Methicillin-resistant *Staphylococcus aureus*, otherwise referred to as MRSA, is a well-known cause of nosocomial infections worldwide and has recently become implicated as a community-acquired and zoonotic pathogen. The adaptive potential of this commensal bacterium enables it to exist in a broad spectrum of environments and survive efforts to reduce its burden. Transmission interventions, such as barrier protection, appear to be the most effective means of outbreak management, particularly in healthcare settings. Whether the origin of the strain is nosocomial, community, or animal, the route of transmission is by way of contact with infected individuals, items, or the immediate environment of an infected individual. There have been several case reports of zoonotic transmission involving multiple species, which most likely occurred by means of direct contact. Additionally, it has been speculated that MRSA may also be spread via aerosol and in both raw and prepared food.

Given that MRSA can infect animals as well as humans, there is concern surrounding the potential for MRSA becoming a bacterial foodborne pathogen, which is separate from the well-documented Staphylococcal food poisoning caused by a toxin produced by the bacteria. However, currently, there are no reports of MRSA disease from handling or eating meat, and there is no evidence to prove or disprove, for that matter, the potential for MRSA to be transmitted via meat, particularly beef and pork.

**What is MRSA?**

**1.1 Defining MRSA**

*Staphylococcus aureus* is a Gram-positive, facultative anaerobe, which is considered both a human commensal organism and opportunistic pathogen and is commonly associated with purulent infections, food poisoning and toxic shock syndrome. The primary environment for this organism is the mucous membranes of the anterior nares of humans. People and animals are frequently asymptomatic carriers of *S. aureus* and suffer no detrimental effects. However, this coagulase-positive organism has the potential to possess a variety of virulence factors allowing it to establish infection and rapidly evolve in response to immune and antimicrobial challenges; these factors enable it to infect a wide variety of locations on and within the body and cause various disorders in humans and animals alike. In a survey conducted between 1997 and 1999, *S. aureus* was found to be the most common source of skin and soft tissue infections, bacteremia, and lower respiratory infections in the United States.

The adaptability of this pathogen was demonstrated in the early 1940s when penicillin-resistant isolates began to appear in hospitals shortly after mass-production of the new “miracle drug” began. By 1970, approximately 70-85% of community strains of *S. aureus* demonstrated resistance to penicillin regardless of geographic location. Unfortunately, researchers and medical professionals are witnessing the same trend develop in MRSA. Methicillin was developed in 1959, introduced in 1961, and was commonly used to treat staphylococcal infections that were resistant to penicillin. In the same year the drug was introduced, methicillin-resistant *Staphylococcus aureus* was isolated from a hospitalized patient in the UK.

Methicillin resistance in *Staphylococcus aureus* developed through the attainment of a mobile genetic element called the SCCmec cassette; this gene cassette harbors the *mecA* gene. Currently, five *mecA* variants have been identified. It is uncertain which staphylococcal species, or other bacterial species for that matter, the gene cassette was originally transferred from. The *mecA* gene enables MRSA to synthesize penicillin binding protein-2 α (PBP2 α) allowing it to survive antimicrobial treatment with β-lactam agents including penicillin derivatives, cephalosporins, monobactams, carbapenems, and β-lactamase inhibitors. Regrettably, β-lactam antimicrobial therapy is the most commonly prescribed treatment for general infections; thus, resistance to this broad class of antimicrobials poses a challenge for
human and animal practitioners and represents substantial health risks as a result of treatment failure to those infected with this resistant organism.

The prevalence of *S. aureus* and MRSA in the nares varies with regard to the population studied, but generally speaking, approximately 20% of the population are consistently colonized with *S. aureus*, 60% of the population are sporadic carriers, and the remaining 20% of the population apparently never harbor the organism, although this later observation may be attributable to poor sampling sensitivity. Young children tend to have higher colonization rates in comparison to older age ranges, which is most likely due to frequent contact with respiratory secretions. In Asia, MRSA accounts for 70-80% of all *S. aureus* isolates. In the United States, estimates for *S. aureus* nasal carriage range from 20% to 45% but typically averages around 30%, and according to a conglomeration of 10 MRSA colonization studies in the US, nasal colonization with MRSA ranges from less than 1% of the population to 1.3%. While the US prevalence of MRSA appears low, it equates to over 3 million human carriers of MRSA in the United States at a given point in time and represents potential for a substantial financial burden due to treatment failure, morbidity, and mortality. Moreover, from 1999 to 2005, it is estimated that MRSA-related hospitalizations more than doubled; MRSA-related hospitalizations for bacteremia cases increased by 81.2%, pneumonia cases increased by 19.3%, and infections outside the blood and lungs attributed to MRSA nearly tripled. Without regard to indirect costs associated with patient pain and suffering, it is estimated that $830 million to $9.7 billion was spent by hospitals, patients, and health insurance companies as a result of MRSA infections in 2005. It is difficult to determine whether the increases noted are the consequence of nosocomial strains manifesting in the community or novel strains that are emerging in community settings.

