Background
The use of systemic peri-operative antibiotic prophylaxis (PAP) in elective joint replacement surgery has been demonstrated to significantly lower the rate of prosthetic joint infections. Surveys have shown that compliance with PAP (that is, the percentage administered in accordance with international standards), though better in orthopaedic surgery compared with other types of surgery, varies from 59.3% - 91.3%. Due to the diversity of guidelines for PAP in joint replacement surgery, with the majority suggesting < 24 - 48 hours of prophylaxis, multiple protocols have been adopted by individual orthopaedic surgeons at our institution.

We aimed to determine the compliance of individual surgeons’ teams with their own PAP protocols, identify poorly supported PAP practices based on a review of the literature and compare PAP in elective joint replacement surgery at our institution against the recently revised Therapeutic Antibiotic Guidelines.

Methods
A retrospective survey of medical records of patients who had undergone elective hip or knee joint replacements between June 2001 and June 2002 at Concord Repatriation General Hospital (a 550 bed teaching hospital affiliated with the University of Sydney), was undertaken. Each surgeon who performed these operations had their own documented protocol for antibiotic prophylaxis in joint replacement surgery (Table 1). A sample of 88 (36%) of 241 records of patients who had elective joint replacement were surveyed using a standardised form. Information collected included patient demographics, meticillin resistant Staphylococcus aureus (MRSA) status, operative details including the surgeon performing the procedure, the presence of invasive devices (including indwelling urinary catheters (IDCs) and PAP details (Table 2). The antibiotic prophylaxis protocol of the surgeon performing surgery and compliance with this protocol for each case of joint replacement was reviewed. Data analysis was performed using the Epi Info 6 statistical programme (Centers for Disease Control).

Results
Cephalosporins
The ß-lactam antibiotic, cephalothin, was the only first generation cephalosporin, provided by pharmacy and hence used in PAP by all of the surgeons surveyed, despite their individual protocols recommending cephazolin. Only one of the surgical protocols (surgeon C’s) specified both the recommended dose and dosing interval for cephalothin; the other protocols specified the interval appropriate for cephazolin. However despite this, the actual cephalothin dosing interval was inappropriate in only 4.5% (4/88) of cases. The duration of cephalothin administration was generally 48 hours and the median number of doses was 8 (range 5 - 20).

“The protocols promoted longer duration of antibiotic use than recommended”

Gentamicin
Overall, 44.3% (39/88) of patients received a single dose of gentamicin in theatre as PAP for operative catheterisation. However 10/39 patients given gentamicin did not have an IDC. Only 5 of these patients were operated on by one of the two surgeons (Table 2) whose protocols called for gentamicin administration irrespective of IDC status. Figure 1 summarises the initial dose of gentamicin given as PAP. Appropriateness of dosing could not be assessed.

Indwelling urinary catheters
The timing of gentamicin dosing in relation to urinary catheter insertion or removal is not clearly stated in any of the surveyed protocols. Two surgeons (D & F) recommend a single dose of gentamicin (80mg) as PAP in catheterised patients - 55.5% (5/9) of
surgeon D and only 10.5% (2/19) of surgeon F’s patients received PAP in accordance with their protocols.

56.8% of patients (50/88) had an indwelling urinary catheter (IDC) inserted in theatre preoperatively. Of this number, 29 were given IV gentamicin at the time of IDC insertion; most of these patients (25/29) received 160 mg of gentamicin, with the remainder being administered 80 mg. A majority (24/29) of these patients were given an additional, lower dose of gentamicin (80 mg) at the time of IDC removal.

Most (64.7%) of the 21 catheterised patients who did not receive gentamicin at the time of IDC insertion later received at least one dose of gentamicin either in relation to IDC removal or subsequent recatheterisation.

Finally, of the 12/50 catheterised patients who received >1 dose of gentamicin post-operatively, one was administered 2 different doses of gentamicin within the time interval of 8 hours and the method of administration of gentamicin was unclear in 5/40 patients: the same dose was ordered to be given as either intravenously or intramuscularly without clarification as to which method was actually utilised.

**Drainage devices**

In the protocols of 4/6 surgeons, PAP duration (IV and oral follow-on therapy) was guided by drain tube removal. Most patients (87/88) had drains inserted intra-operatively. Of this number, all had PAP ceased within 24 hours of drain removal.

**Oral antibiotics**

Oral cephalexin was used in 10/88 patients, but whether the intention was to treat or prevent infection could not be ascertained.

**Tourniquet application**

Tourniquet application was used exclusively in patients undergoing knee arthroplasties. None of these patients received a larger dose of a PAP antibiotic and the timing of the administration of the 1st dose of the PAP in relation to the application of a tourniquet was unable to be accurately determined.

<table>
<thead>
<tr>
<th><strong>Patient Characteristics</strong></th>
<th><strong>Median age (range)</strong></th>
<th><strong>Cases (%)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td>Male 53 (60.2%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Female 35 (39.8%)</td>
<td></td>
</tr>
<tr>
<td><strong>β-lactam allergy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rash</td>
<td>10 / 88 (11.3%)</td>
<td></td>
</tr>
<tr>
<td>anaphylaxis</td>
<td>5/10</td>
<td></td>
</tr>
<tr>
<td>not specified</td>
<td>2/10</td>
<td></td>
</tr>
<tr>
<td><strong>MRSA Status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of preoperative screens</td>
<td>83/88 (94.3%)</td>
<td></td>
</tr>
<tr>
<td>MRSA positive</td>
<td>0/83 (0%)</td>
<td></td>
</tr>
</tbody>
</table>

**Operative details**

<table>
<thead>
<tr>
<th><strong>Arthroplasty type</strong></th>
<th><strong>Hip</strong></th>
<th><strong>Knee</strong></th>
<th><strong>Total</strong></th>
<th><strong>Cases (%)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td>28</td>
<td>42</td>
<td>70/88</td>
<td>(79.5%)</td>
</tr>
<tr>
<td>Revision*</td>
<td>11</td>
<td>7</td>
<td>18/88</td>
<td>(20.4%)</td>
</tr>
</tbody>
</table>

50 arthroplasties were cemented and of this number, 31 used antibiotic- impregnated cement.

