A test for the early detection of MRSA: clinical benefits and financial savings

by Ian Hart

Early diagnosis and appropriate treatment of infections are widely accepted to benefit patient outcome by reducing morbidity, mortality and length of hospitalisation. However, many laboratories are reticent to include new testing regimes without both proof of these benefits and justification on cost grounds. This article discusses a rapid diagnostic test for the earlier detection of MRSA infections, and the findings of some groups regarding the clinical benefits and financial savings that can be realised using this simple test.

Methicillin resistance in *Staphylococcus aureus* (MRSA) is a worldwide problem. The proportion of *S. aureus* isolates resistant to methicillin is still increasing in many parts of the world, most countries now have MRSA rates of >20% and some have rates as high as 50% [1]. However, some countries, such as the Netherlands, Iceland and Scandinavia, have still been able to maintain very low (<1%) rates of MRSA.

A recent report from the European Antimicrobial Surveillance System (EARSS) illustrated how the proportions of MRSA vary enormously between countries across Europe, from <1% in northern Europe to >40% in Southern and Western Europe, and with almost 100-fold difference between the lowest and highest rates observed [2]. The report also observed variations of MRSA rates between hospitals within all countries, particularly those nations with a prevalence of 5-20%. The EARSS suggests that these trends should stimulate initiatives to control MRSA at national, regional and hospital levels.

**Strategies to combat MRSA**
The EARSS summarises that, in order to combat MRSA epidemics, health workers must understand the role of hospital hygiene protocols, antimicrobial drug policies and mechanisms of regional spread. Some of the strategies adopted by countries in Europe with traditionally high MRSA rates, such as the UK and Ireland, are shown below [2]:

- Surveillance of antimicrobial resistance (such as the mandatory surveillance programme for MRSA bacteraemia in the UK).
- Revised policies for antibiotic use.
- Updated national guidelines.
- Initiatives to increase awareness and to encourage efforts to control MRSA by individual hospitals.
- Strategies to reduce healthcare-associated infections, including guidelines for good hospital practice.

Possibly as a result of these initiatives, the rates of increase of MRSA infections in the UK and Ireland have stabilised or even decreased slightly in recent years [2].

In the Netherlands, where a low MRSA rate (<1%) has been maintained, the Dutch Working Party for Infection Prevention attributes this success, in part, to their national policy [1]. In this policy they stress that it is important for all hospitals in the country to comply; if it is to be effective. The policy focuses on optimising detection, and on isolation measures. The Dutch group recognises that early identification is essential for appropriate action to be taken as quickly as possible. They recommend that all patients found to be MRSA-positive are both isolated and treated [1, 3] which includes skin, hair and nasal disinfection, and that care providers (such as ambulance crew, GPs and nursing home staff) should be informed when an MRSA infected patient is discharged [1].

**Earlier identification of MRSA**
The mechanism of methicillin resistance in MRSA is the production of the penicillin binding protein PBP2’ (or PBP2α), which is encoded by the mecA gene. Phenotypic methods for the detection of resistance to methicillin and associated compounds have limitations, since their accuracies can be influenced by the prevalence of strains that express heterogeneous resistance [3]. Methods for the detection of the mecA gene or PBP2’ are more reliable and have become the preferred options for the confirmation of MRSA [4]. In fact, detection of the mecA gene by PCR has been considered the gold standard in the determination of methicillin resistance because of its accuracy, but this method is expensive and labour intensive [5, 6] and many clinical laboratories do not have the resources to perform this technique.

A much simpler and more rapid test is available for the detection of PBP2’ by latex agglutination (PBP2’ Test, Oxoid Limited, UK), which provides a valuable indication of methicillin resistance a day in advance of traditional phenotypic results and AST results.

Requiring minimal labour and no expensive or complicated equipment, the PBP2’ test is also much quicker and easier to perform than genotypic tests, yielding clearly visible results within minutes. Latex particles sensitised with a monoclonal antibody against the PBP2’ protein agglutinate in the presence of MRSA [Figure 1]. The test is flexible enough to be suitable for either batch or individual testing and has the added advantage of being able to detect methicillin resistance in coagulase-negative staphylococci (MRCoNS) in addition to MRSA.

