Methicillin-Resistant Staphylococcus aureus in Animals

J. Scott Weese

Abstract

Methicillin-resistant Staphylococcus aureus (MRSA) is a critically important human pathogen that is also an emerging concern in veterinary medicine and animal agriculture. It is present in a wide range of animal species, including dogs, cats, rabbits, horses, cattle, pigs, poultry, and exotic species, both as a cause of infection and in healthy carriers. Identification of MRSA in various species and in food has led to concerns about the roles of animals, both pets and livestock, in the epidemiology of MRSA infection and colonization in humans. There is evidence of the role of food animals in human MRSA infections in some countries and of pets as a possible source of human infection. Some groups of individuals who work closely with animals, such as veterinarians, have high MRSA colonization rates. This article includes discussions of MRSA in human medicine, animals, and food, as well as its interspecies transmission, colonization, infection, strains, and affected populations. However, clear answers are lacking in many of these areas and limited studies may lead to premature conclusions. It is certain that animals are a source of human MRSA infection in some circumstances—but humans may also serve as sources of infection in animals. Changes in the epidemiology of MRSA in one species may be reflected in changes in other species. The true scope of MRSA in animals and its impact on human health are still only superficially understood, but it is clear that MRSA is a potentially important veterinary and public health concern that requires a great deal more study to enhance understanding and effective response.

Key Words: antimicrobial resistance; companion animals; livestock; methicillin-resistant Staphylococcus aureus (MRSA); zoonosis

Introduction

Staphylococcus aureus is a Gram-positive bacterium and important opportunistic pathogen in various species. Historically it has been a leading cause of both skin and invasive infections in humans, and its impact is no less today. One reason for the continuing important role of S. aureus in disease is its propensity to become resistant to antimicrobials. The introduction of penicillin had a profound effect on staphylococcal infections, but penicillin resistance soon followed. Similarly, after the introduction of new antimicrobials such as methicillin, it was not long before methicillin-resistant S. aureus (MRSA\(^1\)) developed.

Methicillin resistance is conferred by the \(mecA\) gene, which encodes for production of an altered penicillin binding protein (PBP2a or PBP2') that has a low affinity for all beta-lactam antimicrobials (penicillins, cephalosporins, carbapenems), rendering staphylococci resistant to this large and critical antimicrobial class. Frequently, MRSA isolates are also resistant to other antimicrobial classes, further limiting treatment options.

MRSA in Human Medicine

When MRSA emerged in international hospitals in the 1960s, there was initially limited concern because of the relatively low incidence of disease. It was not until the late 1970s and early 1980s that MRSA rates in hospitals increased dramatically, starting a “pandemic” phase (Chambers and DeLeo 2009). MRSA had (and continues to have) a tremendous impact on morbidity and mortality in hospitals, but another major epidemiological shift occurred in the 1990s with the widespread emergence of community-associated MRSA (CA-MRSA\(^1\)) infections.

Early reports of CA-MRSA were associated with strains most commonly found in hospitals and typically involved people with prior healthcare exposure and other healthcare-associated risk factors. Subsequent reports described infections (sometimes fatal) in people with little to no healthcare contact or other recognized risk factors (Diederjen and Kluytmans 2006; Frazee et al. 2005a,b). These infections were often associated with strains different from those that predominated in healthcare facilities, demonstrating a unique community-associated disease, not a hospital-associated infection. Now MRSA is a leading cause of community-associated skin and soft tissue infections in some regions, with rare but dramatic serious infections such as necrotizing

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\(^1\)Abbreviations used in this article: CA-MRSA, community-associated MRSA; MRSA, methicillin-resistant Staphylococcus aureus; ST, sequence type
fasciitis and necrotizing pneumonia (Frazee et al. 2005a,b; Miller et al. 2005).

### MRSA in Animals

It is perhaps not surprising that MRSA has emerged in a variety of animal populations, apparently through different mechanisms. The close contact between humans and various animal species creates the potential for exposure of animals to “human” organisms, and antimicrobial use in animals presumably facilitates the emergence and spread of MRSA. But mechanisms, risk factors, and other information about the emergence of MRSA in animals are rather poorly understood at this point, as repeatedly illustrated in the following discussions.

#### Household Pets

Exposure of household pets to MRSA was probably inevitable as the prevalence of CA-MRSA increased in humans. At least one study has demonstrated that concurrent colonization of people and their pets with indistinguishable methicillin-susceptible *S. aureus* (MSSA) strains is not uncommon (Hanselman et al. 2009), indicating the potential for transmission of MRSA between people and pets in a household.