<table>
<thead>
<tr>
<th><strong>Operation duration</strong></th>
<th><strong>Median (range)</strong></th>
<th><strong>Number of operations &gt; 240 mins##</strong></th>
<th><strong>Cases (%)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>109.5 mins (47 - 375)</td>
<td>5/88 (5.6%)</td>
<td></td>
</tr>
</tbody>
</table>

**Invasive devices**

<table>
<thead>
<tr>
<th><strong>Drain tubes</strong></th>
<th><strong>Cases (%)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>87/88 (98%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Median insertion duration (range)</strong></th>
<th><strong>Cases (%)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Drain insertion</td>
<td>1 day (1 - 3)</td>
</tr>
<tr>
<td>Indwelling urinary catheter</td>
<td>50/88 (56.8%)</td>
</tr>
<tr>
<td>Median insertion duration (range)</td>
<td>3 days (1 - 11)</td>
</tr>
</tbody>
</table>

* Tourniquets were used exclusively in knee replacement surgery
# All operations except 1 were one-stage revisions
## Additional doses of intraoperative antibiotics were not administered in any of these prolonged operations.

<p>| <strong>Table 1. Individual surgeon’s prophylaxis protocols compared to Antibiotic Guidelines.</strong> |
|-----------------------------------------------|-------------------|-----------------|-----------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th><strong>ANTIBIOTIC</strong></th>
<th><strong>DOSE AT INDUCTION</strong></th>
<th><strong>DOSE POST-OP</strong></th>
<th><strong>DURATION</strong></th>
<th><strong>INDWELLING URINARY CATHETER</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>cephazolin 1g</td>
<td>1g 8/24 IV</td>
<td>Until drain removed</td>
<td>cephalothin (if not on IV cephazolin) - 48 hours after IDC removal</td>
</tr>
<tr>
<td>B</td>
<td>cephazolin cephalixin 1g</td>
<td>1g 8/24 IV 500mg 6/24 orally</td>
<td>12 hrs after drain removal</td>
<td>trimethoprim</td>
</tr>
<tr>
<td>C</td>
<td>cephalothin* gentamicin* 160mg</td>
<td>1g 8/24 IV 160mg daily IV</td>
<td>1 dose after drain removal</td>
<td>Total 3 doses</td>
</tr>
<tr>
<td>D</td>
<td>cephazolin 1g</td>
<td>1g 8/24 IV</td>
<td>One day</td>
<td>gentamicin 80mg IV x1</td>
</tr>
<tr>
<td>E</td>
<td>cephazolin gentamicin or other antibiotic 1g</td>
<td>1g 12/24 IV as prescribed by surgeon</td>
<td>Until 1 dose given after drain removal</td>
<td>gentamicin (dose not specified)</td>
</tr>
<tr>
<td>F</td>
<td>cephalothin 1g</td>
<td>8 doses</td>
<td>gentamicin 80mg IV x1</td>
<td></td>
</tr>
<tr>
<td>Australian Guidelines</td>
<td>cephalothin OR cephalixin 2g</td>
<td>Single dose at induction</td>
<td>Repeat dose if operation &gt; 3 hours</td>
<td>no prophylaxis recommended</td>
</tr>
</tbody>
</table>

* No antibiotics for revision TJR until after intra-op specimens taken.
Antibiotic choice and duration

1st generation cephalosporins have been shown to have good serum and bone concentrations, are active against bacteria responsible for up to 80% of prosthetic joint infections, and have a low toxicity profile. The recently updated Australian Antibiotic Therapeutic Guidelines recommend IV cefalothin (2g) or cephalazolin (1g) as prophylaxis for elective joint replacement surgery, with the dose given at the time of induction of anaesthesia. Other literature suggests that dosing of up to 24 hours is appropriate; prolonged use is not associated with reduced infection rates but may result in increased rates of acquisition of MRSA. The choice of cefalothin was appropriate amongst all of the surgeons; the dosage used was 1g and the post-operative duration of administration was mostly 48 hours. Although only two of the six protocols examined accommodated the hospital pharmacy formulary change from cephazolin to cefalothin, only one recognised and recommended the appropriate dose interval. Despite this, in the majority of cases where the PAP protocol recommended 8-hourly cephazolin, cephalothin was substituted and prescribed at the appropriate dose interval.

The use of gentamicin both in PAP and related to IDC manipulation was the area of greatest discrepancy from the protocols in the operations surveyed. The dosage and method of administration of gentamicin was inconsistent in both the surgical protocols (Table 1) and in clinical practice, with no standardised consideration given to either the patient’s weight or creatinine clearance in determining gentamicin dosage - a factor that can affect both efficacy and toxicity. The benefit of the routine use of gentamicin in uncomplicated urinary catheterisation remains debatable. The Australian guidelines do not recommend the routine use of gentamicin in PAP, however single doses are recommended by others. In none of the 5 operations surveyed which were more than 4 hours in duration, were additional doses of antibiotics given after the PAP at induction of anaesthesia. A review of the literature supports the use of additional doses of antibiotics in long operations. For operations more than 3 hours in duration, the Australian guidelines recommend the administration of a second dose of the β-lactam PAP. Extending PAP until invasive drainage devices are removed, a consideration in four of the six surveyed protocols, is of unproven benefit, and more likely to promote MRSA colonisation.

MRSA status

None of the PAP surgical protocols made specific recommendations for PAP in patients colonised with MRSA. The recent guidelines recommend the use of IV vancomycin. Interestingly, screening for MRSA colonisation in elective surgery (that is, in patients without risk factors for MRSA colonisation) did not yield any positive cultures.

