

Methicillin Resistant *Staphylococcus aureus*

MRSA

Last Updated: May 15, 2006



**Institute for International
Cooperation in Animal Biologies**
An OIE Collaborating Center
Iowa State University
College of Veterinary Medicine



**Center for Food
Security and Public Health**
College of Veterinary Medicine
Iowa State University
Ames, Iowa 50011
Phone: (515) 294-7189
FAX: (515) 294-8259
E-mail: cfsph@iastate.edu
Web: <http://www.cfsph.iastate.edu>

Etiology

Staphylococcus aureus is a Gram positive, coagulase positive coccus in the family *Staphylococcaceae*. Methicillin-resistant *S. aureus* (MRSA) strains are resistant to methicillin and essentially all other beta-lactam antibiotics. MRSA isolates are genetically heterogeneous.¹ Some strains, which are called epidemic strains; are more prevalent and can spread within or between hospitals and between countries.²

MRSA was first reported in 1961, soon after methicillin was introduced into human medicine to treat penicillin-resistant staphylococci.¹⁻⁵ MRSA has since emerged as an important pathogen in human medicine.^{1,2,4,5} Methicillin-resistant strains of *S. aureus* were first reported as nosocomial infections in human hospitals. Since the 1990s, they have also become an increasing concern in people who have not been hospitalized or recently had invasive procedures; MRSA strains that cause such infections are called community acquired MRSA.^{2,5,6} Community-acquired MRSA strains may have distinct microbiologic and genetic properties compared with hospital-associated strains.⁷ They tend to cause different types of infections and differ in their typical antibiotic resistance profiles, characteristics discussed in more detail below.⁵⁻¹⁰

More recently, MRSA has become a concern in veterinary medicine. *S. aureus* is not a common bacterial species in animals, and the importance of MRSA in veterinary medicine is not well established.⁵ However, MRSA outbreaks in horses suggest that this organism might be an emerging problem in the equine population.^{5,6,11-13} Both nosocomial and community-acquired MRSA infections have been reported in horses.^{5,12-15} Sporadic cases and small outbreaks have also been reported in other species including dogs and cats.^{2,3,8,14,16-32} In most feline and canine MRSA infections, either the owner or the animal had a link to the hospital environment.³ Recently, there have been reports of possible community-acquired infections in dogs and cats at three referral centers; 16 of 19 cases had no links to human hospitals or nursing homes.³ Probable community-acquired infections have also been reported in cattle and chickens.^{2,20}

There are also concerns about MRSA as a possible zoonosis. Both human-to-animal and animal-to-human transmission are known to be possible; however, it has not yet been determined whether animals are an important primary source of MRSA infections for humans, or if most animals are colonized after contact with human carriers.^{3,12,14,21,23,30-32} Some authors conclude that currently the risk to human health from zoonotic MRSA seems to be very small.³

Mechanisms of methicillin resistance

Beta lactam antibiotics (e.g. penicillins and cephalosporins) damage bacteria by inactivating penicillin binding proteins (PBPs), enzymes that are essential in the assembly of the bacterial cell wall.⁴ Four native PBPs are found in staphylococci; all four can be inactivated by these antibiotics.⁴ As a result of the weakened cell wall, treated bacteria become osmotically fragile and are easily lysed. The staphylococcal beta-lactamase protein, which cleaves the beta-lactam ring structure, confers resistance to penicillin but not to semi-synthetic penicillins such as methicillin, oxacillin, or cloxacillin.

Acquisition of the *mecA* gene, which codes for the penicillin binding protein PBP2a, confers virtually complete resistance to all beta-lactam antibiotics including the semi-synthetic penicillins.^{4,5} PBP2a has a very low affinity for beta-lactam antibiotics, and is thought to aid cell wall assembly when the normal PBPs are inactivated.^{3,4} The *mecA* gene is found on a large mobile genetic element called the staphylococcal chromosomal cassette *mec* (SCC*mec*).^{5,31} Four SCC*mec* types have become widespread.^{5,31} MRSA carrying SCC*mec* type I spread across the world in the 1960s, SCC*mec* II in the 1970s, SCC*mec* III in the 1980s, and SCC*mec* type IV in the 1990s.³¹ Other SCC*mec* types are also found in limited geographic areas.³¹

The presence of the *mecA* gene defines MRSA; however, some studies do not test for this gene, and define MRSA by antibiotic susceptibility testing.³¹ Caution must be used when using susceptibility testing as the criterion for MRSA, as some testing methods can overestimate methicillin resistance.³

Methicillin Resistant *Staphylococcus aureus*

Vancomycin-resistant MRSA

MRSA strains, particularly hospital-acquired strains, are often resistant to other antibiotics as well as beta-lactams. Many hospital-acquired MRSA isolates are only susceptible to vancomycin.¹ Thus, there are strong concerns about the possible development and spread of vancomycin resistance in MRSA. Some vancomycin-resistant MRSA strains have been reported since 1996.^{10,33}

Other *Staphylococci* that carry *mecA*

Staphylococci other than *S. aureus* can also be involved in disease in animals and occasionally humans. Phenotypic methicillin resistance and/or the *mecA* gene have been reported in a few strains of *S. intermedius*, *S. felis*, *S. schleiferi*, *S. simulans*, *S. sciuri*, *S. hominis*, *S. xylosus*, *S. haemolyticus*, *S. epidermidis*, and *S. saprophyticus* isolated from animals.^{3,19,20,34-36} Some of these species can cause rare zoonotic infections.^{3,37}

In addition, there are concerns about the potential transfer of *mecA* from animal to human *staphylococci*.³ MRSA strains appear to have evolved independently many times by gene transfer of the *mecA* gene into different strains of methicillin-susceptible *S. aureus*.¹ In addition, transfer of some genes between human, mouse, and dog *staphylococcal* species has been reported, and there is some molecular evidence that gene transfer may have occurred between *S. intermedius* and *S. aureus*.³ Thus, it may be possible for *mecA* genes from MR-*staphylococci* in animals to be transferred to humans. To date, this has not been reported.

