

Methicillin Resistant *Staphylococcus aureus*

MRSA

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Importance

Staphylococcus aureus is an opportunistic pathogen often carried asymptomatically on the human body. Methicillin-resistant *S. aureus* (MRSA) includes those strains that have acquired a gene giving them resistance to methicillin and essentially all other beta-lactam antibiotics. MRSA was first reported in 1961, soon after methicillin was introduced into human medicine to treat penicillin-resistant staphylococci.¹⁻⁵ This group of organisms has since emerged as a serious concern in human medicine.^{1,2,4,5} MRSA was first reported as a nosocomial pathogen in human hospitals. Although these organisms cause the same types of infections as other *S. aureus*, hospital-associated strains have become resistant to most common antibiotics, and treatment can be challenging.^{2,6-8} Since the 1990s, MRSA has also become a concern in people who have not been hospitalized or recently had invasive procedures; the strains that cause such infections are called community-acquired or community-associated MRSA.^{2,5,9-11} Community-associated MRSA first appeared in high-risk populations such as intravenous drug users, people in nursing homes, and people who were chronically ill, but they are now reported even in healthy children.^{3,10} Until recently, these strains were susceptible to many antibiotics other than beta-lactams; however, resistance seems to be increasing, and multiple antibiotic resistant strains have started to emerge.^{6,10-12}

MRSA can be transmitted between people and animals during close contact.^{3,5,7,9,13-37} The pig-associated lineage MRSA CC398 is a particular concern. This lineage, which apparently emerged in pigs between 2003 and 2005, has spread widely among swine in some locations.^{17,32,38} It was first recognized as a zoonosis in the Netherlands, where the scarcity of human hospital-associated MRSA strains allowed CC398 infections to be recognized.^{34,39} Since that time, methicillin-resistant CC398 has been detected in a number of countries in Europe.^{16-18,29,32,40-45} It has also been recognized in some herds in North America,^{16,20,32,46,47} as well as among pigs in Singapore.⁴⁸ In some locations, large numbers of swine are colonized asymptomatically with CC398, and asymptomatic carriage is common among people who work with these animals.^{16-18,20,30-32,40,42-44,49-52} Clinical cases have also been reported in humans.^{13,16,19,22,29,32,53,54} In addition to pigs, which seem to be the reservoir hosts for CC398, this lineage has been detected in a variety of other domesticated animals, as well as rats living on pig farms.^{23,39,45,55-60} Veal calves have been reported to carry CC398 at high prevalence on some farms.^{16,42,56}

Other MRSA lineages can also be found in animals. MRSA outbreaks in horses suggest that this organism might be an emerging problem in the equine population.^{5,9,36,61,62} Both nosocomial and community-acquired MRSA infections have been reported in horses.^{5,14,36,62-64} MRSA carriage, sporadic clinical cases and/or small outbreaks also occur in other species including dogs, cats, pet birds, cattle, zoo animals and marine mammals.^{2,3,7,8,14,17,21,65-82;} MRSA isolates other than CC398 can be shared between animals and people in close contact.^{2,3,5,7,9,14,21,25-28,36,37,39,72,77-79,82-86} Most strains in pets seem to originate from humans.^{3,15,16,23,35} Although their prevalence in healthy dogs and cats is usually low,^{3,7,8,15,16,23,41,61,78,87-90} clinical cases as well as asymptomatic carriage have been reported.^{3,7,14,16,21,23,35,65,73,91-97} During outbreaks in veterinary hospitals, kennels and other facilities, carriage rates in small animals have been as high as 20%.^{23,96,98} Concerns have also been raised about the ability of pets to transmit MRSA back to people, particularly those who are immunosuppressed, chronically ill, or unusually susceptible for other reasons.

Etiology

Staphylococcus aureus is a Gram positive, coagulase positive coccus in the family *Staphylococcaceae*. Methicillin-resistant *S. aureus* 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 tend to spread within or between hospitals and countries.² Other "sporadic" strains are isolated less frequently and do not usually spread widely. Some clonal lineages of *S. aureus* have a tendency to colonize specific species, and may be adapted to either humans or animals.¹⁷ Other lineages, which are called "extended host spectrum



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genotypes,” are less host-specific and can infect a wide variety of species.¹⁷ For example, the isolate MRSA ST22-IV (EMRSA15) has been reported in people, dogs, cats, bats, turtles, pigs (rarely) and birds.^{17,32}

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*).^{5,78} At least 8 SCC*mec* types (SCC*mec* I through SCC*mec* VIII) have been identified, although some are more common than others.^{5,11,23,32,78} 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.⁷⁸ Different SCC*mec* types tend to occur in human hospital-associated and community-associated MRSA.^{11,16,91}

The presence of the *mecA* gene defines MRSA; however, some studies do not test for this gene, and define MRSA by antibiotic susceptibility testing.⁷⁸ Caution must be used when using susceptibility testing as the criterion for MRSA, as some testing methods can overestimate methicillin resistance.³

Vancomycin-resistant MRSA

MRSA strains, particularly hospital-acquired strains, are often resistant to other antibiotics as well as beta-lactams. Until recently, vancomycin was the only antibiotic available for treating many of these isolates.^{1,12} Vancomycin-resistant MRSA strains, including some community-associated strains, have increasingly been reported.^{6,10,99} New drugs that can be used to treat MRSA infections, such as tigecycline and linezolid, have become available in the last decade, but vancomycin is still a first-line treatment for serious MRSA infections, and resistance remains a concern.¹²

Naming conventions for MRSA

The nomenclature of *S. aureus* strains is not completely standardized; there are at least three different

genetic techniques currently in use for classification.^{20,32,91} For this reason, an isolate can have multiple names. The genetic techniques currently used to classify and name MRSA isolates include pulsed-field gel electrophoresis (PFGE), multilocus sequence typing (MLST), and DNA sequencing of the X region of the protein A gene (*spa* typing).^{5,16} Phage typing was used at one time to differentiate MRSA (and *S. aureus*) isolates, but PFGE became the method of choice in the late 1990s.¹⁰ Widely accepted names based on PFGE included the Archaic, Brazilian, Berlin, Iberian and New York–Tokyo clones, but some groups of organisms were given vague names such as ‘PFGE type A,’ which varied between laboratories.¹⁰ The U.S. Centers for Disease Control and Prevention (CDC) eventually established a nomenclature system, based on PFGE patterns that were common in the USA, listing eight original isolates, USA100 to USA800.¹⁰ Similarly, common PFGE fingerprint clusters were identified in Canada, and named CMRSA1 through CMRSA10.¹⁰⁰ A third designation, by EMRSA (epidemic MRSA) types originated in the U.K., with the initial designation of the most prevalent strain in England and Wales in the early 1980s as “*the* EMRSA.”¹⁰¹ This strain eventually became EMRSA1, when EMRSA2 through EMRSA14 were identified.¹⁰² Additional strains have since been recognized. Sometimes, similar or indistinguishable MRSA isolates have more than one name. For example, CMRSA10 is indistinguishable from USA300, CMRSA2 resembles USA100, and CMRSA8 resembles EMRSA15.¹⁰⁰ Some isolates, notably the livestock associated strain ST398, are not typeable by PFGE.^{16,17}

MLST and *spa* typing have become popular recently.¹⁰ The naming convention for MLST types is sequence type (ST) followed by a number (e.g., ST398), while *spa* types are “t” followed by a number (e.g., t011).¹⁷ PFGE and MLST typing usually sort isolates into similar clusters. MLST is also used to group MRSA into clonal complexes (e.g., CC398), which contain genetically related ST types.¹⁶ The clonal complex contains organisms of the same ST type (i.e., CC8 contains ST8 isolates), but it can contain some related isolates that belong to other ST types. One or two clonal complexes tend to predominate in an area.¹⁰³

Spa typing is useful because it can provide better discrimination between isolates, compared to PFGE or MLST, for epidemiologic investigations. A single MLST type or PFGE type can contain several different *spa* types.^{32,100} A problem with *spa* typing is that unrelated lineages can sometimes contain similar *spa* types.^{17,100} For example, CMRSA5, CMRSA9 and CMRSA10 all contain the *spa* type t008.¹⁰⁰ This may occur because *spa* typing focuses on a small region of the genome, and recombination might result in discrepancies with MLST and PFGE clustering.¹⁰⁰ Additional genetic testing can resolve such discrepancies.¹⁰⁰ Isolates may be identified with a combination of tests for a more complete

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description. MRSA ST8 t064 SCCmecIV, for instance, is a genetic type that has been found in some horses.¹⁷

Although names such as ST9 or CC398 include both methicillin-resistant and methicillin-susceptible *S. aureus* of that genetic type, the isolates referred to in this factsheet are all MRSA unless otherwise noted.

