BREAK POINT

2016 - ISSUE 18

FROM THE NEWSLETTER EDITOR'S DESK

In this issue, the Newsletter features an article from Dr. Glen Carter, Senior Project Officer at the Doherty Applied Microbial Genomics Facility, Melbourne. Many ASA members and readers of "Breakpoint" are gearing for the 17th International Symposium on Staphylococci and Staphylococcal Infections, to be held in Seoul, South Korea, from August 30 to September 2, 2016; and later for the 16th APCCMI meeting in Melbourne, 30 Nov - 3 Dec 2016 (www.apccmi2016.org). The Antimicrobials 2017 and StaphPath 2017 meeting website (www.antimicrobials2017.com) is now available. As always suggestions towards improving the Newsletter are very welcome.

Sharon Chen
ASA Breakpoint Editor

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IN THE NEWS

IMMUNOCOMPROMISED HOSTS

Risk of *Pneumocystis* pneumonia and cytomegalovirus infections with idelalisib

Idelalisib is a phosphatidylinositol 3-kinase inhibitor used for the treatment of chronic lymphocytic leukemia and non-Hodgkin's lymphoma. Seven clinical trials of idelalisib used in combination with other agents have been halted due to an increase in serious adverse events and fatalities in patients receiving idelalisib [1], with the majority being infections, including sepsis and pneumonia. In particular, an increased number of cases of *Pneumocystis* pneumonia and cytomegalovirus (CMV) infection was observed in the idelalisib groups of three trials [2]. Patients taking idelalisib should receive *Pneumocystis* prophylaxis and be monitored for CMV reactivation and that idelalisib be discontinued in patients with evidence of infection or viremia. Changes to the prescribing information are expected, pending review by the US Food and Drug Administration.

1. Important drug warning (Gilead). Decreased overall survival and increased risk of serious infections in patients receiving ZYDELIG (idelalisib). http://zydelig.com/Content/pdf/Zydelig-Safety-Info-FINAL.pdf.

2. Personal communication, Gilead Medical Information Department.

Technique for hand hygiene with alcohol-based hand disinfectant

Alcohol-containing hand disinfection (AHD) is an effective and practical alternative to soap and water for hand hygiene, but the optimal method of AHD has not been established. The US CDC and Prevention endorses a 3-step method (apply sanitizer and rub both palms together, cover all surfaces, and rub until dry), whereas the World Health Organization endorses a 6-step method (apply sanitizer and specifically rub six different aspects of the hands and fingers).

In a randomized trial comparing these two methods among 120 doctors and nurses at an acute care hospital, those assigned to the 6-step method had a greater reduction in the bacterial count of their hands, but took approximately 8 s longer to complete hand hygiene and had lower compliance (65 versus 100%) [1]. Hospital transmission and infection rates were not measured. We continue to favour the 3-step AHD method because it is practical and the difference in the bacterial count reduction is of uncertain clinical significance.

1. Reilly JS, Price L, Lang S, et al. A Pragmatic Randomized Controlled Trial of 6-Step vs 3-Step Hand Hygiene Technique in Acute Hospital Care in the United Kingdom. Infect Control Hosp Epidemiol 2016; :1.

IDENTIFICATION AND ANALYSIS BY WHOLE GENOME SEQUENCING OF A MLST ALLELE DEFICIENT *ENTEROCOCCUS FAECIUM*

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Introduction

Enterococci are part of the normal gastrointestinal microflora of both humans and animals. Despite this, several species are important opportunistic pathogens, with *Enterococcus faecium* in particular being a significant hospital pathogen. [1]

The propensity of *E. faecium* for horizontal gene transfer has resulted in the emergence of multidrug-resistant strains, the most important being vancomycin resistant *Enterococcus faecium* (VRE). [2] Infections caused by *E. faecium* are therefore becoming increasingly difficult to treat. As a consequence hospitals have implemented infection control measures designed to limit the spread of VRE. Molecular typing of clinical and screening *E. faecium* isolates is an important part of infection control since it assists with the identification of possible VRE outbreaks.

Multilocus sequence typing (MLST) is a commonly used method for typing *E. faecium* isolates. [3] However, it is becoming increasingly clear, that this low-resolution typing method is inadequate for accurately monitoring the transmission and spread of *E. faecium.*

Results

As part of ongoing surveillance activities, several hospitals in association with MDU PHL investigated the utility of using whole genome sequencing (WGS) to determine the VRE population structure within Australia. This led to the identification of previously unrecognised *E. faecium* isolates that were non-typeable by MLST due to a missing *pstS* allele. Notably, these *E. faecium* were isolated in hospitals from multiple health jurisdictions and within a short 2-year time frame (2013 – 2015). *In silico* analysis suggested that these isolates were all multidrug resistant, with the vast majority having a vancomycin-resistant genotype associated with the carriage of the *vanA* gene. One isolate carried the *vanB* gene. MLST non-typeable. *E. faecium* (NTEFm) therefore appears to be at least partly driving the emergence of *vanA* VREfm locally within Australia.

