

# continuing education

## MRSA in domestic animals – an update

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### Introduction

*Staphylococcus aureus* is well recognised as a significant pathogen both in human and in animal medicine. It can cause a wide range of conditions in human medicine, from mild skin infection to life-threatening bacteraemia. These conditions, such as localised purulent lesions or metastatic, multi-organ infections (post-bacteraemia), can also occur in all domestic animal species, including poultry. From an economic perspective, however, mastitis in dairy cows is the most significant veterinary disease caused by *S. aureus*. Although *S. aureus* is regularly isolated from both dogs and cats, the most common pathogenic species of staphylococci isolated from these species is *S. intermedius*.

Meticillin was first introduced in human medicine in the 1950s when it was used for treating penicillin-resistant staphylococcal infections. However, Barber (1961) reported meticillin-resistance as early as 1961 and meticillin-resistant *S. aureus* (MRSA) was first isolated in Irish hospitals in 1971 (Hone and Keane, 1974). Its prevalence increased markedly over the 1990s, and in 2002 the European Antimicrobial Resistance Surveillance System (EARSS) reported that 42% of *S. aureus* isolates from blood cultures in Ireland were meticillin-resistant, one of the highest prevalence rates in Europe (Anon, 2003). Thus, as in many countries worldwide, MRSA is a major nosocomial pathogen in Ireland. Isolation of MRSA in animals was first recorded in 1972, when it was detected in the milk of mastitic cows (Devriese *et al.*). There have been increasingly frequent reports of MRSA infections in animals in recent years, including two outbreaks of infection in veterinary teaching hospitals in North America (Goni *et al.*, 2004; Lee, 2003; O'Mahony *et al.*, 2005; Rich *et al.*, 2005; Sequin *et al.*, 1999; Weese *et al.*, 2004).

MRSA strains are resistant to all  $\beta$ -lactam antibiotics, with resistance most commonly mediated by the *mecA* gene. Five types of this gene have been described: staphylococcal chromosomal cassette or SCC *mec* types I to V. This gene encodes for a penicillin-binding protein (PBP) which is expressed in the bacterial cell wall and which has a

low affinity for  $\beta$ -lactam antibiotics, allowing cell wall synthesis to continue despite inactivation of native PBPs. Thus, this group of antibiotics are ineffective against bacteria expressing this gene. In addition, MRSA isolates are frequently resistant to many other antimicrobial classes.

### MRSA in humans

MRSA is a major nosocomial pathogen in many countries, including Ireland. Infection with MRSA is a particular problem in intensive care units, where surgical patients, or those with skin ulceration or indwelling urinary catheters are more frequent (Anon, 2005; Nicolle *et al.*, 1999). In addition, infections arising in the community are causing increasing concern. MRSA detected in the community may be classified as follows (Anon, 2005):

- Patients discharged from hospital with MRSA;
- Nursing home residents with MRSA;
- MRSA transmitted from MRSA patients to non-hospitalised patients or individuals;
- MRSA arising *de novo* in the community.

Clinical cases classified in the final category are considered true community-acquired MRSA (CA-MRSA) infections. Strains isolated from such cases differ from hospital-acquired isolates in that they tend not to be multiresistant and usually contain SCC*mec* IV and other Panton-Valentine leukocidin (PVL) genes (Vandenesch *et al.*, 2003). The PVL genes encode proteins which damage cell membranes and, thus, these strains tend to cause soft tissue infections rather than bacteraemia (Baggett *et al.*, 2003; Lina *et al.*, 1999). CA-MRSA cases have been described in Ireland (Rossney *et al.*, 2005) but the number remains small.