Staphylococcus aureus virulence factors and toxins

Virulence factors found in *S. aureus* allow it to adhere to surfaces, damage or avoid the immune system, and cause toxic effects.³⁸ All strains of *S. aureus* can cause purulent infections. In addition, some strains produce exotoxins that can cause several unique diseases. Strains that carry the toxic shock syndrome toxin 1 (TSST-1), a superantigen, can cause toxic shock syndrome.³⁹ Strains that produce exfoliative toxins A or B, which cause the superficial dead skin layers of the epidermis to separate from the living layers, can cause scalded skin syndrome. In addition, *S. aureus* can produce several enterotoxins when it grows in food. These preformed toxins cause *staphylococcal* gastroenteritis (food poisoning) when they are ingested.⁴⁰ The enterotoxins are also superantigens and can cause toxic shock syndrome if they are released systemically. MRSA isolates that carry TSST-1, exfoliative toxins, or enterotoxins have all been reported.⁴¹⁻⁴⁷

In addition, some strains of *S. aureus* carry Pantone-Valentine leucocidin (PVL), a two-component, pore-forming cytotoxin that can cause tissue necrosis, leukocyte destruction, and severe inflammation.^{32,38} The PVL genes have been found in community-acquired MRSA infections in many countries.³² Strains that carry PVL have been associated with skin and soft tissue infections such as abscesses, furunculosis, and cellulitis, as well as severe necrotizing pneu-

monia.^{32,38} PVL-positive MRSA strains have been involved in severe disease among children and young adults, and have been found in outbreaks of severe skin infections in homosexual men and prison inmates.^{32,38} There are fears that PVL-MRSA might also emerge in human hospital-acquired infections.³² In addition, PVL-positive MRSA strains have been associated with clinical disease and serious infections in a few dogs, a cat, a rabbit, and a parrot.^{26,32}

Geographic Distribution

Methicillin-resistant *S. aureus* (MRSA) can be found worldwide.^{2,3,6,13,31}

Transmission

In humans, *S. aureus* is an opportunistic pathogen.³⁹ Both methicillin-sensitive and methicillin-resistant strains can be found as normal commensals on the skin, nasopharynx, anterior nares, and perineum of some of the population.^{3,30,39} Colonization with *S. aureus* can occur any time after birth.³ Colonization may be transient or persistent; some cases have been reported to last for years.³

Transmission of *S. aureus* or MRSA usually occurs by direct contact, often via the hands, with colonized or infected people.^{2,7,30,39} In human hospitals, colonized and infected human patients are the main reservoirs for MRSA, and this organism is typically spread from patient to patient on the hands of staff.^{3,12,39} In one hospital outbreak, contaminated food appeared to be the source of infection for a patient with septicemia.⁴⁸ Aerosol transmission was also reported in this outbreak.⁴⁸ Community-acquired MRSA has been reported to spread by direct contact, in aerosols, and on fomites.^{3,72} In addition, *S. aureus* can be transmitted from the mother to her infant during delivery.³⁹ The possibility of transmission of community-acquired MRSA in foods of animal origin has also been proposed.²

Asymptomatic colonization with MRSA, including nasal carriage, has also been reported in animals.^{5,6,12,14,15,23,29,30,32} Colonized or infected animals can serve as reservoirs for disease in themselves or other animals.¹² In addition, they may be able to serve as reservoirs for human infections.³ The potential for zoonotic transmission by direct contact is generally accepted.³ However, the clinical significance is controversial.³ Currently, it is not known whether animals are a primary source of MRSA infections for humans, or if most animals are colonized after contact with human carriers.³² The importance of human-to-animal transmission may also vary with the species. While there is evidence that some MRSA strains may be spreading in equine populations, most canine and feline infections are, at present, probably acquired from humans.^{3,5,11,12}

Transmission between people and animals seems to be uncommon.^{2,3} There are a few reports of indistinguishable MRSA strains shared between humans and companion animals in their household. In one case, a MRSA outbreak in a nursing home was followed by asymptomatic nasal carriage in a nurse who worked there.³¹ Although she was successfully

Methicillin Resistant *Staphylococcus aureus*

treated to eliminate carriage, the same strain later recurred. When her family was investigated, the same isolate was found in the asymptomatic family dog as well as her healthy infant daughter. In another case, repeated MRSA infections occurred in a woman who also carried MRSA in her throat.³² Although she was successfully cleared of the carrier state for 6 months, she eventually became a carrier again. The re-colonization is thought to have occurred from her husband, son, or dog, which all carried the same isolate. In a similar case, recurrent MRSA infections were seen in a diabetic patient and his wife; both people and the asymptomatic family dog carried the same strain in their nasal cavity.²³ In each of these three cases, the asymptomatic dog served as one reservoir for the bacteria, and MRSA was eradicated from the humans only when the dogs as well as the humans were included in the treatment.^{23,31,32} A cat was also implicated as a reservoir for continued transmission during an outbreak in a geriatric nursing facility.²⁹ This cat was thought to have been colonized from humans during the outbreak. When it was removed from the ward and infectious disease measures to control the MRSA were introduced, the outbreak resolved.

In some cases, asymptomatic human carriers seem to have transmitted MRSA isolates to animals in veterinary hospitals. At one veterinary clinic in Ireland, five identical MRSA isolates were reported from canine surgical cases, and a veterinarian at the clinic was a carrier of the same strain.²¹ The genetic pattern of the isolate resembled that of a common human epidemic strain of MRSA (EMRSA-15). A retrospective analysis suggested that this organism had probably been present in the clinic for 2 years before it was detected. Although it could not be proven, the timing of the infections suggested transmission from humans to animals. EMRSA-15 transmission was also documented between asymptomatic nasal carriers on the staff of a university small animal hospital and dogs with clinical disease.¹⁴ In this study, the timing suggested that at least two dogs may have been infected from human carriers; however, whether the strain originated in the index case (an infected dog) or a human carrier is unknown. Shared isolates between humans and horses, with probable human-to-animal transmission, were also reported at a midwestern veterinary teaching hospital.³⁰ Similarly, two of 43 staff were found to be long term MRSA carriers during an outbreak at a university veterinary hospital in Vienna in 2004 and 2005; the human isolates could not be distinguished from the isolates found in infected horses.⁶

