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Towards a common susceptibility testing method?

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Richard Wise* and Ian Phillips

BSAC Working Party on Antibiotic Sensitivity Testing, 11 The Wharf, 16 Bridge Street, Birmingham B1 2JS, UK

*Correspondence address. Department of Microbiology, City Hospital, Dudley Road, Birmingham B18 7QH, UK. Tel: +44-121-554-3801; Fax: +44-121-551-7763; E-mail: r.wise@bham.ac.uk

We agree with Gould's comments about the shortcomings of the Stokes' method and the need for the 'comparability of data between different centres across the country so that resistance surveillance data can be reliably compared'. In fact we would go further and suggest that, since bacteria do not respect national borders, there should be worldwide comparability of data. Where we part company with Gould is in how we approach that goal.

In his paper, Gould outlines the relative merits of agar disc diffusion and breakpoint MIC methods and, in doing so, indicates many of the factors that affect the reproducibility of the former method. These include inoculum, temperature, atmosphere and generation time of the bacterium. Surely, however, these affect both methods? Furthermore, we would not agree with the view that only the broth dilution method lends itself well to automation: automatic plate readers, with their data collation system, have a lot in their favour. Other than on these points we would not disagree with Gould's precis of the pros and cons of the different approaches.

The thrust of Gould's paper is to argue for the worldwide use of the NCCLS method for susceptibility testing and here we disagree. We believe that the US-derived method, although having a number of creditable features, is too rigid in its concept to be recommended for use in the UK (or for many other EU countries). Our reasons can be listed:

(i) *Media*. The early choice of Mueller–Hinton agar and broth was 'Hobson's choice'—there was no available alternative. The choice has caused the NCCLS years of headaches because of its inherently variable nature. Similarly, the use of *Haemophilus* test medium base may well yet turn out to be an unfortunate choice. The BSAC decided at an early date that it would not choose Mueller–Hinton. If reproducibility is the criterion, IsoSensitest agar (Oxoid, Basingstoke, UK) has performed well, and the advent of an equivalent competitor (Mast Diagnostics, Bootle, UK) answers another objection. Furthermore many organisms grow better on IsoSensitest agar than on Mueller–Hinton agar, making end points or zone sizes easier to read and measure.

(ii) In Table II, Gould invites us to believe that the inoculum preparation suggested by the BSAC is complex. He misunderstands our point—if a laboratory has a routine method (and there are many) that achieves semi-confluent growth then they should use it. Semi-confluent growth is immediately apparent to even the untrained eye. We continue to recommend that if the inoculum is too heavy, the test should be repeated. The heavy inoculum suggested by the NCCLS has a number of important and fundamental problems. A heavy, or confluent inoculum can vary widely and yet there is no way to ascertain its exact size.[1] Variability in inoculum is probably the greatest source of error in susceptibility testing.

(iii) It is further suggested that the BSAC breakpoints are 'conservative' in nature. This is a criticism we can live with! The higher values obtained with the NCCLS method concern us, in that, first, this may lead to inappropriate prescribing of an agent with an MIC just below the breakpoint value to which the organism will be reported as susceptible and yet the agent may fail. Far better to report such a strain as resistant and hence guide the clinician to a more appropriate choice, until or unless there is better evidence that strains with microbiological resistance mechanisms will respond to therapy with a drug with an MIC below the breakpoint. Secondly, the over-reporting of dubiously susceptible strains can only lead to greater selection pressure and emergence of resistance since low-level resistance is ignored. Recent pharmacodynamic studies demonstrate this.[2]

(iv) We find it difficult to understand the point being made in relation to MIC in Table II. Gould suggests, we believe, that an MIC can be derived by the NCCLS method "by regression line analysis"; this is not our understanding.

(v) At all the BSAC workshops introducing the new method, information on detection of methicillin-resistant *Staphylococcus aureus* (MRSA) was distributed. A careful

study employing *mecA*-positive and -negative strains has underpinned our recommendations and this will be published in the near future.

(vi) The detection of new resistance mechanisms is also helped by low breakpoints but will be addressed by David Livermore in the BSAC supplement explaining the methodology that is to be published later this year.

Before the BSAC agreed to fund the studies into the new method a survey of the membership was undertaken. Despite the NCCLS recommendations being available to all in the UK, none of the laboratories that replied had implemented them. More importantly 90.6% of responding laboratories expressed a willingness to change to a new method.[2] We are heartened to see the steady move by laboratories in the UK and Ireland towards the BSAC standardized method. We acknowledge, however, a relative lack of documentation, one of the strongest points in support of the NCCLS methods. However, we intend to continue to collect information on the performance of the BSAC method, which will eventually temper the imbalance. Finally we emphasize that standardization is not the only way to achieve the results that we all seek. Indeed, we believe that it is not even desirable at present, since only through diversity will we be able to assess all the variables in susceptibility testing. Perhaps then we will be able to move towards the ideal method envisaged by the International Collaborative Study.[1] In the meantime quantification and comparison will show how far we have to travel.

Our final point is 'whatever you do, do it properly'. The close links between the UK quality assurance scheme and ourselves will ensure that relevant strains are circulated and that the proper standard organisms are available and will help to ensure that susceptibility testing goes forward on a sound footing.

References

1. Ericsson, H. & Sherris, J. C. (1971). Antibiotic Sensitivity Testing. Report of an International Collaborative Study. *Acta Pathologica Microbiologica Scandinavica Section B. Suppl.* 217.

2. Andrews, J. M., Brown, D. & Wise, R. (1996). A survey of antimicrobial susceptibility testing in the United Kingdom. *Journal of Antimicrobial Chemotherapy* **37**, 187–8.