### Abbreviations:

**CA-MRSA:** community-acquired MRSA

**EARSS:** European Antimicrobial Resistance Surveillance System

**EMRSA:** epidemic MRSA

**Mec A gene:** the major determinant of meticillin resistance in *S. aureus*

**Meticillin:** formerly written as methicillin

**MLST:** multilocus sequence typing

**MRSA:** meticillin-resistant *Staphylococcus aureus* infection

**PBP:** penicillin-binding protein

**PVL:** Panton-Valentine leukocidin, a cytotoxin that causes leukocyte destruction and tissue necrosis

**SCC:** staphylococcal cassette chromosome

**SCC*mec*:** Staphylococcal cassette chromosome *mecA* gene

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Humans may be either infected or colonised with MRSA. Infection implies that the organism has succeeded in entering the body through a barrier such as the skin and has invaded the tissues. Colonisation occurs when the organism is present on the skin or a mucosal surface but has not invaded the tissues. Colonisation may be transient or long-term. During an intensive study conducted in Ireland in 1999, MRSA was isolated from 508 patients, of which 62% were colonised only. Colonisation rather than infection occurs with CA-MRSA strains also (Rossney *et al.*, 2006).

Although approximately 20% of healthy adults are persistent carriers of *S. aureus* in the nares and some other sites, carriage of the resistant strain, MRSA, is much less frequent. Most studies relating to human carriage of MRSA have involved hospital patients, hospital staff or outpatients. Current data suggest that up to 6% of hospital personnel and up to 3% of outpatients periodically carry MRSA (Cesur and Cokca, 2004; Creech *et al.*, 2005; Eveillard *et al.*, 2004; Kenner *et al.*, 2003).

Transmission of MRSA occurs principally by means of the hands of colonised individuals with colonised and infected in-patients forming the major reservoir of MRSA in hospitals.

#### MRSA in animals

In general, transmission of staphylococcal strains between species is thought to occur infrequently (Quinn *et al.*, 2002). However, it has been reported that pets can act as reservoirs of *S. aureus* for humans (Adekeye, 1981; Simmons-Smit *et al.*, 2000). The strains in these reports were not meticillin-resistant and, until recently, MRSA was not considered as a pathogen of domestic animals. However, in common with reports from other countries worldwide, a number of cases of MRSA in domestic animals have been recorded in Ireland in recent years (O'Mahony *et al.*, 2005). Since early 2003, the diagnostic laboratory in the University Veterinary Hospital, University College Dublin (UCD) has isolated MRSA from approximately 50 domestic animals (including dogs, cats, rabbits, horses) and a seal. It is not clear what the significance of MRSA infection in animals is, or what role animal carriage plays in human infection. Nevertheless, studies from other countries have shown that MRSA strains isolated from animals are often of human origin and could represent a possible source of infection for humans (Devriese and Hommez, 1975; Lee, 2003; Manian, 2003; van Duijkeren *et al.*, 2004). Between January 2003 and January 2004, the majority of 95 isolates from domestic pets, from various geographical regions in the UK, were shown to belong to one or other of the two major epidemic MRSA (EMRSA) strains (EMRSA-15 and EMRSA-16) currently prevalent in UK human hospitals (Kearns *et al.*, 2004).

#### MRSA in dogs and cats

The majority of MRSA infections in dogs and cats, including those recorded in Ireland, are associated with postoperative wound infections, prolonged hospital stays or immunosuppression (O'Mahony *et al.*, 2005; Rich *et al.*, 2005; Tomlin *et al.*, 1999). As in human medicine, the presence of implants such as suture material or orthopaedic devices appears to be associated with persistence of MRSA infection. The source of MRSA infection in small animals is likely to be humans who have been in direct contact with them, either owners or

veterinary personnel associated with treatment of the animals. The evidence for this comes from investigation of the antimicrobial resistance patterns and genetic make-up of strains isolated from humans and from pets. Results of such investigations show that strains isolated from pets are indistinguishable from the most prevalent hospital-associated MRSA strains in the human population (O'Mahony *et al.*, 2005; Rich *et al.*, 2005). In addition, the diagnostic laboratory of



the University College Dublin Veterinary Hospital identified a cluster of cases in which postoperative wound infections in five dogs from a single practice were associated with asymptomatic carriage of MRSA in one of the attending veterinary surgeons (Leonard *et al.*, 2005; O'Mahony *et al.*, 2005).

