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Case Report and Treatment of *Streptobacillus moniliformis* in Laboratory and Wild Thirteen-Lined Ground Squirrels (*Ictidomys tridecemlineatus*)

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***Streptobacillus moniliformis* is a Gram-negative bacterium and the causative agent of rat bite fever. In 2020, members of a laboratory-born thirteen-lined ground squirrel (*Ictidomys tridecemlineatus*) colony tested positive for *S. moniliformis* during routine pathogen screening at the University of Wisconsin–La Crosse. These animals were asymptomatic and continued to be monitored and tested until treatment was attempted with tetracycline in May 2023. Two different treatment regimens were attempted. Squirrels treated with 10-mg treats twice daily for 7 to 10 d were no longer positive for *S. moniliformis*. New squirrels entering the University of Wisconsin–La Crosse animal facility were tested. The only additional positive case was in a wild-caught thirteen-lined ground squirrel in 2024. This squirrel subsequently tested negative following the same tetracycline treatment. Based on the identification of this zoonotic agent in both laboratory and wild-caught species, we recommend regular screening for *S. moniliformis* in captive squirrels and prudent management decisions when handling these animals and their waste. To our knowledge, this is the first published report of confirmed *S. moniliformis* in squirrels.**

Abbreviations and Acronyms: CRRADS, Charles River Research Animal Diagnostic Services; TLGS, thirteen-lined ground squirrel; UWL, University of Wisconsin–La Crosse; UWO, University of Wisconsin–Oshkosh

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Introduction

Streptobacillus moniliformis is a Gram-negative filamentous rod-shaped bacterium known to cause systemic illness that is generally characterized by fever, rigors, and rash and has a mortality rate as high as 13%.[1,2] *Streptobacillus moniliformis* is often transmitted to humans through rodent bites or scratches, which is why the clinical manifestation of the zoonosis is referred to as rat bite fever.[2–4] Infections can also occur as result of ingesting excrement, milk, or tissue containing *S. moniliformis* and has been referred to under these circumstances as Haverhill fever.[5–7] Most cases of *S. moniliformis* infections occur in children handling pet rats and among laboratory technicians and pet shop employees.[2,7,8] Wild rats are thought to be the primary reservoir for *S. moniliformis* and are generally asymptomatic carriers with rates of 50% to 100%.[2,4,8,9] Laboratory rats can also have carriage rates from 10% to 100%, and *S. moniliformis* has also been widely documented in other laboratory species, including mice, guinea pigs, gerbils, and ferrets.[8,10–12] Depending on the mouse strain, *S. moniliformis* can be highly pathogenic, causing acute death or chronic suppurative infections.[13,14] For this reason, and the potential risk of zoonosis, annual *S. moniliformis* monitoring of mouse, rat, hamster, guinea pig, and rabbit colonies is recommended by the Federation for Laboratory Animal Science Association.[15]

In November 2020, routine annual testing was performed on the laboratory rodent colonies at the University of Wisconsin–La Crosse (UWL). These included samples from 3 members of a small colony (n = 17) of thirteen-lined ground squirrels (TLGS; *Ictidomys tridecemlineatus*). A series of pathogen screening tests were performed by Charles River Research Animal Diagnostic Services (CRRADS), including a PCR for *S. moniliformis*. All 3 of the samples came back positive for *S. moniliformis*. Although squirrels in general are noted as a potential carrier of *S. moniliformis*,[8,12] we could not find any documented cases of *S. moniliformis* in ground squirrels in the literature. The following outlines the retesting, treatment, and monitoring process that occurred in response to the positive *S. moniliformis* results at UWL. Our aim is to provide awareness of the potential risk of *S. moniliformis* in ground squirrels and offer some insight on management strategies that may be considered when positive results occur.

Case History

In November 2020, 17 TLGS were being maintained in the UWL vivarium as part of a long-term approved research program (IACUC protocols 1 to 18). All of these squirrels were born in captivity at the University of Wisconsin–Oshkosh (UWO) in spring 2019 and arrived in 1 of 2 cohorts to UWL in the summer of 2020. All animals were housed individually in rooms with a Wisconsin photoperiod (9 h in December gradually increasing to 15.5 h in June and then decreasing again). Squirrels were fed ad libitum irradiated Teklad rodent diet (Envigo Bioproducts, Indianapolis, IN) and supplemented with a seed and dried fruit mix (Harvest Foraging Blend; Bio-Serv, Flemington, NJ). Please refer to Table 1 for information on the age, sex, and arrival date at UWL for each squirrel.

