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Letter to the Editor

Terminology Changes Needed for Descriptions of *Pneumocystis carinii* Infection

Historically, descriptions of *Pneumocystis carinii* pneumonitis have presumed a protozoan parasite etiology, rather than the fungal etiology indicated by the microscopic and molecular biological evidence. The recent article entitled "T- and B-Lymphocyte-Independent Formation of Alveolar Macrophage-Derived Multinucleated Giant Cells in Murine *Pneumocystis carinii* Pneumonia" by Hanano et al. (6) perpetuates this erroneous classification by casually referring to *P. carinii* as a parasite with intracystic bodies and trophozoites and using the term infestation (commonly reserved for parasites). In its broadest sense, parasite denotes a plant or animal that lives in or on another living organism and obtains some advantage from this association (3). Thus, *P. carinii* could be called a parasite, but using this term in conjunction with trophozoite, intracystic bodies, and infestation implies classification of *P. carinii* as a protozoan parasite. The inappropriateness of applying the term nuclei to *P. carinii* has already received comment (1).

P. carinii continues to resist culture in artificial media, and some genera of fungi are difficult to differentiate from protozoan parasites in tissues sections (5). Chronic and active but minimal inflammation, absence of an eosinophilic infiltrate, one or more life forms, a yeast-like stage, association of organisms with reactive macrophages and multinucleated giant cells, requirement for special histochemical stains to visualize the organism in tissues sections, and the ultrastructural features of *P. carinii* are characteristics found more often with fungal infections than with a protozoan infestation. Demonstration of DNA homology of *P. carinii* with ustomycetous red yeast fungi (4, 8) has provided important, if not definitive, evidence for reclassifying *P. carinii* infection as a mycotic infection. Although some references continue to tentatively classify *P. carinii* with protozoans and indicate the possibility of a fungal or uncertain status (3, 5), the weight of evidence is with those who have embraced *P. carinii* within the fungal kingdom (7). In keeping with this taxonomic reclassification, the tissue forms of *P. carinii* should not be referred to by using parasitic terms such as sporozoite, trophozoite, cyst, or intracystic bodies (2).

We propose that the biomedical community should adopt terminology for *P. carinii* that is more applicable to other nonhyphal fungi. Presumably, the thick-walled body (formerly, the cyst) typically identified in tissue sections by silver stains should be referred to as the ascus (sometimes referred to as a sporangium, or spore case). The asci contain eight spores or endospores (formerly the intracystic bodies or sporozoites), which are then released to become yeast cells (formerly, trophozoites). Environmental conditions will determine if the spores immediately germinate into yeast cells (typically stained in tissue by Giemsa stain) or enter an ex vivo dormant phase typical of spores (not yet demonstrated for *P. carinii*).

Although details of the life cycle and mode of transmission of *P. carinii* are uncertain, adoption of a more generic terminology applicable to fungi seems reasonable. This change in terminology will enhance communication between investigators who are immersed in the pneumocystosis field and the uninitiated who sporadically encounter *P. carinii*. Only continued confusion can be expected if authors and journals perpetuate, intentionally or inadvertently, terminology that suggests *P. carinii* is a parasite rather than a fungus-like organism.

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Authors' Reply

In their letter, Schuh et al. emphasize the fact that *Pneumocystis carinii* is a fungus rather than a protozoan. We are fully aware of the fungal affiliation of *P. carinii*, as genetic studies cited by Schuh et al. have demonstrated. We admit to have been tangled in the maelstrom of commonly applied terminology and in this sense rather welcome efforts undertaken to address different developmental stages of this peculiar organism appropriately. Accordingly, we are in favor of changing the terms "trophozoites" and "intracystic bodies/sporozoites" to "yeast cells" and "(endo)spores," respectively. However, substitution of the term "cyst" for "ascus" should be treated with caution. In the fungal kingdom the ascus is not merely any spore case but a specialized form of such a structure typically exhibited by the fungal class *Ascomycetes*, the generation of which is strictly associated with sexual reproduction. Within the ascus, the karyogamy of gametes occurs, followed by meiosis and endogenous formation of haploid meiospores (contrasting exogenous generation of exospores or conidiospores). To our knowledge, there are no reports of definitive sexual reproductive processes in *P. carinii*, even though it was implicated by the suggested finding of synaptonemal complexes in a proposed "early precyst" developmental stage (1). It was further hypothesized that asexual cyst cycles also take place in the life span of the fungus (1). If this were so, terming the cyst an

ascus is, strictly speaking, incorrect. To our knowledge, *P. carinii* has not been definitely allocated a place within the class *Ascomycetes*, yet. Currently, it is believed to fit somewhere between ascomycetes and basidiomycetes (3). Until these questions are settled unambiguously, including the identification of gametes, we would propose the rather general term term "sporangium" more appropriate to describe the cyst.

Certainly, like all living cells, *P. carinii* also has nuclei. There are various ultrastructural studies in the literature showing exactly that. The authors may want to reread the letter by Beals that they have cited. Correctly, Beals reasoned the terming of "dark dots" on cysts (sporangia) that have been silver stained as nuclei to be inappropriate. By using other staining techniques such as Giemsa, nuclei of trophozoites (yeast cells) as well as cysts (sporangia) with intracystic bodies (spores) can be visualized very well, as stated just a few lines further down in his report.

The definition of a parasite as cited by Schuh et al. does not seem reasonable. Whether or not an organism can be denoted as a parasite depends solely on its life style, which is by no means restricted to plants and animals. A parasite is an organism that lives on or in another organism and draws its nourishment therefrom (2). Apart from plants and animals, there are definite parasitic representatives of bacteria and fungi. It seems extraordinarily surprising that a medical dictionary would not consider pathologically important organisms such as fungi as parasites. Surely, a fungus such as *Trichophyton rubrum*, which causes athelete's foot, must essentially be recognized as being parasitic. Other important parasitic fungi infest plants, the most famous of which is *Phytophthora infestans* (potato blight), which caused a devastating famine in Ireland in the last century. *P. carinii* exhibits profound parasitic properties by invading the pulmonary compartment of immunocompromised individuals. In this sense, the term "infestation" in association with this organism is justifiable. Incidentally, Dorland Illustrated Medical Dictionary, cited by Schuh et al., very well includes fungi as parasites (27th ed., parasite > plant parasite); however, fungi were probably erroneously classified as members of the plant kingdom ("vegetable kingdom," according to this dictionary).

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