**Prevalence**

An understanding of the dynamics of *S. aureus* colonization in dogs and cats is limited, but it is clear that the bacterium can cause opportunistic infections or reside in the nasal passages or intestinal tract of healthy humans and animals. As in many other species, MRSA is present in a small percentage of healthy dogs and cats. Prevalence data are variable and comparison between studies is inadvisable because of different populations and methods, but most canine and feline population-based studies have reported rates of 0-4% (Abraham et al. 2007; Baptiste et al. 2005; Boost et al. 2007b; Griffeth et al. 2008; Hanselman et al. 2007; Kottler et al. 2008; Loeffler et al. 2005; Vengust et al. 2006). Rates may be higher in studies of focal populations—for example, 9% in dogs at a veterinary clinic with reported MRSA cases and 7.8% in dogs at a rescue shelter (Loeffler et al. 2005, 2010). But colonization of dogs and cats appears to be transient, as most eliminate the pathogen naturally within a few weeks (Lefebvre et al. 2009; Loeffler et al. 2010).

**Colonization and Infection**

There have been few studies of the risk factors for MRSA colonization, although one showed that living with a human healthcare worker was associated with colonization of dogs (Boost et al. 2007b). Colonization of pets is of concern for two reasons: (1) colonized pets are presumably at increased risk of developing an MRSA infection, although proof of this is currently lacking, and (2) they may be a source of human infection, as discussed below.

While most animals with MRSA are merely colonized, a wide range of clinical infections can occur. As would be expected with staphylococci, most MRSA infections in pets affect the skin and soft tissue. Wound infections, surgical site infections, pyoderma, otitis, and urinary tract infections are most common, but various other opportunistic infections have been reported (Baptiste et al. 2005; Griffeth et al. 2008; Leonard et al. 2006; Morris et al. 2006a,b; Tomlin et al. 1999; Vitale et al. 2006; Weese et al. 2006b). One study cited the administration of antimicrobials, particularly fluoroquinolones, as a risk factor for MRSA (versus MSSA) infection in dogs and cats (Faires et al. 2009).

#### Strains

Typing data provide insight into the epidemiology of MRSA in pets and its relationship to humans. MRSA strains in pets tend to closely reflect those in people in any given region (Baptiste et al. 2005; Grinberg et al. 2008; Leonard et al. 2006; Malik et al. 2006; Moodley et al. 2006; O’Mahony et al. 2005; Strommenger et al. 2006; Weese et al. 2006b). For example, the USA100/CMRSA-2 clone, the predominant strain in colonized humans (Tenover et al. 2008), is commonly reported in pets in North America (Lefebvre et al. 2009; Weese et al. 2006b, 2007). Results are similar in the United Kingdom, but with different strains, as eMRSA-15 and -16 predominate there in both people and pets (Loeffler et al. 2005, 2010; Moodley et al. 2006). These findings provide much support to the hypothesis that MRSA in pets is ultimately human in origin. Recently, however, there have been reports of MRSA infections in dogs caused by sequence type (ST1) 398, a clone associated with food animals and an emerging cause of human CA-MRSA in some regions (Nienhoff et al. 2009; Witte et al. 2007). Whether this represents an uncommon occurrence or the emergence of a new concern in pets is unclear.

**Pet Therapy Animals**

Animals (predominantly dogs) that participate in pet therapy programs raise unique concerns about the risks of interspecies transmission (Lefebvre et al. 2009). A recent article cited healthcare center visitation and contact with children during organized pet therapy sessions as risk factors for MRSA colonization of dogs: animals that were allowed to lick patients or that received treats from them were at higher risk of MRSA acquisition (Lefebvre et al. 2009), possibly through oral exposure to the pathogen on patients’ skin. Another potential concern with pets therapy animals is their possible transient contamination by MRSA in the absence of colonization or infection (Enoch et al. 2005; Lefebvre and Weese 2009). One study demonstrated that petting could lead to the transfer of MRSA applied to a dog’s coat (in the absence of...
the animal’s or person’s known contact with an infected or colonized individual) (Lefebvre and Weese 2009).

Horses

There are some interesting parallels between MRSA in horses and household pets, but also some remarkable differences. As with pets, the first reports of MRSA in horses involved sporadic infections or small clusters and the belief that these were unusual events involving direct transmission from humans (Hartmann et al. 1997; Seguin et al. 1999; Shimizu et al. 1997). Also as with pets, subsequent investigation identified colonization of a small percentage of healthy horses. Most studies report colonization in 0-11% of horses on farms or upon admission to veterinary hospitals (Anderson and Weese 2007; Baptiste et al. 2005; Burton et al. 2008; Van den Eede et al. 2009; van Duijkeren et al. 2010; Vengust et al. 2006; Weese et al. 2005b, 2006c), but there may be higher rates in specific groups (e.g., 43% on one farm; Weese et al. 2005b).