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Table 1. Animal information including sex, date of birth, and arrival at the University of Wisconsin–La Cross organized by age

Animal ID	Sex	Date of birth	UWL cohort	Testing 2020	Testing 2021
19-01	Female	4/3/2019	7/23/2020		–
19-02	Male	4/3/2019	6/4/2020		+
19-03	Female	4/9/2019	7/23/2020	+	
19-04	Male	4/10/2019	7/23/2020		–
19-05	Male	4/10/2019	6/4/2020		–
19-06	Male	4/10/2019	7/23/2020		+
19-07	Female	4/16/2019	6/4/2020		+
19-08	Male	4/30/2019	7/23/2020		+
19-09	Female	4/30/2019	7/23/2020		–
19-10	Female	4/30/2019	6/4/2020		+
19-11	Female	4/30/2019	7/23/2020	+	
19-12	Female	5/1/2019	6/4/2020		+
19-13	Female	5/6/2019	6/4/2020		+
19-14	Female	5/6/2019	6/4/2020		+
19-15	Female	5/10/2019	7/23/2020		–
19-16	Female	5/20/2019	7/23/2020	+	
19-17	Female	5/28/2019	7/23/2020		–

Results are shown of initial *S. moniliformis* testing for the colony of thirteen-lined ground squirrels in November 2020 and April 2021. UWL, University of Wisconsin–La Cross.

These laboratory TLGS were used at UWL for blood and/or tissues samples, and were not subject to any other experimental testing, treatment, or manipulation. UWO performs regular animal health and disease surveillance monitoring and has no reported history of *S. moniliformis* in its TLGS colony. Prior to entering the hibernaculum on November 18, 2020, 3 of the UWL TLGS were randomly selected for infectious disease surveillance monitoring. Serum and oral swabs were submitted from 2 animals (19-03 and 19-11), and fecal pellets from those 2 and a third animal (19-16) were pooled and submitted for analysis by CRRADS. The third animal (19-16) was being euthanized for study purposes. Both oral swabs and the pooled fecal sample from the 3 animals came back positive for *S. moniliformis.* This was the first time that *S. moniliformis* had been found at UWL. The only other species that was maintained in the vivarium at that time was a mouse colony that tested negative.

A committee that included animal care staff, the attending veterinarian, investigators working with the TLGS, and campus administrators met to discuss these results. Additional biosafety measures were immediately implemented. These included additional dedicated personal protective equipment, specialized waste management procedures, and safety risk signage throughout the vivarium. Personnel at UWO were notified of this finding and plans were developed at both UWL and UWO to perform additional diagnostic testing when animals transitioned out of the hibernaculum in the spring of 2021.

In April 2021, 16 of the TLGS remained in the UWL facility including the 2 TLGS that had tested positive in November 2020. Oral swabs from the 14 remaining animals were submitted to CRRADS for *S. moniliformis* PCR testing. Eight of the 14 submitted samples came back positive. Refer to Table 1 for a list of animals and the outcomes of the 2020 and 2021 UWL testing. UWO submitted fecal pellets from animals at their facility to CRRADS: all were negative. In rats *S. moniliformis* is a commensal bacterium in the nasopharynx and upper airways requiring microaerophilic conditions to grow in culture. The extent to which fecal PCR results agree with those from oral swabs in rats of TLGS is unknown.[2,14] The 10 positive animals included males and females from both cohorts that arrived at UWL from UWO and animals from the same litter had both positive and negative results. No correlation could be identified in the housing, transport, care, handling, use, or management of the animals at UWL or at UWO that explained the mixed results in this group.

In November 2022, oral swabs from 2 TLGS (19-07 and 19-08) that tested positive in April 2021 were randomly selected and submitted to CRRADS for PCR testing. Both animals were once again identified as positive for *S. moniliformis.* By early 2023, 6 animals from the original 17 had been euthanized for unrelated reasons. Eleven animals remained from the original 17, and no new animals had been added to the colony.

