Antibiotics: A Double Edged Sword

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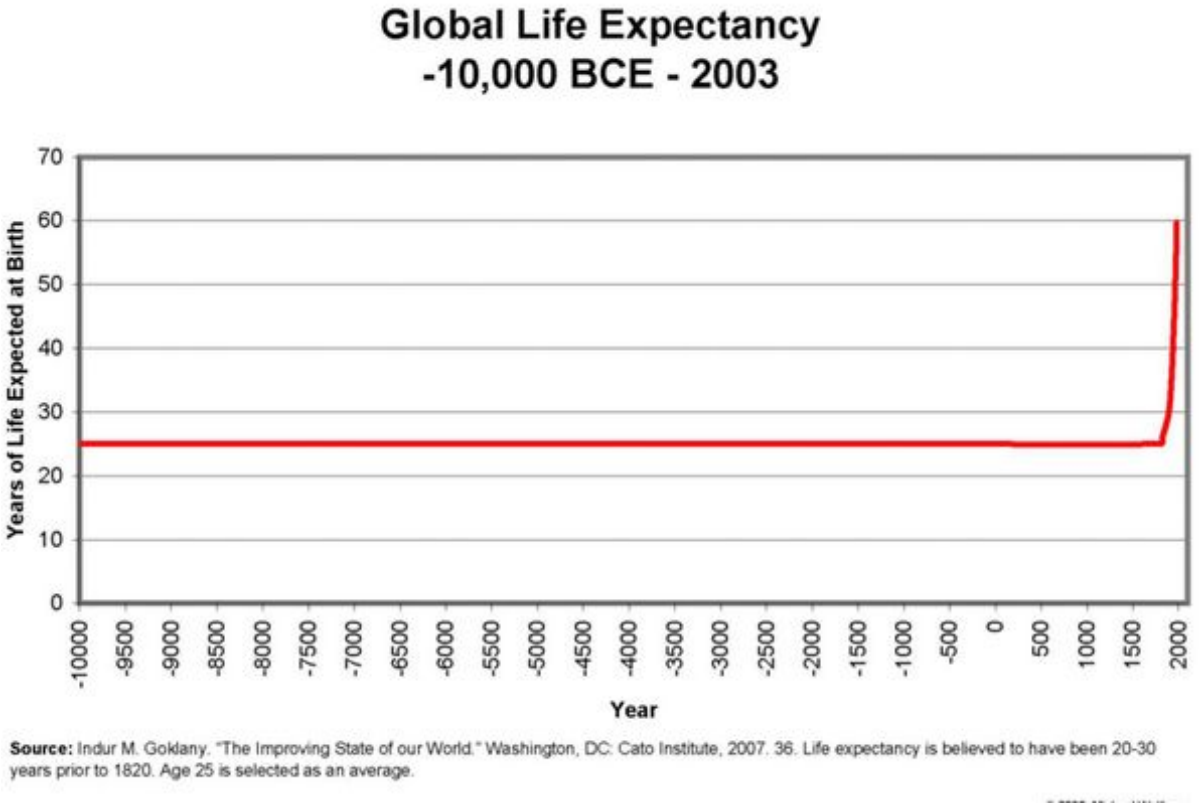
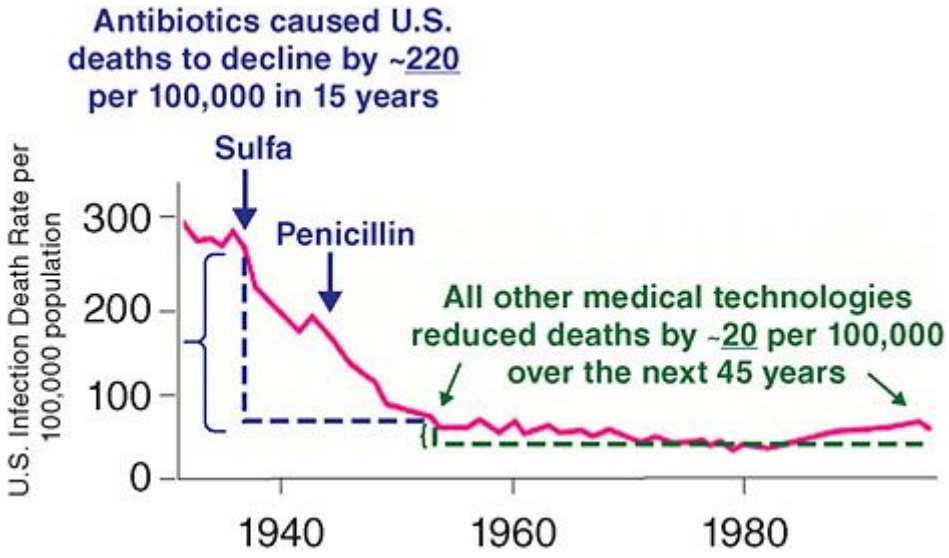
Believe it or not, your life experience is an enormous statistical unlikelihood. If you live in Singapore, your standard of living is almost unprecedented in world history. For example, take a look at life expectancy from 10,000 BC to the present:



Source: Indur M. Goklany. "The Improving State of our World." Washington, DC: Cato Institute, 2007. 36. Life expectancy is believed to have been 20-30 years prior to 1820. Age 25 is selected as an average.