Human hospital-associated and community-associated MRSA

Relatively few clones predominate among hospital-associated MRSA worldwide; they currently belong to CC5, CC8, CC22, CC30 and CC45.¹¹ USA100 (New York–Tokyo clone; ST5-SCCmec II), which belongs to CC5, is the most common hospital-associated MRSA in the U.S.^{10,104} The predominant community-associated strains in North America belong to USA300 (CMRSA10) in CC8, but the CC1 lineage (USA400; CMRSA7) also occurs.^{10,11,100} USA300 differs genetically from hospital-associated CC8 isolates. Community-associated MRSA is heterogeneous in Europe, with ST80 (SCCmec IV) the most common clone, and ST398, USA300 and others also reported.¹¹

Important MRSA strains in animals

Cats and dogs are usually colonized by MRSA strains from humans.^{3,15,16,23,35,105} These isolates usually belong to the predominant human isolates in the area, which differ between regions.²³ The strains found in horses are varied and their origin is largely unknown.²³ Most of the common strains in horses do not seem to belong to the predominant hospital-associated lineages circulating in people.²³ Instead, they tend to belong to older lineages that were common in the past, but have been superseded by other strains, or to less common groups.²³ The majority of the isolates found in Canadian horses have been CMRSA5 (USA500; MRSA ST8 SCCmecIV).^{5,16,36,39,61,62} This strain has also been detected among horses in the U.S.¹⁰⁵ ST8 of a different spa type has been detected in European horses.³⁹ Other isolates that have been reported from horses include ST259, ST254, CC398 and human-associated MRSA.^{16,17,26,93}

Some common lineages found in pigs seem to be distinct from human-associated strains.⁹¹ CC398 is the predominant MRSA lineage in pigs, although CMRSA2 (EMRSA3), which belongs to CC5, is also relatively common among pigs in Canada, and other isolates are found occasionally.^{17,20,32,38,106} Pigs seem to be true reservoir hosts for the CC398 complex.²³ CC398 is also called “non-typeable MRSA” (NT-MRSA) because most isolates cannot be typed by PFGE (although they can be typed by other methods), or livestock-associated MRSA (LA-MRSA).³² Most of the isolates in CC398 are of the ST398 MLST type, but some variants such as ST621, ST752, ST753, ST804 and ST1067 also belong to this group.^{17,107} CC398 contains many spa types.^{17,32,107} CC398 does not seem to be particularly host specific and it has been detected in other species including horses, cattle,

poultry, dogs and humans, as well as rats living on pig farms.^{13,16,17,19,20,22,28-32,34,39,45,55,57-60,97,108,109}

Many MRSA strains causing mastitis in cattle seem to be of human origin, although bovine-associated strains have been suggested and CC398 has also been identified.³²

Other *Staphylococcus* species that carry *mecA*

Staphylococci other than *S. aureus* can also be involved in disease in animals and occasionally in humans. Phenotypic methicillin resistance and/or the *mecA* gene have been reported in strains of *S. pseudintermedius* (formerly *S. intermedius*), *S. felis*, *S. schleiferi*, *S. simulans*, *S. sciuri*, *S. hominis*, *S. xylosum*, *S. haemolyticus*, *S. epidermidis*, *S. vitulinus*, *S. warneri* and *S. saprophyticus* isolated from animals.^{3,41,69,70,83,87-89,110-113} Some of these species can cause zoonotic infections or colonize people asymptotically.^{3,83,98,114-116} Shared colonization between humans and animals has been reported in veterinary hospitals.⁹⁸

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, the 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

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 produce toxic effects.¹¹⁷ All strains of *S. aureus* can cause purulent infections. In addition, some strains produce exotoxins that can result in several unique diseases. Strains that carry the toxic shock syndrome toxin 1 (TSST-1), a superantigen, can cause toxic shock syndrome.¹¹⁸ 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 result in scalded skin syndrome. In addition, *S. aureus* can generate several enterotoxins when it grows in food. These preformed enterotoxins are responsible for staphylococcal gastroenteritis (food poisoning) when they are ingested.¹¹⁹ 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.¹²⁰⁻¹²⁶

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.^{79,117} The PVL genes have usually been associated with community-acquired rather than hospital-linked human MRSA strains.^{12,79,127}

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PVL has been linked to skin and soft tissue infections and severe necrotizing pneumonia, and some authors have also suggested that the PVL gene is associated with increased virulence in general.^{11,79,117,127} Currently, its role and importance in the various syndromes are controversial.^{11,127,128} PVL-positive MRSA strains have been detected in animals (including dogs, a cat, a rabbit, a parrot and a pig), some with serious infections,^{74,79,105} Although all CC398 isolates from animals have been PVL-negative as of 2010, PVL positive MRSA CC398 was isolated from infected humans in China and Sweden.³² These isolates may have acquired the PVL gene from human hospital or community-associated strains, rather than from pigs.³²

Factors contributing to the development of MRSA in livestock

MRSA CC398 is thought to have evolved more than once from methicillin-sensitive strains of CC398.^{23,32} Methicillin-resistant members of this lineage have not been found in strain collections taken from pigs before 2003.³⁸ Why CC398 became widespread in swine populations is not known.³⁸ One hypothesis is that it is related to the use of antimicrobials, particularly tetracycline, in food animals.¹⁶ However, a recent study reported that all Danish isolates of both methicillin-sensitive and methicillin-resistant CC398 were resistant to tetracycline, indicating that tetracycline resistance probably did not provide a survival advantage to MRSA CC398.³⁸ In contrast, the methicillin-resistant isolates had increased resistance to zinc compounds, which are often used to prevent or treat post-weaning diarrhea in young pigs.³⁸ It is possible that selection for resistance to zinc in MRSA CC398 might have co-selected for antibiotic resistance.³⁸ It is also possible that MRSA ST398 evolved in humans, possibly from a methicillin-sensitive strain acquired from pigs, before being transferred back and becoming widespread in swine populations.³²

Geographic Distribution

MRSA can be found worldwide, but its prevalence varies.^{2,3,9,62,78} Human-adapted, hospital-associated strains of these organisms are rare among people in the Netherlands and Scandinavian countries, where extensive control programs have been conducted for years.^{11,42,91} Community-associated strains can occur even where hospital-associated strains have been controlled.¹¹ One or two clonal complexes tend to predominate in an area.¹⁰³

CC398 has been detected among livestock in many European countries.^{16-18,32,40-44} MRSA in this clonal complex has recently been recognized among pigs in North America.^{16,20,32,46,47} and Singapore.⁴⁸ The specific isolates found in horses vary with the geographic area.⁹¹

Transmission

In humans, *S. aureus* is an opportunistic pathogen.¹¹⁸ Both methicillin-sensitive and methicillin-resistant strains

can be found as normal commensals on the skin (especially the axillae and perineum), the nasopharynx and anterior nares of some of the population.^{3,7,118} Colonization with *S. aureus* can occur any time after birth.³ Carriage may be transient or persistent; some cases have been reported to last for years.³ Different colonization patterns have been reported between human hospital-associated and community-associated MRSA.¹¹ Most people who develop symptomatic infections with hospital-associated MRSA also carry the organism in the nares.¹¹ In contrast, community-associated MRSA may colonize sites other than the nares, and clinical cases are often seen in patients who are not colonized.¹¹

Transmission of *S. aureus* or MRSA usually occurs by direct contact, often via the hands, with colonized or infected people.^{2,7,118,129} 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.^{3,36,118} In hospital outbreaks, contaminated food can disseminate the organism to patients as well as to healthcare workers.^{32,130} Aerosol transmission was reported in one hospital outbreak.¹³⁰ Community-acquired MRSA has been reported to spread by direct contact, on fomites and in aerosols.^{2,3,129} In addition, *S. aureus* can be transmitted from the mother to her infant during delivery.¹¹⁸

Asymptomatic colonization with MRSA, including both nasal and rectal carriage, has been reported in animals.^{5,7,9,14,20,36,63,72,77,79,86} The organisms can colonize more than one site.⁸⁴ Interestingly, nasal and gastrointestinal inoculation of 5-week old piglets did not result in stable MRSA carriage, but inoculation of the vagina of a pregnant sow resulted in persistent carriage of CC398 or ST9 isolates in all of her newborn progeny.¹³¹ *S. aureus* adhere less well to the skin of cats and dogs than animal-adapted staphylococci such as *S. pseudintermedius*, and stable colonization is less likely in these species.⁸⁴ Carrier animals may serve as reservoirs for disease in themselves, and they may transmit MRSA to other animals or people.^{3,13,16-20,22-24,28-34,36,38,39}

MRSA as a zoonosis and reverse zoonosis

There is evidence for the transmission of MRSA from humans to animals,^{5,7,9,14,21,25,36,37} as well as from animals to humans.^{5,26,27,36,37} Colonization with livestock associated MRSA, especially CC398 from pigs, has been reported frequently in people who work with these animals.^{13,16-20,22,24,28-34,44,47,49-54,56,91,132,133} Isolates can also be shared between personnel and animals, including dogs, cats and horses, in veterinary hospitals.^{5,7,9,14,21,25-28,36,37,39,83} In most cases, the direction of transfer in veterinary hospitals is based on circumstantial evidence, such as the timing of the infections and/or the type of isolate (e.g., human hospital-associated).^{5,7,9,14,21,26,27,36} It is likely that transmission can occur in both directions during outbreaks. Infection or colonization has been observed in people after as little as 4 hours of close contact with a sick, MRSA colonized foal.³⁶

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One study suggested that there is only a small risk of transmission from colonized surgical staff if infection control protocols are followed.²⁵ Shared isolates have also been reported occasionally between people and pets in households or healthcare facilities (e.g., nursing homes).^{2,3,72,77-79,84-86} Sometimes, MRSA is spread by animals or people with infected wounds or other illnesses; however, transmission can also occur inapparently, from colonized people or animals to humans or animals that become asymptomatic carriers.

Environmental contamination has been reported in veterinary practices, even at times when MRSA patients were not detected.^{23,26,134} In one survey, MRSA was identified in environmental samples from 9% of Canadian veterinary hospitals.¹³⁴ In abattoirs that slaughter CC398 carrier pigs, MRSA could be found in a number of areas by the end of the day, but only limited locations were still contaminated by the next morning.³⁰ A study from China reported MRSA ST9 in dust samples from approximately 56% of pig farms.¹³⁵ Preliminary results also suggest that MRSA may occur in air samples outside MRSA-contaminated swine confinement operations, as well as in shower facilities used by swine workers on farms.⁴⁶ Zoonotic transmission seems to be more common from some species than others.