Conclusions

In short, compliance with the existing PAP protocols was inconsistent and potentially confusing for resident staff to follow at our hospital. The PAP protocols promoted longer duration of antibiotic use than recommended; most guidelines were ambiguous with respect to gentamicin use and did not account for several important patient and operative factors such as the patient’s weight and renal function. The Therapeutic Antibiotic guidelines are an ideal frame-work on which to improve existing PAP protocols. Such best-practice guidelines, if adopted unit-wide, would improve resident prescribing, and promote a more rational and regimented approach to antibiotic use.

References

Correlating the detection of vanB genes in faeces to the presence of vancomycin-resistant enterococci (VRE): interference by vanB-containing anaerobes

S.A. Ballard¹, E.A. Grabsch¹, S. Xie¹, P.D.R. Johnson¹², M.L. Grayson¹²

¹Depts of Infectious Diseases and Microbiology, Austin and Repatriation Medical Centre, Melbourne.
²Dept of Medicine, University of Melbourne, Melbourne.

Introduction

VRE colonisation and infection is increasingly common in Australian hospitals. Acquired vancomycin resistance in enterococci encoded by the vanB operon explains the majority of VRE isolates, and the vanB2 allele linked to a Tn1549-like element appears to dominate.¹,² Recently, the presence of the vanB operon has been described in organisms other than enterococcci. These organisms include Streptococcus bovis isolated from a stool swab and four unrelated anaerobic organisms isolated from faecal samples.⁷,⁹

Three of these organisms were from the genus Clostridium and the fourth from the genus Eggerthella. In both reports, the patients were undergoing routine surveillance for VRE.

Many multiplex PCR protocols and primer sets have been developed for the detection of van genes in pure isolates of enterococci (reviewed in reference⁴). Although conventional culture methods for the detection of VRE are sensitive, the time required to isolate organisms takes 3-5 days. More recently, PCR protocols have been described for the direct detection of van genes from clinical samples or enrichment broth cultures.⁵,⁶,⁸ However, the presence of vanB in non-VRE isolates could lead to an unacceptably high false positive rate when screening by PCR for VRE carriage. In this study, we set out to assess the sensitivity and (specificity) of three vanB PCR protocols on three different enrichment broth cultures of faeces to identify both VRE carriage and vanB gene carriage in a mixed culture. In a random sample of those specimens that were VRE culture negative / vanB PCR positive, attempts were made to isolate the source of the vanB signal to establish the impact vancomycin resistant organisms, other than enterococci, might have on the performance of a vanB PCR for detection of VRE.

Methods

Three growth media (anaerobic brain heart infusion broth, AnaO₂ BHI; aerobic brain heart infusion broth, BHI; and enterococcosel broth, EB) were used to culture faecal specimens from 59 well-characterised patients (12 vanB VRE culture positive and 47 VRE culture negative). Enrichment broth cultures were screened for the presence of vanB using three different PCR protocols. Carriage of VRE was reconfirmed on all broth cultures. Specimens positive for vanB by PCR, but VRE culture negative were further assessed for the presence of other vanB containing organisms.

Results

The sensitivity and specificity of vanB PCR protocols for the detection of VRE in enrichment broths were as follows:

<table>
<thead>
<tr>
<th>Primer/PCR</th>
<th>BHI broth</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>AnaO₂BHI broth</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>EB broth</th>
<th>Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>A: Stinear et al⁹</td>
<td>92%</td>
<td>49%</td>
<td></td>
<td>92%</td>
<td>43%</td>
<td>100%</td>
<td>51%</td>
<td></td>
</tr>
<tr>
<td>B: Bell et al¹</td>
<td>92%</td>
<td>60%</td>
<td></td>
<td>92%</td>
<td>45%</td>
<td>92%</td>
<td>83%</td>
<td></td>
</tr>
<tr>
<td>C: Dutka-Malen et al³</td>
<td>67%</td>
<td>96%</td>
<td></td>
<td>59%</td>
<td>94%</td>
<td>17%</td>
<td>100%</td>
<td></td>
</tr>
</tbody>
</table>

While primer/PCR protocol “A” and “B” gave the best sensitivity, primer “C” had the best specificity for VRE. Six Gram-positive anaerobic bacilli from the order Clostridiales were isolated from 5 specimens that were vanB PCR positive but VRE culture negative. Isolates demonstrated the presence of the vanB operon linked to a Tn1549-like transposon.

“vanB-containing anaerobes may cause false positive results in PCR-based detection of VRE directly from faecal specimens”

Conclusions

The sensitivity of PCR detection of vanB/VRE carriage directly from faecal specimens is dependent on the primer set and media used. Moreover, as the sensitivity of the vanB PCR protocol increases, so the specificity of the test for VRE decreases with the primer/PCR protocol of Bell et al., providing the best balance of sensitivity and specificity. Since carriage of vanB is not the exclusive domain of enterococci, care should be taken interpreting the results of PCR-based detection of VRE when using enrichment broth cultures as the presence of vanB-containing anaerobes may cause false positive results in PCR.

