REVIEW

What's happened to *Staphylococcus intermedius*? Taxonomic revision and emergence of multi-drug resistance

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Staphylococcus intermedius **has been the predominant coagulase-positive** *Staphylococcus* **isolated from canine skin and mucosae and the most commonly reported staphylococcal pathogen in small animal practice for the last 35 years. Although microbiological tests have historically indicated variability in biochemical characteristics amongst** *S. intermedius* **isolates from animals, an acceptable level of diagnostic accuracy for clinical purposes was readily achievable with routine phenotypic testing. However, three recent developments have changed our understanding of the term "***S. intermedius***" and have challenged veterinary bacteriologists to ensure correct species identification of pathogenic staphylococci from small animals. First, the increasing recognition of meticillin-resistant** *Staphylococcus aureus* **in small animal practice and its human health implications demand accurate species identification. Secondly, the application of molecular techniques to analysis of staphylococcal isolates has led to a revised taxonomy and canine isolates of** *S. intermedius* **being re-named** *S. pseudintermedius*. **Thirdly, the recent, rapid emergence of meticillin- and multi-drug-resistant strains of** *Staphylococcus pseudintermedius* **(MRSP) has become a major therapeutic challenge in veterinary practice worldwide, including the UK. This article discusses the background of the recent taxonomic changes within the genus** *Staphylococcus* **and reviews the key features of MRSP and its implications for day-to-day laboratory diagnosis and small animal practice.**

INTRODUCTION TO STAPHYLOCOCCI

Most small animal veterinary surgeons will encounter staphylococcal skin and wound infections on a daily basis (Hill and others 2006). Staphylococci are primarily facultative anaerobic, catalase-positive, non-motile cocci with Gram-positive teichoic acid and peptidoglycan-containing cell walls, and a guanine and cytosine content of 30 to 40%, that appear as clusters upon microscopical examination (Noble 1992). The major pathogenic species possess coagulase, an enzyme that coagulates plasma by converting fibrinogen into fibrin. Coagulase-negative staphylococci (CoNS) are relatively minor pathogens that generally cause opportunistic infections in compromised hosts.

Forty-five species and 24 sub-species have been described, with *Staphylococcus aureus* and *Staphylococcus intermedius* being most important in veterinary medicine. However, following the recent taxonomic changes detailed below, all isolates from dogs (and probably from cats) previously described as *S. intermedius* should currently be called *Staphylococcus pseudintermedius*. For the purpose of this review, the term *S. pseudintermedius* is used to refer to such isolates that are described in the older literature as *S. intermedius*, provided they were of canine or feline origin.

ECOLOGY

Staphylococci, both coagulase-positive (CoPS) and CoNS, are normal inhabitants of the skin and mucosae of animals and man. Mammalian and avian hosts tend to be colonised by preferred staphylococcal species. Staphylococci are shed from carriage sites on skin cells and hair into the environment where they can survive for several months (Neely and Maley 2000, Wagenvoort and others 2000). In human beings, more than 80% of

hospital-acquired *S. aureus* infections are caused by endogenous strains carried nasally by the patient (von Eiff and others 2001). Similarly, Pinchbeck and others (2006) showed that over 94% of *S. pseudintermedius* isolated from skin lesions of dogs with pyoderma were genetically identical to isolates from carriage sites of the same dog.

In dogs, *S. pseudintermedius* is the predominant *Staphylococcus* with reported isolation frequencies between 20 and 90% from healthy canine skin and mucosal sites (Devriese and De Pelsmacker 1987, Cox and others 1988, Allaker and others 1992, Harvey and others 1994, Griffeth and others 2008). Frequencies of isolation of individual CoPS from the skin and coat of healthy cats range from approximately 10% for *S. aureus* to between 5 and 45% for *S. pseudintermedius* (Cox and others 1985a, Lilenbaum and others 1998, Abraham and others 2007).

