Letter in response to the article: "*Nannizzia incurvata* as a rare cause of favus and tinea corporis in Cambodia and Vietnam"

Sir,

We read with great interest the recently published work entitled "*Nannizzia incurvata* as a rare cause of favus and tinea corporis in Cambodia and Vietnam" by Uhrlaß *et al*.[1] The authors describe, for the first time, the isolation of *Nannizzia incurvata* from humans in Cambodia and the description of favus in a child due to this dermatophyte. In this article, the authors have identified *N. incurvata* from a 6-year-old Cambodian boy presenting with symptoms of the favus-like tinea capitis and tinea faciei. Diagnosis was performed using culture and DNA sequencing. The authors performed an excellent clinical investigation; however, we are concerned about epidemiological aspects and would like to discuss some points that would benefit the readers of your esteemed journal.

The authors reported that the patient had previous contact with animals (i.e., chicken, dogs, and cattle). However, we feel that these interactions were not described in detail. In our opinion, it is relevant to elucidate the transmission mechanism of this new dermatophyte species. Did the animals have access to the household? Any animals with clinical signs? Although the genus *Nannizzia* has been assigned as geophilic and humans infections are commonly associated with contaminated soil, it is important to emphasize that animals may play an important role in the persistence and dissemination of these fungi. A study carried out in Tunisia investigated 141 soil samples for the presence of keratinophilic fungi. The authors found that 69% of keratinophilic fungi were isolated from soils where animals were present.[2] The authors also mentioned that residual animal fur and skin debris could act as soil enricher by providing organic matter for keratinophilic fungi. It is noteworthy that infected materials can maintain viable fungi for years, and therefore the presence of animals can significantly contribute to fungal shedding and persistence in the environment.

In another recent study, Dukik *et al.* evaluated the molecular and phenotypic aspects of *Nannizzia* spp. The authors speculated on the direct association between geophilic members of the genus *Nannizzia* and animal hosts.[3] The authors mentioned that animals might act as carriers, contributing to the maintenance and shedding of these fungi to the environment and humans. As a matter of fact, the direct association between geophilic species and animals has already been demonstrated. Bonifaz *et al*. identified *N. nana* in a man that had worked in a pig farm in Mexico, whereas Soankasina *et al.* demonstrated the epidemiological role of cats in the transmission of *N. gypsea* to humans in an African island.[4,5] Thus, the ecological classification of the genus *Nannizzia* remains unclear, since species classified as geophilic may be associated with animals. Recent phylogenetic analyses suggested that *Nannizzia* spp. are derived from an ancestry located between *Trichophyton* spp. and *Microsporum* spp. (a largely zoophilic genus).[3]

We would also like to discuss the fact that the TEF-1 α gene sequence used by the authors was, in theory, erroneously associated with *N. gypsea*. A BLAST search using the same database (NCBI) and accession (KM678069) the authors used as query matched to three *N. incurvata* strains. Two of which were >99% similar (MT497551 and MH512804), but one that was only 96% similar (MH706756). This was significantly higher than the percent identity to other *N. gypsea* strains (90.3%, KM678161 and KM678057). Finally, accessions associated with *N. duboisii* (KM678089) and *N. fulva* (KM678079) were 93% and 91% similar to the query sequence. While it is not our goal here to question the recent taxonomic changes related to these species, it does raise concerns to the use of this gene for speciation.

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Considering that animals may represent a potential source of infection for humans through direct contact or shedding in the environment, we would like to suggest to the medical mycology community to pay special attention to the involvement of animals in this topic. In fact, it seems that the human-animal interface may significantly contribute to recurrent infections, which is one of the leading causes of treatment failure.

To conclude, we would like to congratulate Uhrlaß *et al.* for their work. [1] This is a step further towards better understanding the clinical aspects and therapeutic challenges of *N. incurvata*, a pathogen with potential to emerge as a threat to in human, pets and livestock. In our perspective, the findings by Uhrlaß *et al*. turn the spotlight on the importance of this new fungal species, possibly leading to the identification of new cases in other countries. Finally, we hope that our discussion may add relevant information regarding the epidemiological aspects of animals as carriers and disseminators of *Nannizzia* spp.

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Conflicts of interest
There are no conflicts of interest.

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Authors' Reply

Sir,

We are grateful to Dr. Aline Elisa Santana from Brazil who responded to our article on the occurrence of the rare geophilic dermatophyte *Nannizzia incurvata* in Southeast Asia[1,2]. *N. incurvata* belongs to the so-called *Nannizzia gypsea* (formerly *Microsporum gypseum*) complex. In addition to *N. gypsea*, one also counts *Nannizzia fulva* (formerly *Microsporum fulvum*) and *N. incurvata* described here. *N. gypsea* is perhaps the most prominent representative within the geophilic dermatophyte species. In a typical way, *N. gypsea* causes infection of the skin on the hands and arms, for example, in gardeners who have direct contact with the earth and the dust. Animals do not play a role in *N. gypsea* dermatophytoses. *N. gypsea* and also *N. incurvata* are *per se* not among the zoophilic dermatophytes. Of course, however, it is conceivable that especially in the rural environment at the village, ground living fur animals are surely capable of carrying spores or mycelia of primarily geophilic dermatophytes, thus also of *N. incurvata*. They may then also be indirect carriers for transmission of infections due to *N. incurvata* or *N. gypsea* to humans. However, data on this are not available. The boy we described in Cambodia with tinea capitis favosa and tinea faciei lives in a rural region and is surrounded by various animals in his village and in his parents' house and farm. That is why, such an indirect transmission path from *N. incurvata* from the ground through the fur of animals (dogs, cats and rodents) would be conceivable and theoretically possible. There is no proof of this, however; it is purely speculative.

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