Risk Factors for Colonization and Infection

Reports indicate that antimicrobial exposure is a risk factor both for being colonized with MRSA on admission to an equine hospital and for becoming colonized during hospitalization (Weese and Lefebvre 2007; Weese et al. 2006c). Other risk factors for colonization upon hospital admission include previous colonization of the horse, previous identification of colonized horses on the farm, admission to the neonatal intensive care unit, and admission to a service other than surgery (Weese and Lefebvre 2007). Broader study is required to identify true causal risk factors, particularly those that might be modifiable or avoidable.

Most colonized horses do not develop clinical infections, but colonization at the time of hospital admission is a risk factor for the development of such infections (Weese et al. 2006b). MRSA-colonized horses are also of concern because of the potential for transmission to other horses, humans, and potentially other animal species.

Strains

As with dogs and cats, MRSA colonization in horses appears to be transient in most cases, and decolonization occurs naturally in the absence of reinfection (Weese and Rousseau 2005). One clear difference between MRSA in horses and household pets is the strains that tend to be involved. Most initial reports of MRSA in horses involved ST8 or related (i.e., ST254) strains, especially the USA500/CMRSA-5 clone in North America (Anderson and Weese 2007; Cuny et al. 2006; Moodley et al. 2008; O’Mahony et al. 2005; Weese et al. 2005a,b). These are human epidemic clones but they are currently uncommon in people (Christianson et al. 2007), so their prevalence in horses is disproportionate, suggesting that this strain may be more adept than others at survival in horses. Other common human epidemic clones (e.g., USA100/CMRSA-2) occur in horses, albeit much less frequently (Weese et al. 2005a,c), and recent reports cite ST398 in horses in Europe and Canada (Cuny et al. 2008; Tokaletoff et al. 2009; Van den Eede et al. 2009; van Duijkeren et al. 2010; Walther et al. 2009). Although equine MRSA surveillance has been limited in the past in most areas, it is possible that this documented incidence truly represents the emergence of ST398 in those populations rather than previously undiagnosed endemic infection.

Sources and Transmission

It is likely that there are different origins of MRSA, sources of infection, and routes of transmission in the horse population, where ST8 strains (ultimately human in origin) may be horse adapted and endemic, sporadic infection may be the result of more common human epidemic clones (as is the situation in pets), and ST398 may have originated from food animals, as discussed below.

Clinical MRSA infections can occur as outbreaks but sporadic infections are most common, both in veterinary hospitals and in the community, where they may be accompanied by a wide range of opportunistic infections. Joint, incision, and skin/soft tissue infections are most common in community-onset cases, and surgical site infections predominate in hospitalized horses (Anderson et al. 2009; Hartmann et al. 1997; O’Mahony et al. 2005; Seguin et al. 1999; Weese et al. 2005a). Other possible infections include pneumonia, metritis, omphalophlebitis, sinusitis, bloodstream infection, invasive device infection, osteomyelitis, tenosynovitis, metritis, and mastitis (Anderson et al. 2009; Baptiste et al. 2005; Cuny et al. 2006; Middleton et al. 2005; Shimizu et al. 1997; Weese et al. 2005a). The severity of disease can be quite variable, from mild and superficial to aggressive and life-threatening, and there is no evidence that MRSA infections have a different clinical presentation or outcome than MSSA infections (Anderson et al. 2009a). Risk factors for MRSA infection have not been reported, as opposed to studies involving colonization.

Food Animals

The emergence and dissemination of MRSA in food animals (livestock-associated MRSA) appear to have taken a different course from that in companion animals. Rather than emerging from human sources, MRSA seems to have evolved independently in one or more food animal species, with subsequent dissemination and interspecies transmission.

Cattle

Following the initial report of MRSA in a dairy cow in 1972 (Devriese et al. 1972), sporadic cases of MRSA mastitis in
dairy cattle were described, typically at a low prevalence, among *S. aureus* isolates from clinical or subclinical mastitis. Notwithstanding more recent reports (Juhász-Kaszanitzky et al. 2007; Kwon et al. 2005; Lee 2003, 2006; Moon et al. 2007), the incidence of MRSA mastitis and the prevalence of methicillin resistance among bovine *S. aureus* isolates appears to be quite low (Kwon et al. 2005; Lee 2003), so MRSA does not appear to be a common or important bovine mastitis pathogen at this time. The long-term low prevalence of MRSA mastitis is quite surprising given the number of years since the first identification of MRSA in cattle and the close contact of humans with the udders of dairy cattle.

Minimal information is available about MRSA colonization of healthy cattle. A recent Dutch study found 28% of veal calves colonized with MRSA (Graveland et al. 2008), but in Switzerland the pathogen was isolated from only 1.3% of calves and 0.4% of adult cows (Huber et al. 2009) and in Canada from none of 491 Canadian feedlot cattle (Weese et al. 2009b). Clearly, more study of healthy cattle is required.

