The May 2010 ASA Newsletter

Welcome to the first edition of the ASA Newsletter for 2010! The relative benefits of CLSI versus EUCAST methodologies for susceptibility testing have been a topic of debate. Two short articles explore new developments in both methodologies and consider re-evaluation of existing laboratory methods (John Turnidge). Developments in the CDS method, with doripenem discs now available for testing of Gram-negatives, have also come to the forefront (Syd Bell).

Highlights of the 5th Decennial International Conference on Healthcare-Associated Infections 2010 are included (David Andresen) for those unable to make the trek to Atlanta, Georgia in March. A list of forthcoming national and international meetings is attached which we hope continues to be useful. Finally, I would like to thank David Andresen, Geoff Coombs and all the ASA committee for their enthusiasm and support of the Newsletter.

Sharon Chen
ASA Newsletter Editor

In This Issue

Time to Support Eucast? ............................................................ 2
Australian New Zealand Cooperative on Outcomes in Staphylococcal Sepsis (ANZCOSS) Study................................. 4
ASA 2010 Foundation Members .............................................. 4
Australian Society of Antimicrobials 12th Annual Scientific Meeting (Antimicrobials 2011) ................... 5
What’s New in Susceptibility Testing ..................................... 6
- Clinical and Laboratory Standards Institute (CLSI)
- Calibrated Dichotomous Sensitivity (CDS)
ASA Subscription .................................................................. 11
What’s New on the ASA Website............................................ 11
Conference Report ............................................................... 12
Meeting Calendar .................................................................. 13
May 2010 ASA Newsletter Photo Quiz ................................. 14
December 2009 ASA Newsletter Photo Quiz ......................... 14
The evolution of antibacterial susceptibility testing in Australia has led to the current situation of there being in effect just two standards in routine use: the Clinical and Laboratory Standards Institute (CLSI) standard, and the Calibrated Dichotomous Sensitivity (CDS) standard. Recently, a second major contender has entered the international field, the standard developed by the European Committee on Antimicrobial Susceptibility Testing (EUCAST). Readers would be aware that ASA has supported attendance of one of its members at the CLSI Subcommittee on Antimicrobial Susceptibility Testing (sAST) for almost a decade, giving Australia a first-hand opportunity and contribute in some small way to observe its progress. The efforts of EUCAST and the (slow) progress of the CLSI sAST have revealed the following:

**The CLSI and its sAST**

CLSI is a mature, complex organization, set up as not-for-profit and “independent” of other authorities and organizations in the USA. It focuses on open, transparent decision making through a consensus process. In the last few years it has made an attempt to become a global organization, by changing its name from NCCLS, recruiting more committee members and advisors from outside the USA and, engaging fully with ISO and CEN (the European standards organization). At the same time its charter requires it engage fully with the FDA and industry (pharmaceutical and device manufacturers). It has central administrative staff, but most of its work is done by volunteers. As a stand-alone organization, CLSI funds itself through memberships and the sale of documents. It receives no external official funding.

The sAST has been devising susceptibility testing methods and setting interpretive breakpoints for more than 40 years. It has a wealth of experience behind it, and from susceptibility testing has branched out into setting standards for a range of microbiology laboratory activities. With continued input from a wealth of sources, the sAST has been able to become the de facto standard in many countries outside the USA, driven in part by the development of instrumentation (Vitek, Microscan, Phoenix etc) which are validated by the devices section using CLSI standards.

With maturity comes complexity. The document most widely appreciated by our Australian laboratories is the one containing the yearly update of breakpoints (M100). Because the sAST has been setting breakpoints for decades, many have become out of date due to the steady accumulation of knowledge about pharmacokinetics/pharmacodynamics (PK/PD) over 20 years. Attempts to rectify this problem began in earnest about 6 years ago, but progress has been hampered by the broad consensus process, and the need to keep the FDA engaged. In the USA, but in no other country, the regulator (the FDA), sets antibacterial breakpoints for humans “by law” (that’s the way they put it). The problem has been exacerbated by some multinational pharmaceutical companies who prefer not to deal with the CLSI, as they believe it only complicates their dealings with the FDA (who after all have the final say over marketing). Because CLSI’s client base is still predominantly in the US, the FDA engagement has slowed down changes considerably. The prime example is the 5 years it has taken to publish revised breakpoints for the cephalosporins and Enterobacteriaceae. There are many other breakpoints waiting to be reviewed, and with twice yearly meetings the prospect of rapid updating of breakpoints remains slim.

**EUCAST**

In the years since CLSI’s sAST began the task of revising breakpoints, EUCAST has emerged as a major alternative force. The previously disparate national societies in Europe have worked hard together and have now matured to the point where they come close or even exceed the utility of CLSI standards. Their engagement with the European regulator, EMEA, could be considered more sophisticated, in that EUCAST has a memorandum of understanding with the EMEA to develop and recommend breakpoints, with EMEA reserving the right to veto their recommendations. The EMEA has not yet done so for any EUCAST recommendation. In essence the EMEA agree that EUCAST has the greater expertise. The recent publication of a disc diffusion method by EUCAST means that EUCAST can provide the basic susceptibility testing needs of all routine microbiology laboratories. Their breakpoints have all been developed in the last 5 years and all have taken PK/PD into account (where possible). This puts them ahead of CLSI in the one critical aspect of routine testing: breakpoints. EUCAST is funded by the European Union through the European CDC, while remaining an “effector” arm of the European Society for Clinical Microbiology and Infectious Diseases. Their charter and funding source has allowed them to provide their standards in the public domain (they’re free!)

**CLSI and EUCAST compared**

The maturity of CLSI means that it currently provides more than EUCAST. These are the documents—standards and guidelines—provided by both organizations. Note that both CLSI and EUCAST members contributed to the development of an ISO standard reference method for antibacterial susceptibility testing method (ISO-20776-1), namely the broth microdilution standard.