Pigs

CC398, is often transmitted from pigs to people in close contact.^{13,16-20,22,24,28-34} Most studies report that person-to-person spread of CC398 seems to be infrequent.^{17,24,34,42,49} Although some transmission has been reported within families or in hospitals and institutions, CC398 seems to be uncommon in people without any livestock contact.^{17,32,33,42,49-51} On some German farms with CC398-colonized pigs, 86% of people who worked with pigs, and 4.3% of their unexposed family members, carried the organism.⁴⁹ Approximately 45% of swine veterinarians and 9% of their family members were also colonized with CC398 in this study.⁴⁹ For both livestock workers and veterinarians, no more than one family member tested positive for MRSA.⁴⁹ Only three of 462 German schoolchildren tested in a pig-dense area were carriers, and all three lived on pig farms.⁴⁹ Similarly, colonization was detected in 33% of farmers, but 8% of their family members, in a study from Belgium.⁵⁶ Short chains of transmission have been occasionally reported among people. In one case, MRSA was found in the son of a veterinarian who worked with pigs, and this strain was transmitted to a nurse.³⁴ In another, CC398 was apparently transmitted from a colonized swine veterinarian to his dog, although the dog had no contact with livestock.⁵⁸ A recent outbreak of CC398 in a hospital in the Netherlands suggests that more extensive person-to-person transmission can occur under some conditions.¹³⁶

In China, where MRSA ST9 seems to be common in swine, this organism has been detected in people who work closely with pigs.¹³²

Horses

There is evidence that some MRSA strains may be spreading in equine populations, and some MRSA in horses seem to distinct from the common human strains.^{5,23,26,27,36,61,91} Shared isolates between humans and horses have been described in veterinary clinics,^{5,7,9,26,27,36,39} and an elevated risk of MRSA was reported among equine practitioners at a veterinary conference.^{16,137}

Cattle

Contact with veal calves is a significant risk factor for human colonization with CC398.^{16,42,56} There are sporadic reports of MRSA transmission between other types of cattle and humans, including cases where cows with mastitis and human handlers shared the same isolate.^{55,138} Shared isolates have included both human-associated strains and CC398.^{55,138}

Poultry

Poultry farmers can be colonized by MRSA CC398.³² Elevated rates of MRSA carriage were also reported in poultry slaughterhouse workers in the Netherlands, with much higher carriage rates among workers who contacted live birds than those who worked only with dead fowl.¹⁰⁸

Dogs and cats

In contrast to livestock, transmission between people and pets seems to be relatively infrequent.^{2,3,78,84,85} MRSA isolates in dogs and cats tend to be human hospital-associated or community-associated strains,^{14,16,21,26,27,85,91,95} and most canine and feline infections are thought to be acquired from people.^{3,14,16,21,58,86,91,95} Case reports and case series suggest that, once they become colonized, companion animals can sometimes transmit MRSA back to humans.^{23,72,78} Transmission between staff and dogs or cats has been reported in some veterinary hospitals.^{14,21,26,83} A cat was implicated as a reservoir for continued transmission during an outbreak in a geriatric nursing facility.⁷⁷ It was thought to have been colonized from humans during the outbreak. When the cat was removed from the ward and infectious disease measures to control the MRSA were introduced, the outbreak resolved. In another long-term care facility, nasal colonization was reported in some but not all of the animals that lived on or visited floors with human MRSA cases, and not in animals or humans on another floor.⁸⁶ MRSA was cultured repeatedly from one cat in this facility, but colonization appeared to be transient in another cat, and several exposed animals were never MRSA-positive.⁸⁶ Shared isolates have also been reported in some individual households. In a few case reports, family pets seem to have acted as one reservoir

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for the bacteria, and decolonization of humans was unsuccessful when carriage in these animals was not addressed.^{72,78,79} The frequency with which this occurs is still poorly understood. In Hong Kong, a survey found that less than 1% of dogs or their owners were colonized with MRSA, and in all cases, only the dog or only its owner was colonized.¹⁵ A recent study reported that, of eight U.S. households with recurrent carriage in a person, pets were colonized in only one.⁸⁵ Conversely, 27% of households with a MRSA infection in a pet had at least one person colonized by MRSA.⁸⁵ In these households, 18% of the people, 8% of the other dogs, and 10% of the other cats were colonized.⁸⁵ Another U.S. study found that, although the carriage rate in people was 5-6%, less than 1% of households had simultaneous colonization of humans and pets.⁸⁴

Exotic animals

There is little information about the transfer of MRSA between exotic animals and people. Humans seemed to be the source of the organism for zoo or marine mammals in two case reports. In one case, colonization with a human MRSA strain (CMRSA2; USA100; ST5-MRSA-SCCmecII) was reported in captive dolphins and walrus at a marine park.⁸¹ Another human strain, USA300 (CMRSA10), was transmitted from an elephant calf with cellulitis and skin pustules to human caretakers in a zoo.⁸² A colonized human is thought to have infected the elephant calf.⁸² No other elephants at the zoo were colonized.

MRSA transmission in meat and other foods

Food may serve as a vehicle to disseminate MRSA. Low degree contamination with *S. aureus* is common in retail meat,⁴² and MRSA has been reported in a variety of meats including raw chicken, turkey, pork, veal, beef, mutton/ lamb, rabbit and game.^{32,42,46,92,139-141} The reported levels vary widely from < 0.5% to 35%, depending on the type of meat and the country of origin.^{42,46,92,139-141} Some of the strains detected in meat belong to the CC398 clonal complex or other animal-associated strains, while other isolates seem to originate as contaminants from humans who handle the meat.^{42,139-141} MRSA, including animal-associated strains, has also been detected in raw milk^{59,92,142,143} and cheese.¹⁴³

S. aureus is not ordinarily invasive when eaten, except under rare and unusual circumstances.⁴² For this reason, accidental contamination with MRSA while handling raw meat is the most important consideration. Food may also serve as a vehicle to disperse MRSA, if the organisms have not been destroyed by cooking.

Disinfection

S. aureus and MRSA are susceptible to a variety of disinfectants including sodium hypochlorite, alcohols, quaternary ammonium compounds, iodophors, phenolics, glutaraldehyde, formaldehyde, and a combination of iodine and alcohol.^{118,144} 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).¹¹⁸

In the environment, *S. aureus* can be found for up to 42 days in carcasses and organs, and 60 days in meat products.¹¹⁸ It remains viable for 46 hours on glass, 17 hours in sunlight, and less than 7 days on floors.¹¹⁸ *S. aureus* enterotoxins are stable at boiling temperatures.¹¹⁸

Infections in Humans

Incubation Period

The incubation period for *S. aureus* infections in humans is highly variable.¹¹⁸ Although many clinical cases become apparent in 4 to 10 days, asymptomatic colonization is common and disease may not occur until several months after colonization.¹¹⁸ Staphylococcal food poisoning typically becomes apparent after 2 to 4 hours, but the incubation period can vary from 30 minutes to eight hours.¹¹⁸

Clinical Signs

In people, *S. aureus* is an opportunist.¹¹⁸ MRSA can cause the same types of infections as other isolates of *S. aureus*. This organism can be involved in a wide variety of skin and soft tissue infections including impetigo, folliculitis, furunculosis, cellulitis, abscesses and wound infections.^{2,12,22,65,117,118,129,145} MRSA can also cause invasive infections such as pneumonia, endocarditis, septic arthritis, osteomyelitis, meningitis and septicemia.^{1,2,12,22,65,117,118,129,146} In healthy people, the community-associated strain USA300 (CMRSA10) has been linked to cases of necrotizing pneumonia after influenza virus infections.¹⁰ 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.^{1,118} MRSA strains have been found in some cases of toxic shock syndrome, particularly in Japan.¹²¹⁻¹²³ MRSA has also been detected in cases of staphylococcal scalded skin syndrome in infants and adults.^{120,122,125,126} 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.¹¹⁸ Staphylococcal scalded skin syndrome usually occurs in children. In adults, this disease is generally associated with immunosuppression.¹²²

Acute staphylococcal gastroenteritis (food poisoning) is caused by the ingestion of preformed toxins, which are produced when *S. aureus* grows in food. The toxin, rather than the live organism, is responsible for the illness. Staphylococcal food poisoning usually develops abruptly.¹¹⁹ The symptoms may include nausea, vomiting, diarrhea, abdominal cramps, prostration and, in severe cases, headache and muscle cramps.¹¹⁸ The disease is self-limiting, and most people recover in 1 to 3 days, although some may take longer.^{118,119} Although MRSA has been

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isolated in some cases of staphylococcal gastroenteritis,¹²⁴ antibiotic resistance is unimportant in its treatment because the organism is not present in the body. Invasive disease is very rare after the ingestion of *S. aureus*.⁴² It has been reported only once in the literature, in an unusual situation where a severely immunocompromised patient had received antacids, as well as antibiotics to which the strain was resistant.⁴² The organism in this instance was methicillin sensitive *S. aureus*, but it seems likely that MRSA could cause the same syndrome under these circumstances.

