Antibiotic resistance in hospitals – are surveillance data of any value?

Antibiotic susceptibility profiles of selected bacteria cultured from the blood of patients in private hospitals in five South African centres by various private sector microbiology laboratories over a 6-month period in 2006 are described in this issue of *SAMJ*.[1] This is the first published study of this nature from private sector microbiologists who are members of the National Antimicrobial Surveillance Forum (NASF), and it is to be hoped that it marks the start of an ongoing process.

The NASF was formed in 2003, through a merger of the academic/public sector Antibiotic Study Group (ASG) and the private sector Antibiotic Surveillance Forum (ASF). Its mission is to disseminate information on antimicrobial agents, including the promotion of reliable antibiotic susceptibility testing and documentation of susceptibility patterns in clinically relevant pathogens.

Only selected bacteria and limited antimicrobial agents are included in the study. The former include *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter* spp., *Pseudomonas aeruginosa*, *Acinetobacter baumanii* and *Staphylococcus aureus*. These were chosen because they represent the most common hospital-acquired pathogens and are those in which antibiotic resistance is a recognised problem. However, their ranking among the total blood culture isolates during the study period is not stated.

Some shortcomings are evident. These include lack of standardisation of methodology, no mention of measures to exclude repeat isolates, and no distinction between hospital-acquired and community-acquired isolates. Notably, the extent and patterns of resistance to multiple antibiotics among the pathogens are not addressed. However, these limitations should not detract from the main and important messages that come from this study, which are the high levels of resistance to key 'workhorse' antibiotics used in hospitals, the identification of significant prevalences of extended-spectrum β-lactamases (ESBLs) and other resistance mechanisms in the Enterobacteriaceae studied, and the considerable differences in resistance prevalences between centres.

Bacterial resistance to antimicrobial agents – both in community and health care settings – has long been recognised as a worldwide phenomenon of increasing extent and relevance.[2] Acquired resistance (resistance emerging in bacterial species formerly sensitive to the particular agent/s) is also recognised as a consequence of selective pressure in the form of antibiotic usage. (It comes as no surprise that in the European Union, countries with the lowest overall rates of resistance are those with the lowest per capita usage of antibiotics.) However, many other factors appear to influence both the rate of development and the extent of spread of resistant bacteria.

In respect of the latter, measures to control cross-infection are highly important, particularly in the hospital context.

As noted by the authors, among the Gram-negative bacilli studied, the production of broad-spectrum β-lactamases is clearly a problem in all centres. Being mutant derivatives of narrower spectrum plasmid-mediated β-lactamases, ESBLs have generally remained susceptible to β-lactamase inhibitors such as clavulanate and tazobactam – a feature that has contributed greatly to their laboratory recognition and some clinical role for agents such as co-amoxyclav and piperacillin-tazobactam. Recently, however, inhibitor-resistant ESBLs have been described, seriously underlining the unwelcome capacity of bacteria to keep ahead of man's efforts in the resistance race.

In addition to these typically plasmid-coded β-lactamases, several Enterobacteriaceae, notably *Enterobacter* spp., produce chromosomally coded β-lactamases, mostly of the AmpC class. When first identified AmpC production was an inducible phenomenon, the β-lactamase only being produced on exposure to the β-lactam agent – some being more powerful inducers than others. Subsequently, in the face of such therapy, some isolates mutated to escape the repressor mechanism to become constitutive high-level β-lactamase producers – sharing high-level resistance to a range of penicillins and cephalosporins, including β-lactamase inhibitor combinations. Only cefepime and the carbapenems withstand inactivation by these enzymes. In addition, AmpC-producers may acquire mobile plasmid-mediated ESBL production, leaving carbapenems (imipenem, meropenem, ertapenem) as the only active β-lactams. These strains are also invariably multiresistant to other antibiotics, including aminoglycosides and, increasingly, fluoroquinolones.

What are the implications of such resistance in hospital clinical practice? Some of the therapeutic implications are discussed by the authors. Multiple resistance seriously limits the range of antimicrobial agents available for treatment of infections. In hospital-acquired infections, inappropriate initial antimicrobial therapy is an important determinant of morbidity and mortality.[3,4] Inappropriateness is usually related to bacterial resistance to the prescribed antimicrobial agent(s), although other variables such as dosing and route of administration may also be relevant.[4] Initial empirical choice is best guided by contemporary susceptibility data at institutional or preferably service and unit (e.g. intensive care unit) level.[4]

Concerns regarding the adverse impact of such routine broad-spectrum initial empirical therapy are real. Measures to reduce this include de-escalation to narrower spectrum therapy as early as possible, based on culture results from representative specimens collected before initiation of therapy,

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and shorter courses of therapy.[4-6] The role of so-called antibiotic rotation or cycling appears unproven to date.[5,7]

The above require ongoing documentation of significant bacterial isolates and their susceptibility to a range of potentially applicable antibiotics. Distinction should also be made between hospital-acquired and community-acquired isolates. Appropriate communication of and response to such data should be provided for. Implicit is a requirement for appropriate microbiological investigations on representative clinical specimens, collected before initiation of antimicrobial therapy.

Bantar and co-workers suggest that the value of such laboratory-based surveillance data in guiding therapy can be enhanced with clinical input to assess the relative roles of contamination and true infection.[8] As noted in the NASF study, methods for susceptibility testing should be standardised, thereby improving inter-laboratory comparisons. Consistent methodology will enhance the value of microbiology data at local level. Most microbiology laboratories utilise standardised susceptibility testing methods such as those provided by the Clinical and Laboratory Standards Institute (CLSI) or the British Society for Antimicrobial Chemotherapy (BSAC).[9,10] Nevertheless, it is sobering that optimal susceptibility testing for some agents and resistance mechanisms are still under investigation.[11,12] Given the advent of 'new' resistance mechanisms and, to a much lesser extent, new antimicrobial agents, susceptibility testing promises to be a continually evolving area in which standardisation, quality control and accreditation will be increasingly important.

Examples of other initiatives to promote prudent antibiotic prescribing towards control of antibiotic resistance include computerised systems to support decision-making and the appointment of dedicated personnel (usually pharmacy-based) to monitor and review antibiotic prescribing and to facilitate interaction between pharmacy, microbiology and clinical personnel.[5,13,14]

This initial report from the NASF should be applauded. Going forward, their challenge will be to make such data available on a regular basis, in more centres, to individual hospitals, and in some instances to specific departments and units (e.g. ICUs). Their data expose the problem of antibiotic resistance but also provide a basis for ongoing surveillance, which could underpin the promotion of more effective and judicious use of antibiotics in private hospitals. If the various private microbiologists can collaborate to provide these data, it is to be hoped that the private hospital networks will respond with the will and allocation of resources to utilise this information effectively.

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