Multidrug-Resistant and Methicillin-Resistant *Staphylococcus aureus* (MRSA) in Hog Slaughter and Processing Plant Workers and Their Community in North Carolina (USA)

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**BACKGROUND:** Use of antimicrobials in industrial food-animal production is associated with the presence of antimicrobial-resistant *Staphylococcus aureus* (*S. aureus*) among animals and humans. Hog slaughter/processing plants process large numbers of animals from industrial animal operations and are environments conducive to the exchange of bacteria between animals and workers.

**OBJECTIVES:** We compared the prevalence of multidrug-resistant *S. aureus* (MDRSA) and methicillin-resistant *S. aureus* (MRSA) carriage among processing plant workers, their household members, and community residents.

**METHODS:** We conducted a cross-sectional study of hog slaughter/processing plant workers, their household members, and community residents in North Carolina. Participants responded to a questionnaire and provided a nasal swab. Swabs were tested for *S. aureus*, and isolates were tested for antimicrobial susceptibility and subjected to multilocus sequence typing.

**RESULTS:** The prevalence of *S. aureus* was 21.6%, 30.2%, and 22.5% among 162 workers, 63 household members, and 111 community residents, respectively. The overall prevalence of MDRSA and MRSA tested by disk diffusion was 6.9% and 4.8%, respectively. The adjusted prevalence of MDRSA among workers was 1.96 times (95% CI: 0.71, 5.45) the prevalence in community residents. The adjusted average number of antimicrobial classes to which *S. aureus* isolates from workers were resistant was 2.54 times (95% CI: 1.16, 5.56), the number among isolates from community residents. We identified two MDRSA isolates and one MRSA isolate from workers as sequence type 39B, a type associated with exposure to livestock.

**CONCLUSIONS:** Although the prevalence of *S. aureus* and MRSA was similar in hog slaughter/processing plant workers and their household and community members, *S. aureus* isolates from workers were resistant to a greater number of antimicrobial classes. These findings may be related to the nontherapeutic use of antimicrobials in food-animal production.

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**Introduction**

*Staphylococcus aureus* (*S. aureus*) is an important pathogen that can cause serious and life-threatening infections in humans. Clinical problems caused by *S. aureus* range from localized illnesses, such as necrotizing skin infections and folliculitis, to systemic diseases, including toxic shock syndrome (Lowy 1998). *S. aureus* infections have become more dangerous and costly to treat over the past 20 years because of increasing prevalence of antimicrobial resistance. Of considerable concern is methicillin-resistant *S. aureus* (MRSA), as well as multidrug-resistant *S. aureus* (MDRSA) (Gordon and Lowy 2008). Several studies in hospitals in the United States have reported that MRSA is the most common cause of skin and soft tissue infections (King et al. 2006; Moran et al. 2006; Parchman and Munoz 2009), and MRSA carriage is associated with subsequent infection and increased morbidity and mortality compared with noncarriage (Datta and Huang 2008).

*S. aureus* colonizes skin and can persist in the nares; positive nasal carriage is indicative of exposure and is associated with an increased risk of clinical infection in hospitalized populations (Davis et al. 2004; Stevens et al. 2010). Based on risk factors associated with exposure, MRSA strains are often classified as health care–associated MRSA (HA-MRSA), or community-associated MRSA (CA-MRSA). Since 2001, the increases in MRSA exposures and infections in the United States are largely due to community-associated strains, such that MRSA can no longer be controlled solely on the basis of measures implemented within health care settings (Como-Sabetti et al. 2009; Stefani et al. 2012).