**For consideration**

CLSI does far too much good work in microbiology to be ignored. However, in the area of antibacterial breakpoints for medical use it is falling rapidly behind in the revision process, and sticking with CLSI breakpoints has the potential to compromise patient care. We would like ASA members and any other interested parties to consider the national adoption of EUCAST (human) antibacterial breakpoints and for those relevant users, a switch to the EUCAST disc diffusion method. The reason for the latter suggestion is that this would then result in consistency in susceptibility interpretation if and when national (passive) surveillance ever gets back onto the agenda. It would not be easy to merge susceptibility testing data from CLSI and EUCAST users for many bug/drug combinations.

There are obvious implications for going down this track, not the least of which is the work required to create new laboratory methods and train the staff appropriately. The device manufacturers will also need to assist us in making these adjustments. We would really like to hear from as many people as possible, so they can get a reasonable feel for the overall willingness to change. Please contact us with your thoughts, opinions and concerns, however wordy or brief! If there is sufficient interest in switching, ASA will be pleased to develop a model implementation and training package to assist laboratories with the changeover.

Note that we are still encouraging people to stick with CLSI for anaerobes, mycobacteria and aerobic actinomycetes, antifungals and veterinary antibiotics, simply because they are up with current breakpoint setting methods and can still be relied upon in routine practice. (Some will be aware that EUCAST is working on the antifungal agents and doing quite nicely).
<table>
<thead>
<tr>
<th><strong>CLSI document</strong></th>
<th><strong>EUCAST document</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medical – antibacterial agents</strong></td>
<td></td>
</tr>
<tr>
<td>M2 – Disc susceptibility testing method (Standard)</td>
<td>EUCAST disk diffusion method</td>
</tr>
<tr>
<td>M7 – Dilution susceptibility testing methods (Standard) (ISO standard)</td>
<td>E. Def 3.1: Determination of minimum inhibitory concentrations (MICs) of antibacterial agents by agar dilution. (=ISO standard)</td>
</tr>
<tr>
<td>M11 – Methods for anaerobes (Standard)</td>
<td></td>
</tr>
<tr>
<td>M11-S1 – Breakpoints and QC ranges for anaerobes (Informational supplement)</td>
<td></td>
</tr>
<tr>
<td>M24 – Susceptibility testing of Mycobacteria and aerobic actinomycetes (Standard)</td>
<td></td>
</tr>
<tr>
<td>M24-S1 – QC ranges for rapidly-growing mycobacteria testing (Informational supplement)</td>
<td></td>
</tr>
<tr>
<td>M39 – Analysis and presentation of cumulative antimicrobial susceptibility test data (Guideline)</td>
<td></td>
</tr>
<tr>
<td>M45 – Dilution and disk testing of infrequently isolated or fastidious bacteria (Guideline)</td>
<td></td>
</tr>
<tr>
<td>M100 – Performance standards for antibacterials: Breakpoints and supplementary tests, plus QC ranges (Standard)</td>
<td>EUCAST MIC and Zone diameter breakpoint tables EUCAST Quality Control tables</td>
</tr>
<tr>
<td>M23 – Data requirements for setting breakpoints and QC ranges (Guideline)</td>
<td>E. Def 2.1: Determination of antimicrobial susceptibility test breakpoints Information for pharmaceutical companies intending to bring new antimicrobial drugs to EUCAST for breakpoints EUCAST Procedure for harmonising and defining breakpoints</td>
</tr>
<tr>
<td><strong>Medical – antifungal agents</strong></td>
<td></td>
</tr>
<tr>
<td>M27 – Broth dilution testing of yeasts (Standard)</td>
<td>E. Def 7.1: Broth dilution testing of yeasts</td>
</tr>
<tr>
<td>M27-S1 – Breakpoints and QC ranges for yeasts (Informational supplement)</td>
<td>EUCAST Antifungal MIC breakpoint tables</td>
</tr>
<tr>
<td>M38 – Broth dilution antifungal testing of filamentous fungi (Standard)</td>
<td>E.DEF 9.1: Broth dilution of antifungal agents for conidia forming moulds</td>
</tr>
<tr>
<td>M44 – Disk diffusion testing of yeasts (Guideline)</td>
<td></td>
</tr>
<tr>
<td>M44-S1 – Breakpoints and QC ranges for disk test of yeasts (Informational supplement)</td>
<td></td>
</tr>
<tr>
<td><strong>Veterinary – antibacterials</strong></td>
<td></td>
</tr>
<tr>
<td>M31 – Disk and dilution testing of antibacterials for animals (Standard)</td>
<td></td>
</tr>
<tr>
<td>M37 – Data requirements for setting breakpoints and QC ranges for animal pathogen testing (Guideline)</td>
<td></td>
</tr>
<tr>
<td>M42 – Disk testing of bacteria isolated from aquatic animals (Guideline)</td>
<td></td>
</tr>
<tr>
<td>M49 – Broth dilution testing of bacteria isolated from aquatic animals (Guideline)</td>
<td></td>
</tr>
<tr>
<td><strong>Media standards</strong></td>
<td></td>
</tr>
<tr>
<td>M6 – Protocols for evaluating Mueller-Hinton agar (Standard)</td>
<td>Media preparation for disk testing – Mueller-Hinton agar and MHA supplemented with horse blood and NAD</td>
</tr>
<tr>
<td>M32 – Evaluation of lots of Mueller-Hinton broth (Standard)</td>
<td></td>
</tr>
<tr>
<td><strong>Other documents</strong></td>
<td>Expert rules in antimicrobial susceptibility testing</td>
</tr>
</tbody>
</table>
The ASA Committee wishes to acknowledge the following companies for becoming Foundation (Sustaining) Members of the Society:

PLATINUM
- Janssen-Cilag
- Novartis

SILVER
- GlaxoSmithKline

BRONZE
- AstraZeneca
- BD Diagnostics
- Thermo Fisher Scientific (Oxoid)
- bioMérieux Australia
- Bayer Schering Pharma
- Pfizer Australia
- Immuno
- Merck Sharp & Dohme Australia

Foundation Members websites can be located in the Foundation (Sustaining) Members section of the ASA webpage (http://www.asainc.net.au/foundation_membership/members)

Staphylococcal sepsis remains a significant healthcare problem worldwide, both in the community and in hospital practice. The literature demonstrates that outcomes are suboptimal for some cases of invasive staphylococcal infection. Factors known to impact on outcomes include resistance, especially methicillin resistance, and toxin production such as TSST-1 and PVL.