**Pigs**

Significant concerns about MRSA and food animals emerged in just the past 5 years after an alarming report about infections and high rates of colonization among Dutch pig farmers. An intensive international investigation of MRSA in food animals, predominantly pigs, followed reports of both “unexpected” CA-MRSA infections in people in the Netherlands who had been in contact with pigs and an exceptionally high colonization rate of pig farmers—760 times that of the general Dutch population (Voss et al. 2005).

A unique characteristic of the Dutch report was that the human isolates and one from a pig were nontypable by *smal* pulsed field gel electrophoresis (PFGE) and were ST398, a historically rare clone. This led to further studies of MRSA colonization in pigs, both in the Netherlands (de Neeling et al. 2007; Huijsdens et al. 2006; van Duijkeren et al. 2008) and elsewhere, including Belgium (Dewaele et al. 2008), Canada (Khanna et al. 2007), Germany (Witte et al. 2007), Singapore (Sergio et al. 2007), and the United States (Smith et al. 2008b). But the resulting prevalence data are quite variable between farms—from 0 to 100%—and comparisons of the data are inadvisable because of differing study populations (ages, pig production systems) and methods. The main conclusion should be that MRSA is prevalent among pigs in many countries.

Because ST398 strains have predominated in reports of MRSA in pigs internationally (e.g., de Neeling et al. 2007; Dewaele et al. 2008; Hasman et al. 2010; Khanna et al. 2007; Sergio et al. 2007; Smith et al. 2008a; van Duijkeren et al. 2008), it is plausible that this strain emerged in pigs and was subsequently disseminated to other species. The finding of methicillin-susceptible ST398 in pigs (Guardabassi et al. 2007) supports this hypothesis, although proving it retrospectively is difficult. Other strains have also been identified. Common human epidemic clones are present in pigs in some regions (e.g., the USA100/CMRSA-2 in Canada; Khanna et al. 2007). While it is not possible to draw definitive conclusions, it is most likely that this represents human-to-pig transmission. Studies of pigs in China also report an unrelated clone, ST9, the source and implications of which are unknown (Cui et al. 2009; Wagenaar et al. 2009).

Risk factors for MRSA colonization of pigs have not been adequately investigated. Tetracycline resistance is typical in ST398 and has led to the assumption that the emergence of this strain resulted from heavy tetracycline use in pig production (de Neeling et al. 2007). However, such conclusions may be misleading—tetracycline resistance is also very common in equine ST398 and CMRSA-5/USA500 isolates (Van den Eede et al. 2009; Weese et al. 2005a) despite the sparing use of tetracycline in horses. MRSA is also present on antibiotic-free swine farms (Weese et al. 2009c).

Intuitively, it is reasonable to hypothesize that antimicrobial use on farms would drive the emergence and dissemination of MRSA, but available data are inadequate. A recent study described an increase in the prevalence of colonization among a small group of pigs after tetracycline administration (van Duijkeren et al. 2008), but the increase was not statistically significant and other factors may have been involved. In that study, MRSA colonization was present in pigs at 1 out of 21 farms that did not routinely administer antimicrobials versus 6 out of 10 farms that did. Larger studies are needed to determine the true role of antimicrobials in MRSA in pigs and to differentiate the role of antimicrobials versus other management factors in differences in MRSA rates between farms.

Despite the high prevalence of colonization in pigs, clinical infections are rare, with only sporadic reports of exudative dermatitis, urinary tract infection, and mastitis-metritis-agalactia syndrome (Schwarz et al. 2007; van Duijkeren et al. 2007). The potential impact of MRSA in pigs is therefore greater from a public health standpoint, as discussed below, than an animal health standpoint.

**Poultry**

There have been few investigations of MRSA in poultry. Two reports describe MRSA isolation from healthy and sick chickens (Lee 2003, 2006), but there are limited prevalence and incidence data. Two recent studies reported isolation of ST398 from healthy chickens (Nemati et al. 2008; Persoons et al. 2009), and a third, involving characterized isolates from infected poultry, reported the predominance of a common human epidemic clone (clonal complex 5) (Hasman et al. 2010). Whether the presence of different strains in studies reporting infection versus colonization indicates differences in the strains that cause colonization versus infection or regional differences in MRSA distribution is unclear. More study of poultry is required to determine the epidemiology of infection and colonization.
Interspecies Transmission of MRSA: Affected Populations

There is clear evidence that MRSA can be transmitted between humans and animals, in both directions, yet the frequency, direction, and overall relevance have not been clearly established, and the roles of different animal species in the transmission of MRSA to humans are very superficially understood.