Differentiating between nosocomially-acquired and community-acquired MRSA infections is complicated, and has often been based on the time elapsed between isolation of MRSA and onset of hospitalization in several MRSA screening studies. Generally, a strain is considered to be of community origin if isolation of the organism occurs within 48-72 hours of hospitalization. However, it is possible that carriage of MRSA may go undetected and manifest as an infection months after initial colonization; therefore, time of detection is not an accurate means of distinguishing the origin of MRSA. Due to the increase in community-acquired cases of MRSA and the long history of hospital-acquired infections, some researchers are attributing certain genotypic and phenotypic characteristics to the two MRSA types. The increased number of case reports has allowed epidemiologists to identify risk groups that tend to be associated with the two sources of MRSA infections. Both types of human MRSA strains have been identified in animals; however, researchers have identified strains of MRSA that appear to be specific to a few animal species.

1.2 Nosocomially-Acquired MRSA
Methicillin-resistant *Staphylococcus aureus* was first isolated in the United States in 1968 in a Boston hospital. Currently, healthcare-acquired or hospital-acquired MRSA (HA-MRSA) has become one of the most common causes of nosocomial infections worldwide. In 2005, surveillance data from 300 hospitals across the United States reported that *S. aureus* was isolated from approximately 19% of inpatient infections and approximately 15% of outpatient infections, and MRSA rates among these isolates were approximately 59%, 55%, and 48% among non-ICU, ICU, and outpatients respectively.

Infections caused by MRSA are accompanied with increased monetary expenditures and patient morbidity and mortality. When compared to susceptible *S. aureus*, an infection with MRSA is estimated to cost an additional $3,000 to $35,000 more; this does not take into account indirect costs such as pain control and is associated with an increased length of stay and higher mortality. In 2005, the CDC estimated that MRSA caused more than 94,000 life-threatening infections and nearly 19,000 deaths in the United States; furthermore, most of these infections were associated with healthcare settings.

Nosocomial strains of MRSA 1) are believed to have arisen in medical care facilities and are carried by patients and employees; 2) are typically SCCmeC type II or III; and 3) are multi-drug resistant (MDR) (23). At-risk populations include all personnel, healthcare patients and their families, including pets. Risk is highest in surgical and dialysis patients, patients with invasive medical devices such as catheters, and persons with decreased immune function (e.g. elderly, newborns, immunocompromised patients). Moreover, risk for an individual increases with duration of stay and previous antimicrobial therapy.

1.3 Community-Acquired MRSA
Despite small outbreaks of MRSA reported in communities for a number of years, it was not until recently that MRSA received mainstream media attention as a communicable public pathogen. Transmission of MRSA in the community was first reported among intravenous drug users in Detroit in 1981, but this strain was later found to have originated from a local hospital. Methicillin-resistant *Staphylococcus aureus* seems to have emerged as a community-borne pathogen in the 1990s. As with HA-MRSA, community-associated MRSA, also referred to as community-onset MRSA (CA-MRSA and CO-MRSA, respectfully), can sequester in the nares and on the skin of people and animals and not cause overt health problems. This carrier state allows for silent transmission of the bacteria to others. Community-acquired strains are now isolated worldwide. Specific clones of CA-MRSA tend to dominate certain regions of the globe in both animal and human populations; even though some spatial clustering is evident, strain types are not limited to location. Molecular analysis indicates that the clones associated with CA-MRSA likely arose spontaneously and are not nosocomial strains that have been established within community settings. This conclusion is further
confirmed by the dominating presence of SCCmec type IV and V in CA-MRSA strains. Furthermore, CA-MRSA strains from different geographic locations belong to different clonal complexes which suggest that CA-MRSA strains have evolved from a diverse genetic background rather than the worldwide spread of an individual clone. The dominate CA-MRSA strain in the US is MRSA clone USA 300 and carries SCCmec type IV.

Unlike nosocomial variants, CA-MRSA is typically not multi-drug resistant and thus has a broader range of treatment options; nonetheless, community-acquired strains commonly carry multiple virulence factors instead of antibiotic resistance determinants, particularly Panton-Valentine leukocidin (PVL), and are capable of causing severe disease and death. Panton-Valentine leukocidin is a cytotoxin that kills leukocytes through cellular necrosis and induction of apoptosis resulting in tissue death. This cytotoxin is a virulence factor commonly present in CA-MRSA and is in part responsible for the degree of tissue damage associated with community-acquired strains. It is hypothesized that CA-MRSA strains have less fitness cost than HA-MRSA strains, which is supported by evidence that CA-MRSA strains have a shorter dividing time. Community-acquired MRSA commonly manifests as a skin and soft tissue infection such as furunculosis, abscess formation, or cellulitis; however, there have been multiple reports of potentially serious infections including outer and middle ear infections, bacteremia, endocarditis, septic shock, osteomyelitis, necrotizing fasciitis, necrotizing myositis, and necrotizing pneumonia.

