Suspected transmission of methicillin-resistant
*Staphylococcus aureus* between domestic
pets and humans in veterinary clinics
and in the household

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Abstract

Objective: To describe MRSA infection and colonization in household pets, and transmission of MRSA between animals and humans.

Methods: MRSA infection and colonization in household pets and human contacts were evaluated during investigations initiated after identification of MRSA infection or colonization of a household pet in order to determine if there had been transmission between animals and humans. All MRSA isolates were screened for Panton–Valentine leukocidin (PVL) genes by use of polymerase chain reaction, and isolate relatedness was determined by use of pulsed-field gel electrophoresis (PFGE).

Results: Investigations of six situations where MRSA was identified in one or more animals in a household or veterinary facility were performed. MRSA was isolated from 8 animals (5 dogs and 3 cats) with clinical infections, 1 cat that was in contact with 2 infected cats and 14/88 (16%) of household contacts or veterinary personnel. Both animal-to-human and human-to-animal transmission were suspected. An indistinguishable MRSA isolate was recovered from at least one human that was in contact with each animal case. All isolates were classified as Canadian epidemic MRSA-2, the predominant community-associated MRSA clone in humans in Canada. No isolates possessed genes encoding for the PVL.

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Conclusions: Transmission of MRSA between humans and animals, in both directions, was suspected. MRSA appears to be an emerging veterinary and zoonotic pathogen.
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1. Introduction

Methicillin-resistant Staphylococcus aureus (MRSA) is an established pathogen in most human healthcare facilities. In the United States, MRSA is reported to be associated with over 125,000 hospitalizations annually (Kuehnert et al., 2005). In addition, MRSA infection has been associated with increased morbidity and mortality compared to methicillin-sensitive S. aureus infections (Engemann et al., 2003). Recently, infections due to MRSA have been documented in children and adults who lack traditional risk factors (Centers for Disease Control and Prevention, 1999; Herold et al., 1998; Nguyen et al., 2005). Most infections caused by these community-associated (CA) MRSA appear to involve the skin and soft tissues, however life-threatening infections can develop in otherwise healthy patients (Centers for Disease Control and Prevention, 1999). Perhaps associated with dissemination of MRSA in the community in humans has been the identification of MRSA infection in household pets (Baptiste et al., 2005; Boag et al., 2004; Loeffler et al., 2005; Pak et al., 1999; Rankin et al., 2005; Rich and Roberts, 2004; Tomlin et al., 1999; van Duijkeren et al., 2004a). The emergence of MRSA in household pets is of concern in terms of animal health, and perhaps more importantly, the potential for animals to act as sources of infection or colonization of human contacts.

Most reports of MRSA in pets have involved clinical cases or outbreaks, and less is known about colonization rates in pets in the community. At this point, MRSA colonization appears to be uncommon in this group. A study of dogs and cats presented to primary care veterinary clinics did not identify MRSA in 188 dogs and 39 cats (Murphy et al., 2005). Similarly, a study of dogs that visit human hospitals did not identify MRSA in any of 102 dogs (Lefebvre et al., in press) while a study of dogs presented to a tertiary care veterinary hospital only identified MRSA colonization in 2/203 (1%) dogs (Hanselman et al., 2005). There are previous case reports of suspected interspecies transmission of MRSA. In one, a colonized dog was identified as a source of re-infection of a household contact (Cefai et al., 1994), while in another, recurrent MRSA colonization in two humans in a household was only eliminated after identification and treatment of colonization of their dog (Manian, 2003). A colonized dog was also suspected as being a source of recolonization in a nurse in the Netherlands (van Duijkeren et al., 2004b). A recent study reported isolation of MRSA from the nasal or oral mucosae of 17.9% of staff in a veterinary teaching hospital, suggesting that veterinary staff may be at higher risk for MRSA colonization (Loeffler et al., 2005), while another study reported concurrent colonization of dogs and veterinary hospital staff with indistinguishable strains (Baptiste et al., 2005). By itself, identification of concurrent colonization with indistinguishable MRSA isolates suggests interspecies transmission, however it cannot actually confirm interspecies transmission nor can it confirm the direction of transmission. Epidemiological data are required to provide a better understanding of the dynamics of MRSA transmission in households and veterinary clinics. This study describes evaluation of MRSA infection and colonization in household pets, and transmission of MRSA between animals and humans.