Household Pets

Some of the earliest public health concerns about MRSA and animals focused on household pets. Given the close contact of many people and their pets and the sheer number of pets, this concern is reasonable. Numerous studies report the concurrent isolation of indistinguishable MRSA strains from people and pets (predominantly dogs and cats) in the context of the colonization of both pets of MRSA-infected people and people whose pets are infected (Boost et al. 2007a; Faires et al. 2009; Leonard et al. 2006; Loeffler et al. 2005; Manian 2003; Moodley et al. 2006; O’Mahony et al. 2005; Sing et al. 2008; van Duijkeren et al. 2005; Weese et al. 2006b). However, cross-sectional evaluation of these colonizations cannot determine the direction of transmission nor rule out common-source infection. Pets have been implicated as the cause of human infections (Manian 2003; Sing et al. 2008), but it’s debatable whether pets can truly be implicated in such cases. Finding the same strain in a person and a pet certainly suggests interspecies transmission, but identifying an individual as the cause of infection using single cross-sectional investigation is not reliable: MRSA strains in pets are typically those most common in people, so determination of strain type provides no information about the potential origin of infection.

There is currently no evidence indicating that the general pet-owning population is at increased risk of MRSA infection or colonization, but there has been minimal study of this area. However, a study of Canadian and American households with a MRSA-infected pet found colonization of 18% of the humans (Faires et al. 2009), a rate much higher than the 1-3% estimated for the general population in that region (Gorwitz et al. 2008; Hanselman et al. 2008). Thus, it is reasonable to assume that exposure to an infected animal is a risk factor for MRSA colonization of owners, with unknown clinical relevance.

Particular attention has been paid to households with recurrent MRSA infections in humans. Case reports have described isolation of MRSA from pets in such households (Faires et al. 2009; Manian 2003; Sing et al. 2008), but care must be taken when interpreting the relevance of case reports. In one small prospective study, MRSA was isolated from pets in only one out of eight households (13%) with recurrent MRSA infections (Faires et al. 2009). While that study was quite small and further investigation is needed, it is important to note the low prevalence and the fact that in the only household with colonized pets, there was also a colonized healthy person. The presence of MRSA in a pet does not necessarily indicate that the animal was or could be a source of human infection, although concerns should not be dismissed.

In summary, current data strongly suggest that MRSA can move between people and pets in households, whether the individuals are colonized or infected. Research is needed to understand the frequency of this cross-species transmission and its risk to animal and human populations.

Horses

There is clear evidence of interspecies transmission of MRSA between horses and humans, resulting in both colonization and infection. Higher rates of MRSA colonization than would be expected have been identified in horse owners and equine veterinarians. One study reported colonization of 13% of horse owners and the presence of a colonized person on every farm that had one or more colonized horses, with indistinguishable human and equine strains (Weese et al. 2005b). The prevalence in that study should be interpreted with caution because a subset of farms was chosen based on previous diagnosis of MRSA on the farm, and the true population prevalence among horse owners is unknown. Studies of veterinary personnel have also strongly suggested an occupational risk of horse contact, as discussed below.

Laboratory Animals

The potential for colonization, amplification, and interspecies transmission of MRSA should be of concern for people involved with laboratory animal colonies. The mixing of animals, use (and potential overuse) of antimicrobials, use of invasive devices and implants, and contact with humans all create a clear opportunity for introduction and transmission of MRSA.

There are very few reports of MRSA infection or colonization in laboratory animal colonies, but this may simply be a reflection of the uncommon publication of MRSA infections in such facilities. Anecdotally, outbreaks of MRSA infection and colonization in laboratory animals, especially nonhuman primates, are not uncommon but are rarely reported in the literature. This author has been contacted numerous times about MRSA infections in research animals, none of which have ever been published. This understandable reluctance to publicize infections, given sensitivities regarding management of research animals and the high-profile nature of MRSA, complicates assessment of the scope of the problem, risk factors, and ways to prevent or control infections.

2Two exceptions are MRSA pneumonia in a rhesus macaque at a research facility (Rivas et al. 2007) and ST398 MRSA colonization of pigs used in research (Sergio et al. 2007).
One retrospective study identified MRSA infections of intravenous catheters in two rhesus macaques (*Macaca mulatta*; Taylor and Grady 1998), but there was no apparent further investigation or characterization of the MRSA isolates. Infections of invasive devices, particularly those that are left in place for prolonged periods of time, may pose a high risk. Sporadic cases or outbreaks raise concerns about animal health, the need for device/implant removal, costs of treatment, and the potential for zoonotic transmission.