Limited information is available in the literature on antibiotic usage in TLGS. Based on *Carpenter's Exotic Animal Formulary*,[16] the 2 positive retested animals (19-07 and 19-08) were each given a cherry flavored medicated treat containing 10 mg of tetracycline (¼ tablet of MD975-40, Bio-Serv) twice a day for 10 d in May 2023. Both animals were heavily monitored for changes in intake (food and water), output (feces and urine), and behavior with no adverse effects noted. Testing results prior to and following treatment are summarized in Table 2. Oral swabs submitted to CRRADS for PCR testing following treatment of both animals came back negative for *S. moniliformis.* It was decided that the remaining 9 animals were each going to be treated with tetracycline. An alternative treatment regime involving 0.5 mg/mL tetracycline in the drinking water was identified as a potential logistically favorable alternative.[16,17] The 9 remaining TLGS were all treated for 7 d, after which oral swabs were once again submitted to CRRADS for PCR testing. Two of the 9 treated with 0.5 mg/mL tetracycline for 7 d (19-12 and 19-13) came back positive for *S. moniliformis.* Both animals had been positive in April 2021.

Given the limited sample size, it is unknown whether the alternative liquid form of the medication, the shortened treatment period (7 rather than 10 d), or some other factor contributed to the positive results in the 2 medicated water–treated TLGS. Both animals (19-12 and 19-13) were subsequently treated with medicated treats for 7 d and were negative in follow-up testing. This would suggest that medicated tetracycline-containing

Table 2. Results from *S. moniliformis* testing in thirteen-lined ground squirrels prior to and following treatment with 10 mg of tetracycline twice a day or 0.5 mg/mL tetracycline in the drinking water for 7 to 10

Animal ID	Initial	11/2022	Tetracycline treatment	Posttreatment	Tetracycline treatment	Recheck
19-07	+	+	10-mg treats	–		–
19-08	+	+	10-mg treats	–		–
19-03	+		0.5 mg/mL	–		–
19-10	+		0.5 mg/mL	–		–
19-12	+		0.5 mg/mL	+	10-mg treats	–
19-13	+		0.5 mg/mL	+	10-mg treats	–
19-14	+		0.5 mg/mL	–		–
19-01	–		0.5 mg/mL	–		–
19-04	–		0.5 mg/mL	–		–
19-15	–		0.5 mg/mL	–		–
19-17	–		0.5 mg/mL	–		–
24-01	+[a]		10-mg treats	–		

[a]Wild-caught animal tested positive twice prior to tetracycline treatment.

treats may be more effective than medicated water in TLGS. No adverse effects to either tetracycline treatment regimen was identified.

In June 2023, an additional cohort of 8 TLGS arrived at UWL from UWO. These animals were all born at UWO in May 2022. No TLGS at UWO were positive for *S. moniliformis*, and therefore none of these animals had previously been treated. After arrival at UWL, oral swabs were submitted to CRRADS for PCR testing, and none was positive for *S. moniliformis.* In September 2024, 7 TLGS were wild caught in La Crosse County, WI and brought into the UWL animal facility. In addition to other diagnostic tests and quarantine procedures, oral swabs were submitted to CRRADS for *S. moniliformis* PCR testing. One of these 7 wild animals (24-01) was positive for *S. moniliformis.* This is the first time that a ground squirrel outside of the original 10 positive cases came back positive for *S. moniliformis*, and the first time that a wild-caught ground squirrel was reported positive for *S. moniliformis.* The animal was retested the following week to confirm that diagnosis with the same result. The positive TLGS (24-01) was treated with 10 mg of tetracycline-containing treats twice a day for 7 d. A follow-up oral swab and fecal sample both came back negative for *S. moniliformis* from CRRADS.