The first documented report of transmission of CA-MRSA in the United States occurred in 1993 and involved members of a high school wrestling team and the surrounding Vermont community. Community-associated MRSA received much interest from healthcare practitioners and researchers alike when the bacterium resulted in the deaths of four children in Minnesota and North Dakota. The initial distinction made between community-associated and hospital-associated MRSA was that the community strains affected persons without any of the predisposing risk factors associated with healthcare-borne strains; thus, these individuals were typically healthy (aside from the MRSA infection), had no recent contact with a healthcare facility or employee, did not have a history of previous antimicrobial therapy, had not recently undergone dialysis or surgery, and lacked the presence of invasive medical devices.

Numerous studies have made attempts to describe the risk factors associated with CA-MRSA. Some of these risk groups include but are not limited to children, inmates, athletes (especially those in contact sports), daycare workers, and members of semi-closed populations such as Native Americans, Pacific Islanders, and aboriginal tribes in Canada and Australia.

### 1.4 MRSA in Animals

*Staphylococcus aureus* is considered a human commensal organism and opportunistic pathogen in both human and veterinary medicine. However, it was postulated by Mann in 1959 following the isolation of *S. aureus* from the nares of 23 of 100 dogs that “the common house pet can serve as an important reservoir or carrier of staphylococci infection for man.” Mann’s hypothesis that staphylococci are zoonotic appears true.

The first detection of MRSA in animals was in mastitic cows in 1972. Since then, there have been sporadic reports of MRSA in animals worldwide, and MRSA is now becoming recognized as a contagious pathogen in veterinary practices. Case reports of human nosocomial and community strains of MRSA isolated from animals can be found in the literature and encompass a variety of species from mammalian, reptilian, and avian families. In certain instances, colonized animals were asymptomatic carriers of MRSA, and on other occasions, animals presented with an active MRSA infection. Typically, carrier animals were identified during outbreaks, screening studies, or when family members were continually re-infected with MRSA despite decontamination measures and antimicrobial therapy. There are also reports of MRSA strains that are specific to certain animals, primarily horses and pigs; these strains have been isolated from humans.

Reports have been documented MRSA in the following animal species: cats, dogs, cattle, horses, monkeys, goats, seals, chickens, pigs, sheep, rabbits, a guinea pig, a turtle, a bat, a parrot, and a chinchilla. Clinical presentation of the disease is as varied as it is in humans and includes mastitis, pyoderma, arthritis, osteomyelitis, abscesses, pneumonia, and bacteremia. Even though there was probable horizontal transmission of MRSA strains between animals within the same facility or herd, MRSA cases were hypothesized to have originated from human strains in the majority of animal case reports.

Several of the reports involving pigs and horses (which are discussed in detail below) describe MRSA clones that appear to be endemic in certain swine and equine populations, respectfully. There are conflicting reports of methicillin-susceptible *S. aureus* (MSSA) and MRSA clones in cattle. Some evidence suggests that only a somewhat small subset of the present MSSA strains are able to colonize, cause significant infection, or become an endemic cause of mastitis in dairy cattle herds and persist despite intervention practices. However, there are conflicting reports of observed variation in bacterial populations responsible for mastitis in cows.

At present, there are very few reports documenting the prevalence of MRSA in bovine populations reared for beef production. A recent study by McCarthy and coworkers investigated the burden of MRSA in cattle populations. The study involved 301 cattle from various sources that were sampled at three different sites on the animal (nasal, perianal, and dorsal midline) for MRSA and methicillin-susceptible *S. aureus* carriage. Cattle populations encompassed feedlot cattle, both finished beef and arrival cattle, culled range beef cattle and culled dairy cattle. Feedlot origin animals were sampled during processing at the...
feedlot, either at arrival or departure; all other cattle types were sampled at an auction facility that receives cattle from Texas, Colorado, New Mexico, and Oklahoma. In their study, no MRSA was recovered (prevalence=0%; 95%CL=0, 1.3%) from any of the three locations of the 301 animals sampled. Susceptible *S. aureus* was recovered from 14.3% of the animals sampled. Dairy cattle were found to have the lowest carriage of *S. aureus* which may reflect efforts to control this pathogen on dairies in the area; however, milk samples and/or teat swabs were not taken from culled dairy cows. The isolates recovered during the study were subjected to microbroth susceptibility testing to access resistance to a panel of antimicrobial drugs. Of the 82 isolates recovered, 17.1% were pansusceptible. The most commonly observed resistance was to chloramphenicol (53.7%), followed by daptomycin (50%), tetracycline (1.2%) and erythromycin (1.2%). No isolate was resistant to four or more drugs. It was determined that the burden of MRSA in the cattle population sampled is negligible, and the most sensitive site for surveillance was the nares.