RECENT TAXONOMIC REVISIONS OF "*S. INTERMEDIUS*"

In his 1992 review of staphylococcal taxonomy, Noble refers to a paper from 1962 entitled "An introduction to chaos: or the classification of micrococci and staphylococci"; this paper was written when only three species were recognised, namely *S. aureus*, *S. epidermidis* and *Staphylococcus saprophyticus*. Application of molecular biological techniques has underpinned the extensive revision of staphylococcal classification. The genus currently contains 45 species and 24 sub-species, which can be assigned to 11 clusters by sequencing of the 16S rRNA gene, and 4 clusters by sequencing the *gap* gene (Ghebremedhin and others 2008). It might be argued from the perspective of the veterinary dermatology community that chaos remains, albeit in a somewhat modified form, in view of the phenotypic variation amongst and between species of bacteria closely related to *S. intermedius*.

Staphylococcus intermedius was first described by Hajek (1976) who recovered staphylococci from pigeons, dogs, mink and horses that had biochemical properties "between" *S. aureus* and *S. epidermidis*, hence the term "*intermedius*." It soon became apparent that the majority of CoPS isolated from dogs were in fact *S. intermedius*, and not *S. aureus* as defined under the previous classification. However, the significant phenotypic variability amongst *S. intermedius* noted by Hajek (1976) and shortly thereafter by Devriese and van de Kerckove (1979) was shown later to be paralleled by significant genotypic variation (Meyer and Schleifer 1978, Chesneau and others 2000, Bannoehr and others 2007).

Staphylococcus pseudintermedius was first described in 2005 following molecular analyses of isolates from a cat, a dog, a horse and a parrot. Their phenotypic profiles were similar to *S. intermedius* and *Staphylococcus delphini,* a species first reported from dolphins in 1988 (Varaldo and others 1988, Devriese and others 2005). In 2007, two groups published detailed phylogenetic analyses of collections of "*S. intermedius*" from Japan (Sasaki and others 2007) and Europe (Bannoehr and others 2007), with remarkably similar findings; these authors showed that all their strains from dogs, cats and human beings were examples of *S. pseudintermedius*. Most feral pigeon-derived strains were examples of

S. intermedius, and most equine and domestic pigeon-derived strains were examples of *S. delphini*. Whilst detailed biochemical testing may differentiate *S. intermedius* from *S. pseudintermedius* and *S. delphini*, the latter two species can only be reliably distinguished by molecular tests, such as sequencing of the thermonuclease (*nuc*) or heat shock protein (*hsp*60) genes (Sasaki and others 2007) or *Mbo*I restriction of a fragment of the *pta* gene (Bannoehr and others 2009, Slettemeas and others 2010). These molecular studies support the introduction of the term "*S. intermedius* group" (SIG), comprising at least three closely related species, *S. intermedius*, *S. delphini* and *S. pseudintermedius* (Takahashi and others 1999, Bannoehr and others 2007, Sasaki and others 2007, Ghebremedhin and others 2008).

Taken together, these observations indicate that isolates with traditional phenotypic characteristics of "*S. intermedius*" should be identified as *S. pseudintermedius* when obtained from dogs. Isolates from other species with such characteristics are best identified as bacteria of the "*S. intermedius* group" unless molecular test results are available (Hermans and others 2010).

Although molecular techniques have clarified the taxonomy of the SIG, chaos remains at the phenotypic level in the diagnostic laboratory due to variable expression of biochemical properties, both between and within species of the SIG. For example, the type culture of *S. pseudintermedius* is reported to produce acetoin (Voges-Proskauer test) using API STAPH (bioMerieux) galleries (Devriese and others 2005). In contrast, Sasaki and others (2007) reported that 28 out of 83 strains of *S. pseudintermedius* identified by molecular tests did not produce acetoin in standard tests and acetoin production is generally not detected using the API STAPH test. In addition, the type culture was reported to be negative for clumping factor using rabbit plasma whereas Cox and others (1985b) reported that 55 out of 105 dog-derived "*S. intermedius*" (and therefore likely *S. pseudintermedius*) expressed clumping factor when tested with rabbit plasma, in line with the common perception of many veterinary bacteriologists. Previously reported biochemical data for *S. intermedius* should be re-appraised since some strains formerly classified as *S. intermedius* are likely to be examples of *S. pseudintermedius* or *S. delphini* (Devriese and others 2009).