2. Materials and methods

2.1. Case investigations

Investigations were instigated following reports from primary care veterinarians of MRSA infection in household pets. Initial isolation of MRSA was made by the referring veterinarian through submission of specimens to veterinary diagnostic laboratories. Following identification of MRSA, the veterinarian or laboratory personnel contacted the authors, who initiated an investigation. Veterinary personnel and
owners of infected pets were contacted, and diagnostic samples were requested from animals and humans that have been in contact with the affected pet. Single nasal swabs were collected from humans, while one or more of nasal, pharyngeal, rectal and perineal swabs were collected from animals. Swabs were placed in liquid Stuart’s or Amies’ medium. Samples were stored at 4 °C, shipped to the laboratory on ice, and processed within 24 h of arrival at the laboratory. Information regarding direct or indirect contact with the human healthcare system (i.e. employment in healthcare system, hospitalization, cohabitation with a healthcare worker or recently hospitalized individual, antimicrobial therapy) was collected from the owners and veterinary personnel whenever possible.

2.2. Specimen processing

Swabs were inoculated onto mannitol-salt agar with 2 µg/ml oxacillin and incubated aerobically at 35 °C for 48 h. Colonies were identified as *S. aureus* based on colony morphology, Gram stain appearance, ability to ferment maltose, and positive tube coagulase test or latex agglutination test (Pastorex Staph Plus, Bio-Rad Laboratories Ltd., Mississauga, Canada).

Antimicrobial susceptibility testing was performed by broth microdilution as per Clinical and Laboratory Standards Institute (CLSI) guidelines (National Committee for Clinical Laboratory Standards, 2000). Susceptibility to oxacillin, erythromycin, clindamycin, ciprofloxacin, vancomycin, mupirocin, tetracycline, doxycycline, rifampin, gentamicin, fusidic acid, trimethoprim-sulfamethoxazole, dalfopristin-quinupristin and linezolid was evaluated. Methicillin-resistance was confirmed via penicillin binding protein 2a (PBP2a) latex agglutination test (PBP2’ Test Kit, Oxoid, Hants, UK).

Isolates were typed via pulsed field gel electrophoresis (PFGE) following *SmaI* digestion (Mulvey et al., 2001). SCCmec typing was performed as has been previously described on a representative isolate from each case investigation (Oliveira and DeLencastre, 2002). These isolates were also tested for the presence of the Panton–Valentine leukocidin (PVL) genes by PCR and by molecular beacon using the *lukF* component of *pvl* (O’Brien et al., 2004). Amplification of the *pvl* gene was performed using the following primers: LukS-PV: GGCCITTCAATACACATATTG; LukF-PV: CCAAATACCTTCATAAATTG. The beacon experiment was carried out using the following beacon and primers:

- **lukF** beacon: 5’-6-FAMd(CGCGAAGAATTTATTGGTGTCCTATCTCGCG)DABCYL 3’;
- LukF F: 5’-GCCAGTGTTATCCAGAGG-3’;
- LukF R: CTATCCAGTTGAAGTTGATCC-3’.

The University of Guelph Research Ethics and Animal Care Committees approved this study.

3. Results

The authors received thirty-seven reports of MRSA infection in household pets in Canada and the United States between July 2000 and Jan 2004; with the majority being reported in 2003 and 2004. In six of these cases, owners and veterinary personnel consented to provide additional diagnostic samples, and transmission of MRSA within the veterinary clinic and household were evaluated (Table 1). Overall, MRSA