Given the zoonotic nature of MRSA, periodic monitoring of random beef populations would provide further insight into the burden of MRSA in beef cattle. The majority of research done in food animals that can be found in the literature is performed during the processing of carcasses and is addressed in the unprepared food segment, section 4.

**MRSA in Water and the Environment**

### 2.1 Water

There are limited reports of contaminated water as a reservoir for MRSA infection. Begier et al. 2004, reported cases of CA-MRSA among members of a college football team that used a communal whirlpool. In 2005, Methicillin-susceptible *S. aureus* was documented in a professional football team; again, contaminated whirlpool water was believed to have lead to infection in this case as well. Unfortunately, there was not enough evidence gathered in either of these isolated cases to conclude beyond doubt that water was the vector of transmission. Research completed by Tolba et al. indicates that water could possibly be a route of transmission for MRSA. Both HA-MRSA and CA-MRSA strains were able to survive and multiply in sea and fresh river water for the 14 days of the study and were not at culturable concentrations at any of the samplings of chlorinated water with a free chlorine concentration of 2.90 ppm. Even though MRSA can exist in marine and fresh water, it appears unlikely that these are important sources of transmission. No reports were found in the literature involving water as a means transmission of MRSA to animals, but it might occur under certain conditions.

### 2.2 Environment

Much research has been done concerning the healthcare environment and the spread of MRSA, but the exact function(s) of the environment in community transmission of MRSA are yet to be determined. Methicillin-resistant *Staphylococcus aureus* has the ability to exist in the air and on environmental fomites contaminated by contact with the bacterium from a variety of vectors for an extended period of time which hypothetically increases in ideal conditions; it is also capable of forming biofilms on surfaces which prolong habitation in a less-than-optimal environment.

Environmental contamination with MRSA depends on multiple factors such as surface composition, the ability of MRSA to remain viable in a dry environment, and the frequency of surface recontamination and disinfection. The location on or in the body of a MRSA positive patient, animal or human, is believed to contribute to the degree of environmental contamination. Decontamination of environmental surfaces including uncommon places such as ventilation grills and nebulizers has shown to control MRSA outbreaks; however, in hospitals, regular cleaning of contaminated high-touch surfaces does not always eliminate MRSA.

The knowledge gained from human healthcare situations can be applied to veterinary situations and food safety scenarios. Decontamination practices in the veterinary setting should mirror those practiced in human healthcare to control and prevent MRSA outbreaks in veterinary personnel and among animal patients. Additionally, the site of animal contamination in beef production might require additional interventions during the in-plant processing of the carcass at the abattoir.

**Diagnostics and Transmission**

### 3.1 Diagnostics

Diagnosis of a MRSA related-illness is determined by patient symptoms, visual assessment and ultimately a positive culture of MRSA from the individual. Many methods for detection and isolation of MRSA are documented in the literature, and protocols are relatively similar in human and animal research and healthcare settings. Food safety techniques are different from clinical sample (taken directly from animal or human) isolation methods in regard to the nature of the specimen (e.g. emulsified foodstuffs versus nasal swab), and selective medias used in the primary isolation step (possibly mannitol salt agar versus Baird-Parker agar). There are far more media available for staphylococcal isolation than what are mentioned here. Media selection depends on the nature of the research and the capabilities and established protocols of the laboratory performing the culture.

In research settings, samples are typically enriched in a selective broth containing high levels of sodium chloride (7% or more) and possibly methicillin or a surrogate drug. Oxacillin and cefoxitin are adequate proxies, and sometimes preferred, to indicate methicillin resistance. After the initial incubation, the sample is typically streaked for isolation onto a differential or selective-differential agar such as mannnitol salt agar or Baird-Parker agar to isolate typical *S. aureus* colonies. Subsequent isolates are subjected to a variety of manual or automated biochemical tests to confirm the species of the isolate. Likely evaluation for confirmation of
S. aureus might include Gram stain, identification of type of hemolysis, anaerobic glucose and mannitol fermentation, catalase test, Lysostaphin sensitivity test, and plasma coagulase tube test. If antibiotic selection was not performed in the initial broth incubation, resistance can be confirmed by broth dilution, disk diffusion techniques or E test techniques; the Clinical Laboratory Standards Institute (CLSI) has established breakpoints for oxacillin at 4 µg/mL or 10 mm or less, and cefoxitin at 4 µg/mL or 21 mm or less. While standards for zone diameter and µg/mL concentration were updated in 2007, there were no changes in regards to S. aureus. There are also several selective-differential chromogenic media available that allow researchers to combine the isolation and antibiotic challenge steps, but biochemical confirmation of S. aureus is still needed to verify the species of the isolate. CHROMagar, MRSA Select agar, Denim Blue agar, MRSA ID are examples of the commercial differential, selective agars available for this purpose. Due to the expense associated with the chromogenic agars, some laboratories create their own “in-house” MRSA media that consists of a agar base (e.g. tryptic soy agar, mannitol salt agar, Muller-Hinton agar) supplemented with oxacillin or cefoxitin at 4 mg/L concentration.

