This is the end: our post-antibiotic world

Since the dawn of the antibiotic age, we knew the end would come.

In the 1930s, the serendipitous discovery of penicillin provided clinicians with a powerful weapon to combat previously fatal illnesses. Antibiotics became household drugs. Yet our cavalier use of these key weapons are facilitating the development of antibiotic resistance. In medicine, some estimate that in the US 50% of prescribed antibiotics are squandered on viral infections and other cases where they are not needed, or ineffective as prescribed1. Outside the clinics, over 75% of antimicrobials in Canada are used in agricultural animals to stimulate their growth and prophylactically guard against infections2, which may help breed drug-resistant strains that are infectious to humans and much harder to treat.

Antibiotic resistance is growing at an alarming rate and the public health consequences are dire. Globally, in 2011, 3.7% of new cases and 20% of previously treated cases were estimated to have multi-drug resistant tuberculosis (TB). Our “last line” antibiotic defenses – such as ciprofloxacin for *Shigella* or cephalosporins for *Neisseria gonorrhoeae* – are crumbling in the face of rapidly developing resistance3. In 2013, the World Health Organization issued an urgent warning over Carbapenem-resistant *Enterobacteriaceae* (CRE), which are resistant to nearly all antibiotics we have today2.

Adding fire to the flame, the antibiotic development pipeline has slowed to a trickle. To engineer novel classes of antibiotics that are unfamiliar to microbes, pharmaceutical companies need to rely on rational drug design, an endeavor with an estimated $1 billion price tag4. Furthermore, antibiotics are simply not profitable.

Since they cure the root of the disease, they are not suitable for long-term use. Once a new antibiotic hits the market, resistance rapidly develops and may render the drug ineffective in a few years. Even a truly innovative class of antibiotics may not sell: health care professionals may save them as a last resort for multi-drug resistant cases – a good practice for medicine, but certainly not one for business. In 1999, Roche, Lilly, Abbott and Bayer pulled out of antibiotic research. In 2004, only five new antibiotics were under development, in stark contrast to four new drugs for eretile dysfunction5. As recently as 2011, Pfizer closed down its main antibiotic research division6.

Is the post-antibiotic era inevitable? The answer is hopefully no, but not without global cooperation and an attitude change towards our use of antibiotics. In this regard, Canada has been vigilant in government regulations of medical and agricultural antibiotic use. First established in 1994, the Canadian Nosocomial Surveillance Program (CNISP) surveys *CPE* and other infections from 54 sentinel hospitals spread across 10 provinces, which provides a framework for developing national guidelines for sustainable antibiotic use in medicine. The Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) compliments CNISP and monitors antimicrobial use and resistance across the food supply chain. These and other international efforts continue to provide useful information about emerging resistance, outbreaks and their impact on public health2, and they need to be sustained.

An alternative strategy is to spur the development of novel antibiotics. The GAIN (Generating Antibiotic Incentives Now) Act in the United States was enacted in 2012 to incentivize and accelerate approval for antibiotics development. Last year, Roche invested up to US$550 million dollars to develop macrocyclic peptidomimetic antibiotics against *Pseudomonas aeruginosa*6. This January, AstraZeneca and Sanofi each partnered with biotechnology companies to identify and optimize novel naturally occurring antimicrobial compounds6. This is not a fast fix – drug leads often require over a decade to go from concept to market7. In the meantime, perhaps the most important intervention is to educate both medical professionals and the general public in antibiotic use. It is time to treat them with respect.

References:

[1] Centers for Disease Control and Prevention. Antibiotic resistance threats in the United States [Internet]. April 23, 2013. Available from: <http://www.cdc.gov/drugresistance/threat-report-2013/pdf/ar-threats-2013-508.pdf>

[2] Public Health Agency of Canada. Antimicrobial Resistance – A Shared Responsibility [Internet]. October 23, 2010. Available from: <http://www.phac-aspc.gc.ca/cphorsphc-respcacsp/2013/resistance-eng.php>

[3] World Health Organization. Antimicrobial resistance [Internet]. May, 2013. Available from: <http://www.who.int/mediacentre/factsheets/fs194/en/>

[4] McKenna M. Imagining the Post-Antibiotics Future. Medium [Internet]. February 10, 2014. Available from: <https://medium.com/editors-picks/892b57499e77>

[5] Spellberg B, Guidos R, Gilbert D, Bradley J et al. (2008). The Epidemic of Antibiotic-Resistant Infections: A Call to Action for the Medical Community from the Infectious Diseases Society of America. Clin Infectious Diseases, 46(2), 155-164.

[6] News and Analysis (2014). An Antibiotic Comeback? Nature Reviews Drug Discovery 13, 165.

[7] Kaitin KI (2010). Deconstructing the Drug Development Process: The New Face of Innovation. Clin Pharmacol Ther, 87(3): 356-361.