Zoonosis Update

Sporotrichosis

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In human medicine, general practice physicians and dermatologists consider sporotrichosis to be an environmentally acquired disease. The disease is most often observed in gardeners and may develop via a thorn prick to the finger; because of this, sporotrichosis is commonly known as rose-growers' disease. Following inoculation with *Sporothrix schenckii* via pricking of a finger, a pustule develops and ulcerates; the infection invades the lymphatic system and ascends the arm, resulting in a chain of cutaneous ulcers. This lymphocutaneous form is the most common manifestation of infection with *S schenckii* in humans. On occasion, a cutaneous form of the disease persists at the site of inoculation.[1] Lesions are most commonly located in the arm but can also develop elsewhere.

Results of a study[2] of sporotrichosis in humans indicate that forestry workers accounted for 17%, gardeners and florists for 10%, and other occupations associated with soil (such as farmers) for 16% of all infections with *S schenckii*. Human infections with *S schenckii* have occurred primarily after handling plant material; in 1983, for example, 12 cases of cutaneous sporotrichosis were reported among hay-mulching workers in Oklahoma and New Mexico.[3] The most extensive outbreak of horticulture-related sporotrichosis occurred in 1988, in which 84 workers acquired cutaneous sporotrichosis after handling conifer seedlings that were packed in Pennsylvania with sphagnum moss that had been harvested in Wisconsin.[4,5] In that outbreak, people in 15 states were affected, including forestry workers, garden-club members, and nursery workers. Sphagnum moss was also identified by investigators with the Centers for Disease Control and Prevention as the source of sporotrichosis in 10 horticultural workers in a Disney World topiary.[6]

In addition to the horticultural sources of sporotrichosis, increasing attention is being focused on the role of domestic cats in the transmission of *S schenckii* to humans.[7] Zoonotic transmission of sporotrichosis has been documented, and this mechanism of infection could become more prevalent in populations of immunosuppressed individuals as suggested by reports[8,9] of sporotrichosis in AIDS patients. *Sporothrix schenckii* has been listed as an emerging zoonotic disease.[10] Six important factors that influence the emergence of zoonotic diseases have been identified; these include the transportation of humans and animals between geographic locations, increased contact between animals and humans, changes in the environment and husbandry practices, a growing population of immunocompromised humans, increased awareness of the zoonotic origin of many diseases, and the identification of organisms that were not previously known.

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Etiologic Agent of Sporotrichosis

Sporothrix schenckii is a dimorphic fungus that, like many other medically important fungi, is in the Moniliaceae family of the Deuteromycete class of fungi.[11,12] The mycotic agent of sporotrichosis has 2 important mechanisms through which its potential to infect the mammalian host is maximized. First, *S schenckii* has the ability to change phases to an ascomycete telemorph that survives on living or decaying plant material. This fungus has been isolated from decaying vegetation such as thorns, straw, hay, wood, moss, and soil. Second, after entering the skin via puncture, bite, or scratch, the fungus converts to a yeast phase, thereby causing lesions locally and possibly systemically in the mammalian host. *Sporothrix schenckii* survives in the environment and becomes pathogenic in animals as a result of the dimorphic abilities of the organism; this dimorphism is the conversion from a yeast-like form at temperatures between 35 and 37°C to a mycelial phase (with branching, septate hyphae) at environmental or laboratory temperatures of 25 to 30°C. Environmental isolates of *S schenckii* will form hyphal mycelia but readily convert to a yeast-like form following injection into mice or other susceptible mammalian hosts. On the other hand, the yeast-like form identified in the lesions of animals is easily adapted to growth in hyphal-conidial form on suitable media incubated at 25 to 30°C. Some strains of *S schenckii* grow best at temperatures no higher than 35°C; these strains are believed to be involved in development of localized (fixed) cutaneous lesions in humans and animals.

Subcutaneous and other rarer forms of infection with *S schenckii* are present worldwide in man and animals. The host range for infection with this mycotic agent is wide and includes humans, horses, dogs, pigs, mules, cats, cattle, camels, fowl, rats, mice, hamsters, and chimpanzees.[13,14]

Sporotrichosis in Cats

Outdoor cats are exposed to *S schenckii* via

wound contamination or penetrating foreign bodies. Three clinical syndromes of feline sporotrichosis are known; these are localized or fixed cutaneous, lymphocutaneous, and multifocal disseminated sporotrichosis. Among cats, the lymphocutaneous and localized forms are the most common and important to zoonotic transmission.[15] Subcutaneous lesions generally develop in association with the lymphatic chain and are detected initially as nodules that are painful upon palpation; the nodules eventually ulcerate and suppurative lymphadenitis develops. Lesions may be verrucose with microabscesses at the border; the exudate from these lesions is usually thick and brownish red.[16]

