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Spontaneous *Staphylococcus xylosus* Infection in Mice Deficient in NADPH Oxidase and Comparison with Other Laboratory Mouse Strains

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***Staphylococcus xylosus* typically is described as a nonpathogenic common inhabitant of rodent skin. Reports of *S. xylosus* as a primary pathogen in human and veterinary medicine are scarce. Here we report 37 cases, affecting 12 strains of laboratory mice, of spontaneous infections in which *S. xylosus* was isolated and considered to be the primary pathogen contributing to the death or need for euthanasia of the animal. Infection with *S. xylosus* was the major cause of death or euthanasia in 3 strains of mice deficient in the production of phagocyte superoxide due to defects in NADPH oxidase. NADPH-oxidase–deficient mice (*n* = 21) were most susceptible to spontaneous *S. xylosus* infections. The infections were characterized by abscesses and granulomas in soft tissues, with bacterial migration to internal organs (primarily regional lymph nodes and lungs and, to a lesser degree, muscle, bone, and meninges). In contrast, 9 strains of phagocyte-superoxide–producing mice (*n* = 16) also had *S. xylosus* infections, but these were largely confined to eyelids, ocular conjunctiva, and skin and rarely involved other tissues or organs. Because exhaustive bacterial culture and isolation may not be performed routinely from mouse abscesses, *S. xylosus* infections may be underdiagnosed. *S. xylosus* should be considered in the differential diagnosis in laboratory mice with abscesses and other skin lesions. This report expands the range of mouse strains and tissues and organs susceptible to spontaneous *S. xylosus* infection and compares the pathology among various mice strains.**

Abbreviations: CGD, chronic granulomatous disease; KO, knockout.

Staphylococcus xylosus is a coagulase-negative nonmotile gram-positive coccus belonging to the *Staphylococcus saprophyticus* group. This bacterial group is ubiquitous in nature, persisting in soils and on surfaces.[22] *S. xylosus* is a common commensal bacterium that generally is found inhabiting the skin and mucous membranes of a variety of mammals and occasionally humans.[23] It probably colonizes the skin and surfaces by forming a biofilm.[25] Although *S. xylosus* is considered a nonpathogenic *Staphylococcus* and commonly is used as a starter culture for meat products[6], several reports describe opportunistic infections in animals[3,4,8,13,21] and humans.[7,16,36]

A primary defense mechanism of phagocytic cells is superoxide, which is produced by the enzyme complex NADPH oxidase.[2] Activation of the phagocyte NADPH oxidase requires coordinated assembly of 4 structural proteins: the membrane-bound flavocytochrome b558, composed of a heavy chain (gp91^{phox}) and a light chain (p22^{phox}), and 3 cytosolic proteins, p47^{phox}, p67^{phox}, and the GTP-binding regulatory protein *rac*.[2, 27, 28, 29, 31] Defects of some NADPH oxidase components in humans results in a group of genetic disorders, known collectively as chronic granulomatous disease (CGD), that are manifested clinically by recurrent bacterial and fungal infections and tissue granuloma formation.[29] Superoxide production also is thought to be involved in other diseases, including Parkinson disease, cancer, inflammatory bowel disease, hypertension, cataracts, and multiple sclerosis.[17, 18, 20, 34, 35] In addition, patients with CGD are known to have excessive inflammatory responses manifesting as granulomatous enteritis, genitourinary obstruction, and cutaneous lesions.[15]

Several strains of mice have been genetically altered not to express the genes involved in the production of superoxide (called knockout [KO] mice).[12, 26] The p47^{phox} KO and gp91^{phox} KO mice have defects in NADPH oxidase that cause the animals to develop a disease similar to human CGD, manifesting as an increased susceptibility to infection with bacteria and fungi and making them excellent models for the study of CGD pathogenesis and therapy.[3, 12, 19, 22, 26]

In the current report, we describe spontaneous infections with *Staphylococcus xylosus* as the main cause of morbidity and mortality in a specific pathogen-free phagocyte superoxide-deficient mouse colony model of CGD. In addition, we report spontaneous *S. xylosus* infections in 9 strains of mice and compare the lesions with those observed in CGD mice, which include meningitis, bone lysis, and myositis. Management practices were modified to prevent additional cases of *S. xylosus* infection in our CGD mice colony.

