alveolar macrophages; focal thickening of alveolar septa; focal adenomatous hyperplasia of alveoli; and perivascular and peribronchiolar lymphoplasmacytic infiltrates. These changes have been identified in mice up to 1 year after infection with Sendai virus (Appel et al. 1971; Parker and Richter 1982; Robinson et al. 1968).

Athymic nude mice, unlike euthymic mice, develop progressive lung changes due to persistent in-

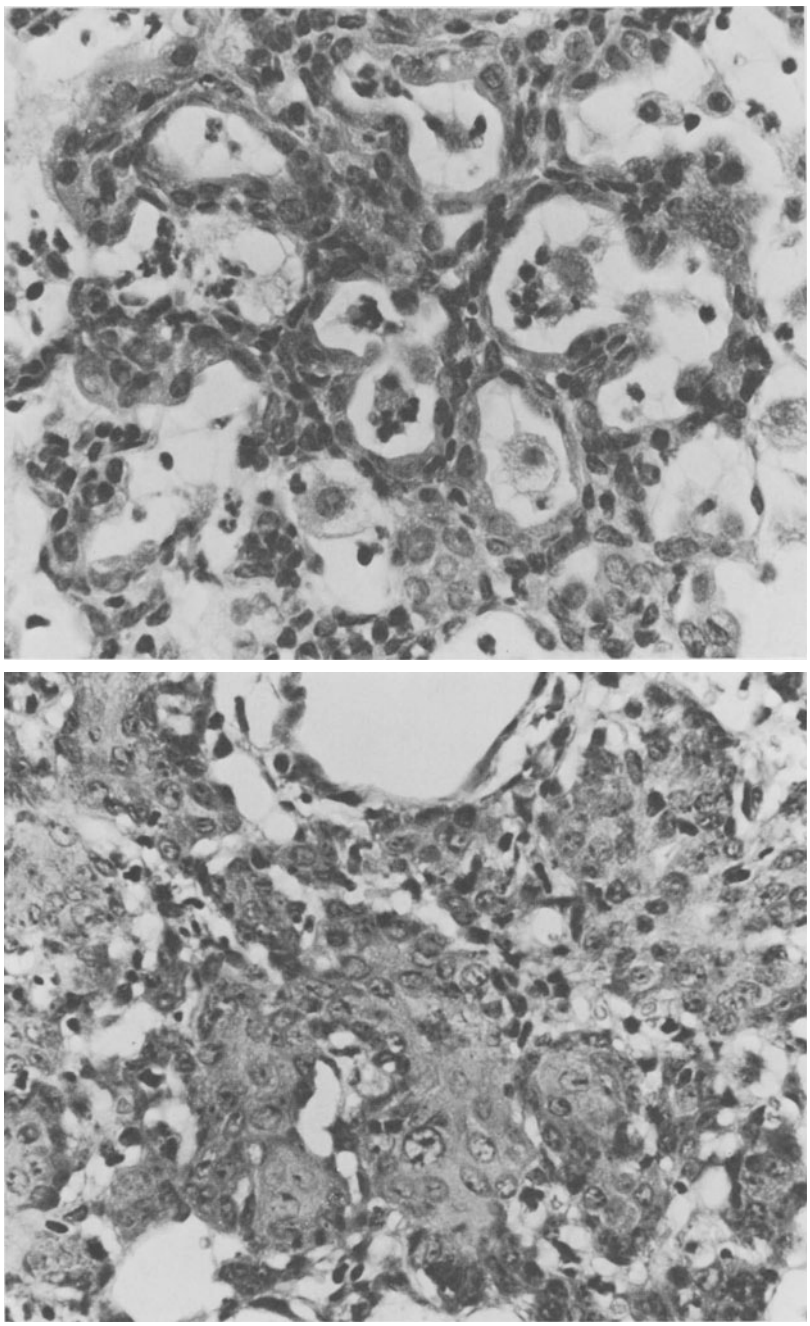


Fig. 245 *(Above).* Sendai virus infection, reparative phase. Alveoli are lined by cuboidal epithelium and septa are infiltrated with lymphoid cells. H and E, × 600 (reduced by 15%)

Fig. 246 *(Below).* Sendai virus infection, reparative phase. Alveolar squamous metaplasia. H and E, × 600 (reduced by 15%)

fection with Sendai virus (Iwai et al. 1979; Ward et al. 1976). Pulmonary changes are most often diffuse due to extensive parenchymal involvement. Alveolar septa are thickened by edema, neutrophils, and macrophages. Alveolar epithelialization is striking and squamous metaplasia is prominent in some cases. Bronchiolar epithelium is hyperplastic with numerous mitotic figures. Airways may be filled with neutrophils. Lymphoid infiltrates are usually sparse.