Within the category of CA-MRSA, studies in several countries have identified specific strains associated with livestock and which have been termed livestock-associated MRSA (LA-MRSA) (Armand-Lefevre et al. 2005; Bisdorff et al. 2012; DeBoer et al. 2009; Ogata et al. 2012; Smith and Pearson 2011; Waters et al. 2011). Studies have reported increased risks of MRSA carriage among persons working with livestock, including swine (Aubry-Damon et al. 2004; Denis et al. 2009; Geenen et al. 2012; Morcillo et al. 2012; Mulders et al. 2010; Nijsten et al. 1996; Voss et al. 2005); among veterinarians treating livestock (García-Gaëlls et al. 2012; Hanselman et al. 2006); and, more recently, among persons without direct livestock contact but residing in areas of high livestock density (Feingold et al. 2012). In addition, several recent studies have reported on the prevalence of MDRSA carriage among livestock, farm workers, and slaughterhouse workers (Khanna et al. 2008; Oppliger et al. 2012; Smith and Pearson 2011; VanCleef et al. 2010).

In comparison with the European Union, relatively fewer studies examining MDRSA and MRSA exposures in hog production have been conducted in the United States (Leedom Larson et al. 2010; Osadebe et al. 2013; Rinsky et al. 2013; Smith et al. 2009) and, to our knowledge, no studies have been published examining the prevalence of MRSA among workers in U.S. hog slaughter and processing plants or the household members of MRSA carriers.

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of these workers. Therefore, we undertook a study of workers in a large hog slaughter and processing plant, their household members, and community residents. The objective of our study was to test the hypothesis that workers have a higher prevalence of carriage of nonsusceptible strains of *S. aureus*, including MDRSA and MRSA, compared with residents in the same area who do not work in hog slaughter and processing. We also tested the hypothesis that workers are more likely to carry *S. aureus* isolates that are resistant to more antimicrobials as compared with community residents from the same area. We included household members in this study based on studies of household transmission of *S. aureus* and MRSA that reported transmission rates within households as high as 43% (Davis et al. 2012). We hypothesized that household members of workers would also have greater exposure to nonsusceptible strains of *S. aureus* than community referents.

### Methods

#### Study design and recruitment

We conducted a cross-sectional study between September and November 2011 in Tar Heel, North Carolina, the location of the Smithfield plant, the largest hog slaughter and processing plant in the United States. Tar Heel is sparsely populated (117 residents, according to the 2010 U.S. Census (U.S. Census Bureau 2011)), with most workers and community referents residing in nearby cities and towns in southern North Carolina and northern South Carolina. The workforce at the Tar Heel plant included approximately 4,500 workers and was unionized, which facilitated enrollment of workers in the study. Study participants were recruited through outreach efforts by our partner, the United Food and Commercial Workers International Union (UFCW) local 1208. Prior to data collection, we met with local and national officials of the UFCW, as well as with shop stewards of the local union (employees who represent the union at each work area within the plant). These individuals informed the union membership about the study. We asked workers to invite up to two members of their community (people who lived nearby, but who did not live with them or work at the plant), and up to two people living with them who did not work at the plant. Through these efforts we enrolled three categories of participants: a) plant workers, b) household members of plant workers (up to two per worker), and c) community residents. All data collection activities were conducted at the union office, located within one mile of the plant. Before initiating the study, we informed Smithfield about the study through telephone contact with the Vice President for Environmental Affairs.

Participant enrollment took place between Thursdays and Sundays in three waves. All workers had been at work within the past week and many came directly from work. Prior to enrollment, a verbal screening was conducted to determine eligibility of persons approaching the enrollment sessions: all participants were required to be ≥18 years of age, able to speak and understand either English or Spanish, reside in the local area (for community residents) defined as southern North Carolina and northern South Carolina, and were not working at a health care facility. Those who met these inclusion criteria were assigned a unique participant code and were directed to interview stations where oral informed consent was obtained prior to data collection. No personal identifiers were collected in order to protect confidentiality. The study was reviewed and approved by the Johns Hopkins Bloomberg School of Public Health Committee on Human Research.

#### Data collection and biological sampling

An extensive interview was conducted using a standardized questionnaire to collect information on demographic data, current and past occupational history, recent health history (including infections and any use of antimicrobials), contact with live animals (livestock and companion animals), and typical diet. Fluent English/Spanish speakers administered the questionnaire in both languages. We pretested the questionnaire in English and Spanish for clarity and consistency on six non-Hispanic and six Hispanic union members.