Materials and Methods

The colony comprised 3 different mouse models of CGD: B6.129S6-*Cybb*^{tm1Din}/J (gp91^{phox}KO),[26] B6.129S2-Ncf1^{tm1shl}N14, and B6p47^{phox}[KO]HLL (both p47^{phox} KO),[12,30] all of which lacked phagocyte superoxide production. In addition, other colonies comprised of different strains, transgenics, and knockout mice,

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all of which have normal production of phagocyte superoxide, were maintained and bred in the same facility. Other strains affected were: AKR/J-*Lvif*, which carries a segment of chromosome 10 with a null allele of a gene that inactivates some murine leukemia viruses; B6;129-*Adora2a*^{tm1Dyj}/J, adenosine deaminase-deficient mice causing severe combined immunodeficiency accompanied by T-cell depletion and accumulation of both intracellular and extracellular adenosine and deoxyadenosine; AKR/J-*Xpr1*^{Sxv}, which carries a wild-mouse version of a chromosome 1 locus that encodes the receptor for xenotropic–polytropic murine leukemia viruses; C57BL/6NTac-[KO]FPR, with defective neutrophil chemotaxis; C57BL/6NTac-[KO]P50NF-kB-[KO]P52NF-kB, a double-knockout mouse that lacks nuclear factor proteins, causing complete block of maturation of B cells in the spleen and partial block of B cell development in bone marrow; C57BL/6J-[KO]RAG1 N10, which lacks recombination-activating gene 1 (*Rag1*), which controls recombination of immunoglobulin and T-cell receptor genes (as a consequence of this defect, these mice have no mature T or B cells); NOD.Cg-*Prkdc*^{scid} *Il2rg*^{tm1Sug}/JicTac, which mice are severe combined immunodeficient with dysfunctional cytokine production and incompetence of T, B, and NK cells; NFS/N-*Xpr1*^{Sxv} *Rmcf2*$^{+}$, which carry an endogenous retrovirus on chromosome 18 originally identified in the Asian species *M. castaneus*; and BALB/c, which are immunocompetent.

The mice were housed in an AAALAC-accredited animal facility (National Institute of Allergy and Infectious Diseases, Bethesda, MD). The mice were individually or group-housed in sterile ventilated microisolation caging (Thoren Caging Systems, Hazleton, PA) with autoclaved hardwood bedding (SaniChip, Harlan Teklad, Madison, WI) and food (Rodent NIH31 Autoclavable NA, Zeigler Brothers, Gardners, PA) and acidified water provided ad libitum. All mice were maintained in the same animal facility but not necessarily in the same animal room; however, health status was the same for all mice in this study. Colony sentinels were tested quarterly and were free of the following agents: mouse hepatitis virus, pneumonia virus of mice, Sendai virus, Theiler murine encephalomyelitis virus, mouse rotavirus, lymphocytic choriomeningitis virus, ectromelia virus, mouse cytomegalovirus, minute virus of mice, polyoma virus, reovirus 3, mouse adenovirus, rodent parvoviruses, *Mycoplasma pulmonis*, and cilia-associated respiratory bacillus. Hantavirus testing was performed once a year. Endoparasite and ectoparasite examination was performed every 6 wk in sentinel animals and throughout the year on culled research animals. Mouse norovirus and *Helicobacter* spp. were not excluded from the animal colony; therefore, all mice were considered potentially infected with these agents. When tested, sentinel mice were routinely positive to mouse norovirus, but individual experimental mice were not tested. Necropsies of clinical cases were performed as part of the routine colony health surveillance program.

The mouse colony was maintained as part of several experimental protocols approved by the institutional animal care and use committee. All procedures and use of animals were in accordance with the *Guide for the Care and Use of Laboratory Animals*.[10] Sick animals were euthanized with CO_2 overdose according to the American Veterinary Medical Association guidelines on rodent euthanasia.[1] Complete necropsies were performed immediately after euthanasia, and tissue samples from lesions and all major organs were collected and fixed in 10% neutral-buffered formalin, embedded in paraffin, sectioned at 5 µm, and stained with hematoxylin and eosin for light microscopy. In addition, samples taken from lesions and exudates were submitted (Microbiology Laboratory, NIH Division of Veterinary Resources, Bethesda, MD) for culture, isolation, and sensitivity tests.