To understand the local epidemiology of severe *Staphylococcus aureus* disease in Australia and New Zealand a cooperative, under the auspices of the Australian Society for Antimicrobials, has been established; the Australian New Zealand Cooperative on Outcomes in Staphylococcal Sepsis (ANZCOSS).

As from the 21st May 2007 19 sites from 6 Australian states/territories and 3 sites from New Zealand commenced contributing data. Participating institutions are submitting, online, basic demographic, risk factor and outcome data on patients with *S. aureus* sepsis seen at their sites on a continuous basis, with the first full review of outcome data occurring after 12 months of data have been entered. To date, more that 5000 cases have been entered. The first complete analysis of data was published in the Medical Journal of Australia in October 2009.

With a crude mortality rate of nearly 20% identified, there is still much to do and learn about this condition. A substudy examining the relationships between vancomycin treatment and outcome is currently being co-ordinated through the Austin Hospital contributors in Melbourne (vssANZCOSS). Work has also commenced with statistician researchers at the Queensland University of Technology on outcomes of hospital-onset bacteraemia.

We are hopeful that many current contributors will see the long term benefits of continuing their contribution, including intervention studies and attempts to improve mortality rates.

ANZCOSS invites all institutions in Australia and New Zealand to participate, or to continue to contribute if they are able.

For further information please contact
John Turnidge (john.turnidge@health.sa.gov.au) or the ANZCOSS Data Administrator, Despina Kotsanas (despina.kotsanas@southernhealth.org.au).
On behalf of the Australian Society for Antimicrobials I would like to invite you to the Society’s 12th Annual Scientific Meeting “Antimicrobials 2011” to be held at the Hilton on the Park, Melbourne on Thursday 24th - Saturday 26th February 2011.

I am pleased to announce Fred Tenover from Cepheid in the United States of America and Rafael Canton from the University Hospital Ramon y Cajal (Madrid, Spain) will be participating at the meeting. Fred will be presenting the plenary “USA300 – What does the Genome Tell Us?” while Rafael will be presenting the plenary “Antibiotic Resistance Genes from the Environment with Emerging Clinical Importance”. Both speakers will also be participating in the symposium sessions.

The Australian plenary speaker for “Antimicrobials 2011” is John Turnidge from SA Pathology. John will be presenting the plenary “The Things that Bug Me”.

The programme’s symposia cover many different aspects on antimicrobials and sessions include “ST93 Community MRSA: Australia’s Answer to USA300”, “Carbapenem Resistance in Gram-negatives: The Role of the Carbapenemases”, “Multidrug Resistance in the Community”, “Clostridium difficile”, and “Emerging Antimicrobial Resistance Worldwide”. In addition we have two workshops on Saturday afternoon titled “CLSI vs EUCAST and Beyond” and the “Changes and Controversies in Antimicrobial Use” and “Anti-Infectives Prophylaxis” Pharmacy Workshops. Three proffered papers and two poster sessions are also planned for the meeting. Once again ASA is offering travel awards to financial members of the Society who are submitting abstracts for the meeting. These awards include return economy airfare, registration and accommodation. In addition the ASA/bioMérieux travel award will be awarded during the meeting to an abstract dealing with the identification of antimicrobial resistance in a routine clinical setting.

To promote discussion and interaction between delegates and the invited speakers the meeting’s registration includes lunches, morning and afternoon teas and admission to the Welcome and Industry Receptions. I am confident that you will find the meeting’s programme both scientifically stimulating and informative and we look forward to meeting you in Melbourne.

Graeme Nimmo
President ASA

Newsletter Contributions
Submission of articles, material for the Picture Quiz, reviews for the journal club, or letters to the Editor should be sent to:

Sharon Chen
ASA Newsletter Editor
e-mail: info@asainc.net.au
WHATS NEW FROM CLSI

Professor John Turnidge, SA - Pathology

New CLSI Breakpoints for Cefalosporins, Aztreonam and Carbapenems for the Enterobacteriaceae
Action For Laboratories And Device Manufacturers

In January 2010 the Antimicrobial Susceptibility Testing (AST) subcommittee of the CLSI released new breakpoints (interpretive criteria) for parenteral cephalosporins and carbapenems. This followed literally years of data digestion, discussion, disputation and decision-making. The breakpoints agreed upon were driven by merging laboratory data, detailed pharmacokinetic/pharmacodynamic (PK/PD) analyses, and published data on clinical outcomes. Breakpoints have been either lowered or eliminated altogether. Comments on the specific agents follow:

Cephalothin

Cephalothin has had MIC breakpoints retained but has been relegated on PK/PD grounds to a predictive role for other oral cephalosporins. This means that in practice cephalothin, even in maximal doses, has no useful clinical activity against Enterobacteriaceae, even those without intrinsic resistance mechanisms and despite what we all used to believe. The old breakpoints have been retained for the specific purpose of predicting susceptibility and resistance to first-generation oral cephalosporins–cephalexin and cefadroxil in the Australian context. Data presented recently to the subcommittee has shown that, at least for the interim, cephalothin breakpoints (MIC and zone diameter) cannot be used to predict cephalosporin susceptibility.

