

Pneumocystis carinii

Host species

- Laboratory animals (Smulian & Walzer 1992)
- Wide range of domestic animals, monkeys, humans

Organotropism

- Lungs
- Occasionally other organs or generalization to eyes, skin etc.

Clinical disease

- Inapparent in immunocompetent host
- Slowly progressive chronic pneumonia with weight loss in immunocompromised host

Morbidity and mortality

- Con conventionally bred colonies may be persistently infected because of subclinical nature in immunocompetent hosts (Frenkel et al. 1966).
- High morbidity and mortality with chronic progressive pneumonia in immunosuppressed animals

Zoonotic relevance

- *Pneumocystis (P.) carinii* is not universally transmissible between mammalian species (Gigliotti et al. 1993).
- Respiratory mode of transmission (Hughes 1982)
- Most common opportunistic infection and leading cause of morbidity and mortality in AIDS patients

Interference with research

Physiology

- *P. carinii* pneumonia leads to alterations in compliance and lung mechanisms (Brun-Pascaud et al. 1985, Stokes et al. 1986).

- *P. carinii* may alter the amount and type of surfactant produced: *P. carinii* pneumonia in rats leads to a decrease in surfactant phospholipids in bronchoalveolar lavage (Kernbaum et al. 1983, Sheehan et al. 1986). *P. carinii* organisms can directly inhibit secretion of phosphatidylcholin from type II cells (Rice et al. 1993). Broncho-alveolar lavage phosphatidylglycerol is reduced in rats with *P. carinii* pneumonia (Su et al. 1996). Surfactant protein-A levels increase during *P. carinii* pneumonia in the rat (Phelps et al. 1996).
- Attachment of *P. carinii* to alveolar macrophages occurs by a fibronectin- and calcium dependent mechanism, but does not trigger a phagocytic response (Pottratz & Martin 1990a, 1990b). *P. carinii* glycoprotein A binds macrophage mannose receptors, thereby mediating binding and uptake of *P. carinii* by alveolar macrophages (Ezekowitz et al. 1992, O'Riordan et al. 1995). Surfactant protein A can function as a ligand between *P. carinii* and alveolar macrophages (Williams et al. 1996).
- Attachment of *P. carinii* to type I pneumocytes leads to their degeneration and to proliferation of type II pneumocytes.
- Following attachment of *P. carinii* to type I cells, surface glycocalyx is decreased and alveolar-capillary permeability is increased (Lanken et al. 1980, Yoneda & Walzer 1980, 1981, 1984). As a consequence of dysplasia and disruption of the epithelium, underlying material gains access to the alveolar space and impairs normal lung function.
- *P. carinii* attachment increases expression of fibronectin-binding integrins on cultured lung cells (Pottratz et al. 1994).
- *P. carinii* and IFN-g induce rat alveolar macrophages to produce nitric oxide (Sherman et al. 1992).
- The mitochondrial ATPase 6 gene is upregulated in *P. carinii*-infected rat lungs (Asnicar et al. 1996).
- *P. carinii* infection alters GTP-binding proteins in the lung (Oz & Hughes 1997).
- *P. carinii* inhibits cyclin-dependent kinase activity in lung epithelial cells (Limper et al. 1998).
- Fibrinogen expression is induced in the lung epithelium during *P. carinii* pneumonia (Simpson-Haidaris et al. 1998).

Pathology

- Slight infection: multifocal alveolar aggregates of cysts and interstitial/perivascular non-purulent infiltration (Walzer et al. 1980, Chen et al. 1990)
- Severe infection: consolidated lungs; extensive lung areas involved with alveolar aggregates of cysts (eosinophilic, honeycombed material), proliferation of type II pneumocytes and severe interstitial fibrosis
- Extrapulmonary manifestation of *P. carinii* infection by hematogenous or lymphatic spread is possible; major sites are lymph nodes, bone marrow, liver, and spleen, characterized by eosinophilic honeycombed material with inflammatory response.
- Multinucleated giant cells in murine *P. carinii* pneumonia (Hanano et al. 1996)

Immunology

- High risk for all congenitally immunodeficient hosts and for experimental models of immunosuppression.
- *P. carinii* from different host species are immunologically distinct (Gigliotti & Harmsen 1997).
- *P. carinii* induces activating and inhibitory innate cellular immune response mechanisms (Warschkau et al. 1998).

- Cellular immunity is important for protection against *P. carinii* pneumonia (Furuta et al. 1984, 1985).
- *P. carinii*-reactive CD4+ lymphocytes may contribute to the host's response via secretion of macrophage-activating cytokines (IFN-g and others) as well as by the production of signals that induce foster expansion of the antibody-forming pool of B cells and cytotoxic CD8+ lymphocytes (Beck et al. 1993).
- Protective immunity against *P. carinii* is mediated by CD4+ T cells (reviewed by Hanano & Kaufmann 1998).
- Neutrophils, alveolar type II epithelial cells, B cells, CD8+ lymphocytes, antibodies and cytokines, such as IFN-g and TNF, participate in host effector mechanisms against *P. carinii* (Masur & Jones 1978, Von Behren & Pesanti 1978, Shear et al. 1989, Pesanti 1989, 1991, Chen et al. 1992, Beck et al. 1996, Garvy et al. 1997, Kolls et al. 1997 Marcotte et al. 1996).
- *P. carinii* induces TNF- α production from monocyte and macrophage cultures with a peak within 8 h of incubation (Tamburrini et al. 1991).
- *P. carinii* glycoprotein A stimulates IL-8 production and inflammatory cell activation in alveolar macrophages and cultured monocytes (Lipschik et al. 1996).
- *P. carinii* induces expression of ICAM-1 and IL-6 in lung epithelial cells (Yu & Limper 1997 Pottratz et al. 1998).

Infectiology

- Neutrophils in bacterial pneumonia may participate in host effector mechanisms against *P. carinii* (Pesanti 1982).

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