



GV-SOLAS

Gesellschaft für Versuchstierkunde
Society for Laboratory Animal Science

Expert Information

From the Working Group on Hygiene

**Implication of infectious agents on
results of animal experiments**

Corynebacterium bovis

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Corynebacterium bovis

Background

- First description and isolation from cattle in 1962¹
- First isolation from (athymic) mice in 1995²

Prevalence

- *Corynebacterium (C.) bovis* is one of the most prevalent organisms isolated from bovine milk, its pathogenicity regarding bovine mastitis is discussed.^{1,3}
- Monitoring of immunodeficient mice with scaly skin lesions revealed that 2% of microbiological cultures and 9% of PCR assays were positive for *Corynebacterium bovis*.⁴
- *Corynebacterium bovis* was also isolated from a chronic testicular abscess and the lung of a laboratory rabbit.⁵
- Up to 4% of cultured cell lines and 13% of solid tumor tissue samples were contaminated with *Corynebacterium bovis* DNA.⁶

Host species

- Mouse^{2,7}, rat⁸, rabbit⁵
- Evidence in mouse colonies is reported for North America², Europe⁹ and Asia¹⁰
- Major host: cattle^{1,3}
- *Corynebacterium bovis* was identified as the causal agent for hyperkeratotic dermatitis (so-called scaly skin disease) in athymic mice in 1995.²

Properties

- Gram-positive, rod-shaped, non spore-forming, facultative anaerobic bacterium^{11,2,9} with different virulence and pathogenicity of strains^{12,13}
- Transmitted between animals by direct contact⁵, spreads rapidly to naïve nude mice.⁹
- Transmission via fomites, for instance, gloves of animal caretakers or by transplantable tumor lines⁹
- Persistent in the environment, lipophilic, survives well on skin flakes or other organic material, only sensitive to heat and certain chemical disinfectants.⁹
- Very difficult to eradicate^{14,15}

Susceptibility

- Immunocompetent and immunodeficient mice and rats can be infected, both glabrous and hirsute.^{7,8}
- Glabrous mice are prone to develop hyperkeratosis.^{7,9}
- Nude (*Foxn1^{nu}*), hairless (*Hr^{hr}*)², SCID (*Prkdc^{scid}*), and NSGS mice develop clinical signs and histological findings.^{9,16}

Organotropism

- Skin^{1,2}
- Mucous membranes of oral cavity and nose²

Clinical disease

- Scaly skin disease of athymic mice has been reported since 1976^{2,13}
- Hyperkeratotic dermatitis (also called scaly skin disease) is most commonly observed in homozygous nude mice.^{2,9}
- Euthymic hairless mice may also develop scaly skin disease.²
- SCID mice may develop alopecic areas, with small white flakes involving the dorsum, flanks, neck and cheeks; acanthosis and hyperkeratosis may be observed histologically.⁷
- NSGS mice develop periocular and facial hyperkeratosis and alopecia.¹⁶
- Cattle mastitis¹, rabbit abscesses⁵, inflammations in different organs of human¹⁷

Pathology

- Dyskeratotic hair follicles with squamous metaplasia along the hair root¹⁸
- Marked acanthosis, moderate orthokeratotic hyperkeratosis, dermal mononuclear cell infiltrate²

Morbidity and mortality

- Usually inapparent infection for immunocompetent and hirsute animals¹⁹
- High morbidity (80%) but low mortality (1%) in affected adult hairless mice^{7,20}
- Suckling mice have high mortality up to 100%.¹⁸
- The lesions tend to resolve spontaneously and disappear within 7-10 days.^{2,8}

Zoonotic potential

- Unclear; some cases of human diseases have been reported.^{14,17,21,22}

Interference with research

Oncology

- Tumor growth rate may be depressed.^{18,20}
- Engraftment of xenografts is retarded, NK cell activity may be affected.^{18,20}
- In the NSGS mouse model of chronic myelomonocytic leukemia (CMML), *C. bovis* infection results in diminished human CMML engraftment, including less thrombocytopenia, less splenomegaly, fewer CMML infiltrates in histopathologic sections of murine organs, and fewer human CD45+ cells in samples from spleen, bone marrow, and peripheral blood.¹⁶

Teratology

- No data

Infectiology

- No data

Immunology

- No data

Interactions with other infectious agents

- *Corynebacterium bovis* infection of the mammary gland in mice has an influence on subsequent infection with *Staphylococcus aureus*.¹²

Toxicology

- No data

Physiology

- Increased water consumption (2x) and urine production^{2,20}
- Significant weight loss¹⁹, probably due to anorexia and dehydration or depressed growth rate

Cell biology

- No data

Assisted reproductive technology

- No data

Special considerations

- No data

Updated by Karin Jacobi, Berlin, March 2019 and Michael Mähler, Hannover, February 2021

