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## Overconsumption of Antibiotics

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## Overconsumption of antibiotics

It is with great interest that I read the Article by Thomas Van Boeckel and colleagues,<sup>1</sup> reporting global antibiotic consumption. It is quite concerning that two-thirds of the increase in antibiotic usage between 2000 and 2010 occurred in BRICS countries (Brazil, Russia, India, China, and South Africa). As Van Boeckel and colleagues explain, this problem is partly due to the population increase in these countries, better access to drugs, and the improved socioeconomic status of BRICS countries. The absence of functioning antibiotic policies has fostered indiscriminate antibiotic use and misuse in most BRICS countries. The large increase in cephalosporin and fluoroquinolone consumption in India and China is particularly noteworthy, but is not unexpected as long as a course of these antibiotics is cheaper than a culture and sensitivity report. A large population size, socioeconomic disparity, and heterogeneity within the health-care system in most BRICS countries are major impediments for strict implementation of antibiotic policies.

Yet the highest use of antibiotics per person is in the USA, a country with good socioeconomic status that does

not have the usual excuses for antibiotic misuse that developing countries have. The USA is also the country with the highest level of antibiotics misuse in veterinary practice.<sup>2</sup> Antibiotic usage in Australia and New Zealand has also increased over the same period. The publication of Van Boeckel and colleagues' Article coincided with a meeting between BRICS leaders in Brazil. If this coincidence was orchestrated with the good intention of mobilising political will in BRICS leaders, the authors should be congratulated. In the war against microbes, the end justifies the means.

This is an opportunity for BRICS countries to consider the situation carefully. At the same time, the world should take an uncritical approach, as India did with the Chennai declaration.<sup>3</sup> This set of recommendations produced a serious change in the way the issue of antibiotics resistance is perceived by the medical community and authorities in India. The 5 year plan<sup>4</sup> proposed by the Chennai declaration is an ideal template for the improvement of infection control and standard of antibiotic stewardship in developing countries. Even developed countries, such as the USA, might benefit from similar initiatives (eg, World Alliance against Antibiotic Resistance, Antibiotic Action, and ReAct) to reduce antibiotic usage in medical and veterinary practice.

I declare no competing interests.

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We applaud Thomas Van Boeckel and colleagues<sup>1</sup> for their large analysis of antibiotic consumption in 71 countries. A 36% increase in use of antibiotics worldwide, 76% of which was in Brazil, Russia, India, China, and South Africa, is a concerning finding. In Europe and the USA, practitioners are increasingly aware of the importance of infection control and antimicrobial stewardship. However, 50% of antimicrobials, irrespective of setting, are used inappropriately.<sup>2,3</sup> We agree that most increases in global antibiotic consumption are probably caused by inappropriate use and that coordinated efforts to improve antimicrobial use internationally are desperately needed.<sup>1,2</sup>

Several European countries have instituted national campaigns to encourage appropriate use of antimicrobials.<sup>1</sup> In the USA, antimicrobial stewardship programmes have been recommended across all facets of health care, including acute, long-term, and ambulatory-care centres.<sup>3,4</sup> However, California is the only state with formal state-wide legislation that supports antimicrobial stewardship.<sup>5</sup> Although legislation is an important first step in the promotion of antimicrobial stewardship, staffing constraints, limited funding and administrative support, and other barriers to stewardship still persist.<sup>5</sup>

Formal legislation that mandates stewardship does not exist in other US states, but Rhode Island has adopted a state-wide approach to overcome stewardship barriers. Hospital administration, public health agencies, and multidisciplinary health-care providers from various practice settings are collaborating to advance antimicrobial stewardship efforts in the state. Providers from settings with established programmes assist those without established programmes. In May, 2011, the **Rhode Island Antimicrobial Stewardship Task Force** was formed to allow pharmacists from each of the state's 12 acute-care hospitals to