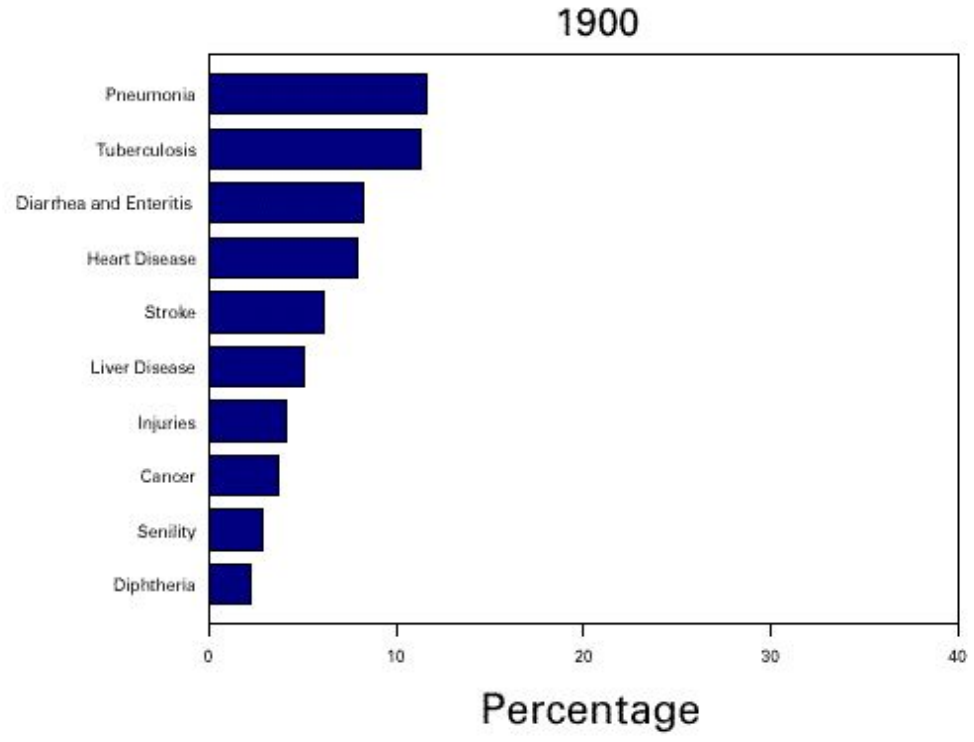
Isn't this amazing? I want to draw your attention specifically to the role of antibiotics. Take a look at mortality rates in the 20th century:

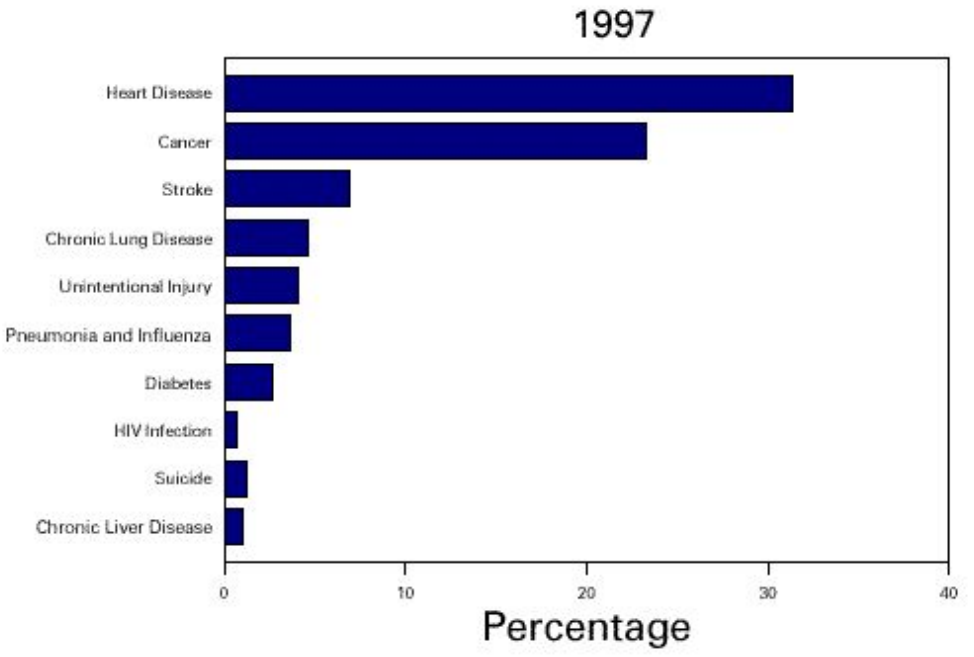


Clearly, the serendipitous discovery and introduction of antibiotics revolutionised the treatment of human ailments. For the first time, an entire class of diseases (those caused by bacteria) could be so effectively and systematically eradicated. One only needs to see the change in perception of these very illnesses to identify the scale of