References

1. Cobb RW, Walley JK. 1962. *Corynebacterium bovis* as a probable cause of bovine mastitis. Vet Rec 74:101-102.
2. Clifford CB, Walton BJ, Reed TH, Coyle MB, White WJ, Amyx HL. 1995. Hyperkeratosis in athymic nude mice caused by a coryneform bacterium: microbiology, transmission, clinical signs and pathology. Lab Anim Sci 45(2):131-139.
3. Brooks BW, Barnum DA, Meek AH. 1983. An observational study of *Corynebacterium bovis* in selected Ontario Dairy Herds. Can J Comp Med 47(1):73-78.
4. Pritchett-Corning KR, Cosentino J, Clifford CB. 2009. Contemporary prevalence of infectious agents in laboratory mice and rats. Lab Anim 43(2):165-173.
5. Arseculeratne SN, Navaratnam C. 1975. *Corynebacterium bovis* as a pathogen in rabbits. Res Vet Sci 18(2):216-217.
6. Manuel CA, Bagby SM, Reisinger JA, Pugazhenti U, Pitts TM, Keysar SB, Arcaroli JJ, Leszczynski JK. 2017. Procedure for horizontal transfer of patient-derived xenograft tumors to eliminate *Corynebacterium bovis*. J Am Assoc Lab Anim Sci 56(2):166-172.
7. Scanziani E, Gobbi A, Crippa L, Giusti AM, Pesenti E, Cavalletti E, Luini M. 1998. Hyperkeratosis-associated coryneform infection in severe combined immunodeficient mice. Lab Anim 32(3):330-336.
8. Burr HN, Lipman NS, White JR, Zheng J, Wolf FR. 2011. Strategies to prevent, treat, and provoke *Corynebacterium*-associated hyperkeratosis in athymic nude mice. J Am Assoc Lab Anim Sci 50(3):378-388.
9. Scanziani E, Gobbi A, Crippa L, Giusti AM, Giavazzi R, Cavalletti E, Luini M. 1997. Outbreak of hyperkeratotic dermatitis of athymic nude mice in northern Italy. Lab Anim 31(3):206-211.
10. Kim TH, Kim DS, Han JH, Chang SN, Kim KS, Seok SH, Kim DJ, Park JH, Park JH. 2014. Detection of *Corynebacterium bovis* infection in athymic nude mice from a research animal facility in Korea. J Vet Sci 15(4):583-586.
11. Anderson JC, Honkanen-Buzalski T, Bramley AJ. 1985. The pathogenesis of a high-virulence strain of *Corynebacterium bovis* in the mammary gland of the mouse. J Comp Pathol 95(2):227-234.
12. Honkanen-Buzalski T, Anderson JC, Bramley AJ. 1985. The virulence of strains of *Corynebacterium bovis* in the mammary gland of the mouse and the effect of corynebacterial mastitis on subsequent infection with *Staphylococcus aureus*. Br Vet J 141(5):519-528.
13. Dole VS, Henderson KS, Fister RD, Pietrowski MT, Maldonado G, Clifford CB. 2013. Pathogenicity and genetic variation of 3 strains of *Corynebacterium bovis* in immunodeficient mice. J Am Assoc Lab Anim Sci 52(4):458-466.
14. Burr HN, Wolf FR, Lipman NS. 2012 *Corynebacterium bovis*: epizootiologic features and environmental contamination in an enzootically infected rodent room. Lab Anim Sci 51(2):189-198.
15. Manuel CA, Pugazhenti U, Leszczynski JK. 2016. Surveillance of a ventilated rack system for *Corynebacterim bovis* by sampling exhaust-air manifolds. J Am Assoc Lab Anim Sci 55(1):58-65.
16. Vedder AR, Miedel EL, Ragland NH, Balasis ME, Letson CT, Engelman RW, Padron E. 2019. Effects of *Corynebacterium bovis* on engraftment of patient-derived chronic myelomonocytic leukemia cells in NSGS mice. Comp Med 64(4): 276-282.
17. Vale JA, Scott GW. 1977. *Corynebacterium bovis* as a cause of human disease. Lancet 2(8040):682-684,
18. Field G. 2006. An update on scaly skin disease. ACLAM Newsletter 37:5-8.

19. Gobbi A, Crippa L, Scanziani E. 1999. *Corynebacterium bovis* infection in immunocompetent hirsute mice. *Lab Anim Sci* 49(2):209-211.
20. Field K, Greenstein G, Smith M, Herrmann S, Gizzi J. 1995. Hyperkeratosis-associated coryneform in athymic nude mice. *Lab Anim Sci* 45:469 (abstract).
21. Dalal A, Urban C, Ahluwalia M, Rubin D. 2008. *Corynebacterium bovis* line related septicemia: a case report and review of the literature. *Scand J Infect Diseases* 2008; 40(6-7):575-577.
22. Sbaai M, Lahlou YB, Ghazouniani M, Houba A, Frikh M, Elouenass M. 2011. Septicémie à *Corynebacterium bovis*: à propos d'un cas avec revue de littérature. *Ann Biol Clin* 69(6):732-734

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