In clinical settings, it is important to attain a positive confirmation of the pathogen in question in as little time as possible. Since these samples are typically taken from infected areas, samples are directly plated onto a selective-differential agar such as MRSA Select or the laboratory “in-house” agar instead of being enriched first. They are also simultaneously plated onto a non-selective agar, commonly blood agar, for further analysis. The number of colony-forming units (CFU) per unit (volume, weight, or area) may be important information to gather in a food safety situation; therefore, it is not uncommon for these sample to be transferred in a basic buffered solution to lessen the likelihood of increased CFU per sample so that quantification can be performed.

In order for a phenotypically methicillin- (or oxacillin- or cefoxitin-) resistant strain to be confirmed as MRSA, the mecA gene or its gene product, PBP2α, must be detected. The two “gold standards” for confirmation of MRSA that are recommended by CLSI are PCR for the mecA gene or a latex agglutination test to confirm the presence of PBP2α.

### 3.2 Transmission
#### a. Mechanisms of Transmission
As mentioned previously, regardless of species or direction of transmission, some form of direct contact or indirect contact via fomite with the bacteria is typically required to become colonized with MRSA. This can be through direct forms of contact such as skin-to-skin with an infected individual or an animal’s skin/hide or through indirect contact with contaminated objects such as medical devices or milking equipment in dairies. Methicillin-resistant S. aureus can also be spread via aerosolized droplets from the respiratory secretions of infected individuals, occasionally through contaminated water and the air. Airborne transmission of MRSA is further supported by a reduction of MRSA environmental contamination under HEPA-filtration.

It is important to note that direct contact with an infected area is obviously not required for an individual to become colonized, and colonization does not always result in disease. However, the most common mode of transmission is from direct contact between infected (carrier or diseased) individuals to a susceptible individual.

#### b. Zoonotic Transmission
In recent years, zoonotic transmission of MRSA has emerged and been reported throughout the world. Multiple instances have been documented involving human MRSA strains occurring in companion animals and livestock. A more current phenomenon is the appearance of MRSA strains of animal origin occurring in people. Zoonotic transmission likely occurs through the same mechanisms that horizontal transfer in humans and animals occurs. Veterinary personnel are prime candidates as a carrier of MRSA and facilitate the spread of MRSA to and within animal populations. In one case involving equine veterinary staff members, a single strain (CMRSA-5) was responsible for the colonization of 13 employees, 3 of which required medical attention. It was determined in this case study that the original infected foal was the source of colonization of the asymptomatic employees, but was questioned in the 3 invasive cases because of slightly different antibiograms. CMRSA-5 appears to be the predominant strain in horses and horse personnel. It is important to note that the CMRSA-5 strain is relatively uncommon in humans. In a study by Anderson et al., personnel attending an equine veterinary conference in San Antonio, TX, were sampled to gage MRSA prevalence among veterinarians. The pathogen was isolated from 10.1% personnel sampled (n=257). CMRSA-5 (USA 500) was the most common strain type isolated, the second most common being CMRSA-2 (USA100). USA 100 is a common HA-MRSA strain in North America and has also been isolated from cats, dogs, and horses. In the same study, one isolate of CMRSA-10 (USA 300) was found. As previously mentioned, USA 300 is a predominant CA-MRSA clone in North America.