ANTIMICROBIAL RESISTANCE

In the past, most *S. pseudintermedius* infections of dogs were successfully treated with antibacterial drugs chosen either empirically, or based on antibacterial susceptibility testing. Multi-drug-resistance, defined by Coombs and others (2004) as resistance to at least three different classes of antimicrobials in addition to the β-lactams, has been extremely rare, at least in Europe (Lloyd and others 1996, Pellerin and others 1998, Guardabassi and others 2004, Rantala and others 2004, Greiner and others 2007). In the UK, a survey of over 1200 clinical staphylococcal isolates, found no resistance to cefalexin, co-amoxiclav, oxacillin/meticillin and enrofloxacin between 1987 and 1995 (Lloyd and others 1996). In fact, resistance to any of the first generation cephalosporins had never been reliably documented. In Europe, cefalexin resistance was first reported

in *S. pseudintermedius* isolates from dogs seen at a dermatology referral centre in Germany in 2005 when it occurred in combination with resistance to meticillin and several other antibacterial compounds (Loeffler and others 2007).

METICILLIN-RESISTANT *S. PSEUDINTERMEDIUS* (MRSP)

The semi-synthetic penicillin antibiotic, meticillin (methicillin), was introduced in 1959 to deal with β-lactamase producing staphylococci that were resistant to penicillin. Shortly thereafter, meticillin-resistant strains of *S. aureus* (MRSA) were isolated, primarily in hospital settings. Meticillin-resistance reflects expression of the *mecA* gene that codes for a modified penicillin-binding cell wall protein (PBP2a) whose low affinity for β-lactam antibiotics renders penicillins and cephalosporins ineffective. The *mecA* gene is located within the staphylococcal chromosomal cassette *mec*, (SCC*mec*), a large mobile genetic element, and additional genetic determinants frequently confer concurrent resistance to other clinically relevant antibiotics.

Acquisition of *SCCmec* by *S. pseudintermedius* strains has led to the dramatic emergence of MRSP across Europe, principally since 2005 to 2006 (Loeffler and others 2007, Schwarz and others 2008, Ruscher and others 2009, Perrenten and others 2010). In a North American study of *S. intermedius*, meticillin-resistance was reported in 57 out of 336 isolates (17%) in 2003 to 2004 (Morris and others 2006) whereas only one MRSP had been identified amongst 25 meticillin-resistant staphylococci isolated between 1995 and 1998 (Gortel and others 1999). In Europe, MRSP accounted for 23% of *S. pseudintermedius* submissions from a dermatology clinic in Northern Germany in 2006 (Loeffler and others 2007). The frequency of isolation of MRSP (n = 61, 7·4% of SIG isolates) was over four times greater than that of MRSA (n = 15, 18·75% of *S. aureus* isolates) in a review of 901 CoPS isolated from dogs in Germany during 2007 (Ruscher and others 2009). MRSP accounted for 10 out of 48 SIG isolates (21%) in a survey of 590 canine specimens submitted to an Italian veterinary diagnostic laboratory in a 2-month period during 2008; all of these meticillin-resistant strains were also resistant to fluoroquinolones, gentamicin, lincosamides, tetracyclines and potentiated-sulphonamides (De Lucia and others 2010), reflecting acquisition of additional resistance genes. Prevalence data from the UK does not appear to been published in peer-reviewed journals, although a commercial laboratory in Devon, UK recently reported that MRSP accounted for 14% of 125 CoPS isolated in a 12-month period up to July 2008 (Steen and Webb 2010). These isolates were resistant to more antibiotics than MRSA isolates obtained during the same period.

MOLECULAR TYPING METHODS FOR EPIDEMIOLOGICAL STUDIES OF MRSP

A combination of molecular methods has been developed for the powerful and precise typing of *S. pseudintermedius* clones. These typing methods have demonstrated marked genetic diversity amongst meticillin-sensitive *S. pseudintermedius* (Ruscher and others 2010). Multi-locus sequence typing characterises isolates by sequencing internal fragments of multiple house-keeping genes (currently five in the case of *S. pseudintermedius*). For each house-keeping gene, the different sequences present within a bacterial species are assigned as distinct alleles and, for each isolate, the alleles at each of the five loci define the allelic profile or sequence type (ST); profiles can be readily compared to those held in Internet databases. *Spa*-typing involves the amplification, sequencing and analysis of the variable region *X* of the staphylococcal protein A gene. Pulsed-field gel electrophoresis (PFGE) is accomplished by digestion of genomic DNA using the endonuclease *Sma*I and subsequent electrophoretic separation of the DNA fragments in an agarose gel.