Results

From November 2005 to July 2008, a total of 37 mice representing 12 strains were found to be infected with *S. xylosus* (Table 1), which was considered to be the primary pathogen contributing to the death or euthanasia of the animal. Briefly, 25 male and 12 female mice were affected. Among the 1190 phagocyte-superoxide–deficient mice in the colony, 21 (1.76%) had abscesses affecting soft tissues or cervical lymph nodes (n = 19; 90.5%) and lungs (n = 13; 61.9%), followed by meninges and bone (n = 4 each; 19.0%). Gross lesions were characterized by subcutaneous masses or swollen cervical lymph nodes containing purulent material and tan to gray masses (diameter, 1 to 2 mm) in lung parenchyma. Histologically, the masses were multiple, confluent microabscesses which sometimes were surrounded by a dense fibrous connective tissue, with large colonies of cocci in the center of the abscess (Figures 1 and 2). In 4 of 13 CGD mice, inflammatory nodules in the lung were granulomatous with primarily histiocytic cell infiltrates. The center of most of the abscesses had eosinophilic crystals or spicules occasionally admixed with basophilic round cocci (diameter, 1 to 1.5 µm; Figure 3). In animals in which the microabscesses affected bone, bone lysis and new bone formation were a result of inflammatory infiltrates extending from soft tissues (Figure 4). Histologically, 4 animals had granulomas with bacterial colonies in the meninges (Figure 5), and 5 of 21 (23.8%) CGD mice had ulcerative skin lesions with granulocytic infiltrate and fibrosis. In general, the incidence of *S. xylosus* infection was higher in B6p47^{phox}[KO]HLL (8 of 98 males [8.16%] and 4 of 123 females [3.25%]) compared with B6.129S6-*Cybb*^{tm1Din}/J (4 of 209 males [1.91%] and 2 of 162 females [1.23%]) and B6.129S2-Ncf1^{tm1shl}N14 (1 of 288 males [0.34%] and 2 of 310 females [0.64%]) during the reporting period, and mostly breeders were affected.

In mice with normal phagocyte superoxide production (AKR/J-*Lvif*, B6;129-*Adora2a*^{tm1Dyj}/J, BALB/c, AKR/J-*Xpr1*^{Sxv}, C57BL/6NTac-[KO]FPR, C57BL/6NTac-[KO]P50NF-kB-[KO]P52NF-kB, C57BL/6J-[KO]RAG1 N10, NOD.Cg-*Prkdc*^{scid} *Il2rg*^{tm1Sug}/JicTac, and NFS/N-*Xpr1*^{Sxv} *Rmcf2*$^{+}$), the lesions mainly affected eyelids or ocular conjunctiva (10 of 16; 62.5%) and, to a lesser degree, caused dermatitis (7 of 16; 43.7%). Eyelids and conjunctiva of affected animals were swollen and irritated and had creamy yellow exudates around the margins. Some mice also had exophthalmus. Microscopically, the eyelids were ulcerated with serocellular crust formation of the lid margin and superficial colonization with colonies of cocci. Some cases demonstrated suppurative keratitis whereas more severely affected animals had histiocytic and lymphocytic infiltrates at the mucocutaneous junction with folliculitis, melanin drop-off, and rare thrombi in small vessels in adjacent skin.

The skin lesions in mice with normal production of phagocyte superoxide were characterized by ulcerations with underlying dermal and subcutaneous granulation tissue and neutrophilic infiltrate. In a C57BL/6J-[KO]RAG1 N10, there was necrotizing and vesicular dermatitis with a mixed inflammatory infiltrate. One AKR/J-*Lvif* mouse had perineal ulceration that affected the skin, anus, rectum, and vagina and formed a fistula into the adjacent skeletal muscle. Large colonies of coccoid bacteria were present on the fistula surface and invading the muscle. The adjacent soft tissues contained abundant granulation tissue (Figure 6). A C57BL/6NTac-[KO]P50NF-kB-[KO]P52NF-kB mouse had flaky skin on the tail with ulceration, which was characterized by suppurative dermatitis with multifocal ulceration, acanthosis, hyperkeratosis, and intracorneal bacterial colonization with cocci. A NOD.Cg-*Prkdc*^{scid} *Il2rg*^{tm1Sug}/JicTac mouse presented preputial gland thickening with a yellowish content. Micro-

Table 1. Clinical, histologic, and microbiologic characteristics of necropsied mice