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.⁶⁵ Human community-acquired-MRSA infections are mainly associated with superficial skin or soft tissue disease.^{5,9,12,129,145,146} Some community-acquired MRSA strains have caused other types of illnesses, including severe sepsis, necrotizing fasciitis and necrotizing pneumonia.^{12,129,146} Community-acquired strains can also occur in hospitalized populations.¹²

Zoonotic MRSA

Zoonotic MRSA can presumably cause the same types of infections as human-associated MRSA strains. Asymptomatic colonization is common,^{13,17,20,22,28,30-32,34} but opportunistic infections also occur.^{13,16,19,22,29,53} MRSA CC398 seems to be less virulent in humans than traditional hospital-associated and community-associated human strains.³² Most human CC398 infections have been superficial skin and soft tissue infections, but more severe or invasive illnesses (aggressive wound infection, destructive otomastoiditis, sinusitis, endocarditis, nosocomial bacteremia, pneumonia, and severe invasive infection with multiorgan failure) have also been reported.^{13,16,19,22,29,32,53,54} Illnesses that have been reported from non-CC398 zoonotic strains include wound infections and skin disease, including necrotizing fasciitis.^{5,36,62,78,147}

Communicability

A colonized or infected person can transmit MRSA to other people, mainly by direct contact.^{2,118} People have also transmitted MRSA to a variety of animal species.^{3,7,14,16,23,25-27,58,77,81,82,91,95} Most studies suggest that CC398 seems to spread less readily between people than human-associated MRSA isolates.^{17,32,33,42,49,50,56} However, outbreaks are possible in hospitals.¹³⁶ Humans remain infectious as long as the carrier state persists or the clinical lesions remain active.¹¹⁸

Diagnostic Tests

S. aureus infections are diagnosed by culturing the affected site, while staphylococcal food poisoning is diagnosed by examination of the food for the organisms and/or toxins.^{119,129} *S. aureus* is a Gram positive, non-spore forming coccus. It may be found singly, in pairs, in short chains or in irregular clusters.¹⁴⁸ The colonies are circular, smooth and glistening.¹⁴⁸ On blood agar, they are usually beta-hemolytic.¹⁴⁸ Young colonies are colorless; older colonies may be shades of white, yellow or orange.¹⁴⁸ Enrichment media, as well as selective plates for MRSA, are available. 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. Detection of the organism in clinical specimens can vary, depending on the isolation method used.¹⁴⁹

If *S. aureus* is isolated from an infection, genetic testing or antibiotic susceptibility testing should be done to identify MRSA.¹²⁹ Fluoroquinolone-resistant *S. aureus* strains should, in particular, be suspected of being MRSA.⁷⁸ Genetic tests to detect *mecA*, such as polymerase chain reaction (PCR) assays, are the 'gold standard' for identification.^{6,23,78,150} PCR methods to detect *mecA* in *S. aureus* are commercially available.^{151,152} A latex agglutination test can be used to detect PBP2a.^{6,23,150} Antibiotic susceptibility tests such as the agar screen test, disk diffusion test, or MIC determination can also be used to identify MRSA.^{2,6,78,150} Most antibiotic susceptibility tests use oxacillin or cefoxitin, as methicillin is no longer commercially available in the United States.⁶ Antibiotic susceptibility testing has some drawbacks compared to the detection of *mecA* or PBP2a. Methicillin-susceptible and resistant subpopulations can co-exist *in vitro*; although the entire colony carries the resistance genes, only a small number of bacteria may express resistance in culture.⁶ The expression of resistance in phenotypic tests can also vary with growth conditions such as temperature.¹⁵⁰ 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.¹⁵⁰

Clones or strains of MRSA are differentiated using genetic tests such as pulsed-field gel electrophoresis, SCCmec typing, multilocus sequence typing, *spa* typing and other tests.^{5,16,91} These techniques are mainly useful for epidemiological studies, such as tracing outbreaks.¹⁶ Some isolates may be untypeable by certain methods.^{16,17} Notably, PFGE cannot identify strains belonging to CC398. PFGE and MLST typing tends to be congruent, but unrelated lineages can sometimes contain similar *spa* types.^{17,100} Additional genetic testing can resolve such discrepancies.¹⁰⁰ *Spa* typing can distinguish isolates that are indistinguishable by MLST or PFGE.¹⁶ A combination of methods may be necessary to identify a strain.

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Treatment

Certain MRSA skin infections, such as some abscesses, can sometimes be treated by incision and drainage, or other management techniques that do not require systemic antibiotics.^{12,118,129,153} Factors such as the location, severity and speed of progression of the infection, as well as the age and health of the patient, can affect the type of treatment chosen.¹⁵³ Invasive staphylococcal infections require antibiotics.^{12,118,129,153} Antibiotic treatment should be based on susceptibility testing. Adjunct measures such as the removal of catheters may also be necessary.¹²

Very few antibiotics are effective in treating infections caused by hospital-acquired MRSA.⁸ All MRSA strains are considered to be resistant to penicillins, cephalosporins, cephems, 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.^{2,7} In addition, hospital-acquired MRSA strains are frequently resistant to most common antibiotics including tetracycline, aminoglycosides, macrolides, chloramphenicol and fluoroquinolones.^{2,6-8} Antibiotics used to treat serious, multiple drug resistant MRSA infections include vancomycin, as well as newer drugs such as linezolid, tigecycline, quinupristin/dalfopristin and daptomycin.^{6,12,16,153} Isolates with resistance to some of these drugs, including vancomycin, have been reported.^{6,10,16,99} Community-acquired MRSA strains have often been resistant only to β -lactam agents and macrolides and azalides (erythromycin, and azithromycin and clarithromycin).^{6,12} Resistance to other antibiotics such as fluoroquinolones and tetracycline may be increasing in these strains, and multiple antibiotic resistant strains have started to emerge.¹⁰⁻¹² Current recommendations for the treatment of MRSA are available from the CDC or other clinical sources.

Staphylococcal food poisoning, which is caused by toxins, is self-limiting and it is not treated with antibiotics.^{118,124} Supportive therapy may be given, if needed.

Prevention

The Netherlands and Scandinavian counties have greatly reduced the incidence of hospital-associated human MRSA, using screening and control programs targeted at hospital staff and patients.^{11,42,91} In the Netherlands, hospital personnel are screened and treated for MRSA carriage.³³ Patients at risk for colonization are screened on admission to the hospital and isolated if they are carriers.³³ High risk patients, including people who work with pigs or veal calves, are isolated until the screening test demonstrates that they are MRSA-free.³³ Carriers who do not eliminate the organism are decolonized.³³ MRSA outbreaks are also investigated aggressively, and antibiotic use is restricted.⁵¹ Opinions in

other countries remain divided on the benefits of screening on admission, compared to universal infection control procedures used alone.¹⁵⁴⁻¹⁵⁹ Decolonization of humans is also controversial, and may be recommended in some situations or groups of patients, but not others.^{12,127,153,160} Decolonization is not routinely recommended for community-associated MRSA.¹⁵³

A variety of decolonization methods have been used in people. Intranasal mupirocin and fusidic acid, alone or in combination with other topical antimicrobials such as bacitracin and chlorhexidine, have been used in some cases.^{16,21} Systemic antibiotics have also been employed.¹² If other family members are also carriers, they should be treated simultaneously.^{3,78} Carriage in pets may need to be considered if a household must be decolonized (see below, for decolonization in animals). Decolonization is not always successful; the organism may be reintroduced by carriage in other parts of the body, and resistance to drugs, including mupirocin, can occur.^{12,21} One trial, which tested the simultaneous use of intranasal mupirocin, 2% chlorhexidine gluconate for bathing, and oral rifampin and doxycycline, found that 74% of individuals remained free of MRSA after 3 months, and 54% after 8 months.¹² People who are in contact with pigs carrying CC398 often become recolonized from this source, and it is uncertain whether livestock workers should be decolonized.³³ In one family colonized with CC398, the efficacy of mupirocin treatment was poor in family members who worked on a pig farm, and better in family members who had only occasional contact with pigs.²⁴

Good hygiene, particularly hand washing, is important in preventing the transmission of MRSA between people in hospitals and other institutions, as well as in the community.^{6,12,21,146,153} Specific guidelines have been published by the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force, as well as a CDC-convened experts' meeting on the management of MRSA in the community (see Internet Resources).^{153,161} Other important measures in hospitals include environmental cleaning and disinfection, and isolation precautions for MRSA-infected, hospitalized patients.¹² Outpatients with MRSA skin lesions should keep them covered with clean, dry bandages and practice good hygiene to prevent transmission to others.¹⁵³ In some circumstances, such as the inability to adequately cover a MRSA-infected wound, close contact with other people should be avoided.¹⁵³

Precautions recommended for preventing transmission from livestock and other animals include hand washing and other basic hygiene, and protective clothing where appropriate.¹⁶ Skin lesions should be covered to prevent them from becoming infected.¹⁶ One article suggested using gloves and face masks when working with livestock.⁵² Although hand washing

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between cases or farms was reported to reduce colonization among equine veterinarians, there are reports that hygiene measures including protective clothing and disinfection of the hands did not decrease CC398 carriage in swine workers.^{16,18,137} The reason is still uncertain, and it is possible that the implementation was ineffective. The use of hot water baths to scald carcasses, as practiced in China, might help protect abattoir workers from MRSA in swine.¹³² People who are unusually susceptible to MRSA, such as immunocompromised persons and post-surgical patients, should be educated about the risks of zoonotic MRSA and the role of good hygiene, such as hand washing before and after contact with pets, and avoidance of direct contact with nasal secretions and wounds.