The insertion of the SCC*mec* element into the chromosome of susceptible strains accounts for the emergence of meticillin-resistant staphylococcal lineages. In SCC*mec* typing, the types of recombinase (*ccr*) genes, along with the class of the *mec* gene and its associated regulatory sequences are determined. In marked contrast to the genetic variability observed amongst MSSP, studies of MRSP isolates have shown that a single clone predominates in dogs and cats in Europe, specifically sequence type ST71(MLST)-J(PGFE)-t02(*spa*)-II-III(SCC*mec*). This clone has been isolated from Germany, Switzerland, Netherlands, Denmark, Sweden and Italy, and more sporadically from North America and Hong Kong (Bannoehr and others 2007, Kadlec and others 2010, Perreten and others 2010, Ruscher and others 2010, Boost and others 2011). A single predominant clone has also emerged in North America, specifically ST68-C-t06-V (Perreten and others 2010, Ruscher and others 2010). The current lack of ST71 meticillin-sensitive *S. pseudintermedius* does not support the simultaneous and rapid acquisition of SCC*mec* by an already widespread and successful *S. pseudintermedius* lineage, but rather suggests the dramatic dissemination of this particular clone. These molecular epidemiological data suggest that rigorous hygienic precautions are indicated whenever colonisation and infection is detected in veterinary patients to limit further epidemic spread of this bacterium.

ZOONOTIC POTENTIAL

Staphylococcus pseudintermedius rarely colonises human skin and human beings, although carriage rates are generally increased amongst individuals regularly exposed to dogs (Harvey and others 1994, Goodacre and others 1997, Guardabassi and others 2004). Out of 3397 isolates of CoPS obtained from a general human hospital population, 3357 were *S. aureus* and only 2 were *S. pseudintermedius* (Mahoudeau and others 1997), although initial mis-identification of *S. pseudintermedius* as *S. aureus* has been reported in medical laboratories more accustomed to the isolation of the latter species (Tanner and others 2000, Potthumarthy and others 2004, van Hoovels and others 2006, Kempker and others 2009, Slettemeas and others 2010). Nasal carriage of *S. pseudintermedius* was not identified in a study of 56 healthy

human volunteers, although the saliva and dental plaque were colonised in 8·9% of the subjects (Ohara-Nemoto and others 2008). Nasopharyngeal colonisation rates of less than 1·5% were reported in studies targeting members of the veterinary college staff (Talan and others 1989, Loeffler and others 2005), but higher rates have been reported amongst dog owners in more recent studies. One persistent nasal carrier and four transient nasal carriers of *Staphylococcus* "*intermedius*" were identified in a study of staphylococci isolated from the anterior nares of 16 owners of dogs with atopic dermatitis and 13 veterinary practice staff in constant contact with dogs (Harvey and others 1994); strains recovered from the human beings generally correlated with those of the in-contact dogs (Goodacre and others 1997). In a study of 242 dog and cat owners in Ontario, *S. pseudintermedius* was isolated from nine human beings, and indistinguishable strains were isolated from dogs in four of nine households with colonised human beings (Hanselman and others 2009). Guardabassi and others (2004) showed that nasal carriage of *S. pseudintermedius* was more frequent amongst owners of dogs with deep pyoderma (7 out of 13) than in human beings without daily dog contact (1 out of 13), and that 6 of 13 owners carried strains with identical PFGE patterns to those isolated from their dogs.

The emergence of MRSP strains has led to recognition of carriage amongst human beings in contact with dogs, as well as sporadic cases of human infection (Gerstadt and others 1999, Campanile and others 2007, Kempker and others 2009, Stegmann and others 2010). MRSP was isolated from five dogs and one cat with infected surgical wounds by a laboratory in the Netherlands (van Duijkeren and others 2008). Further investigations resulted in MRSP with the same resistance pattern being isolated from the nose of the veterinary surgeon and 3 out of 6 veterinary nurses, from 4 out of 22 environmental samples, and from the nose of a healthy dog belonging to a staff member that was regularly present at the clinic. MRSP and MRSA were isolated from 3 and 8 out of 34 samples, respectively, from veterinary surgeons in a Japanese academic veterinary hospital but from 0 out of 36 personnel in non-clinical laboratories (Ishihara and others 2010). A survey of 171 veterinary dermatology staff and their pets in North America showed that nine individuals were colonised by MRSP and six by MRSA (Morris and others 2010). Concordant strains of MRSP were isolated from pets in the household of three human carriers.

