Cat-associated zoonotic conditions

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Keywords: bacteria, cat, claw, dermatophyte, feline, felis, flea, fungi, helminith, mite, parasite, protozoa, punctatis, puncture, sporothrix, sporotrichosis, tick, unicellular, virus, zoonotic

To the Editor:
I read with interest the excellent report by Heckens et al. [1] and appreciated the author's accompanying accurate and alluring alliteration in the paper's title.

A 45-year-old woman from the Netherlands developed cat-transmitted cutaneous sporotrichosis on her right upper thigh, caused by *Sporothix brasiliensis*, one week after returning from a one-month visit to Brazil. During her stay in Brazil, she had been in close contact with street cats; indeed, she had held one of the cats—with skin lesions on its nose region—on her lap while it was being taken to a veterinarian. The fungal culture from not only the ulcerated, pus-draining carbuncle on her thigh, but also from the affected nasal area on the cat both grew *S. brasiliensis* [1].

Cats have been associated with the development of zoonotic conditions in humans. These include not only fungal infections, such as sporotrichosis, but also conditions caused by bacteria, dermatophytes, fungi, helminiths, fleas, mites, mycobacteria, ticks, unicellular parasites, and viruses (**Table 1**), [1-29]. Indeed, cow pox and leishmaniasis are recently-observed cat-transmitted diseases to humans [2,9,10,27].

In addition, cat-related non-infectious cutaneous lesions have also been observed. Felis punctatis refers to groups of individual red punctures secondary to repeated minor skin trauma during the act of kneading; this is the rhythmic and repetitive activity in which there is insertion and withdrawal of extended claws as the cat pushes its paws in and out of a soft object [30]. Even this affectionate action has been postulated to be associated with the zoonotic spread of feline-transmitted lymphocutaneous sporotrichosis [19].

Sporothrix is a temperature-dependent dimorphic fungus; it occurs as pathogenic yeasts in host organisms, or at 37 degrees Celsius, and as septate hyphae in the environment, or in vitro at 25 degrees Celsius [20,21]. Four species of *Sporothrix* cause most of the infections in human and animals: *S. schenckii* (more recently referred to as *S. schenckii sensu stricto* or *S. schenckii species complex*), *S. brasiliensis*, *S. globose*, and *S. luriei* [20-23]. *S schenckii* has been observed world-wide whereas *S. brasiliensis* is more common in South America (such as in Argentina and Brazil) and *S. globose* is more frequent in East Asia [20-26].

Humans most commonly acquire sporotrichosis as the result of a traumatic inoculation. The source of the fungal spores can be a contaminated organic material (such as soil or the thorn of a plant) or a fomite (such as debris). A scratch from a cat or another infected animal can also result in zoonotic transmission of the infection. Less often, a primarily pulmonary sporotrichosis infection can result from inhalation of the fungal spores [1,12,19-29].

The classification of sporotrichosis is predominantly based on the clinical manifestations of the infection.

Earlier classifications had four forms of the infection: cutaneous, lymphocutaneous, mucosal, extracutaneous, and disseminated. More recently, the disease classification has been modified into four different types: 1) skin which includes fixed cutaneous, lymphocutaneous, and multiple inoculations; 2) mucous membrane which includes nasal, ocular, and other mucosal sites; 3) systemic which includes disseminated cutaneous, neurological, osteoarticular, pulmonary, other locations, and septic; and 4) immunoreactive which includes conditions that do not contain fungi such as acute febrile neutrophilic dermatosis (Sweet syndrome), erythema multiforme, erythema nodosum, and reactive arthritis [21,23].

Lymphocutaneous sporotrichosis is the most common presentation of the fungal infection, similar to the 41-year-old woman from California with kneading-associated cat-related transmission of the infection that initially appeared as a single painless red papule on her left chest wall that subsequently was followed by additional erythematous papules in the same region that eventually ulcerated during a period of three weeks [19]. In contrast, although lymphocutaneous sporotrichosis can occur in immunocompromised patients, systemic sporotrichosis more commonly is observed in those individuals; common reasons for immunosuppression in sporotrichosis patients include anti-tumor necrosis factor treatment, chronic alcoholism, corticosteroid therapy, diabetes mellitus, hematologic malignancies, and human immunodeficiency virus infection [27]. Both *S. schenckii* and *S. brasiliensis* have been the causative organism in renal transplant patients [28,29].

Factors that influence the treatment of sporotrichosis include the species of sporotrichosis, the immunological status of the host, and the clinical type of disease. The first-line treatment of choice is itraconazole: 100mg to 200mg per day for cutaneous disease and 400mg per day for pulmonary or systemic disease. Alternative treatments include potassium iodide and terbinafine; immunosuppressed patients with either cutaneous or systemic sporotrichosis may initially require intravenous amphotericin B prior to converting to oral itraconazole. Prolonged treatment, at least four to six weeks after remission, is usually necessary to minimize the chance of relapse [1,23].