Bioinformatic analyses showed that all NTEfm isolates belong to the hospital-associated A1 clade [4] and that multiple lineages have arisen through the independent deletion of the *pstS* gene. Subsequent analyses revealed substantial diversity within the core genome of the NTEfm group,

IDENTIFICATION AND ANALYSIS BY WHOLE GENOME SEQUENCING OF A MLST ALLELE DEFICIENT *ENTEROCOCCUS FAECIUM* CONT'D

with NTEfm isolates clearly clustering by hospital, suggestive of a founding event followed by intra-hospital transmission. To a lesser extent there was also evidence of clustering between isolates from different hospitals and across jurisdictions, suggesting inter-hospital transmission has also occurred.

While acknowledging potential sampling bias, we noted a dramatic increase in NTEfm isolates in 2015 and across multiple health jurisdictions, which is perhaps indicative of an emerging national outbreak and suggests NTEfm has become a successful clinical lineage within Australia.

Conclusion

We have identified NTEfm isolates that have arisen following deletions encompassing the *pstS* gene used in the *E. faecium* MLST scheme. Almost all NTEfm isolates carry either the *vanA* or *vanB* resistance genes. The isolation of NTEfm in several hospitals across different states and territories is suggestive of an ongoing multi-jurisdictional outbreak in Australia. Identification of NTEfm further highlights the limitations of MLST for monitoring *E. faecium*. We advocate the use of WGS for ongoing and future public health-based surveillance activities relating to *E. faecium*.

References

1. Arias CA, Murray BE. The rise of the *Enterococcus*: beyond vancomycin resistance. *Nat Rev Microbiol* 2012; 10: 266–78.

2. Cattoir V, Leclercq R. Twenty-five years of shared life with vancomycin resistant enterococci: is it time to divorce? *J Antimicrob Chemother* 2013; 68: 731–42.

3. Homan WL, Tribe D, Poznanski S et al. Multilocus sequence typing scheme for *Enterococcus faecium. J Clin Microbiol* 2002; 40: 1963–71.

4. Lebreton F, van Schaik W, McGuire AM et al. Emergence of epidemic multidrug-resistant *Enterococcus faecium* from animal and commensal strains. *mBio* 2013; 4: e00534-13.

2016 - 2018 MEETING CALENDAR

16th ISSSI
August 30 – September 2 2016 Seoul, South Korea
http://www.isssi2016.org

10th International Transplant Infectious Diseases Conference
Aug 17- 19, Hong Kong, China
Website: www.tts.org/

International congress for Tropical Medicine and Malaria
Sept 18-22, Brisbane, Australia
Website: http://tropicalmedicine2016.com/

Infection Prevention 2016
Sept 26-28, Harrogate, England
Website: www.ips.uk.net

ID week 2016
Oct 26-30, New Orleans, LA
Website: www.idsociety.org

IMED 2016: International Meeting on Emerging Diseases and Surveillance
4-7 November, Vienna, Austria
Website: http://imed.isid.org

16th Asia Pacific Conference on Clinical Microbiology and Infection (APCCMI)
30 Nov- 3 Dec, Melbourne, Australia
Website: http://www.asainc.net.au

2017

ASA Annual Meeting, in conjunction with the StaphPath Meeting
23-25 February, Adelaide, South Australia
Website: www.asainc.net.au

Australasian Society for Infectious Diseases
29 March – 1 April 2017
Website: www.asid.net.au

British Society for Microbiology Annual Meeting
3-6 April, Edinburgh, Scotland
Website: www.microbiologysociety.org

27th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID 2017)
22-25 April 2017, Vienna, Austria
Website: http://escmid.org/dates_events/

ASM Microbe 2017
1-6 June 2016, New Orleans, LA
Website: www.asm.org/microbe2017

ID week 2016
Oct 4-8, San Diego, CA
Website: www.idsociety.org

2018

28th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID 2018)
21-24 April 2018, Madrid, Spain
Website: http://escmid.org/dates_events/

ASM Microbe 2018
7-11 June 2016, Atlanta, GA
Website: www.asm.org/microbe2018