



# BREAK POINT

## 2013 - ISSUE 06

### WELCOME TO ANOTHER EDITION OF BREAKPOINT

Welcome to the last issue of Breakpoint for 2013.

A very timely article on phenotypic detection of *mecC*-MRSA is provided by Geoff Coombs, Royal Perth Hospital, WA.

David Paterson, Royal Brisbane Hospital, is coordinating the “M-E-R-I-N-O clinical study”, and is interested in hearing from interested parties. Please read on.

A conference calendar follows as do major ASA notices.

The Committee as always, welcomes feedback.

**Sharon Chen**

ASA Newsletter Editor

## Antimicrobials 2014

Thurs 20<sup>th</sup> - Sat 22<sup>nd</sup> February 2014 Melbourne Convention Exhibition Centre, Melbourne, Victoria  
[www.antimicrobials2014.com](http://www.antimicrobials2014.com)

### PLENARY SPEAKERS

Resistance Amplification by Cross Transmission. Susan Huang. University of California, USA

Epidemiology and Susceptibility Testing of Fungal Infections. Maiken Arendrup. Statens Serum Institute, Denmark

Antibiotic Dosing in ICU: Moving towards Individualised Therapy? Jason Roberts. University of Queensland, Australia

### KEYNOTE SPEAKERS

Targeted versus Universal Decolonization to Prevent ICU Infection. Susan Huang. University of California, USA

BSAC Outpatient Parenteral Antimicrobial Therapy Guidelines. Andrew Seaton. Gartnavel General Hospital, UK

Bacteria ARE More Promiscuous than Humans: So what are we going to do about it?. Steve Projan, MedImmune, USA

### SYMPOSIUM

<i>Clostridium difficile</i> Still Very Difficult	MDR – Many Different Responses	Investing in Fungal Futures	Therapeutic Drug Monitoring – Peaks and Troughs in the Real World	Bug Time Stories
Epidemiology: “Where the Wild things Are?” (Tom Riley)	Modelling a Response to MDR (Emma McBryde)	Australian Perspective: Antifungal Susceptibility (Sarah Kidd)	β-lactam TDM in Clinical Practice (Jason Roberts)	<i>Streptococcus pneumoniae</i> : the Attributable Disease Burden Due to Resistance (Susan Huang)
Hypervirulence or Just Hype? (Allen Cheng)	Antibiotics in Agriculture – Is there an Ethics Dilemma (Peter Collignon)	Non-Culture Based Diagnostics in Mycology (Catriona Halliday)	Aminoglycoside Dosing – Current Controversies (Evan Begg)	Staphylococcal Bacteraemia: New Knowledge on Optimum Treatment (Natasha Holmes)
Infection Control Issues (Rhonda Stuart)	How can Whole Genome Sequencing Enhance our Understanding – Information Overload (Ben Howden)	Treatment of Candidaemia: What’s New (Maiken Arendrup)	Practical Challenges (John Turnidge)	Multi resistance Plasmids in Enterobacteriaceae (Sally Partridge)
Establishing a Faecal Matter Unit (Patrick Charles)				



## CONTENTS

<a href="#">ASA Subscription</a> .....	Page 02
<a href="#">In the News</a> .....	Page 02
<a href="#">Introducing the Merino Trial</a> .....	Page 03
<a href="#">Phenotypic Detection of <i>mecC</i>-MRSA</a> .....	Page 04
<a href="#">Meeting Calendar</a> .....	Page 06

## ASA SUBSCRIPTION

Payment of ASA Subscription renewals can be performed on-line in the Members' Area of the website (<http://www.asainc.net.au/members>)

Alternatively subscription renewal forms can be downloaded from the Members' Area (<http://www.asainc.net.au/members>)

and:

**Faxed:** 08 9450 8853

**Emailed:** [info@asainc.net.au](mailto:info@asainc.net.au)

**Posted:** Australian Society for Antimicrobials  
PO Box 8266, Angelo Street, South Perth, Western Australia 6151

ASA Application Membership Forms can be downloaded from the ASA website (<http://www.asainc.net.au/membership>)

## IN THE NEWS

The Quod Pill (who is responsible for dreaming up names?)... is the newest 4-in-1 single- pill option for the treatment of HIV-1 infection. Comprising tenofovir, emtricitabine, cobicistat (COBI) and a new integrase inhibitor elvitegravir (EVG), it is of at least comparable efficacy with other comparator agents, and offers the convenience of just once daily dosing. Read more in "Clinical Infectious Diseases" – Advance Access. September 2013.

BJ Gardiner *et al.* also in "Clinical Infectious Diseases" Advance Access October 28 2013 discuss the potential of fosfomycin in (i) prophylaxis against Gram negative infection prior to TRUS biopsy – a single 3 g dose achieves good concentration in uninflamed prostatic tissue - and (ii) as an option for multi-drug resistant Gram negative prostatitis.