In 2006, two separate studies reported higher rates of MRSA carriage in large-animal personnel when compared to small-animal practitioners and the general population. There have been reports of MRSA detection in livestock (pigs and cattle) and chickens in other countries. Clones that are commonly present in cattle (primarily dairy cattle) and chickens are typically shown to be of human origin, and these strains can become endemic on dairies. In 2003, a nontypable strain of MRSA emerged in the Netherlands and was highly associated with pig and cattle farmers. The geographic distribution of these nontypable isolates corresponded to the density of pig farms, and cases most often involved individuals from rural areas, whereas typable strains were common in densely populated areas and were associated with healthcare settings. The strain has been named ST398 MRSA; ST398 was presumably once a susceptible S. aureus strain that is commensal in pigs (but not humans).
acquired resistance\textsuperscript{104} and is now endemic in certain areas.\textsuperscript{24,101} At present, there are increasing reports of zoonotic transmission of ST398 MRSA, some of which harbor the PVL gene and have resulted in hospitalization.\textsuperscript{115} The cases of ST398 MRSA with the PVL gene that required hospitalization occurred in Sweden in persons without previous animal contact.\textsuperscript{115}

b. Foodborne Transmission

To date, foodborne transmission of MRSA resulting in disease is a rare occurrence. In 1995, a food-initiated outbreak of MRSA occurred in a hospital in the Netherlands.\textsuperscript{56} This outbreak involved 26 patients and 13 healthcare workers and resulted in 4 deaths, two of which were directly attributed to MRSA infection. The outbreak was present in patients in two separate wards that were located in different parts of the hospital and resulted in wound and blood infections. Despite complete disinfection of both wards (including patients and employees), a second outbreak took place. In addition to intensified bacteriologic surveillance, cultures of prepared food were taken. Seven months after the first outbreak, MRSA was isolated from a piece of a banana that had been handled by a dietary worker who was later found to carry MRSA only in his throat and was determined to be the likely source of the outbreak. The author noted that this is the first time that contaminated food is believed to be the route of transmission resulting in subsequent MRSA infection.

The second case report of MRSA food contamination took place in the United States in 2001.\textsuperscript{48} The outbreak involved three patrons who purchased shredded pork barbeque and coleslaw from a local grocery deli. Three to four hours after consuming the meal, all three adults experienced nausea, vomiting, and stomach cramps and were taken to the emergency room and treated. Stool samples of the ill family members were collected; in addition, food specimens and nasal swabs of the food preparers were also cultured. The resulting 12 \textit{S. aureus} isolates were sent to the Centers for Disease Control and Prevention for further testing. Pulse-field analysis revealed that 5 of the 12 isolates were indistinguishable and came from all 3 stool samples, the coleslaw, and a nasal swab of one of the food preparers. This strain (determined to be the outbreak strain) was found to produce staphylococcal enterotoxin C and was later identified as MRSA.

Two other workers were identified as carrying \textit{S. aureus} strains that were found to be susceptible, but produced either enterotoxin A or B. The \textit{S. aureus} isolated from the pork was also susceptible and produced enterotoxin C. After inspection, no lapses in correct procedures appeared to have lead to the outbreak. A follow up with one of the three infected patrons was negative for MRSA. This outbreak of foodborne transmission of MRSA did not result in MRSA infection, but typical staphylococcal food-poisoning caused by toxin production.

It is possible that staphylococcal food poisoning outbreaks attributed to MRSA go unreported because the illness is self-limiting and affected people rarely seek medical attention; furthermore, in events where \textit{S. aureus} is identified, it is not always subjected to antimicrobial susceptibility testing.\textsuperscript{48} These two cases demonstrate that MRSA can be transmitted in food and has the potential, under the right conditions, to be a foodborne pathogen. However, this route of transmission currently appears to be a rare occurrence.

MRSA in Unprepared Food

4.1 Meats

a. Beef

The majority of \textit{S. aureus} isolates from cattle are from mastitic dairy cows. Prevalence among beef cattle has not been thoroughly investigated. In one study that molecularly analyzed 128 bovine \textit{S. aureus} isolates (50 were from mastitis cases), only two isolates tested positive for the \textit{mecA} gene, and despite the 144 gene targets analyzed, this study was unable to distinguish between bovine and human \textit{S. aureus} isolates.\textsuperscript{76}

In an earlier study by Lee, 1,913 specimens of various origins were collected from beef and dairy cattle, pigs and chickens. \textit{S. aureus} was recovered from 421 of the samples, and 15 of these were determined to be MRSA, 12 were from milk samples and 3 were from chicken meat specimens.\textsuperscript{60} The 12 MRSA isolates were compared to human MRSA isolates via RAPD (random amplification of polymorphic DNA) analysis. There was only one cattle isolate that did not share a RAPD pattern with the 38 human isolates used for comparison.\textsuperscript{60} In a similar study by Lee in 2005, 19 isolates from 2,523 specimens were found to harbor the \textit{mecA} gene. Three of these isolates were from chicken and the remaining 16 isolates were from cattle, 13 of which were from milk specimens.\textsuperscript{61} As far as processing is concerned, there is no literature indicating whether or not MRSA is common in US abattoirs. A 2007 study in the Netherlands, where MRSA in known to be present in certain cattle populations, failed to recover MRSA from retail meat samples.\textsuperscript{105} A study in Australia that looked into coagulase-positive staphylococcal species at different points in processing suggested that much of the contamination to carcasses is from worker’s hands and varies by abattoir; furthermore, the method of hide removal and evisceration might be key points in the occurrence and degree of contamination to beef carcasses.\textsuperscript{26,107}

b. Pork

There has been an increase in reports of MRSA in Dutch and Danish swine populations and farmers. Carriage can be both asymptomatic and result in disease in the animals and humans in contact with them\textsuperscript{64,102,103} As previously mentioned, the strain associated with the recent increase in reports of MRSA is ST398.