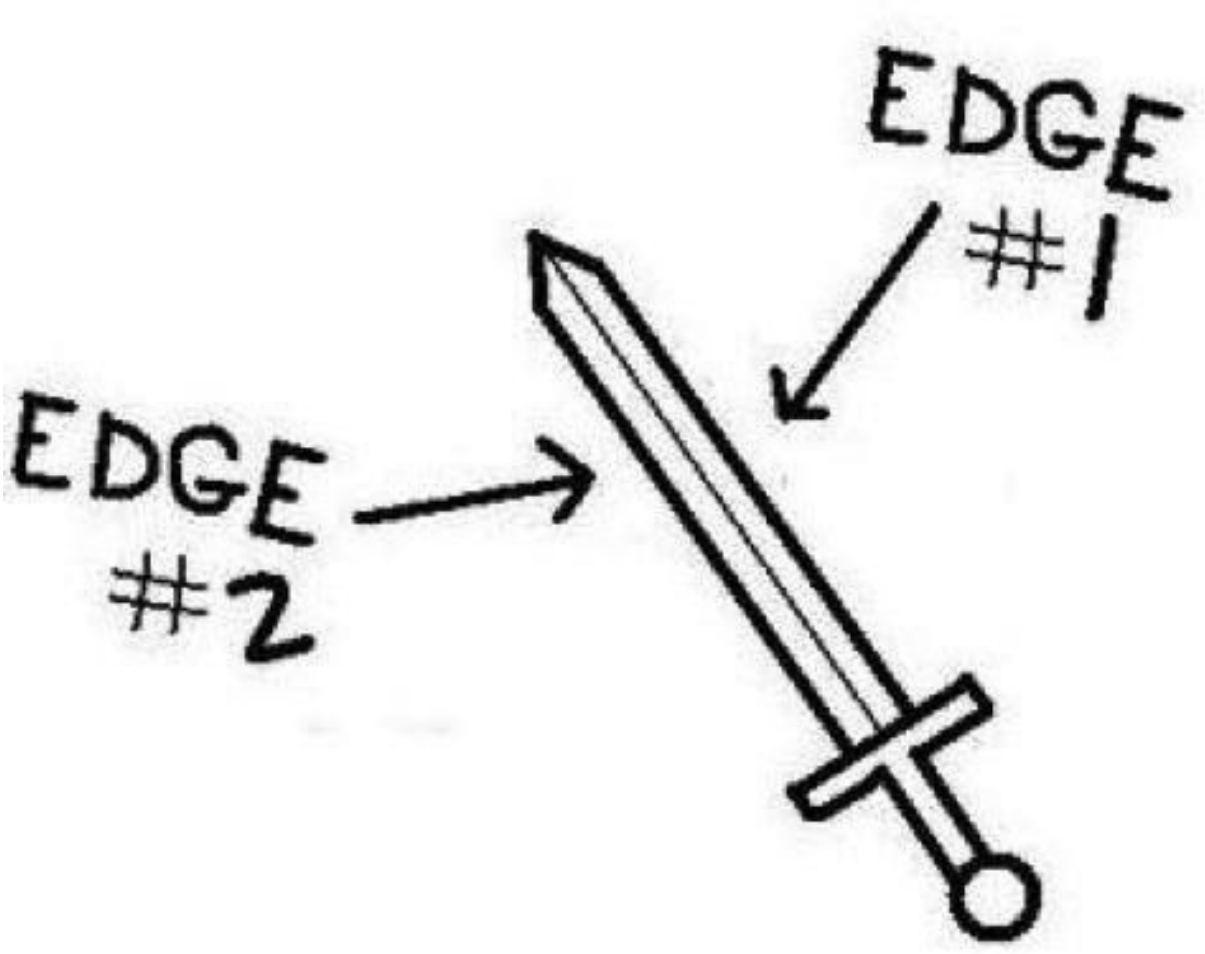
this medical transformation. The spectre of contagious diseases like tuberculosis, cholera, and dysentery that once inspired apocalyptic dread in entire cities is now reduced to the mere inconvenience of a hospital stay. In other words, antibiotics changed the way humanity experienced bacterial diseases, not only physiologically, but also psychologically.

FIGURE 2. The 10 leading causes of death as a percentage of all deaths — United States, 1900 and 1997