\*recommended reading



## INTRODUCING THE MERINO TRIAL – RECRUITMENT COMMENCING IN 2014!

David Paterson  
University of Queensland Centre for Clinical Research, Queensland

### Introduction

In 2013, the ASA awarded its research award to the ASID Clinical Research Network for the MERINO Trial – a “Randomised controlled trial of Meropenem versus Piperacillin-tazobactam for definitive treatment of bloodstream infections due to ceftriaxone non-susceptible *Escherichia coli* and *Klebsiella spp.*” (M-E-R-I-N-O is in the title somewhere – trust me!). After a year of preparation, the trial is set to start.

The key objective of the study is to determine if piperacillin-tazobactam is non-inferior to meropenem for bloodstream infections due to ESBL or plasmid-mediated Amp-C producers, with the primary outcome being mortality at 30 days after the blood culture is drawn.

Inclusion criteria for the study are:

- Bloodstream infection with *E. coli* or *Klebsiella*
- Bacteria confirmed as non-susceptible to ceftriaxone, susceptible to piperacillin/tazobactam and susceptible to meropenem using EUCAST criteria
- No more than 72 hours from the time the positive blood culture was collected

Exclusion criteria are:

- Patient not expected to survive more than 4 days or receiving palliative care
- Patient allergic to a penicillin or a carbapenem
- Patient with polymicrobial bacteraemia

We thank the ASA for their support, and invite interested hospitals to contact us at [merinotrial@gmail.com](mailto:merinotrial@gmail.com) for the full protocol so that recruitment can commence!

David Paterson, on behalf of the MERINO Trial team.



## PHENOTYPIC DETECTION OF *mecC*-MRSA

Geoffrey Coombs. Royal Perth Hospital, PathWest Laboratory Medicine – WA  
Australian Collaborating Centre for *Enterococcus* and *Staphylococcus* Species (ACCESS) Typing and Research, Curtin University.

Methicillin resistance in staphylococci is typically due to a modified penicillin binding protein (PBP2' or PBP2a) encoded by the *mecA* gene (1). Apart from ceftobiprole (2) and ceftaroline (3), the presence of PBP2a confers resistance to all  $\beta$ -lactam antibiotics including the semi-synthetic  $\beta$ -lactamases resistant penicillins, such as methicillin and oxacillin.

In most strains *mecA* is part of a chromosomally integrated mobile genetic element called staphylococcal cassette chromosome *mec* (SCC*mec*) (4). The *mecA* gene is widely disseminated among *Staphylococcus aureus* and other staphylococcal species, and its expression is essential for the methicillin-resistant phenotype. Recently *mecA* gene homologues that are only distantly related to *mecA* have been identified in the genomes of staphylococci (5). One of these homologues, *mecC*, has been identified in *S. aureus* from human and animal sources (6, 7).

Previously known as *mecA*<sub>LG251</sub>, *mecC*-MRSA has been isolated in several European countries including the Republic of Ireland, France, Sweden, the Netherlands, Germany, Austria, Switzerland, Finland, Spain, Norway and Belgium (8). Although the origin and epidemiology of these strains is poorly understood, animal-to-human transmission has been reported (9). *mecC*-MRSA causes a range of infections which are predominately community acquired, and in at least in Denmark, their prevalence appears to be increasing (10). The majority of *mecC*-MRSA are susceptible to non- $\beta$ -lactam antibiotics and belong to multilocus sequence type (MLST) clonal complex (CC) 130 and CC425 (8).

*mecC* exhibits only 69% identity to *mecA* at the DNA level and 63% identity at the protein level to PBP2a (6). **From a primary diagnostic perspective it is important to note that *mecC*-MRSA isolates are not detected by routine *mecA*-specific PCR assays or by the PBP2a slide agglutination tests.**

In 2013 Skov *et al* (11) reported on the susceptibility of 62 *mecC*-MRSA to cefoxitin and oxacillin using broth microdilution, agar dilution, Etest and disc diffusion on different types of media. The isolates belonged to 13 different *spa* types and were assigned to MLST CC130, CC425 or CC1943.

**The study demonstrated cefoxitin was a reliable agent for the detection of *mecC*-MRSA when tested on Mueller-Hinton agar as recommended by EUCAST.** However substantial differences in the performance of different brands of Mueller-Hinton agar were recorded and therefore it is important that a laboratory uses a known *mecC*-positive isolate as a control.

The authors also showed oxacillin was only reliable for the detection of *mecC*-MRSA if MICs were determined using agar dilution with Columbia agar containing 2% NaCl. The inability of oxacillin to reliably detect *mecC* MRSA is thought to be due to a 4-fold higher affinity of the *mecC*-encoded PBP2a<sub>var</sub> for oxacillin compared to cefoxitin (12).

