

Out of Hours

Dangerous Ideas:

resistant superbugs and the potential of the microbiome

The Society for Academic Primary Care invited submissions of 'Dangerous Ideas' at its annual scientific meeting in July. This article is the first in a short series of the best of these.

When the Chief Medical Officer, Sally Davies, talks about a 'ticking time bomb' and the Prime Minister, David Cameron, warns us of the dangers of going back to 'the Dark Ages', you know that the problem is serious. Both were referring to the global threat of antibiotic resistance.

Antibiotic resistance is increasing. There are sufficient tales from secondary care to remind us of the doomsday scenario when antibiotics might lose all potency against invading bacteria. In intensive care, the emergence of gram negative septicaemias resistant to the last effective antibiotics, the carbapenem group, has caused considerable alarm.¹ In a military setting, multidrug resistant skin infections in healthy army recruits have become a serious concern, sometimes resulting in amputations.²

The rise of antibiotic resistance is real. Increasingly the discussion turns to the unnecessary prescribing of antibiotics in general practice. We know that many consultations for acute self-limiting infections, mostly viral, result in a prescription for an antibiotic; also that high volumes of antibiotic prescribing are associated with community and individual resistance. In spite of the concern about emergent resistance, other factors in primary care continue to drive antibiotic prescribing, including perceived demand from patients and the expectation that antibiotic prescription will shorten consultations.³

Yet curiously, antibiotic-induced resistance attenuates over time.⁴ For the first few months after taking an antibiotic, urine infections are five times more likely to be antibiotic resistant. Within 6 months of taking an antibiotic, the rate of resistance reverts to pre-treatment levels.

What drives this reduction of resistance? It is probable that these emerging resistant organisms lack reproductive fitness or are unable to find a sustainable niche in the bowel microbiome. A process of decolonisation takes place as antibiotic-sensitive organisms displace their resistant counterparts.⁵

Role of the microbiome The microbiome is the term used to describe the ecological

community of microbes found in body spaces that communicate with the outside world, primarily our gastrointestinal tract and our skin. More than 10 000 species of bacteria live in and on the human body. Bacteria constitute 60% of the dry weight of our faeces. Many functions have been ascribed to the gut microbiome including a role in protecting us from obesity, metabolic syndrome, and even mental health conditions.⁶

Interest has been sparked in the protective role of the microbiome following the observation that 'faecal transplant' (the introduction of dilute faeces either through a naso-jejunal tube or a colonoscope) is an effective treatment for multidrug resistant *Clostridium difficile* infections.¹¹ Recolonisation by healthy commensal organisms displaces the pathogenic *C. difficile* bacteria.

The 'Krapsole' How can we harness the potential of the microbiome? First we should minimise the collateral damage to the microbiome which results from avoidable or inappropriate treatment with broad-spectrum antibiotics.

Secondly if faecal transplant is so effective for multiresistant *C. difficile* infections, might it work for other resistant infections? Faecal transplant has inherently repulsive aesthetics. Could the essence of the microbiome's defence capability be captured through selectively-developed cultures?⁷ Or could the current interest in probiotics be redirected to develop cultures which restore healthy microbiomes, maximising their potential to displace resistant organisms? Or could the microbiome be captured within a capsule to deliver the healthy commensals directly into the small intestine: a mode of administration which could be termed, the 'Krapsole'?⁸

And so, the dangerous idea? We need to overturn the century-old idea in medicine that bacteria, as the source of infectious diseases, are always bad. This means we should refocus the debate about antibiotic stewardship away from the concept of antibiotics as a threatened resource and instead recognise the potential of the microbiome in all its diversity to contain bacterial resistance. This could mark the beginning of a new appreciation of the value of bacteria, both in terms of keeping healthy, and in curtailing the rise of antibiotic resistance.

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