The risk of MRSA in laboratory animal facilities is not restricted to those with active MRSA research programs. Certainly, the presence of experimentally infected animals in a facility could increase other animals' risk of exposure, whether from colonized animals, environmental contamination, fomites, or colonized personnel. However, considering the prevalence of MRSA in the general population and the potential for higher rates of carriage in animal care personnel, exposure of laboratory animals from colonized humans probably poses the greatest risk. Routine infection control and surveillance activities must address the ever-present risk of introduction of MRSA into a facility.

### Food Animals

Livestock-associated MRSA has emerged as a pressing concern in some countries. Since the first reports of human infections associated with MRSA in pigs, subsequent studies have confirmed that pig contact is a risk factor for MRSA infection and colonization (Lewis et al. 2008; van Rijen et al. 2008). The studies have largely focused on the role of pigs in the Netherlands, with less information about other food animals and other regions.

There have been dramatic increases in human ST398 infection and colonization in the Netherlands, where the prevalence of PFGE nontypable (and therefore presumed ST398) MRSA isolates recovered from humans rose from 0% in 2002 to more than 21% in 2006 (van Loo et al. 2007a). Changes in surveillance likely accounted for some of this increase, but it is clear that ST398 rates are rising and are to a large degree associated with animal contact, as colonization rates have been particularly high in various groups with livestock contact, such as veterinarians (discussed in the next section), farmers, and people living on farms (Table 1). Specifically, contact with pigs or cattle is a risk factor for ST398 or nontypable MRSA colonization (Köck et al. 2009; van Loo et al. 2007a; van Rijen et al. 2008; Vandenbroucke-Grauls and Beaujean 2006): studies reported colonization in 32% of people with veal calf contact in the Netherlands (Graveland et al. 2008) and in 32% of hospitalized people who had contact with pigs and veal calves (van Rijen et al. 2008). These rates themselves are remarkable, but they are astounding considering that the prevalence of colonization in the general Dutch population is less than 1% (Wulf et al. 2008).

A recent Dutch study indicated that the annual incidence of MRSA increased more than threefold from 2001 to 2006 and that this increase was entirely attributable to animal-related MRSA (van Rijen et al. 2009). According to the study, animals accounted for 26% of the cases in people who were identified as colonized upon hospital admission. Because of the risk associated with pig contact, Dutch hospitals have adopted strict MRSA control measures, and a Dutch report recommended that people with pig contact be isolated at the time of their hospital admission until MRSA screening results are available (Vandenbroucke-Grauls and Beaujean 2006).

Farm-based risk factors for MRSA acquisition have been only minimally investigated. Not surprisingly, working in barns with colonized pigs is a risk factor (van den Broek et al. 2008), and more intensive and longer contact is probably an important factor, as evidenced by transient MRSA carriage in people who visit farms to collect samples versus higher rates of colonization in workers with more intensive or longer contact (van den Broek et al. 2008).

The geographic variation in the prevalence of ST398 colonization and incidence of infection in humans is quite interesting. Although it is a leading cause of CA-MRSA infection in some European countries, ST398 MRSA infections are currently rare in North America, where, despite the presence of ST398 in livestock, there are very few reported infections in humans (Golding et al. 2009). The reason for

<table>
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<tr>
<th>Study population</th>
<th>Country</th>
<th>Prevalence</th>
<th>Reference</th>
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<tbody>
<tr>
<td>Swine farm personnel</td>
<td>Belgium</td>
<td>38%</td>
<td>Denis et al. 2009</td>
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<tr>
<td>Swine farm personnel</td>
<td>United States</td>
<td>37%</td>
<td>Harper et al. 2009</td>
</tr>
<tr>
<td>People with veal calf contact</td>
<td>The Netherlands</td>
<td>32%</td>
<td>Graveland et al. 2008</td>
</tr>
<tr>
<td>Hospitalized people with pig or veal calf contact</td>
<td>The Netherlands</td>
<td>32%</td>
<td>van Rijen et al. 2008</td>
</tr>
<tr>
<td>People working and living on pig farms</td>
<td>The Netherlands</td>
<td>30%</td>
<td>van den Broek et al. 2008</td>
</tr>
<tr>
<td>Swine farm personnel</td>
<td>Canada</td>
<td>20%</td>
<td>Khanna et al. 2007</td>
</tr>
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*Country where sampling was performed. Some individuals may have been from other countries.*
this is unclear. Various possibilities exist, including differences in direct and indirect contact with food animals, much lower population density in North American pig-rearing regions, and the more common presence of other (perhaps competing) MRSA strains in people in the general population. Another possibility is that this is an emerging disease in North America, with a later onset than in Europe.

Veterinary Personnel

It has become clear that MRSA exposure is an occupational risk in veterinary medicine. Most, but not all, studies of colonization of veterinary personnel have indicated relatively high colonization rates (Table 2). While these studies have typically not involved a non-animal-contact control group, the reported prevalences have tended to be well in excess of those for the general population, strongly suggesting an increased risk of exposure.

