

Improving our understanding of antibiotic resistance: The relevance of surveillance at the population level

Bacterial infections are primarily treated with antibiotics. However, bacteria develop mechanisms enabling them to thrive in the presence of therapeutic doses of antibiotics, leading to antibiotic resistance, and to broad antibiotic resistance when a bacterium is not susceptible to more than one class of antibiotics.

The level of antibiotic resistance is on the rise globally to an alarming extent, including in South Africa (SA), and calls for strategies to mitigate the decline in the effectiveness of antibiotics have grown louder.^[1,2] For example, new insights from research and policy development on antibiotic resistance continue to feature prominently in international meetings, such as the recently held global Grand Challenges meeting in October 2016. Proposals to establish a framework aimed at the judicious use of antibiotics, as a measure to mitigate antibiotic resistance, include production and distribution of quality drugs, correct diagnosis, appropriate prescription of drugs and channels for their distribution, and the involvement of all health professionals for viable antibiotic stewardship.^[3-5]

Our knowledge about optimal antibiotic usage and the scope and diversity of circulating antibiotic-resistant bacteria in apparently healthy individuals is limited. This editorial is intended to highlight the importance of antibiotic resistance surveillance at population level as part of an approach to improve our understanding of the complexity and dynamics of the antibiotic resistance landscape in SA.

Recent data from the Etiology, Risk Factors, and Interactions of Enteric Infections and Malnutrition and the Consequences for Child Health and Development (MAL-ED) project^[6] revealed varying degrees of antibiotic use in different countries, including SA, and evidence for overuse and underuse in children <24 months old. Data were collected through twice-weekly home visits and from examination of clinic/hospital treatment records. MAL-ED is a multicountry, prospective, observational birth cohort study carried out to improve understanding of the interactions of enteric infections, childhood illnesses, vaccine responses, environmental enteropathy, physical growth and cognitive development.^[7]

In this edition of the *SAMJ*, DeFrancesco *et al.*^[8] demonstrate that strains of *Escherichia coli*, a common cause of bacterial gastroenteritis, produce extended-spectrum beta-lactamase (ESBL). The production of ESBL allows bacteria to thrive in the presence of therapeutic doses of several clinically important antibiotics, potentially complicating management. Clones of *E. coli* (each bacterial colony emanating from a single genome) were obtained from normal (non-diarrhoeal) stools of young children enrolled in MAL-ED SA, followed by antibiotic susceptibility and minimum inhibitory testing, and detection of genes coding for antibiotic resistance. Worthy of note is the fact that *E. coli*-producing ESBL was observed prospectively in children as young as 4 months of age, and who had never received antibiotics. A previous report highlighted quinolone-resistant bacteria in young Peruvian children naive to antibiotics and the fact that antibiotic-resistant bacteria are increasingly becoming part of our normal microbiota,^[9] suggesting carriage and transmission of multidrug-resistant bacteria at the population level from early in life.

Questions that arise are: what is the burden of antibiotic resistance in apparently healthy individuals, and how does this burden affect the formulation of strategies to minimise the spread of antibiotic-resistant bacteria? We propose that it is worthwhile to understand

the burden and carriage of drug-resistant bacteria at the population level. Data obtained from this approach, in addition to hospital-based and environmental observations, will contribute enormously to our understanding of the scope, ecology and transmission dynamics of antibiotic resistance in SA. This is relevant for advocacy, policy development and practice. The approach of understanding the microbial resistance levels in the general population is not new: for example, it is being applied in HIV drug resistance surveillance.^[10] In view of the enormous challenge posed by the surge in antibiotic resistance in SA and globally, new strategies are needed to improve our understanding of the antibiotic resistance landscape.

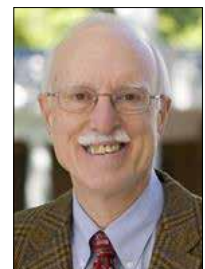
Pascal O Bessong

Professor of Microbiology and Director, HIV/AIDS & Global Health Research Programme, Department of Microbiology, School of Mathematical and Natural Sciences, University of Venda, Thohoyandou, Limpopo, South Africa
bessong@univen.ac.za



Richard L Guerrant

Professor of International Medicine, Division of Infectious Diseases and International Health, School of Medicine, University of Virginia; and Founding Director, Center for Global Health, University of Virginia, Charlottesville, USA



1. Laxminarayan R, Duse A, Wattal C, et al. Antibiotic resistance – the need for global solutions. *Lancet Infect Dis* 2013;13(12):1057-1098. [http://dx.doi.org/10.1016/S1473-3099\(13\)70318-9](http://dx.doi.org/10.1016/S1473-3099(13)70318-9)
2. Chioro A, Coll-Seck AM, Høie B, et al. Antimicrobial resistance: A priority for global health action. *Bull World Health Organ* 2015;93(7):439. <http://dx.doi.org/10.2471/BLT.15.158998>
3. O'Donnell LA, Guarascio AJ. The intersection of antimicrobial stewardship and microbiology: Educating the next generation of health care professionals. *FEMS Microbiol Lett* 2017;364(1):fw281. <http://dx.doi.org/10.1093/femsle/fw281>
4. Goff DA, Kullar R, Goldstein EJ, et al. A global call from five countries to collaborate in antibiotic stewardship: United we succeed, divided we might fail. *Lancet Infect Dis* 2016;17(2):e56-e63. [http://dx.doi.org/10.1016/S1473-3099\(16\)30386-3](http://dx.doi.org/10.1016/S1473-3099(16)30386-3)
5. Levy Hara G, Kanj SS, Pagani L, et al. Ten key points for the appropriate use of antibiotics in hospitalised patients: A consensus from the Antimicrobial Stewardship and Resistance Working Groups of the International Society of Chemotherapy. *Int J Antimicrob Agents* 2016;48(3):239-246. <http://dx.doi.org/10.1016/j.ijantimicag.2016.06.015>
6. Rogawski EA, Platts-Mills JA, Seidman JC, et al. Diverse antibiotic use practices in the first two years of life across 8 sites in the MAL-ED birth cohort study. *Bull World Health Organ* 2017;95(1):49-61. <http://dx.doi.org/10.2471/BLT.16.176123>
7. MAL-ED Network Investigators. The MAL-ED study: A multinational and multidisciplinary approach to understand the relationship between enteric pathogens, malnutrition, gut physiology, physical growth, cognitive development, and immune responses in infants and children up to 2 years of age in resource-poor environments. *Clin Infect Dis* 2014;59(suppl 4):S193-S206. <http://dx.doi.org/10.1093/cid/ciu653>
8. DeFrancesco AS, Tanih NF, Samie A, Guerrant RL, Bessong PO. Antibiotic resistance patterns and β -lactamase identification in *E. coli* isolated from young children in rural Limpopo, South Africa: The MAL-ED cohort. *S Afr Med J* 2017;107(3):205-214. <http://dx.doi.org/10.7196/SAMJ.2017.v107i3.12111>
9. Mathers AJ, Guerrant RL. Dissecting the evolutionary stealth of our flora against antibiotics. *Trans R Soc Trop Med Hyg* 2014;108(3):121-122. <http://dx.doi.org/10.1093/trstmh/tru002>
10. Steegen K, Carmona S, Bronze M, et al. Moderate levels of pre-treatment HIV-1 antiretroviral drug resistance detected in the first South African national survey. *PLoS One* 2016;11(12):e0166305. <http://dx.doi.org/10.1371/journal.pone.0166305>

S Afr Med J 2017;107(3):167. DOI:10.7196/SAMJ.2017.v107i3.12357