In this study, we investigated the molecular mechanism behind bayberry treatment of cholera described in ancient Chinese medicine. We found that an extract derived from a simple and rapid extraction of bayberry fruits could repress *V. cholerae* virulence gene expression at low concentrations and inhibit *V. cholerae* growth at high concentrations. Intriguingly, this bayberry extract did not inhibit or kill many non-pathogenic bacteria tested, including *Escherichia coli* and *Bacillus subtilis* (data not shown). The narrow-spectrum bactericidal activity of the bayberry extract may thus preserve normal intestinal flora during treatment. Thus far, there has been little success in finding cheap and effective treatments for poverty-associated infectious diseases like cholera. For example, although Hung *et al.* reported a small-molecule inhibitor of *Vibrio cholerae* virulence and intestinal colonization, such compounds must be artificially synthesized. Further study is necessary to reveal the exact nature of bayberry extract inhibition of *V. cholerae* infection, but consumption of bayberry fruits or fruit extracts may prove to be a cheap alternative therapy for cholera in many developing countries.

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**Research letters**

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**Transparency declarations**

None to declare.

**Supplementary data**

A colour version of Figure 1 is available as Supplementary data at JAC Online (http://jac.oxfordjournals.org/).

**References**


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**Thermostable nuclease: a study of clinical impact**

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Keywords: bacteraemia, *Staphylococcus aureus*, rapid diagnosis

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Sir,

Bacteraemia due to *Staphylococcus aureus* is associated with a high morbidity and mortality. Early detection and treatment is critical for successful management. Unfortunately, coagulase-negative staphylococci (CoNS) are the most frequent isolates grown from blood cultures, many of which are considered skin contaminants. A test that rapidly and accurately discriminates the two would potentially allow earlier treatment of *S. aureus*, while reducing unnecessary antimicrobial use. Thermostable nuclease (TSN) is a rapid test (requiring 2–4 h)
that differentiates between \textit{S. aureus} and CoNS, as \textit{S. aureus} produces a nuclease that is uniquely and consistently thermo-stable. TSN testing involves removing 2–3 mL of blood broth from a blood culture and heating the blood broth in a boiling water bath for 15 min. Once cooled, two to three drops are placed in a 6 mm well cut in the media (Southern Group Laboratory, Corby, UK) and the plate is incubated for 2–4 h at 37°C. A positive reaction, indicating thermonuclease activity, shows an area of clearing at the edge of the well.

Addenbrooke’s Hospital is a tertiary referral hospital with 1100 beds. The impact of the TSN test on the immediate management of positive blood cultures was assessed for the calendar month of August 2007. Blood cultures were processed using BacT/Alert 3D (bioMérieux, Basingstoke, UK), and TSN testing was performed when Gram-positive cocci in clumps were seen on microscopy. Blood cultures growing the same organism within a 2 week period were counted as one episode. Patients were identified prospectively and assessed to determine the reliability of the test (in terms of sensitivity, specificity and positive- and negative-predictive values), when compared with tube coagulase, and the impact of the TSN result following a clinical evaluation of the patient (i.e. no impact, start antimicrobial therapy, withhold therapy or stop therapy).

Ninety patient episodes (123 staphylococcal bacteraemias) occurred in the study period. CoNS accounted for 75 episodes, \textit{S. aureus} for 11 and \textit{Micrococcus} spp. for 4. TSN was performed in 88 of 90 episodes (Gram-positive cocci in chains and Gram-negative bacilli were seen on the original Gram film in one case each; the subsequent cultures from these blood cultures were mixed). The sensitivity, specificity and positive- and negative-predictive values were 81.8\% (9/11), 97.4\% (77/79), 100\% (9/9) and 97.4\% (77/79), respectively (Table 1). Antimicrobial treatment was withheld in 8 of 88 (9.1\%) cases pending the TSN result and was not commenced when a negative result was obtained. Antimicrobial therapy was commenced as a result of a positive TSN result in 2 of 88 (2.3\%) cases. A negative TSN did not result in treatment cessation when patients were already on antimicrobial agents at the time of the positive blood culture. The TSN made no immediate clinical impact in 78 of 88 (88.6\%) cases. One of the two false-negative TSN results was a transcription error and the other was a patient with neutropenic sepsis. Both of these patients were receiving empirical antimicrobial treatment, so the TSN result had no effect on therapy.

The performance of TSN has been described previously. However, to the best of our knowledge, no previous study has attempted to address its clinical impact. An obvious benefit would be that it allows earlier targeted treatment of \textit{S. aureus} bacteraemia and this occurred in 2 of 11 episodes (18.2\%); the other nine cases were already receiving appropriate empirical therapy based on clinical suspicion. Although a negative TSN result did not lead to treatment cessation, it prevented inappropriate and unnecessary antimicrobial use in eight patients, which has not been described before. This is important in an attempt to control the spread of \textit{Clostridium difficile} and other causes of healthcare-associated infection. The apparent single true false-negative TSN result is of concern due to potential delays in treatment. This has been described previously with the BacT/Alert blood culture system.

TSN is simple and cheap and does not require complex and expensive equipment or expertise, enabling it to be used in any clinical laboratory. Although this study is small, with only 90 episodes, it is prospective in nature. We believe that TSN is a useful adjunct to routine staphylococcal identification methods and leads to a reduction in unnecessary antimicrobial use.

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**References**


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**In vitro activities of combinations of amphotericin B, posaconazole and four other agents against Rhizopus**

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Keywords: zygomycosis, itraconazole, \textit{Rhizopus oryzae}, \textit{Rhizopus microsporus} var. \textit{rhizopodiformis}

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**Table 1. Performance table comparing TSN and coagulase results**

<table>
<thead>
<tr>
<th>TSN result</th>
<th>Coagulase positive</th>
<th>Coagulase negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSN positive</td>
<td>9</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>TSN negative</td>
<td>2</td>
<td>77</td>
<td>79</td>
</tr>
<tr>
<td>No TSN result</td>
<td>0</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
<td>79</td>
<td>90</td>
</tr>
</tbody>
</table>