Unintended consequences can show up in surprising places

We have all experienced the law of unintended consequences; we take an action in anticipation of a specific result and while that result may or may not occur, there are results that we did not anticipate. Sometimes these unanticipated results are positive while other times they are not.

When Midwest farmers first started using chemical fertilizers, the expected result—higher yields—occurred. They did not expect that over a period of decades the washing of some of the fertilizer off their fields and into adjacent streams would create a dead zone in the Gulf of Mexico. Years later we discovered that the dissolved nitrogen in the waterways also created problems for municipal water treatment systems downstream.

While most people can agree on the facts and make the connection between applied nitrogen to farm fields and the problem municipal water systems have in removing the nitrogen from drinking water, that leaves us no closer to agreeing on a solution to the unintended consequence of increasing crop yields through the use of chemical fertilizers.

This last week we ran across another example of the law of unintended consequences, or maybe it's just Murphy's Law: "If something can go wrong it will." The story was about an outbreak of a multi-drug resistant yeast, *Candida auris* (CA) (http://tinyurl.com/yxgb5zm9). The yeast was first identified in the ear (auris is Latin for ear) of a patient in Japan. Later CA was been identified in patients in South Korea, Pakistan, and India. In this era of global air travel, it subsequently spread to many other countries including the US.

An article in *Clinical Infectious Diseases*, "Simultaneous Emergence of Multidrug-Resistant *Candida auris* on 3 Continents Confirmed by Whole-Genome Sequencing and Epidemiological Analyses" (http://tinyurl.com/y3uugwjf), reported that of the 41 patients studied, 24 (59 percent) died. The authors reported: "using stringent break points, 50 of the isolates [of CA] (93%) were resistant to fluconazole, 29 (54%) to voriconazole … 19 (35%) to amphotericin B … 4 (7%) to echinocandins … and 3 (6%) … were resistant to flucytosine. Two isolates … were resistant to fluconazole, voriconazole, echinocandins, and amphotericin B. In all, 22 (41%) isolates were resistant to [2 or more] classes of antifungals."

The azole drugs usually used to treat patients with yeast and fungal infections are nearly identical to the drugs used in agriculture worldwide. While we have read about herbicide and insecticide resistance developing in plants as the result of their widespread use, this appears not to be the situation in the case of CA.

In performing genetic sequencing of the multi-drug resistant CA, scientists found that 4 strains appeared nearly simultaneously. The genetic differences among these strains indicate that they diverged from each other thousands of years ago. So, while the widespread agricultural use of azoles did not contribute to the development of the four resistant strains, it appears that by killing susceptible strains of *Candida,* agricultural use did create an environmental space for the spread of *Candida auris*.

Whether agriculture directly (nitrogen fertilizer and herbicide resistance in weeds) or indirectly (multi-drug resistant *Candida auris*) brings about the unintended consequence, we (input suppliers, farmers, politicians, policy analysts, agricultural and medical scientists, and society at large) bear the responsibility of finding effective and acceptable ways of dealing with the results of modern life when the law of unintended consequences takes a bite out of us.

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