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Risk factors for meticillin-resistant *Staphylococcus aureus* (MRSA) carriage in MRSA-exposed household pets

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Abstract

Background: Household pets can carry meticillin-resistant *Staphylococcus aureus* (MRSA) introduced to the home by their human companions. Specific factors promoting pet carriage of this pathogen have not been fully elucidated.

Objective: This study evaluated MRSA cultured from pets and the home environment in households where an MRSA human infection had been identified, and aimed to determine potential risk factors for pet MRSA carriage.

Materials and Methods: Humans diagnosed with community-associated MRSA (CA-MRSA) skin or soft-tissue infection (SSTI) in the mid-Atlantic United States were identified. One hundred and forty two dogs and cats from 57 affected households were identified of which 134 (94.4%) pets and the household environment were sampled for bacterial culture, PCR confirmation and *spa*-typing for MRSA strain determination. Samples were obtained three months later from 86 pets.

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CONFLICTS OF INTEREST

No conflicts of interest were reported in regard to publication of this research.

Results: At baseline, 12 (9.0%) pets carried MRSA. Potential risk factors associated with carriage included pet bed (environmental) MRSA contamination, flea infestation and prior antimicrobial use in the pet. Pets tended to carry human-adapted MRSA strains and *spa*-types of MRSA isolates cultured from pets were concordant with strains cultured from the home environment in seven of eight homes (87.5%) at baseline.

Conclusions and clinical relevance: Results may inform risk-based veterinary clinical recommendations and provide evidence for selective pet testing as a possible alternative to early removal of pets from the homes of humans infected with MRSA. MRSA contamination of the home environment probably is an important risk factor for pet MRSA carriage, and household interventions should be considered to reduce risk of MRSA carriage in exposed pets.

Keywords

meticillin-resistant *Staphylococcus aureus* (MRSA); community-associated; zoonotic; antimicrobial use; environment; *spa* types

INTRODUCTION

Transmission of meticillin-resistant *Staphylococcus aureus* (MRSA) is known to occur bidirectionally between humans and animals, including in household settings, yet the role of household pets as reservoirs for human MRSA infection and factors promoting pet MRSA carriage are not fully elucidated.[1,2]

Pet- and household-related characteristics previously found to be associated with pet MRSA carriage include pet species, pet age and sex, treatment with antimicrobials, exposure to veterinary clinics and close contact with a human MRSA patient (see Supporting information Methods S1 for details). Environmental contamination with MRSA[3,4] is a risk factor for MRSA carriage and reinfection in humans. Previous studies have demonstrated correlation of MRSA strains among animals, humans and their shared home environments.[5,6]

This study assessed risk factors for MRSA carriage in pets living with humans previously diagnosed with MRSA skin or soft-tissue infection (SSTI). Furthermore, staphylococcal protein A (*spa*-)types of MRSA isolates cultured from humans, pets and household environments were compared. We hypothesised that antimicrobial use, environmental MRSA contamination and close human–pet contact may be risk factors for pet MRSA carriage and that MRSA isolates obtained from pet and environmental samples would have the same *spa*-type.

METHODS

Human participants provided written informed consent for their participation in the study. Pet sampling was approved by the Johns Hopkins School of Public Health Animal Care and Use Committee (ACUC), and pet owners provided written informed consent. Human index patients diagnosed around one month previously with CA-MRSA SSTI, their cohabitating family members and their domestic animals were enrolled.

Between January and December 2012, in collaboration with the University of Pennsylvania School of Medicine and other institutions, 88 human index participants representing 95 households in the mid-Atlantic region were enrolled into the "Pets and Environmental Transmission of Staphylococci" (PETS) study.[7] PETS was a sub-study of a randomised controlled trial (RCT; Epidemiology and Transmission of MRSA in the Community, NCT00966446) which evaluated the effectiveness of MRSA decontamination (one week nasal mupirocin and two chlorhexidine-based body washes) through sampling of household members for MRSA at bi-weekly home visits for six months.

