LETTER TO THE EDITOR

The Natural Environment May Be the Most Important Source of Antibiotic Resistance Genes

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I found the recent paper by Wichmann et al. (1) of great interest, and it illustrates an aspect of antibiotic resistance that has concerned me for a long time, namely, the origin of that resistance.

The authors approach the problem from the point of view of misuse of antibiotics in animal food production systems. For years, attempts have been made to make that connection, with a view to restricting antibiotic use in agriculture. Establishing a link has not been truly successful, yet we frequently hear about how antibiotic use should be restricted. The underlying assumption here is that the direct use of antibiotics leads to the development of antibiotic resistance in the animal, which can then be transferred to important human pathogens. On the face of it, the argument seems reasonable, but I suggest it could not be further from the truth.

It must be remembered where these antibiotics came from. The major groups of antibiotics Wichmann et al. studied are the beta-lactams, phenicols, aminoglycosides, and tetracyclines. All of these antibiotics are derived from various environmental microbial species: the beta-lactams from species of the fungus *Penicillium*, phenicols from species of the complex bacterium *Streptomyces venezuelae*, aminoglycosides from species of *Streptomyces* and *Micromonospora*, and tetracyclines from species of the *Actinobacteria* group. These organisms have surely been in existence for millions of years, and their production of these natural antibiotics would have been normal as they competed in the natural environment. A consequence of their activity would have been the development of resistance by other microbes in the environment so they could compete against the antibiotic producers. This would have led to the development of antibiotic-resistant bacteria and antibiotic resistance genes in the natural environment.

So I suggest that all along, the most important source of antibiotic resistance genes has been the natural environment. If this is the case, then it should change how we think about the origins of antibiotic resistance and how we should manage it.

I think the large number of resistance genes discovered by Wichmann et al. (1), i.e., 80, supports this idea. The large number of antibiotic resistance genes that are found in manure, and that can be found in the feces of many other animals, comes directly from their environment. Cows eat grass and during that feeding activity take in soil and other material as well, just as chickens do, and the material ingested over time would include antibiotic-resistant organisms and their genes. All of this food material containing these antibiotic-resistant bacteria could easily accumulate in the cow rumen, to be excreted in cow feces, and a similar situation would apply to chickens.

Ultimately, manure and feces may well be sources of resistance genes for human pathogens, but I suggest that how we manage antibiotic resistance must rely on the assumption that the genes come from the environment and are not generated in the food animals.

Reference

1. **Wichmann F, Udikovic-Kolic N, Andrew S, Handelsman J.** 2014. Diverse antibiotic resistance genes in dairy cow manure. mBio 5(2):e01017-13. http://dx.doi.org/10.1128/mBio.01017-13.

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