#### MRSA in horses

Infection with MRSA in horses has been reported previously, particularly in North America where two major outbreaks have been documented in veterinary hospitals (Sequin *et al.*, 1999; Weese *et al.*, 2004). MRSA isolation from horses has been recorded in Japan, Ireland and the UK (O'Mahony *et al.*, 2005; Shimizu *et al.*, 1997; Waller, 2005). As in dogs and cats, wound infections and post-surgical

infections appear to be the most common clinical manifestations. However, in contrast to isolates obtained from small animals, equine MRSA strains differ from strains commonly isolated from humans (O'Mahony *et al.*, 2005; Waller, 2005; Weese, 2004). The relationship between equine isolates worldwide is unclear as limited data have been published to date, insufficient to allow comparison of isolates obtained in different countries. Irish equine isolates were resistant to a greater number of antimicrobial agents than common human isolates and molecular techniques showed that they were unlike human MRSA isolates currently prevalent in Ireland (O'Mahony *et al.*, 2005; Rossney *et al.*, 2006). Epidemiological typing of Irish equine isolates, as well as isolates from associated veterinary personnel, suggested that transmission between humans and horses occurred. This finding was similar to those reported from previous studies in North America (Sequin *et al.*, 1999; Weese, 2004). There are no published Irish studies on the carriage rates of MRSA in veterinary personnel, although unpublished observations indicate prolonged nasal carriage of at least 12 months in one veterinary surgeon. In a Canadian study, 18% (12/66) of humans sampled on farms where MRSA had been isolated from horses were found to be colonised. In contrast, only 5% (2/41) of humans on farms where MRSA had not been isolated from horses were colonised (Weese *et al.*, 2005). As in human medicine, transmission of infection on the hands of veterinary personnel caring for horses is likely to be a major route of infection. However, a recent Canadian study found that widespread contamination of the veterinary hospital environment can occur and that this may be an important source of MRSA infection (Weese *et al.*, 2004).

#### MRSA in farm animals

To date, MRSA has not been reported in farm animals in Ireland. However, strains of MRSA have been detected in dairy cows, sheep, pigs and chickens in a number of countries worldwide (Devriese and Hommez, 1975; Goni *et al.*, 2004; Kwon *et al.*, 2005; Lee, 2003; Voss *et al.*, 2005). A comparison of human and farm animal isolates was carried out in some studies and findings suggest that the relationship may not always be straightforward. While isolates from cows' milk appeared to be of human origin in a Korean study, MRSA circulating in pigs and pig farmers in the Netherlands were different from strains routinely isolated in human hospitals (Kwon *et al.*, 2005; Voss *et al.*, 2005).

#### Diagnosis and typing of MRSA in animals and veterinary personnel

Identification of MRSA is not routinely carried out in all laboratories. Detection of meticillin resistance should be carried out according to the guidelines of the National Committee for Clinical Laboratory Standards (Anon, 2004). The presence of PBP can be detected using commercially available kits such as the Mastalex<sup>TM</sup>-MRSA kit (Mast diagnostics, Merseyside, UK). Initial investigation of transmission between animals and humans in Ireland involved comparison of strains by chromosomal DNA analysis using the restriction endonuclease *Sma*I, followed by pulsed-field gel electrophoresis (PFGE) (Murchan *et al.*, 2003) and antibiogram-resistogram (AR) typing (Rossney *et al.*, 1994, 2003; O'Mahony *et al.*, 2005). O'Mahony *et al.* (2005) reported that MRSA from non-equine animals resembled isolates of the