After completing the questionnaire, trained personnel collected a swab sample (BD Diagnostic Systems, Sparks, MD) dual swab with Amies agar gel) from both nares of each participant. The ray-tipped swab applicator was then placed into its plastic tube containing transport medium. The transport tube was labeled with the participant code, and shipped to our laboratory at Johns Hopkins by express courier service.

#### Microbiological and molecular analyses

Upon arrival at the laboratory, all samples were kept at room temperature until they were processed by the Johns Hopkins Hospital Laboratory of Medical Microbiology, within 72 hr of collection. Nasal swabs were cultured on BBL 5% sheep blood agar (SBA) and CHROMagar Staph aureus plates (both from BD Diagnostic Systems) and incubated aerobically at 35°C for ≤48 hr before reading. Any suspected colony (β-hemolytic on 5% SBA or mauve colored on ChromAgar Staph aureus plates) was further subjected to Gram staining and the catalase assay and slide agglutination test (Rabbit Coagulase Plasma: ProLab, Richmond Hill, Ontario, Canada). Gram-positive cocci in clusters that were catalase positive and coagulase positive were identified as *S. aureus* (Becker and von Eiff 2011) and subcultured on 5% SBA to isolate pure colonies before being transferred into 30% glycerol and frozen at —80°C.

We transferred one isolate from each *S. aureus*-positive culture to our laboratory for antimicrobial susceptibility testing using the disk diffusion method (Clinical and Laboratory Standards Institute (CLSI) 2008). Isolates were first regrown in Mueller Hinton broth and then examined for susceptibility to cefoxitin, ciprofloxacin, clindamycin, erythromycin, gentamicin, sulfamethoxazole/trimethoprim, quinupristin/dalfopristin, and tetracycline. We used the zone of growth inhibition around specific-antibiotic disks to assess the minimum inhibitory concentration (MIC). Based on these MICs and according to CLSI (2008) standards, we classified the isolates as susceptible, intermediate, or resistant to each antimicrobial except for cefoxitin, for which isolates were classified as either susceptible or resistant. Cefoxitin-resistant isolates were identified as phenotypic MRSA because resistance to cefoxitin predicts resistance to methicillin (Fernandes et al. 2005; Magiorakos et al. 2012).

We performed polymerase chain reaction (PCR) assays targeting *S. aureus* nuc (endonuclease) and mecA (penicillin-binding protein) genes, using the primers mecA-1: 5′-TCGACAAATGCACTACAAACAG-3′; mecA-2: 5′-GCATTAGCACCTTGTAAGC G-3′; mecA-1: 5′-GGGATCATACGG TCATTATTCC-3′ and mecA-2: 5′-AACG ATTTGACAGCAGCATGCC-3′ and methods previously reported (Poulsen et al. 2003). We defined as genotypic MRSA those specimens that were positive for the mecA gene. Because of variation in mecA sequences (Fluit 2011; García-Alvarez et al. 2011; Hansen et al. 2004) that could lead to false negatives, we examined both phenotypically and genotypically characterized MRSA in our analyses. We performed multilocus sequence typing (MLST) of the seven housekeeping genes to identify *S. aureus* genetic strains as described by Enright et al. (2000).

#### Statistical analysis

The distributions of demographic, exposure, and outcome variables were examined and compared across the three categories of participants (workers, household members, community residents). As noted above, we classified isolates as either susceptible or resistant to cefoxitin; and as susceptible, intermediate, or resistant to other antimicrobials on the basis of MIC values (CLSI 2008). In addition, we also classified the isolates as either susceptible or nonsusceptible (the latter category including both intermediate and resistant isolates) as proposed by Magiorakos et al. (2012). Consistent with Magiorakos et al. (2012), we classified isolates as MDRSA if they were nonsusceptible to ≥3 classes of antimicrobials.
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or were MRSA (i.e., resistant to cefoxitin). Although the susceptible and nonsusceptible categories may be more important for epide-
micrological purposes (Magiorakos et al. 2012) the CLSI definition is reliable in determining therapeutic failure (Kahlmeter et al. 2003). To facilitate comparison to the clinical literature, we examined both classifications.

