Our Dwindling Miracle of Antibiotics

Every antibiotic use helps destroy a miracle by breeding resistance

AND also alters the composition of our vast microbial microbiome

Both have substantial future adverse health outcome effects for us all

The World Health Organisation warns that **a "post-antibiotic" era is rapidly approaching** in which common infections can no longer be treated with tried and trusted antibiotics, turning the clock back to a time when even a slight cut or graze might prove fatal.

> ***"Antimicrobial resistance is not a future threat looming on the horizon. It is here, right now, and the consequences are devastating"*** - Margaret Chan, Director-General of the World Health Organisation

> ***"Antibiotic resistance has been described as a ticking time-bomb"*** - Dame Sally Davies, the UK Chief Medical Officer. She added that it posed a "***catastrophic threat***" on a par with terrorism and climate change, only sooner.

Prior to antibiotic discovery most bacteria were fully susceptible to all antibiotics.
Now even common bacterial species (e.g. *Staph aureus*, MRSA) are not only rapidly becoming resistant to 'standard' antibiotics but also many are also becoming resistant to 'top shelf intravenous' antibiotics (e.g. *E. coli* multi resistant ESBL and CRE forms).

Infections have two main sources:

1. **Exogenous infections** – those microbes which we catch from **other people**. Many of these are viral and can be vaccinated against (e.g. mumps, measles, rubella, hepatitis B, influenza, etc) but there are also other viruses for which there is no vaccine (e.g. Norovirus, hepatitis C, HIV, colds, etc).
   In addition exogenous bacteria which are mainly but not all food poisoning (e.g. *Campylobacter, Salmonella*) but also other non food poisoning e.g. *Clostridium tetani*, *Mycobacterium tuberculosis*, etc.
   Also there are the newly emerging exogenous infectious diseases - 335 emerged globally in humans between 1940 and 2004 e.g. SARS, Dengue, Ebola, Zika - although these are generally **comparatively uncommon** in our region these have **ongoing high media profile**, and so increase our historical fear of microbes and help confirm our belief that
   'all microbes are bad and should be avoided and/or treated'

2. **Endogenous infections** – those microbes mainly bacterial (e.g. *Staph aureus, E. coli, Klebsiella, Strep, Pseudomonas*) which **are part of our normal microbial pasture**, in us (gut, mucosal surfaces) and on us (skin). Each of us has a microbial pasture of about **90 trillion bacteria**, our **'microbiome'**, compared to only about 10 trillion of our larger size human tissue cells. Because of this vast number, **'my bugs are your bugs'** – we cannot but help but share them in any community. Occasionally when our tissue cells are compromised (e.g. skin ulcer, cut, wound, eczema, dermatitis) a tiny part of our normal microbial pasture (e.g. *Staph aureus*) finds it has no competing microbial flora to suppress its numbers anymore, so its numbers multiply and overcome our immune system at that site, and that is what we now call a 'clinical infection' – which has emerged from ourselves, from **our own normal good healthy protective pasture**.

When any infection is treated with an oral antibiotic, it generally still works like a miracle, although we are increasingly relying on higher level antibiotics as our routine first line. And there are almost no new antibiotics being added to our total available antibiotic resource i.e**. this precious, limited, antibiotic resource is running out**.

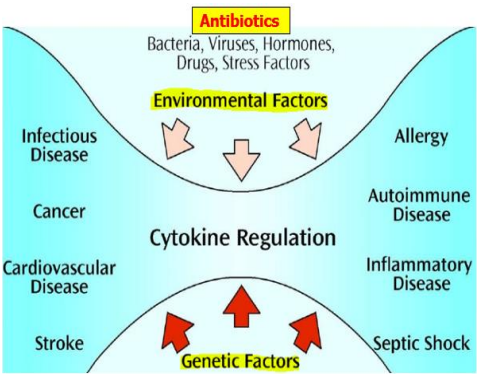
For instance, all *Staph aureus* worldwide used to be susceptible to penicillin as first line, now 90% are resistant. So we now commonly use flucloxacillin as first line instead, **but** from all routine community isolates of *Staph aureus* infections (which people have caught from themselves) 5 of every 100 (5%) are now MRSA positive in the South Island, 8% MRSA positive in Wellington community, 13% MRSA positive in AKL community, 24 % MRSA positive in SE Asia community.
And the bowel flora source infections e.g. *E. coli* (resistant form ESBL, CRE) are becoming much more resistant and much faster globally. We are increasingly isolating essentially antibiotic untreatable infections (e.g. UTIs, ulcers).