The possibility of transmission from animals that participate in animal-assisted therapy must also be considered. MRSA has been identified in a few pet therapy dogs after visits to healthcare facilities, as well as in a few resident animals.^{77,86,162,163} For visiting therapy animals, a committee of Canadian and U.S. experts (2007) recommended that emphasis be placed on hand hygiene and good infection control procedures.¹⁶⁴ Routine screening to identify specific pathogens, including MRSA, was not recommended. However, screening should be conducted if the animal has been in contact with a MRSA case or there is any other reason to believe it may be colonized.¹⁶⁴ The current CDC Guidelines for Environmental Infection Control in Health-Care Facilities, which addresses resident animals, does not make specific recommendations for MRSA prevention or control in this group.¹⁴⁴ In 2004, one paper recommended that resident pets in hospital or nursing home environments be monitored for MRSA as if they were part of the staff (i.e., if screening programs are conducted in staff, they should include resident animals).³ In 2010, there were no published guidelines when MRSA-colonized animals are detected among resident animals in a healthcare facility.⁸⁶ In one recent outbreak, options presented to the facility, after consultation with experts, included removing the animal until it clears the bacterium, or allowing it to remain in the facility, with or without antibiotic treatment, and with continued monitoring (culture) and the encouragement of good hand hygiene among human contacts.⁸⁶

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.¹¹⁹ Hygiene and good meat handling practices are expected to reduce the risk of infection or colonization from MRSA on contaminated meat.³² Pasteurization will destroy organisms in milk. The detection of MRSA in cheese (pecorino and Romano cheese in Italy) might be a greater concern.¹⁴³

Morbidity and Mortality

MRSA colonization

Approximately 25-50% of the human population is a nasal carrier of *S. aureus*.^{3,42,118,129} About 20% are thought to carry one strain persistently, while up to 60% are intermittent carriers.⁹¹ MRSA carriage rates in the general population vary from less than 1% to 5%.^{42,84,91,165} The prevalence varies with the geographic region.^{2,9,91} Human-adapted, hospital strains of MRSA are rare among people in the Netherlands and Scandinavian countries, where extensive control programs are in effect.^{42,91} Danish control programs decreased the percentage of MRSA among *S. aureus* from 15% in 1971 to 0.2% in 1984.⁹¹ In the Netherlands, less than 1% of *S. aureus* isolates from clinical specimens are methicillin resistant, and nasal carriage occurs in 0.03% of people admitted to the hospital (excluding people with risk factors for zoonotic carriage).⁹¹ In contrast, more than 50% of human *S. aureus* isolates were reported to be methicillin resistant in Korea in the early 2000s.² In the U.S., approximately 1.5% of the population carried MRSA in 2003-2004.¹¹ One recent U.S. study reported that, overall, 5.6% of its study population was colonized.⁸⁴

MRSA colonization among human healthcare workers and veterinary personnel

Human healthcare workers are expected to be at an increased risk for colonization, due to occupational exposure. One study reported a carriage rate of 11% among healthcare workers and 5% in non-healthcare workers in India.¹⁶⁶ In another study from Taiwan, the carriage rates were 7.6% and 3.5%, respectively.¹⁶⁷ Like the general population, healthcare workers can also be colonized with community-associated or livestock-associated MRSA. In the Netherlands, MRSA was detected in 1.7% of healthcare workers who had some contact with pigs or veal calves, and 0.15% of healthcare workers who had no contact with livestock, although the difference was not statistically significant.⁵¹

A number of studies have reported elevated MRSA carriage among veterinary personnel, even in people with no known link to a MRSA case.^{16,23,49,52,84,137,168-172} Reported colonization rates among staff at veterinary hospitals and referral clinics in Europe and North America range from 0% to 10%, and have occasionally been reported to be as high as 27%.²³ Although carriage rates can be higher during outbreaks, some hospitals had no carriers even when MRSA patients were hospitalized.²³ Surveys that examined swine, equine and small animal practitioners have reported increased carriage in all three groups. MRSA carriage was detected in approximately 10% of veterinary practitioners attending an international equine veterinary conference, with an increased risk among practitioners who had treated a horse with MRSA in the last year.^{16,137} Approximately 12% of the participants at an international

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conference on pig health also carried MRSA, mainly CC398.¹⁷⁰ Small animal practitioners had lower carriage rates in some but not all studies. At the 2005 American College of Veterinary Internal Medicine Forum, MRSA colonization was reported in 7% of veterinarians, 12% of technicians, and no participants without animal contact.¹⁷¹ In this study, 15.6% of large-animal personnel and 4.4% of small-animal personnel were colonized. A survey of practitioners in Denmark reported carriage rates of approximately 4% in all veterinarians, 3% among small animal practitioners, and <1% in people not professionally exposed to animals.^{23,168} However, a study of participants at the 2008 American College of Veterinary Surgeons Symposium reported colonization rates of 17% in veterinarians and 18% in technicians, with similar rates among small animal and large animal practitioners.¹⁷² Other studies have reported colonization rates of 3% (veterinarians in Switzerland), 4.6% (veterinarians and veterinary students in contact with livestock in the Netherlands) and 45% (veterinarians who care for pigs in Germany).^{49,52,169}

In the U.S., one study examined whether people from households containing healthcare workers or veterinary healthcare workers have elevated rates of carriage, compared to the general population. In this study, the colonization rate was similar among all three types of households, and ranged from 5% (no healthcare workers) to 6% (households with either human or veterinary healthcare workers).⁸⁴

MRSA colonization among livestock workers

In countries where livestock are colonized with MRSA (especially CC398), people who work with these animals on farms or in abattoirs have elevated MRSA carriage rates.^{16,18,20,31,44,47,49-51,56,91,108,132,133} A few studies also suggest increased MRSA carriage among people who work with CC398-colonized poultry.^{32,108} In the Netherlands, the prevalence of MRSA is less than 1% in the general population, but rates of 15-27% have been reported in farm and abattoir workers who handle live swine.^{31,50-52} One study reported that some swine workers were carriers on 30% of the farms with MRSA colonized pigs, but no human carriers could be detected on non-colonized farms.³¹ Similarly, studies from Germany and Belgium have reported carriage rates as high as 33-86% among people who work with CC398-colonized pigs or live on colonized farms.^{18,49,56} On Dutch veal calf farms, the prevalence in farmers was greater than 10% when at least 20% of the calves were colonized, but approximately 1% when less than 20% of the calves were colonized.⁵⁶ The authors suggest that carriage in humans might be transient. Another study reported transient colonization in people who collected samples from workers on swine farms.³¹ MRSA carriage was not detected in pig farmers or slaughterhouse workers in Switzerland, where the prevalence of MRSA was very low (0-1.3%) in pigs or cattle.¹⁶⁹ In abattoirs in the Netherlands, MRSA carriage

is reported to be much higher among workers who handle live pigs or poultry than in those who do not work with live animals.^{30,108}

Relatively little is known about the colonization rates among swine workers in North America. In Canada, 20% of the swine workers, 25% of pigs, and 45% of farms were reported to be colonized, often with MRSA CC398 but also with CMRSA2 (EMRSA3; USA 100).²⁰ In the US, one study examined two conventional midwestern farms, and found MRSA CC398 in one of the two production systems.⁴⁷ In the production system with colonized pigs, CC398 was detected in 64% of the workers.⁴⁷ It was not found in people at the other farm's facilities.⁴⁷ Preliminary findings, presented at a 2009 conference, suggest that the prevalence of MRSA carriage may be higher among workers in confinement operations than antibiotic-free facilities in the U.S.⁴⁶ In Manitoba and Saskatchewan, Canada, the prevalence of CC398 carriage among the general population was 0.14% in 2007-2008.¹⁷³

Relatively little is known about colonization among livestock workers in Asia. In Malaysia and China, where studies detected ST9 but not CC398 in swine, some people who work with pigs carry ST9.^{16,132,133} Colonization was reported in both pigs and people in China, but no farms had MRSA in both pigs and workers in Malaysia.^{132,174}

Illness caused by MRSA

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} Risk factors for infection include hospitalization, residence in a long-term care or assisted living facility, dialysis, and the presence of indwelling percutaneous catheters or other medical devices.⁶⁵ Most MRSA infections are seen in high risk patients, including the elderly and people with open wounds.⁶¹ Patients in ICUs are particularly susceptible.^{3,36} In the U.S., healthcare-associated MRSA infections became increasingly prevalent between the late 1970s and the mid-2000s: MRSA accounted for 2.4% of nosocomial infections in the late 1970s, 29% in 1991, and 43% in 2002.^{3,9} Nosocomial MRSA infection rates reported in human hospitals, prior to 2006, were 5.9 per 1000 admissions in France, 4.7 per 1000 admissions in Hong Kong, 0.76 per 1000 admissions in Ontario, Canada, 0.53 per 1000 admissions in Taiwan, and 1.7 per 1000 admissions in the US.³⁶ Invasive healthcare-associated MRSA infections in the U.S. decreased between 2005 and 2008.¹⁷⁵

Although some individuals in the community carry hospital-associated MRSA, these strains do not usually spread extensively within communities; different isolates are generally responsible for community-associated MRSA.^{11,176} Community-acquired MRSA infections are becoming more common in people, although their prevalence still seems to be low in many European

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countries.^{5,9,11,78} These infections initially appeared in high-risk populations such as intravenous drug users, people in nursing homes, and those who were chronically ill, but they are now reported even in healthy children^{3,10} Outbreaks have been seen in various closed living groups including athletes, military recruits, children, homosexual men and prisoners.¹²⁹ 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.^{10,129} Community-associated MRSA are also an increasing problem in U.S. hospitals, where they seem to contribute to additional infections rather than displacing hospital-associated strains.^{11,64,176}

