By Dr Hsu Li Yang, Editorial Board Member

Antibiotics Commoditised

In my line of work, I have had colleagues voluntarily step up to talk to me about their (or their relatives') infections. In the past year, a new and disturbing trend has emerged. One colleague described having a urinary tract infection (UTI) as – "one of the most painful experiences in that person's life" – that did not resolve with oral antibiotics. The perpetrating bug? A common garden variety *Escherichia coli* that was resistant to ciprofloxacin and produced extended-spectrum beta-lactamase (ESBL – therefore resistant to practically all penicillin and cephalosporin antibiotics). Another colleague mentioned a case of severe UTI occurring in his child. This time, the infection was caused by a *Proteus mirabilis* (another bug that commonly causes UTI's) that was resistant to commonly used oral antibiotics.

Are these the result of people bringing back bugs from the hospital and failing to bathe properly? Unfortunately, this comforting assertion of laying sole responsibility on a few errant unwashed colleagues is both dangerous and wrong. Antibiotic-resistant bacteria are not just confined within hospital walls, but are out there in the community and the number and variety of such bacteria is increasing with time. A 2007 study from Tan Tock Seng Hospital highlighted that up to 12% of emergency department attendees – the majority of whom had no previous hospitalisations – carried ESBL-positive gram-negative bacteria in their gut. The only risk factor associated with this phenomenon? Recent consumption of oral antibiotics prescribed by general practitioners (GPs)[1].

Of course, GPs over-prescribing antibiotics is not the main cause of this rising problem of drug-resistant bugs. More prevalent than human antibiotic abuse is the use of antibiotics as growth promoters in animal husbandry. This has led to an increase in the prevalence of antibiotic-resistant bacteria in uncooked meat and dairy products, and it is well known that once these bacteria get into our gut, even if they do not cause any infection, they may pass the genetic determinants for antibiotic resistance to other gut flora. When antibiotics are commonly prescribed in the community, there is an ecologic pressure that keeps these antibiotic resistance determinants (or the resistant bugs themselves) in circulation.

A somewhat similar situation is present in local hospitals. It is not uncommon for patients hospitalised after office hours to receive antibiotics, regardless of whether there were clinical grounds to suspect a bacterial infection. One colleague complained that during his morning ward rounds he would find patients who received intravenous ceftriaxone (Rocephine – a 3rd generation cephalosporin) for migraine, heart failure and upper respiratory tract infections (URTIs). More commonly, doctors do not switch to narrower-spectrum antibiotics once culture results are available – "let's not change what is working" is the common mantra – or stop antibiotics after an appropriate period of therapy. This widespread broad-spectrum antibiotic pressure also contributes to the maintenance of multidrug-resistant bacteria in the hospital setting.

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Recently, in the midst of a *har cheong gai* (deep fried, therefore theoretically having lower risk of drug-resistant bugs) and XO fish beehoon lunch, the talk turned to antibiotic prescription by GPs. "It is difficult," declared my friend, who occasionally moonlights as an ED physician and a GP. "Many patients with URTIs ask for antibiotics. If it is my own patient, then I will usually counsel them. If it is one of my partners' long-term patients, then I will probably just prescribe. Can afford to lose my own patient, but not my partners', you know." Meditatively chewing on a chicken wing, he expounded further, "Of course, it also depends on the queue. If there are many patients waiting to be seen, then I am sorry – no time to talk through these things. Easier to just prescribe and clear the backlog." What about the ED, I wondered. "Some patients get very upset if we don't prescribe antibiotics. If I know the senior ED physician is strict about antibiotic prescribing, I will refer them up. If not, then why waste time? Just prescribe *lor*."

We soon moved on to other more interesting topics. But that bit of the conversation stuck with me. This friend was just describing the realities on the ground. It is not just about educating doctors to prescribe antibiotics judiciously – probably all doctors already know that antibiotics are useless in viral infections, and that three days of oral antibiotics are adequate for the majority of cases of uncomplicated cystitis. Harping on it repeatedly is unlikely to improve their knowledge or compliance – there are other external and more compelling factors that hinder doctors in actual clinical practice with regards to prescribing antibiotics in any case. Some are detailed in the conversation above. Others are more insidious.

Doctors are trained to do their best for their patients at the present time. There are almost no doctors who will under-treat their patients in the here and now for a nebulous future's communal good – and that is only right and proper. However, the problem is that what is considered "under-treatment" tends to be subjective. I once received a call from a private oncologist for a curbside consult: his patient was still having a high fever after a single day of hospitalisation. What antibiotics was he on, I wondered? Vancomycin, meropenem and bactrim (in case there was pneumocystis pneumonia) – and he was contemplating throwing in an antifungal agent as well. Had the patient been in any hospital recently? Not really – just outpatient visits, and he wasn't neutropenic. I tried to rationalise the antibiotic selection, but I am not so sure he took my advice.

My former boss and mentor, the esteemed Dr Tan Ban Hock (now Head of Infectious Diseases at the Singapore General Hospital), once shared an insight with me that underlined a cultural perspective among hospital doctors. During mortality meetings, senior physicians would occasionally take their juniors to task if antibiotics were not prescribed (or if narrow-spectrum antibiotics were prescribed), but they would be satisfied if a broad-spectrum antibiotic was prescribed, even if the infection (such as it was) was caused by a very susceptible organism. The more "powerful" the antibiotic, the better. Medico-legal concerns, albeit not as rife as in the US, also appear to be part of the decision-making process for withdrawing or prescribing antibiotics.

Are there other factors that may affect the decision-making process in both primary and hospital settings? Unfortunately, financial remuneration has been shown to be one such factor in other countries – in Taiwan, for example, GPs with on-site pharmacies or those who derived a significant proportion of their revenue from the sale of medications were more likely to prescribe antibiotics for the common cold[2]. No such data is available in Singapore, but anecdotally, such inappropriate prescriptions are not unknown. Another factor is the influence of the pharmaceutical industry. Drug representatives trawl the corridors and clinics of hospitals while others visit the GP chains and clinics, distributing the latest papers that support their product(s) along with office mementos and pens. Most of us doctors would like to think we are immune to these and other more expensive blandishments, but we can be considered delusional in this instance[3].

So what can we do to improve the situation? My colleagues and I recently published a position paper with several recommendations (note: this is not a shameless plug for the paper!) and "motherhood statements" in the SMJ after analysing the local situation from different perspectives[4]. Clearly, a broader approach is required rather than just focusing on hospitals or GPs trying to make ends meet in the heartlands. The public at large will need to be educated (and

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re-educated) in order to reduce the "demand" for antibiotics, better training will have to be provided for our junior doctors and medical students, and the pharmaceutical industry should be regulated (by self or otherwise) more strictly. Some developed countries have been successful with such strategies, so while these are not easily implemented solutions, they are not quite "moonshine" either. The alternative scenario is worse.

Antibiotics revolutionised medical care in the last century, and remains an integral component in the development of any therapy where the human immune system is deliberately breached or weakened to effect cure or control of disease, including surgery and cancer treatment. The rise of antibiotic resistance and the shrinking pharmaceutical antibiotic development pipeline have tarnished the miracle that they once represented. Antibiotics have become the quintessential commodity in health care – unless used wisely and preserved (but not "mothballed" to the extent that the already waning interest of the pharmaceutical industry will be further dampened), they may soon become as worthless as Lehman mini-bonds. And to stretch the abused analogy, no amount of picketing at Hong Lim Park will reverse the situation. ■

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