The same strain has been isolated in Canadian pig populations. In a recent report by Kannha et al., both CMRSA-2 and ST398 were isolated from swine populations on 20 different farms in the provence of Ontario; overall prevalence of MRSA in the 285 animals sampled was nearly 25%.\textsuperscript{52} The finding of MRSA in
Canadian swine raised several questions regarding American swine populations. An initial investigation into the burden of MRSA in pig populations in the United States was recently undertaken at the University of Iowa. The samples were taken from two different production farms in Iowa. On farm A, samples were taken from piglets ages 9 weeks, 12 weeks, 15 weeks, 18 weeks, 21 weeks, 24 weeks, and adults. The overall prevalence of MRSA was 70%, and swine 15 weeks or younger had increased odds (OR: 2.17, CL=95%; 1.6 to ∞) of carriage when compared to adult swine.96 On farm B, fewer age groups (11 and 20 weeks, and adult) were sampled given the prevalence of MRSA in piglets on farm A. There was no MRSA isolated from farm B.96 Farm workers were invited to participate in the study. There were no positive workers from farm B, and 9 of 14 workers sampled on farm A were positive. All the positive workers worked with breeding swine. Molecular typing of the MRSA isolates from the pigs and workers were indistinguishable and revealed that the strain was ST398.96 This is the first report of ST398 MRSA in swine and swine workers in the U.S. However, there has been no report of illness resulting from ST398 in the U.S., and ST398 MRSA has only been reported in swine workers. Carriage of this strain type in the general U.S. population and its prevalence in abattoirs have yet to be thoroughly investigated. An analysis of retail pork meat in the Netherlands only resulted in 1 positive MRSA isolate from 64 samples.105 Past studies have isolated S. aureus from processing facilities, and contamination rates of S. aureus isolated from pork have been shown to vary by abattoir which suggests that slaughter technique could increase the potential for carcass contamination,93 which is a factor that may need to be addressed in the near future.

c. Poultry
Methicillin-resistant Staphylococcus aureus has been isolated from chicken meat in Korea and Japan53,59 but not from other countries in which screening of chicken meat for MRSA has been documented.86 The two isolates recovered from 714 samples taken from retail chicken meat in Japan were identical to two different human strain types; additionally, only two of the 930 samples taken from Korean slaughterhouses and meat markets were confirmed as MRSA.53,59 Despite the evidence that MSSA is a pathogen in poultry,81 the prevalence of MSSA and MRSA in US chicken populations or abattoirs has not been documented.

d. Fruits and Vegetables
There is currently no information available with regards to fruit and vegetable contamination with MRSA; however, given the ubiquitous nature of S. aureus, it is feasible that fresh or fresh-frozen produce could be contaminated from manure spread to fertilize crops and human handling and thus serve as a source of MRSA. If so, this may be of consequence because many fruits and vegetables are eaten raw.

e. Other foods
A study of 160 enterotoxigenic strains of S. aureus isolated from 1,634 food stuffs of animal-origin in Italy resulted in the isolation of 6 MRSA isolates, 4 of which were unpasteurized bovine milk, 1 from mozzarella cheese, and 1 from pecorino cheese.80

4.2 Potential for Control of MRSA in Foods

a. Pre-Harvest
There are currently no pre-harvest interventions in place for the control of MRSA. Likely interventions, if needed, would involve active screening of farm animals and workers for MRSA; nevertheless, this would be very costly and interventions during processing are a more practical option for control if deemed necessary. This said, however, in the initial investigation by McCarthy et al., dairy cattle had the lowest prevalence of S. aureus and may reflect efforts to control S. aureus mastitis. It is possible, therefore, that targeted control is an option for pre-harvest control of MRSA.

b. Post Harvest
As with other foodborne pathogens, the in-plant interventions currently used in abattoirs and plants would likely control MRSA from animal populations, but MRSA is different from the majority of food pathogens, in that it is a common commensal of humans. Therefore, to effectively control MRSA, should it become a food-safety concern, it would be essential to periodically screen workers in contact with food items for MRSA to prevent in-plant contamination of foodstuffs.