In a recent study by Cartwright *et al*, (13) the bioMérieux Vitek 2 system was anecdotally shown to frequently report *mecC*-MRSA isolates as susceptible to oxacillin but resistant to cefoxitin. This profile differs from the oxacillin-resistant/cefoxitin-resistant profile that is usually observed with *mecA* positive MRSA isolates. The authors suggest that the Vitek 2 system may provide a zero-cost screening method for the identification of *mecC*-positive MRSA. The system's "expert rules" however are programmed to override raw data and report an oxacillin-sensitive /cefoxitin-resistant profile as oxacillin-resistant/cefoxitin-resistant with an explanatory comment. Laboratory staff will need to examine the uncorrected data to identify possible *mecC* MRSA.

In conclusion, cefoxitin has been shown to reliably detect *mecC*-MRSA, however until further studies are performed to determine if phenotypic tests such as the Vitek 2 system can reliably distinguish *mecC*-MRSA from *mecA*-MRSA, *mecC* PCR should be performed on all *mecA* negative cefoxitin resistant isolates.



## PHENOTYPIC DETECTION OF *mecC*-MRSA CONT'D

Geoffrey Coombs. Royal Perth Hospital, PathWest Laboratory Medicine – WA

Australian Collaborating Centre for *Enterococcus* and *Staphylococcus* Species (ACCESS) Typing and Research, Curtin University.

1. **Beck WD, Berger-Bachi B, Kayser FH.** 1986. Additional DNA in methicillin-resistant *Staphylococcus aureus* and molecular cloning of *mec*-specific DNA. *J Bacteriol* 165:373-378.
2. **El Solh A.** 2009. Ceftobiprole: a new broad spectrum cephalosporin. *Expert Opin Pharmacother* 10:1675-1686.
3. **Coombs GW, Pearson JC, Robinson JO, Christiansen KJ.** 2013. Activity of ceftaroline against community associated and healthcare associated methicillin resistant *Staphylococcus aureus*. *Pathology*.
4. **International Working Group on the Classification of SCC.** 2009. Classification of staphylococcal cassette chromosome *mec* (SCC*mec*): guidelines for reporting novel SCC*mec* elements. *Antimicrob Agent Chemother* 53:4961-4967.
5. **Ito T, Hiramatsu K, Tomasz A, de Lencastre H, Perreten V, Holden MT, Coleman DC, Goering R, Giffard PM, Skov RL, Zhang K, Westh H, O'Brien F, Tenover FC, Oliveira DC, Boyle-Vavra S, Laurent F, Kearns AM, Kreiswirth B, Ko KS, Grundmann H, Sollid JE, John JF, Jr., Daum R, Soderquist B, Buist G, International Working Group on the Classification of Staphylococcal Cassette Chromosome E.** 2012. Guidelines for reporting novel *mecA* gene homologues. *Antimicrob Agent Chemother* 56:4997-4999.
6. **Garcia-Alvarez L, Holden MT, Lindsay H, Webb CR, Brown DF, Curran MD, Walpole E, Brooks K, Pickard DJ, Teale C, Parkhill J, Bentley SD, Edwards GF, Girvan EK, Kearns AM, Pichon B, Hill RL, Larsen AR, Skov RL, Peacock SJ, Maskell DJ, Holmes MA.** 2011. Methicillin-resistant *Staphylococcus aureus* with a novel *mecA* homologue in human and bovine populations in the UK and Denmark: a descriptive study. *Lancet Infect Dis* 11:595-603.
7. **Shore AC, Rossney AS, O'Connell B, Herra CM, Sullivan DJ, Humphreys H, Coleman DC.** 2008. Detection of staphylococcal cassette chromosome *mec*-associated DNA segments in multiresistant methicillin-susceptible *Staphylococcus aureus* (MSSA) and identification of *Staphylococcus epidermidis ccrAB4* in both methicillin-resistant *S. aureus* and MSSA. *Antimicrob Agent Chemother* 52:4407-4419.
8. **Paterson GK, Morgan FJ, Harrison EM, Cartwright EJ, Torok ME, Zadoks RN, Parkhill J, Peacock SJ, Holmes MA.** 2013. Prevalence and characterization of human *mecC* methicillin-resistant *Staphylococcus aureus* isolates in England. *J Antimicrob Chemother*.
9. **Harrison EM, Paterson GK, Holden MT, Larsen J, Stegger M, Larsen AR, Petersen A, Skov RL, Christensen JM, Bak Zeuthen A, Heltberg O, Harris SR, Zadoks RN, Parkhill J, Peacock SJ, Holmes MA.** 2013. Whole genome sequencing identifies zoonotic transmission of MRSA isolates with the novel *mecA* homologue *mecC*. *EMBO Molecular Med* 5:509-515.
10. **Petersen A, Stegger M, Heltberg O, Christensen J, Zeuthen A, Knudsen LK, Urth T, Sorum M, Schouls L, Larsen J, Skov R, Larsen AR.** 2013. Epidemiology of methicillin-resistant *Staphylococcus aureus* carrying the novel *mecC* gene in Denmark corroborates a zoonotic reservoir with transmission to humans. *Clin Microbiol Infect* 19:E16-22.
11. **Skov R, Larsen AR, Kearns A, Holmes M, Teale C, Edwards G, Hill R.** 2013. Phenotypic detection of *mecC*-MRSA: cefoxitin is more reliable than oxacillin. *J Antimicrob Chemother* doi: 10.1093/jac/dkt34
12. **Kim C, Milheirico C, Gardete S, Holmes MA, Holden MT, de Lencastre H, Tomasz A.** 2012. Properties of a novel PBP2A protein homolog from *Staphylococcus aureus* strain LGA251 and its contribution to the beta-lactam-resistant phenotype. *J Biologic Chem* 287:36854-36863.
13. **Cartwright EJ, Paterson GK, Raven KE, Harrison EM, Gouliouris T, Kearns A, Pichon B, Edwards G, Skov RL, Larsen AR, Holmes MA, Parkhill J, Peacock SJ, Torok ME.** 2013. Use of Vitek 2 antimicrobial susceptibility profile to identify *mecC* in methicillin-resistant *Staphylococcus aureus*. *J Clin Microbiol* 51:2732-2734.