<table>
<thead>
<tr>
<th>Case</th>
<th>Location</th>
<th>Index animal</th>
<th>Colonized animal contacts</th>
<th>Colonized human contacts</th>
<th>Subsequent clinical infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pennsylvania</td>
<td>Dog</td>
<td>No</td>
<td>Yes 4/37 (11%)</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>Washington state</td>
<td>Two kittens</td>
<td>Yes 1/2 (50%)</td>
<td>Yes 4/25 (16%)</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td>New York state</td>
<td>Dog</td>
<td>No</td>
<td>Yes 3/23 (13%)</td>
<td>Yes: 1 dog</td>
</tr>
<tr>
<td>4</td>
<td>Ontario</td>
<td>Dog</td>
<td>No</td>
<td>Yes 1/1 (100%)</td>
<td>No</td>
</tr>
<tr>
<td>5</td>
<td>Ontario</td>
<td>Dog</td>
<td>No</td>
<td>Yes 1/1 (100%)</td>
<td>No</td>
</tr>
<tr>
<td>6</td>
<td>Quebec</td>
<td>Cat</td>
<td>No</td>
<td>Yes 1/1 (100%)</td>
<td>No</td>
</tr>
</tbody>
</table>

*Identified as colonized with an indistinguishable isolate during the study period.

*Nosocomial infections occurring after identification of the index case and caused by an isolate indistinguishable from that from the index case.*
was isolated from 8 clinically affected animals (5 dogs and 3 cats) as well as 1 cat that was in contact with 2 affected cats and 14/88 (16%) human contacts from these investigations.

3.1. Case studies

3.1.1. Case 1

A post-operative infection was identified in a dog 14 days after a limb amputation. The dog had remained hospitalized throughout the entire post-operative period. One week after the report of MRSA infection, screening of clinic personnel was performed and 4/37 (11%) individuals were identified as colonized. The dog’s owners declined submission of MRSA screening samples. The human and canine isolates were indistinguishable isolates of Canadian epidemic MRSA-2 (CMRSA-2), possessed SCCmecII and were negative for PVL. Isolates were resistant to oxacillin, erythromycin, clindamycin and ciprofloxacin, and susceptible to vancomycin, mupirocin, tetracycline, doxycycline, rifampin, trimethoprim-sulfamethoxazole, gentamicin, fusidic acid, dalfopristin-quinupristin and linezolid. Nasal colonization persisted for 9 months in one of the kittens, but was not detected subsequently, despite not receiving eradication therapy. No risk factors for MRSA colonization were reported in members of the household.

3.1.2. Case 2

Two 6 month old kittens were presented to a veterinary clinic with signs of chronic rhinitis. MRSA was isolated from nasal swabs from both animals. Nasal swabs were collected from 22 clinic personnel and the two owners, as well as one other cat in the household. MRSA was isolated from one technician in the veterinary clinic who had been in contact with both kittens, as well as both owners and the other cat in the household. Upon further discussion, it was reported that the kittens were siblings that had been obtained from a feline rescue center and that a number of littermates had died of an unknown infectious disease prior to weaning. Samples were collected from the operator of the facility and the mother of the kittens. MRSA was isolated from the facility operator but not the cat. All isolates were indistinguishable isolates of CMRSA-2, possessed SCCmecII and were negative for PVL. Isolates were resistant to oxacillin, erythromycin, clindamycin, ciprofloxacin and mupirocin, and susceptible to vancomycin, rifampin, trimethoprim-sulfamethoxazole, gentamicin, fusidic acid, dalfopristin-quinupristin and linezolid. Nasal colonization persisted for 9 months in one of the kittens, but was not detected subsequently, despite not receiving eradication therapy. No risk factors for MRSA colonization were reported in members of the household.

3.1.3. Case 3

An adult dog was referred to a veterinary clinic for evaluation of a post-operative infection. An amputation had been performed at a different clinic 6 days prior presentation, and the dog had only been discharged from the first clinic 24 h earlier. MRSA was isolated from purulent debris at the surgical site at the time of admission to the second clinic, and the owner reported contact with purulent discharge while assisting the dog into the clinic. Approximately 10 days after initial presentation, nasal swabs were collected from 22 veterinary personnel and the dog owner; MRSA was isolated from 2 (9%) clinic personnel and the owner of the first dog. No swabs were collected from personnel at the first clinic. No clinical abnormalities were present or developed in any of the colonized individuals. Shortly after collection of the nasal swabs from clinic personnel, a post-operative MRSA infection was identified in another dog from the second clinic. The first dog had been euthanized because of severe non-responsive cellulates and osteomyelitis prior to admission of the second affected dog. The second dog had been attended by both of the colonized clinic personnel. All isolates were indistinguishable on PFGE, classified as CMRSA-2, possessed SCCmecII and were negative for PVL. Isolates were resistant to oxacillin, erythromycin, clindamycin, ciprofloxacin and mupirocin, and susceptible to vancomycin, tetracycline, doxycycline, rifampin, trimethoprim-sulfamethoxazole, gentamicin, fusidic acid, dalfopristin-quinupristin and linezolid. The dog’s owner reported no putative risk factor for MRSA colonization. After identification of the second case, barrier precautions were used for any contact with the infected animal. Colonized clinic personnel were referred to their physician for
eradication therapy and no further MRSA infections were identified at that clinic over the next year.