The prevalence of S. aureus, nonsusceptible S. aureus, MDRSA, and MRSA was determined for each participant group and for the study population as a whole. We also determined the proportions of S. aureus isolates that were nonsusceptible, MDRRSA, and MRSA among participants with positive S. aureus swabs. Depending on the number of individuals in each category, we used chi-
squared or Fisher’s exact tests to compare proportions across participant categories.

We used unadjusted and adjusted Poisson regression to compare the average number of antimicrobials to which S. aureus isolates were resistant (based on the CLSI definition) among workers, household members, and community residents. We also used unadjusted and adjusted log binomial regression models to compare the prevalence of MDRSA among workers, household members, and community residents. All multivar-
iable models were adjusted for age (in groups), any self-reported use of antimicrobials in the previous 6 months (yes/no), and any self-
reported visit to a medical facility in the previous 6 months (yes/no). A medical facility was defined as any place where medical care is provided, including hospitals, clinics, doctor offices, and nursing homes. The variables included in the adjusted models were selected based on a priori assumptions.

Finally, we examined the patterns of anti-
microbial resistance found in the S. aureus isolates and the distribution of S. aureus and genotypic MRSA strains based on MLST analysis. All statistical analyses were performed using Stata version 11 (StataCorp, College Station, TX), with a significance level of 0.05.

Results

Study population. We enrolled 336 partici-
pants. Of those, 162 participants were hog slaugh-
ter/processing plant workers, 63 were household members from 50 different house-
holds, and 111 were community residents.

Community residents were more often white non-Hispanic (18%) than workers (3.1%) or their household members (1.6%) (p < 0.01) (Table 1). On average, workers were older than household members or community residents [mean = 41 vs. 38.6 and 32.3 years of age, respectively; analysis of vari-
ance, F(2,2) = 9.01, p < 0.01]. There were more women (58.5%) overall than men in each group, but there were no statistically

significant differences among groups with regard to sex, visit to a medical facility or using antimicrobials in the last 6 months, having a MRSA diagnosis in the past year, or animal contact at home unrelated to hog slaughter and processing work.

Prevalence of S. aureus, nonsusceptible S. aureus, MDRSA, and MRSA. The overall prevalence of S. aureus nasal carriage among the study population was 23.5% (79/336) and was higher among household members (30.2%) than workers (21.6%) or community members (22.5%) (p = 0.38) (Table 1). We tested 78 isolates from the 79 S. aureus-
positive participants for antimicrobial sus-
cceptibility (one isolate did not grow). The overall prevalence of MDRSA among workers, household members and community residents, respectively. The overall prevalence of phenotypic MRSA was 4.8% (16/336), with 5.6%, 4.8%, and 3.6% among workers, household members and community residents, respectively. Nine of the 16 phenotypic MRSA isolates were posi-
tive for meca, providing an overall prevalence of genotypic MRSA of 2.7% (9/335); with a prevalence of 3.1%, 3.2%, and 1.8% among workers, household members and community residents, respectively.