CC398 may be less virulent in people than traditional hospital-associated and community-associated human strains, although severe infections can occur.^{16,19,32} In one hospital in the Netherlands, approximately 13% of the patients who carried CC398 had symptomatic infections, while 42% of the patients colonized with other isolates were affected.³³ In Belgium, where 38% of humans who lived on swine farms were colonized with CC398, skin infections with this organism occurred in 0.8%.¹⁸

As with many bacterial infections, the mortality rate for MRSA infections 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 colonization or infections have been reported in many species including pigs,^{16,17,20,31,32,38,47,49-51,91,106,132,133} dogs,^{3,8,14,17,21,23,27,35,58,69-76,78,79,92,94,114} horses,^{5,7,9,14,17,23,27,36,61-64,75} cats,^{3,17,23,27,35,65,71,74-77,95} cattle,^{2,17,55,56,59,66,67,70,138} sheep,⁶⁸ rabbits,^{23,27,35,74} rats,⁶⁰ guinea pigs,^{23,35} a chinchilla,²³ a bat,³⁵ a seal,²⁷ dolphins,⁸¹ a walrus,⁸¹ an elephant,⁸² poultry,^{2,57,108,109} pigeons,¹⁷⁷ parrots,^{35,74,80} and turtles.^{23,35}

Cats and dogs seem to be colonized mainly by isolates from humans.^{3,15,23,35,95} In contrast, some equine-adapted strains may be spreading among horses.^{5,23,26,27,36,61,91} Whether cats, dogs and horses should be considered reservoirs for MRSA, or colonization is only temporary, is still uncertain.²³ Pigs seem to be true reservoir hosts for CC398.^{16,17,23,32,34,38,39} This clonal complex is the predominant MRSA among pigs in Europe, but CMRSA2 is also relatively common among pigs in Canada.^{20,32} Different strains may predominate in other geographic areas. ST9 has been recognized among pigs in China, Hong Kong and Malaysia.^{16,132,133} CC398 does not seem to be particularly host specific, and it has been detected in other species

including horses, poultry, cattle, humans, dogs and rats.^{13,16,18-20,22,28-32,34,39,44,45,49,55,56-60,97,108,109}

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 without developing clinical signs.

Clinical Signs

MRSA has been found in asymptomatic carriers including pigs, dogs, cats, horses, calves and other animals.^{3,5,14,16,17,20,23,32,38,56,62,72,77-79,91,97,106}

S. aureus can cause a wide variety of suppurative infections in animals.^{2,16} MRSA has been isolated from various skin and wound infections including abscesses, dermatitis including severe pyoderma, exudative dermatitis in pigs, postoperative wound infections, fistulas, and intravenous catheter or surgical implant infections.^{2,3,5,7,9,14,16,21,23,28,35,37,39,62-65,73,80,92,94-97} It has also been found in other conditions including pneumonia, rhinitis, sinusitis, otitis, bacteremia, septic arthritis, osteomyelitis, omphalophlebitis, metritis, mastitis (including gangrenous mastitis) and urinary tract infections.^{5,9,14,16,23,32,35,37,39,55,59,62-64,66-68,92,97,138} Both

Bordetella bronchiseptica and MRSA were isolated from the nasal and oropharyngeal tract of puppies after an outbreak of fatal respiratory disease; the role of MRSA in the outbreak was uncertain.⁹⁷ In addition to causing mastitis in dairy cattle,^{32,55,59,138} one study suggested that MRSA in milk was associated with higher somatic cell counts than methicillin-sensitive *S. aureus*.⁵⁹ MRSA was also isolated from a suppurative area in chicken meat and from the joints of a chicken with signs of arthritis.² In a recent study, most equine MRSA infections at veterinary hospitals were opportunistic.⁶⁴

Communicability

MRSA from colonized or infected animals can be transmitted to humans, as well as to other animals.^{3,5,13,16,17-20,22-24,26-34,36,37,72,77,82} Some strains, such as CC398, seem to be transmitted efficiently within pig populations and from pigs to people.^{16,18,20,31,32,44,47,49-51,56,91,108,132,133} How readily the various MRSA lineages can be transmitted between dogs or cats is still unclear. One case report found high levels of colonization with CC398 in a kennel of dogs, although different animals were colonized when samples were collected two weeks apart.⁹⁷ Another study conducted at a rescue facility suggests that transmission of human-associated MRSA may not occur readily between healthy dogs.⁹⁶ In this study, MRSA was not transmitted from colonized dogs to their kennel mates, or from a dog with a surgical wound infection to its kennel-mate.⁹⁶

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Diagnostic Tests

S. aureus infections, including colonization, are diagnosed by culture. MRSA can colonize more than one site, and the best site for detecting carriers among dogs and cats is unknown.⁸⁴ Nasal and rectal sampling should both be done whenever possible.⁸⁴ In swine, one study reported that nasal swabs detected most colonized pigs, but some animals carried MRSA in both locations, and a few carrier pigs (all weanlings) could only be found using rectal swabs.²⁰ *S. aureus* is a Gram positive, non-spore forming coccus. It may be found singly, in pairs, in short chains, or in irregular clusters.¹⁴⁸ The colonies are circular, smooth and glistening.¹⁴⁸ On blood agar, they are usually beta-hemolytic.¹⁴⁸ Young colonies are colorless; older colonies may be shades of white, yellow or orange.¹⁴⁸ Enrichment media, as well as selective plates for MRSA, are available. Detection of the organism in clinical specimens can vary, depending on the isolation method used.¹⁷⁸ 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 can identify methicillin resistant strains.¹²⁹ Genetic tests to detect *mecA*, such as PCR, are the 'gold standard' for identification.^{6,23,78,150} PCR methods to detect *mecA* in *S. aureus* isolates from humans are commercially available.^{151,152} A real-time PCR test validated for the detection of human nasal carriage had poor agreement with culture results in horses.¹⁷⁹ A latex agglutination test can be used to detect PBP2a.^{6,23,150} Antibiotic susceptibility tests such as the agar screen test, disk diffusion test, or MIC determination can also be used to identify MRSA.^{2,6,78,150} Most antibiotic susceptibility tests use oxacillin or cefoxitin, as methicillin is no longer commercially available in the U.S.⁶ Antibiotic susceptibility testing has some drawbacks compared to detection of *mecA* or PBP2a. Methicillin-susceptible and resistant subpopulations can co-exist *in vitro*; although the entire colony carries the resistance genes, only a small number of bacteria may express resistance in culture.⁶ The expression of resistance in phenotypic tests can also vary with growth conditions such as temperature.¹⁵⁰ 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.¹⁵⁰

Clones or strains of MRSA are differentiated by genetic tests such as PFGE, MLST, SCCmec typing, spa typing and other assays.^{5,16,91} These techniques are usually used for epidemiological studies, such as tracing outbreaks.¹⁶ Some isolates may be untypeable by certain methods.^{16,17} Notably, PFGE cannot identify CC398. PFGE and MLST typing tends to be congruent, but unrelated lineages can sometimes contain similar spa types.^{17,100} Additional genetic testing can resolve such

discrepancies.¹⁰⁰ Spa typing can distinguish strains that are indistinguishable by MLST or PFGE.¹⁶ A combination of methods may be necessary to identify a strain.

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.^{2,7}

MRSA isolated from animals vary in their antibiotic susceptibility.^{2,5,14,16,32,55,64,180} Most CC398 MRSA are resistant to tetracyclines, and many are also resistant to trimethoprim.^{16,32,180} However, the precise susceptibility patterns of these isolates can vary widely. In one study, MRSA CC398 isolates from bovine mastitis cases in Germany demonstrated 10 different antibiotic resistance patterns, with approximately 41% of isolates resistant only to beta-lactam antibiotics and tetracyclines.⁵⁵ Another study reported 22 different antibiotic resistance patterns among CC398 isolates from pigs.¹⁸⁰ Susceptibility to fluoroquinolones and resistance to tetracycline has been identified as characteristic of the epidemic MRSA strain CMRSA5 (CC8 lineage; USA500), found among horses especially in Canada.⁶⁴ Some MRSA can appear sensitive to clindamycin during routine sensitivity testing, but carry a gene that allows them to become resistant during treatment.¹⁸¹ In one study, inducible clindamycin resistance was very common among erythromycin-resistant, clindamycin-susceptible MRSA isolates from dogs and cats in Canada.¹⁸¹

Some antimicrobials such as vancomycin, tigecycline and certain other drugs are considered to be critically important antimicrobials for use, sometimes as a last resort, in human MRSA infections.¹⁶ These drugs are controversial for the treatment of MRSA-infected animals.¹⁶ Using them may place selection pressure for antibiotic resistance on MRSA that may also infect humans.¹⁶ Recent publications should be consulted for the current list of such drugs.