Rare cases of probable animal-to-human transmission have also been reported. During an outbreak at a veterinary teaching hospital in Ontario, the timing of the cases suggested that both horse-to-human and human-to-horse transmission had occurred.⁵ Twenty-six staff were asymptotically colonized; indistinguishable subtypes were isolated from horses that had recently been under the care of all but 3 of the colonized staff. A tattoo infection occurred in one veterinarian; the same isolate was seen in two horses that had been under that person's care for a week before the wound infec-

tion developed. At the same hospital, skin lesions were later reported in three personnel who had contact with a sick foal colonized by MRSA at admission.¹² Infection or colonization was observed in people after as little as 4 hours of close contact with the foal. The predominant isolate found at this hospital is CMRSA-5.^{5,11-13} There has been some speculation that this strain might be particularly well-adapted to transmission in horses.¹¹

Disinfection

S. aureus is susceptible to various disinfectants including 1% sodium hypochlorite, glutaraldehyde, formaldehyde, and a combination of iodine and alcohol.³⁹ This organism is also susceptible to moist heat (121° C for a minimum of 15 min) or dry heat (160-170° C for at least 1 hour).³⁹

In the environment, *S. aureus* can be found for up to 42 days in carcasses and organs and 60 days in meat products.³⁹ It remains viable for 46 hours on glass, 17 hours in sunlight, and less than 7 days on floors.³⁹ *S. aureus* enterotoxins are stable at boiling temperatures.³⁹

Infections in Humans

Incubation Period

The incubation period for *S. aureus* infections in humans is highly variable.³⁹ Although many infections become apparent in 4 to 10 days, asymptomatic colonization is common and disease may not occur until several months after colonization.³⁹ Staphylococcal food poisoning typically becomes apparent after 2-4 hours, but the incubation period can vary from 30 minutes to 8 hours.³⁹

Clinical Signs

MRSA can cause the same types of infections as other isolates of *S. aureus*. This organism causes a wide variety of skin and soft tissue infections including impetigo, folliculitis, furunculosis, cellulitis, abscesses, and wound infections.^{2,7,8,38,39,49} MRSA can also cause invasive infections such as pneumonia, endocarditis, septic arthritis, osteomyelitis, meningitis, and septicemia.^{1,2,7-9,38,39} Strains of *S. aureus* that carry the exotoxin TSST-1 can cause toxic shock syndrome, a life-threatening disease characterized by a sudden onset of high fever, rash, desquamation, hypotension, and multiple organ failure.^{1,39} MRSA strains have been found in some cases of toxic shock syndrome, particularly in Japan.⁴²⁻⁴⁴ MRSA has also been found in cases of staphylococcal scalded skin syndrome in infants and adults.^{41,43,46,47} This disease, which is caused by strains that carry exfoliative toxins A or B, is characterized by widespread blistering and loss of the outer layers of the epidermis.³⁹ Staphylococcal scalded skin syndrome usually occurs in children. In adults, this disease is usually associated with immunosuppression.⁴³

Acute staphylococcal gastroenteritis (food poisoning) can be caused by contamination of food with *S. aureus*. Staphylococcal food poisoning usually develops abruptly.⁴⁰ The symptoms may include nausea, vomiting, diarrhea,

Methicillin Resistant *Staphylococcus aureus*

abdominal cramps, prostration and, in severe cases, headache and muscle cramps.³⁹ Most people recover in 1-3 days, although some may take longer.^{39,40} MRSA has been isolated in some cases of staphylococcal gastroenteritis.⁴⁵ However, as this disease is self-limiting and caused by a preformed toxin in food, methicillin resistance is unimportant in treatment.

Hospital vs. community-acquired MRSA infections

Hospital- and community-acquired MRSA, which occur in different populations, tend to cause different types of infections. Hospital-acquired MRSA can cause a wide variety of infections, from surgical site infections to invasive disease.² These strains are major causes of nosocomial infections associated with indwelling medical devices and surgical sites.⁸ Human community-acquired-MRSA infections are mainly associated with superficial skin or soft tissue disease.^{5-7,9,49} However, some community-acquired MRSA strains have caused disease, including severe sepsis and pneumonia, in other body systems.^{7,9}

Zoonotic MRSA

Zoonotic MRSA can presumably cause the same types of infections as other MRSA. To date, zoonotic transmission has been associated with asymptomatic human colonization as well as wound infections and skin disease.^{5,12,13,31} Reported skin lesions include folliculitis, small lesions suggestive of excoriation with mild inflammation, lesions suggestive of impetigo, and infection in pre-existing eczema.¹²

Communicability

A colonized or infected person can transmit MRSA to other people, mainly by direct contact.^{2,39} Humans can spread *S. aureus* as long as the carrier state persists or the clinical lesions remain active.³⁹

Diagnostic Tests

S. aureus infections are diagnosed by culture of the infection site, while staphylococcal food poisoning is diagnosed by examination of the food for the organisms and/or toxins.^{7,40} *S. aureus* is a Gram positive, non-spore forming coccus. It may be found singly, in pairs, in short chains, or in irregular clusters.⁵⁰ The colonies are circular, smooth, and glistening.⁵⁰ On blood agar, they are usually beta-hemolytic.⁵⁰ Young colonies are colorless; older colonies may be shades of white, yellow, or orange.⁵⁰ Biochemical tests such as the coagulase test are used to differentiate *S. aureus* from other staphylococci. *S. aureus* can also be identified with the API Staph Ident system.