Table 1. Study population characteristics by participant category.

| Category                        | Total [n = 336 (%)] | Worker [n = 162 (%)] | Household member [n = 63 (%)] | Community resident [n = 111 (%)] | χ² test statistic (df) | p-Value |
|---------------------------------|---------------------|----------------------|-------------------------------|----------------------------------|------------------------|---------|
| Age (years)                     |                     |                      |                               |                                  |                        |         |
| 18–25                           | 89 (26.5)           | 24 (14.8)            | 31 (49.2)                     | 34 (30.6)                        | 48.13 (10)             | < 0.01  |
| 26–35                           | 66 (19.6)           | 32 (19.8)            | 10 (15.9)                     | 24 (21.6)                        | 0.09 (2)               | 0.82    |
| 36–45                           | 65 (19.3)           | 40 (24.7)            | 7 (11.1)                      | 18 (16.2)                        | 4.31 (1)               | 0.04    |
| 46–55                           | 62 (18.5)           | 43 (26.5)            | 6 (9.5)                       | 13 (11.7)                        | 2.78 (1)               | 0.09    |
| 56–62                           | 50 (14.8)           | 23 (14.2)            | 8 (12.7)                      | 19 (17.1)                        | 4.75 (1)               | 0.03    |
| Sex, female                     | 196 (58.5)          | 98 (54.7)            | 41 (65.1)                     | 67 (60.8)                        | 2.26 (1)               | 0.13    |
| Race/ethnicity                  |                     |                      |                               |                                  | 31.07 (6)              | < 0.01  |
| African American                | 231 (68.8)          | 114 (70.4)           | 46 (73.0)                     | 71 (64.0)                        | 0.07 (6)               | 0.78    |
| Hispanic                        | 52 (15.5)           | 30 (18.5)            | 13 (20.6)                     | 9 (8.1)                          | 0.43 (6)               | 0.51    |
| White non-Hispanic              | 26 (7.7)            | 5 (3.1)              | 1 (1.6)                       | 20 (18.0)                        | 0.07 (6)               | 0.78    |
| Native American                 | 18 (5.4)            | 9 (5.6)              | 2 (3.2)                       | 7 (6.3)                          | 0.07 (6)               | 0.78    |
| Other                           | 9 (2.7)             | 4 (2.5)              | 1 (1.6)                       | 4 (3.6)                          | 0.07 (6)               | 0.78    |
| Animal contact on home property | 161 (47.9)          | 74 (45.7)            | 28 (44.4)                     | 59 (53.2)                        | 1.85 (2)               | 0.38    |
| Medical facility visit in last 6 months | 192 (57.3)          | 89 (54.9)            | 40 (64.5)                     | 64 (58.7)                        | 4.13 (2)               | 0.12    |
| MDRSA diagnosis in the last year | 3 (13.9)            | 2 (11.2)             | 1 (11.1)                      | 0 (0.0)                          | 0.00 (1)               | 0.99    |
| Use of antimicrobials in last 6 months | 80 (47.3)           | 37 (22.8)            | 17 (27.0)                     | 26 (23.4)                        | 0.44 (2)               | 0.82    |

S. aureus

| Total [n = 78 (%)] | Worker [n = 35 (%)] | Household member [n = 18 (%)] | Community resident [n = 25 (%)] | p-Value |
|-------------------|---------------------|--------------------------------|---------------------------------|---------|
| Nonsusceptible S. aureus | 65 (83.3)          | 28 (80.0)                      | 13 (72.2)                       | 24 (96.0) | 0.09 |
| MDRSA phenotype | 16 (20.5)          | 9 (25.7)                       | 3 (16.7)                        | 4 (16.0) | 0.67 |
| MDRSA mecA | 9 (11.5)           | 5 (14.3)                       | 2 (11.1)                        | 2 (8.0) | 0.90 |
| MDRSA mecA | 23 (29.3)          | 13 (37.1)                      | 4 (22.2)                        | 6 (24.0) | 0.41 |

*p-Value was calculated with Fisher’s exact test. Additionally, MRSA was defined as S. aureus resistant to cefoxitin. MDRSA denotes S. aureus resistant to three or more of the antimicrobials used in this study or resistant to cefoxitin.
The prevalence of MDRSA carriage in workers was 1.96 times higher (95% CI: 0.71, 5.45) than in community residents after adjusting for other variables ($p = 0.20$) (Table 4). The prevalence of MDRSA in household members was comparable to community residents (prevalence ratio ($PR$) = 1.04; 95% CI: 0.25, 4.28).