References


2003 AstraZeneca ASA ICAAC Travel Award

Congratulations to Susan Ballard, of the Dept of Infectious Diseases at the Austin and Repatriation Medical Centre in Victoria. She was the winner of the 2003 AstraZeneca ASA ICAAC Travel Award for her ICAAC (Interscience Conference on Antimicrobial Agents and Chemotherapy) abstract. The Award consisted of a return economy airfare, accommodation and conference registration to attend ICAAC, and will be offered again in 2004. The next ICAAC is in Washington DC in November 2004. ASA members who wish to apply for the award are invited to submit their ICAAC abstracts to the ASA secretary, Dr Keryn Christiansen at keryn.christiansen@health.wa.gov.au prior to the ICAAC abstract closing date. We thank AstraZeneca for their ongoing support.
The inability of the NCCLS disc diffusion oxacillin interpretive breakpoint for *Staphylococcus aureus* to reliably detect oxacillin susceptible *Staphylococcus lugdunensis*

Cheryll McCullough, Geoffrey Coombs, Sandra Rodgers and Keryn Christiansen

*Dept of Microbiology and Infectious Diseases, Royal Perth Hospital, Western Australia*

**Introduction**

*Staphylococcus lugdunensis* was first described by Freney et al in 1988 and is now widely accepted as a significant pathogen, although there continues to be a problem of low awareness of the organism among clinicians and laboratory staff. It is a coagulase negative staphylococcus that more closely resembles *S. aureus* in its pathogenicity. It has been implicated in a variety of infections including endocarditis, septiccaemia, breast abscesses, orthopaedic, skin and soft tissue infections.

In 1999, NCCLS introduced an oxacillin interpretative breakpoint for disc diffusion testing of coagulase negative staphylococci (CNS). However this breakpoint was established primarily for *S. epidermidis* and may not be suitable for other CNS (eg *S. lugdunensis*).

**NCCLS guidelines for staphylococi**

**Table 1. Prior to 1999 - Single NCCLS breakpoint for all staphylococci**

<table>
<thead>
<tr>
<th>Ox Disc (zone diameter)</th>
<th>OX MIC (mg/L)</th>
<th>Interpretation</th>
<th>mecA gene</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 12mm</td>
<td>≥ 4mg/L</td>
<td>RESISTANT</td>
<td>DETECTED</td>
</tr>
<tr>
<td>&gt; 13mm</td>
<td>&lt; 2mg/L</td>
<td>SUSCEPTIBLE</td>
<td>NOT DETECTED</td>
</tr>
</tbody>
</table>

**Table 2. 1999 - Introduction of CNS breakpoint by NCCLS**

<table>
<thead>
<tr>
<th>Ox Disc (zone diameter)</th>
<th>OX MIC (mg/L)</th>
<th>Interpretation</th>
<th>mecA gene</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 17mm</td>
<td>≥ 0.5mg/L</td>
<td>RESISTANT</td>
<td>DETECTED</td>
</tr>
<tr>
<td>&gt; 18mm</td>
<td>&lt; 0.25mg/L</td>
<td>SUSCEPTIBLE</td>
<td>NOT DETECTED</td>
</tr>
</tbody>
</table>

In 2002 - NCCLS added the following comment to the guidelines for interpreting oxacillin zone diameters: “Interpretive criteria for CNS correlate with the mecA gene for *S. epidermidis*. These criteria may overall resistance for other CNS eg *S. lugdunensis* or *S. saprophyticus*. For serious infections with CNS other than *S. epidermidis*, testing for mecA or the protein expressed by mecA, the penicillin binding protein 2a (PBP2a) may be appropriate for strains with zone diameters in the intermediate or resistant range. Isolates that are not shown to carry mecA or do not produce PBP2a should be reported as oxacillin susceptible.”

Most laboratories, however, do not have access to molecular methods for the detection of the mecA gene, and the accuracy of phenotypic assays for the detection of PBP2a in CNS has not been determined. As the NCCLS CNS disc diffusion oxacillin breakpoints often misclassify mecA gene negative strains as oxacillin resistant, we investigated if the “Oxacillin susceptibility testing of *S. lugdunensis* can be determined by MIC testing on MHA with 2% NaCl added using NCCLS *S. aureus* interpretive breakpoints”

**Results**

**mecA / nuc gene PCR testing (n = 70)**
- All isolates were mecA and nuc gene negative.

**Kirby-Bauer Disc Diffusion testing (n = 70)**
- Using the CNS oxacillin interpretive breakpoint (≥ 18mm = susceptible), only 3 isolates (4%) were classified as oxacillin susceptible.
- Using the *S. aureus* oxacillin interpretive breakpoint (≥ 13mm = susceptible), 47 isolates (67%) were classified as oxacillin susceptible.
- Using the *S. aureus* oxacillin interpretive breakpoint (< 2mm = susceptible), all 67 isolates (100%) were classified as oxacillin susceptible.

**Minimum Inhibitory Concentration (MIC) (n = 67)**
- Using the CNS oxacillin interpretive breakpoint (< 0.25mg/l = susceptible), only 1 isolate (1%) was classified as oxacillin susceptible.
- Using the *S. aureus* oxacillin interpretive breakpoint (< 2mg/l = susceptible), all 67 isolates (100%) were classified as oxacillin susceptible.

**Discussion**

- The NCCLS CNS disc diffusion and MIC oxacillin interpretive breakpoints were not suitable for *S. lugdunensis*.
- Although the NCCLS *S. aureus* disc diffusion oxacillin interpretive breakpoint was not reliable for *S. lugdunensis*, the NCCLS MIC interpretive breakpoint correctly classified all isolates as oxacillin susceptible.
Conclusions

• Clinically significant CNS requiring susceptibility testing should be fully identified.
• NCCLS CNS and \textit{S} \textit{aureus} disc diffusion interpretive breakpoints for oxacillin are not reliable for \textit{S} \textit{lugdunensis}.
• Oxacillin susceptibility testing of \textit{S} \textit{lugdunensis} can be determined by \textit{mecA} gene PCR or by MIC testing on Mueller Hinton Agar with 2% NaCl added using NCCLS \textit{S} \textit{aureus} interpretive breakpoints.

Acknowledgements

Dr Michelle Porter from the Women’s and Children’s Hospital and Dr Sue Benson from St John of God Pathology for supplying clinical isolates.