3.1.4. Case 4
A post-operative MRSA incision infection was identified in a dog following peri-ocular surgery. After identification of the infection, an indistinguishable isolate was also isolated from the owner who had previously been identified as colonized during hospitalization. Both isolates were indistinguishable, CMRSA-2, possessed SCCmecII, spa type 2 and negative for PVL. Isolates were resistant to oxacillin, erythromycin, clindamycin, ciprofloxacin and mupirocin, and susceptible to vancomycin, tetracycline, doxycycline, rifampin, trimethoprim-sulfamethoxazole, gentamicin, fusidic acid, dalfopristin-quinupristin and linezolid. No additional screening was performed and follow-up information was not available.

3.1.5. Case 5
MRSA lower urinary tract infection was identified in a dog whose owner had acquired MRSA following surgery earlier in the year. A nasal swab was collected from the owner after recognition of the pet’s infection, and an indistinguishable isolate was recovered. Both isolates were indistinguishable, CMRSA-2, possessed SCCmecII, and negative for PVL. Isolates were resistant to oxacillin, erythromycin, clindamycin and ciprofloxacin, and susceptible to vancomycin, mupirocin, tetracycline, doxycycline, rifampin, trimethoprim-sulfamethoxazole, gentamicin, fusidic acid, dalfopristin-quinupristin and linezolid. No additional screening was performed and follow-up information was not available.

3.1.6. Case 6
MRSA lower urinary tract disease was identified in a cat whose owner worked in a nursing home. The owner had previously been identified as colonized with MRSA, and an isolate indistinguishable from the cat’s isolate was subsequently recovered from a rectal swab from the owner. Both MRSA isolates were indistinguishable, CMRSA-2, SCCmecII and negative for PVL. Isolates were resistant to oxacillin, erythromycin, clindamycin and ciprofloxacin, and susceptible to vancomycin, mupirocin, tetracycline, doxycycline, rifampin, trimethoprim-sulfamethoxazole, gentamicin, fusidic acid, dalfopristin-quinupristin and linezolid. No additional screening was performed and follow-up information was not available.

4. Discussion
While concurrent colonization with MRSA has been identified in humans and animals, this study further information suggesting that MRSA can be transmitted between humans and animals many times within a household or veterinary clinic. Because of the nature of the study, a temporal association can only be made, however results of this study, particularly in Cases 2 and 3, strongly suggest interspecies transmission and support previous concerns that pets could become household reservoirs of MRSA for subsequent infection (or re-infection) of susceptible household members. Both human-to-animal and animal-to-human transmissions were suspected, but the origin of infection was not always clear. In Case 1, the dog could have been colonized at the time of admission to the first veterinary clinic and subsequently developed clinical infection, or veterinary personnel could have been the source. Nosocomial infection is suspected, but regardless of the source of infection in the dog, it is likely that the dog was the source of colonization of some or all of the affected veterinary personnel. While this cannot be proven, it seems unlikely that four personnel in the clinic would be independently colonized from other sources with an indistinguishable strain and one that was indistinguishable from a dog under their care.

The number of instances of MRSA transmission and the timeframe over which colonized animals and humans were encountered in Case 2 was interesting. Based on the pattern of contacts, the timing of isolation and the apparent low prevalence of MRSA in the general pet population, it is apparent that MRSA infection originated in the animal rescue operation, unless the colonized person was independently with an indistinguishable strain; something that is considered unlikely. It is unclear whether the facility operator or other cats were the original source, however because there was no reported contact between the colonized animal rescue facility operator and the kittens’ owners, it is presumed that MRSA was transmitted by the kittens to both owners, one other cat and one person in the veterinary clinic. It is concerning that
MRSA was isolated from one of the kittens for up to 9 months after initial diagnosis. If household pets can be colonized for prolonged periods of time, the potential for transmission of MRSA to household members and other contacts could be high.