Age (mo)	Sex	Strain	Lesion	Tissues or organs involved	Granuloma?	Microbiology
4	M	B6p47^{phox}[KO]HLL	Abscess	Head, neck, brain, and lung	Yes	*S. xylosus*
5	M	B6p47^{phox}[KO]HLL	Abscess	Cervical lymph nodes, mandible	No	*S. xylosus, E. coli, Micrococcus* sp.
7	M	B6p47^{phox}[KO]HLL	Abscess	Lung	No	*S. xylosus*
9	M	B6p47^{phox}[KO]HLL	Abscess	Cervical lymph nodes, maxilla, lung	No	*S. xylosus*
10	M	B6p47^{phox}[KO]HLL	Abscess	Lymph nodes, lung, limb skin and bone	No	*S. xylosus*
12	M	B6p47^{phox}[KO]HLL	Abscess	Lung	No	*S. xylosus*
16	M	B6p47^{phox}[KO]HLL	Abscess	Cervical lymph nodes, mandible	No	*S. xylosus*
6	F	B6p47^{phox}[KO]HLL	Abscess	Skin, lung, brain	No	*S. xylosus*
7	F	B6p47^{phox}[KO]HLL	Abscess	Cervical lymph nodes, maxilla, lung	No	*S. xylosus*
7	F	B6p47^{phox}[KO]HLL	Dermatitis	Muzzle skin	Yes	*S. xylosus*
7	F	B6p47^{phox}[KO]HLL	Dermatitis	Muzzle skin	Yes	*S. xylosus*
2	M	B6.129S6-*Cybb*^{tm1Din}/J	Abscess	Head, brain, lung	Yes	*S. xylosus, Enterococcus fecalis, Micrococcus* sp., *Bacillus* sp.
8	M	B6.129S6-*Cybb*^{tm1Din}/J	Abscess	Muzzle, skull	Yes	*S. xylosus*
12	M	B6.129S6-*Cybb*^{tm1Din}/J	Abscess	Maxilla, lymph node, lung	No	*S. xylosus*
12	M	B6.129S6-*Cybb*^{tm1Din}/J	Abscess	Maxilla, lymph node, lung, brain	No	*S. xylosus*
8	F	B6.129S6-*Cybb*^{tm1Din}/J	Abscess	Skull, leg, lymph node	Yes	*S. xylosus*
19	F	B6.129S6-*Cybb*^{tm1Din}/J	Abscess	Neck, lung	Yes	*S. xylosus*
7	M	AKR/J-*Lvif*	Conjunctivitis, blepharitis, dermatitis	Eyelid and conjunctiva, perineum	No	*S. xylosus, Corynebacterium pseudotuberculosis, Lactobacillus* sp., *Pasteurella* sp.
9	M	AKR/J-*Lvif*	Conjunctivitis, blepharitis	Eyelid and conjunctiva	No	*S. xylosus, S. epidermidis*
9	M	AKR/J-*Lvif*	Conjunctivitis, blepharitis	Eyelid and conjunctiva	No	*S. xylosus, S. sciuri, Enterococcus* sp., *Candida* sp., *Stenotrophomonas maltophilia*
12	M	AKR/J-*Lvif*	Conjunctivitis, blepharitis	Eyelid and conjunctiva	No	*S. xylosus*
12	M	AKR/J-*Lvif*	Conjunctivitis, blepharitis	Eyelid and conjunctiva	No	*S. xylosus*