Coronavirus disease-19 (COVID-19) positive cats have been reported in four continents: Asia, Europe, North America, and South America [31-35]. It has also been demonstrated the airborne transmission of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) can occur following prolonged contact of experimentally infected cats with a previously non-infected cat [33,36]. Therefore, earlier investigators postulated the possibility of cats as animal vectors in the zoonotic transmission of COVID-19 to humans [35].

To date, at least 68 COVID-19 cats have been found to be positive for SARS-CoV-2. However, prior to infection, many of these felines had previously been exposed to humans with COVID-19. Thus, current researchers favor reverse zoonotic transmission of SARS-CoV-2 from infected humans-to-animals as the etiology of COVID-19 in the cats [31-33].

In conclusion, cat-associated zoonotic conditions can result from various pathogens. In Brazil, where Henckens et al.'s [1] patient had visited, *S. brasiliensis* is endemic in the cat population and frequently transmitted to humans as a zoonotic infection. In contrast to several virus infections in humans that have been demonstrated to occur following cat-to-human transmission the observation of SARS-CoV-2 in cats appears to be caused by reverse zoonotic transmission from humans-to-cats.

Acknowledgement:
I would like to acknowledge Douglas S. Ramsay, DMD PhD MSD for his input on this article. I also sincerely appreciate his contribution to the article we coauthored describing cat claw-induced punctures: felis punctatis.

Potential conflicts of interest

The author is a paid consultant for ParaPRO; however, this activity has no influence as a potential conflict of interest regarding the manuscript.

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Table 1. *Cat-associated zoonotic conditions: causative organism.*

Organism	Ba	De	Fu	He	My	Pe	Pu	Vi	References
Avian influenza								X	[2]
Bacteroides sp.	X								[3-6]
Bartonella henselae[a]	X								[2,7]
Bordetella bronchiseptica	X								[3-6]
Brucella abortus	X								[2]
Campylobacter jejuni	X								[2]
Capnocytophaga canimorsus	X								[3-6]
Cestodes[b]				X					[2]
Coxiella	X								[2]
Cryptosporidium sp.							X		[2-6]
Cystoisospora sp.							X		[8]
Entamoeba							X		[2]
Escherichia coli	X								[2]
Fleas[c]						X			[2-6]
Fusobacterium sp.	X								[3-6]
Giardia duodenalis							X		[8]
Giardia lamblia							X		[2-6]
Helicobacter pylori	X								[2]
Hepatitis E								X	[2]
Histoplasmosis			X						[3-6]
Klebsiella	X								[2]
Leishmania infantum							X		[2,9,10]
Leptospirosis	X								[2]
Microsporidia			X						[2]
Microsporum canis		X							[2,11,12]
Mites[d]						X			[3-6]
Mycobacteria sp.					X				[2,13,14]
Nematodes[e]				X					[2,8,15,16]
Orthopox[f]								X	[17]
Pasteurella multocida	X								[2]
Porphyromonas sp.	X								[3-6]
Rabies								X	[2-6]
Rickettsia sp.	X								[2]
Rotavirus								X	[2]
Salmonella sp.	X								[2]
SFTS								X	[18]
Shigella	X								[2]
Sporotrichosis			X						[1,12,19-29]
Staphylococcus sp.	X								[2]
Streptococcus sp.	X								[2]
Ticks[g]						X			[3-6]
Toxoplasma gondii							X		[2-6]
Trematodes[h]				X					[2]

Abbreviations: Ba, bacteria; De, dermatophyte; Fu, fungus; He, helminth; My, mycobacteria; Pe, Parasite-external; Pu, Parasite-unicellular protozoa; SFTS, severe fever with thrombocytopenia syndrome; Sp., species; Vi, virus

[a]The condition is known as bartonellosis or cat scratch fever.

[b]Cestodes include *Diplopylidium sp., Dipylidium caninum, Hymenolepis sp., Joyeuxiella sp.*, and *Taenia taeniaeformis.*

[c]Flea-associated conditions include bartonellosis, endemic typhus (which is also known as murine typhus), and yersiniosis.
[d]Mite-associated conditions include cheyletiella and scabies (which is also known as mange).
[e]Nematodes include *Aelurostrongylus abstrusus [8], ancylostoma braziliense* (a hookworm that causes cutaneous larva migrans), [15], *gnathostomata sp.[2], and toxascaris leonine* [2], and *toxocara cati* (a roundworm that causes visceral lava migrans), [2,8,16].
[f]The condition observed was cowpox.
[g]Tick-associated conditions include ehrlichiosis, Lyme disease, rocky mountain spotted fever, and tularemia.
[h]Trematodes include *Alaria sp., Asocotyle, Echinochasmus, Euparadistomum, Haplorchis, Heterophyes sp., Proceroverum, Prohemistomum,* and *Pygidiopsis*.