In another North American study, nasal carriage of MRSP was demonstrated in 2 out of 15 owners of dogs infected by MRSP of the same SCC*mec* type and antimicrobial susceptibility pattern; these isolates were not detected on repeat sampling 2 months after the dogs were treated, suggesting that MRSP carriage in human beings may be transient (Frank and others 2009). In a similar study conducted in the Netherlands, human nasal colonisation was detected in 2 out of 45 samples, whereas approximately one-third of samples from in-contact dogs and cats and 44% of environmental samples yielded MRSP (van Duijkeren and others 2011).

These observations clearly indicate that staphylococci are exchanged between human beings and dogs. Whilst transient inapparent carriage is the likely outcome of human exposure to *S. pseudintermedius* from dogs, there is potential for infections to develop in rare cases, with the resultant therapeutic difficulties in the case of MRSP (Stegmann and others 2010). Furthermore, canine-derived MRSP must be considered as a potential source for SCC*mec* transfer and possibly other mobile determinants of antimicrobial resistance to susceptible staphylococci on human skin and mucosae (Guardabassi and others 2004).

IMPLICATIONS FOR LABORATORY IDENTIFICATION

Species differentiation amongst pathogenic staphylococci is less straightforward than standard microbiology texts suggest (Vandenesch and others 1995, Pottumarthy and others 2004). Before the emergence of MRSA as a canine pathogen, identification of CoPS isolated from dogs to species level was of minimal clinical relevance. However, accurate species identification and differentiation of MRSA and MRSP is now essential since there are substantial differences in zoonotic potential of these two species, and the breakpoints for in vitro susceptibility testing may be different.

Initial identification of staphylococci to genus level can be achieved by assessing colony morphology (smooth, convex, slightly glistening, white to yellow surface of 1 to 2 mm diameter on blood or other nutrient agar after 24-hour incubation (37°C) (Barrow and Feltham 1993); microscopy (Gram-positive cocci), and tests for catalase production (enabling differentiation from streptococci and enterococci; reviewed by Freney and others 1999).

DNase and coagulase production are important markers for pathogenicity amongst staphylococci. Coagulase expression by the three CoPS routinely isolated from small animals (*S. pseudintermedius, S. aureus and S. schleiferi* ssp. *coagulans*) can be demonstrated either by the tube test (for free coagulase), or the slide test (for bound coagulase or "clumping factor") (Barrow and Feltham 1993). While the tube test with rabbit plasma is considered the "gold standard," the slide test is quicker, easier and cheaper to perform. However, even this basic test does not yield uniform results. Reference texts report only 11 to 89% of "*S. intermedius*" isolates to be positive in contrast to 100% positivity in the tube test (Freney and others 1999, Kloos and Bannerman 1999) and some CoPS may be disregarded as CoNS due to a lack of test sensitivity (Cox and others 1985).

Differentiation between members of the SIG currently requires molecular tests (such as multi-locus sequence analyses or *Mbo*I restriction of a *pta* gene fragment (Sasaki and others 2007, Bannoehr and others 2009, Slettemeas and others 2010), but differentiation of MRSA and MRSP is feasible using combinations of carefully performed phenotypic tests. Biochemical characteristics, particularly sugar fermentation, can assist in the differentiation of CoPS. Biochemical properties for *S. aureus*, "*S. intermedius*" and for *S. schleiferi* sp. *coagulans* are summarised in standard microbiology texts (MacFaddin 1980, Barrow and Feltham 1993, Kloos and Bannerman 1999), those for *S. pseudintermedius* in more recent publications (Devriese and others

FIG 1. Examples of two *Staphylococcus aureus* isolates; one showing typical golden colony pigmentation, the other growing as white colonies on blood agar, mimicking *S. pseudintermedius*

2005, Sasaki and others 2007) and those used in the authors' laboratory in Table 1. However, it is well documented that none of these tests is 100% accurate and a combination of several tests is desirable (Mackay and others 1993, Rao and others 2002). The classical golden pigmentation of *S. aureus* was not observed in 21% of 133 animal-derived MRSA collected by the authors (Fig. 1). The Vogues-Proskauer reaction in particular is a cost and time-effective test, and although some variability has been observed (Sasaki and others 2007), the test should be positive for *S. aureus* and negative for SIG (Barrow and Feltham 1993).