**MLST and S. aureus strains by group.**

We identified 19 unique sequence types (ST) from 68 *S. aureus* isolates (Figure 2). Sequence types for the 11 remaining isolates could not be determined. ST1 and ST5 were found in all three participant groups. ST8 was the predominant sequence type among all three participant groups, S. aureus isolates from workers and household members (21% and 22%, respectively) but absent among isolates from community residents. ST72 was also observed only among isolates from workers ($n = 1$) and household members ($n = 3$). Notably, three isolates, all from workers, were identified as ST398, including two MDRSA isolates and one MRSA isolate. Among MRSA isolates, ST8 was the predominant sequence type (38%), followed by ST1 (19%).

**Discussion**

To our knowledge, this is the first published study in the United States to examine carriage of *S. aureus*, MDRSA, and MRSA in hog slaughter and processing plant workers and their communities. Although the prevalence of *S. aureus* and MRSA was similar among all three participant groups, *S. aureus* isolates from workers were resistant to a greater number of antimicrobial classes than isolates carried by household members or community residents. Workers also had a higher prevalence of MDRSA than community residents, although the difference was not statistically significant. The overall prevalence of *S. aureus* in our population was 23.5%, which is...
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carriage in our study was also greater than estimates from two studies of young, healthy, adult military recruits that reported prevalences of MRSA carriage between 0.5% and 2% (Findlay et al. 2010; Zinderman et al. 2004).

PCR using previously reported primers (Foulsen et al. 2003) did not detect mecA in 7/16 phenotypically characterized MRSA isolates, consistent with the presence of variant mecA genes that are not detected by standard probes (Garcia-Álvarez et al. 2011; Petersen et al. 2013). Therefore, we reported both phenotypic and genotypic MRSA as suggested by Fluit (2011). We did not conduct further PCR analyses to identify any mecA variants.

We looked for ST398, a strain variant of the clonal complex (CC) 398 that has been associated with exposure to hogs and other livestock (Armand-Lefèvre et al. 2005; Feingold et al. 2012; Smith and Pearson 2011). Three ST398 isolates were identified in workers using MLST, including one that was MRSA, and two that were susceptible to methicillin (cefoxitin) but classified as MDRSA on the basis of resistance to ≥ 3 other antimicrobial classes. Studies in European countries have showed that pigs are a source of MRSA CC398 infections in humans, with the predominant ST being ST398 (Lewis et al. 2008), and that MRSA CC398 is much more prevalent among people exposed to hogs than their family members or non-exposed community residents (Cuny et al. 2009; Oppliger et al. 2012; VanCleef et al. 2010). Similar to our results, a Swiss study of antimicrobial-resistant S. aureus in pigs and pig farmers reported that 22% of all MRSA and methicillin-susceptible S. aureus CC398 strains were multidrug resistant (Oppliger et al. 2012).

We observed evidence of greater S. aureus genotype diversity in isolates from workers (11 MLST sequence types) than in isolates from household members or community residents (7 and 9 sequence types respectively). Oppliger et al. (2012) reported more S. aureus genotype diversity in isolates from non-farmers than pig farmers. We identified ST5 in all three participant groups, ST8 in workers and household members, and ST398 in workers only. Similarly, a French study

| Participant group | Category          | n   | Unadjusted mean ratio (95% CI) | p-Value | Adjusted mean ratio (95% CI) | p-Value |
|-------------------|-------------------|-----|-------------------------------|---------|-------------------------------|---------|
| Community resident| Community resident| 111 | Referent                      | Referent| Referent                      | Referent|
|                   | Household member  | 62  | 1.19 (0.35, 4.07)             | 0.78    | 1.04 (0.25, 4.28)             | 0.96    |
|                   | Worker            | 162 | 1.48 (0.58, 3.79)             | 0.41    | 1.96 (0.71, 5.45)             | 0.20    |

PR, prevalence ratio.