If *S. aureus* is isolated from an infection, genetic testing or antibiotic susceptibility testing should be done to identify MRSA.⁷ Fluoroquinolone-resistant *S. aureus* strains should, in particular, be suspected of being MRSA.³¹ Genetic tests to detect *mecA*, such as polymerase chain reaction (PCR) assays, are the 'gold standard' for identification; however, such tests may not be widely available outside reference laboratories.^{10,31,51} A latex agglutination test can be used to

detect PBP2a.^{10,51} Antibiotic susceptibility tests such as the agar screen test, disk diffusion test, or MIC determination can also be used to identify MRSA.^{2,10,31,51} Most antibiotic susceptibility tests use oxacillin or ceftiofur, as methicillin is no longer commercially available in the United States.¹⁰ Antibiotic susceptibility testing has some drawbacks compared to detection of *mecA* or PBP2a. Methicillin-susceptible and resistant subpopulations can co-exist *in vitro*; although all of the colony carries the resistance genes, only a small number may express the resistance in culture.¹⁰ The expression of resistance in phenotypic tests can also vary with growth conditions such as temperature.⁵¹ In addition, some susceptibility tests can overestimate methicillin resistance; isolates that do not carry *mecA* (and thus, are not MRSA) can appear to be phenotypically resistant to methicillin.⁵¹

Clones or strains of MRSA are differentiated by genetic tests such as pulsed-field gel electrophoresis (PFGE), SCC-mec typing, and DNA sequencing of the X region of the protein A gene (*spa* typing).⁵

Treatment

Some MRSA skin infections such as abscesses can sometimes be treated by incision and drainage, or other management techniques that do not require antibiotics.^{7,39} Invasive staphylococcal infections require antibiotics.^{7,39}

Very few antibiotics are effective in treating infections caused by hospital-acquired MRSA.²⁴ All MRSA strains are considered to be resistant to penicillins, cephalosporins, cepheids, and other β -lactam antibiotics (such as ampicillin-sulbactam, amoxicillin-clavulanic acid, ticarcillin-clavulanic acid, piperacillin-tazobactam, and the carbapenems) regardless of the susceptibility testing results.^{2,30} In addition, hospital-acquired MRSA strains are frequently resistant to most common antibiotics including tetracycline, aminoglycosides, macrolides, chloramphenicol, and fluoroquinolones.^{2,10,30} Since 1996, vancomycin-resistant MRSA strains have also been found.^{10,33} In contrast, community-acquired MRSA strains are often resistant only to β -lactam agents and erythromycin.¹⁰

Antibiotic treatment should be based on susceptibility testing. Serious MRSA infections are often treated with vancomycin, linezolid, and daptomycin.¹⁰ Some strains are also susceptible to trimethoprim/sulfamethoxazole, gentamicin, or rifampin, but these drugs are not typically used as first-line treatment in human MRSA infections.¹⁰

Staphylococcal food poisoning, which is caused by toxins, is self-limiting and is not treated with antibiotics.^{39,45} Supportive therapy may be given, if needed.

Prevention

Screening of healthcare workers and treatment for intranasal carriage can reduce the risk to patients.⁹ Pets in hospital or nursing home environments should be monitored for MRSA as if they were part of the staff.³ Screening of patients also reduces MRSA reservoirs and decreases the risk of nosocomial transmission.¹⁰ Intranasal mupirocin can be used to

Methicillin Resistant *Staphylococcus aureus*

eliminate nasal carriage of MRSA in humans.²¹ This treatment is not always successful; the organism may be reintroduced by carriage in other parts of the body, and resistance to mupirocin can occur.²¹ If other family members or pets are also carriers, they should be treated simultaneously.^{3,31}

Good hygiene, particularly hand washing, is important in preventing transmission of MRSA.^{9,10,21} Specific guidelines have been published by the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force.⁵²

The risk of staphylococcal food poisoning can be decreased by keeping hot foods at 60°C (140°F) or above, and cold foods at 7.2°C (45°F) or below.⁴⁰

Morbidity and Mortality

Approximately 25-50% of the human population is a nasal carrier of *S. aureus*.^{3,7,39} The prevalence of MRSA strains varies with the geographic region.^{2,6} In the U.S., approximately 1% of the population carries MRSA.⁷ In contrast, more than 50% of human *S. aureus* isolates are methicillin resistant in Korea.²

MRSA accounts for 30-40% of all hospital-acquired infections in humans, and is one of the most prevalent nosocomial pathogens worldwide.^{2,3,14} Nosocomial MRSA infection rates reported in human hospitals are 5.9 per 1000 admissions in France, 4.7 per 1000 admissions in Hong Kong, 0.76 per 1000 admissions in Ontario, 0.53 per 1000 admissions in Taiwan, and 1.7 per 1000 admissions in the US.¹² Risk factors for MRSA include hospitalization, residence in a long-term care or assisted living facility, dialysis, and the presence of indwelling percutaneous catheters or other medical devices.⁸ Most MRSA infections are seen in high risk patients, including the elderly and people with open wounds.¹¹ Patients in ICUs are particularly susceptible.^{3,12} Healthcare-associated MRSA infections are becoming more prevalent.^{3,6} In the U.S., MRSA accounted for 2.4% of nosocomial infections in the late 1970s, 29% in 1991, and 43% in 2002.³ Toxic shock syndrome caused by MRSA is rare in the U.S. and Europe, but it is more common in Japan.⁴⁴

Community-acquired MRSA infections are also becoming prevalent.^{5,6,31} Although these infections initially appeared in high-risk populations such as intravenous drug users, people in nursing homes, and those who were chronically ill, they are now reported even in healthy children.³ Outbreaks have been seen in various closed living groups including athletes, military recruits, children, homosexual men, and prisoners.⁷ Factors that have been associated with the spread of community-acquired MRSA skin infections include close skin-to-skin contact, cuts or abrasions, contaminated items and surfaces, crowded living conditions, and poor hygiene.⁷ PVL-positive strains, which have been associated with some outbreaks and serious human infections, are a particular concern. A small percentage of *S. aureus* strains currently appears to carry the PVL genes. In one U.K. survey, 1.6%

of *S. aureus* were PVL-positive and 47% of these isolates were MRSA.³⁸

As with all bacterial infections, the mortality rate varies with the syndrome. Lower mortality rates would be expected in superficial infections and high mortality rates in septicemia and other serious invasive diseases. The mortality rate also depends on success in finding an effective antibiotic for the strain.

Infections in Animals

Species Affected

MRSA infections have been reported in dogs,^{3,14,19-28,31,32,37} horses,^{5,6,11-15,27,30} cats,^{3,8,22,26-29} cattle,^{2,16,17,20} sheep,¹⁸ rabbits,²⁶ chickens,² and a parrot²⁶. MRSA that carry PVL were reported in animals for the first time in 2005; these strains have been found in dogs, a cat, a rabbit, and a parrot.²⁶

Incubation Period

As it does in humans, the incubation period for animal MRSA infections varies with the syndrome. Animals can be colonized for variable periods of time without developing clinical disease.