The PETS study occurred in a MRSA-enriched environment (based on known MRSA patient status) and involved two household pet and home environment sampling events: one baseline visit roughly 30 days after SSTI diagnosis for initial enrollment, and one three months later for longitudinal comparison of MRSA *spa*-types.

At each household visit, all pets were sampled at the nares or nasal planum, the tongue, gingiva or hard palate, and inguinal and perineal regions. Sterilised electrostatic cloths (Swiffer, Proctor & Gamble; Cincinnati, OH, USA) were used as described previously[8,9] for environmental surface sampling of settled dust from nine environmental sites.

Meticillin resistance was confirmed by the presence of a *mecA* or *mecC* gene (which encode altered penicillin-binding proteins) by universal *mec*-testing,[10] and isolate species (*S. aureus*) was confirmed by multiplex PCR analysis of the nuclease (*nuc*) gene.[11,12]

Presence of detectable MRSA in this pet population is defined as pet MRSA carriage, as this study cannot distinguish between contamination, infection or transmission. Variables evaluated as potential risk factors of interest included pet characteristics (Table 1a) and household characteristics (Table 1b).

Data from the baseline visit and a three month follow-up visit were analysed using STATA (v14) software (StataCorp; College Station, TX, USA). Estimates of associations between detection of MRSA in pets and potential risk factors were obtained using survey-weighted unadjusted and adjusted logistic regression (see Methods S1 for more detail). The *spa*-types of MRSA isolates were compared between human, pet and environmental samples, and a longitudinal comparison of *spa*-types from pet isolates was conducted.

RESULTS

Sixty-seven (70.5%) of 95 enrolled households reported ownership of at least one pet of any species; only dogs and cats were included in analyses. Participating pets at baseline included 71 dogs and 63 cats from 57 households. Tables 1a and 1b provide pet signalment/demographics and unadjusted risk factor data for pet MRSA carriage.

Eight (14.0%) of 57 households had at least one MRSA-positive pet. The prevalence of MRSA positivity at baseline was 9.0% (12 of 134 sampled pets; Table 1a). Five (7.0%) of seventy-one sampled dogs and seven (11.1%) of 63 sampled cats carried MRSA at baseline. On unadjusted logistic regression, risk factors significantly associated with pet carriage of MRSA included antimicrobial use in the pet and pet bed (environmental) MRSA

contamination. At baseline, 100% of MRSA-positive pets lived in homes where one or more human-associated environmental site (not counting the pet bedding) was MRSA-positive, and 11 pets (91.7%) with detectable MRSA carried a *spa*-type concordant with that detected in the home environment. At the three month visit, 86 pets were tested (38 dogs and 48 cats). In only one of seven MRSA-culture positive pets (14.3%) was the environment MRSA-negative at this time point.

Seventy four pets were tested both at baseline and three months, and of these 13 (17.6%) were MRSA-positive at either or both time points. Of the nine longitudinally-sampled pets that were MRSA-positive at the first visit, five (55.5%) pets cleared MRSA carriage during this time and four (44.4%) pets had persistent carriage. Four (5.4%) pets had incident MRSA carriage (i.e. MRSA not present at baseline and then isolated at three month sampling). All pets with persistent carriage carried the same MRSA *spa*-type on both visits. Longitudinal comparisons of *spa*-types recovered from animal isolates at baseline and three months are provided in Table S5. See Results S1 and Table S4 for final risk factor model variable analysis at three months.

A priori, pet signalment variables (pet species, age and sex) were fixed in the multivariate model. On unadjusted analyses, pet neuter status, antimicrobial use, kennel exposure, fleas on pet exam and MRSA isolation from pet bedding were all associated with MRSA carriage at a p-value <0.20 and therefore evaluated in adjusted analyses.