MRSP can be suspected from the typical antimicrobial susceptibility profile. In the UK, they are normally resistant to the antibacterial compounds commonly used to treat canine pyoderma (potentiated-sulphonamides, lincomycin, clindamycin, co-amoxyclav, cephalexin, enrofloxacin, marbofloxacin), while MRSA isolated from small animals most often show susceptibility to potentiated sulfonamides, tetracyclines and sometimes clindamycin. Detection of the *mecA* gene by polymerase-chain reaction or its product (PBP2a) by latex agglutination is commonplace in medical but not veterinary laboratories. The molecular typing tools described above in the taxonomy section have, to date, not gained wide usage in commercial veterinary bacteriology laboratories, although for the reasons discussed previously, there is a clear need for accurate differentiation of MRSP and MRSA.

MANAGEMENT OF MRSP INFECTIONS

Although meticillin-resistance in staphylococci is not always associated with multi-drug-resistance, most MRSP described in the literature have shown resistance to the majority of clinically relevant veterinary drugs. The dominant European clone of MRSP is normally resistant to β-lactam antibiotics, aminoglycosides, macrolides, lincosamides, tetracyclines, chloramphenicol, trimethoprim and fluoroquinolones, and susceptible to only amikacin, fusidic acid, rifampicin, vancomycin, teicoplanin and linezolid, and none of these latter drugs is licensed for systemic use in pets (Descloux and others 2008, Perreten and others 2010). In 2009, the World Health Organisation (WHO) Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR) produced a reference document to help formulate and prioritise risk assessment and risk management strategies for containing antimicrobial resistance. They classified antibacterial agents as *critically important*, *highly important* and *important* based on their role as either sole therapy or one of few alternatives to treat serious human disease, or diseases caused by organisms transmitted via non-human sources, or by organisms that may acquire resistance determinants from non-human sources (WHO 2009). Amikacin and rifampin are listed as being of *critical importance* for the treatment of mycobacterial infections in human medicine, whereas vancomycin, teicoplanin and linezolid are of *critical importance* in the management of multi-drug-resistant MRSA and enterococci. Fusidic acid is the only antibiotic likely to be active against European dog-derived MRSP that falls outside the *critically important* category, being listed as *highly important* in relation to the treatment of MRSA.

Table 1. Characteristics used for phenotypic identification of coagulase-positive staphylococcal species isolated from dogs and cats (adapted from Devriese and Hajek 1980, Barrow and Feltham 1993, Freney and others 1999, Devriese and others 2005)

		SIG			
Test	*Staphylococcus aureus*	*Staphylococcus pseudintermedius*	*Staphylococcus intermedius*	*Staphylococcus delphini*	*Staphylococcus schleiferi* ssp. *coagulans*
Haemolytic effect	+	+	+	+	+
Clumping factor	+	Variable	Variable	−	−
Tube coagulase	+	+	+	+	+
VP	+	Weak	−	−	+
DNase	+	+	+	Weak	+
Trehalose	+	+	+	−	−
Lactose	+	Variable	+	+	−
Mannitol	+	−	−	+	Variable

VP Voges-Proskauer reaction (Acetoin production), SIG *S. intermedius* group

For superficial skin infections and some wound infections, topical antibacterial therapy combined with correction of the underlying cause, or removal of foreign material such as sutures or implants, has been successful in some cases. Loeffler and others (2007) resolved superficial pyoderma caused by MRSP in five out of seven dogs using topical fusidic acid and chlorhexidine products, or ethyl lactate shampoo.