Cutaneous lesions of sporotrichosis in the cat are most often observed on the legs,[15,17] face, or nasal plenum.[15,18] Localized cutaneous sporotrichosis in cats is confined to the area of inoculation and develops after an incubation period of approximately 1 month. Although the localized cutaneous form remains localized to the skin, there may be regional multicentric lesions. If the localized cutaneous form is not treated, there may be progression to the lymphocutaneous form; the latter is characterized by cutaneous nodules that progress to draining ulcers that affect skin, subcutis, regional lymphatics, and lymph nodes.

In cats, the lungs and liver are the primary sites for dissemination of *S schenckii*; however, involvement of bones, eye, CNS, gastrointestinal tract, spleen, kidney, mammary gland, testis, and epididymis has been reported in veterinary medical literature and some textbooks.[13-16]

Immunosuppression in cats has been implicated in cases of disseminated sporotrichosis, but this association has not been well documented. Also, it does not appear that FIV or FeLV infection is a predisposing cause of sporotrichosis in cats; most cats with sporotrichosis are not infected with either virus.[18] At the Oklahoma Animal Disease Diagnostic Laboratory, evaluation of medical records of 12 cats with cutaneous lesions from which *S schenckii* was isolated revealed that 6 cats were assessed for FIV and FeLV infection, and those tests yielded negative results. In 5 of those 6 cats, results of CBCs were within accepted reference ranges.

Further review of those medical records revealed that the age of the 12 cats ranged from 1.5 to 5 years; there were 6 females and 6 males. There were 9 domestic shorthair cats, and all 9 cats resided outdoors. The other 3 cats were Siamese, Himalayan, and Persian. The location of the primary lesion was on the legs or paws (n = 6 cats), face (4), shoulder (1), and back (1). The interval from the estimated exposure to report of lesion development in the 12 cats was 10 days to 2 months. One cat had multiple abscesses in both forelimbs that developed 2 weeks after onychectomy. Eight of the 12 cats had received antimicrobial treatment of 5 to 7 days' duration. Two cats underwent surgery to remove infected tissue. In 4 cats for which histologic evaluation of lesions was performed, a diagnosis of pyogranulomatous dermatitis with yeast was made. Review of the medical records held at the Oklahoma Animal Disease Diagnostic Laboratory also revealed another cat (not included in the group of 12) that had *S schenckii* detected in the nasal cavity.

Diagnosis of Sporotrichosis in Cats

Differential diagnoses of skin lesions in cats may include bacterial pyoderma, mycobacteriosis, nocardiosis, actinomycosis, cryptococcosis, sporotrichosis, foreign body, squamous cell carcinoma, immune-mediated disease, systemic lupus erythematosis, pemphigus vulgaris, allergy, allergy to parasites, or drug eruption.[18] Cutaneous sporotrichosis in cats is often treated with antimicrobials when first observed, but the condition usually fails to respond to empiric antimicrobial therapy.

A unique aspect of sporotrichosis in cats is the large number of yeast-like cells detected in the subcutaneous lesions (**Fig 1**), compared with that detected in lesions in other species. Because *S schenckii* organisms have distinctive cytologic features,[19] sporotrichosis in cats is most often diagnosed via cytologic evaluation of samples obtained from aspiration of abscesses or nodules, impression smears of ulcerated skin or exudate, smears of swab specimens, or skin scrapings. Smears are air-dried and stained with Wright's or a Romanowsky-type stain. Smears prepared from lesions in cats with sporotrichosis typically contain high numbers of yeast-like organisms that are usually round to oval, 3 to 5 µm in diameter, and 5 to 9 µm in length. The yeast-like cells are often described as cigar-shaped but may appear as round budding yeast. Cytologic examination of smears prepared from lesions in dogs and horses infected with *S schenckii* typically contain low numbers of yeast-like cells. It has been suggested that this disparate number of yeast-like cells in lesions of cats versus those of horses or dogs contributes to the greater zoonotic potential of feline sporotrichosis, compared with that associated with the disease in other domestic animals.[13-15,19]

Results of fungal culture of specimens from lesions are needed for definitive diagnosis of sporotrichosis in humans and animals. This dimorphic fungus is readily isolated from swabs or biopsy specimens obtained from