Conclusions

5.1 Outlook
It is possible that the spread of methicillin resistance to MSSA strains could follow the trend of penicillin resistance that occurred in Staphylococcus aureus in the 20th century. It is also possible that the virulence determinants observed in CA-MRSA could transfer to HA-MRSA and, furthermore, that MRSA could exchange (give and receive) resistance genes with other bacterial species. For example, this has been reported in a hospital patient that was co-infected with both MRSA and vancomycin-resistant Enterococcus (VRE) which resulted in a vancomycin-resistant MRSA mutant.96 Vancomycin is commonly used to treat MDR-MRSA strains. This is of consequence because intermediate resistance to vancomycin in MRSA is an emerging phenomenon threatening the healthcare system96 and needs to be closely monitored.

It is a common practice for hospitals and extended care facilities to use animals as a means of patient therapy. Therapy animals, typically dogs, are at high risk for MRSA colonization and thus could possibly serve as MRSA carriers between patients and the outside community; furthermore, these animals might potentially carry CA-MRSA strains into the hospital environment. Horses are commonly used as therapy animals in behavioral, psychological, and mental disorders and could serve as a source of transmission to these specific groups of individuals. At present, there are no standard regulation guidelines established for therapy animals. Screening of these animals for MRSA or other potential zoonotic pathogens is not a frequent practice if done at all, and there...
Methicillin-resistant *Staphylococcus aureus* strains can be found in the food chain, and food, therefore, could serve as a potential vehicle for exposure to MRSA. It appears, however that most *S. aureus* and presumably MRSA recovered from beef carcasses and beef products are the result of workers. Further work is needed to validate the effectiveness of interventions at critical control points (CCPs) to prevent, reduce, or eliminate contamination with MRSA.

5.2 Implications

The zoonotic nature of MRSA adds another facet to the already multi-dimensional challenge of ensuring food safety. Not only does the scientific community have to address and develop management protocols in humans, but for certain animals, primarily horses, pigs, and dogs, as well. There are currently no national guidelines for control of MRSA in animals in veterinary practices. The veterinary community could learn much from the screening and containment protocols in human medical facilities. Public-health specialists will require the cooperation of medical personnel in veterinary and human medicine in order to be successful in addressing the zoonotic spread of MRSA in communities. The most apparent need to address MRSA in animal populations appear to be in veterinary settings, equine populations, and swine production (including North America).

5.3 Research Needs

- Identification of reservoirs for the transfer of antibiotic resistance and virulence genes might allow scientists to better anticipate and monitor the ongoing evolution of *Staphylococcus aureus* and subsequently enable science and medicine to better control the spread of emerging MRSA variants. More specifically, coagulase negative (CoN) *Staphylococcus* species are emerging as a notable pathogen and should be monitored in this regard, especially since there are genetic indications that a CoN *Staphylococcus* sp. donated the *mecA* gene to *S. aureus*.

- Pertinent attention to address the need for novel therapies for MRSA would prove beneficial with the looming threat of vancomycin resistance among *Staphylococcus* strains. There are some laboratories attempting to design a staphylococcal vaccine, which would initially be used to protect high-risk patients due to the cost associated with manufacture of the vaccine; unfortunately, the first attempts concerning vaccine development have been unsuccessful in that they supply only limited protection from the bacterium. Trials for a vaccine to be used in dairy cattle are ongoing as well. Preliminary results show promise using a whole cell vaccine, but complete protection has yet to be attained.

- Accurate, worldwide prevalence data for MRSA in both humans and animals is necessary to gauge a starting point for further research. A current national assessment of prevalence in our raw produce and food animals in various stages of production, as well as during and after processing, is needed to adequately estimate the foodborne hazard posed by MRSA.

- Broad-based, periodic surveillance to establish a baseline burden of MRSA and any fluctuations in the burden of MRSA are needed in the beef industry. Research to ascertain a baseline burden of other methicillin-resistant staphylococcal species that harbor *mecA* genes, aside from MRSA, in addition to evaluating the burden of *mecA* variants in other bacterial populations present in cattle still warrants investigation.

- In-plant interventions need to be evaluated to assess their ability to prevent, reduce, or eliminate MSSA, MRSA, and other staphylococcal species during and after processing. Additionally, researchers need to work with post-harvest segments to estimate CCPs of concern with *S. aureus* and other staphylococci, and if the need warrants, establish measures to prevent, reduce, or eliminate contamination at these CCPs.

- It is also important to work with the dairy industry and encourage on-farm control of *S. aureus* where MSSA-associated, and potentially MRSA-associated, mastitis is prevalent endemic.

References


79. NCCLS/CLSI. 2004. Performance standards for antimicrobial susceptibility testing: 14th informational supplement, Wayne, PA, USA.


