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Editorial

Gastrointestinal Infections

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This section contains timely reviews of three topical subjects. The use of probiotics to prevent *C. difficile* infection (CDI) is a controversial area, with conflicting data, and a paucity of robust, controlled, appropriately powered, clinical trials to provide a clear picture. Mills et al examine the evidence for the use of probiotics, including recent clinical trial data and new approaches to microorganism based therapy for CDI.[1] A new systematic review and meta-analysis concluded that probiotic use may reduce the rate of CDI in high risk populations by as much as 50%. Nevertheless, prior clinical trials, and indeed meta-analyses have yielded conflicting results.[3-5] Notably, meta-analyses of the efficacy of probiotics aggregate data from studies employing different microorganisms, formulations and dosages. Furthermore, individual study deficiencies, including some that have high influence on the conclusions of the reviews,[6] are often not addressed. Lastly, the largest randomized controlled trial of a probiotic combination product of lactobacilli and bifidobacteria showed no benefit in the prevention of *C. difficile* infection.[7]

Mills et al. also helpfully review potentially promising new approaches to the prevention of CDI including probiotic and prebiotic combinations, strains that directly inhibit *C. difficile*, modulation of bile acid metabolism to augment colonization resistance, microbiome niche competition, and bacteriophage therapy.[1] In addition, they consider ongoing developmental programmes to produce regulated products, including stool-derived products, purified spore preparations, and sterile fecal filtrates, as alternatives to faecal microbiota transplantation (FMT). The hope is that such products can achieve the efficacy of FMT, without the need to obtain and screen donor samples, and with an improved (long term safety) risk-benefit profile.

Karkey and colleagues, who have considerable experience of working in the developing countries, review the evolution of antimicrobial resistance in *Salmonella Typhi*.[8] They note

that resistance to first and second line antibiotics is common and leads to treatment failure of typhoid. Chloramphenicol was the first widely used antibiotic for typhoid fever, but as resistance emerged to this agent, and to ampicillin and co-trimoxazole, fluoroquinolones became the drugs of choice. In turn, widespread fluoroquinolone resistance has led to increased use of azithromycin and third generation cephalosporins. In turn, reports of resistance to the latter antibiotics are increasingly occurring. Ironically, there is a reversion to chloramphenicol and co-trimoxazole (and now sometimes to fluoroquinolones) susceptibility in *S. Typhi* in some settings. However, a particular concern is the continuing spread of a multi-drug resistant clone of *S. Typhi* (H58, also known as genotype 4.3.1) across and between countries. Hence, the possible role of newer antibiotics and of vaccines gains added impetus.

The third topic in this section is the increasing role of molecular-based assays for the routine detection of gastrointestinal pathogens.[9] These assays permit rapid and sensitive detection of gastrointestinal pathogens, but the significance of some of the positive results, especially for potential as opposed to proven pathogens can be confusing. The absence of defined interventions in many such instances means there can often be questionable value of identifying a possible cause for diarrhoeal or other gastrointestinal symptoms. Crucially, also, assay accuracy, the repertoire and so cost of the target organisms, and workflow considerations mean that there is not a one size fits all solution for these molecular detection panels. Clearly, thorough evaluation of these is needed to determine their cost-effectiveness, and thus whether/which panels can replace conventional enteric microbiological methods. Notably, the ability to detect hitherto 'missed' possible causes of gastrointestinal infection may revolutionise the surveillance of these frequents causes of morbidity across both developing and developed countries.

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