Discussion

TLGS are not a common laboratory species, although they have been used for research on hibernation and metabolism since the 18th century.[18] It is important for researchers and laboratory managers to be aware that there is at least some risk for ground squirrels to carry *S. moniliformis.* This may be of particular importance in facilities housing mice, especially strains of mice or immunocompromised animals that may have an increased risk or response to *S. moniliformis*.[9,13,14] This case report may also be useful to animal control and wildlife management staff who may interact with TLGS in the wild. Wild ground squirrels can serve as prey to other species. *Streptobacillus moniliformis* has been documented in carnivores presumably following the ingestion of excrement or *S. moniliformis*–positive rodents.[7,8,12] Understanding the carrier rate of *S. moniliformis* in wild and laboratory TLGS is beyond the scope of this study, but these results do suggest that TLGS are at least capable of being repeated or persistent carriers of this zoonotic agent. Eisenberg and colleagues discussed the spectrum of host species for streptobacilli in their 2016 review on *S. moniliformis* diagnostics.[12] They affirm that anecdotally, exotic rodents such as gerbils and squirrels are included in this list of hosts, based on infections following bites, but confirmation was not made of *S. moniliformis* or isolates stored from squirrels.[12,19,20] To our knowledge, this is the first confirmed report of *S. moniliformis* in wild and laboratory ground squirrels.

The use of antibiotics to treat the *S. moniliformis*–positive animals was done as a management decision and not a comprehensive investigation on the safety or efficacy of tetracycline in TLGS. All positive TLGS ($n = 5$) that were treated orally with 10 mg of tetracycline twice a day for at least 7 d were no longer positive in follow-up testing. At least 2 animals were positive after treatment for 7 d with water bottles containing 0.5 mg/mL tetracycline. Three others that were previously positive tested negative after this water treatment. A significant limitation was the lack of fluid intake quantification. TLGS are highly efficient at conserving metabolic water and may not have the same fluid intake of other rodent species.[21] All animals were frequently monitored, and drinking was noted, but we are unable to speculate on the dose or rate of tetracycline consumed. Consequently, we cannot advocate for the water-based tetracycline treatment option for *S. moniliformis* in TLGS without additional testing. No side effects from antibiotic usage were noted during or following these tetracycline treatments. TLGS have been documented as potential harbors of antibiotic-resistant bacteria, which can include resistance to tetracycline.[22] Considerable care and prudent management are recommended with all antibiotic usage in laboratory animal species.[23]

The TLGS used in this study were part of an ongoing research project and were not maintained to study *S. moniliformis* diagnostics, treatment, or preventions. Consequently, the events, timeline, and sample sizes in this case report do not have the scientific rigor to make statistically supported conclusions. Decisions were made based on resources and available evidence at that time. All TLGS that tested positive for *S. moniliformis* were subsequently positive when retested until after antibiotic treatment. We do not know whether those were persistent or recurrent events. For this reason, we recommend and will continue to maintain annual monitoring for *S. moniliformis* in TLGS as a component of our health monitoring program.

The use of PCR as a diagnostics tool for *S. moniliformis* has been documented in the literature.[12] CRRADS indicated that they do not share their proprietary primers and probes used for agent detection. All animals in this study were asymptomatic, and consequently these results are based on the assumption of CRRADS diagnostic accuracy. We cannot comment on the validity of their process, only on the consistency of their results.

Conclusions

Streptobacillus moniliformis is a zoonotic agent causing some risk of disease to humans and other laboratory species. Both wild TLGS and those raised in a research colony can be asymptomatic carriers of *S. moniliformis*. It is therefore recommended that routine monitoring be performed and appropriate care and protection be implemented when interacting with TLGS and their waste. A 7- to 10-d course of tetracycline may be effective in treating *S. moniliformis* in adult TLGS when appropriate.

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Conflict of Interest

The authors have no conflicts of interest to declare.