The strains present in veterinary personnel further support the hypothesis of occupational exposure, at least for equine and food animal veterinarians. Studies of the former have predominantly identified ST8 (or related) strains (Anderson et al. 2008; Cuny et al. 2006, 2008; Hanselman et al. 2006; Moodley et al. 2006; O’Mahony et al. 2005; Weese et al. 2005a,b), suggesting an equine origin because of the relative rarity of these strains in the general human population (Christianson et al. 2007). Similarly, studies of swine veterinarians and farmers have reported predominantly ST398 strains, supporting occupational exposure (Huysdens et al. 2006; Khanna et al. 2007; Smith et al. 2008a; Wulf et al. 2008).

Studies of small animal veterinary personnel have reported predominance of common human epidemic clones (Burstiner et al. 2009; Hanselman et al. 2006; O’Mahoney et al. 2005), as would be expected based on the strains most commonly found in pets. That finding complicates determination of likely origin of colonization. Other studies of this group have reported relatively low rates of colonization, similar to or only slightly higher than expected for the general population (Hanselman et al. 2006; Wulf et al. 2006; Zemlicková et al. 2009). In contrast, a recent study of people attending a veterinary surgery conference in the United States reported 17% colonization of small animal veterinary personnel, a rate that was no different from equine personnel (Burstiner et al. 2009). This could represent inherent differences in study populations but could also indicate a true increase in MRSA in small animal veterinary personnel, a possibility that requires further investigation.

Factors associated with MRSA colonization in veterinary personnel have not been thoroughly investigated. One study of equine veterinarians identified hand hygiene as an important protective factor: veterinarians who reported that they regularly washed their hands between farms and after handling potentially infectious cases had significantly lower colonization rates (Anderson et al. 2008), a clear indication of the usefulness of routine hand hygiene. A previous diagnosis of

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<th>Study population</th>
<th>Countrya</th>
<th>Prevalence</th>
<th>Reference</th>
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</thead>
<tbody>
<tr>
<td>Small animal veterinary clinic staff</td>
<td>United Kingdom</td>
<td>18%</td>
<td>Loeffler et al. 2005</td>
</tr>
<tr>
<td>Veterinary surgery conference attendees</td>
<td>United States</td>
<td>17%</td>
<td>Burstiner et al. 2009</td>
</tr>
<tr>
<td>Large animal veterinarians</td>
<td>United States</td>
<td>15.6%</td>
<td>Hanselman et al. 2006</td>
</tr>
<tr>
<td>Equine veterinary hospital personnel</td>
<td>Canada</td>
<td>14%</td>
<td>Weese et al. 2005a</td>
</tr>
<tr>
<td>Horse owners and veterinarians</td>
<td>United States and Canada</td>
<td>13%</td>
<td>Weese et al. 2005b</td>
</tr>
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<td>Swine veterinary conference attendees</td>
<td>The Netherlands</td>
<td>12.5%</td>
<td>Wulf et al. 2007</td>
</tr>
<tr>
<td>Veterinary technicians</td>
<td>United States</td>
<td>12%</td>
<td>Hanselman et al. 2006</td>
</tr>
<tr>
<td>Equine veterinarians</td>
<td>United States</td>
<td>10.1%</td>
<td>Anderson et al. 2008</td>
</tr>
<tr>
<td>Veterinarians and veterinary students with livestock</td>
<td>The Netherlands</td>
<td>4.6%</td>
<td>Wulf et al. 2006</td>
</tr>
<tr>
<td>contact</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small animal veterinarians</td>
<td>United States</td>
<td>4.4%</td>
<td>Hanselman et al. 2006</td>
</tr>
<tr>
<td>Veterinarians</td>
<td>Denmark</td>
<td>3.9%</td>
<td>Moodley et al. 2008</td>
</tr>
<tr>
<td>Veterinarians</td>
<td>Czech Republic</td>
<td>0.7%</td>
<td>Zemlicková et al. 2009</td>
</tr>
</tbody>
</table>

aCountry where sampling was performed. Some individuals may have been from other countries.
MRSA (infection or colonization) or treatment of a horse with MRSA were both associated with MRSA colonization in that study (Anderson et al. 2008).

There are limited reports of zoonotic infections in veterinary personnel, but it is not known whether that indicates a low incidence of disease or underreporting. In one case a veterinarian working with an infected horse acquired a tattoo-site infection (Weese et al. 2005a). In another instance, an outbreak of MRSA skin infections occurred in three people, wearing gloves and coveralls, who worked with a colonized newborn foal over a 4-hour period to provide general nursing care in a neonatal intensive care unit (Weese et al. 2006a). Overall, 19% of people that had similar contact with the foal were infected or colonized.