For The Rhode Island Antimicrobial Stewardship Task Force see <http://web.uri.edu/pharmacy/meet/the-rhode-island-antimicrobial-stewardship-task-force-riastf-advancing-antimicrobial-stewardship-efforts-through-state-wide-collaboration/>

For more on The Infection Control Professionals of Southern New England see <http://www.icpsne.org/>

collaborate towards the advancement of antimicrobial stewardship through monthly leader-facilitated meetings, development of treatment pathways, dosing guidelines, example policies, and educational material, and sharing of ideas and experience of hospital barriers and facilitators of antimicrobial stewardship. **The Infection Control Professionals of Southern New England** is an infection-control collaborative that promotes education, collaboration, and best practice for the prevention and control of infections. The Rhode Island Department of Health has convened a Task Force for Antimicrobial Stewardship and Environmental Infection Control, which has provided recommendations for environmental cleaning in Rhode Island hospitals and long-term care facilities. All groups work together to improve regulation of antimicrobial use in the state.

With the alarming increase in antimicrobial use worldwide, efforts are urgently needed to prevent unnecessary antimicrobial consumption. Multidisciplinary groups should come together to promote the adoption and expansion of antimicrobial stewardship. State-wide collaboration focused on antimicrobial stewardship might be an effective means to improve utilisation of antimicrobials, which could be adopted by other states and regions worldwide.

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## Probiotics to prevent early-life infection

Anna Seale and colleagues<sup>1</sup> reported estimates of possible severe bacterial infection in neonates in resource-limited settings. Worldwide about 15 million infants are born preterm each year and about 1 million of them die in infancy.<sup>2</sup> Additionally, roughly 18 million infants are born with low birthweight, predominantly in low-income and middle-income countries. This population has a high burden of morbidity and mortality associated with invasive infections in the neonatal period and early infancy.<sup>3</sup> Despite partial success in improvement of childhood mortality as part of WHO millennium goals, neonatal and early infant mortality has remained mostly unchanged since 2000.<sup>3</sup>

A review by Alfaleh and colleagues in 2014 (24 randomised trials, n=5000) supports that enteral probiotic supplementation significantly reduces necrotising enterocolitis (relative risk [RR] 0.43, 95% CI 0.33–0.56) and all-cause mortality (RR 0.65, 95% CI 0.52–0.81) in very low birthweight infants (weighing <1500g), with an

excellent safety profile and without adverse effects.<sup>4</sup>

Most of these trials (22 of 24) were done in high-income countries and in this setting probiotics had no significant effect on late-onset sepsis, a common complication of preterm birth, affecting up to 50% of the most immature infants (infants born before 28 weeks gestation; RR 0.91, 95% CI 0.80–1.03).<sup>4</sup> By contrast, trials of probiotics done in resource-poor and emerging settings show a significantly reduced incidence of bacterial and fungal late-onset sepsis in very low birthweight infants.<sup>5–7</sup> The benefits of probiotics in resource-poor settings are supported by a trial in a community setting in India in 2013 (n=4556), in which low birthweight infants (weighing >2000g) were given *Lactobacillus plantarum* and the prebiotic fructo-oligosaccharide, resulting in a significant reduction in serious infections (sepsis, pneumonia, and diarrhoea) during the first 60 days of life (personal communication).<sup>8</sup> The reported reductions in late-onset sepsis caused by probiotic supplementation are probably affected by the gestational age and birthweight of the infants, the local pattern of invasive pathogens, the pathogen's antibiotic susceptibilities, and the type of probiotic strain or strains used.

In view of the global burden of preterm and very low birthweight infants with invasive infection and the increasing numbers of multidrug-resistant microorganisms, probiotics have much potential in resource-poor settings as a simple, safe, and affordable public health intervention. Additional research is essential to address the present gaps in knowledge on probiotics for treating preterm and low birthweight infants, especially in the context of resource poor settings. In view of the cost associated with the import, storage, and distribution of proven probiotic strains, future randomised controlled trials could compare the efficacy and safety of proven strains with that of local