Rats. Information on the microscopic appearance of Sendai-virus-induced lung lesions in rats is limited. Lesions in a colony of mixed rat strains that

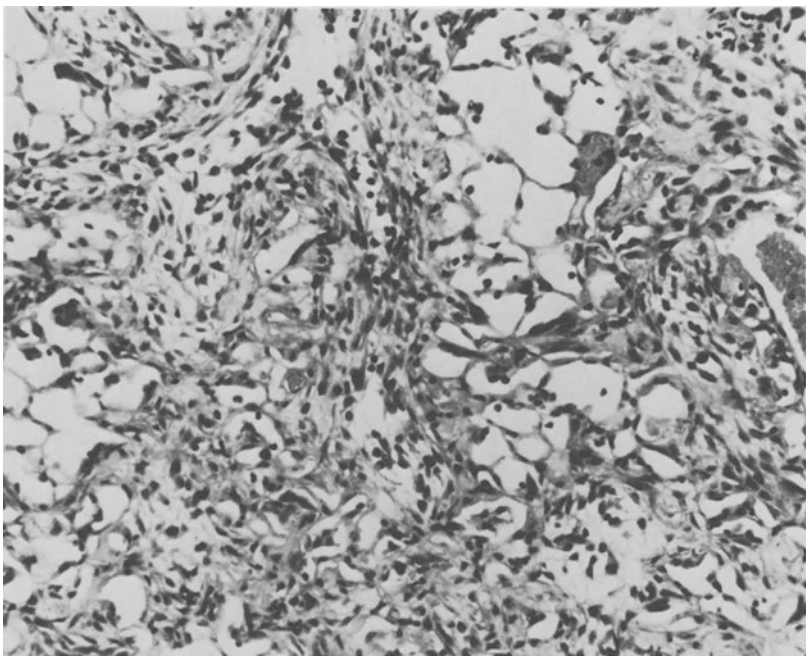


Fig. 247. Sendai virus infection, resolution phase. Organizing alveolitis. H and E, × 244 (reduced by 15%)

develop antibodies to Sendai virus have been reported but virus isolation was not attempted (Burek et al. 1977). These rats had mild to severe peribronchial and perivascular cuffing by lymphocytes and plasma cells, and interstitial pneumonia. Bronchiolar epithelium was hyperplastic and focally ulcerated. Unfortunately, the rats also developed antibodies to pneumonia virus of mice. In the author's experience this virus is capable of producing inflammatory lung disease in the rat. Necrotizing bronchitis has been reported in germfree rats inoculated intranasally with Sendai virus (Jacoby et al. 1979).

Ultrastructure

Limited ultrastructural pathology has been reported of experimental and spontaneous Sendai virus infections in euthymic mice (Brownstein et al. 1981; Parker and Richter 1982; Richter 1970, 1973; Zurcher et al. 1977). The ultrastructure of naturally infected athymic nude mice has also been reported (Ward et al. 1976). The primary site of replication is the epithelium of bronchi and bronchioles and it is within ciliated and Clara cells that ultrastructural evidence of replication is most easily seen. Nucleocapsid assembly occurs in the cytosol at a rate far in excess of the rate of virus assembly. The result is massive accumulations of nucleocapsids, which appear as poorly delineated aggregates or crystalline arrays of rigid hollow fibrils 16–18 nm in diameter. Intranuclear aggregates of similar-appearing fibrils have been reported and these apparently correspond to the intranuclear inclusions seen by light microscopy. The significance of these aggregates is not known; they are rare and appear late in infection, suggesting that they may be transported from sites of synthesis in the cytosol (Choppin and Compans 1975). Nucleocapsids align beneath modified segments of plasma membrane to initiate exotrophy. These modified segments are thickened by glycoprotein surface spikes and an electron-dense layer on the inside of the plasma membrane. Budding forms may be spherical, filamentous, or pleomorphic (Darlington et al. 1970).

