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Expert Information

from the Working Group on Hygiene

Implication of infectious agents on results of animal experiments

Bordetella bronchiseptica

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Contents

Bordetella bronchiseptica

Background

- Etiological agent of respiratory tract infections in a wide range of mammals and birds, with zoonotic potential[1]

Prevalence

- *B. bronchiseptica* infection prevalence may vary from 0 to 100% depending on the species and population being tested; infections are generally higher in young animals, debilitated animals, and animals kept in close confinement.[1]
- Dogs, pigs and guinea pigs are frequently infected.[1]
- Commonly isolated from cats, rabbits and horses[1,2]
- Rarely isolated from other animals and humans[1]
- Less plausible reports of natural infections in laboratory rats and mice[1]

Host species

- Wide range of domestic and wild mammals and birds[1]
- Laboratory animals[3]; it is unclear whether rats and mice are natural hosts for *B. bronchiseptica.*[1,4]
- Amoebae may serve as potential environmental reservoirs, amplifying and disseminating vectors for *B. bronchiseptica.*[5]

Properties

- Survives on paper bedding in an animal room environment for at least 2 weeks[6]

Susceptibility

- Differential host susceptibility: pigs, dogs, and guinea pigs are most susceptible; rats, rabbits and horses have moderate susceptibility; chickens, mice, and humans are least susceptible[3,7,8]

Organotropism

- Respiratory tract

Clinical disease

- Many infected animals remain asymptomatic.[7]
- Clinical disease is most commonly associated with respiratory symptoms such as sneezing, oculonasal discharge, coughing, and dyspnoe; signs of systemic disease include pyrexia, anorexia, chorioretinitis, vomiting, and diarrhea.[3,8-10]
- Pig: atrophic rhinitis with resultant twisting or shortening of the snout; most severe disease in combination with toxigenic *Pasteurella multocida* infection[11,12]
- Dog: infectious tracheobronchitis (kennel cough)[3,9]
- Cat: variable clinical signs, from a mild disease form with fever, coughing, sneezing, ocular discharge and lymphadenopathy to severe pneumonia with dyspnea, cyanosis and death[13]

- Rabbit: snuffles; most infections become problematic only in association with *Pasteurella multocida* infection[14]
- Not conclusively demonstrated to be a natural pathogen of mice and rats; at most opportunistic pathogen that can affect physiological functions in rats[1,4]

Pathology

- Pig: rhinitis, atrophy of nasal turbinate bones, pneumonia[3,11,12]; ultrastructural changes in the turbinates are characterized by progressive degenerative changes in osteoblasts and osteocytes[15,16]
- Dog: rhinitis, sinusitis, tracheobronchitis, pneumonia[3,7]; bronchopneumonia with infiltration of neutrophils and macrophages into the bronchi and alveoli[17]
- Cat: tracheitis, suppurative bronchopneumonia, lymphadenitis[2,10]
- Rabbit: serous to purulent rhinitis, catarrhal to purulent bronchopneumonia, pleuritis, hyperplasia of lymphoid tissues[8,14,18,19]; severe heterophilic bronchopneumonia in immunodeficient rabbits in association with severe interstitial pneumonia caused by *Pneumocystis oryctolagi*[20]
- Guinea pig: serous to purulent otitis media, necrotizing tracheitis, suppurative necrotizing bronchopneumonia[8,21,22]
- Rat: acute to subacute bronchopneumonia, atrophic rhinitis[23,24]

Morbidity and mortality

- Variation in the pathogenicity of *B. bronchiseptica* isolates[1]
- Disease associated with *B. bronchiseptica* is frequently accompanied by infection with other agents
- In general, low mortality

Zoonotic potential

- Transmissible between species
- Airborne and contact transmission
- Infections in humans are often associated with an immunocompromised host[25-27]

Interference with research

Oncology

- No data

Teratology

- No data

Infectiology / Interactions with other infectious agents

- *B. bronchiseptica* colonization may increase the severity of canine parainfluenza-2 virus in dogs[28]
- *B. bronchiseptica* infection predisposes the nasal mucosa to colonization with *Pasteurella multocida* in pigs[29,30] and rabbits[8,14]
- Enhanced adherence of *P. multocida* to porcine tracheal rings pre-infected with *B. bronchiseptica*[31]

- *B. bronchiseptica* infection alters clearance and increases replication of swine influenza virus during co-infections in pigs[32]
- *B. bronchiseptica* antigen enhances the production of *Mycoplasma hyopneumoniae* antigen-specific immunoglobulin G in mice[33]
- Prior infection with *B. bronchiseptica* increases nasal colonization by *Haemophilus parasuis* in swine[34]

