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Staphylococcus aureus in veterinary medicine

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ABSTRACT

Staphylococcus aureus is a major opportunistic pathogen in humans and one of the most important pathogenic *Staphylococcus* species in veterinary medicine. *S. aureus* is dangerous because of its deleterious effects on animal health and its potential for transmission from animals to humans and vice-versa. It thus has a huge impact on animal health and welfare and causes major economic losses in livestock production. Increasing attention is therefore being paid to both livestock and companion animals in terms of this pathogen. In this review, we summarise the current knowledge on the animal host adaptation of *S. aureus*. Different types of *S. aureus* infections in animals are also presented, with particular emphasis on mastitis in dairy herds, which is probably the costliest and therefore the best documented *S. aureus* infection seen in animals.

1. The adaptation of *Staphylococcus aureus* to animal hosts

1.1. Biotypes and host-specific genotypes

S. aureus strains isolated from animal hosts were shown at an early stage to present phenotypic characteristics, which vary depending on the host of origin. Six biotypes were defined and categorised according to their reaction to six simple assays (Table 1): human, β-haemolytic human, bovine, ovine-caprine, avian-abattoir and non-host-specific. Since then, this concept of biotypes has not been questioned by other characterisation methods (Devriese, 1984; Isigidi et al., 1990; Shimizu et al., 1991). Indeed, using multilocus enzyme electrophoresis (MLEE), natural populations of *S. aureus* from humans, cows and sheep have been shown to be indexed according to electrophoretic types that are rarely shared between human and animal strains, suggesting host specificity and a limited transmission of *S. aureus* between the three host species tested (Musser and Selander, 1990). Genotyping methods based on the polymorphism of DNA macrorestriction profiles, such as pulse field gel electrophoresis (PFGE), have confirmed that strains belonging to a given biotype are grouped in the same (or a closely related) pulsotype (Hennekinne et al., 2003). Other DNA-based typing methods such as amplified fragment length polymorphism (AFLP), applied to isolates from farmers, non-farmers and cow mastitis also showed that human isolates were very similar and quite distinct from the cow isolates (Sakwinska et al., 2011).

DNA sequence-based techniques enable determination of a precise and refined population structure. Multi Locus Sequence Typing (MLST) is a powerful typing method, which is widely used for epidemiological studies. The *S. aureus* mlst database (http://saureus.mlst.net) now contains more than 2200 different sequence types (ST) determined on strains isolated from a variety of hosts (although human isolates markedly predominate) (McCarthy et al., 2012). MLST data clearly show that some clonal complexes (CC; consisting of closely related ST) are predominant in, and clearly associated with, a given host. Livestock-associated *S. aureus* isolates belong to a small number of clones found in animal hosts (Fitzgerald et al., 1997; McCarthy et al., 2012; Sakwinska et al., 2011). For example, ruminant mastitis isolates are mostly associated with clonal complexes CC97, CC133, CC130, CC126 and CC705. The latter CC705 includes ST151, which comprises isolates that are restricted to cows. Furthermore, isolates belonging to CC133 are found in cows, sheep or goats and are more widely disseminated among ruminant species (Ben Zakour et al., 2008; Guinane et al., 2010).

In addition, *S. aureus* strains isolated from poultry or rabbit infections mostly belong to ST5 and ST121, respectively. Both STs include strains of human origin, suggesting that they share a recent common ancestor (Smyth et al., 2009; Vancraeynest et al., 2006). Recently, strains belonging to CC8 were frequently found in bovine mastitis isolates. CC8 is well documented in human carriage and infections, but despite a close relationship with human CC8, this new bovine CC8 genotype was only found in one of the farmers and non-farmers sampled for the study, suggesting that this new bovine-adapted clone was due to a recent human-to-cow host jump with a loss of the ability to colonise humans (Sakwinska et al., 2011).

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Table 1
Phenotypic tests enabling the discrimination of different *S. aureus* biotypes, after Devriese (1984), modified from Devriese et al., Shimizu et al. (1991) and Isigidi et al. (1990).

Biotypes	Phenotypic characteristics			
	Staphylokinase	β-Haemolysin	Coagulation of bovine plasma within 6 h	Type of growth on crystal violet
Host specific				
Human	+	–	–	C/A
Human β-haemolytic	+	+	–	C/A
"True" avian (protein A–)/Abattoir (protein A+)	–	–	–	A
Bovine	–	+	+	A
Ovine	–	+	+	C
Non host specific				
K^- β^+ Bov^- CVType : C	–	+	–	C
K^- β^+ Bov^- CVType : A	–	+	–	A
K^+ β^- Bov^+ CVType : A	+	–	+	A
K^+ β^+ Bov^+ CVType : A	+	+	+	A
K^- β^- Bov^- CVType : C	–	–	–	C

Abbreviations: K = staphylokinase; β = β-haemolysin; Bov = coagulation of bovine plasma within 6 h; CV Type = type of growth on nutrient agar with crystal violet.