Reference group are those who did not take antimicrobials in last 6 months.

Table 4. Unadjusted and adjusted PRs estimating the association between exposures and carriage of multidrug-resistant S. aureus.

| Participant group | Category          | n   | Unadjusted PR (95% CI) | p-Value | Adjusted PR (95% CI) | p-Value |
|-------------------|-------------------|-----|------------------------|---------|----------------------|---------|
| Community resident| Community resident| 111 | Referent               | Referent| Referent             | Referent|
|                   | Household member  | 62  | 1.08 (0.35, 3.45)      | 0.55    | 0.97 (0.30, 3.15)    | 0.98    |
|                   | Worker            | 162 | 0.89 (0.34, 2.31)      | 0.50    | 0.85 (0.34, 2.31)    | 0.99    |

| Participant group | Category          | n   | Unadjusted mean ratio (95% CI) | p-Value | Adjusted mean ratio (95% CI) | p-Value |
|-------------------|-------------------|-----|-------------------------------|---------|-------------------------------|---------|
| Community resident| Community resident| 111 | Referent                      | Referent| Referent                      | Referent|
|                   | Household member  | 62  | 1.19 (0.35, 4.07)             | 0.78    | 1.04 (0.25, 4.28)             | 0.96    |
|                   | Worker            | 162 | 1.48 (0.58, 3.79)             | 0.41    | 1.96 (0.71, 5.45)             | 0.20    |

PR, prevalence ratio.

Reference group are those who did not visit a medical facility in last 6 months. Reference group are those who did not take antimicrobials in last 6 months.

Table 3. Unadjusted and adjusted estimates of the association between exposures and the mean number of antimicrobials classes to which a S. aureus isolate was resistant.

| Participant group | Category          | n   | Unadjusted mean ratio (95% CI) | p-Value | Adjusted mean ratio (95% CI) | p-Value |
|-------------------|-------------------|-----|-------------------------------|---------|-------------------------------|---------|
| Community resident| Community resident| 111 | Referent                      | Referent| Referent                      | Referent|
|                   | Household member  | 62  | 1.19 (0.35, 4.07)             | 0.78    | 1.04 (0.25, 4.28)             | 0.96    |
|                   | Worker            | 162 | 1.48 (0.58, 3.79)             | 0.41    | 1.96 (0.71, 5.45)             | 0.20    |

PR, prevalence ratio.

Reference group are those who did not visit a medical facility in last 6 months. Reference group are those who did not take antimicrobials in last 6 months.

Figure 2. S. aureus sequence type diversity and distribution. Sequence types were based on seven housekeeping genes that were derived from whole genome sequences of each isolates.
observed \textit{S. aureus} ST5 in both pig farmers and non-farmers, and ST8 and ST398 in pig farmers only (Armand-Lefevre et al. 2005). ST1 was identified in isolates from all three groups in our study, and was the most common isolate identified in pork meat in a U.S. study (Waters et al. 2011). However, ST1 was not prevalent in pigs, pig farmers, or non-farmers in the Swiss study (Oppliger et al. 2012).

The most common \textit{S. aureus} genotypes in hog slaughter and processing plant workers in our study were ST8 (belonging to CC8) and ST5 (belonging to CC5), with the predominant MRSA genotype being ST8 (4/9 isolates). In contrast, studies from other countries reported CC9 and CC398 as the predominant \textit{S. aureus} and MRSA genotypes in pigs and pig farmers (Armand-Lefevre et al. 2005; Oppliger et al. 2012). ST8 and ST5 have been consistently reported to be the most common MRSA strains in isolates from pigs and pork in the United States (Molla et al. 2012; Fu et al. 2009; Waters et al. 2011). We did not identify ST9 (belonging to CC9) among \textit{S. aureus} isolates, although this sequence type was previously found in pigs and pork in the United States (Molla et al. 2012; Waters et al. 2011).