This appearance of productively infected cells is also seen in infected type II alveolar epithelium (Brownstein et al. 1981). An additional cytoplasmic inclusion consisting of membrane-bound, randomly arranged hollow fibrils, 15–20 nm in diameter, surrounded by 40-nm electron-dense cuffs has been reported in these cells (Zurcher et al. 1977). Incomplete reports indicate viral components in type I alveolar epithelium and septal capillary endothelium (Parker and Richter 1982; Ward et al. 1976). Only intranuclear nucleocapsids have been described in the former (nude mice). Viral assembly has not been observed in ei-

ther cell type. Both of these may be examples of abortive infections.
Alveolar macrophages are susceptible to abortive infections in vitro (Eustatia et al. 1972; Mims and Murphy 1973), but ultrastructural evidence of viral replication is lacking. The author has seen numerous virions and nucleocapsids within heterophagosomes of alveolar macrophages in experimentally infected mice. This perhaps represents phagocytosis of debris containing viral particles.

Differential Diagnosis

Mice. Sendai virus pneumonia must be distinguished from pneumonias caused by mouse coronaviruses, K virus, pneumonia virus, *Mycoplasma pulmonis,* and *Corynebacterium kutscheri.* The chronic wasting disease produced in athymic nude mice must be distinguished from similar syndromes caused by mouse coronarviruses, mouse adenovirus, *Pneumocystis, Giardia, Spironucleus,* and *Toxoplasma.*

Rats. Sendai virus pneumonia must be distinguished from pneumonias caused by rat coronavirus, pneumonia virus, *Mycoplasma pulmonis, Streptococcus pneumoniae,* and *Corynebacterium kutscheri.*
Some pulmonary changes caused by Sendai virus infection mimic those changes caused by exposure of rodents to halogenated aromatic hydrocarbons (Reid et al. 1973), oxidant gases (Stephens et al. 1974), and other toxicants which have the terminal conducting airways as target structures.

Biologic Features

Natural History. Sendai virus causes acute limited infections in immunocompetent rodents. There is no evidence for latency or chronic infections (Fujiwara et al. 1976; van der Veen et al. 1974). Enzootic and epizootic forms exist. Enzootic infections occur in partially immune rodent colonies where susceptible individuals are regularly introduced to perpetuate the infection. This can occur in breeding or open colonies. In breeding colonies, the susceptible population is the weaning age animals (3–6 weeks), due to their declining passive immunity (Parker and Reynolds 1968). Enzootic infections are usually subclinical. Epizootic infections occur in naive rodent colonies and either die out after 2–7 months or become enzootic if the proper conditions exist (Parker and Reynolds 1968; Parker et al. 1978). Clinical signs may be associated with epizootic infections in mice but have not been reported in rats. Such factors as strain susceptibility, age, husbandry, shipping, and copathogens are important in precipitating overt disease in mice (Jakab 1974; Jakab and Dick 1973; Parker et al. 1978; Ward 1974; Zurcher et al. 1977). Breeding colonies may exhibit neonatal or weanling mortality, prolonged gestation, fetal resorption, or runting in young mice (Bhatt and Jonas 1974; Iwai et al. 1979). Adult mice may exhibit anorexia, depression, ruffled fur, hunched posture, chattering, conjunctivitis, and photophobia.
Sendai virus is transmitted by aerosol and contact routes. Naso- and oropharyngeal secretions develop high infectivity titers during the 1st week. Fifty to seventy percent of mice will become infected after 24 h of contact with a transmitter mouse (van der Veen et al. 1970, 1972). Attack rates are lower for aerosol transmission unless multiple transmitters are present (van der Veen et al. 1974).
Athymic nude mice infected with Sendai virus are persistently infected. Most exhibit dramatic weight loss, depression, wrinkled skin, dyspnea, and cyanosis and usually die between 2 and 10 weeks later (Iwai et al. 1979; Ward et al. 1976).