## 2014 - 2015 MEETING CALENDAR

### 2014

#### **Australian Society for Antimicrobials Annual Meeting**

20-22 Feb, Melbourne, Victoria  
[www.antimicrobials2014.com](http://www.antimicrobials2014.com)

#### **Royal College of Pathologists Update Meeting**

21-23 Feb, Melbourne, NSW  
[www.rcpa.edu.au](http://www.rcpa.edu.au)

#### **Principles of Molecular Microbiology Diagnostics**

5-7 March, Maastricht, The Netherlands  
[escmid.org/dates\\_events/](http://escmid.org/dates_events/)

#### **Australasia Society for infectious Diseases Annual meeting**

26 -29 March, Adelaide, SA  
[www.asid.net.au](http://www.asid.net.au)

#### **16<sup>th</sup> International Congress on Infectious diseases (ICID)**

2-5 April, Cape Town, South Africa  
[www.isid.org/org/icid](http://www.isid.org/org/icid)

#### **SHEA, Society for Healthcare Epidemiology of America**

3-6 April, Denver, USA  
[www.shea-online.org](http://www.shea-online.org)

#### **Antimicrobial Stewardship Programmes: Developing, Implementing and Measuring.**

9-10 May, Barcelona, Spain  
[escmid.org/dates\\_events/](http://escmid.org/dates_events/)

#### **24<sup>th</sup> European Congress of Clinical Microbiology and Infectious Diseases (ECCMID 2014)**

10-13 May 2014, Barcelona, Spain  
[escmid.org/dates\\_events/](http://escmid.org/dates_events/)

#### **114<sup>th</sup> American Society for Microbiology Annual Meeting**

17-20 May, Boston, USA  
[www.asm.org](http://www.asm.org)

#### **Molecular Typing Methods for Pathogens**

30 June - 4 July, Lyon, France  
[escmid.org/dates\\_events/](http://escmid.org/dates_events/)

#### **Australian Society for Microbiology, Annual Meeting**

6-9 July, Melbourne  
[www.theasm.org.au](http://www.theasm.org.au)

#### **20<sup>th</sup> IEA World Congress of Epidemiology**

17-21 Aug, Anchorage, Alaska  
[ieaweb.org/](http://ieaweb.org/)

#### **16<sup>th</sup> International Symposium on Staphylococci and Staphylococcal infections**

26-29 August, Chicago, USA  
[isssi2014.com/](http://isssi2014.com/)

#### **54<sup>th</sup> ICAAC**

6-9 Sept, Washington D.C. USA  
[www.asm.org](http://www.asm.org)

#### **15<sup>th</sup> Asia Pacific Congress of Clinical Microbiology and Infection.**

26-29 Nov, Kuala Lumpur  
[www.apccmi2014.org/](http://www.apccmi2014.org/)

### 2015

#### **Australian Society for Antimicrobials Annual Meeting**

26-28 Feb, Brisbane, Queensland  
[www.asainc.net.au](http://www.asainc.net.au)

#### **25<sup>th</sup> European Congress of Clinical Microbiology and Infectious Diseases (ECCMID 2015)**

25 - 28 April 2015, Copenhagen, Denmark  
[escmid.org/dates\\_events/](http://escmid.org/dates_events/)

#### **55<sup>th</sup> ICAAC**

18-21 Sept, San Diego, USA  
[www.asm.org](http://www.asm.org)