Table 1. Continued

Age (mo)	Sex	Strain	Lesion	Tissues or organs involved	Granuloma?	Microbiology
6	F	AKR/J-*Lvif*	Skin/mucosal ulcers	Perineum, anus, rectum, vagina	No	*S. xylosus, E. coli, Enterococcus* sp.
21	M	B6.129S2-Ncf1^{tm1shl}N14	Abscess	Lung, pelvic muscles	No	*S. xylosus*
12	F	B6.129S2-Ncf1^{tm1shl}N14	Abscess	Leg muscles and bone	No	*S. xylosus*
19	F	B6.129S2-Ncf1^{tm1shl}N14	Dermatitis	Skin	No	*S. xylosus*
19	M	B6;129-*Adora2a*^{tm1Dyj}/J	Conjunctivitis, blepharitis	Eyelid and conjunctiva	No	*S. xylosus*
19	M	B6;129-*Adora2a*^{tm1Dyj}/J	Conjunctivitis, blepharitis	Eyelid and conjunctiva	No	*S. xylosus, Micrococcus* sp.
2	M	BALB/c	Conjunctivitis, dermatitis	Eye conjunctiva, skin	No	*S. xylosus*, *Aerococcus* sp., *Pasteurella* sp.
7	M	BALB/c	Dermatitis	Skin	Yes	*S. xylosus*
12	M	NOD.Cg-*Prkdc*^{scid} *Il2rg*^{tm1Sug}/JicTac	Adenitis	Preputial gland	No	*S. xylosus, Raoultella ornithinolytica*
1	M	C57BL/6Ncr-[KO] P47^{phox}N14	Abscess	Maxilla, lung	Yes	*S. xylosus*
24	M	NFS/N-*Xpr1*^{Sxv} *Rmcf2*$^{+}$	Vesiculitis	Seminal vesicle, urethra	No	*S. xylosus, E. coli, Enterobacter* sp.
1	F	C57BL/6NTac-[KO] P50NF-kB-[KO]P52NF-kB	Dermatitis	Skin	No	*S. xylosus, S. sciuri*
7	F	C57BL/6J-[KO]RAG1 N10	Dermatitis	Skin	No	*S. xylosus*
7	M	AKR/J-*Xpr1*^{Sxv}	Conjunctivitis, blepharitis	Eyelid and conjunctiva	No	*S. xylosus*
1	F	C57BL/6NTac-[KO]FPR	Blepharitis, keratitis	Eyelid, cornea	No	*S. xylosus*

M, male; F, female

scopically, large numbers of cocci and bacilli were observed within the preputial gland but without an obvious inflammatory response. However NOD.Cg-*Prkdc*^{scid} *Il2rg*^{tm1Sug}/JicTac mice are severe combined immunodeficient,[11] thereby explaining the lack inflammatory infiltrate. A NFS/N-*Xpr1*^{Sxv} *Rmcf2*$^{+}$ mouse had enlarged seminal vesicles containing a white opaque creamy and yellow-tinged creamy fluid. Multifocal to coalescing areas of fibrosis and fibroplasia of the seminal vesicle wall was noted, along with mucosal ulceration and a lymphocytic infiltrate with a large focus of plump macrophages containing amphophilic globular bodies. *S. xylosus* was isolated from all of these mice.

Granuloma formation was most common in gp91$^{-/-}$ mice (4 of 6; 66.6%) followed by p47$^{-/-}$ mice (4 of 15; 26.7%). Of 37 cases, *S. xylosus* was the only organism isolated from 27, and the remaining 10 had, in addition to *S. xylosus*, one or more other bacteria (Table 1). Colonies of cocci were observed on histologic examination in 26 of the 37 cases (70.27%). Sensitivity tests performed on 5 *S. xylosus* isolates from clinical cases revealed that the organism was susceptible to 13 commonly used antibiotics, including trimethoprim–sulfamethoxazole (Table 2). To manage the *S. xylosus* outbreaks in the CGD mice colony, management practices were modified and included replacing acidified drinking water with antibiotic (trimethoprim–sulfamethoxazole)-containing water and replacing woodchip bedding (SaniChip, Harlan Teklad) with paper-based bedding (Diamond Soft, Harlan Teklad). After instituting these changes, no additional cases of *S. xylosus* infection occurred in our CGD colony.

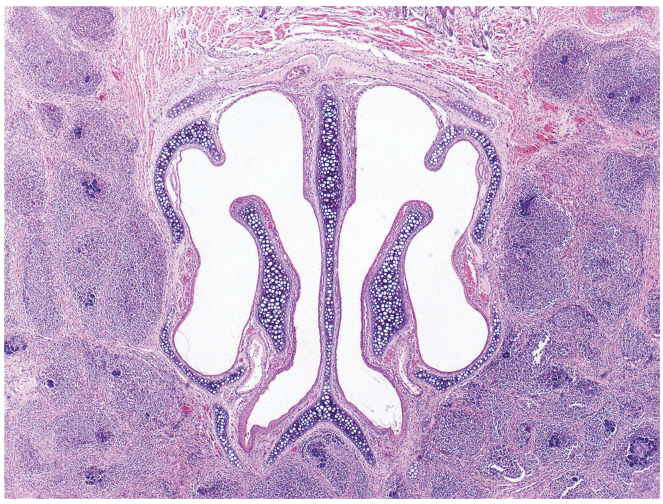

Figure 1. B6p47^{phox}[KO]HLL. Phagocyte superoxide-deficient mouse, nose. Transverse section showing multiple microabscesses surrounded by fibrosis affecting the masseter muscles. Hematoxylin and eosin stain; magnification, ×40.