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References

1. Levaditi C, Nicolau S, Poinsloux P. Sur le rôle étiologique de *Streptobacillus moniliformis* (nov. spec.) dans l'érythème polymorphe aigu septicémique. *C R Acad Sci.* 1925;180:1188–1190.
2. Elliott SP. Rat bite fever and *Streptobacillus moniliformis*. *Clin Microbiol Rev.* 2007;20(1):13–22.
3. Freels LK, Elliott SP. Rat bite fever: three case reports and a literature review. *Clin Pediatr (Phila).* 2004;43(3):291–295.
4. Centers for Disease Control and Prevention (CDC). Rat-bite fever—New Mexico, 1996. *MMWR Morb Mortal Wkly Rep.* 1998;47:89–91.
5. Parker F, Hudson NP. The etiology of Haverhill fever (*Erythema arthriticum epidemicum*). *Am J Pathol.* 1926;2(5):357–380.7.
6. Place EH, Sutton LE. *Erythema arthritcum epidemicum* (Haverhill fever). *Arch Intern Med.* 1934;54(5):659–684.
7. Wouters EGH, Ho HTK, Lipman LJA, Gaastra W. Dogs as vectors of *Streptobacillus moniliformis* infection? *Vet Microbiol.* 2008;128(34):419–422.
8. Washburn RG. Rat-bite fever: *Streptobacillus moniliformis* and *Spirillum minus*. In: Bennett JE, Dolin R, Blaser MJ, eds. *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases.* 8th ed. W.B. Saunders; 2015:2629–2632.e1. Available at: https://www.sciencedirect.com/science/article/pii/B9781455748013002332.
9. AlHadithi HT. Incidence of *Streptobacillus moniliformis* in laboratory rats and mice. *Biomed Lett.* 1997;55:7–11.
10. Cooper TK, Meyerholz DK, Beck AP, et al. Research-relevant conditions and pathology of laboratory mice, rats, gerbils, guinea pigs, hamsters, naked mole rats, and rabbits. *ILAR J.* 2021;62(1–2):77–132.
11. Nation PN. Pathology of ground squirrels in a research colony. *Comp Med.* 2020;70(6):542–550.
12. Eisenberg T, Ewers C, Rau J, Akimkin V, Nicklas W. Approved and novel strategies in diagnostics of rat bite fever and other *Streptobacillus* infections in humans and animals. *Virulence.* 2016;7(6):630–648.
13. Glastonbury JR, Morton JG, Matthews LM. *Streptobacillus moniliformi*s infection in Swiss white mice. *J Vet Diagn Invest.* 1996;8(2):202–209.
14. Fornefett J, Krause J, Klose K, et al. Comparative analysis of clinics, pathologies and immune responses in BALB/c and C57BL/6 mice infected with *Streptobacillus moniliformis*. *Microbes Infect.* 2018;20(2):101–110.
15. Mähler Convenor M, Berard M, Feinstein R, et al; FELASA working group on revision of guidelines for health monitoring of rodents and rabbits. FELASA recommendations for the health monitoring of mouse, rat, hamster, guinea pig and rabbit colonies in breeding and experimental units. *Lab Anim.* 2014;48(3):178–192.
16. Frohlich J, Mayer J. Rodents. In: Carpenter J, Harms C, eds. *Carpenter's Exotic Animal Formulary.* 6th ed. W.B. Saunders; 2023:530–573. Available at: https://www.sciencedirect.com/science/article/pii/B9780323833929000095.
17. Gabrisch K. *Krankheiten der Heimtiere.* Schlütersche Verlagsgesellschaft; 2014. Available at: https://de.book-info.com/isbn/3-89993-678-7.htm.
18. Pra RD, Bagriantsev SN, Gracheva EO. Ground squirrels. *Curr Biol.* 2022;32(12):R605–R607.
19. Gray HH. Squirrel-bite fever. *Trans R Soc Trop Med Hyg.* 1967;61(6):857–858.
20. McMillan B, Boulger LR. Squirrel-bite fever. *Trans R Soc Trop Med Hyg.* 1968;62(4):567.
21. Junkins MS, Feng NY, Merriman DK, Bagriantsev SN, Grachev EO. Suppression of neurons in circumventricular organs enables months-long survival without water in thirteen-lined ground squirrels. *Science.* 2024;386(6725):1048–1055.
22. Cloud-Hansen KA, Villiard KM, Handelsman J, Carey HV. Thirteen-lined ground squirrels (*Spermophilus tridecemlineatus*) harbor multiantibiotic-resistant bacteria. *J Am Assoc Lab Anim Sci.* 2007;46(3):21–23.
23. Narver HL. Antimicrobial stewardship in laboratory animal facilities. *J Am Assoc Lab Anim Sci.* 2017;56(1):6–10.