PNEUMOCYSTIS

Animal Group(s) Affected	Transmission	Clinical Signs	Severity	Treatment	Prevention and Control	Zoonotic
Humans, non-human primates, and numerous mammalian species, especially immune-compromised individuals.	Aerosol transmission, environmental exposure, or direct contact with infected individuals.	Dyspnea, dry cough, cyanosis, pyrexia, weight loss.	Can be fatal in immuno-compromised individuals.	Trimethoprim -sulfa methoxazole (TMP-SMX) is the drug of choice.	Prophylactic treatment with TMP-SMX.	No as human strain is believed to be host-specific.

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Susceptible animal groups: Humans, primates and numerous mammalian species. The organism is presumed to be ubiquitous in the environment. Serological evidence shows that most healthy children have had exposure to the organism by 4 years of age. Studies screening numerous zoological, wildlife and laboratory mammalian species have also shown a high prevalence of exposure to the organism. The organism proliferates in the lungs of host species with compromised immune systems. Studies have found an absence of the organism in animals with body temperatures below 35^{o}C and above 41^{o}C. Studies conducted in birds, reptiles, amphibians and fish have not identified the organism.

Causative organism: Human derived: *Pneumocystis jirovecii* (formally known as *P. carinii*). Multiple other mammalian host-specific species exist. For example, *P. carinii* in the rat and *P. murina* in the mouse. The organism was previously thought to be a protozoan, but in 1988, through DNA analysis, it was determined to be a yeast-like fungus. It is unusual when compared to other fungi in that the cell membrane lacks ergosterol and currently is unable to be grown in culture. Genomic and phenotypic differences exist between the organisms that infect different mammalian species indicating that the organisms are host-species specific.

Zoonotic potential: *Pneumocystis* organisms infecting each mammalian species are host specific. No animal reservoir for *P. jiroveci* has been identified and no animal strains have been identified as human pathogens.

Distribution: Worldwide in humans and animals.

Incubation period: 3 to 12 weeks; but unclear if this includes carriage time in healthy individuals as compared to immunocompromised hosts.

Clinical signs: Immunocompetent individuals are most often asymptomatic. Immunodeficient individuals develop *Pneumocystis* pneumonia (PcP), a chronic progressive pneumonia. The most common clinical signs include dyspnea, an unproductive cough, cyanosis, pyrexia, and weight loss. Severe cases can lead to respiratory failure and death. Extrapulmonary lesions occur in a minority (<3%) of patients, involving most frequently the lymph nodes, spleen, liver, and bone marrow. The organisms reside in the alveoli and stimulate both a humoral and cellular immune response. The host's inflammatory response leads to alveolar damage, impaired gas exchange and decreased respiratory function which results in the common clinical signs of this disease.

Post mortem, gross, or histologic findings: Lungs show evidence of interstitial pneumonia. Grossly, the lungs will be edematous and heavy. They will have a pale gray or tan granular, firm, consolidated cut surface.

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Histological examination of lung tissue often reveals a foamy eosinophilic exudate within the alveolar spaces and interstital fibrosis of the alveolar septa. Basophilic dots within the exudate represent the *Pneumocystis* cysts. With special stains, the cysts can be identified as ovoid bodies. Additional stains can also be used to identify isolated trophozoites. The organism can be specifically identified using immunohistochemistry, immunofluorescense and PCR assay. Studies have also identified the organism in a large percentage of asymptomatic infants on post-mortem.

Diagnosis: Specific diagnosis is by the recovery and identification of the organism in samples obtained through trans-tracheal aspirate (TTA), bronchoalveolar lavage (BAL), induced sputum or lung tissue obtained through biopsy or necropsy. Identification of the organism via PCR assay, immunohistochemistry, immunofluorescence, or special stains that stain the cyst wall of the organism (Gomori's methanamine silver (GMS), toluidine blue O) or those that stain the nuclei of the trophozoites and sporozoites (Geimsa, Wright, Diff-Quick, polychrome methylene blue, and Gram's stain).

Material required for laboratory analysis: Bronchopulmonary secretions obtained via TTA, BAL or induced sputum. Lung tissue obtained via biopsy or necropsy.

Relevant diagnostic laboratories: Laboratories with the capability to perform nested PCR assay are used to identify the organism. Immunohistochemical methods require the host species-specific monoclonal antibody used to identify the organism to avoid false negative results. Identification of the organism using special stains requires reviewer expertise.

Treatment: Since the organism lacks ergosterol, common anti-fungal treatments are not effective. Trimethoprim-sulfamethoxazole (TMP-SMX) is the drug of choice for both the treatment of infection and prophylaxis. Alternative drugs used for the treatment of infection include pentamidine, trimethoprim plus dapsone, atovaquone and primaquine plus clindamycin. Alternative drugs used for prophylaxis include dapsone, dapsone plus pyrimethamine, pentamidine and atovaquone. Recurrence is common if the immunosuppressive condition of the host persists.