Because no pets carrying MRSA were unexposed to household environmental MRSA, this variable could not be included in multivariate models. A number of factors were of marginal significance ($p > 0.05$ and $p < 0.20$) in unadjusted analysis at baseline and were considered for multivariate evaluation. These included flea infestation at household examination, neutered status and exposure to a boarding kennel within the past year. False discovery rate analysis suggested that only pet bed MRSA contamination would remain significant after consideration of multiple comparisons. After adjusting for all other variables, pet neuter status and kennel exposure were no longer significant ($p = 0.729$ and $p = 0.354$, respectively).

On sensitivity analysis for an adjusted model including veterinary clinic visits instead of pet antibiotic use, the associations between MRSA isolation from pet bedding and fleas on pet exam were unchanged, and an association between vet clinic visit association and pet MRSA carriage was not significant ($p = 0.118$).

Stepwise forward and backward logistic regression selection resulted in retention of pet antimicrobial use, presence of fleas on the pet and pet bed isolation of MRSA in a multiple logistic regression model. Inclusion of the human–animal contact variable did not improve model fit.

The final multivariate logistic regression model at baseline included pet species, age, sex, antimicrobial use, fleas on pet exam and MRSA isolation from pet bedding (Table 2).

Strain typing and *spa*-type comparisons

MRSA isolate *spa*-types are reported in Table 3, with comparison of pet, human index patient and environmental samples at baseline from eight homes. All isolates carried the *mecA* gene. Only one MRSA isolate from a pet, of 12 (8.3%) at baseline, had a discordant *spa*-type from home environmental sample isolates. *spa*-types of MRSA isolates from humans in the same household were all concordant with the human index patient isolate. Table S3 presents MRSA isolate *spa*-types recovered at three months.

The *spa*-type most frequently identified from environmental isolates (four of eight homes, 50%) was *spa*-type t008, associated with the USA300 clone. Most of the isolates typed in this study previously have been associated with distinct clonal complexes, except for t008 and t334, which are both associated with the CC8 clonal complex.[13]

DISCUSSION

All pets in this study had documented household exposures to a person with a MRSA SSTI, putting all of them at risk for MRSA acquisition. Pet bed (environmental) MRSA positivity was associated with higher odds of pet MRSA carriage in this population, and all positive pets resided in a house with at least one human-associated (nonpet-bed) environmental surface positive at baseline. This provides evidence that contaminated home environments, whether contaminated by a person or a pet, probably play some role in MRSA carriage, transmission or colonisation in pets exposed to MRSA. If the index human had a draining wound this could contribute to environmental MRSA contamination; however, this detail was not available from extracted data. Other risk factors identified here included antimicrobial use in the pet, and pet infestation with fleas.

The results reported in Table 3 strongly support the hypothesis that MRSA strain type can be shared amongst people, pets and their home environments. Most homes in our study had the same MRSA *spa*-type in all three reservoirs. A recent study in households of children with CA-MRSA[6] also found that MRSA strains were shared among these three reservoirs (humans, pets and environment). The majority of pet isolates had *spa*-type t008, associated with the USA300 clone, which is the most common CA-MRSA strain in humans in the USA.

Human index participants with MRSA infection initially were treated by a physician, typically with antimicrobial drug therapy, which limits the ability to generalise these findings to pet populations in homes where antibiotics were not prescribed for human use. Additionally, results from this mid-Atlantic population may not reflect those found elsewhere.

Currently available guidelines[14] state that while human-to-pet transmission of MRSA is possible, re-infection of the human patient from the pet is less likely, pet carriage of MRSA is usually temporary, and pet screening is recommended only within a broader household approach to prevent recurrent MRSA infection. We agree that early removal of pets from the homes of humans infected with MRSA may not be necessary if clinical management

includes targeted testing. Testing the pet may not be beneficial without consideration of planning for concurrent environmental and pet MRSA decontamination.

