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Commentary: Science, politics can team up to solve antibiotic resistance

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By Andrew F. Read

The doctor tried antibiotic after antibiotic, but the bacteria in the woman's body continued to proliferate. With only two drugs left, the doctor asked for my advice. An evolutionary biologist collaborating with the physician to study antibiotic resistance, I suggested he use both drugs simultaneously. I reasoned that since the two drugs had different modes of action, more mutations would be required for the bacteria to generate resistance to both drugs.

In truth, we had no idea what to do, and there wasn't enough justification to go with my theory. We know simultaneous drugs can stop resistance with HIV, but we have no idea about chronic bacterial infections.

So my physician colleague went with best practice - try one antibiotic until it fails, then switch to the other. The patient duly died, not from the heart failure that brought her into the hospital in the first place, but from the evolution of drug resistance among the bacteria in her body.

Awareness of antibiotic resistance is increasing, and the recent finding of colistin-resistant *E. coli* in a Pennsylvania woman brought the urgency of the situation to new heights. Indeed, the Centers for Disease Control and Prevention claims that 23,000 Americans a year die from drug-resistant bacteria. I believe the number is more likely around 40,000.

That's about the same number of people who die in car crashes each year. But unlike car crash deaths, infection deaths are on the rise.

People talk about returning to a pre-antibiotic era; that's not going to happen. There is a lot we can do, from developing new drugs and vaccines to reducing the use of antibiotics on farms to improving our hygiene. The bad news is, none of these actions will solve the problem alone, and all of them are tricky to achieve.

Although we do need science to provide solutions, the problems are fundamentally political. For example, it costs $1 billion to bring a new drug to market, and yet no market exists for antibiotics because their purchase prices are so cheap and they are used for only short periods of time. Without government intervention, new antibiotics are unlikely to happen.

Reducing or even eliminating the use of antibiotics on farms could substantially reduce resistance among some bacteria to drugs that are administered to both farm animals and humans, but it's not going to be the major solution some people think it will be because so many of the drugs we rely on are used only in health-care settings. Even for those drugs used on farms, their use in humans is probably a stronger driver of resistance than agricultural use.

Hygiene in hospitals is extremely important, but when a patient crashes and needs to be revived immediately, the nurse can't stand at the door and scrub down; he or she has to get in there. We can do hygiene better, but we can't do it perfectly.

An area where we can make a big difference is in antibiotic stewardship - prescribing the right drug, at the right dose, for the right duration, at the right time. The question is, "What is right?" We know what is wrong - prescribing antibiotics to treat viral infections, for instance - but it is my belief that what we typically consider to be right is actually a major driver of resistance.

Consider duration of antibiotic use. We're all accustomed to 10-day or two-week courses, but where did these numbers come from? It turns out that almost all of them are completely arbitrary, and abiding by them may in fact be driving drug resistance.

Here's why. Antibiotic resistance can arise when susceptible bacteria are killed off by drugs, thereby relieving resistant bacteria of competition and enabling them to proliferate. In clinical trials, shorter durations of antibiotics (as little as three days) often are just as effective at improving health as longer durations, and some studies also show that drug resistance is reduced.

While the science of antibiotics is advanced, the science of evolutionary management of antibiotic resistance is rudimentary. Our patient might not have died had we a better understanding of evolutionary management. Clearly, more studies are needed to determine what constitutes appropriate antibiotic use.

A British economist recently published an analysis suggesting that if we don't change our antibiotic use, by the year 2050 more people will die of drug-resistant infections than of cancer globally. That is scary.

As we saw during the "War on Cancer" that began during the Nixon era and continues today, science and politics need to work together to address health problems. Compared with cancer, antibiotic resistance is an easy science problem. We just need the political will to solve it.

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