Cephazolin

Cephazolin MIC breakpoints have been lowered to S ≤ 1, I = 2, R ≥ 4 mg/L on PK/PD grounds, relating to a standard adult dosing schedule of 1g every 8 hours. These new breakpoints create a significant problem because many previously wild-type E. coli, Klebsiella species and P. mirabilis will then be classified as intermediate or resistant. This would drive more prescribing of third-generation cephalosporins and carbapenems. This followed literally years of data digestion, discussion, disputation and decision-making. The new breakpoints are adequate for this purpose.

Ceftriaxone and Cefotaxime

The breakpoints for these agents have been lowered to S ≤ 1, I = 2, R ≥ 4 mg/L on PK/PD and clinical outcome grounds. The data confirm that almost all Enterobacteriaceae harbouring ESBLs and/or plasmid-borne AmpC enzymes will be detected using the ‘S’ breakpoint, because they will test as intermediate or resistant to these agents. One immediate consequence is that ESBL screening and confirmation tests are no longer required for interpreting results. Some laboratories may wish to continue with ESBL supplementary tests, but should be aware that they are not designed to confirm presence/absence of plasmid-borne AmpC enzymes, which we now know are present in Australian isolates of Enterobacteriaceae. However, there is a high likelihood that strains testing as I or R with the new breakpoints harbour one of these (an ESBL or plasmid-borne AmpC) on a transmissible element, so for infection control purposes, appropriate precautions could easily be based on the finding of ‘I’ or ‘R’ without supplementary testing.

Ceftazidime

Based on a standard adult dose of 1g every 8 hours, ceftazidime breakpoints have been lowered by one dilution to S ≤ 4, I = 8, R ≥ 16 mg/L. These breakpoints will not detect all ESBL or plasmid-borne AmpC-producing strains. However, testing ceftriaxone or cefotaxime using the new breakpoints is adequate for this purpose.

Cefepime

Breakpoints for cefepime were evaluated at the same time as the other cephalosporins and the decision was not to change them. This may be reviewed in the near future because of ongoing concerns about the fact that they are not compatible with 12-hourly dosing. There is ongoing concern about the adequacy of dosing of cefepime on a 12-hourly schedule, and the general consensus is that this agent should be administered 8-hourly, similar to ceftazidime.

Aztreonam

Breakpoints for aztreonam, another β-lactam vulnerable to extended-spectrum β-lactamases, have also been adjusted down by one dilution on PK/PD grounds. The new breakpoints are S ≤ 4, I = 8, R ≥ 16 mg/L.
WHATS NEW IN SUSCEPTIBILITY TESTING  (Cont)

Carbapenems

After repeated analysis of data, as well as input from some of the producers, the breakpoints for carbapenems have all been lowered. The decision was made in January 2010, and followed the printing of the annual M100 book. This is the reason that the older breakpoints appear in the current version of M100 (S20). The new breakpoints will be published as an official supplement to M100 soon.

They are:

<table>
<thead>
<tr>
<th></th>
<th>S (mg/L)</th>
<th>I (mg/L)</th>
<th>R (mg/L)</th>
<th>S (mm)</th>
<th>I (mm)</th>
<th>R (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eraspenem</td>
<td>≤ 0.25</td>
<td>0.5</td>
<td>≥ 4</td>
<td>≥ 23</td>
<td>20-22</td>
<td>≤ 19</td>
</tr>
<tr>
<td>Imipenem</td>
<td>≤ 1</td>
<td>2</td>
<td>≥ 4</td>
<td>≥ 23</td>
<td>20-22</td>
<td>≤ 19</td>
</tr>
<tr>
<td>Meropenem</td>
<td>≤ 1</td>
<td>2</td>
<td>≥ 4</td>
<td>≥ 23</td>
<td>20-22</td>
<td>≤ 19</td>
</tr>
<tr>
<td>Doripenem</td>
<td>≤ 1</td>
<td>2</td>
<td>≥ 4</td>
<td>≥ 23</td>
<td>20-22</td>
<td>≤ 19</td>
</tr>
</tbody>
</table>

Reporting the results as found

A further important recommendation though is that cephalosporin, aztreonam and carbapenem results should be reported “as found”. This will be a significant departure for many of us, as there has been a wish to automatically report all third-generation cephalosporins R when an ESBL has been detected. Now it is possible to have a result such as ceftriaxone I or R, and ceftazidime S using the new breakpoints. While this result is predictive of the presence of an ESBL or plasmid-borne AmpC, and a comment should be appended to the report, this should not cause the ceftazidime result to be changed to R! While this might be surprising to many people, the subcommittee has agreed, based on evidence presented to it, that “the MIC is the MIC”, i.e. it is the actual MIC that predicts in vivo activity, and not the presence/absence of an enzyme per se. The EUCAST committee is of the same view and is currently canvassing feedback on a proposal to report cephalosporin results “as found”.

There is still value in “detecting” ESBLs and carbapenemases for Infection Control purposes. However, instead of screening for ESBLs and the like, the strategies for detecting these are simply to add a comment to reports for strains that test as I or R to cefotaxime OR ceftriaxone OR ceftazidime OR aztreonam, suggesting that the presence of an ESBL or plasmid-borne AmpC is likely. We should also notify Infection Control of these results via the usual mechanisms for MRO notification. A similar action applies when getting a result of I or R to any of the carbapenems (most of us test just meropenem).

Actions arising from the new breakpoints

Agar dilution users

Those using agar dilution will be able to adjust the concentrations in their plates to the new breakpoints. Many will be using the I mg/L cefotaxime/ceftriaxone concentrations already for ESBL screening. If the laboratory is reporting cephalaxin or cefaclor (for instance, for urinary isolates), they should test cephalexin and report the results as cephalexin or cefaclor. If they are reporting cephazolin on isolates of Enterobacteriaceae on non-urinary isolates, or all isolates, then they must test cephazolin.