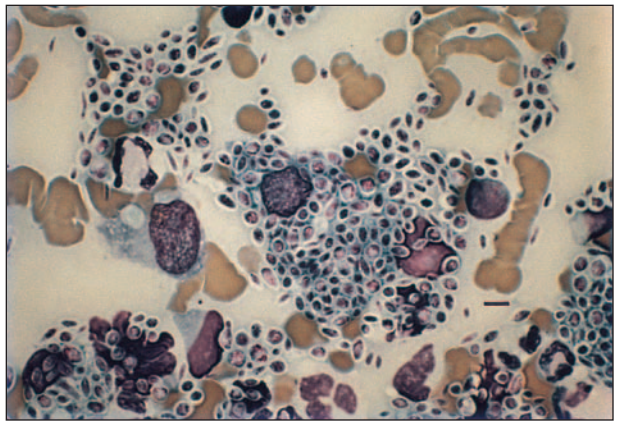

Figure 1—Photomicrograph of an impression smear of exudate from an ulcerated lesion of a cat with sporotrichosis. Notice the high number of yeast-like forms of *Sporothrix schenckii* in macrophages and the extracellular spaces. Wright stain; bar = 25 µm. (From Clinkenbeard KD. Diagnostic cytology: sporotrichosis. *Compend Contin Educ Pract Vet* 1991;13:207–211. Reproduced with permission.)

lesions via culture on Sabouraud mycologic medium when incubated at both 25 and 37°C for 10 to 14 days. In this manner, both the yeast and mycelial forms of *S schenckii* are identified, which is necessary for definitive diagnosis of sporotrichosis. When sporotrichosis is suspected, but yeast-like cells are not observed cytologically or cultured from specimens obtained from lesions, results of sporothrix whole yeast agglutination[20] or latex agglutination testing may be required for diagnosis. Because yeast-like cells are not plentiful in the lesions of horses with sporotrichosis, compared with the number in lesions of affected cats, cytologic evaluation of specimens from lesions can be inconclusive, and serologic testing is necessary to confirm diagnosis of the disease in horses. Other diagnostic tests such as indirect fluorescent antibody testing are rarely needed and require access to a laboratory that has the necessary reagents for performing that test.

Histologic examination of fixed biopsy specimens of lesions may assist with diagnosis of sporotrichosis, but the findings are not disease-specific, because the yeast-like cells of *S schenckii* may be mistaken for *Cryptococcus neoformans, Candida* spp, *Histoplasma capsulatum*, or other less common yeast such as *Trichosporon* spp. Special stains such as periodic acid-Schiff, Gomori methenamine silver, or Gridley's stain are needed to identify the yeast structure of *S schenckii* in tissue sections.

Treatment of Sporotrichosis in Cats

Treatment of mycotic infections in animals has proven to be a challenge to veterinary practitioners, because most drugs have notable toxic adverse effects and are not approved for use in animals. Traditionally, sodium iodide has been used in the treatment of sporotrichosis in cats; however, serious adverse effects associated with that agent have led to its replacement with more effective and safer antifungal drugs such as the imidazoles. Ketoconazole has been used to treat sporotrichosis in cats but has not resulted in complete elimination of *S schenckii* infection.[21,22] Itraconazole has also been used to treat sporotrichosis in cats and is presently considered to be the drug of choice in cats and also in humans.[18,23] Itraconazole is a potent inhibitor of most fungal pathogens in animals because of its greater selectivity for the fungal cytochrome system, compared with that of ketoconazole.[24] This lipophilic drug is well absorbed after oral administration and widely distributed to tissues, including skin, where it achieves concentration much greater than that in plasma. In cats that were administered 10 mg of itraconazole/kg (4.5 mg of itraconazole/lb) PO every 24 hours,[25] a steady-state serum concentration of the drug was achieved after 2 to 3 weeks.

Itraconazole is administered orally to cats at dosages of 5 to 10 mg/kg (2.3 to 4.5 mg/lb) every 12 hours, preferably with food that increases absorption. Compared with the capsule formulation (at an equivalent dose), the liquid form of itraconazole is often used to treat cats because it permits more accurate dose measurement, is best absorbed when food has been withheld, and attains higher peak plasma concentrations. Few adverse effects associated with the use of itraconazole in cats have been reported; in 1 study,[26] no adverse effects were detected in cats treated orally with 10 mg/kg/d for 3 months, whereas cats treated with the same dosage of ketoconazole developed anorexia and weight loss. Administration of any imidazole (including itraconazole) is contraindicated during pregnancy. In cats treated with antifungal agents, drug toxicoses have been reported and necessitate that serum biochemical analyses are performed regularly during treatment of sporotrichosis. Treatment should be continued for 1 month after apparent clinical cure to prevent recurrence of clinical signs.