Given reports of zoonotic infections and the apparent high incidence of colonization of some veterinary groups, MRSA should be considered an occupational risk in veterinary medicine.

**MRSA in Food**

Considering the increasing evidence of MRSA in food animals, it is logical that concerns would emerge about MRSA contamination of food and to assume that colonized animals were the source of contamination. But this connection has yet to be clearly demonstrated. ST398 MRSA has predominated in some, but not all, reports of MRSA in meat. Studies have reported the presence in meat of strains more commonly found in people, including strains not yet reported in food animals (Lozano et al. 2009; Pu et al. 2009; Weese et al. 2009a), raising questions about whether contamination is from food animals, other sources such as people involved in food processing, or both. Clearly, more information is required, necessitating research beyond the cross-sectional study of retail food contamination.

It is also reasonable to suspect that MRSA food poisoning could become more common with an increase in food contamination and colonization of food handlers. As with methicillin-susceptible staphylococci, classical staphylococcal “food poisoning” caused by ingestion of preformed enterotoxins can occur. While MRSA isolates can possess various enterotoxin genes there is only one report of staphylococcal food poisoning caused by MRSA (Jones et al. 2002). This may be in part because of limited attempts to culture stool for *S. aureus* in cases of suspected food poisoning. Clinically, food poisoning caused by MRSA should be no different from that caused by MSSA, but MRSA-contaminated food could also be a source of intestinal colonization.

In addition to these risks, food may be a concern as a vehicle of MRSA extraintestinal colonization and infection. Contaminated food was implicated as a source of an outbreak in a hospital in the Netherlands, where MRSA was isolated from a banana peeled by a colonized food preparer (Kluytmans et al. 1995). Based on that finding and the lack of another identified route of transmission, food was suspected as being a vehicle for MRSA, although definitive proof was lacking. It is certainly plausible that surface contamination of food could lead to colonization if people touch their noses after contaminating their hands. Infection of hand wounds could also be a concern, but neither of these has been proven.

Recent attention has largely focused on contamination of meat, based on the presence of MRSA in food animals and on reports of MRSA-contaminated retail meat, involving a range of meat products and with prevalences ranging from 0.4% to 12% (de Boer et al. 2009; Lin et al. 2009; Lozano et al. 2009; Pu et al. 2009; van Loo et al. 2007b). Although it is not advisable to compare prevalence data because of varying methods, sample collection schemes, and sample types, these studies indicate that MRSA is present in a varying but generally small percentage of retail meat samples. The use—or not—of enrichment culture methods, for example, can result in differing data, because very low levels of contamination are detectable in the culture. A Canadian study identified MRSA in 6.3% of ground pork and 5.6% of ground beef, yet 32% and 45% of positive pork and beef samples, respectively, had up to 20 CFU/g; most quantifiable samples had fewer than 100 CFU/g and the highest had 3590 CFU/g (Weese et al. 2009a). While the potential infective dose is completely unknown, it is reasonable to assume that low levels of MRSA are of less concern than higher levels, but it is nonetheless important to consider low levels when evaluating the potential of food as a source of infection.

Despite increases both in MRSA food contamination and in human incidence of CA-MRSA and ST398 infections, there are no reports of a direct link between the two. There is no question that food can be contaminated with MRSA, and a role in human disease can be hypothesized, but no objective data are available to support or refute such a hypothesis. More intensive surveillance and the inclusion of queries about food exposure (ingestion and contact) in CA-MRSA investigations are necessary to elucidate the true role of food in human disease. Even so, determination of an association may be difficult, since infection occurs only in certain situations and often well after exposure.

**Conclusions**

The overall role of animals in human MRSA infections varies tremendously between animal species and regions. And because the epidemiology of MRSA in animals is only superficially understood, it is inappropriate to draw conclusions or take actions based on rather limited data. However, it is clear that MRSA is an excellent example of the “One Health” concept as it can reciprocally affect human and animal populations.

Concerns about MRSA in animals are reasonable and require careful study of various aspects to better understand the emergence and dissemination of MRSA in different species and to characterize interspecies transmission. At the same time, it is important to remember that a minority of human MRSA infections are directly associated with animals. Thus,
a balanced approach is key in efforts to reduce the implications of MRSA in both animals and humans while avoiding an excessive response that might unnecessarily harm human interactions with pets, food animals, and food.

As MRSA becomes (or has become) established in different animal and human populations, elimination of all risk will be impossible. However, proper study of MRSA in animals, characterization of interspecies transmission, identification of true human and animal health risks, and development of evidence-based control measures can surely reduce the impact on animal health and welfare, human health, agriculture, and the human-animal bond.

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