predominant strain found in human patients in Ireland. This strain, which is similar to UK EMRSA-15, exhibits a limited number of AR and PFGE patterns making interpretation of epidemiological typing results difficult. One of the assumptions underlying interpretation of PFGE patterns is that epidemiologically unrelated isolates should have different genotypes (Tenover *et al.*, 1995). This may not be the case with MRSA in Ireland because of the high prevalence of this one strain. Hence, there is a difficulty in trying to assess whether apparent clusters of isolates of this strain are occurring as a result of cross-infection or because of independent acquisition. It should be remembered that, although PFGE is considered the 'gold standard' for epidemiological typing of MRSA, it is a relatively insensitive typing method where differences rather than similarities are conclusive. Typing of MRSA based on multilocus sequence typing (MLST), where the genotype of an isolate is determined by sequencing internal fragments of seven housekeeping genes in conjunction with staphylococcal cassette chromosome *mec* (SCC*mec*) typing is widely used for the international comparison of MRSA strains (Enright *et al.*, 2002). MLST and SCC*mec* types of a large bank of Irish human isolates have been published recently (Shore *et al.*, 2005). Although some studies have been carried out on a small number of Irish animal isolates using MLST and characterisation of the *mecA* gene (unpublished), further work is required in order to facilitate comparison with Irish human isolates and with other animal and human isolates worldwide. Epidemiological typing of MRSA isolates in Ireland is carried out in the National MRSA Reference Laboratory (NMRSARL) in St James's Hospital in Dublin (Rossney *et al.*, 2003). PFGE typing techniques are now in place in the UCD Veterinary Hospital and data collected on animal isolates are submitted to the NMRSARL twice yearly for comparison with human isolates. This system allows for early detection of changes that may take place in transmission patterns between humans and animals and *vice versa*. Screening of veterinary personnel may be required if multiple cases of MRSA infection occur in animals attending a practice. Swabs from each nostril detect approximately 75% of human naso-pharyngeal (i.e., mucosal) carriers. Including throat and perineal swabs increases the detection rate to 98%. Close co-operation between the medical and veterinary professions is required where screening is undertaken. The advice of a medical practitioner should always be followed where treatment of veterinary personnel for MRSA carriage is considered.

#### Control of MRSA infection in animals

Guidelines for the control of MRSA in hospitals and the community in Ireland have been published recently (Anon., 2005). Many of the principles of control contained in this document can be adapted for the control of MRSA in a veterinary hospital setting. In addition, guidelines for the control of MRSA have been published by the British Small Animal Veterinary Association (2005). Control measures may be summarised as follows:

- MRSA infection should be considered as a possibility particularly in animals suffering from post-surgical infections, chronic wounds or other infectious conditions which are not responding to antimicrobial therapy;
- Animals with suspect MRSA infection should be isolated and samples for bacteriology and antimicrobial susceptibility testing

should be collected from all such cases, before antimicrobial therapy commences;

- When dealing with confirmed cases of MRSA infection, gloves should always be worn. Equipment used should be either autoclaved or disposed of carefully;
- All those carrying out, or assisting in, surgical procedures should wear masks and gloves. As the principal route of transmission of MRSA is via the hands of colonised individuals, veterinary personnel should wash their hands thoroughly after dealing with suspect or confirmed cases of MRSA infection. Alcohol-based hand sanitisers such as those used in human medicine, or other suitable hand disinfectants should be used during hand-washing procedures;
- All equipment used on confirmed MRSA cases must be cleaned and disinfected before re-use. Accommodation used for confirmed MRSA cases must also be cleaned and disinfected immediately animals are discharged;
- Where recurring instances of MRSA infection are confirmed despite adherence to appropriate controls, personnel should be screened for carriage of MRSA in order to identify the possible source of infection.

Close co-operation between the medical and veterinary professions is required to identify human carriers and to implement effective control measures. Although carriage of MRSA by animals is unlikely to pose a hazard to immunocompetent individuals, it is the responsibility of the veterinary practitioner to inform owners of the risks which may arise from contact with companion animals infected with MRSA.

### Conclusions

MRSA infection has been documented in small animals and horses in Ireland. Isolates of MRSA from farm animals in Ireland have not been reported to date. There is evidence that humans may be the source of infection in small animals, as strains isolated from dogs and cats are indistinguishable from the most prevalent strain isolated from humans in Irish hospitals. Strains isolated from horses and horse personnel are indistinguishable from each other but unlike human healthcare-associated strains. Veterinary practitioners should be aware that MRSA infections can occur in animals and that improved infection control measures are required to limit transmission of MRSA in veterinary hospitals.

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