

Superbugs & Antibiotic Resistance: Try Negotiating

Dr. Lon Jones, DO

Published: November 3, 2015

More and more we are learning that bacteria are not all enemies. There are good bacteria; ten times more bacteria living on us and in us than we have cells and mostly they are good. Bacteria are the unquestioned masters of life on earth, both in durability and variety. As one doctor put it, we are likely to just be taxicabs for our resident bacteria. We are finding that friendly bacteria help to keep us slim, that they protect us from their more dangerous relatives and guide our developing immune system, and we have known for a long time how useful they are in helping to digest the food we eat and making vitamins for us that we can't.

Then there are bad ones that infect and kill us. It may be helpful to see it from their point of view: they are only recycling—it's what they do. These are the pathogens and we are at war with them. But we cannot win this war for simple reasons, explained earlier in our book, *The Boids and the Bees*:

The process of developing a new drug takes lots of time, involves lots of people, expensive clinical testing, and requires a patent so the company can make a profit. The process of developing resistance, on the other hand, is much faster. With over three billion years of experience bacteria are the experts at playing with their DNA—they grew up with it. While bacteria have no brains or central nervous system, or even ganglia or neurons, that lets them learn as we commonly think of the term, they are capable of both recognizing a threat and playing with the elements in their environments to deal with it, and those elements are primarily their DNA. When threatened they increase their mutation rate, pick on areas of their DNA that are more open to manipulation, and share the changes in plasmids with other bacteria, allowing others to refine and improve the changes. Resistance involves an adaptation, or mutation in one out of a billion or so bacteria, which can then multiply unimpeded because the other competing bacteria have been killed off. The resistant bacterium thus passes the resistance on to its own progeny, as well as sharing it with others in the plasmids—with no concern at all for intellectual property rights or profit. They are a formidable foe and we have little chance of winning this war.

Antibiotics do help us win a few more years of life. We do need them and we need them to work. And therein lies the problem: the more we need and use them the more resistance is developed. Israel's recently resigned Defense Minister, Moshe Yaalon, commented some time ago on the difference between strategy and tactics. Strategy is looking at the whole picture, while tactics deal with individual battles. When he said, 'Our tactical decisions are not in our strategic interest', he could have been talking about our use of antibiotics as well as Israel's Palestinian policy.

We have reached the point where the pharmaceutical companies have given up trying to compete with the bacteria. The government is now trying to spur interest by coming up with over a billion dollars to find a solution to the problem. The first goal of Obama's program is to: "Slow the Emergence of Resistant Bacteria and Prevent the Spread of Resistant Infections." The pathway to doing this involves restraint on use (so there are fewer tactical decisions that are not in our strategic interest), an emphasis on immunizations, and a small bit about the possible use of probiotics to compete. What is missing is anything about negotiating.

Negotiate is what we do when we realize we can't win a war. While we have not openly realized our war with bacteria is not winnable it is pretty clear from the trend we are experiencing. And perhaps we have not seen this because we draw a blank when we think about negotiating with brainless microscopic bugs.

That may not be the word or even the idea he used, but Paul Ewald described the process very well in his book, *The Evolution of Infectious Disease*. Simply put, if we threaten bacteria they will adapt with resistance, but if we constrain them without a deadly threat, they will adapt in a more peaceful way, toward what is called commensalism, or living with us in a helpful way. Constraining them, according to Ewald, is done by isolating them, making it harder for them to get from person to person, and using such things as soap and water, gloves, gowns and masks, and condoms. We need to do more of this. But there is another way too.

Forty years ago Nathan Sharon was doing research on how bacteria hold on to us in order to infect us. He found that they held on to sugar complexes on our cell surfaces. The one he focused on, for example, was the way *E. coli*, the bacteria that cause so many urinary infections, hold on. He found that the sugar mannose was involved. Mannose is plentiful on the cells lining the urinary tract so it is there for the bacteria to hang on to. Sharon also argued for competing with this attachment by adding mannose to the environment. This additional mannose would fill up the binding sites so that the bacteria would have fewer empty ‘hands’ to hold on with; it’s a process called competitive inhibition, and it works. Sharon said that these sugar complexes provide the bacteria and the cells with a language that tells them where to attach or where to go. We argue that the language can also be used to negotiate and that interfering with adherence puts the same pressure on the bacteria to adapt in friendly ways that Ewald finds with constraint.

Xylitol is a common sugar substitute that has been shown to interfere with the adherence of several significant pathogens. It is a natural substance that cannot be patented so the pharmaceutical industry is not interested. In this way it is similar to the mannose that Sharon tried to get people to use, without success, for the last forty years of his life. I have written about xylitol’s use in taming bacteria. More recently, and independently, a group in Sao Paulo has written of how it can by-pass resistance; and even more recently a dental researcher in Italy has shown that, at least for problem causing oral bacteria, several other uncommon sugars work like xylitol in curtailing their adherence.

Using these sugars on a regular basis is negotiating with our unfriendly bacteria and it can result in a simple, safe, and inexpensive solution for Obama’s first goal.