Vitek users

The combination of changes in cephalothin and cephazolin creates a problem with the current Vitek 2 cards, because users were recently been requested to choose between the two agents. ‘Cephazolin’ cards are able to predict cephalaxin (and cefaclor for those wishing to use this agent for Enterobacteriaceae—hopefully not many!), but not cephazolin. ‘Cephazolin’ cards can only be used to predict cephazolin, not cephalothin, cephalaxin (or cefaclor). In future, it may be necessary to test both agents in laboratories servicing hospitals using cephalaxin as their injectable first-generation cephalosporin.

One issue facing users is the fact that the cephalaxin concentrations in the wells of the current (Australian) card do not go down low enough to accommodate the new cephalaxin breakpoints. While awaiting future developments on these breakpoints, we recommend that In the mean time, after discussion with bioMérieux, we recommend that the software be adjusted to create the following output: Susceptible ≤ 4 mg/L, Resistant ≥ 4 mg/L. This brings the interpretive criteria down one dilution from the current (too high) breakpoint. It will take some time for bioMérieux to make adjustments to the well concentrations in their cards, and they will need to wait for the outcome of the June CLSI meeting before starting on these adjustments (which take time as they need validation studies and then FDA approval).

Disc diffusion users

At this stage, if the laboratory has been testing and reporting cephalothin, they will either have to stop reporting this agent (and start reporting a 3rd generation cephalosporin routinely because it is important to have at least one cephalosporin reported for penicillin-allergic patients!!), or set up an alternative method such as Etest/MICE, which is not inexpensive, or make/purchase some agar dilution plates with the new breakpoint concentrations in them. The disc diffusion users can at least report cephalaxin on urinary isolates (by testing cephalothin).

Summary of actions for ESBL testing in Enterobacteriaceae

No ESBL testing is routinely required. The recognition of ESBLs, plasmid-borne AmpC enzymes, and carbapenemases (metallo- enzymes and serine enzymes) is indirectly via the detection of strains with the result I or R.
<table>
<thead>
<tr>
<th>Agent</th>
<th>New MIC BPs S/I/R</th>
<th>Test</th>
<th>Report</th>
<th>Isolates</th>
<th>Possible Report Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cephalothin</td>
<td>≤ 8 / 16 / ≥ 32</td>
<td>Cephalothin</td>
<td>Cephalothin</td>
<td>Urinary only</td>
<td>__</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>≤ 1 / 2 / ≥ 4</td>
<td>Cefazolin</td>
<td>Cefazolin</td>
<td>AI</td>
<td>__</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>≤ 1 / 2 / ≥ 4</td>
<td>Cefotaxime</td>
<td>Cefotaxime or ceftriaxone</td>
<td>A</td>
<td>If result is I or R “ESBL or plasmid-borne AmpC likely to be present. Infection Control will be notified”</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>B</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>≤ 1 / 2 / ≥ 4</td>
<td>Ceftriaxone</td>
<td>Cefotaxime or ceftriaxone</td>
<td>A</td>
<td>If result is I or R “ESBL or plasmid-borne AmpC likely to be present. Infection Control will be notified”</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>B</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>≤ 4 / 8 / ≥ 16</td>
<td>Ceftazidime</td>
<td>Ceftazidime</td>
<td>AI</td>
<td>If result is I or R “ESBL or plasmid-borne AmpC likely to be present. Infection Control will be notified”</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>B</td>
</tr>
<tr>
<td>Cefepime</td>
<td>No change ≤ 8 / 16 / ≥ 32</td>
<td>Cefepime</td>
<td>Cefepime</td>
<td>AI</td>
<td>If result is I or R “ESBL or plasmid-borne AmpC likely to be present. Infection Control will be notified”</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>≤ 4 / 8 / ≥ 16</td>
<td>Aztreonam</td>
<td>Aztreonam</td>
<td>AI</td>
<td>If result is I or R “ESBL or plasmid-borne AmpC likely to be present. Infection Control will be notified”</td>
</tr>
<tr>
<td>Ertapenem</td>
<td>≤ 0.25 / 0.5 / ≥ 1</td>
<td>Ertapenem</td>
<td>Ertapenem</td>
<td>AI</td>
<td>If result is I or R “Carbapenemase likely to be present. Infection Control will be notified”</td>
</tr>
<tr>
<td>Imipenem</td>
<td>≤ 1 / 2 / ≥ 4</td>
<td>Imipenem</td>
<td>Imipenem</td>
<td>AI</td>
<td>If result is I or R “Carbapenemase likely to be present. Infection Control will be notified”</td>
</tr>
<tr>
<td>Meropenem</td>
<td>≤ 1 / 2 / ≥ 4</td>
<td>Meropenem</td>
<td>Meropenem</td>
<td>AI</td>
<td>If result is I or R “Carbapenemase likely to be present. Infection Control will be notified”</td>
</tr>
<tr>
<td>Doripenem</td>
<td>≤ 1 / 2 / ≥ 4</td>
<td>Doripenem</td>
<td>Doripenem</td>
<td>AI</td>
<td>If result is I or R “Carbapenemase likely to be present. Infection Control will be notified”</td>
</tr>
</tbody>
</table>

A  E. coli, Klebsiella spp., P. mirabilis, C. koseri, Shigella spp., Salmonella spp.
B  Enterobacter spp, Serratia spp., C. freundi, P. vulgaris and penneri, Providencia spp. and Morganella morganii
* Most often resistance implies that the isolate is a stably de-repressed mutant; however, isolates are being found with increasing frequency that contain ESBLs and/or plasmid-borne AmpC enzymes
### VITEK 2 CURRENT AUSTRALASIAN CARD ACTIONS (AST N149 and ASTN150)

