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## Antibiotic prophylaxis approaches for urinary tract infections

Recurrent urinary tract infections among patients using clean intermittent self-catheterisation (CISC) are a major concern, especially in patients with spinal cord injury. In this population, urinary tract infections are the most common cause of morbidity and the second most common cause of mortality.<sup>1</sup> Moreover, the prevalence of multidrug-resistant organisms in patients with spinal cord injury is high, at up to 40.5%.<sup>1</sup> Additionally, diagnosis of urinary tract infection is challenging because urine culture is nearly always positive because of urinary colonisation, and symptoms are often non-specific.<sup>2</sup>

The AnTIC Trial<sup>3</sup> is the first large-scale randomised controlled trial to study a CISC population, with 158 (39%) of 404 patients with neurological bladder dysfunction, comparing prophylaxis with no prophylaxis for recurrent urinary tract infections.<sup>3</sup> In this trial, the investigators showed the efficiency of a daily, low-dose antibiotic treatment (50 mg nitrofurantoin, 100 mg trimethoprim, or 250 mg cefalexin) to prevent urinary tract infections.

Surprisingly, only 76 (37%) of 203 patients in the prophylaxis group and 77 (38%) of 201 patients in the

control group had a positive urinary culture at baseline.

Overall, the investigators found a 48% reduction in frequency of urinary tract infections in the prophylaxis group, with a significant reduction of symptomatic antibiotic-treated urinary tract infections ( $p < 0.0001$ ).

However, considering urinary culture, bacterial resistance was significantly more frequent in this group, especially to three drugs (nitrofurantoin, trimethoprim, and co-trimoxazole).

To address the challenges of antibiotic prophylaxis in individuals using CISC, we did an observational prospective study of 38 patients with spinal cord injuries before and after prophylaxis, to assess the safety and efficacy of a weekly oral cyclic antibiotic regimen with two or three different antimicrobial agents used alternatively at high dose, to prevent urinary tract infections.<sup>4</sup> Over a period of at least 2 years, there was a significant decrease in incidence of urinary tract infections (from 9.4 infections per patient-year to 1.8 per patient-year). Moreover, at inclusion, six (16%) patients were colonised with multidrug-resistant organisms and only two (5%) of them were still colonised after a 2-year follow-up.<sup>4</sup> Another effect we noted was a significant reduction in number of febrile urinary tract infection episodes ( $p = 0.04$ ), whereas the reported strategy by Fisher and colleagues does not reach such an outcome ( $p = 0.24$ ).

We also assessed our strategy after a mean of 63 months of weekly cyclic prophylaxis and confirmed that it did not lead to emergence of bacterial resistance.<sup>5</sup>

Thus, we believe that, when antibiotic prophylaxis is required, a weekly intermittent high dose of cyclic antibiotic treatment is effective and does not engender emergence of resistance. These results should soon be confirmed by the PACHIU trial (NCT01388413).

We declare no competing interests.

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## Enterococcus faecium tolerance to isopropanol: from good science to misinformation

Following the publication by Sacha Pidot and colleagues,<sup>1</sup> alarmist articles appeared in the lay press, including *The Guardian*, *Reuters*, *NBC*, and *The Times*.<sup>2,3</sup> These stories have (probably inadvertently) mischaracterised the study analysis and implied that alcohol-based handrub is becoming ineffective. In reality, alcohol-based handrub is the most effective agent available for hand hygiene and is a key element in infection prevention.

As experts in hand hygiene, we feel these misinterpretations could lower health-care worker compliance



Published Online  
September 4, 2018  
[http://dx.doi.org/10.1016/S1473-3099\(18\)30542-5](http://dx.doi.org/10.1016/S1473-3099(18)30542-5)

with hand hygiene practices and put patients at risk.

The study compared older and newer *E faecium* isolates (obtained between 1997 and 2015) and their tolerance to a 23% alcohol solution, and found that some newer strains were more tolerant to alcohol.<sup>1</sup> Hospital alcohol-based handrub formulations contain 60–90% alcohol. There is no evidence of resistance at these concentrations, thus tolerance to a 23% alcohol solution is not clinically relevant. The study itself states that there was no difference in the bacterial log reduction between human isolates exposed to 70% isopropanol solution (similar to what might be used in an alcohol-based handrub), regardless of those strains' tolerance to alcohol.<sup>1</sup> Hospitals must select high quality, validated alcohol-based handrub formulations and encourage high rates of hand hygiene compliance among health-care workers to lower rates of health-care-associated infections and the spread of antimicrobial resistance.<sup>4</sup>

The study also showed that some alcohol-tolerant vancomycin-resistant enterococci strains spread more quickly to mice than non-tolerant strains after mouse cages were wiped down with an alcohol-impregnated wipe. Hospital environmental disinfection for VRE is a comprehensive protocol, not a quick wipe. Furthermore, alcohol is not recommended for VRE environmental control.

Good research often falls victim to misinterpretation or distortion; if it then generates attention, it can do more harm than good. We tend to blame journalists, but it is worth also looking at the press releases and the journals themselves. In this case, the online version of the article on the Science Translational Medicine website was given the tag line “alcohol loses its luster” as well as a few lines mentioning possible implications for alcohol-based handrub efficacy.<sup>1,5</sup> Furthermore, the press release by the American Association for the Advancement of Science was entitled “Hospital superbugs becoming resistant to

alcohol disinfectants”. These are distorted statements, considering that alcohol-based handrub is on the WHO essential medicines list and saves millions of lives worldwide every year.<sup>6</sup>

Misinterpreting the relevance of laboratory study results can lead to major negative consequences. The road between a bit of sensationalism and full distortion is as dangerous as it is short.

We declare no competing interests.

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## Pakistan's national action plan for antimicrobial resistance: translating ideas into reality

The threat of antimicrobial resistance has appeared as a global health crisis that could lead to 10 million deaths every year by 2050. WHO instituted a global action plan to

tackle antimicrobial resistance in the 68th World Health Assembly in 2015. This global action plan was endorsed by all countries, including Pakistan—the world's sixth most populous country, and which is expected to rise to fourth place by 2050.

The first follow-up action was the development of the National Strategic Framework for Containment of Antimicrobial Resistance, which was translated into the national action plan of Pakistan for antimicrobial resistance.<sup>1</sup> An intra-sectoral core committee on antimicrobial resistance was formed by the Government of Pakistan, with the mandate to identify key stakeholders and experts in policy making, assess the existing status of antimicrobial resistance, prepare a policy document, and provide recommendations.<sup>1</sup> Pakistan also completed the process of joint external evaluation of the International Health Regulations and the global health security agenda for assessment of priority areas for action on antimicrobial resistance.<sup>2</sup>

By participating in the Global Antimicrobial Surveillance System, the Pakistan National Institute of Health is the custodian of antimicrobial resistance surveillance in Pakistan.<sup>3</sup> However, these activities are not prioritised because there are no domestic resources allocated for antimicrobial resistance, and the funding from the health department of Pakistan and donors might not be sufficient. Therefore, WHO's mission report has warned that Pakistan is not completely prepared to detect, prevent, and respond to internal or external health threats that could threaten the country's population, and have the potential to jeopardise travel and trade, because Pakistan is a signatory to the International Health Regulations but is yet to meet the essential core capacities, despite several extensions.<sup>2</sup>

In April, 2018, the Pakistan Global Antibiotic Resistance Partnership launched a *situation analysis report*