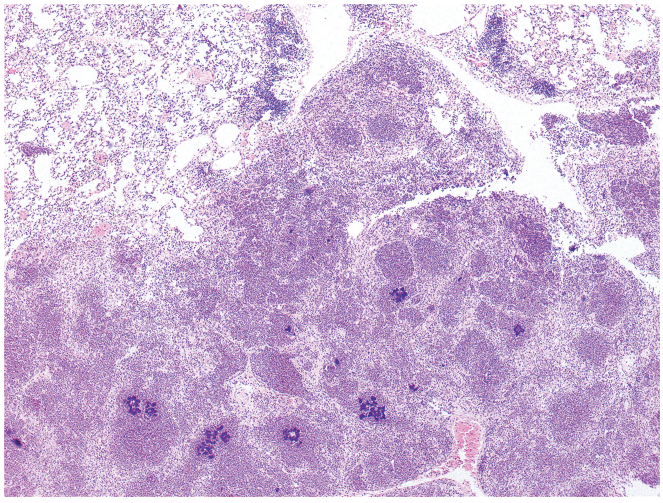

Figure 2. B6p47^{phox}[KO]HLL. Phagocyte superoxide-deficient mouse, lung. Low-power photomicrograph showing multiple coalescing microabscesses. Hematoxylin and eosin stain; magnification, ×40.

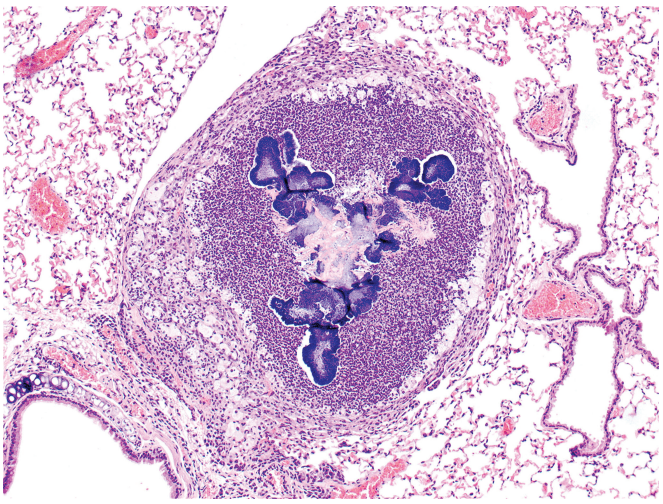

Figure 3. B6p47^{phox}[KO]HLL. Phagocyte superoxide-deficient mouse, lung. Eosinophilic crystals and spicules admixed with basophilic cocci in the center of a granuloma. Hematoxylin and eosin stain; magnification, ×100.

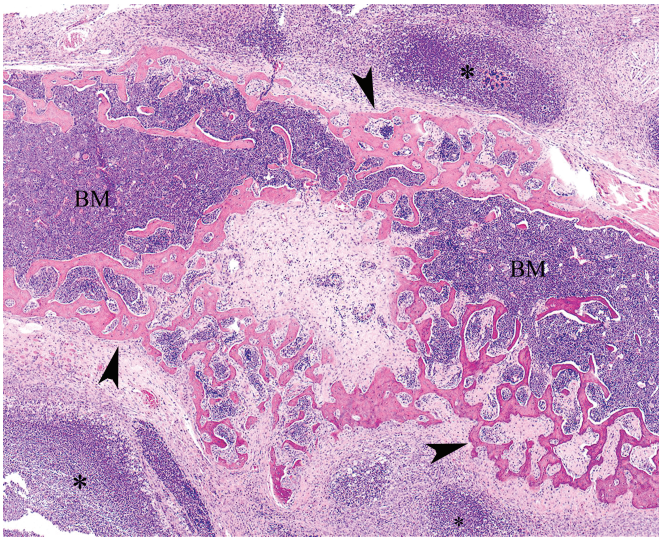

Figure 4. B6.129S2-Ncf1^{tm1shl}N14. Phagocyte-superoxide–deficient mouse, front leg. Chronic suppurative cellulitis, with bone lysis and new bone formation (arrowheads) associated with *Staphylococcus xylosus* abscesses (asterisk). BM, bone marrow. Hematoxylin and eosin stain; magnification, ×40.