Clinical Signs

MRSA has been found in asymptomatic carriers including dogs, cats, horses, and other animals.^{3,5,13,14,23,29,31,32}

S. aureus can cause a wide variety of suppurative infections in animals.² MRSA has been isolated from a variety of skin and wound infections including abscesses, dermatitis, postoperative wound infections, fistulas, and intravenous catheter or surgical implant infections.^{2,3,5,6,8,13-15,21,25,30} Less frequently, it has been found in cases of pneumonia, rhinitis, bacteremia, septic arthritis, osteomyelitis, omphalophlebitis, metritis, and mastitis.^{5,6,13-18} MRSA was also isolated from a suppurative area in chicken meat and from the joints of a chicken with signs of arthritis.²

Communicability

MRSA from infected animals and asymptomatic carriers can be transmitted to humans.^{3,5,12,23,29} Skin lesions have been reported in some people after as little as 4 hours of close contact with a colonized foal.¹²

Diagnostic Tests

S. aureus infections are diagnosed by culture of the infection site. *S. aureus* is a Gram positive, non-spore forming coccus. It may be found singly, in pairs, in short chains, or in irregular clusters.⁵⁰ The colonies are circular, smooth, and glistening.⁵⁰ On blood agar, they are usually beta-hemolytic.⁵⁰ Young colonies are colorless; older colonies may be shades of white, yellow or orange.⁵⁰ Biochemical tests such as the coagulase test are used to differentiate *S. aureus* from other staphylococci. *S. aureus* can also be identified with the API Staph Ident system.

Methicillin Resistant *Staphylococcus aureus*

If *S. aureus* is isolated from an infection, genetic testing or antibiotic susceptibility testing can identify methicillin resistant strains.⁷ Genetic tests to detect *mecA*, such as polymerase chain reaction (PCR) assays, are the 'gold standard' for identification; however, such tests may not be widely available outside reference laboratories.^{10,31,51} A latex agglutination test can be used to detect PBP2a.^{10,51} Antibiotic susceptibility tests such as the agar screen test, disk diffusion test, or MIC determination can also be used to identify MRSA.^{2,10,31,51} Most antibiotic susceptibility tests use oxacillin or ceftiofur, as methicillin is no longer commercially available in the United States.¹⁰ Antibiotic susceptibility testing has some drawbacks compared to detection of *mecA* or PBP2a. Methicillin-susceptible and resistant subpopulations can co-exist *in vitro*; although all of the colony carries the resistance genes, only a small number may express the resistance in culture.¹⁰ The expression of resistance in phenotypic tests can also vary with growth conditions such as temperature.⁵¹ In addition, some susceptibility tests can overestimate methicillin resistance; isolates that do not carry *mecA* (and thus, are not MRSA) can appear to be phenotypically resistant to methicillin.⁵¹

Clones or strains of MRSA are differentiated by genetic tests such as pulsed-field gel electrophoresis (PFGE), SCC-mec typing, and DNA sequencing of the X region of the protein A gene (*spa* typing).⁵

Treatment

Antibiotic therapy should be based on susceptibility testing; however, all MRSA strains are considered to be resistant to penicillins, cephalosporins, cepheems, and other β -lactam antibiotics (such as ampicillin-sulbactam, amoxicillin-clavulanic acid, ticarcillin-clavulanic acid, piperacillin-tazobactam, and the carbapenems) regardless of the susceptibility testing results.^{2,30}

MRSA isolated from animals vary in their antibiotic susceptibility. For example, while some isolates have been susceptible to amikacin, vancomycin, and trimethoprim-sulfamethoxazole², or ciprofloxacin, clindamycin, fusidic acid, linezolid, mupirocin, quinupristin-dalfopristin, and vancomycin⁵, others were resistant to numerous drugs including gentamicin, rifampicin, ciprofloxacin, fusidic acid, co-trimoxazole, and tetracycline.¹⁴

One dog with MRSA septic arthritis was treated successfully with a surgically implanted absorbable gentamicin-impregnated sponge.²⁵ Other canine surgical site infections have been treated with antibiotics combined with removal of the surgical implants; in some cases, antibiotic treatment was continued for up to 5 weeks.²¹

Prevention

Veterinary hospitals should establish guidelines to minimize cross-contamination by MRSA or other methicillin-resistant staphylococci.³ Good hygiene including hand washing and environmental disinfection is important in prevention.²¹ Researchers also recommend that veterinary hos-

pitals initiate surveillance programs for MRSA infections, particularly in horses.^{3,11} Screening at admission allows prompt isolation of MRSA carriers and the use of barrier precautions to prevent contact with other animals.¹² It also allows rapid recognition of cases if clinical infection occurs. Similar precautions have been used on some farms where MRSA was found.⁵

There are no proven, safe, and acceptable options to eradicate MRSA from horses that carry this bacterium in the nares.⁵ In one asymptotically colonized dog, oral doxycycline and rifampin eliminated MRSA carriage.³¹ Topical treatment to eliminate nasal carriage is considered to be impractical in pets.³¹

Morbidity and Mortality

There is relatively little information on the prevalence of MRSA in veterinary medicine; however, currently this organism does not seem to be common in the animal population.^{3,11,24,30,31} *S. aureus* itself is not a common staphylococcal species in animals. This organism is typically recovered from less than 10% of dogs and cats in most studies, although carriage rates as high as 90% have been reported in a few surveys.³