In conclusion, this study – which focused on potential risk factors for pet MRSA carriage in order to guide best practices for risk-based MRSA testing – concluded that environmental contamination and pet antimicrobial use are risk factors for pet MRSA carriage. Longitudinal and interventional studies are needed to build better causal understanding of transmission pathways and dynamics. Next steps should identify whether interventions targeting the home environmental reservoir (including the pet's bedding) can reduce risk of MRSA carriage in exposed pets.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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TABLE 1a.

Dog and cat signalment and pet-associated baseline population characteristics assessed as risk factors for meticillin-resistant *Staphylococcus aureus* (MRSA) carriage, unadjusted

Characteristic (N = 134)		**MRSA-positive (n = 12)**	**MRSA-negative (n = 122)**	**OR (95% CI)**	***p*-value**	**Cats: OR; (95% CI); *p*-value**	**Dogs: OR; (95% CI); *p*-value**
Species, no. (%)	Cats, 63 (47%)	7	56	1.65 (0.46, 5.96)	0.438	–	–
	Dogs, 71 (53%)	5	66				
Dog breeds (n = 71), no. (%)	Labarador mix, 9 (12.7%)	3	6		–	–	15; (2.26, 99.68); 0.006*
	non-Labarador, 62 (87.3%)	2	60				
Cat breeds (n = 63), no. (%)	DSH, 54 (85.7%)	7	47		–	–	–
	non-DSH, 9 (14.3%)	0	9				
Other dogs/cats in home, no. (%)	Other dogs/ cats in home, 98 (73.1%)	9	89	1.11 (0.19, 6.46)	0.904	1.18; (0.19, 7.31); 0.852	1.18; (0.10; 14.50); 0.896
	Single cat/dog, 36 (26.9%)	3	33				
Pet age (months), no. (%)	≥24, 99 (73.9%)	6	64	0.91 (0.41, 2.02)	0.806	0.50; (0.12, 2.10); 0.330	2.77; (0.42 18.27); 0.280
	<24, 35 (26.1%)	6	58				
Pet sex, no. (%)	Female, 76 (56.7%)	7	69	1.08 (0.40, 2.87)	0.883	1.74; (0.34, 8.95); 0.495	0.56; (0.12, 2.50); 0.432
	Male, 58 (43.3%)	5	53				
Neuter status, no. (%)	Neutered, 52 (38.8%)	7	45	2.4 (0.66, 8.70)	0.18	2.88; (0.52, 16.11); 0.220	1.65; (0.29, 9.27); 0.560
	Unneutered (ref), 82 (61.2%)	5	77				
Indoor/outdoor, no. (%)	Outdoor, 36 (26.9%)	3	33	0.9 (0.17, 4.66)	0.897	0.77; (0.07, 8.14); 0.821	1.24; (0.11, 14.70); 0.857
	Indoor, 98 (73.1%)	9	89				

DSH, domestic short hair; OR, odds ratio, logistic regression; –, not estimable due to 0 stratum

TABLE 1b.

Household-associated baseline risk factors for meticillin-resistant *Staphylococcus aureus* (MRSA) carriage, unadjusted

