

1 **Methicillin-Resistant
Staphylococcus:**

Notes from London

Laura B. Stokking PhD, DVM, DACVD
Veterinary Specialty Hospital

2 **Methicillin-Resistant Staphylococci in Animals**

ASM/ESM

Microbiology
Internal Medicine
Dermatology
Public Health

3 ***Staphylococcus* sp**

- Gram-positive cocci
- Facultative anaerobe
- Resident cutaneous and mucosal microflora of mammals and birds
- Coagulase-positive, coagulase-negative

4 **Ancient History**

□ Before 1976

Staphylococcus aureus

- All hemolytic coagulase positive staphylococci

□ 1976

Staphylococcus intermedius

- Dogs, minks, horses, pigeons, dolphins

□ 2005: 16S rDNA

Staphylococcus pseudintermedius

- Important canine pathogen

5 **Resident Staphylococcal Species**

1

■ Humans

- *S aureus*
- *S epidermidis*

■ Canine

- *S pseudintermedius*
- *S schleiferi*

2

■ Feline

- *S pseud-intermedius*
- *S schleiferi*
- *S aureus*
- *S hyicus*

6 Methicillin Resistance

- Staphylococcus aureus*
 - MRSA
- Staphylococcus intermedius* group
 - Staphylococcus delphini*
 - Staphylococcus intermedius*
 - Staphylococcus pseudintermedius*
 - MRSPI, MRSI
- Staphylococcus schleiferi*
 - MRSS

7 *Staphylococcus aureus*: Humans

- Opportunist
- Disease requires disruption of epidermal integrity
 - Needles, catheters, surgery, point of entry
- Carriage
 - Skin, mucosae, anterior nares, pharynx
 - 30% carry *Staphylococcus aureus*
 - 3% to 4% carry MRSA (1% in 2002)

8 Nasal Carriage: Humans

1. Never
 - Cannot be colonized
2. Intermittent
 - Acquire *S aureus*, lose it
3. Persistent
 - Always carry *S aureus*
 - Can keep same strain for long time
 - Disperse in environment
 - High risk of infection

9 Pathogenesis

- Colonization
 - Organism present
 - No pathologic reaction
- Infection
 - Barrier to infection breached
 - Organism acts as pathogen
 - Host inflammatory reaction, lesion.

10 *Staphylococcus aureus*: Pathogenicity

- *Staphylococcus* protein A
 - Surface-associated

- Exfoliative toxins A and B
- Toxic shock syndrome toxin 1
- Panton Valentine leukocidin toxin
 - Tissue destruction, CA-MRSA
- *mecA*

11 Staphylococcal gene cassette *mecA*

12 Staphylococcal gene cassette *mecA*

- Codes for penicillin binding protein 2a
 - Intrinsic resistance to all beta-lactam antibiotics and their derivatives
- Oxacillin
 - Semisynthetic penicillin
 - Surrogate for resistance to beta lactams
- Multiple different types of *mecA*
 - Multiple different genetic recombination events.

13 Epidemiologic Types: Humans

- Health-care associated
 - HA-MRSA
 - Resistant to multiple classes of antibiotics
- Community associated
 - CA-MRSA
 - Superantigen
- Livestock associated
 - Europe, Canada; food chain
- Niche drift

14 HA-MRSA

- Multi-drug resistance
 - Plasmid mediated
 - Resistance genes for several drugs are organized into clusters on plasmids, several genes can be co-located on the same plasmid

15 CA-MRSA

- Community acquired
 - Panton-Valentine leukocidin (PVL) toxin
 - Lyses lipid bilayers
 - Blistering, necrosis
 - **Superantigen**

16 Canine MRS Infections
University of Pennsylvania

Staphylococcus aureus: 41%

Staphylococcus pseudintermedius: 16%

Staphylococcus schleiferi:
40%

17 **MRSA vs. MSSA**

Companion Animals

- Skin
- Risk factors
 - Antimicrobial administration
 - Fluoroquinolones
- High survival rate
 - 93% for MRSA, 91% for MSSA
 - No difference in outcome
- Site of infection was not risk factor
- Duration of hospitalization or surgery not risk factor

18 **MRSA in Companion Animals**

- Colonization??
- Contamination
- Carriage
- Culture positive does not equal colonization
- Dogs may be possible vector of transmission after contamination

19 **MRSA**

- MRSA in dogs/cats paired with human family members
 - Plasmid-associated target genes more frequent in human MRSA than in MRSA from dogs and cats
- Animal-specific genetic variation can occur within same MRSA lineage
- Not as virulent in dogs and cats?

20 **MRSA in Companion Animals**

Absence of several virulence-associated genes in canine MRSA

- Proteases, haemolysins, adhesion factors, enterotoxins

21 **Intrahousehold Transmission**

- Colonization requires adherence and multiplication
 - Atopy
- Recurrent contamination in pets?
 - No clothes, no showers, licking
- Dogs with healthcare workers more often "colonized"
- Having bird or cat also risk factor
- Transmission goes both ways, most MRSA found in animals is from epidemiologically human strain

22 **MRSA and Pet Therapy**

- Enrolled before starting, monthly screening
- Contaminated
 - All self-cleared by next visit (naturally decolonized)
- Transient colonization is norm
- No evidence that decolonization is effective in dog, cat, horse or that it is needed

23 **MRSA in Companion Animals**

- Don't know long-term carrier state.
- Topical therapy
 - Local
 - Shampoo
- Systemic antimicrobials
 - Based on culture
- Hand hygiene
- Whole house contaminated
 - Environment

24 **MRSPI**

- Canine carriage
- Nasal, oral, anal mucosa
- Dogs can continue to carry the same MRSP clones without active infection

25 **MRSPI**

- Multiple acquisition of *SCC mec*
 - Distinct genetic lineages

SP accepts transposons, rather than plasmids.

26 **MRSPI**

- Cassettes in *S pseudintermedius* usually simpler than those in *S aureus*
- Antibiotic resistance genes outside cassette in *S pseudintermedius*
- Spreads clonally

27 **MRSPI: Resistance Genes**

- Beta-lactams: 100%
- Ciprofloxacin, erythromycin, gentamicin, kanamycin, sulfonamides: 60%
- Doxycycline: 71%

37 **Screening?**

- ID risk of zoonotic infection
- Source of human infection
- Part of overall household outbreak investigation
- Monitor elimination of MRSA
- Veterinary hospital infection control

38 **Current Questions**

- Host specificity
- Colonization sites
- Virulence factors
- Transmission factors
- Epidemiological studies on SPI in humans
- Vaccines
- Gap in knowledge at molecular level between SA and SP