Prevention and control: Avoidance of the organism is impractical since the natural reservoir is unknown and the organism is presumed to be ubiquitous in the environment. TMP-SMX or other chemoprophylaxis can be used as a preventative treatment in susceptible individuals.

Suggested disinfectant for housing facilities: A study found the following chemical disinfectants to be effective in the inactivation of *Pneumosytis* cysts: 70% ethyl alcohol, 10% iodoform, 1% quaternary ammonium salts, 3% hydrogen peroxide, sodium chlorite and 1% cresol soap.

Notification: None

Measures required under the Animal Disease Surveillance Plan: None

Measures required for introducing animals to infected animal: Prevent exposure of healthy animals to animals exhibiting clinical signs of pneumocytosis.

Conditions for restoring disease-free status after an outbreak: This approach may not be possible since a large percentage of humans and other mammalian species harbor this organism while remaining asymptomatic. Testing can be used to screen individuals for the presence of the organism. Serological screening is not effective since a large percentage of humans and other mammalian species are shown to have had exposure to the organism. Sterilization of any air filters in the area of the outbreak is an important measure to reduce the number of cysts in the environment. Disinfecting the area of the outbreak with appropriate disinfectants will help to inactivate any remaining cysts.

Experts who may be consulted:

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References:

1. http://dpd.cdc.gov/dpdx/HTML/pneumocystis.htm Accessed 16 September 2013.
2. Armstrong, M.Y.K., and M.T. Cushion. 1994. Animal models. *In*: Walzer, P.D. (ed.) *Pneumocystis carinii* Pneumonia, 2nd ed. Marcel Dekker, Inc. New York, New York. Pp. 181-203.
3. Cailliex, J.C, N. Seguy, C.M. Denis, E.M. Aliouat, E. Mazars, L. Polonelli, D. Camus, and E. Dei-Cas. 1996. *Pneumocystis carinii*: an atypical fungal micro-organism. J. Med. Vet. Mycol. 34(4): 227-239.
4. Dei-Cas, E., M. Brun-Pascaud, V. Bille-Hansen, A. Allaert, and E.M. Aliouat. 1998. Animal models of pneumocystosis. FEMS Immunol. Med. Microbiol. 22(1-2): 163-168.
5. Demanche, C., M. Berthelemy, T. Petit, B. Polack, A.E. Wakefield, E. Dei-Cas, and J. Guillot. 2001. Phylogeny of *Pneumocystis carinii* from 18 primate species confirms host specificity and suggests coevolution. J. Clin. Microbiol. 39(6): 2126-2133.
6. Edman, J.C., J.A. Kovacs, H. Masur, D.V. Santi, H.J. Elwood, and M.L. Sogin. 1988. Ribosomal RNA sequence shows *Pneumocystis carinii* to be a member of the fungi. Nature. 334(6182): 519-522.
7. Haque A.K., and P.A. Adegboyega. 2008. *Pneumocystis jiroveci* pneumonia. *In*: Tomashefski, J.F. (ed.). Dail and Hammar's Pulmonary Pathology: Volume I: Nonneoplastic lung disease. 3rd ed. Springer, New York, New York. Pp. 487-514.
8. Joffrion, T.M., and M.T. Cushion. 2010. Sterol biosynthesis and sterol uptake in the fungal pathogen *Pneumocystis carinii*. FEMS Microbiol. Lett. 311(1): 1-9.
9. Kaneshiro, E.S., and J.N. Maiorano. 1996. Survival and infectivity of *Pneumocystis carinii* outside the mammalian host. J. Eukaryot. Microbiol. 43(5): 35S.
10. Kuramochi, T., K. Hioki, and M. Ito. 1997. *Pneumocystis carinii* cysts are susceptible to inactivation by chemical disinfectants. Exp. Anim. 46 (3): 241-245.
11. Laakkonen, J. 1998. *Pneumocystis carinii* in wildlife. Int. J. Parasitol. 28(2): 241-252.
12. Poelma, F.G. 1975. *Pneumocystis carinii* infections in zoo animals. Z. Parasitenkd. 46: 61–68.
13. Ponce, C. A., M. Gallo, R. Bustamante, and S.L. Vargas. 2010. *Pneumocystis* colonization is highly prevalent in the autopsied lungs of the general population. Clin. Infect. Dis. 50(3): 347-353.
14. Sakura, A., A.K. Jarvnen, M. Olsson, M. Karkkainen, and T. Ilvesniemi. 1996. *Pneumocystis carinii* pneumonia in dogs- a diagnostic challenge. J. Vet. Diagn. Invest. 8(1): 124-130.
15. Settnes, O.P., P.B. Nielsen, R. Bucala, M.J. Linke, and M.T. Cushion. 1994. A survey of birds in Denmark for the presence of *Pneumocystis carinii*. Avian Dis. 38(1): 1-10.
16. Stringer, J.R., Beard, C.B., Miller, R.F. and Wakefield, A.E. 2002. A new name for *Pneumocystis*

from humans and new perspectives on the host-pathogen relationship. Emerg. Infect. Dis. 8(9): 891-896.