A few studies have examined the prevalence of MRSA in animal populations. In one study from the U.S., MRSA strains were found in at least one patient in 6 of 7 veterinary teaching hospitals surveyed; however, the overall prevalence of this organism was low.²⁴ In this study, veterinary diagnostic laboratories at the seven institutions were asked to submit samples of *S. aureus* found from October 2001 to March 2002. Seventy clinical isolates of *S. aureus* were reported from 65 birds, cattle, dogs, horses, and cats; 14% of these isolates (which occurred in 4 horses, four dogs and a cat) were MRSA. A survey from the U.K. found 95 MRSA (1.4%) in 6519 samples from companion animals.²⁷ In this study, MRSA was found in 69 dogs, 24 cats, one rabbit, and one horse. A Hungarian antibiotic resistance monitoring scheme found no cases of *mecA*-positive staphylococci in animals or animal food products in 2001.⁵³ In 2003-2004, this ongoing survey found five MRSA, which all originated from cattle in two dairy herds.²⁰ MRSA was also found in 11 horses seen at an active midwestern veterinary teaching hospital over a 13-month period, and one of 38 *S. aureus* isolated from symptomatic sheep in Spain.^{18,30} Other studies have reported somewhat higher prevalence rates. In Korea, where MRSA is common in humans, 421 of 1913 specimens from cattle, pigs, and chickens collected from 2001 to 2003 contained *S. aureus*.² Twelve isolates from cattle and three isolates from chickens were MRSA. The overall incidence of MRSA in this study was 3.6%. A survey of 148 healthy cats in Brazil found 14 *S. aureus*, of which three isolates (2%) were phenotypically methicillin resistant.³⁶ Another study reported MRSA carriage in 11 (16%) of 67 horses tested at a university equine clinic in the U.K.¹⁴ Three horses had clinical infections. While some studies have found MRSA at veterinary hospitals but not in animals sampled

Methicillin Resistant *Staphylococcus aureus*

from the community¹⁴, others document proven or suspected community-associated MRSA.^{2,5,12,20,24}

A few outbreaks or clusters of clinical cases have been reported in horses or dogs at veterinary hospitals.^{5,6,11-14,21,24} Some of these studies suggest that MRSA may be an emerging pathogen, particularly in horses.^{5,11-13} At a veterinary teaching hospital in Ontario, an outbreak with the Canadian MRSA-5 strain was first reported in horses in 2000; MRSA was isolated from the nasal cavity of 2 (4%) of 57 horses.⁵ A nosocomial colonization rate of 17 horses per 1000 equine admissions was reported at this hospital in 2002.¹² Ten colonized horses were found per 1000 admissions in 2003, and 36 per 1000 admissions in 2004.¹² Clinical nosocomial infections occurred in 1.8 horses out of every 1000 admissions, with no increase over the 3 year period. Community-associated MRSA colonization was seen in 1.7% of equine admissions in 2002, 1.5% in 2003, and 5.7% in 2004. An increased incidence of community-associated MRSA was reported in Thoroughbreds and horses less than a year of age.¹² In these studies, community-acquired infections in horses were clustered. In 2002, MRSA was found in 41 (13%) of 321 horses on one farm in the province.⁵ Three (5%) of 64 of horses on another farm were colonized, and eight other farms had no MRSA carriers. During an outbreak at a university veterinary hospital in Austria from 2003 to 2005, the overall incidence of MRSA was approximately 4.8 cases per 1,000 admissions (4.8%).⁶ Anecdotal reports suggest that MRSA infections are becoming more common in horses, including foals in neonatal intensive care units.¹¹

There are no reports on the mortality rates for MRSA in animals. However, the death rate would be expected to vary with the syndrome, with lower mortality rates in superficial infections and high mortality rates in septicemia and other serious invasive diseases.

Post-Mortem Lesions

The post-mortem lesions of MRSA infections are those seen with any purulent bacterial infection, and vary with the organ system or tissue involved.

Internet Resources

Centers for Disease Control and Prevention (CDC)

http://www.cdc.gov/ncidod/diseases/submenus/sub_staphylococcus.htm

Guideline for Hand Hygiene in Health-Care Settings.

Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force
<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5116a1.htm>

Material Safety Data Sheets – Public Health Agency of

Canada, Office of Laboratory Security
<http://www.phac-aspc.gc.ca/msds-ftss/index.html>

Medical Microbiology

<http://www.gsbs.utmb.edu/microbook>

The Merck Manual

<http://www.merck.com/pubs/mmanual/>

The Merck Veterinary Manual

<http://www.merckvetmanual.com/mvm/index.jsp>

References

1. Fitzgerald JR, Sturdevant DE, Mackie SM, Gill SR, Musser JM. Evolutionary genomics of *Staphylococcus aureus*: insights into the origin of methicillin-resistant strains and the toxic shock syndrome epidemic. *Proc Natl Acad Sci U S A*. 2001 Jul 17;98(15):8821-6.
2. Lee JH. Methicillin (Oxacillin)-resistant *Staphylococcus aureus* strains isolated from major food animals and their potential transmission to humans. *Appl Environ Microbiol*. 2003 Nov;69(11):6489-94.
3. Duquette RA, Nuttall TJ. Methicillin-resistant *Staphylococcus aureus* in dogs and cats: an emerging problem? *J Small Anim Pract*. 2004 Dec;45(12):591-7.
4. Pinho MG, de Lencastre H, Tomasz A. An acquired and a native penicillin-binding protein cooperate in building the cell wall of drug-resistant staphylococci. *Proc Natl Acad Sci U S A*. 2001 Sep 11;98(19):10886-91.
5. Weese JS, Archambault M, Willey BM, Hearn P, Kreiswirth BN, Said-Salim B, McGeer A, Likhoshvay Y, Prescott JF, Low DE. Methicillin-resistant *Staphylococcus aureus* in horses and horse personnel, 2000-2002. *Emerg Infect Dis*. 2005 Mar;11(3):430-5.
6. Cuny C, Kuehmerle J, Stanek C, Willey B, Strommenger B, Witte W. Emergence of MRSA infections in horses in a veterinary hospital: strain characterisation and comparison with MRSA from humans. *Euro Surveill*. 2006 Jan 20;11(1).
7. Centers for Disease Control and Prevention [CDC]. Community-associated MRSA information for clinicians [online]. CDC; 2005 Feb. Available at: http://www.cdc.gov/ncidod/dhqp/ar_mrsa_ca_clinicians.html. Accessed 17 Apr 2006.
8. Bender JB, Torres SM, Gilbert SM, Olsen KE, LeDell KH. Isolation of methicillin-resistant *Staphylococcus aureus* from a non-healing abscess in a cat. *Vet Rec*. 2005 Sep 24;157(13):388-9.
9. Bratu S, Eramo A, Kopec R, Coughlin E, Ghitan M, Yost R, Chapnick EK, Landman D, Quale J. Community-associated methicillin-resistant *Staphylococcus aureus* in hospital nursery and maternity units. *Emerg Infect Dis*. 2005 Jun;11(6):808-13.
10. Centers for Disease Control and Prevention [CDC]. Health-care-associated methicillin resistant *Staphylococcus aureus* (HA-MRSA). CDC; 2005 June. Available at: http://www.cdc.gov/ncidod/dhqp/ar_mrsa.html. Accessed 17 Apr 2006.
11. O'Rourke K. Methicillin-resistant *Staphylococcus aureus*: an emerging problem in horses? *J Am Vet Med Assoc*. 2003 Nov 15;223(10):1399-400.
12. Weese JS, Caldwell F, Willey BM, Kreiswirth BN, McGeer A, Rousseau J, Low DE. An outbreak of methicillin-resistant *Staphylococcus aureus* skin infections resulting from horse to human transmission in a veterinary hospital. *Vet Microbiol*. 2006 Apr 16;114(1-2):160-4. Epub 2005 Dec 27.