Characteristic (N = 134)		MRSA-positive (n = 12)	MRSA-negative (n = 122)	OR (95% CI)	*p*-value	Cats: OR; (95% CI); *p*-value	Dogs: OR; (95% CI); *p*-value
Environmental MRSA positivity, no. (%)	Env. positive, 100 (74.6%)	12	88	–	–	–	–
	Env. neg, 34 (25.4%)	0	34				
Pet bed MRSA+, no. (%)	MRSA detected on pet bed, 21 (15.7%)	6	15	7.13 (1.87, 27.26)	0.005*	13.06; (2.59, 65.69); 0.003*	2.50; (0.28, 22.41); 0.401
	MRSA not detected on pet bed, 113 (84.3%)[†]	6	107				
Pet antibiotic use over previous 12 months, no. (%)	Antibiotics, 10 (7%)	3	7	5.48 (1.33, 22.59)	0.02*	20.25 (4.40, 93.28); 0.00*	–
	No antibiotics, 124 (93%)	9	115				
Nature of person–pet contact (cutoff score=2), no. (%)	Close human contact, 89 (66 %)	9	80	1.58 (0.29, 8.67)	0.596	–	0.36; (0.04, 3.30); 0.353
	Casual human contact, 45 (34%)	3	42				
Kennel/boarding/ daycare, no. (%)	Any kennel, 12 (9%)	3	9	4.19 (0.54, 32.30)	0.166	1.7; (0.10, 29.03); 0.707	10.33; (0.78, 136.36); 0.075
	No kennel, 122 (91%)	9	113				
House pests, no. (%)	Any pests, 102 (76%)	8	94	0.6 (0.19, 1.83)	0.36	1.39; (0.32, 6.05); 0.653	0.21; (0.04, 1.20); 0.077
	No pests, 32 (24%)	4	28				
Presence of mould, no. (%)	Any mould, 79 (59%)	7	72	0.97 (0.23, 4.10)	0.969	5.2; (0.59, 46.06); 0.134	0.14; (0.01, 1.73); 0.122
	No mould, 55 (41%)	5	50				
Rural versus urban/ periurban, no. (%)	Rural, 35 (26%)	2	33	0.54 (0.05, 5.59)	0.599	–	1.17; (0.09, 15.64); 0.905
	Nonrural, 99 (74%)	10	89				
Season (spring/summer versus autumn/winter), no. (%)	Spring/ summer, 89 (66.4%)	9	80	1.58 (0.39, 6.41)	0.52	1.62; (0.28, 9.45); 0.584	1.74; (0.18, 16.70); 0.622
	Autumn/winter, 45 (33.6%)	3	42				
Fleas on pet during household exam, no. (%)	Fleas, 12 (9.0%)	2	10	12 (0.91, 158.90)	0.059	9.17; (0.43, 193.31); 0.149	16.25; (0.68, 387.80); 0.083
	No fleas, 115 (91.0%)	2	120				

OR, odds ratio, logistic regression; –, not estimable due to 0 stratum

[†]Includes both pets with beds sampled with no MRSA detected and pets without any bed available to sample

TABLE 2.

Unadjusted and multivariable dog and cat baseline risk factors for meticillin-resistant *Staphylococcus aureus* (MRSA) carriage

Risk factors **N = 134**	**Unadjusted logistic regression** **OR (95% CI)**	**Adjusted, multiple logistic regression** **OR (95% CI)**
Species (cat versus dog)	1.65 (0.46, 5.96)	1.38 (0.29, 6.57)
Pet age	0.91 (0.41, 2.02)	2.22 (0.58, 8.42)
Pet sex (female versus male)	1.08 (0.40, 2.87)	0.79 (0.29, 2.21)
Pet bed MRSA positivity (MRSA isolated versus not)	7.13 (1.87, 27.26) **	10.05 (2.72, 37.14) ***
Pet antibiotic use (pet use versus not)	5.48 (1.33, 22.59) *	5.59 (1.52, 20.53) **
Fleas on pet exam (fleas observed versus not)	12 (0.91, 158.9)	43.17 (2.76, 674.24) **

*, $p < 0.05$

**, $p < 0.01$

***, $p < 0.001$

Table 3.

staphylococcal protein A (*spa*-)typing at baseline

House ID	Index patient	Pet(s)*	Environment	No. cats pos.	Total no. cats	No. dogs pos.	Total no. dogs
A	NT	t334	t008/t216	0	3	1	5
B	t008	t008	t008	1	1	0	0
C	t008	t008	t008	2	2	0	0
D	t008	t008	t008	2	14	0	0
E	t12500	t12500	t12500	0	0	1	3
F	t216	t216	t216	0	0	2	2
G	NT	t216	t216	1	1	1	1
H	t121	t121	t121	1	3	0	0

*No positive housemate pets were discordant with each other

NT, not tested