Importantly, we found that, among participants carrying \textit{S. aureus}, workers had the highest proportion of \textit{S. aureus} resistant to at least one antimicrobial class. Moreover, workers had isolates resistant to more antimicrobial classes and also had a higher prevalence of carriage of MRDSA as compared with community residents. Multidrug resistance also was more pronounced in isolates from Swiss hog farmers than isolates from non-farmers (Oppliger et al. 2012).

Infections caused by multidrug resistant bacteria are associated with worse health outcomes and higher expenditures (Cardoso et al. 2008). However, few studies have examined the prevalence of MRDSA in human populations in the United States. One previous North Carolina study reported a 16% prevalence of MRDSA carriage among industrial livestock operation workers compared with 9% among antibiotic-free livestock operation workers (Rinsky et al. 2013). The greater number of drugs to which isolates from workers in our study were resistant is also noteworthy and may be associated with the use of multiple antimicrobials in hog feeds (Silbergeld et al. 2008).

We found resistance to erythromycin was more prevalent than resistance to any other antimicrobial class, similar to Oppliger et al. (2012). However, patterns of resistance to other antimicrobials differed between the two studies, possibly reflecting differences in the use of antimicrobials as swine feed additives between the United States and Switzerland.

In the present study, we observed the prevalence of carriage of resistant strains of \textit{S. aureus} to be greater in all studied groups than in the general U.S. population, but we did not observe differences between groups for some carriage outcomes. Although differences may have been obscured in part because of small sample sizes within groups, it is also possible that the non-worker groups in our study were exposed through environmental pathways from both farms and slaughter and processing operations. Studies by our group and others support this possibility. For example, \textit{S. aureus} and MRDSA have been measured in air releases from intensive hog farms in the United States (Chapin et al. 2005; Gibbs et al. 2004, 2006), detected at distances of 150 m downwind from swine houses in Germany (Schulz et al. 2012), and found in hogs being transported in open trucks from farms to the slaughter house and in untreated swine waste waters and other releases (Burkholder et al. 2007). This explanation is also supported by other work by our group on clusters of MRSA infections among persons residing in areas of intensive hog production in the Netherlands and in northern North Carolina (Feingold et al. 2012).

The overall elevated rates of MRDSA and MRSA across participant groups, and the higher rate in the worker group, may be explained by the concentration of swine farms over the greater Tar Heel region and the common use of different antimicrobial formulations as growth promoters. The slaughterhouse plant in the present study served as a hub for collecting swine from these farms. As a result, workers at the Tar Heel plant were exposed to swine from different farms, and these animals may have carried strains of \textit{S. aureus} with different patterns of antimicrobial resistance. In contrast, non-workers, depending on where they lived, may have been indirectly exposed to relatively few farms and a less diverse set of \textit{S. aureus} strains.

Conclusions

Our results raise concerns about the exposure of hog slaughter and processing plant workers to antimicrobial-resistant \textit{S. aureus}. \textit{S. aureus} isolates from workers were, on average, resistant to more classes of antimicrobials than isolates from community residents. In addition, among \textit{S. aureus}-positive participants, a greater proportion of workers carried strains of \textit{S. aureus} resistant to at least one antimicrobial class. Further, the overall prevalence of MRSA carriage identified in our study population in 2011 was higher than the estimate for the general U.S. population based on NHANES data for 2003–2004 (Gorwitz et al. 2008).

The observation of a similar higher prevalence of MRSA among all groups in our study may be in part related to nonoccupational exposures in the region, which has the highest density of industrial hog farms and hogs in the United States (Wing et al. 2000). Further studies will be crucial for the identification of factors associated with nonoccupational exposures.

Our results suggest a need for surveillance of antimicrobial-resistant \textit{S. aureus} in populations with direct or indirect exposure to livestock. Finally, our study adds to concerns about the use of antimicrobials for nontherapeutic purposes as part of food-animal production, a practice that might contribute to selection for antimicrobial-resistant strains of \textit{S. aureus} in the community, especially in the food-production system.
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