Transmission of Sporotrichosis from Cats to Humans

In humans, sporotrichosis is primarily manifested as subacute to chronic cutaneous and subcutaneous infection. Skin exposure or inoculation of *S schenckii* by scratch, puncture wound, or abrasion is followed by development of a papule that enlarges to a nodule and usually ulcerates over a period of 1 to 2 weeks. If not treated, the infection may progress to the lymphatic system and cause the lymphocutaneous form of sporotrichosis. This form of the disease must be differentiated from *Bartonella henselae* (cat-scratch disease), *Yersinia pestis* (plague), *Francisella tularensis* (tularemia), nontubercular mycobacteriosis, nocardiosis, and leishmaniasis.

It is rare for humans to develop other forms of the disease such as pulmonary, osteoarticular, visceral, or disseminated sporotrichosis. The extracutaneous forms of sporotrichosis are most often seen in patients who have other conditions such as alcoholism, diabetes mellitus, chronic obstructive pulmonary disease, or human immunodeficiency virus infection.

Sporothrix schenckii infects a multitude of animal species, but cats are the most notable source of transmission of sporotrichosis to humans. There are many reports[27-31] of the zoonotic potential of sporotrichosis in cats. A recent study[32] was conducted in Brazil that included 66 humans, 117 cats, and 7 dogs with sporotrichosis. In that study, 52 humans reported contact with cats with sporotrichosis, and 31 humans reported a scratch or bite from cats; these data strongly suggest that sporotrichosis in humans can occur via cat scratches. The importance of cats as a source of sporotrichosis in humans was highlighted in development of the disease in a veterinarian in Stillwater, Okla. One week after being scratched on the left thumb by a cat with ulcerated cutaneous abscesses, the veterinarian developed a swollen red painful lesion on the dorsum of the thumb in the area of the scratch (**Fig 2**). However, trauma may not be required for transmission of *S schenckii* from cats to humans. In a clinical report,[33] a veterinarian developed sporotrichosis from a cat without evidence of trauma; via analyses of restriction fragment-length profiles, the isolates of *S schenckii* identified in samples obtained from the cat and veterinarian were identical. From this finding, it was suggested that exposure to the large number of organisms that generally reside in skin lesions of cats with sporotrichosis can result in transmission of infection to humans in the absence of a skin-penetrating injury.

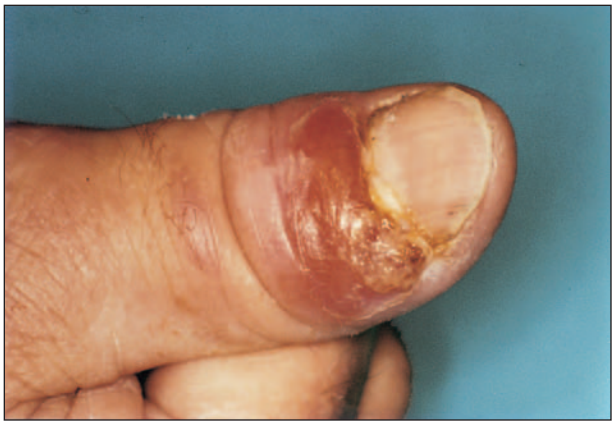

Figure 2—Photograph of thumb of a veterinarian infected with *S schenckii* during treatment of a cat infected with sporotrichosis. (From Clinkenbeard KD. Diagnostic cytology: sporotrichosis. *Compend Contin Educ Pract Vet* 1991;13:207–211. Reproduced with permission.)

In human medicine, dermatologists and primary care physicians may mistake lesions of sporotrichosis with many causes of wounds. Misdiagnoses and difficulty of treating fungal infections should emphasize to physicians and veterinarians the importance of a proper diagnostic evaluation when presented with patients with cutaneous lesions.

Because cats with sporotrichosis contain a plethora of infectious yeast forms of *S schenckii* in their lesions, veterinarians, veterinary technicians, and animal owners should always wear gloves when handling cats with ulcerative lesions or open draining tracts. Without doubt, owners should be advised of the zoonotic potential of cutaneous sporotrichosis and the need to take precautions when handling their affected pets. After handling pets with sporotrichosis, hands and arms should be washed with an antiseptic solution of known antifungal activity such as povidone iodine or chlorhexidine solutions.[34]

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