Pathogenesis. Viral replication is restricted to the respiratory tract in natural infections, although a low-level transient viremia may occur. Peak titers are reached in 3–6 days and virus is usually not recoverable after 8–12 days (Appel et al. 1971; Parker et al. 1978; Robinson et al. 1968; Sawicki 1962; Stewart and Tucker 1978; van Nunen and van der Veen 1967). Adult mice eliminate virus earlier than suckling mice and develop lower peak titers (Sawicki 1961). Outbred mice eliminate virus earlier than inbred mice (Stewart and Tucker 1978). Seroconversion (hemagglutination inhibition, complement fixation) is usually detectable on days 7–9 (Appel et al. 1971; Robinson et al. 1968; Stewart and Tucker 1978; van Nunen and van der Veen 1967). Mice are usually leukopenic by the 7th day of infection; leukocytosis follows on days 8–11 (Robinson et al. 1968). Offspring of naturally infected dams rapidly acquire neutralizing and complement-fixing antibodies of the IgG_1 and IgG_2 subclasses with the onset of nursing. These titers plateau on days 7–14 and then rapidly decline (Iida et al. 1973).

Etiology. Sendai virus is a parainfluenza 1 virus of the genus *Paramyxovirus,* family Paramyxoviridae. It is a pleomorphic, enveloped virus measuring approximately 100–300 nm in length. The helical nucleocapsid contains a continuous single strand of RNA. The envelope is studded with two types of surface-projecting glycosylated polypeptides. The larger projection has hemagglutination and neuraminidase activity; the smaller projection has hemolysin and cell fusion activity. The virus rapidly inactivates at temperatures between 20° and 37 °C (Chanock et al. 1963).

Frequency. Sendai virus is ubiquitous in colonies of mice and rats. A survey of various institutional and commercial colonies, published in 1978, indicated that 66% of mouse colonies and 63% of rat colonies had experienced infections (Parker et al. 1978). Attack rates usually exceed 50% (Parker et al. 1964, 1978).

Comparison with Other Species

Parainfluenza viruses naturally infect humans, other primates, dogs, cattle, sheep, and birds in addition to rodents. All mammalian parainfluenza viruses replicate and cause disease primarily in the respiratory tract. They have a tropism for the epithelium of the conducting airways. Besides Sendai virus, histopathology is well described for parainfluenza 3 virus infection in calves (Dawson et al. 1965; Omar et al. 1966; Tsai and Thomson 1975). These lesions are similar to those caused by Sendai virus in rodents. Intranuclear inclusions are more prevalent and intracytoplasmic inclusions are more distinct in parainfluenza 3 virus infections.

References

Appel LH, Kovatch RM, Reddecliff JM, Gerone PJ (1971) Pathogenesis of Sendai virus infection in mice. Am J Vet Res 32: 1835–1841

Bhatt PN, Jonas AM (1974) An epizootic of Sendai infection with mortality in a barrier-maintained mouse colony. Am J Epidemiol 100: 222–229

Brownstein DG, Smith AL, Johnson EA (1981) Sendai virus infection in genetically resistant and susceptible mice. Am J Pathol 105: 156–163

Burek JD, Zurcher C, van Nunen MCJ, Hollander CF (1977) A naturally occurring epizootic caused by Sendai virus in breeding and aging rodent colonies. II. Infection in the rat. Lab Anim Sci 27: 963–971

Chanock RN, Parrott RH, Johnson KM, Kopikian AZ, Bell JA (1963) Myxoviruses: parainfluenza. Am J Respir Dis 88 (Suppl): 152–166

Choppin PW, Compans RW (1975) Reproduction of paramyxoviruses. Compr Virol 4: 95–178

Darlington RW, Portner A, Kingsbury DW (1970) Sendai virus replication: an ultrastructural comparison of productive and abortive infections in avian cells. J Gen Virol 9: 169–177

Dawson PS, Darbyshire JH, Lamont PH (1965) The inoculation of calves with parainfluenza 3 virus. Res Vet Sci 6: 108–113

Eustatia JM, Maase E, van Helden P, van der Veen J (1972) Viral replication in mouse macrophages. Arch Virusforsch 39: 376–380

Fujiwara K, Takenaka S, Shumiya S (1976) Carrier state of antibody and viruses in a mouse breeding colony persistently infected with Sendai and mouse hepatitis viruses. Lab Anim Sci 26: 153–159

Iida T, Tajima M, Murata Y (1973) Transmission of maternal antibodies to Sendai virus in mice and its significance in enzootic infection. J Gen Virol 18: 247–254

Iwai H, Goto Y, Ueda K (1979) Response of athymic nude mice to Sendai virus. Jpn J Exp Med 49: 123–130