The test has demonstrated excellent sensitivity and specificity in evaluations around the world [3, 7, 8, 9] and it conforms to both the EARSS guidelines for confirmation of non-susceptible isolates [4] and the NCCLS guidelines for the detection of oxacillin resistance (M100-S14/M2-A8).

One group from the Netherlands found the detection of PBP2’ by latex agglutination to be highly sensitive and specific for the detection of methicillin resistance, offering higher sensitivity than the Oxacillin Screen Agar Test and the E Test [3] and yielding results in just 20 minutes. It was concluded that the speed and ease of use of this test make it a valuable tool in the ongoing battle against MRSA [3].

**Realising and reducing the cost of MRSA**
In the USA, where the proportion of *S. aureus* isolates found to be methicillin resistant is >40% [10], the PBP2’ Test is used regularly to provide an early indication of resistance and is helping hospitals to minimise the clinical and financial impact of MRSA [11].

In addition to improving patient care, by allowing earlier initiation of appropriate treatment, it has also been recognised that earlier detection of MRSA, facilitated by the PBP2’ Test, provides considerable potential for financial savings. A recent review explored the costs of MRSA [11] and estimated actual cost savings associated with obtaining...
MRSA confirmation a day earlier than traditional methods. These included physical and emotional costs resulting from delays in effective treatment and increased morbidity and mortality, the cost of therapy, the cost of isolation and extended hospitalisation and the cost of nosocomial infection, resulting from spread within the hospital. It was shown that savings could be made in the areas of pharmacy costs, infection control costs and nosocomial infection costs.

**Reducing pharmacy costs**

In countries where the MRSA rate is high, prophylactic treatment with vancomycin is often initiated on confirmation of *S. aureus* infection, pending the Antimicrobial Susceptibility Test (AST) result. This is not ideal, since vancomycin is a more expensive treatment option than those agents used to treat methicillin-sensitive *S. aureus*, such as oxacillin. Vancomycin also has implications in the elimination of commensal flora sometimes leading to infection by opportunistic pathogens and in the further development of resistance. Increased incidence of VRE has been associated with increased use of vancomycin [10]. MRSA with reduced sensitivity to vancomycin has also been reported [12].

With the PBP2’ Test, since MRSA confirmation is available a day earlier, fewer patients need to receive vancomycin on day 1 and with a MRSA rate of 35%, this could save the equivalent of around €17 500 every year (assuming a difference of €8 between the daily dose of vancomycin and oxacillin) [11].

**Reducing isolation costs**

By allowing MRSA confirmation a very short time after isolating *S. aureus* colonies, the PBP2’ Test ensures that fewer patients require isolation while awaiting AST results. High-risk patients may be placed in isolation before the methicillin/oxacillin status is known, at an estimated cost of €4194 per day [13]. If PBP2’ testing helped to prevent one unnecessary isolation per week (a reasonable estimation for a busy hospital) the annual saving would be €218 088 [11].

**Reducing nosocomial infection costs**

Rapid detection allows correct assessments and appropriate actions to be taken at the earliest opportunity and helps to reduce the incidence of subsequent nosocomial MRSA infections. One group of researchers estimated the cost of an MRSA nosocomial infection to be the equivalent of €22 433 [14]. If just one nosocomial infection was prevented every 4 weeks, using the PBP2’ Test, the annual saving would be €291 629 [11].

**Total annual savings**

Considering these savings, and taking into account the cost of the test, estimated potential annual savings equivalent to €487 915 could be made in a typical, busy hospital with a moderately high proportion of MRSA infections [11].

The clinical benefits to the patient in terms of improved treatment and care are, of course, priceless. Even in countries where there is a very low prevalence of MRSA, earlier diagnosis helps to prevent prophylaxis and treatment of *S. aureus* infections from being ineffective [1].

These findings provide strong evidence for the usefulness and cost effectiveness of PBP2’ screening prior to obtaining AST results. Such measures will help to reduce the financial burden of MRSA by detecting resistant strains at the earliest opportunity and allowing costly treatment and care to be targeted more appropriately.

**References**

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