References


Tee WS, Soh SY, Lin R, Loo LH. \textit{Staphylococcus lugdunensis} carrying the \textit{mecA} gene causes catheter-associated bloodstream infection in premature neonate. \textit{J Clin Micro} 2003;41:519-520

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NCCLS. Performance Standards for Antimicrobial Susceptibility Testing; Ninth Informational Supplement. NCCLS document M100-S9, Jan 1999. Vol.19 No 1

NCCLS. Performance Standards for Antimicrobial Susceptibility Testing; Eighth Informational Supplement. NCCLS document M100-S8, Jan 1998. Vol.18 No 1

\begin{table}[h]
\centering
\begin{tabular}{|l|l|l|l|}
\hline
\textbf{Investigators} & \textbf{Lay Title} & \textbf{Years} & \textbf{Total funding} \\
\hline
Melissa Brown & Multidrug resistance in hospital strains of Golden Staph & 3 & $490,500 \\
Ron Skurray & Control of multidrug resistance genes in hospital strains of Golden Staph & 3 & $451,750 \\
Lesley Roy & Do long-term antibiotics prevent urinary tract infection? & 3 & $367,725 \\
Jonathan Carapetis & Antibiotic resistance in hospital strains of Golden Staph & 3 & $425,250 \\
Graham Reynolds & Drug resistance in scabies & 3 & $506,625 \\
Judy Simpson & What should be done to prevent bloodstream infections in hospitalised patients? & 2 & $117,000 \\
Elisabeth Hodson & Development of lactobacilli as pathogen killers & 3 & $267,750 \\
Mark Turner & Acute bronchitis in general practice: can antibiotics help some patients? & 3 & $388,875 \\
Roger Nation & Improving use of an ‘old’ last-line antibiotic & 3 & $262,125 \\
Jian Li & Ways of improving the use of a last-line antibiotic & 2 & $133,513 \\
Craig Rayner & & & \\
\hline
\textbf{TOTAL FUNDING} & & & $3,411,113 \\
\end{tabular}
\end{table}

2003 NHMRC project grants awarded for research into antimicrobial agents

2003 BioMérieux ASA Identifying Resistance award

Congratulations to Cheryll McCullough of the Dept of Microbiology and Infectious Diseases at the Royal Perth Hospital, the winner of the 2003 BioMérieux ASA Identifying Resistance award. This award is given to an individual ASA member for the best proffered paper (oral or poster) at the ASA annual scientific meeting on the identification of bacterial resistance to antimicrobials in a routine clinical setting. It consists of A$1000 cash prize, a commemorative plaque, and a travel award (flights, accommodation and registration) to attend the next ASA annual scientific meeting. This award will be offered again in 2004 and all abstracts submitted for the ASA 2004 meeting on the identification of bacterial resistance to antimicrobials in a routine clinical setting will be considered for this award. We thank BioMérieux for their ongoing support.
In July 2003, an elderly man presented to hospital with a purulent discharge from a suprapubic catheter site. This was swabbed for culture.

The swab was inoculated onto horse blood agar and MacConkey plates. After 24 hours incubation at 35°C, there was a pure growth of *S aureus* and Group G Streptococcus. Figure 1 shows a disc susceptibility test for *S aureus* (penicillin 10 ug disc on the left, tetracycline 10 ug disc on the right). Figure 2 shows an oxacillin E test for *S aureus*.

- Comment on the disc sensitivity patterns in Figure 1.
- Comment on the E test result in Figure 2.
- What needs to be done to sort out this finding?

Please email your responses to the ASA Newsletter Editor Wendy Munckhof at wendy_munckhof@health.qld.gov.au. Answers will be published in the next issue, and correct responses will be acknowledged.

*Picture quiz provided by Dr Joan L Faoagali and Jan Bodman, Royal Brisbane Hospital. Photographs by Cassy Faux.*
On the right is a photo of an isolate of *Candida albicans* from a mouth swab of an AIDS patient with oral candidiasis. A RPMI agar plate has been incubated aerobically for 48 hours at 35°C. The disc is a Fluconazole 25 mg NeoSensitab and the Etest is for Fluconazole.

- **Please read the Etest MIC for Fluconazole.**
  Fluconazole MIC is 0.05 mg/ml or 1.0 mg/ml.

- **According to current NCCLS recommendations, when should Etests be read for yeasts?**
  The recommended incubation time for yeast Etests is 48 hours. However the new revised NCCLS M27-A2 document does provide 24 hr QC ranges, so that tests for Candida may be read at 24 hrs.

- **Why is trailing seen with the Etest and not the disc?**
  Etests commonly overestimate the yeast MIC for Fluconazole due to trailing. Trailing can also occur in disc methods for yeast Fluconazole susceptibility testing but is less common. The reason for trailing MICs is unknown.

- **How common is it for Candida albicans to have trailing end points when tested against fluconazole?**
  When read at 48 hrs, 20% of *Candida albicans* strains show trailing end points when tested against Fluconazole.

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**ASA Hospital Antibiotic Usage Survey reminder**

ASA is conducting the third Antibiotic Usage Survey in major hospitals around Australia, following previous surveys in 1986 and 1992. Survey forms were sent to Chief Pharmacists, Infectious Disease Physicians and / or Clinical Microbiologists in major hospitals around the country in January 2002 and have subsequently been resent.

Thank you to the 32 hospitals that have returned completed the 2-page survey forms. Unfortunately, 17 hospitals have still not replied to date. Could any ASA members on staff at these hospitals please ensure they do so! Data cannot be analysed until most of these hospitals return completed surveys. Please contact Dr Mike Whitby (07) 3240 2595 if you need another survey form.

This is a list of the hospitals that were sent the survey.