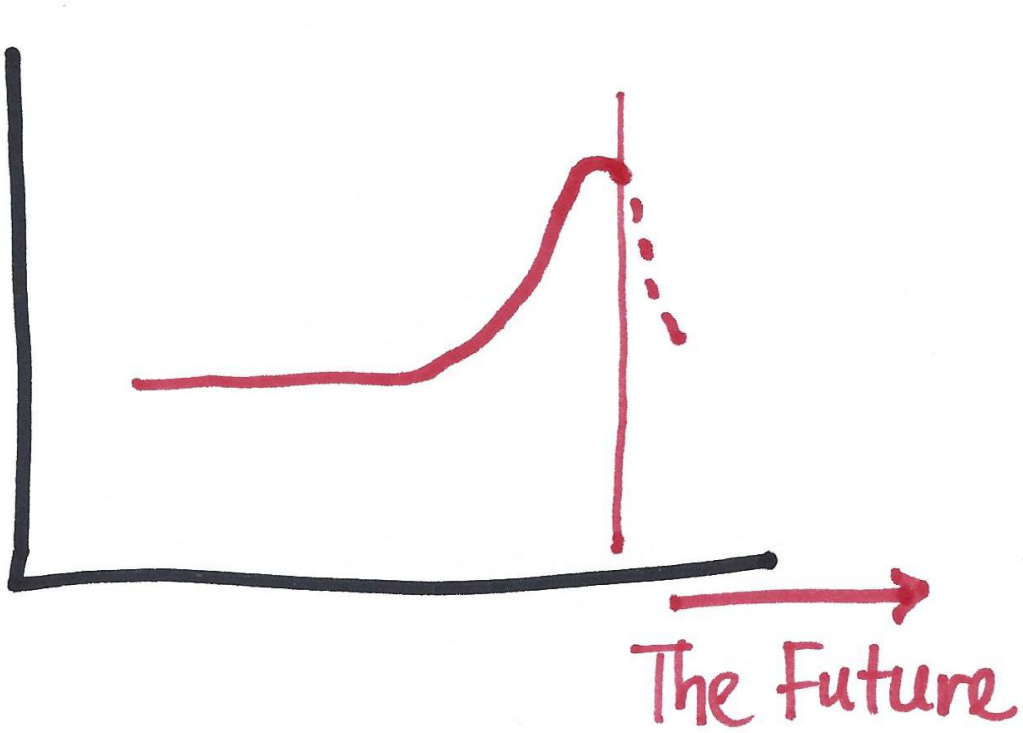




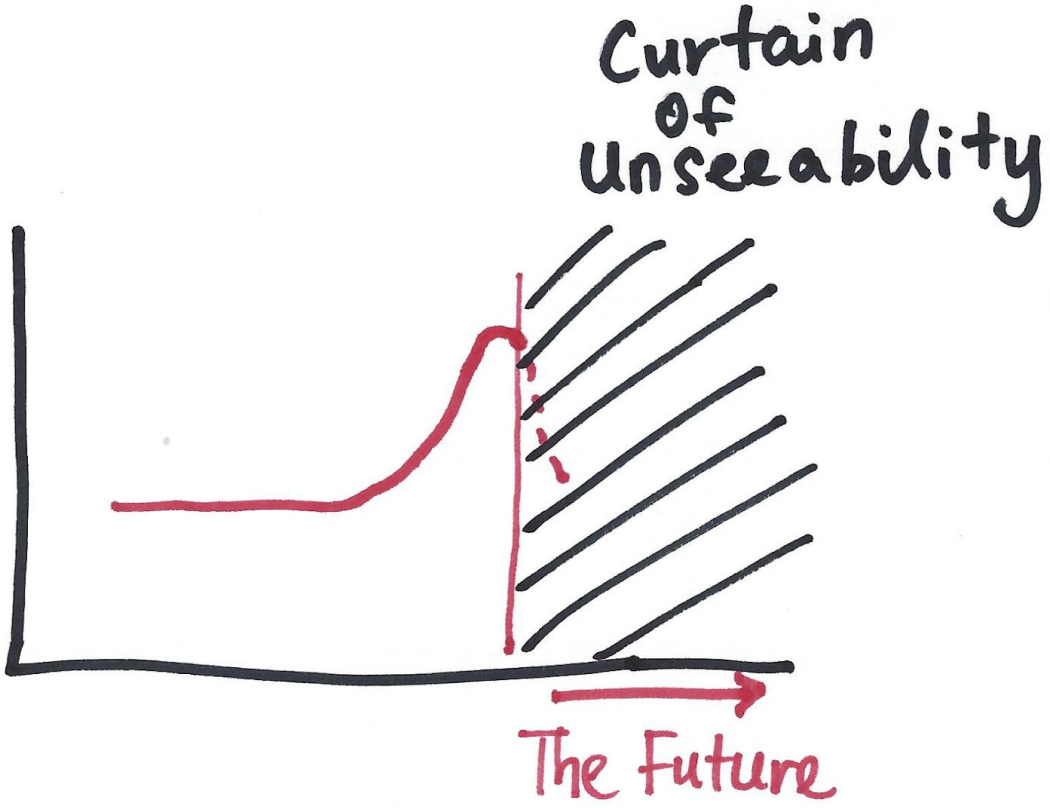
That’s exactly why antibiotics is a double-edged sword.



The unreasonable effectiveness of antibiotics in treating so many diseases has evoked a kind of nonchalance toward these afflictions, rooted in an arguably misplaced trust in the unstoppable progress of medicine in improving our biological standard of living. How would it feel to stand at the edge of, for the first time in human history, a huge step *backwards*?



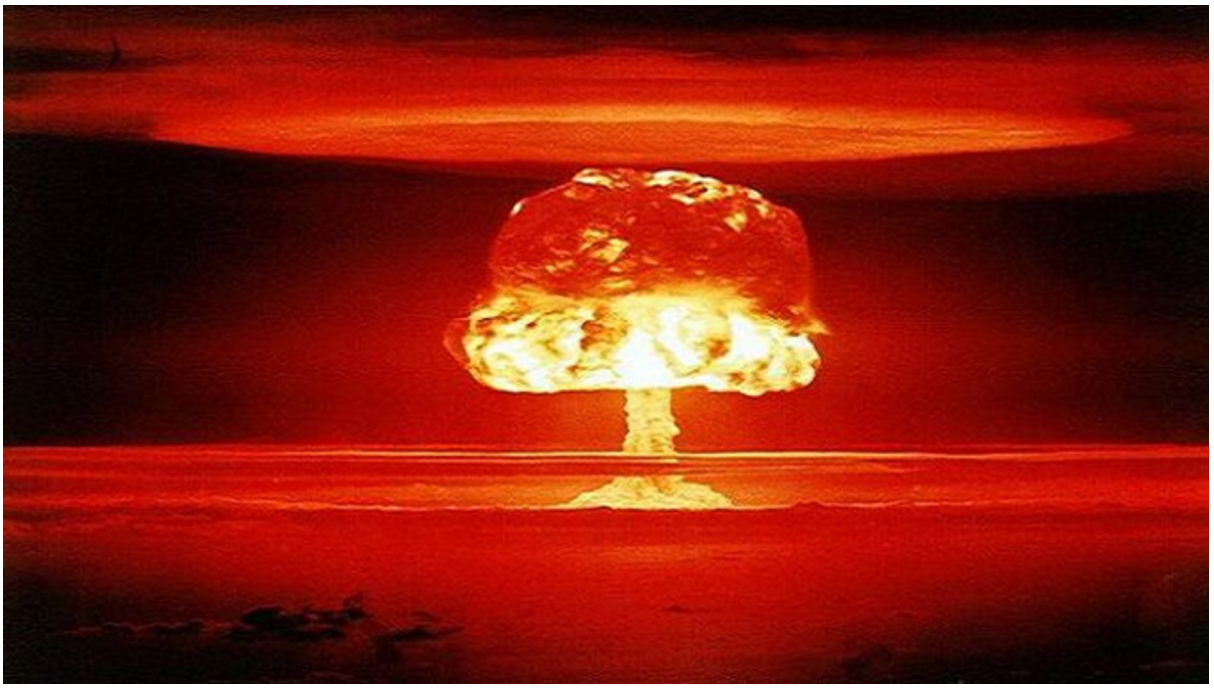
Terrifying, right? Before I explain exactly what this scary dotted line is, and how we might possibly avert this calamitous crisis, here's another question: why doesn't it seem that anyone is alarmed at all? Consider this:



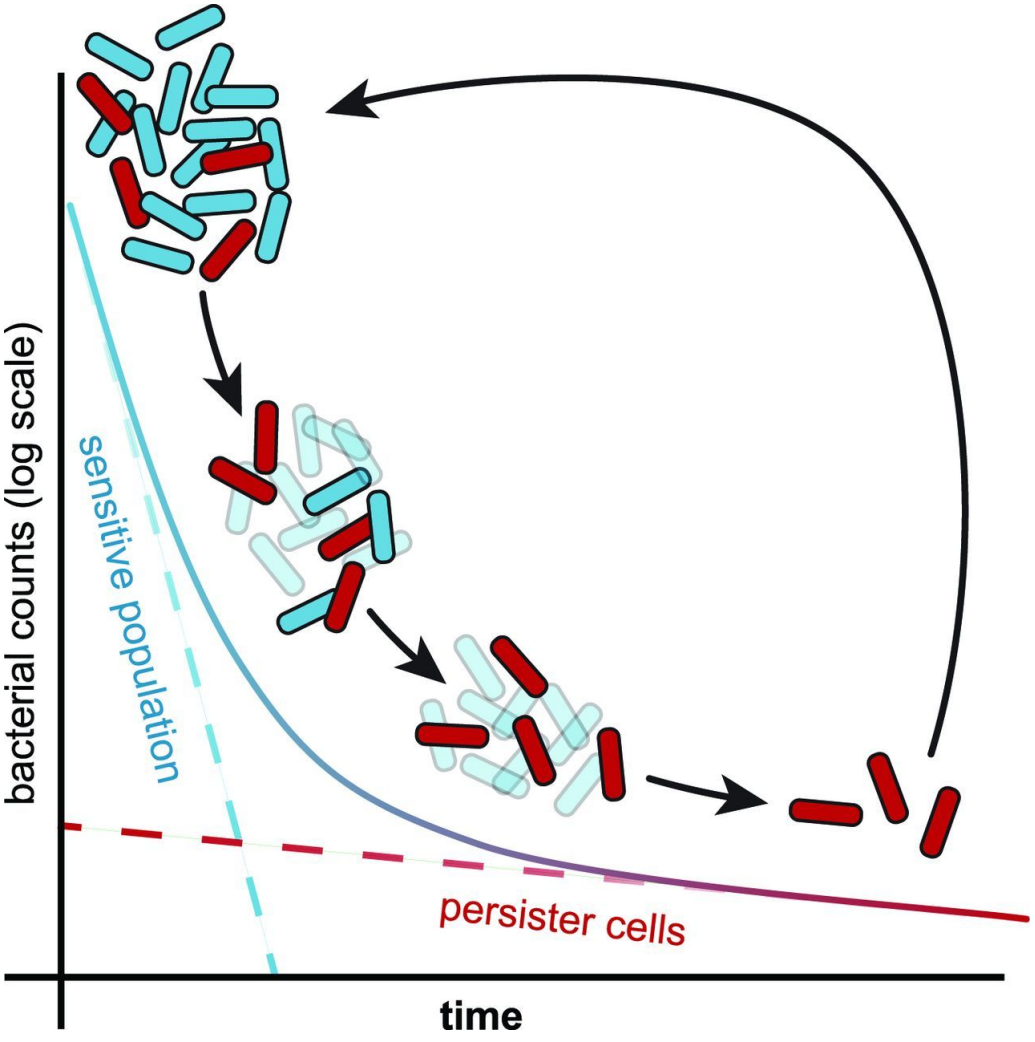
Here is perhaps the most important takeaway: *that what we are most unable to foresee prompts the least significant efforts at prevention*. The false sense of security resulting from the widespread use of antibiotics has lulled humanity into hubristic complacency and inaction. But whatever we have been able to see, we have been able to fight, and for the most part humanity has been able to address most problems once we put our minds to it.

What is antibiotic resistance, anyway?

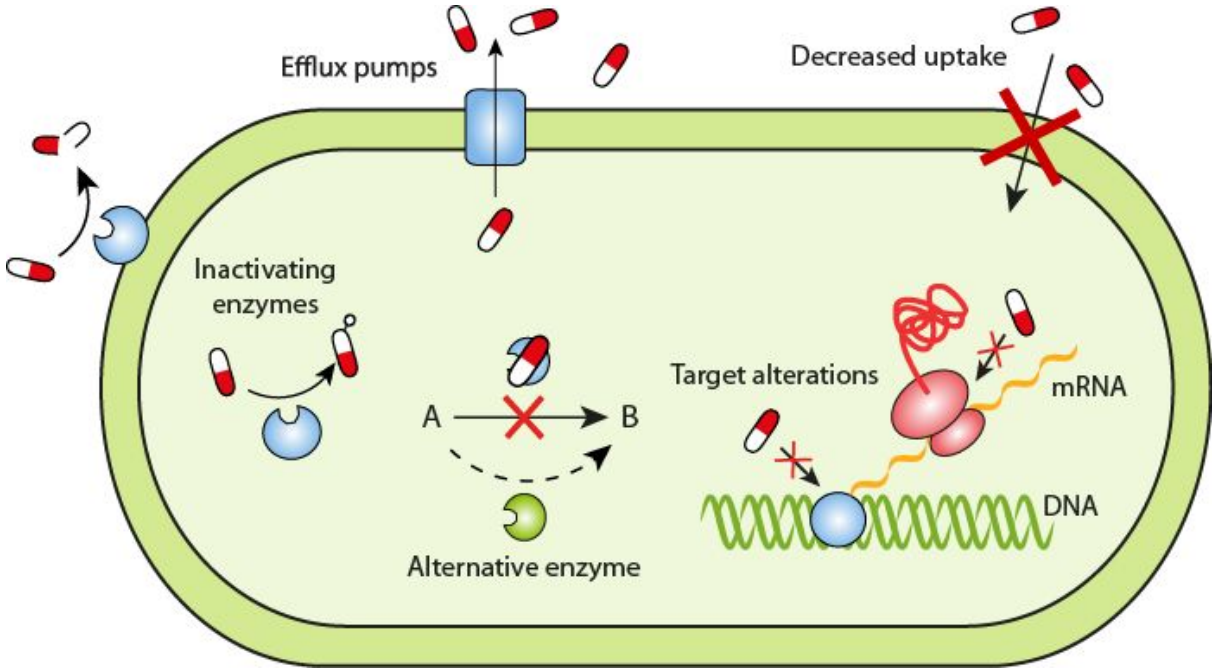
You've probably heard the grave warnings of your doctor to finish your antibiotics course for fear of medical repercussions. The reason for this is simple: *our antibiotics are not infallible*. The truth is, bacteria can become resistant to the antibiotics that are supposed to kill them. Some might understand antibiotics to work like this:



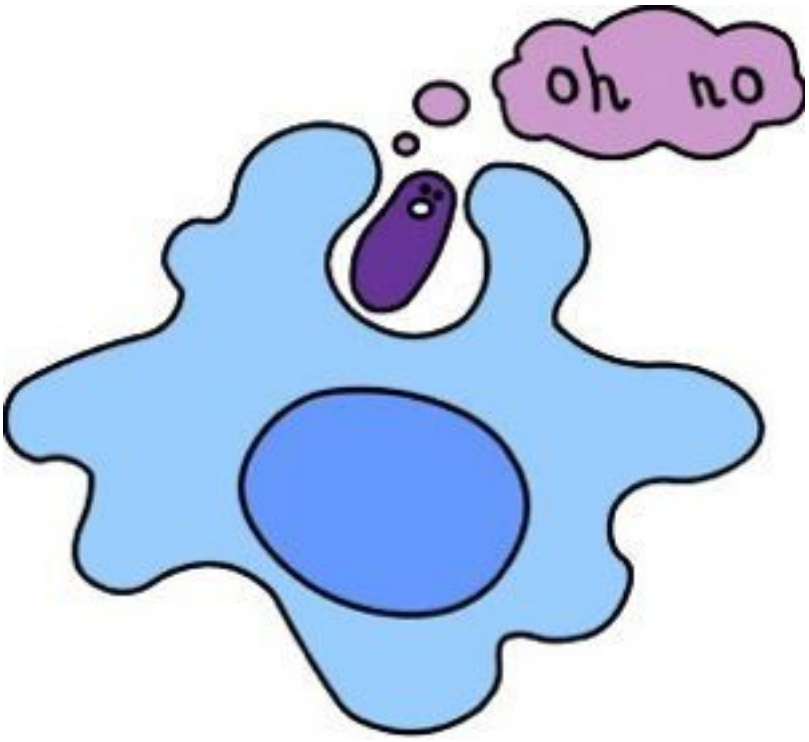
In reality, it works something more like this:



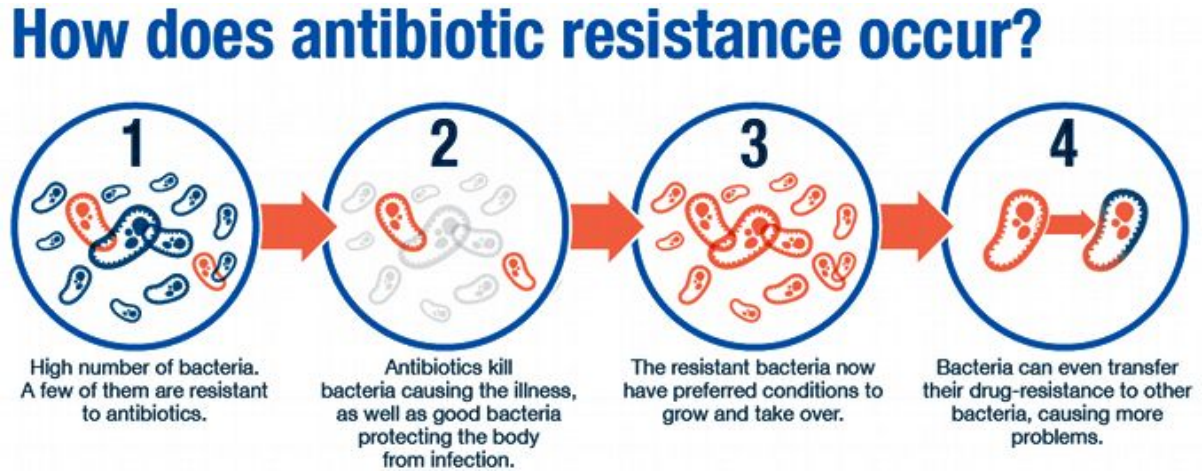
The reason for this random variation is mutation. Because bacteria reproduce extremely fast (some even reproduce once every 20 minutes), there are many avenues for errors in DNA replication that may give rise to mutations. Most are harmful, but because of the sheer number of replications ongoing at any one time in your body, the few beneficial ones almost certainly happen.



Yet one reason why your body is able to still eliminate these persisting bacteria is your immune system, which can still target these bacteria. That's because it works a different way that isn't affected by the resistant mechanism. Additionally, it's good to remember that even the tougher bacteria are only *resistant*, so at prescribed dosages and for a sufficiently long period of time, they can be addressed.