<table>
<thead>
<tr>
<th>New MIC BPs S/I/R</th>
<th>Available concentrations</th>
<th>Report</th>
<th>Software interpretive setting</th>
<th>Isolates</th>
<th>Report Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cephalothin</td>
<td>No change ≤8 / 16 / ≥32</td>
<td>2, 8, 32</td>
<td>Cephalothin or Cefadroxil</td>
<td>No change ≤8 / 16, R ≥32</td>
<td>Urinary only</td>
</tr>
<tr>
<td>Cephazolin</td>
<td>≤1 / 2 / ≥4</td>
<td>4, 16 / 64</td>
<td>Cephazolin</td>
<td>≤4, (No I), R ≥8</td>
<td>All</td>
</tr>
</tbody>
</table>
| Ceftriaxone        | ≤1 / 2 / ≥4              | 1, 2, 8, 32 | Ceftriaxone or ceftroxime | ≤1, I =2, R ≥2 | A | If result(s) I or R

“ESBL or plasmid-borne AmpC likely to be present. Infection Control will be notified” |
|                     |                          |        |                               |          | B | (no consensus approach yet) * |
| Cefepime            | No change ≤8 / 16 / ≥32  | 2, 8, 16, 32 | Cefepime | No change ≤8 / 16, R ≥32 | All | If result(s) I or R

“ESBL or plasmid-borne AmpC likely to be present. Infection Control will be notified” |
|                     |                          |        |                               |          | B | (no consensus approach yet) * |
| Meropenem           | ≤1 / 2 / ≥4              | 0.5, 4, 16 | Meropenem | ≤0.5, I = 1-2, R ≥4 | All | If result(s) I or R

“Carbapenemase likely to be present. Infection Control will be notified”

---

**A** E. coli, Klebsiella spp, P. mirabilis, C. koseri, Shigella spp, Salmonella spp.

**B** Enterobacter spp, Serratia spp, C. freundii, P. vulgaris and penneri, Providencia spp. and Morganella morganii

* Most often resistance implies that the isolate is a stably de-repressed mutant; however, isolates are being found with increasing frequency that contain ESBLs and/or plasmid-borne AmpC enzymes
## DISK DIFFUSION

<table>
<thead>
<tr>
<th>Agent</th>
<th>New Disc BPs/ VR</th>
<th>Test</th>
<th>Report</th>
<th>Isolates</th>
<th>Report Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cephalothin</td>
<td>No change</td>
<td>Cephalothin</td>
<td>Cephalexin</td>
<td>Urinary only</td>
<td>--</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>None</td>
<td>Cefazolin</td>
<td>Cefazolin</td>
<td>All</td>
<td>--</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>≥ 26 / 23-25 / ≥ 22</td>
<td>Cefotaxime</td>
<td>Cefotaxine or ceftriaxone</td>
<td>A</td>
<td>“ESBL or plasmid-borne AmpC likely to be present. Infection Control will be notified”</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Cefotaxine</td>
<td></td>
<td>(no consensus approach yet) *</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>≥ 23 / 20-22 / ≥ 19</td>
<td>Ceftriaxone</td>
<td>Ceftriaxine or ceftriaxone</td>
<td>A</td>
<td>“ESBL or plasmid-borne AmpC likely to be present. Infection Control will be notified”</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ceftriaxine</td>
<td></td>
<td>(no consensus approach yet) *</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>≥ 21 / 18-20 / ≥ 17</td>
<td>Ceftazidime</td>
<td>Ceftazidime</td>
<td>All</td>
<td>“ESBL or plasmid-borne AmpC likely to be present. Infection Control will be notified”</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ceftazidime</td>
<td></td>
<td>(no consensus approach yet) *</td>
</tr>
<tr>
<td>Ceftepime</td>
<td>No change</td>
<td>Ceftepime</td>
<td>Ceftepime</td>
<td>All</td>
<td>“ESBL or plasmid-borne AmpC likely to be present. Infection Control will be notified”</td>
</tr>
<tr>
<td></td>
<td>≥ 18 / 15-17 / ≥ 14</td>
<td></td>
<td></td>
<td></td>
<td>(no consensus approach yet) *</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>≥ 21 / 18-20 / ≥ 17</td>
<td>Aztreonam</td>
<td>Aztreonam</td>
<td>All</td>
<td>“ESBL or plasmid-borne AmpC likely to be present. Infection Control will be notified”</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(no consensus approach yet) *</td>
</tr>
<tr>
<td>Ertapenem</td>
<td>≥ 23 / 20-22 / ≥ 19</td>
<td>Ertapenem</td>
<td>Ertapenem</td>
<td>All</td>
<td>“Carbapenemase likely to be present. Infection Control will be notified”</td>
</tr>
<tr>
<td>Imipenem</td>
<td>≥ 23 / 20-22 / ≥ 19</td>
<td>Imipenem</td>
<td>Imipenem</td>
<td>All</td>
<td>“Carbapenemase likely to be present. Infection Control will be notified”</td>
</tr>
<tr>
<td>Meropenem</td>
<td>≥ 23 / 20-22 / ≥ 19</td>
<td>Meropenem</td>
<td>Meropenem</td>
<td>All</td>
<td>“Carbapenemase likely to be present. Infection Control will be notified”</td>
</tr>
<tr>
<td>Doripenem</td>
<td>≥ 23 / 20-22 / ≥ 19</td>
<td>Doripenem</td>
<td>Doripenem</td>
<td>All</td>
<td>“Carbapenemase likely to be present. Infection Control will be notified”</td>
</tr>
</tbody>
</table>

A  E. coli, Klebsiella spp., P. mirabilis, C. koseri, Shigella spp., Salmonella spp.

