Key to antimicrobial stewardship success: Surveillance by diagnostic microbiology laboratories

The important role of laboratories in enhancing antimicrobial stewardship activities through improved diagnostics and provision of surveillance data is globally recognised.[1] Consider the aim of an antimicrobial stewardship programme: 'optimize clinical outcomes while minimizing the unintended consequences of antimicrobial use'.[2] The clinical microbiology laboratory plays a critical role in achieving these aims through the provision of culture and susceptibility data that are both patient-specific (optimisation of clinical outcomes) and informative for surveillance activities that guide empirical antimicrobial selection (minimising unintended consequences of antimicrobial use). For this reason, the World Health Organization (WHO) included the strengthening of surveillance and laboratory capacity in its 2011 World Health Day six-point plan to combat antimicrobial resistance (AMR).[3] South African laboratories in the public and private sectors have the means to provide surveillance data and, through a collaborative approach, the capacity to create antimicrobial resistance maps. In line with the WHO's recommendations and under the auspices of the South African Society of Clinical Microbiology, efforts are currently underway to improve national AMR surveillance data for typical healthcare-associated pathogens. The generation and provision of these data is, however, only half of the challenge. The analysis and interpretation thereof is equally important, as highlighted in this month's *SAMJ* by McKay and Bamford[4] in their study comparing community- with healthcare-acquired bloodstream infections at Groote Schuur Hospital (GSH), Cape Town, a tertiary public sector hospital.

The study is a retrospective description of bloodstream isolates submitted to the GSH laboratory over a 1-year period. Using predefined criteria, the isolates were classified as community or healthcare acquired and a comparative analysis of resistance patterns was undertaken. The issue of differing resistance patterns in the community v. hospital is a well-established and much-publicised phenomenon.[5] The article serves to reinforce these established differences, highlighting the profound resistance associated with hospital pathogens: (*i*) a 47.6% difference in the methicillin-resistant *Staphylococcus aureus* (MRSA) rate; and (*ii*) a ~35% difference in extended-spectrum β-lactamase (ESBL) production by Enterobacteriaceae. The authors have provided substantive local surveillance data to support their recommendations for empirical antimicrobial prescribing based on an assessment of whether the infection is community or healthcare acquired. They have therefore highlighted a crucial element that, for various reasons relating to surveillance capacity, has unfortunately not been available in similar published local AMR surveillance data.[6-8] This element is the clinical and epidemiological context that is required for interpretation of the data. Unfortunately without this context the data become blurred and the issue of resistance is magnified disproportionately. Aggregated data (which is what we have seen to date) give an indication of whether overall resistance is on the increase or decrease, but do not provide sufficient information to guide practice at a local level. Nearly three-quarters of all bloodstream infections (BSIs) from GSH, as McKay and Bamford show, were healthcare acquired; when

aggregated these data roughly translate into a 33% MRSA rate and a 30% ESBL rate. Compare this with the 0% MRSA rate and 4% ESBL rate for community-acquired infections at the same hospital, and the importance of making the distinction between community- and healthcare-acquired BSIs becomes obvious.

Aggregated data without context are therefore inadvertently detrimental to antimicrobial stewardship initiatives, as the perceived threat of resistance compels many prescribers to go straight for the 'big-gun' antibiotics. While AMR is a very real threat to the prospects of treating infections, as McKay and Bamford confirm, good ol' cloxacillin (a far superior drug to vancomycin in the treatment of *S. aureus*[9]) is still a perfectly suitable option in the right patient. Similarly, with a <5% ESBL rate for Enterobacteriaceae associated with community-acquired BSIs, the third- and fourth-generation cephalosporins still have an important role to play.

Importantly, McKay and Bamford have indicated that their surveillance data are being constructively utilised at GSH, as suggested recommendations 'are in line with contemporary hospital antibiotic recommendations'. As an example, the intensive care units (ICUs) account for almost three-quarters of all *Acinetobacter baumannii* bloodstream infections, supporting the decision to include colistin or tobramycin as empirical treatment options for ICU patients with suspected Gram-negative sepsis. The dissemination and utilisation of surveillance data is crucial if they are to impact on patient management and outcomes. Unfortunately this aspect is often sorely neglected, requiring a collaborative effort from clinical, laboratory and hospital staff. For the general practitioner serving the community, it would require close liaison with the microbiology laboratory with provision of practice-specific surveillance data. Local hospital AMR surveillance data should ideally go a step further through stratification of susceptibility data by ward/unit. In their study McKay and Bamford stratified by discipline rather than by individual wards and demonstrated some distinct differences in organism profile, although no major differences in susceptibility profiles. Ward-specific surveillance data have been shown to be a more useful tool for empirical antimicrobial selection, owing to distinct within-hospital antimicrobial susceptibility differences between wards/units.[10] For example, one cannot compare the cardiology ICU with the surgical ICU, or the haematology-oncology unit with the rest of the general medical unit. Nevertheless, the stratification data presented in this paper are illuminating and could potentially be stratified further for additional enhancement of antimicrobial stewardship efforts.

McKay and Bamford's study raises some additional challenges and areas of focus for hospitals, laboratories and prescribers. Classification of infections into community v. healthcare acquired is becoming more difficult, and the term 'healthcare associated' has been widely used to account for an increasingly complex healthcare environment that includes patients from long-term care facilities, rehabilitation centres, dialysis centres, etc.[11,12] The definitions used in different studies vary considerably.[12] This lack of standardisation is a major stumbling block to adequate risk assessment. Similarly, the cited risk factors for likelihood of a multidrug-resistant organism that are often used to guide empirical antimicrobial selection lack specificity and are generally used too loosely.[13-15] Distinctive epidemiological criteria upon which to base antimicrobial choices are desperately required, and local surveillance data are crucial in addressing this need. Enhanced surveillance data based on standardised definitions, with subsequent analysis at a local (facility/practice) level, could potentially identify risk factors with better diagnostic accuracy. This would enable hospitals (facilities) to develop facility-specific guidelines for antimicrobial prescribing. Development of such site-specific guidelines is particularly challenging in the private sector, where hospitals are governed by corporate processes and policies. However, hospitals are not all the same, varying significantly in their case mix, which influences risk factors, and crucially in their microbiological 'ecosystem'. This type of enhanced surveillance would require substantial investment in personnel and IT infrastructure.

Laboratories face the challenge of providing accurate, reliable and standardised data. As indicated in McKay and Bamford's study, piperacillin-tazobactam (a valuable agent) susceptibility data were not reported because of methodological limitations. Similarly, ESBL production was not tested but inferred from the cefepime result, a limitation acknowledged by the authors. Many laboratories would not use cefepime but rather ceftriaxone to infer ESBL production, whereas others would confirm it with phenotypic testing. It is evident that this methodological variance can have a major impact on the generation and interpretation of collated surveillance data, highlighting the need for some form of standardisation, if not in methods then at least in reporting. In the private sector there are usually two or three laboratories serving a hospital, each with its own subtle differences in practice and reporting. Ultimately the onus is on the hospital to collate these data and provide meaningful surveillance reports.

Notwithstanding the important antimicrobial stewardship initiatives undertaken by various stakeholders as part of a commitment to address AMR, the success of antimicrobial stewardship (if measured according to the aims thereof) begins with the microbiology laboratory. The message is very clear, as McKay and Bamford have subtly suggested in their concluding remarks – the onus is on diagnostic microbiology laboratories to provide good-quality, clinically relevant and stratified surveillance data.

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