Antibiotics and other measures have been used successfully in case reports in animals.^{16,21} In some cases, surgical implants were also removed.²¹ One dog with MRSA septic arthritis was treated successfully with a surgically implanted, absorbable gentamicin-impregnated sponge.⁷³ Local treatment with antiseptic compounds such as chlorhexidine, povidone iodine or glycerol may be helpful in some types of infections.¹⁶ Meticulous wound management without antimicrobials was successful in at least one case in a dog.¹⁶ Animals treated with topical therapy alone must be monitored closely for signs of localized progression or systemic spread.¹⁶

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Prevention

Veterinary hospitals should establish guidelines to minimize cross-contamination by MRSA and other methicillin-resistant staphylococci.³ Good hygiene including hand washing and environmental disinfection is important in prevention.^{16,21} Dedicated clothing that can be laundered at the clinic should be worn, and gloves and other personal protective measures should be used when there is a risk of contact with body fluids.⁹¹ Good infection control measures should be employed, especially with invasive devices such as intravenous catheters and urinary catheters.¹⁶ Barrier precautions should be practiced when treating animals with recognized MRSA infections, and these animals should be isolated.^{16,91} MRSA-infected wounds should be covered whenever possible.^{16,91} Although colonized people can transmit MRSA to animals, one study suggests that there may be only a small risk of transmission from colonized surgical personnel if infection control protocols are followed.²⁵ In this study, MRSA wound infections occurred in four of 180 surgical cases in which the primary surgeon was persistently colonized, and none of 141 cases seen by a surgeon who was not colonized; this difference was not statistically significant.²⁵

Researchers have recommended that veterinary hospitals initiate surveillance programs for MRSA infections, particularly in horses.^{3,61} Screening at admission allows prompt isolation of MRSA carriers and the use of barrier precautions to prevent contact with other animals.³⁶ It also allows clinical cases to be recognized rapidly. Routine screening of all admitted animals may be costly, and it may be practical only for referral practices.^{16,91} For this reason, some authors recommend screening targeted populations, including animals with non-antibiotic responsive, non-healing or nosocomial infections, and animals belonging to healthcare workers or known MRSA-positive households.^{16,91} Animals that have been in contact with MRSA cases or infected/colonized staff should also be tested.¹⁶ If staff are screened for any reason (e.g., during an outbreak), this must be undertaken only with full consideration of privacy and other concerns.

There are currently no proven, completely reliable methods to decolonize animals, and the efficacy of decolonization in animals is unknown. Various measures have been used successfully in individual cases. Colonization in dogs, cats and horses often seems to be transient, and some animals have spontaneously eliminated MRSA when the environment was regularly cleaned and disinfected, and re-infection was prevented.^{16,96} Captive dolphins and walrus colonized at a marine park also cleared the carriage with only infection control procedures, although long term carriage (15 months) was reported in one dolphin.⁸¹ Whether all MRSA types can be eliminated in all species with similar measures is still uncertain.¹⁶ Routine decolonization with antimicrobials is currently not

recommended for pets, but it may be considered in individual cases to control transmission to humans or other animals (e.g., when an animal remains a persistent carrier or infection control measures are impossible).¹⁶ In rare cases where an entire family is being decolonized, kenneling an animal, preferably in isolation, might allow it to spontaneously eliminate MRSA without additional measures.¹⁶ A variety of antimicrobials have been used to decolonize animals in individual cases, but the efficacy of the various drugs is still unknown. Oral doxycycline and rifampin eliminated MRSA carriage in one asymptotically colonized dog.⁷⁸ Rifampin and ciprofloxacin, or fusidic acid and chlorhexidine were successful in two other dogs.^{16,96} Topical treatment (e.g., mupirocin) to eliminate nasal carriage has been considered to be impractical in pets.⁷⁸ Mupirocin resistance can occur in some MRSA isolates.^{16,37}

A combination of techniques has been used to control MRSA in some infected facilities. On two horse farms, the use of enhanced infection control measures, segregation of carriers and repeated screening, without antimicrobial treatment, eliminated colonization in many animals.¹⁸² People who had been colonized were referred to a physician for decolonization. Intranasal amikacin was used to eliminate long term carriage in two horses that remained colonized after 100 days. Amikacin was unsuccessful in one horse, which was then treated with two courses of oral chloramphenicol. This animal eventually eliminated the MRSA by 30 days after the end of treatment. Once MRSA was eliminated, screening of new horses and periodic testing of residents was established to prevent its reintroduction.

Management techniques may affect MRSA colonization on a farm.³² In some cases, MRSA appears to be introduced when buying new stock, and to be spread during livestock movements.³² Biosecurity measures, such as dedicated clothing and showering in, may decrease the risk of MRSA introduction to a farm by visitors, or reduce transmission between units. Infection control measures, including improved hygiene, might also decrease transmission between farms.¹⁶ Because MRSA CC398 has been detected in rats living on pig farms or mixed pig/veal operations, rats should be considered in control programs.⁶⁰ Whether MRSA in manure poses a risk when used as fertilizer, and the effectiveness of measures such as composting or heat treatment in prevention, are unknown. It is possible that avoiding routine antimicrobial use in food animals, to decrease selection pressures, might decrease the prevalence of MRSA among livestock.¹⁶

Morbidity and Mortality

Prevalence of MRSA in dogs and cats

S. aureus is not a common staphylococcal species in dogs and cats; this organism is typically recovered from less than 10% of these animals in most studies,^{3,84,91}

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Colonization with MRSA seems to be uncommon among healthy dogs and cats when not linked to a source of MRSA, but it may be found more readily in hospitalized animals, especially during outbreaks.^{3,7,8,16,23,61,78} In healthy dogs and cats in the community, carriage rates from 0% to 2% were reported in studies from the U.S., Canada, Denmark, Ireland, Hong Kong and Brazil.^{15,23,41,87-90} In one U.S. study, MRSA was isolated from none of 50 healthy dogs in the community, and 1.6% of dogs with inflammatory skin conditions.⁸⁷ Another U.S. study reported a higher prevalence, with 3.3% of dogs and 4% of cats colonized with MRSA.⁸⁴ In this study, there were no differences in the colonization rate among pets (or people) from households with or without a human or veterinary healthcare worker.⁸⁴

Higher colonization rates have been reported in some veterinary clinics, kennels and other facilities, especially during outbreaks. Carriage rates among dogs in several private clinics, teaching hospitals or rescue facilities in the U.S., the U.K. and Japan ranged from 8% to 20%, with the highest rate reported in a referral clinic during an outbreak.^{23,96,98} In some dogs, the carriage was transient.⁹⁶ One recent study reported that MRSA could be detected in 2.5% of clinical samples containing coagulase positive staphylococci taken from sick dogs, and 12.5% of such samples from sick cats, at veterinary clinics in the U.S. Midwest and Northeast.¹⁰⁵ Another study from the U.S. found that 14% of the *S. aureus* isolates submitted by veterinary teaching hospitals in 2001-2002 were MRSA; the positive samples originated from four horses, four dogs and a cat.⁸ Similar surveys from the U.K. and Ireland reported that MRSA occurred in less than 1.5% of clinical samples from dogs and cats, and was isolated from very few healthy animals,^{75,90} while a study from the Republic of Korea found that 4% of *S. aureus* isolates in clinical samples from hospitalized dogs were methicillin resistant.⁹² Particularly high carriage rates were reported in a kennel of dogs infected with MRSA CC398 in Canada.⁹⁷ In this kennel, clinical cases were reported in several animals, and MRSA was isolated from 40% of the remaining asymptomatic dogs, including 75% of the puppies, but not from two pet cats or two people.⁹⁷ In a second test two weeks later, 29% of the dogs carried MRSA; however, the only dog that was positive on both occasions was a bitch that developed gangrenous mastitis.⁹⁷ One of the owners of the kennel worked with pigs, but it is not known whether the MRSA came from that source.⁹⁷

There are a few anecdotal reports of colonization among resident animals in human healthcare or assisted living facilities. A cat was implicated as a reservoir for continued transmission during an outbreak in one geriatric nursing facility.⁷⁷ This cat was probably colonized from humans during the outbreak. In another long-term care facility with a 5.6% MRSA prevalence among its human residents, two of 11 cats became nasal carriers.⁸⁶ Both

colonized cats were residents on floors with infected people. A human strain was isolated repeatedly from one of these cats, but the other cat was positive at only 2 of 8 sampling periods. The one dog in the facility did not carry MRSA. Some animals in this facility lived on or visited the same floors as the MRSA-positive cases, but did not become colonized.⁸⁶

Risk factors that have been identified for MRSA infections in dogs and cats include contact with human carriers, repeated courses of antibiotics, hospitalization for several days, intravenous catheterization and surgery.^{23,94} The presence of suture material or orthopedic implants seems to be linked to persistent infections.⁹¹ Reports of MRSA infections in companion animals, mainly as postoperative complications and wound infections, appear to be increasing.⁹¹

Prevalence of MRSA in horses

Some surveys in healthy horses report a low prevalence of MRSA carriage. In surveys conducted between 2004 and 2007, MRSA was not detected in any horses (samples of 100-500 healthy animals) in the Netherlands, Slovenia, or Canada.^{16,112,113,183} Another survey reported that 1.3% of horses in western Canada carried MRSA in 2006 and 2007, although the colonization was often transient.¹⁸⁴ In Ireland, carriage was detected in 1.7% of healthy horses in 2005-2006.⁹⁰ One investigation of community-acquired infections among horses in North America found that these infections were clustered: colonization with MRSA was detected in 13% or 5% of the horses on two farms, but it was not found in any horses on eight other farms.⁵

MRSA is fairly common in equine clinical samples in some reports. In the U.S., one study reported that 14% of the *S. aureus* isolates submitted by veterinary teaching hospitals in 2001-2002 were MRSA; the positive samples originated from four horses, four dogs and a cat.⁸ Another study, conducted in 2006-2008, detected MRSA in 42% of the clinical samples containing coagulase positive staphylococci from sick horses in the U.S. Midwest and Northeast.¹⁰⁵ In a study from Ireland, MRSA was isolated from approximately 5% of equine clinical samples between 2003 and 2006.⁹⁰ At one diagnostic facility in the Netherlands, the percentage of MRSA isolates in equine clinical samples increased from 0% in 2002 to 37% in 2008.¹⁶

