The New York Times

**March** 8, 2016 Tuesday   
Late Edition - Final

**Antibiotic Resistance** Is Worrisome, but Not Hopeless  
  
**BYLINE:** By AARON E. CARROLL.

Aaron E. Carroll is a professor of pediatrics at Indiana University School of Medicine. He blogs on health research and policy at The Incidental Economist, and you can follow him on Twitter at @aaronecarroll.

**SECTION:** Section A; Column 0; National Desk; THE NEW HEALTH CARE; Pg. 3  
  
**LENGTH:** 1252 words

A century ago, the top three causes of death were infectious diseases. More than half of all people dying in the United States died because of germs. Today, they account for a few percent of deaths at most.

We owe much of that, of course, to antibiotics. The discovery of prontosil, the first synthetic modern antibiotic, earned Gerhard Domagk the Nobel Prize in 1939. Mass-produced penicillin earned Alexander Fleming, Ernst Boris Chain and Howard Walter Florey one in 1945.

It is hard to overstate how much less of a threat infectious diseases pose to us today. But we take antibiotics for granted. We use them inappropriately and indiscriminately. This has led many to worry that our days of receiving benefits from them are numbered.

When I was a medical student, doctors around me were panicking about methicillin-resistant Staphylococcus aureus (MRSA). Before then, infection with that bacteria had been almost exclusively contained to health care facilities. In the 1990s, it was then starting to appear in the wider community. Today, community-acquired MRSA is so common that we pretty much just assume the presence of MRSA for any infections we believe are caused by staph.

Concern about the rise of resistance often focuses on overuse of antibiotics. There's plenty of evidence that we, the users, are the problem. In a recent multicountry study conducted by the World Health Organization, almost two-thirds of people believed that antibiotics could be used to treat colds and the flu, which are, of course, caused by viruses. Antibiotics kill bacteria, not viruses.

The same number of people also knew that **antibiotic** **resistance** was a real problem that could affect them, but this knowledge did not seem to prevent them from misusing the drugs.

Every time we use antibiotics, we increase the chance for resistant strains to develop. Bacteria are very good at the evolution game, and killing off more susceptible strains leaves the more resistant ones to fill the gap. Bacteria have also become good at transmitting resistance abilities through plasmids, small, circular DNA molecules that can be transferred from bacteria to bacteria.

The widespread use of antibiotics in the raising of animals has clearly contributed to the development of resistance as well. The Food and Drug Administration estimates that more kilograms of antibiotics are sold in the United States for food-producing animals than for people.

Animals are also where the most recent worry has focused. Until very recently, even as some E coli have become resistant to nearly every antibiotic, they have remained susceptible to colistin, an old but rarely used (in humans) drug. Being old, though, the drug is cheap, and for that reason it has become popular to add colistin to animal feed in some countries, like China, in order to produce cheaper pork and other meats.

In a recent report published in Lancet Infectious Diseases, scientists discovered colistin-resistant E coli in 21 percent of slaughtered pigs in China. They found isolates in 15 percent of meat sold from those animals in retail sites. They even detected resistant E coli in more than 1 percent of hospitalized patients.

Most horrifying, it appears that the resistance is transmitted by plasmids. That means the bacteria don't just pass on resistance to their ''**children''**; they can pass it among one another and to completely different strains of bacteria. Scientists were also able to detect colistin resistance from the same gene in Klebsiella pneumonia in hospitalized patients. The accompanying editorial to the colistin report called this ''a major breach in our last line of defense.''

While the concern is reaching a fever pitch, it's important to remember that resistance isn't new. We can't blame all of our problems on antibiotic overuse and misuse. Even the proper use of antibiotics will eventually lead to resistance.

Our response to these setbacks has been to create new types of drugs. Penicillin-resistant staphylococcus were already being seen in labs in 1940, a few years before mass-produced penicillin was introduced. Tetracycline was introduced in 1950, and resistant shigella were identified in the same decade. Erythromycin's introduction in 1953 was followed by resistant streptococcus in 1968. Gentamicin, developed in 1967, saw resistance in 1979; Vancomycin, developed in 1972, saw resistance in 1988; and Imipenem, released in 1985, saw resistance in 1998.

It's also in this game of catch-up that we are failing. Fifteen of the 18 largest pharmaceutical companies have abandoned the antibiotic market entirely. Research funding in all areas of academia has been cut back significantly as well. While 19 new antibiotics were approved by the F.D.A. from 1980 to 1984, only 13 were approved from 2000-2014. We aren't keeping pace with resistance.

While we can quibble about the exact cost of bringing a new drug to market, we can all agree that it's a lot of money. Drugs in the United States are profitable when they are sold in great volume or when they are very expensive. Antibiotics, as a class of drug, provide a poor return on investment for pharmaceutical companies. They face low-priced and generic competition. Any breakthrough drug will almost certainly be held in reserve for only the most resistant cases, meaning there's not a huge immediate market for it, when a company still has exclusivity.

Many people have proposed new ways to incentivize and reward innovation. The Group of 7 is poised to coordinate action, as is the Group of 20 and the World Health Organization. In Davos, Switzerland, nearly the entire drug industry agreed. It released a statement in January calling for big changes in how we pay for antibiotic research and development, including the idea of ''delinkage'' or paying for value as opposed to volume of antibiotics sold.

There are other glimmers of good news. The federal budget agreement passed late last year increased spending in this area by more than $375 million. Almost half of that went to the Centers for Disease Control and Prevention to help prevent and monitor outbreaks.

The National Institutes for Health received $100 million for **antibiotic** **resistance**research. The Biomedical Advanced Research and Development Authority also received an additional $96 million to help explore new drugs. Later this year, the agency will start an antibiotic research and development accelerator with $30 million a year over the next few years.

It's this new drug investment that might bring the most hope. For many years, spending on **antibiotic** **resistance** research was flat. Only in the last year or two have both the president and Congress seemed especially interested in pushing for more funding. New antibiotics are a public good, not necessarily an area for private rewards. Huge public support for researching new classes of antibiotics will be necessary to combat this growing threat.

As a sage observer once noted, though, bringing new antibiotics to market without changing how we use them is akin to providing alcoholics with a finer grade of brandy. For this reason, most new funding goes toward prevention, infection control and managing antibiotic use. The best outcome is preventing infections through vaccination or public health measures so that we improve human health without increasing resistance to antibiotics.

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**GRAPHIC:** DRAWING (DRAWING BY SELMAN DESIGN)