Jacoby RO, Bhatt PN, Jonas AM (1979) Viral disease. In: Baker HJ, Lindsey JR, Weisbroth SH (eds) The laboratory rat, vol 1, Biology and diseases. Academic, New York, chap 11

Jakab GJ (1974) Effect of sequential inoculations of Sendai virus and *Pasteurella pneumotropica* in mice. J Am Vet Med Assoc 164: 723–728

Jakab GJ, Dick EC (1973) Synergistic effect in viral-bacterial infection: combined infection of the murine respiratory tract with Sendai virus and *Pasteurella pneumotropica.* Infect Immun 8: 762–768

Mims CA, Murphy FA (1973) Parainfluenza virus Sendai infection in macrophages, ependyma, choroid plexus, vascular endothelium and respiratory tract of mice. Am J Pathol 70: 315–328

Omar AR, Jennings AR, Betts AO (1966) The experimental disease produced in calves by the J-121 strain of parainfluenza virus type 3. Res Vet Sci 7: 379–388

Parker JC, Reynolds RK (1968) Natural history of Sendai virus infection in mice. Am J Epidemiol 88: 112–125

Parker JC, Richter CB (1982) Viral diseases of the respiratory system. In: Foster HL, Small JD, Fox JG (eds) The mouse in biomedical research, vol 2, Diseases. Academic, New York, chap 8

Parker JC, Tennant, RW, Ward TG, Rowe WP (1964) Enzootic Sendai virus infections in mouse breeder colonies within the United States. Science 146: 936–938

Parker JC, Whiteman MD, Richter CB (1978) Susceptibility of inbred and outbred mouse strains to Sendai virus and prevalence of infection in laboratory rodents. Infect Immun 19: 123–130

Reid WD, Ilett KF, Glick JM, Krishna G (1973) Metabolism and binding of aromatic hydrocarbons in the lung. Relationship to experimental bronchiolar necrosis. Am Rev Respir Dis 107: 539–551

Richter CB (1970) Application of infectious agents to the study of lung cancer: studies on the etiology and morphogenesis of metaplastic lung lesions in mice. USAEC Symposium Series 21: 365–382

Richter CB (1973) Experimental pathology of Sendai virus infection in mice. J Am Vet Med Assoc 163: 1204

Robinson TWE, Cureton RJR, Heath RB (1968) The pathogenesis of Sendai virus infection in the mouse lung. J Med Microbiol 1: 89–95
Sawicki L (1961) Influence of age of mice on the recovery from experimental Sendai virus infection. Nature 192: 1258–1259
Sawicki L (1962) Studies on experimental Sendai virus infection in laboratory mice. Acta Virol (Praha) 6: 347–351
Stephens RJ, Sloan MF, Evans MJ, Freeman G (1974) Early response of lung to low levels of ozone. Am J Pathol 74: 31–58
Stewart RB, Tucker MJ (1978) Infection of inbred strains of mice with Sendai virus. Can J Microbiol 24: 9–13
Tsai KS, Thomson RG (1975) Bovine parainfluenza type 3 virus infection: ultrastructural aspects of viral pathogenesis in the bovine respiratory tract. Infect Immun 11: 783–803
van Nunen MCJ, van der Veen J (1967) Experimental infection with Sendai virus in mice. Arch Virusforsch 22: 388–397
van der Veen J, Poort Y, Birchfield DJ (1970) Experimental transmission of Sendai virus infection in mice. Arch Virusforsch 31: 237–246
van der Veen J, Poort Y, Birchfield DJ (1972) Effect of relative humidity on experimental transmission of Sendai virus in mice. Proc Soc Exp Biol Med 140: 1437–1440
van der Veen J, Poort Y, Birchfield DJ (1974) Study of the possible persistence of Sendai virus in mice. Lab Anim Sci 24: 48–50
Ward JM (1974) Naturally occurring Sendai virus disease of mice. Lab Anim Sci 24: 938–942
Ward JM, Houchens DP, Collins MJ, Young DM, Reagan RL (1976) Naturally-occurring Sendai virus infection of athymic nude mice. Vet Pathol 13: 36–46
Zurcher C, Burek JD, van Nunen MCJ, Meihuizen SP (1977) A naturally occurring epizootic caused by Sendai virus in breeding and aging rodent colonies. I. Infection in the mouse. Lab Anim Sci 27: 955–962

Rat Coronavirus Infection, Lung, Rat

David G. Brownstein

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).