**ACT**
- The Canberra Hospital

**NT**
- Royal Darwin Hospital

**NSW**
- Westmead Hospital
- St Vincent’s Hospital
- Prince of Wales Hospital
- St George Hospital
- Nepean Hospital
- Royal Prince Alfred Hospital
- Concord Repatriation General Hospital
- Wollongong & Port Kembla Hospital
- Royal North Shore Hospital
- John Hunter Hospital
- Liverpool Hospital
- New Children’s Hospital Westmead

**VIC**
- Alfred Hospital
- Monash Medical Centre
- Royal Children’s Hospital
- Royal Women’s Hospital
- Western Hospital
- Box Hill Hospital
- Geelong Hospital
- Royal Melbourne Hospital
- St Vincent’s Hospital
- Austin & Repatriation Medical Centre

**QLD**
- Toowoomba Hospital
- Rockhampton Hospital

**SA**
- The Queen Elizabeth Hospital
- Repatriation General Hospital
- Royal Adelaide Hospital
- Women’s and Children’s Hospital
- Flinders Medical Centre
- Modbury Hospital
- Lyell McEwin Health Service

**WA**
- Royal Perth Hospital
- Princess Margaret Hospital for Children
- Sir Charles Gardiner Hospital
- Fremantle Hospital

**TAS**
- Royal Hobart Hospital
- Launceston Public Hospital

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**Reference**


Picture quiz and answers provided by David Ellis, Women’s & Children’s Hospital, Adelaide.
Stability of some commonly used home intravenous antibiotics

Henry K. Lie¹, Julia Carroll²

¹ Senior Pharmacist, Centralised Intravenous Additive Services (CIVAS), Dept of Pharmacy, King Edward Memorial Hospital for Women and Princess Margaret Hospital for Children, Women’s and Children’s Health Service, Perth

² Senior Pharmacist, Alternative Site Infusion Service (ASIS), Infection Management Service, Princess Alexandra Hospital, Brisbane

<table>
<thead>
<tr>
<th>DRUG</th>
<th>DILUENT</th>
<th>STABILITY in syringes</th>
<th>STABILITY in elastomeric devices</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aciclovir 500mg</td>
<td>NaCl 0.9%, Water for injection (WFI)</td>
<td>7 days at room temperature.¹,² Refrigeration causes crystallisation of drug</td>
<td>29 days at room temperature.³ Refrigeration causes crystallisation of drug</td>
</tr>
<tr>
<td>Amikacin 2.5mg/mL</td>
<td>NaCl 0.9%</td>
<td>14 days refrigerated⁴,⁵,⁶</td>
<td>10 days refrigerated, 30 days frozen³</td>
</tr>
<tr>
<td>Amoxicillin 10-50mg/mL</td>
<td>NaCl 0.9%</td>
<td>Unstable (3-8 hours stability only at room temperature, up to 3 days refrigerated)⁷,⁸,⁹</td>
<td></td>
</tr>
<tr>
<td>Ampicillin 125 mg/ml</td>
<td>WFI</td>
<td>Unstable, similar to amoxicillin at room temperature, up to 2 days refrigerated¹⁰</td>
<td></td>
</tr>
<tr>
<td>Aztreonam 20mg/mL</td>
<td>WFI NaCl 0.9%</td>
<td>7 days refrigerated¹¹,¹²</td>
<td>14 days refrigerated, 30 days frozen¹³</td>
</tr>
<tr>
<td>Benzyl Penicillin 3g</td>
<td>Sodium citrate 4%</td>
<td>14 days refrigerated¹⁴</td>
<td>7 days refrigerated¹⁵</td>
</tr>
<tr>
<td>Cefotaxime 100mg/mL</td>
<td>WFI</td>
<td>7 days refrigerated. 3 months at -20°C plus 7 days refrigerated when thawed. Once thawed, should not be refrozen¹⁰,¹⁶</td>
<td>10 days refrigerated, 30 days frozen plus 24 hours post thawing.¹³</td>
</tr>
<tr>
<td>Cefepime 100mg/mL</td>
<td>WFI</td>
<td>3 months at -20°C plus 7 days refrigerated when thawed. Once thawed, should not be refrozen¹⁰,¹⁸</td>
<td>14 days refrigerated⁰³</td>
</tr>
<tr>
<td>Cefoxitin 2g</td>
<td>WFI</td>
<td>7 days refrigerated¹⁹</td>
<td>10 days refrigerated¹⁵</td>
</tr>
<tr>
<td>Ceftriaxone 100mg/mL</td>
<td>WFI</td>
<td>7 days refrigerated. 3 months at -20°C plus 7 days refrigerated when thawed. Once thawed, should not be refrozen¹⁶,¹²⁰</td>
<td>7 days refrigerated¹³</td>
</tr>
<tr>
<td>Cephazolin 1g</td>
<td>WFI</td>
<td>7 days refrigerated. 3 months at -20°C plus 7 days refrigerated when thawed. Once thawed, should not be refrozen¹²,²²</td>
<td></td>
</tr>
<tr>
<td>Dicloxacillin</td>
<td>WFI</td>
<td>7 days refrigerated. 3 months at -20°C plus 7 days refrigerated when thawed. Once thawed, should not be refrozen¹¹,¹⁶,¹³,¹⁹,²³</td>
<td></td>
</tr>
<tr>
<td>Dicloxacillin</td>
<td>WFI</td>
<td>Unsuitable for home IV use due to particle precipitation</td>
<td></td>
</tr>
<tr>
<td>Flucloxacillin 100mg/mL</td>
<td>WFI</td>
<td>7 days refrigerated¹⁰</td>
<td>Manufacturer states 3 days refrigeration.</td>
</tr>
<tr>
<td>Gentamicin 10mg/mL</td>
<td>NaCl 0.9%</td>
<td>14 days refrigerated²⁴</td>
<td>10 days refrigerated¹³</td>
</tr>
<tr>
<td>Meropenem 50mg/mL</td>
<td>WFI</td>
<td>6 months at -60°C²⁵ 48 hours refrigerated²⁶</td>
<td>4 days refrigerated plus 6 hours at room temperature²⁶</td>
</tr>
<tr>
<td>Teicoplanin</td>
<td>WFI</td>
<td>Unstable in plastic due to leaching of silicone particles. Manufacturer recommends storage in glass vial or glass syringe for up to 7 days refrigerated²⁷</td>
<td></td>
</tr>
<tr>
<td>Ticarcillin/Clavulanic Acid 100mg/mL</td>
<td>WFI</td>
<td>7 days refrigerated. 3 months at -20°C plus 7 days refrigerated when thawed. Once thawed, should not be refrozen¹⁶</td>
<td>7 days refrigerated³</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>Diluted to 30mL with NaCl 0.9%</td>
<td>14 days refrigerated²⁸</td>
<td>10 days refrigerated¹³</td>
</tr>
<tr>
<td>Vancomycin 5mg/mL</td>
<td>NaCl 0.9%</td>
<td>3 months refrigerated²⁹</td>
<td>14 days refrigerated³</td>
</tr>
</tbody>
</table>

