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#### Review

# Presence of methicillin-resistant *Staphylococcus aureus* in the food chain



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#### ARTICLE INFO

Article history:
Received 19 October 2016
Received in revised form
7 December 2016
Accepted 8 December 2016
Available online 5 January 2017

Keywords: Staphylococcus aureus Antibiotics β-lactam Transmission Safety Surveillance

#### ABSTRACT

*Background:* Antimicrobial resistance is one of the major challenges in medicine and **methicillin-resistant** *Staphylococcus aureus* (MRSA) is a particularly problematic nosocomial pathogen. Many recent studies document successful MRSA lineages in farm animals and derived foodstuffs, highlighting the need for adequate control and prevention programmes to avoid food transmission.

Scope and approach: We review the presence of MRSA along the food chain, and the potential of food-producing animals and associated foodstuffs for the transmission of MRSA. The massive use of **antibiotics** in feed to promote growth, and the inappropriate use of antimicrobial agents in veterinary and human medicine are considered to be major contributors to the emergence of resistance. Developments in the epidemiology of MRSA, in hospital (human) settings and primary food production, and MRSA spread along the food chain are described here. Information from EU surveillance programmes is also taken into consideration.

*Keys findings and conclusions*: The emergence of MRSA has implications for **food safety** and surveillance programmes are required for rapid MRSA detection and control.

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#### 1. Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) is becoming clinically problematic worldwide. The appearance of antimicrobial-resistant bacteria as a result of inappropriate use of antibiotics either as antimicrobial therapy or for growth promotion is affecting the food chain sectors, with implications for food-producing animals and associated foodstuff. Here, we review recent evidence of the increasing prevalence of MRSA, with particular attention to the food chain and the genetic background.

#### 2. Methicillin-resistant Staphylococcus aureus (MRSA)

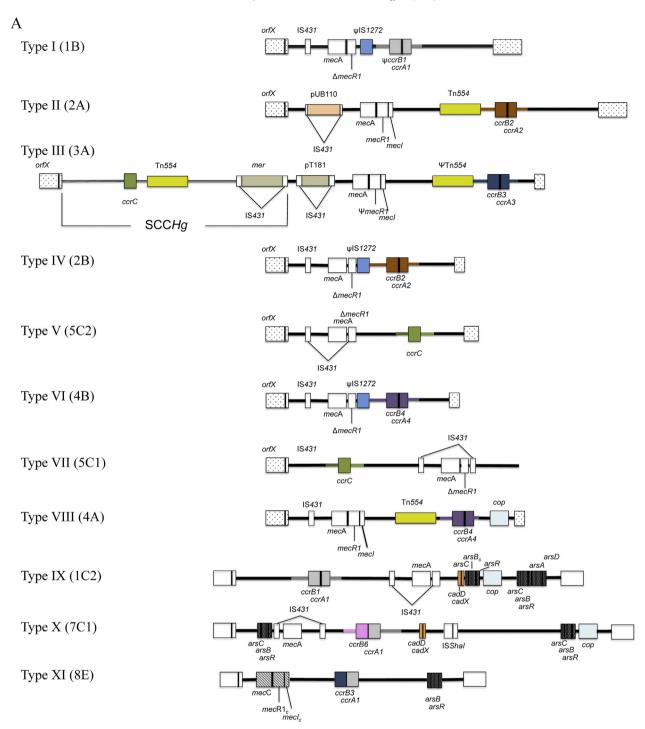
Resistance to penicillinase-stable penicillins, also called "methicillin resistance" or "oxacillin resistance", in *S. aureus* is

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manifested as resistance to all  $\beta$ -lactam antimicrobial agents including cephalosporins and carbapenems and potential susceptibility to the newest class of MRSA-active cephalosporins (e.g. ceftaroline).

The appearance of methicillin-resistant *Staphylococcus aureus* (MRSA) dates back to 1961 in the United Kingdom (Petinaki & Spiliopoulou, 2012), one year after the first introduction of methicillin in clinical practice to treat infections with penicillin-resistant *S. aureus* (Jevons, 1961). MRSA became a serious threat in the early 90s in the USA and UK (Kluytmans, 2010). Resistance is conferred by a mobile genetic element, named the staphylococcal chromosomal cassette (SCCmec) (Milheiriço, Oliveira, & de Lencastre, 2007), carrying mecA or mecC genes, encoding a penicillinbinding protein 2a (PBP2a) (Paterson, Morgan, et al., 2014;; Petinaki & Spiliopoulou, 2012). Beta-lactam drugs bind to PBPs, essential for cell wall peptidoglycan synthesis, leading to bacterial cell lysis. However, PBP2a has low affinity for β-lactam agents, such that peptidoglycan synthesis can continue in MRSA strains (Paterson, Morgan, et al., 2014) even in the presence of diverse β-



**Fig. 1.** A. Features of the different types of the Staphylococcal Cassette Chromosome *mec* (SCC*mec*). The structures of SCC*mec* elements illustrated are based on the following published nucleotide sequences: AB033763 (Type I -1B); D86934 (Type II-2A); AB037671 (Type III - 3A); AB063172 (Type IV - 2B); WBG8318 (Type V-5C2); AF411935 (Type VI-4B); AB373032 (Type VII-5C1); FJ390057 (Type VIII-4A); AB505628 (Type IX-1C2); AB505630 (Type X-7C1); FR821779.1 (Type XI-8E). B. Comparison between amino acid sequences of MecA (Genbank accession number AGC51118.1) and MecC (Genbank accession number WP\_000725529.1). Identity is 63.17% (422 identical positions and 187 similar positions). \*(asterisk) indicates positions which have a single, fully conserved residue;: (colon) indicates residues with strongly similar properties - scoring > 0.5 in the Gonnet PAM 250 matrix. The online Clustal Omega tool, hosted at http://www.uniprot.org, was used.

lactam inhibitor combinations. The *mec*A gene can be found on one of the eleven SCC*mec* types (I-XI) (Fig. 1A), which carry five different *mec* gene complexes, composed of *mec*A and its regulatory genes *mec*I and *mec*R1, and eight different *ccr* gene complexes, containing two different *ccr* recombinases responsible for the

mobility of the element (Kondo et al., 2007). The ancestry of *mecA* has been elucidated: MRSA is generated by the integration of a *mecA*-carrying SCC*mec* element into a methicillin-susceptible *S. aureus* (Enright et al., 2002). A novel methicillin-resistance gene, named *mecC* by the International Working Group (IWG) on the

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