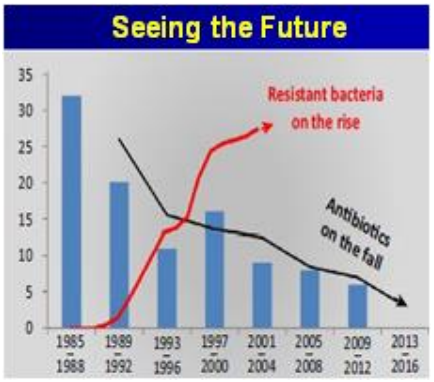
Every use and prescription of antibiotics is having the combined effect of breeding this increasing resistance to the increasing concern and detriment of all future patients in the community.

Collateral antibiotic resistance damage

So every antibiotic use not only selects for resistance amongst the millions of bacteria from the identified pathogen at the site of infection by killing only the susceptible bacteria present allowing any resistant ones to increase in number, but when provoked by any antimicrobial, bacteria have the ability to switch on genes in their chromosomes when they are induced to do so by this antimicrobial provocation. So bacteria that were initially susceptible can then become resistant by a different provoked induction process. And these resistances, often multiple, can then be horizontally transferred (often by a plasmid genetic DNA structure) to other susceptible bacteria of the same species or different species, both pathogens and non pathogens for future sharing by them.

So every antimicrobial use, especially oral use because of the vast microbial numbers in our bowel flora, not only kills all the susceptible bacteria targeted at the infection site, but also all the susceptible bacteria from our entire 90 trillion microbiome that it has contact with – the collateral damage resistance.





Our Microbiome

And we used to think emerging multi drug resistant organisms (MDROs) that we are creating were the worst part. But now we know an even larger significant secondary harm to our good health is our ongoing manipulation of our at least 500 - 1,000 bacterial species in us and on us, all present in a complex harmonious, symbiotic relationship – similar to a complex ancient jungle. What we feed this established jungle (our diet) can somewhat alter its composition, but what we 'defoliate' it with (e.g antibiotics, similar to Agent Orange and DDT) has a massive effect, often from which it never fully recovers. Humans only have half the bacterial species diversity compared to pre antibiotic use. We are just starting to realise the huge beneficial health effects of an 'untouched microbial jungle' on us, but the medium to long term ill effects of our microbial jungle that has been adversely manipulated (e.g. especially by any antibiotic use) – when this 'jungle' is perturbed there are increasing strong correlations and evidence of this causing many other significant adverse health parameters including, but not limited to:

- **Obesity, diabetes**
- **Eczema, dermatitis, asthma**
- **Moods, behaviour**
- **Autoimmune illnesses including Crohn's disease, irritable bowel disease and syndrome, multiple sclerosis, arthritis**
- **Colorectal cancer**

Summary

- Every antimicrobial use helps breed microbial resistance, which is shared in the greater community and affects future antibiotic treatment availability and options
- Our amazing miracle of antibiotics is increasingly being squandered by our over use of them
- Most light to moderate bacterial infections will resolve by themselves without any antibiotic treatment, so consider monitoring these infections and only antibiotic intervention if clinically worsening. Infection resolution may take longer, but the short term benefits (less MDRO breeding) and long term benefits (antibiotics available for us all for longer, **and** less microbiome perturbation diseases) are well worth it
- We are microbial farmers of our complex microbial ecosystem – there is a rapidly increasing realisation of the significant adverse health effects of disturbing this ecosystem. Somewhat similar to DDT killing mosquitoes (malaria, dengue, zika benefits) but major secondary long term damage (insects, birds, fat accumulation, poor decomposition in the environment, genetic damage, etc)
- Infection – before treating with antibiotic always ask yourself: **"Is this serious enough to definitely require antibiotics? Are you certain? Is topical antisepsis an option? And/or monitor and review**??"

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