Immunology

- Alveolar macrophages from rabbits colonized with *B. bronchiseptica* exhibit ultrastructural and functional changes (alteration of metabolic activities upon stimulation, decreases in cell adherence, phagocytic uptake, and bactericidal activity)[35,36]
- Neutrophils are critical to the early defense against *B. bronchiseptica* infection[37]
- *B. bronchiseptica* induces primarily a Th1-type T-cell response[38]
- Serum concentrations of C-reactive protein are increased in dogs and monkeys infected with *B. bronchiseptica*[39,40]
- *B. bronchiseptica* dermonecrotizing toxin (DNT) suppresses antibody responses in mice[41]
- CD11b host cells receptor is required for the control of bacterial numbers and the regulation of cellular responses in the lungs of mice experimentally infected with *B. bronchiseptica*[42]
- The type III secretion system (TTSS) of *B. bronchiseptica* inhibits the generation of IFN-gamma-producing splenocytes[43] and leads to attenuated non-classical macrophage activation in experimentally infected mice[44]
- *B. bronchiseptica* infection leads to recruiting of lymphocytes and NK cells into the lungs of experimentally infected mice[45]
- *Bordetella* fimbriae like filamentous hemagglutinin (FHA) promotes *B. bronchiseptica* mediated suppression of lung inflammation and increase resistance to inflammatory cell-mediated clearance in a mouse model[46]

Toxicology

- No data

Physiology

- Lactic dehydrogenase activity and lactic acid and total protein concentrations were higher and alkaline phosphatase activity was lower in blood plasma of severely affected pigs early in *B. bronchiseptica* infection compared with controls[47]
- Neutral mucins are decreased in nasal mucosa of pigs infected with *B. bronchiseptica*[48]
- In dogs, *B. bronchiseptica* infection leads to bronchial hyper-responsiveness to histamine[49,50] and methacholine[51]
- In guinea pigs, infection leads to hyper-responsiveness to histamine in the nasal mucosa with increased vascular permeability and recruitment of nociceptive nerve-parasympathetic reflexes[52]

- *B. bronchiseptica* DNT impairs bone formation[53] and is necessary to produce the lesions of turbinate atrophy and bronchopneumonia in pigs infected with this organism.[54] The DNT appears to directly damage lung tissues, at least in mice.[55]

Cell biology

- Adherence of *B. bronchiseptica* to ciliated respiratory epithelial cells[56,57] and induction of ciliostasis[58]
- Evidence for binding of *B. bronchiseptica* to sialyl glycoconjugates on swine nasal mucosa[59] and to glycosylated receptors on dendritic cells[60]
- Internalization and persistence of *B. bronchiseptica* in dendritic, epithelial, and phagocytic cells[61-63]
- *B. bronchiseptica* exerts a cytotoxic effect on various human cell lines[64]
- In osteoblast-like MC3T3-E1 cells, *B. bronchiseptica* DNT induces a morphological change, inhibits elevation of alkaline phosphatase activity, reduces accumulation of type I collagen[65], stimulates DNA synthesis[66] and protein synthesis[67], induces membrane organelle proliferation and caveolae formation[68], and causes actin stress fiber formation and focal adhesions through the activation of the GTP-binding protein Rho[69]
- In Swiss 3T3 fibroblasts, *B. bronchiseptica* DNT induces p21rho-dependent tyrosine phosphorylation of focal adhesion kinase and paxillin[70]
- *B. bronchiseptica* flagellin is a pro-inflammatory determinant for airway epithelial cells[71]
- Ciliostasis is a key early event during colonization of canine tracheal tissue by *B. bronchiseptica*[72]
- *B. bronchiseptica* secretes BopB via a type III secretion system during infection. BopB may play a role in the formation of pores in the host plasma membrane which serve as a conduit for the translocation of effector proteins into host cells[73]
- *B. bronchiseptica* adheres to and survive intracellularly in swine alveolar macrophages[74]

Assisted reproductive technology

- No data

Special considerations

- An animal model for rhinogenic sinusitis was developed in rabbits naturally colonized with *B. bronchiseptica.*[75]
- Experimental models of rats infected with *B. bronchiseptica* were developed for coughing[76], atrophic rhinitis[24] or for the study of molecular aspects of *Bordetella* pathogenesis.[57,77]
- Mice have been extensively used as experimental models for *B. bronchiseptica* infections.[1]

Michael Mähler, Hannover, actualized by Laurentiu Benga, Düsseldorf, November 2019

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