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Murine Respiratory Mycoplasmosis in F344 and LEW Rats: Evolution of Lesions and Lung Lymphoid Cell Populations

JERRY K. DAVIS, RANDALL B. THORP, PHILLIP A. MADDOX, MARY B. BROWN, AND GAIL H. CASSELL*

Departments of Microbiology and Comparative Medicine, Schools of Medicine and Dentistry, University of Alabama in Birmingham, Birmingham, Alabama 35294

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By comparison of two rat strains, LEW and F344, which are known to differ in susceptibility to *Mycoplasma pulmonis* respiratory disease, it was shown that differences in lesion severity and progression were associated with changes in lung lymphocyte populations. Lung lesions in LEW rats developed earlier after infection, became more severe, and were characterized by continued proliferation of all classes of lymphoid cells, T lymphocytes, B lymphocytes, and plasma cells, throughout the 120-day observation period. In contrast, lymphoid proliferation in F344 rats reached a plateau at 28 days and was restricted to an increase in T lymphocytes, immunoglobulin A (IgA)-bearing B lymphocytes, and IgA and IgG plasma cells. Although approximately 10 times as many IgG B cells and 4 times as many IgG plasma cells were found in infected LEW rats as compared with F344 rats, the specific anti-*M. pulmonis* IgG response in the two strains was roughly parallel. The same relationships held true, although to a lesser extent, for specific IgA antibody responses and cellular responses. Whereas lung lesions showed a tendency to resolve in F344 rats by 120 days, severe lesions persisted in LEW rats. The disparity between the cellular response and specific antibody response, the seemingly uncontrolled lymphocyte proliferation in LEW rats, and the mitogenic potential of *M. pulmonis* suggest that differences between LEW and F344 rats in lung lesion severity and progression are related to differences in the degree of nonspecific lymphocyte activation in the two strains, an imbalance in regulation of lymphocyte proliferation in LEW rats, or both.

Murine respiratory mycoplasmosis, due to *Mycoplasma pulmonis*, is a naturally occurring, slowly progressing, chronic disease in laboratory rats (28, 29). By 28 days postinfection, LEW rats develop quantitatively and qualitatively more severe lung lesions than do F344 rats (J. K. Davis, and G. H. Cassell, Vet. Pathol., in press). The increased severity of lung lesions in LEW rats appears to correlate with a greater amount of peribronchial and perivascular lymphoid tissue in these animals, although lymphoid hyperplasia is a prominent lesion in infected rats of both strains. This observation suggests that lymphocytes have a central function in the development of lung lesions.

The present studies were designed to compare the kinetics of lymphoid hyperplasia and parenchymal lung lesions in LEW and F344 rats, define the lymphocyte populations present at various times after infection, identify the classes of antibody produced, and correlate each of these parameters with severity and progression of disease. Antibody production to *M. pulmonis* was used as an indicator of immune recognition and degree of specific responsiveness. The results show that lung lymphocyte numbers and subpopulation distributions are related to development of lung lesions in both F344 and LEW rats and suggest that differences in lung lesion severity and progression are related to differences in degree of nonspecific lymphocyte activation in the two strains, an imbalance in regulation of lymphocyte proliferation in LEW rats, or both.

MATERIALS AND METHODS

Animals. Pathogen-free F344 rats were reared and maintained in Trexler plastic film isolators as previously described (28). Pathogen-free LEW rats, reared and maintained in a similar fashion, were obtained from the Trudeau Institute, Inc., Saranac Lake, N.Y. Intracage ammonia levels were monitored twice weekly, and the bedding was changed as necessary to maintain levels between 19 and 38 mg/liter (25 and 50 ppm) (4). At 2 months of age, F344 or LEW rats were sedated with a combination of fentanyl and droperidol (Innovar-Vet; Pittman Moore, Inc., Washington Crossing, N.J.) and intranasally inoculated with either 0.05 ml of sterile Hayflick broth or 9×10^8 colony-forming units of *M. pulmonis* (UAB 6510) in 0.05 ml of Hayflick broth (7). Control rats (those receiving sterile broth) were killed at 0, 60, or 120 days, and *M.*