B  Enterobacter spp, Serratia spp., C. freundii, P. vulgaris and penneri, Providencia spp. and Morganella morganii

* Most often resistance implies that the isolate is a stably de-repressed mutant; however, isolates are being found with increasing frequency that contain ESBLs and/or plasmid-borne AmpC enzymes
WHAT’S NEW FROM CDS

Syd Bell
South Eastern Area laboratory Services
Prince of Wales Hospital, Sydney

1. Problems with our Register of Members on the CDS Website
We have encountered problems with the CDS Registration on the CDS Website at http://web.med.unsw.edu.au/cdstest/ because our ISP will not provide access to online registration on their new server. If you are not registered and wish to be, please contact us on: cds@sesiahs.health.nsw.gov.au.

2. Doripenem (Doribax)
This recently released carbapenem (doripenem 10 µg discs) has now been calibrated for the testing of the Gram-negative bacteria including Pseudomonas species, the Enterobacteriaceae and Acinetobacter species:

<table>
<thead>
<tr>
<th>Annular radius of susceptible strains</th>
<th>MIC (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 6 mm</td>
<td>≤ 4 mg/L</td>
</tr>
</tbody>
</table>

The acceptable ranges of the annular radii in mm obtained with a doripenem 10 µg disc for the reference strains are:

- E. coli ACM 5185: 11.1 – 14.7
- P. aeruginosa ACM 5189: 12.6 – 16.6

3. Campylobacter and Tetracycline
The acceptable range of tetracycline 10 µg discs versus Campylobacter jejuni ACM 5183 tested in micro-aerophilic atmosphere at 37°C has been changed.

The new acceptable range of the annular radii in mm is:

- Campylobacter jejuni ACM 5183: 10.8* - 16.8

(*note this has been corrected since original entry [11.8] here)

4. CDS Workshop at ASM Sydney 2010
The CDS workshop will be held as usual at the ASM Scientific Meeting which is in Sydney this year. Attendees are requested to let us know if there is any aspect of susceptibility testing that they would like to see addressed at this meeting.

ASA SUBSCRIPTIONS

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
- 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)

What’s New on the ASA Website
http://www.asainc.net.au

Antimicrobials 2010: PDFs of the proposed programme and the Registration and call for Abstract Flyers can be downloaded from the ASA website (http://www.asainc.net.au/meeting)

Non-ASA Meetings: Information on non ASA Meetings can be placed on the ASA website. Please send information on meetings to info@asainc.net.au

Antimicrobials Surveillance Programmes:
- AGAR
- Western Australian MRSA Epidemiology Report
- South Australian Antimicrobial Utilisation Surveillance Program (AUSP)
The “5th Decennial” was held in Atlanta, Georgia in mid-March, co-organised by SHEA, the CDC, APIC and IDSA. While not as large as ICACAC or the annual IDSA meeting, this multidisciplinary conference provided a high-quality overview of Healthcare-Associated Infection (HAI) epidemiology, prevention, and research methodology. Some of the policy issues, such as reimbursement for HAI, appeared rather parochial to outside eyes (particularly given the meeting’s billing as an “international” conference), but there was still much of relevance to an overseas delegate such as myself. It was surprising that relatively few Australians attended. The following is a subjective highlights list:

**Research Methods:**
This was a major focus of the meeting, and there was a general recognition that we need to move beyond case-control studies of risk factors for HAIs and embrace more sophisticated and robust research methods, such as time-series designs and cluster-randomisation. Australia’s Emma McBryde (VIDS, Melbourne) presented an excellent overview of methodological issues surrounding surveillance methods, in particular the effect of serial correlation of data (due to cross-transmission) on conventional monitoring techniques, and ways to assess the sensitivity and specificity of surveillance tools. Ebbing Lautenbach (University of Pennsylvania) reviewed the difficulties in inferring causality in quasi-experimental studies, and potential difficulties in obtaining ethics approval for these study designs. Anthony Harris (University of Maryland) discussed quasi-experimental designs more broadly and proposed designs with improved internal validity such as repeated-switch multiple-unit time series studies. The SHEA Research Committee is seeking expressions of interest from USA and International hospitals to participate in investigator-driven, high quality trials in infection control.

**CLABSI prevention**
Highlights of the draft HICPAC/CDC guidelines for prevention of Central Line-Associated Bloodstream Infection (CLABSI) were presented by David Pegues (Ronald Reagan UCLA Medical Centre). This document has just completed a public consultation phase and should appear later this year. Points of interest include the use of maximal sterile precautions and 2% chlorhexidine prep for CVC insertion, use of ultrasound guidance if available, avoiding routine line changes, use of split septum valves in preference to mechanical valves, and daily bathing with 2% chlorhexidine post-insertion. Chlorhexidine sponges at the exit site, impregnated catheters, and antibiotic locks remain optional manoeuvres that can be added if CLABSI rates remain high after implementation of the core prevention measures.

**Implementation Science**
Sanjay Saint (University of Michigan) provided a terrific guide for the uninitiated to this important area, which moves beyond the question of “what is best practice?” to “how do we get people to do it?” Methods to promote the clinical uptake of research evidence have advanced substantially in recent years, most visibly with the “bundle” approach to CLABSI, but require further research and refinement.

**Isolation Precautions for MRO’s**
There was an entertaining debate between David Pegues and Kathryn Kirkland (Dartmouth-Hitchcock Medical Centre, New Hampshire) who took positions for and against the proposition that “all patients colonised with multidrug-resistant pathogens should be placed in contact precautions”. While there was no clear knockout winner, an approach of flexible, locally-appropriate isolation precautions rather than a one-size-fits-all rule clearly gained considerable audience support. Publication of the results of the cluster-randomised STAR*ICU study is eagerly awaited. In this study ICU’s were assigned either to intensive MRSA and VRE screening and isolation, or to reinforced generic precautions such as hand hygiene. There was no apparent significant difference in MRO transmission although the statistical power of the study has been questioned.