However, what happens if the antibiotics course isn't finished?



Evidently, many resistant bacteria still survive; sufficiently enough to overwhelm the body's defences. Without the weaker bacteria competing for food in Darwinian natural selection, they quickly build up their strength.

What's worse, resistant strains of bacteria can confer resistance to other bacterial species by horizontal gene transfer. Bacteria have circular DNA called plasmids that can be exchanged with other bacteria in a process called conjugation, or are released when they die (and can be taken up by other bacteria).

Right. So what's the problem exactly?

We only have a limited number of antibiotics. In fact, in the case of cephalosporin-resistant gonorrhea, there's only *one drug left* for effective treatment. It's not entirely unimaginable that this might one day be true of more diseases,

including the more commonplace ones like strep throat. And when that day comes, even a simple cut might leave you fighting for your life, but we'll also lose much more: (From WIRED)

- Treatments requiring immunosuppressant drugs (cancer, organ transplants)
- Treatments involving a permanent port into the bloodstream (kidney transplants)
- Open-cavity surgery and implantable devices (knee replacements, heart valves)
- Liposuctions and tattoos
- Safe childbirth
- Cheap food (and the farmer incomes)

For the last item, it's worth pointing out that most livestock and agricultural products can be so cheaply produced because of the use of antibiotics to stem the tide of infectious plant and animal diseases.

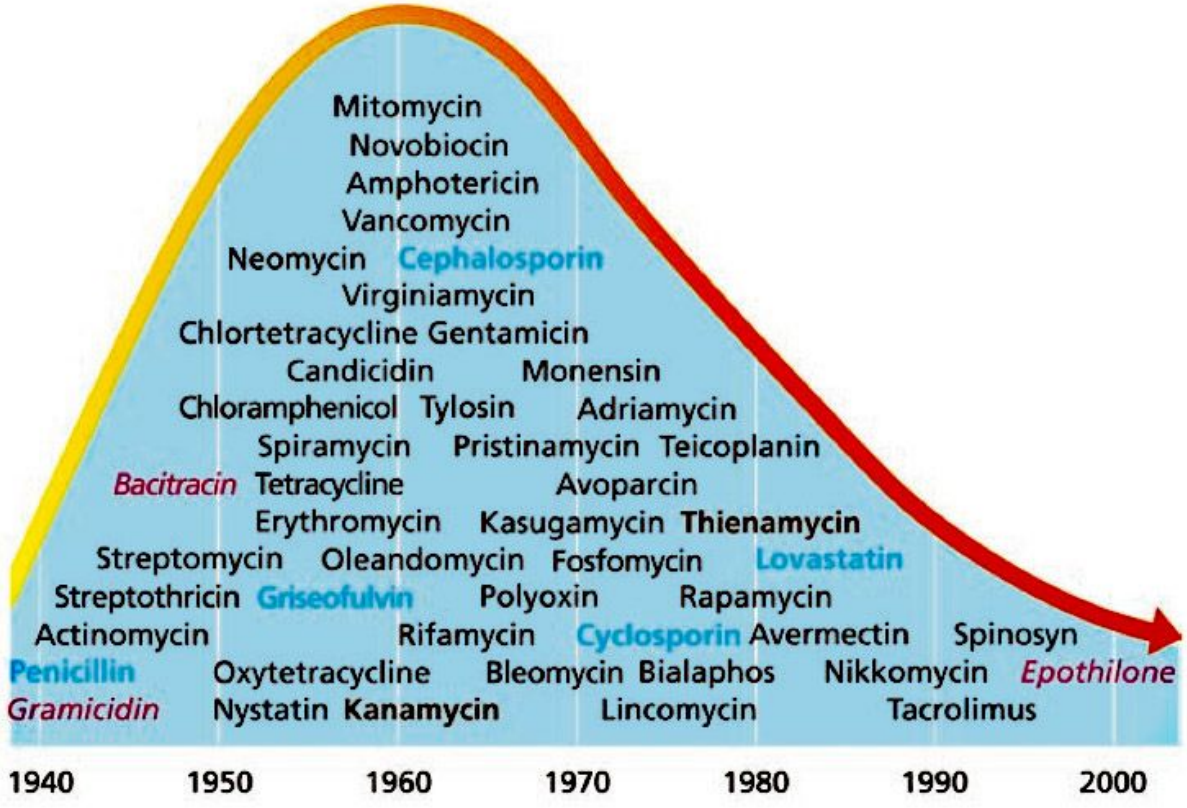
Wow. So how exactly did we end up with this problem?

There are many more reasons besides not finishing an antibiotic course. Here are a few:

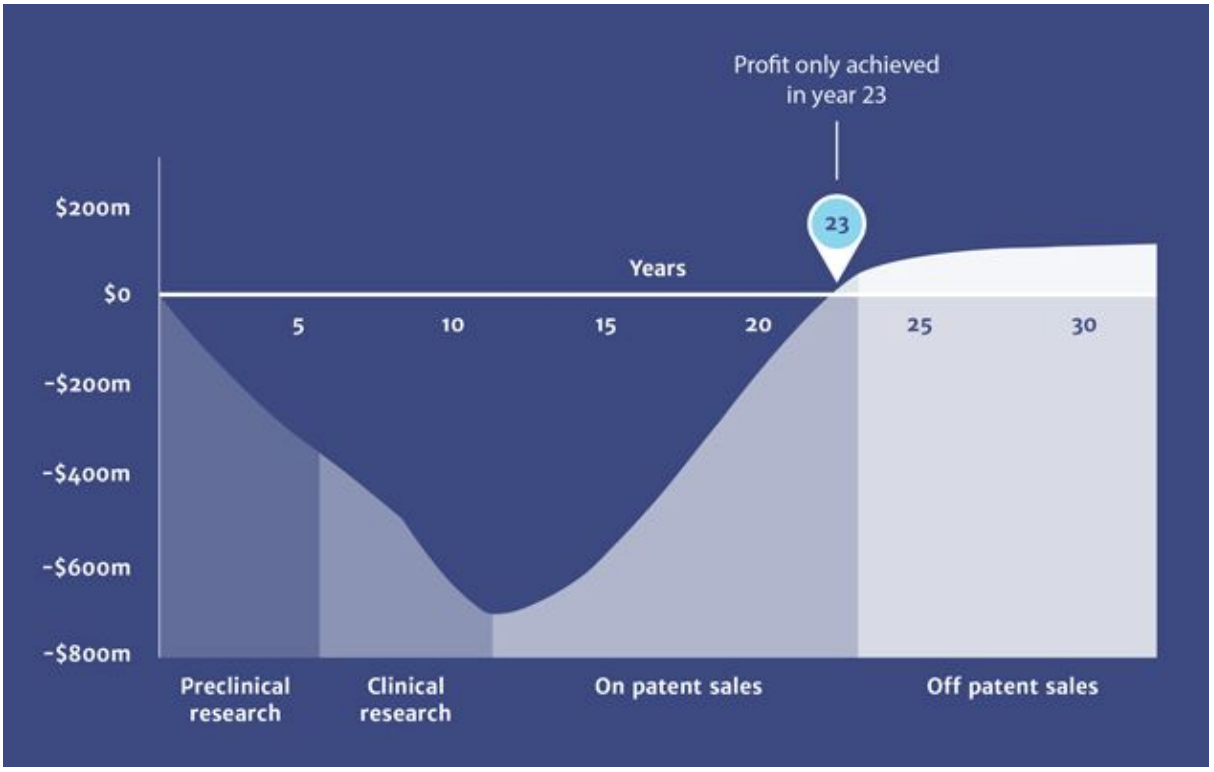
- *Overprescription by doctors*. It's a common misconception that antibiotics are effective against viral infections (they aren't). That's because the cellular mechanisms targeted by antibiotics, like cell wall synthesis, are not present in viruses. So not only do they not work against the common flu, antibiotic use might cause intestinal bacteria, like *E. coli*, to become resistant and one day pose a threat. ‘
- *Black market and lax regulation.* Besides errors by doctors, patients sometimes demand antibiotics for their treatments believing that it leads to higher chances of recovery. In areas with lax regulations, they are sometimes prescribed antibiotics when it would be unwise. Black market antibiotics like gentamacin, lincomycin and moxifloxacin are seized regularly in countries like Cambodia, so the strongest antibiotics we guard most safely might soon be no longer effective.
- *Self-prescription*. Some people might find it cheaper to reuse antibiotics from family members or a previous illness to treat their infection, since it would save the cost of visiting a doctor and the prohibitively high cost of antibiotics for lower-income families. In reality, since different ailments like the (virus-caused) flu and (bacteria-caused) strep throat may present with similar symptoms, this may lead to antibiotic resistance.
- *Livestock use.* As mentioned earlier, antibiotics are used to rear farm animals to reduce healthcare costs. A study by the US Federal Drug Administration found that over 80% of antibiotics were used for farm animals. Since the probability of antibiotic abuse and resistance emerging increases with the use of antibiotics, using the same antibiotics for farm animals and humans make it far more likely for antibiotic resistance to emerge in bacteria that infect both animals and humans.

Wait. Why don't we just invent new antibiotics?

This is very much a supply-and-demand problem: while we are abusing antibiotics in every imaginable way, we aren't producing as many antibiotics as we used to. Here's a graph showing antibiotics production from 1940:



Additionally, the cost of antibiotic research is prohibitively high and takes time scales of around ten years to develop, an option available to only the few large pharmaceutical companies. In fact, with companies like Novartis leaving the field due to low profitability, the supply of antibiotics is set to decrease.With most low-hanging fruit already picked, newer antibiotics are few and far between. In fact, no new classes of antibiotics were discovered in around 2 decades. It therefore seems highly likely that we will have sufficient antibiotics to last into the future.



Uh oh. Isn't anyone doing anything about this?

Yes. For one, international law frameworks like the Transatlantic Taskforce on Antimicrobial Resistance are working toward tightening regulations on antibiotic prescription on a global scale. Additionally, some antibiotics are labelled indicating that they be used exclusively with only humans, dogs, or horses. If used rightly, this would increase the number of antibiotics exclusively used by humans, reducing the emergence of antimicrobial resistance.

Another promising study is the effectiveness of improved hygiene. It turned out that after a review of hygiene practices in hospitals in England and Wales, the number of deaths from methicillin-resistant staphylococcus aureus (MRSA) went from 1600 to 364 from 2007 to 2011. Perhaps, there is a wide berth for hospitals to take actions to reduce the impact of antibiotic resistant bacteria and associated health costs.

What will the future look like?

It's therefore quite likely that we will one day run out of antibiotics, and that that day will be soon. I kid you not, the consequences can be potentially devastating. Even a return to the leech-and-bloodletting days of medicine wouldn't seem too far fetched. Yet, with proper management and the strength of collective will, this crisis can be averted.

Ultimately, what we're fighting is something *alive*, that by definition is in a constant state of change and flux. The battle of antibiotic resistance is an arms race, and one we're not likely to win. Perhaps antibiotics will not serve us well into the future, but what awareness we can raise to counter this threat will go a long way in delaying that day.

(1476 words)