Methicillin Resistant *Staphylococcus aureus*

13. Weese JS, Rousseau J, Willey BM, Archambault M, McGeer A, Low DE. Methicillin-resistant *Staphylococcus aureus* in horses at a veterinary teaching hospital: frequency, characterization, and association with clinical disease. *J Vet Intern Med.* 2006 Jan-Feb;20(1):182-6.
14. Baptiste KE, Williams K, Willams NJ, Wattret A, Clegg PD, Dawson S, Corkill JE, O'Neill T, Hart CA. Methicillin-resistant staphylococci in companion animals. *Emerg Infect Dis.* 2005 Dec;11(12):1942-4.
15. Shimizu A, Kawano J, Yamamoto C, Kakutani O, Anzai T, Kamada M. Genetic analysis of equine methicillin-resistant *Staphylococcus aureus* by pulsed-field gel electrophoresis. *J. Vet. Med. Sci.* 1997;59:935-937.
16. Devriese LA, Hommez J. Epidemiology of methicillin-resistant *Staphylococcus aureus* in dairy herds. *Res Vet Sci.* 1975;19:23-27.
17. Devriese LA, Van Damme LR, Fameree L. Methicillin (cloxacillin)-resistant *Staphylococcus aureus* strains isolated from bovine mastitis cases. *Zentbl Vetmed. Reihe B.* 1972;19:598-605.
18. Goni P, Vergara Y, Ruiz J, Albizu I, Vila J, Gomez-Lus R. Antibiotic resistance and epidemiological typing of *Staphylococcus aureus* strains from ovine and rabbit mastitis. *Int J Antimicrob Agents.* 2004 Mar;23(3):268-72.
19. Gortel K, Campbell KL, Kakoma I, Whittam T, Schaeffer DJ, Weisiger RM. Methicillin resistance among staphylococci isolated from dogs. *Am J Vet Res.* 1999 Dec;60(12):1526-30.
20. Kaszanyitzky EJ, Egyed Z, Janosi S, Keseru J, Gal Z, Szabo I, Veres Z, Somogyi P. Staphylococci isolated from animals and food with phenotypically reduced susceptibility to beta-lactamase-resistant beta-lactam antibiotics. *Acta Vet Hung.* 2004;52(1):7-17.
21. Leonard FC, Abbott Y, Rossney A, Quinn PJ, O'Mahony R, Markey BK. Methicillin-resistant *Staphylococcus aureus* isolated from a veterinary surgeon and five dogs in one practice. *Vet Rec.* 2006 Feb 4;158(5):155-9.
22. Malik S, Peng H, Barton MD. Partial nucleotide sequencing of the *mecA* genes of *Staphylococcus aureus* isolates from cats and dogs. *J Clin Microbiol.* 2006 Feb;44(2):413-6.
23. Manian FA. Asymptomatic nasal carriage of mupirocin-resistant, methicillin-resistant *Staphylococcus aureus* (MRSA) in a pet dog associated with MRSA infection in household contacts. *Clin Infect Dis.* 2003 Jan 15;36(2):e26-8.
24. Middleton JR, Fales WH, Luby CD, Oaks JL, Sanchez S, Kinyon JM, Wu CC, Maddox CW, Welsh RD, Hartmann F. Surveillance of *Staphylococcus aureus* in veterinary teaching hospitals. *J Clin Microbiol.* 2005 Jun;43(6):2916-9.
25. Owen MR, Moores AP, Coe RJ. Management of MRSA septic arthritis in a dog using a gentamicin-impregnated collagen sponge. *J Small Anim Pract.* 2004 Dec;45(12):609-12.
26. Rankin S, Roberts S, O'Shea K, Maloney D, Lorenzo M, Benson CE. Pantone valentine leukocidin (PVL) toxin positive MRSA strains isolated from companion animals. *Vet Microbiol.* 2005 Jun 15;108(1-2):145-8.
27. Rich M, Roberts L. Methicillin-resistant *Staphylococcus aureus* isolates from companion animals. *Vet Rec.* 2004 Mar 6;154(10):310.
28. Rich M, Roberts L, Kearns A. Methicillin-resistant staphylococci isolated from animals. *Vet Microbiol.* 2005 Feb 25;105(3-4):313-4.
29. Scott GM, Thomson R, Malone-Lee J, Ridgway GL. Cross-infection between animals and man: possible feline transmission of *Staphylococcus aureus* infection in humans? *J Hosp Infect.* 1988;12:29-34.
30. Seguin JC, Walker RD, Caron JP, Kloos WE, George CG, Hollis RJ, Jones RN, Pfaller MA. Methicillin-resistant *Staphylococcus aureus* outbreak in a veterinary teaching hospital: potential human-to-animal transmission. *J Clin Microbiol.* 1999 May;37(5):1459-63.
31. van Duijkeren E, Wolfhagen MJ, Box AT, Heck ME, Wannet WJ, Fluit AC. Human-to-dog transmission of methicillin-resistant *Staphylococcus aureus*. *Emerg Infect Dis.* 2004 Dec;10(12):2235-7.
32. van Duijkeren E, Wolfhagen MJ, Heck ME, Wannet WJ. Transmission of a Pantone-Valentine leucocidin-positive, methicillin-resistant *Staphylococcus aureus* strain between humans and a dog. *J Clin Microbiol.* 2005 Dec;43(12):6209-11.
33. Centers for Disease Control and Prevention [CDC]. Laboratory detection of: vancomycin-intermediate/resistant *Staphylococcus aureus* (VISA/VRSA) [online]. CDC; 2005 Feb. Available at: http://www.cdc.gov/ncidod/dhqp/ar_visavrsa_labFAQ.html. Accessed 17 Apr 2006.
34. Frank LA, Kania SA, Hnilica KA, Wilkes RP, Bemis DA. Isolation of *Staphylococcus schleiferi* from dogs with pyoderma. *J Am Vet Med Assoc.* 2003 Feb 15;222(4):451-4.
35. Kawano J, Shimizu A, Saitoh Y, Yagi M, Saito T, Okamoto R. Isolation of methicillin-resistant coagulase-negative staphylococci from chickens. *J Clin Microbiol.* 1996 Sep;34(9):2072-7.
36. Lilenbaum W, Nunes EL, Azeredo MA. Prevalence and antimicrobial susceptibility of staphylococci isolated from the skin surface of clinically normal cats. *Let Appl Microbiol.* 1998 Oct;27(4):224-8.
37. Tanner MA, Everett CL, Youvan DC. Molecular phylogenetic evidence for noninvasive zoonotic transmission of *Staphylococcus intermedius* from a canine pet to a human. *J Clin Microbiol.* 2000 Apr;38(4):1628-31.
38. Holmes A, Ganner M, McGuane S, Pitt TL, Cookson BD, Kearns AM. *Staphylococcus aureus* isolates carrying Pantone-Valentine leucocidin genes in England and Wales: frequency, characterization, and association with clinical disease. *J Clin Microbiol.* 2005 May;43(5):2384-90.
39. Public Health Agency of Canada, Office of Laboratory Security. Material Safety Data Sheet: *Staphylococcus aureus* [online]. Office of Laboratory Security; 2001 March. Available at: <http://www.phac-aspc.gc.ca/msds-ftss/msds143e.html>. Accessed 16 Apr 2006.
40. United States Food and Drug Administration [FDA], Center for Food Safety and Applied Nutrition. Foodborne pathogenic microorganisms and natural toxins handbook [monograph online] FDA; 1992 [last update 2005 Dec]. *Staphylococcus aureus*. Available at: <http://www.cfsan.fda.gov/~mow/intro.html>. Accessed 15 Apr 2006.
41. Chi CY, Wang SM, Lin HC, Liu CC. A clinical and microbiological comparison of *Staphylococcus aureus* toxic shock and scalded skin syndromes in children. *Clin Infect Dis.* 2006 Jan 15;42(2):181-5.