**Chlorhexidine**
Trish Perl (Johns Hopkins Hospital, Baltimore) and Michael Climo (Hunter Holmes McGuire VA Medical Centre, Virginia) chaired a session where there was discussion of the recent RCT showing the superiority of alcoholic chlorhexidine for surgical preparation over providone iodoine. Alcoholic preparations (either iodine-based or chlorhexidine-based) are used extensively in the USA and Europe, but Australian surgeons continue to be concerned about fire risk with alcoholic products. Other than surgical skin preparation, chlorhexidine clearly has a clear role in hand hygiene products and as skin preparation for line insertion. Investigators are currently examining additional roles such as routine bathing in the ICU to reduce MRO acquisition and/or CLABSI, and for oral hygiene as a VAP prevention tool. The emergence of chlorhexidine resistance in bacteria remains a theoretical concern with widespread use.

**Other Highlights**
Stephan Harbarth (Geneva University Hospital) presented a randomised crossover trial in Kenya of alcohol-based hand rub versus soap and water as surgical hand preparation, showing no difference in wound infection rates but a staff preference for ABHR as it was more convenient. Bernard Camins (Washington University School of Medicine) presented an RCT of 3 Staphylococcus aureus decolonisation approaches after an SSTI. As well as a control group, the interventions were nasal mupirocin alone, nasal mupirocin with chlorhexidine showers, and nasal mupirocin with soaking in dilute bleach baths. All active treatment arms were associated with better MRSA clearance than placebo at 1 month, but only the bleach-based regimen gave improved clearance at 4 months follow up.
## MEETING CALENDAR

### Virology Masterclass
20 June – 2 July, 2010
University of Adelaide, South Australia

### ESCMID-SHEA-ASID Comprehensive Course in Hospital Epidemiology
21 – 25 June, 2010
Port Douglas, QLD

### 16th Symposium on Infections in the Immunocompromised Host
27 – 30 June, 2010
Budapest, Hungary
website: [http://www.ichs.org/budapest.htm](http://www.ichs.org/budapest.htm)

### Australian Society for Microbiology 2010 – Bridging Diverse Cultures
4 – 8 July, 2010
Sydney, NSW

### Viral Hepatitis – 7th Australasian Conference
6 – 8 September, 2010
Melbourne, VIC

### 14th International Symposium on Staphylococci and Staphylococcal Infections (ISSSI)
6 – 9 September, 2010
Bath, UK

### 50th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC)
12 – 15 September, 2010
Boston, Massachusetts

### Australian Infection Control Association Conference (AICA)
4 - 6 October, 2010
Perth, WA

### Australasian Sexual Health Conference 2010
18 – 20 October, 2010
Sydney, NSW

### 2010 Australasian HIV/AIDS Conference (ASHM)
20 – 22 October, 2010
Sydney, NSW

### Infectious Diseases Society of America (IDSA) 48th Annual Meeting
21 - 24 October, 2010
Vancouver, Canada
website: [http://www.idsociety.org](http://www.idsociety.org)

### Society for Hospital Pharmacists of Australia (SHPA) National Conference – Medicines Management 2010
11 - 14 November, 2010
Melbourne, Victoria

### 6th World Melioidosis Congress
30 November – 3 December, 2010
Townsville, QLD

### 12th Western Pacific Congress on Chemotherapy and Infectious Diseases
2 - 5 December, 2010
Singapore

### Antimicrobials 2011: ASA 12th Annual Scientific Meeting
24-26 February, 2011
Melbourne, VIC

### Society for Healthcare Epidemiology of America (SHEA), 21st Annual Scientific Meeting
1 – 4 April, 2011
Dallas, Texas
website: [http://www.shea-online.org](http://www.shea-online.org)

### 21st European Congress of Clinical Microbiology and Infectious Diseases (ECCMID)
7 - 10 May, 2011
Milan, Italy
website: [http://www.escmid.org](http://www.escmid.org)

### 4th Congress of the European Microbiologists (FEMS 2011)
26 – 30 June, 2011
Geneva, Switzerland
website: [http://www2.kenes.com/fems2011/Pages/Home.aspx](http://www2.kenes.com/fems2011/Pages/Home.aspx)

### 7th European Congress on Tropical Medicine and International Health
October 2011
Barcelona, Spain

### 22nd European Congress of Clinical Microbiology and Infectious Diseases (ECCMID)
31 March – 3 April, 2012
London, UK
website: [http://www.escmid.org](http://www.escmid.org)
A specimen was obtained from a young woman with a symptomatic UTI. Urine culture revealed pure growth of a coagulase –ve Staphylococcus with the following susceptibility results.
1. Which organism and beta-lactam resistance mechanism is demonstrated?
2. How would you report susceptibilities on this isolate?

**Answer**

*Staphylococcus saprophyticus* (novobiocin resistant). The reduced zone to cefoxitin suggests methicillin/oxacillin resistance due to an altered penicillin binding protein 2a.

The presence of the **mecA** gene was confirmed by PCR. **mecA** positive *S. saprophyticus* are infrequently isolated. Interestingly, a recent study from Japan demonstrated the **mecA** gene to be present in 8 of 101 isolates, all of which had a novel SCCmec type.

According to CLSI, routine testing of urine isolates of *S. saprophyticus* is not advised. Coagulase negative staphylococci that test resistant to cefoxitin should be reported as resistant to all beta lactams.

The CDS method suggests testing for susceptibility to beta-lactams using ampicillin and cephalexin discs and reporting results as tested.

**References**


Prepared by Paul Ingram, Diane Hume and Barbara Henderson, PathWest Laboratory, Nedlands, WA.