In the third case, it is presumed that the dog was infected at the first veterinary clinic because purulent discharge was apparent at the surgical site within 24 h of discharge. The owner was presumably colonized via contact with the purulent discharge, but the possibility that the owner or dog or both were colonized prior to admission to the first clinic cannot be excluded. Regardless, contact with this dog resulted in colonization of two veterinary personnel. Because the first dog was no longer hospitalized by the time the second infected dog was admitted, it is presumed that one of the colonized personnel was the source of infection of the second dog. MRSA has been identified in the environment in veterinary hospitals (Loeffler et al., 2005; Weese et al., 2004), however the significance of environmental contamination is unclear and personnel-based transmission is considered more likely.

In Cases 4–6, owners were presumed to have infected pets after developing nosocomial MRSA infection (Cases 4 and 5) or becoming colonized while working in hospital (Case 6). These cases highlight the potential for household pets to become community-based reservoirs of infection or re-infection of household contacts. This may be of particular concern with healthcare workers who could subsequently transmit MRSA to patients.

The high-level (>256 mg/L) mupirocin resistance in isolates from Cases 3, 4 and 6 was noteworthy. While uncommon, high-level mupirocin resistance has been identified in humans (Kresken et al., 2004; Mulvey et al., 2005), and there is one report of colonization of a dog with mupirocin resistant MRSA (Manian, 2003). Mupirocin resistance is of significance because mupirocin is commonly used for eradication of nasal MRSA colonization and treatment of skin and soft tissue infections (Mody et al., 2003; Rohr et al., 2003), and in vitro mupirocin resistance has been associated with treatment failure (Walker et al., 2003).

All isolates were classified as CMRSA-2 (ST5-MRSA-II), which is related to the USA100 clone, otherwise referred to as the New York or Japanese clone (Simor et al., 2005). This is a hospital-origin clone that is the most common cause of community-onset MRSA infection in people in Canada, likely reflecting the movement of CMRSA-2 from hospitals into the community (Simor et al., 2002, 2005), although clones with properties more typical of community-associated isolates (SCCmecIV, PVL positive, resistant to fewer antimicrobials or only to beta-lactams) are increasing in frequency in humans in North America (Kourbatova et al., 2005; Mulvey et al., 2005). It is unclear whether the predominance of CMRSA-2 in these pets indicates that pets are more susceptible to infection with CMRSA-2 compared to other MRSA types, as is apparent with CMRSA-5 (ST8-MRSA-IV) in horses in North America (Weese et al., 2005a, 2005b), or whether this is based on exposure of these pets to CMRSA-2 and not other MRSA clones. Further study of MRSA in animals, particularly in areas where different MRSA clones are increasing in prevalence, is required to clarify this situation.

Regardless, the predominance of common human MRSA clones in household pets is consistent with observations in the United Kingdom (Boag et al., 2004; Loeffler et al., 2005; Rich and Roberts, 2004) and suggests that household pets likely acquire MRSA via direct contact with infected or colonized humans, as opposed to dissemination of veterinary-specific clones or acquisition of methicillin resistance de novo by methicillin-susceptible community isolates of S. aureus. Genes encoding for PVL production were not identified in this study. This toxin has been associated with community-associated disease, including skin and soft tissue infections, severe pneumonia and sepsis (Centers for Disease Control and Prevention, 1999; Francis et al., 2005), and has been recently identified in MRSA isolates from dogs, cats, a rabbit and a parrot in the United States (Rankin et al., 2005).

As MRSA becomes more common in humans in the community, it is becoming apparent that this can be reflected in household pets. This is a disturbing situation because of the potential for both human and animal disease, and complicates control of this pathogen. Investigation of CA-MRSA in humans should involve consideration both of animals as sources of infection, and animals as potential subsequent reservoirs of infection should they acquire MRSA in the household. Surveillance and infection control measures aimed at evaluating humans and their pets must be evaluated to limit the impact of MRSA on both populations.
References


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