Methicillin Resistant *Staphylococcus aureus*

42. Durand G, Bes M, Meugnier H, Enright MC, Forey F, Liasine N, Wenger A, Kikuchi K, Lina G, Vandenesch F, Etienne J. Detection of new methicillin-resistant *Staphylococcus aureus* clones containing the toxic shock syndrome toxin 1 gene responsible for hospital- and community-acquired infections in France. *J Clin Microbiol.* 2006 Mar;44(3):847-53.
43. Ito Y, Funabashi Yoh M, Toda K, Shimazaki M, Nakamura T, Morita E. Staphylococcal scalded-skin syndrome in an adult due to methicillin-resistant *Staphylococcus aureus*. *J Infect Chemother.* 2002 Sep;8(3):256-61.
44. Jamart S, Denis O, Deplano A, Tragas G, Vandergheynst A, De Bels D, Devriendt J. Methicillin-resistant *Staphylococcus aureus* toxic shock syndrome. *Emerg Infect Dis.* 2005 Apr;11(4):636-7.
45. Jones TF, Kellum ME, Porter SS, Bell M, Schaffner W. An outbreak of community-acquired foodborne illness caused by methicillin-resistant *Staphylococcus aureus*. *Emerg Infect Dis.* 2002 Jan;8(1):82-4.
46. Richardson JF, Quoraishi AH, Francis BJ, Marples RR. Beta-lactamase-negative, methicillin-resistant *Staphylococcus aureus* in a newborn nursery: report of an outbreak and laboratory investigations. *J Hosp Infect.* 1990 Aug;16(2):109-21.
47. Yokota S, Imagawa T, Katakura S, Mitsuda T, Arai K. [A case of staphylococcal scalded skin syndrome caused by exfoliative toxin-B producing MRSA] *Kansenshogaku Zasshi.* 1996 Feb;70(2):206-10.
48. Kluytmans J, van Leeuwen W, Goessens W, Hollis R, Messer S, Herwaldt L, Bruining H, Heck M, Rost J, van Leeuwen N, et al. Food-initiated outbreak of methicillin-resistant *Staphylococcus aureus* analyzed by pheno- and genotyping. *J Clin Microbiol.* 1995 May;33(5):1121-8.
49. Centers for Disease Control and Prevention [CDC]. Community-associated methicillin-resistant *Staphylococcus aureus* infection among healthy newborns--Chicago and Los Angeles County, 2004. *MMWR Morb Mortal Wkly Rep.* 2006 Mar 31;55(12):329-32.
50. Bottone EJ, Girolami R, Stamm JM, editors. Schneierson's atlas of diagnostic microbiology. 9th ed. Abbott Park IL: Abbott Laboratories; 1984. *Staphylococcus*; p. 10-13.
51. Lee JH, Jeong JM, Park YH, Choi SS, Kim YH, Chae JS, Moon JS, Park H, Kim S, Eo SK. Evaluation of the methicillin-resistant *Staphylococcus aureus* (MRSA)-Screen latex agglutination test for detection of MRSA of animal origin. *J Clin Microbiol.* 2004 Jun;42(6):2780-2.
52. Boyce JM, Pittet D. Guideline for Hand Hygiene in Health-Care Settings. Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force *Morb. Mortal Wkly Rep.* October 25, 2002/ 51(RR16);1-44
53. Kaszanyitzky EJ, Janosi S, Egyed Z, Agost G, Semjen G. Antibiotic resistance of staphylococci from humans, food and different animal species according to data of the Hungarian resistance monitoring system in 2001. *Acta Vet Hung.* 2003;51(4):451-64.