Discussion

Staphylococcus xylosus is considered a common skin commensal of rodents and other mammals.[23] Reports of *S. xylosus* as a primary pathogen in human and veterinary medicine are scarce. Acute pyelonephritis,[36] endocarditis,[7] and septicemia[16] have been reported to occur in humans. In domestic animals, *S. xylosus* has been isolated from mastitis in dairy cows[21] and ewes.[8] In laboratory animals, *S. xylosus* has been associated with nasal dermatitis in gerbils.[32] However, despite the large number of mice used in research compared with other species, only 5 reports describe spontaneous infections due to *S. xylosus* in mice. One outbreak of *S. xylosus* caused severe necrotizing dermatitis and high mortality in an athymic nude mice colony.[4] Another report[12] described 2 cases of *S. xylosus* infections affecting the periauricular soft tissue, plantar surface of the feet, and lung in a p47^{phox} knockout mouse colony. A subsequent study[13] reported similar lesions affecting feet, tail, lymph nodes, and lung due to spontaneous *S. xylosus* infections in p47^{phox}-deficient mice, with a lower incidence in animals that had received prophylactic γ-interferon. In addition, *S. xylosus* was occasionally isolated from subcutaneous abscesses and, in one case, from lung in a gp91$^{-/-}$ Cybb mouse colony.[3] *S. xylosus* was isolated from multiple ulcerated skin lesions in a C57BL/6J-*Nos2*^{tm1Lau} mouse colony (mice with deletion of the nitric oxide synthase gene).[37] Recently pure cultures of *S. xylosus* have been inoculated experimentally into artificially created skin lesions on the tails of SJL/J mice to determine pathogenicity.[33] The intradermal tail inoculations produced focal to multifocal erythema, hyperemia, edema, ulcerative dermatitis, and scar tissue formation. Bacterial colonies were observed in and around the artificially created wounds.[33] However, the infection was confined to the inoculated area, with no lesions observed in other organs, the pattern expected in immunocompetent mice.

We found that most of the spontaneous infections in our CGD mice were due to *S. xylosus* and not to *S. aureus*, which is a common cause of skin infections in animals and humans.[14] Mixed infections occasionally were observed, but *S. xylosus* was, in most cases, the only organism isolated. *S. aureus* was not isolated from any of these cases. This situation is in contrast to previous reports from

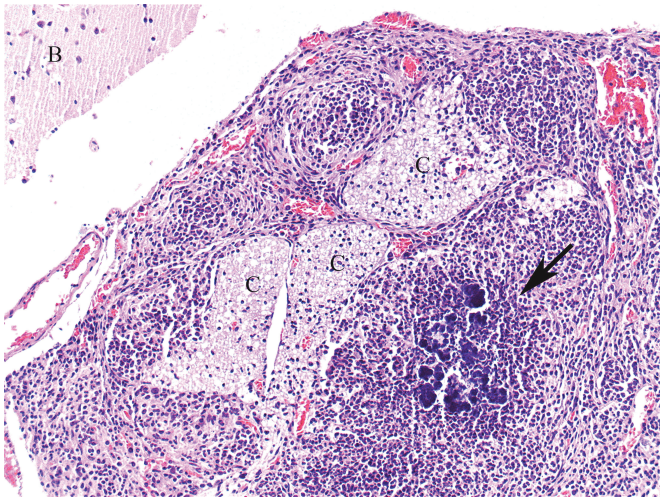

Figure 5. B6.129S6-*Cybb*^{tm1Din}/J. Phagocyte-superoxide–deficient mouse, brain (B) and meninges. Granuloma containing cocci colonies (arrow) in the meninges next to cranial nerves (C). Hematoxylin and eosin stain; magnification, ×200.

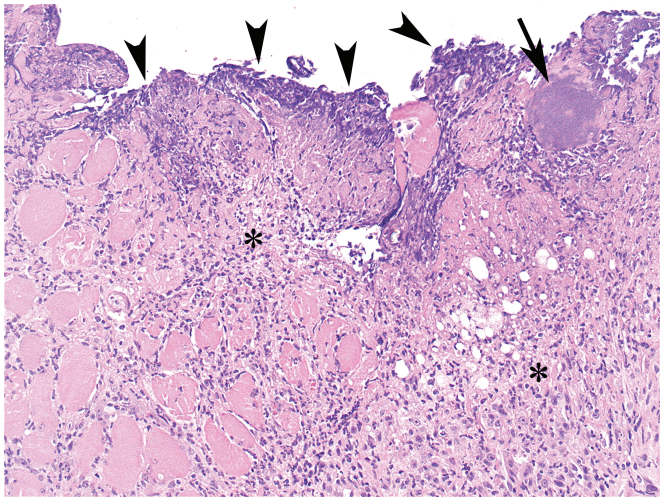

Figure 6. AKR/J-*Lvif* mouse, skeletal muscle; fistula. Photomicrograph showing colonies of coccoid bacteria on the fistula surface (arrowheads) and deeper in the tissue (arrow). Note the abundant granulation tissue and fibrosis with mild neutrophilic infiltrate and edema on the adjacent tissue (asterisk). Hematoxylin and eosin stain; magnification, ×200.