Footnote. Refrigeration refers to 2°-8°C
Information on stability in syringes supplied by Henry K. Lie of the Princess Margaret Hospital for Children (PMH) CIVAS department, Perth. This department routinely supplies home antibiotics for cystic fibrosis patients, cancer patients, and patients with cellulitis and osteomyelitis. The antibiotics are first diluted using either normal saline or in most cases water for infusion to 30mL. These are supplied in 30mL Braun syringes which fit into a springfusor and are infused over 15 minutes (2 to 3 times daily). The antibiotics are supplied in ready to use syringes usually one week at a time, depending on stability. Most commonly used home antibiotics are stable in the refrigerator for at least one week with the following exceptions: amoxicillin (2-3 days), ampicillin (2-3 days), meropenem (2 days), aciclovir (stored at room temperature) and dloxacillin (unsuitable for home use due to particle precipitatin).

Information on stability in elastomeric devices supplied by Julia Carroll of the Princess Alexandra Hospital Alternative Site Infusion Service (ASIS). This service supplies antibiotics in elastomeric devices for in the home administration, mostly for adult patients with surgical wound infections, osteomyelitis, synovitis, cellulitis, diabetic foot infections, and occasionally for cystic fibrosis patients. Antibiotics requiring reconstitution are reconstituted with water for injection (exception being Benzyl Penicillin which is reconstituted with a Sodium Citrate buffer) and added to elastomeric devices filled with required amount of normal saline. Most antibiotics are infused over 24 hours in disposable elastomeric devices or programmable pumps, with the exceptions vancomycin (infused over 2 hours) and aminoglycosides (infused over 30 - 60 minutes). All preparation is carried out in a clean room in a vertical laminar flow cabinet. An additional concern with stability in elastomeric devices is stability at 31°C over 24 hours, 31°C being skin temperature under clothing. The devices are worn in a waist pouch. This demand for stability at higher than normal room temperature accounts for some of the differences in stability compared with syringes.

References


Novotel Brighton-Le-Sands, Sydney
Thursday 26th - 28th February, 2004

Plenary Speakers

• Steven J Projan
New Drug Development
Director of Antimicrobial Research,
Wyeth-Ayerst Research,
New York, USA

Steve has co-written over 60 original scientific papers and has several areas of interest including antimicrobial chemotherapy and resistance, genomics, microbial pathogenesis, and biotechnology. In recent years his research has included investigating antibiotic resistance in bacteria from magpies and rabbits from west Wales; identifying compounds that inhibit the last steps of cell wall biosynthesis; and using genomics to detect novel antibacterial targets and drugs. Steve is an enthusiastic orator who brings both optimism and a fresh approach to the conquest against antimicrobial resistance.

In the words of Steve Projan……..

“Steven J Projan, PhD (Columbia 1990, Molecular Genetics) is widely known for his dilettantish approach to bacterial pathogenicity, antimicrobial drug resistance and anti-infective drug discovery. Since 1988 he has directed a group of dedicated scientists in antibacterial drug discovery at Wyeth Research in Pearl River, New York, who clearly deserve better. Dr Projan identified tigecycline (GAR-936) as a potential clinical candidate in 1994 by blind dumb luck and fortunate timing, he hopes to parlay that success into a lucrative career in drug discovery and standup comedy.”

• John Perfect
Antifungal Developments
Director of the Mycology Interdisciplinary Research Unit,
Professor of Medicine and Associate Professor of Microbiology,
Duke Medical Center, North Carolina, USA

John has over 200 published papers in peer-reviewed journals to his credit and has also co-authored a book on Cryptococcus neoformans. John is a member of numerous professional societies and committees including the American Society of Microbiology and ISHAM. He is also an active researcher in the field of medical mycology and a lecturer on medical infectious diseases, mycology and tropical medicine.

• Ivan Bastian
Laboratory and clinical aspects of MDR TB in high- and low-prevalence settings
Clinical Microbiology Consultant,
IMVS, South Australia

Ivan is the laboratory representative for the Australian National Tuberculosis Advisory Committee which has recently drafted guidelines for Australian mycobacteriology laboratories. His works in the field of tuberculosis extend internationally including assisting with drug susceptibility testing in East Timor, East Java and the Pacific Islands. In 1998, Ivan was awarded a Neil Hamilton Fairley Fellowship to investigate improved diagnostics for tuberculosis in low resource countries. Subsequently, he has reviewed prison TB services in Moldova for Caritas Luxemburg and worked in a TB prison laboratory in Siberia. In 2000, Ivan was an editor for the publication “Multidrug-Resistant Tuberculosis”.