The construction of phylogenetic trees based on MLST data has shown that most *S. aureus* strains possess a human host association, and that animal-associated strains share lineages that appear to be basically human-specific (Fig. 1) (Shepheard et al., 2013; Smyth et al., 2009). Recent phylogenetic analysis has revealed probable host switching events, including a majority of anthroponoses (human-to-animal host jump) and zoonoses (Shepheard et al., 2013).

However, it should be noted that this current image of the population structure must take account of a possible bias induced by the imbalance between the large numbers of human strains present in the mlst database and the still small numbers of animal strains. It appears that animal strains (or at least livestock-associated clones) emerged from human strains following a human-to-animal host jump, with a subsequent specialisation that somehow limited any further reverse transmission from animal-to-human, as shown for cow-to-human transmission (Sakwinska et al., 2011). Limited transmission has also been shown between other animal hosts, e.g. cat-to-dog transmission (Sasaki et al., 2012). Similarly, studies based on biotype and pulsotype determinations revealed limited poultry-to-human transmission (Rodgers et al., 1999). Nevertheless, *S. aureus* appears to be capable of host jump and adaptation to novel hosts, even after long periods of isolation in a given host species (Shepheard et al., 2013).

Specificity regarding host colonisation was investigated experimentally *in vitro* by assaying the adherence of six *S. aureus* strains belonging to human-associated or pig-associated clonal lineages to human and pig corneocytes, and *in vivo* by determining their vertical transmission in a newborn piglet colonisation model. These combined experiments demonstrated that some lineages have clear host preferences for human (ST22, ST36) or pig (ST433) hosts, whereas others seem to have a broader host range (ST398 and ST8)

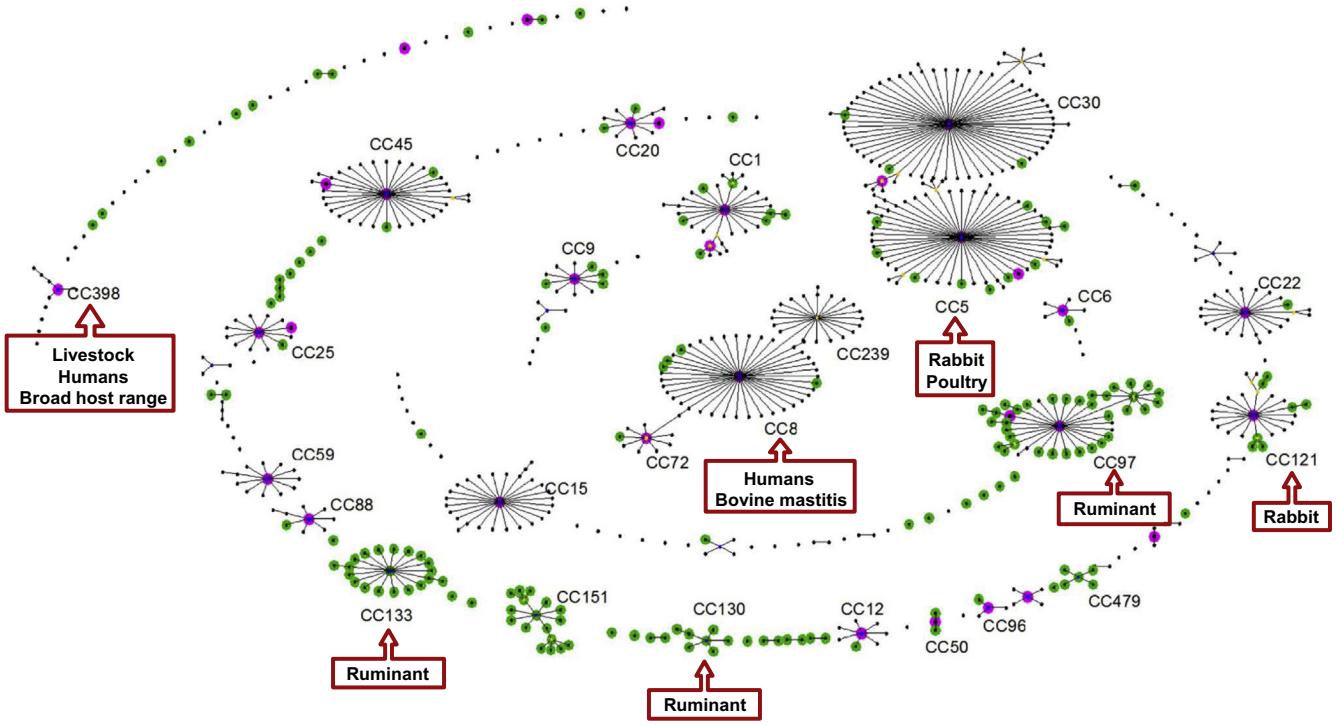

Fig. 1. eBURST plot of 696 STs from human and animal hosts, from Shepheard et al., 2013 (doi: 10.1371/journal.pone.0062369.g002). Comparative eBURST of 696 STs. Genotypes from the human host are shown in black, genotypes from animal hosts are shown in green. Genotypes found in both human and animal hosts are highlighted in pink. The authors have tagged the Clonal Complexes (CC) that predominate in a given animal host (see text for details).