other investigators, in which *S. xylosus* occurred only occasionally and was not the main cause of morbidity or mortality in the CGD mouse colony.[3,12] In addition, to our knowledge, *S. xylosus* has not been reported previously as a cause of myositis, bone lysis, and meningitis in CGD or other mouse strains, as we describe here. These lesions highlight the importance of *S. xylosus* as an emerging and serious pathogen in laboratory mice, particularly in immunodeficient strains. Abscesses observed in CGD mice are also sometimes referred to as botryomycosis. The eosinophilic material admixed with colonies of bacteria is known as Splendore–Hoeppli material and is thought to be composed of antigen–antibody complexes.[24] Alternatively, the spicules and crystals observed in the abscesses may be composed of Ym1 protein as described in p47^{phox}-deficient mice.[9]

Mice deficient in phagocyte superoxide may develop severe disease after *S. xylosus* infection characterized by soft tissue abscesses and granulomas, as part of the expected phenotype, with extension to regional lymph nodes, lungs, and, to a lesser degree, muscle, bone, and meninges. In contrast, in mice with normal production of phagocyte superoxide, the infections tend to be superficial and are confined to eyelids, ocular conjunctiva and skin and rarely affect other tissues or organs. Some skin infections may have been secondary to idiopathic ulcerative dermatitis in mice with a C57BL/6 background. In any case, mice with normal production of phagocyte superoxide but with other immune deficiencies are occasionally susceptible to develop superficial lesions in which *S. xylosus* is the primary pathogen or at least contributes to the pathogenesis of the inflammation. Although 37 cases in a 32-mo period in a rodent barrier colony with an estimated daily census around 20,000 mice may appear to be negligible, the majority of cases occurred in the CGD rodent model colony, which contains an average of only 25 breeder pairs, making infection with *S. xylosus* the exclusive cause of morbidity or mortality in our CGD rodent breeding colony during that period.

Table 2. Antibiotic susceptibility of *Staphylococcus xylosus* isolates from 5 clinical cases

Antibiotic	Growth inhibition (mm)
Ampicillin	29–42
Chloramphenicol	20–24
Clindamycin	23–28
Cephalothin	26–42
Ceftriaxone	21–30
Erythromycin	23–26
Kanamycin	22–27
Penicillin G	29-43
Streptomycin	20
Trimethoprim–sulfamethoxazole	23–26
Tetracycline	20–28
Vancomycin	16–20
Oxacillin	15–21

The *S. xylosus* isolates from our colony were sensitive to most common antibiotics. This result is in contrast to reported infections by drug-resistant strains which is common in domestic animals and humans.[5,16,38] The woodchip bedding in our CGD mice colony was replaced with paper-based bedding due to our concern that the sharp edges of the woodchip bedding material may have caused microabrasions in the skin or conjunctiva of the animals, leading to subsequent infection by *S. xylosus*. In addition to hematogenous or lymphatic spread, pneumonia might have been a result of cocci migrating from the nasal cavity to the lungs, and meningitis might have been a result of active bacterial migration or extension from muzzle lesions possibly through cranial nerves. Bone lysis occurred due to the action of the bacterial infection and the resultant inflammatory response against the infection.

In conclusion, *S. xylosus* is an important pathogen in mice with defective production of phagocyte superoxide and in other immunocompromised strains. Because bacterial culture and isolation are not performed routinely from mice with abscesses in some animal facilities, *S. xylosus* infections are likely to be underdiagnosed compared with the more typical pathogen, *S. aureus*. *S. xylosus* should be considered in the differential diagnosis in mice, especially immunodeficient animals, with abscesses and other skin lesions. This report expands the range of mice strains and tissues and organs susceptible to spontaneous *S. xylosus* infections and notes differences in the pathology of the infection between strains.

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