ESBL Workshop

Extended spectrum beta-lactamases (ESBLs) originally detected in Klebsiella pneumoniae and Escherichia coli are now being detected in other species of Enterobacteriaceae and Gram negative glucose nonfermenters throughout the world. New types are emerging such as CTX-M and plasmid-borne AmpC beta-lactamases. What is the epidemiology of ESBLs in Australia and what are the clinical implications? When should laboratories test for these organisms and what methods should be used?

The ESBL workshop will discuss these and other issues including discussion on what confirmatory molecular tests are available for the diagnostic microbiology laboratory. The workshop will include audience participation.

Registration and abstract submission


Updated conference and accommodation information will also be on the website

Dates to remember

Deadline for abstract submission: 19th December 2003
Abstract notification: 31st December, 2003
Close of early bird registration: 19th December 2003
(persons submitting accepted abstracts will be able to register at early bird rate)
Accommodation booking deadline: 16th January, 2004

Antimicrobials 2004 Travel Awards

Travel awards are available for ASA members presenting a proffered paper (oral or poster) at the conference. The awards consist of return economy class airfare, accommodation, conference registration and a ticket to the Meeting Dinner. Applicants should forward a copy of their abstract to the Secretary (keryn.christiansen@health.wa.gov.au) before 19th December 2003.

2004 BioMérieux ASA Identifying Resistance Travel Award

This is awarded to an ASA member on the basis of a proffered paper (oral or poster) presented during Antimicrobials 2004 dealing with the identification of bacterial resistance to antimicrobials in a routine clinical setting. The award consists of a $1000 cash prize, a commemorative plaque, and flights, accommodation and registration for the recipient to attend Antimicrobials 2005. The award will be announced during the ASA Meeting’s Dinner.

ASA Newsletter, December 2003
## PRELIMINARY PROGRAM

**Antimicrobials 2004**
**SYDNEY 26 - 28 FEBRUARY 2004**
**Novotel, Brighton Beach, Sydney**

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<td><strong>0900 - 1000</strong></td>
<td>Plenary 1</td>
<td>Plenary 2</td>
<td>Plenary 3</td>
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<tr>
<td></td>
<td><strong>New Drug Development</strong></td>
<td><strong>Antifungal Developments</strong></td>
<td><strong>Laboratory and Clinical Aspects of MDR TB in High-and-Low Prevalence Settings</strong></td>
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<tr>
<td></td>
<td>Steve Projan</td>
<td>John Perfect</td>
<td>Ivan Bastian</td>
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<tr>
<td><strong>1000 - 1030</strong></td>
<td>MORNING TEA</td>
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<tr>
<td><strong>1030 - 1200</strong></td>
<td>Symposium 1</td>
<td>Symposium 3</td>
<td>Symposium 5</td>
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<tr>
<td></td>
<td><strong>All Things Fungal</strong></td>
<td><strong>Genetics of Resistance 101</strong></td>
<td><strong>Who Benefits from Controlling Resistance</strong></td>
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<tr>
<td></td>
<td>Current Perspectives on Fungal Infections (Tania Sorrell)</td>
<td>Basic Principles (Ruth Hall)</td>
<td>Lessons from the Fields (Steve Powles)</td>
</tr>
<tr>
<td></td>
<td>What we know about Antifungal Therapies (John Perfect)</td>
<td>Macrolide Resistance (Julian Rood)</td>
<td>Software Solutions (James Black)</td>
</tr>
<tr>
<td></td>
<td>Antifungal Prophylaxis - When and with What? (Ken Bradstock)</td>
<td>Efflux Pumps (Melissa Brown)</td>
<td>The Industry? (Steve Projan)</td>
</tr>
<tr>
<td><strong>1200 - 1400</strong></td>
<td>LUNCH (POSTERS (Authors in Attendance))</td>
<td>LUNCH (Pfizer Pharmaceuticals Symposium POSTERS)</td>
<td>LUNCH POSTERS</td>
</tr>
<tr>
<td><strong>1400 - 1530</strong></td>
<td>Proffered Papers 1</td>
<td>Proffered Papers 2</td>
<td><strong>ESBL Workshop</strong></td>
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<tr>
<td></td>
<td>(six speakers)</td>
<td>(Six speakers)</td>
<td>Introduction: The Expanding Spectrum of the Extended Spectrums (Jan Bell)</td>
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<tr>
<td></td>
<td></td>
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<td>Clinical Impact of ESBLs (John Turnidge)</td>
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<tr>
<td><strong>1530 - 1600</strong></td>
<td>AFTERNOON TEA</td>
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<tr>
<td><strong>1600 - 1730</strong></td>
<td>Symposium 2</td>
<td>Symposium 4</td>
<td><strong>ESBL Workshop (cont)</strong></td>
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<tr>
<td></td>
<td><strong>Therapy of Emerging Diseases</strong></td>
<td><strong>State of the Art: Management of Staphylococcal Infections - The ASA Guidelines</strong></td>
<td>Phenotypic Tests (Jan Bell)</td>
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<tr>
<td></td>
<td>Anthrax (Richard Lawrence)</td>
<td>Introduction (Iain Gosbell)</td>
<td>Confirmatory/Molecular Tests (Phil Giffard)</td>
</tr>
<tr>
<td></td>
<td>SARS and other Respiratory Viruses (John Mills)</td>
<td>Bacteraemia (David Mitchell)</td>
<td>Question Time</td>
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<td>Four Fatal Fungi - Scedosporium/Fusarium/Penicillium/ Zygomycetes (John Perfect)</td>
<td>Implant/Skin Soft Tissue (Sally Roberts)</td>
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<td>Pharmacokinetic/Pharmacodynamic Considerations (Craig Rayner)</td>
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<td><strong>1730 - 1830</strong></td>
<td>AGM</td>
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<tr>
<td><strong>1830 - 1930</strong></td>
<td><strong>Welcome Reception</strong></td>
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<tr>
<td><strong>1900 - 2330</strong></td>
<td></td>
<td><strong>Conference Dinner</strong></td>
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