Off-label use of systemic antibacterial compounds may be necessary in deep pyoderma or other serious infections, although there is often limited data on optimal dosage and frequency of administration of such drugs. Amikacin is not absorbed orally and must be injected. Rifampicin may be administered orally but there is a high risk of resistance developing during treatment, especially when used alone (Kadlec and others 2011) and the risk of hepatotoxicity necessitates regular monitoring of blood biochemistry. Individual isolates of MRSP with rifampicin resistance have been reported (Perreten and others 2010).

Whilst 54 out of 57 isolates of MRSP from North America were susceptible to chloramphenicol (Morris and others 2006), only 30 to 40% of 25 European isolates were susceptible (Descloux and others 2008, de Lucia and others 2010). This geographical variation highlights the importance of basing drug selection for MRSP infection on extended *in vitro* susceptibility testing of individual isolates.

Resistance to vancomycin, teicoplanin and linezolid has not been recognised in MRSP to date (Ruscher and others 2009, Perreten and others 2010), although Perreten and others have questioned whether it is appropriate to use these drugs in animals. In view of the reserved status of these drugs in human medicine (for the treatment of MRSA bacteraemia), and the current intense scrutiny of veterinary use of antimicrobials by the European Medicines Agency (EMEA), the authors take the view that there is no place for the use of vancomycin, teicoplanin and linezolid in veterinary medicine.

Decolonisation is often recommended in the human literature as an adjunct in the management of MRSA infection, although its efficacy remains controversial. Topical antibacterial agents, such as mupirocin, fusidic acid or chlorhexidine, are applied to carriage sites in order to eradicate MRSA and to allow recolonisation by less resistant staphylococci. Studies of nasal/anal decolonisation in dogs with MRSP are not yet reported, although topical fusidic acid application to the nose and anus has been shown to reduce skin carriage of *S. pseudintermedius* in healthy beagle dogs (Saijonmaa-Koulumies and others 1998). Systemic antibacterial therapy with cefpodoxime has been reported not to remove susceptible CoPS from carriage sites (Hillier and others 2007); furthermore, third generation cephalosporins are also *critically important* antibiotics for human medicine.

PREVENTION AND CONTROL OF MULTI-DRUG-RESISTANT STAPHYLOCOCCAL INFECTIONS

The dispersal of *S. pseudintermedius* from the skin of dogs and cats accounts for the frequent occurrence of this bacterium in the environment of veterinary practices (van Duijkeren and others 2008). Rigorous hygienic precautions must be adopted whenever MRSP colonisation or infection is detected or suspected in animal patients to prevent nosocomial infection and further spread of this multi-drug-resistant bacterium (Lloyd 2010). This should include personal hygiene (hand washing, use of masks, gowns and gloves for surgical procedures) and environmental hygiene measures through thorough and regular cleansing and disinfection of all practice areas, as recommended for MRSA (NASPHV 2008) and other contagious pathogens (CCAR 2008). Resistance to detergents and disinfectants has not been of major concern in multi-drug-resistant staphylococci to date and low minimum inhibitory concentrations of animal-MRSP were found in four biocides commonly used in veterinary practices (Baines and others 2008).

CONCLUSIONS

Isolates formerly classified as *S. intermedius* from canine hosts should now be described as *S. pseudintermedius*. The term "*S. intermedius* group" should be used for isolates from other hosts in the absence of molecular tests. The rapid emergence and wide dispersal of MRSP in Europe and North America, as predicted by Waller (2005) is of major concern for animal and human health. In view of the frequency of staphylococcal disease in dogs, MRSP has the potential to significantly impair the ability of veterinary surgeons to effectively deal with common skin and soft tissue infections. The phenotypical variability of the SIG and the need for accurate differentiation between MRSP and MRSA present a challenge for veterinary diagnostic laboratories whose routine laboratory procedures might need to be reviewed and updated. Veterinary practices should apply stringent infection control policies as recommended for MRSA to prevent further spread of MRSP in view of its role as a major animal pathogen, a potential zoonosis and as a new reservoir of transmissible resistance genes. The emergence of MRSP serves as a further reminder of the importance of responsible antibiotic use by the veterinary profession.

Conflict of interest
None of the authors of this article has a financial or personal relationship with other people or organisations that could inappropriately influence or bias the content of the paper.

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