Outbreaks or clusters of clinical cases have been reported occasionally among horses at veterinary hospitals,^{5,8,9,14,36,61,62} and some studies suggest that MRSA may be an emerging pathogen in this species.^{5,16,36,61,62} At a veterinary teaching hospital in Ontario, Canada, MRSA was isolated from the nasal cavity of 4% of horses during an outbreak with CMRSA5 (USA500; ST8-MRSA SCCmecIV) in 2000.⁵ Nosocomial colonization rates varied from 1% to 3.6% among horses admitted in 2002-2004, and clinical nosocomial infections

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occurred in 0.2%, with no increase over the 3 year period.³⁶ In the same hospital, community-associated MRSA colonization was detected in 1.7% of equine admissions in 2002, 1.5% in 2003, and 5.7% in 2004.³⁶ During an outbreak in 2003-2005 at a university veterinary hospital in Austria, the overall incidence was 4.8%.⁹ At a university equine clinic in the U.K., carriage was reported in 16% of the horses tested during an outbreak, and clinical cases occurred in 4%.¹⁴ MRSA carriage has also been reported in 2.2% to 11% of horses presented at equine practices and university hospitals in Belgium, Germany (Berlin) and western Europe,^{16,45,185} but in less than 0.5% of horses tested at four equine clinics in Sweden.¹⁶ Anecdotal reports suggest that MRSA infections are becoming more common in horses, including foals in neonatal intensive care units.⁶¹

Risk factors for MRSA infections in horses may include treatment with antibiotics, contact with carriers, and previous hospital admission.²³ Carriage of MRSA predisposes an animal to nosocomial infection while in the hospital.²³ Surgery and orthopedic implants also seem to be associated with an elevated risk.²³

Prevalence of MRSA in swine

The prevalence of CC398 varies with the geographic region. Reported carriage rates in Europe vary from 1.3% of pigs sampled in Switzerland,¹⁶⁹ to approximately 40% of pigs in Belgium and the Netherlands.^{18,32} Up to 81% of the farms in some countries may be infected with CC398, and many or most of the pigs can be colonized on infected farms.^{16,32,40,42,43} In five German abattoirs, 49% to 80% of the pigs carried CC398, and the colonization rate in each group of pigs ranged from 0% to 100%.⁴⁴ In Canada, one study reported that 25% of the swine and 45% of the farms tested were colonized with MRSA, with approximately 7% to 100% of the pigs colonized on MRSA-positive farms.²⁰ It is not certain whether MRSA was recently introduced on farms with a low prevalence, or if management practices or other factors limit transmission or colonization.²⁰ Most of the isolates identified in this study were CC398, but CMRSA2 (US100; EMRSA3; in CC5) was also relatively common. One study examined two conventional farms in the U.S. Midwest, and detected CC398 in only one of the two production systems.⁴⁷ In the colonized production system, this organism was detected in 36% of the adult sows and 100% of the young animals.⁴⁷ Preliminary findings from one study, reported at conference in 2009, indicated that the prevalence of MRSA in confinement-raised and antibiotic-free swine in Iowa and Illinois was 11% overall.⁴⁶ All of these isolates were found in confinement facilities and no MRSA was detected on antibiotic-free farms. Some studies have reported that colonization varies with the age of the pigs, while others detected no significant difference.^{20,32,47}

MRSA ST9 may colonize swine populations in Malaysia, China and Hong Kong.^{16,132,133} In China, two

studies did not detect MRSA CC398 in pigs, but found that MRSA ST9, which is a minor population in other countries, was the most prevalent type in this species.^{132,135} MRSA ST9 was detected in dust samples from approximately 56% of farms, and 11% of pigs were colonized.^{132,135} Methicillin-sensitive CC398 was found, but methicillin-resistant members of this clonal complex were not.¹³⁵ MRSA ST9 was also identified in 16% of pigs from markets in Hong Kong, and MRSA CC398 was not found.¹³³ In Malaysia, a study reported that more than 1.4% of swine were colonized with ST9 MRSA strains, and MRSA was detected in at least one pig on 30% of farms.¹⁷⁴ Colonization in Malaysia appeared to be transient; when MRSA-positive pigs were retested, they had eliminated the organism.¹⁷⁴ This strain did not have the same spa type as the ST9 strain found in China.¹⁷⁴ Another study from Malaysia reported that the prevalence of MRSA was 0.8% among 4-5 week old pigs.¹⁸⁶ MRSA CC398 has been reported in pigs in Singapore.⁴⁸

Prevalence of MRSA in cattle

One study reported that MRSA (mainly CC398) could be isolated from 88% of veal calf rearing units in the Netherlands, and from 28% of these calves overall.^{16,42,56} The prevalence of MRSA was lower on farms with good hygiene, and calves were more likely to be colonized on larger farms.⁵⁶ The use of antibiotics was also linked to MRSA carriage.⁵⁶ Another Dutch study reported that 50% of the beef calves on one farm were colonized.³²

Although MRSA has caused some outbreaks of mastitis, its prevalence in this condition is not yet known.^{32,55,59,138} Many strains isolated from cases of mastitis seem to be of human origin, although bovine-associated strains have been suggested and CC398 has also been identified.^{32,55,59} A Hungarian antibiotic resistance monitoring scheme found no *mecA*-positive staphylococci in animals or animal food products in 2001, but five MRSA, which all originated from cattle in two dairy herds, were detected in 2003-2004.^{70,187} In Belgium, MRSA CC398 was detected on almost 10% of farms with mastitis problems, and 4-7% of the cattle on infected farms was reported to be infected.³² In South Korea, where MRSA is common among people, the quarter-level prevalence of MRSA in milk was reported to be less than 0.5%.³² In a study from Switzerland, which also found that CC398 was uncommon among pigs in that country, MRSA was detected in 1% of calves and 0.3% of cattle.¹⁶⁹

Prevalence of MRSA in poultry

MRSA has been detected in poultry in several countries, but its prevalence and importance are still poorly understood.^{16,32,57} In Belgium, CC398 was isolated from healthy poultry on 13% of the farms sampled.⁵⁷ Another study from Belgium detected MRSA in 20% to 100% of broiler chickens but not in laying hens.¹⁰⁹ All of these isolates were CC398, but of a spa type not usually detected

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in other livestock.¹⁰⁹ In the Netherlands, 0% to 24% of broilers entering abattoirs carried MRSA, with an overall prevalence of 6.9%, and 23% of their flocks of origin were colonized.¹⁰⁸ Within the colonized flocks, the prevalence of MRSA varied from 10% to 100%.¹⁰⁸ Most of the isolates in this study were CC398, but 28% were ST9.¹⁰⁸

Prevalence of MRSA in other species

There are occasional reports of MRSA colonization in other species, including captive wildlife and marine mammals.^{81,82} The incidence of these infections is unknown. In the Netherlands, MRSA CC398 was detected in rats on 66% of the farms that had pigs, but not on poultry farms or a goat farm.⁶⁰

Morbidity and mortality in clinical cases

The mortality rates for MRSA in animals are expected to vary with the syndrome, with lower mortality rates in superficial infections and higher mortality rates in septicemia and other serious invasive diseases. In a recent study, 84% of horses with MRSA infections at 6 veterinary hospitals in Canada survived to discharge.⁶⁴ High survival rates have also been reported in dogs and cats, probably because most infections are not invasive.¹⁶ In dogs with MRSA infections mainly affecting the skin and ears at veterinary referral hospitals, 92% (of 40 affected dogs) were discharged, with no significant differences in the survival rate for these animals compared to dogs with methicillin-sensitive *S. aureus*.⁹⁴ In a study reporting the treatment of several wound or surgical site infections and pyoderma in dogs, 9 of 11 animals were treated successfully.¹⁶ The mortality rate was 20% in an outbreak of exudative dermatitis caused by CC398 in young pigs.²⁸

Post Mortem Lesions [Click to view images](#)

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

American Veterinary Medical Association. MRSA
http://www.avma.org/reference/backgrounders/mrsa_bgnd.asp

Association for Professionals in Infection Control and Epidemiology. Guidelines for the Control of MRSA
<http://goapic.org/MRSA.htm>

British Small Animal Veterinary Association. MRSA
<http://www.bsava.com/Advice/MRSA/tabid/171/Default.aspx>

Centers for Disease Control and Prevention (CDC)
<http://www.cdc.gov/mrsa/index.html>

CDC. Guidelines for Hand Hygiene in Health-Care Settings.
<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5116a1.htm>

CDC. Management of MultidrugResistant Organisms in Healthcare Settings

<http://www.cdc.gov/ncidod/dhqp/pdf/ar/mdroGuideline2006.pdf>

CDC. Strategies for Clinical Management of MRSA in the Community

http://www.cdc.gov/ncidod/dhqp/pdf/ar/CAMRSA_ExpMtgStrategies.pdf

Guidelines for Animal-Assisted Interventions in Health Care Facilities

<http://www.deltasociety.org/Document.Doc?id=659>

Material Safety Data Sheets – Public Health Agency of Canada, Office of Laboratory Security

<http://www.phac-aspc.gc.ca/msds-ftss/index.html>

Multi Locus Sequence Typing [database]

<http://www.mlst.net/>

Spa-MLST Mapping [database]

<http://spaserver2.ridom.de/mlst.shtml>

The Merck Manual

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

The Merck Veterinary Manual

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

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