Research

Primer: FDA and Antibiotic Development

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Introduction

In 2011, two million Americans were infected with—and 23,000 killed by—drug-resistant bacteria.[1] Over the past 20 years incidents of drug-resistant infections acquired in hospitals have increased from a low of 10 percent of all hospital acquired infections to 60 percent today.[2] Despite the evident need for new, novel antibiotics, almost no major pharmaceutical companies are investing in antibiotic development. Only 11 new antibiotics were approved between 1998 and 2014, and no new classes of antibiotics have been approved since 1987.[3]

What's Going Wrong?

Antibiotics developers, like all pharmaceutical manufacturers, are market actors sensitive to incentives. Currently there are very few incentives to invest in antibiotic research and development (R&D) and many reasons to direct those funds elsewhere.

Antibiotics are Expensive to Produce

Because we rarely face entirely new bacteria, antibiotic development is often intended to better combat a well-known bacterium that has adapted defenses against currently available treatments through repeated exposures. Bacteria's ability to evolve quickly renders once therapeutic drugs useless against later generations.[4] Scientists must meet this challenge by developing either a more powerful generation of an existing drug, or a new drug with a unique method of attacking for which the bacteria has no adaptation.[5] Unfortunately, both these options—especially the latter—are expensive and scientifically complex, and therefore do not create much incentive for investment in R&D relative to other drugs that can more readily be improved upon.

Antibiotics Provide Low Return on Investment

Antibiotics offer drug manufacturers a particularly low return on their investment. They are intended to be single use drugs that cure the condition they treat.[6] Even an expensive antibiotic is unlikely to earn profits equal to a cheap treatment for a chronic disease; which must be purchased regularly throughout the patient's lifetime.

Unlike other classes of drugs, antibiotics are often their own worst enemy financially. The more often an antibiotic is prescribed and used, the more opportunities the bacterium has to evolve and develop a resistance to the drug.

FDA Approval Process is Long and Expensive

Pathways to Food and Drug Administration (FDA) approval are slow and difficult. By the time a new antibiotic comes to market, the strain of bacteria it treats may have had over a decade to develop its resistance; particularly if the new drug is an update of a similar drug, rather than a novel form of attack.

Another important market influence acting against antibiotic R&D is the seeming irrationality of consumers. Bacterial threats to individual and population health are not as immediate as they once were, and deaths caused by uncomplicated bacterial infections are still relatively rare.[7] Public consciousness is currently more focused on "scarier" threats like cancer and heart disease, and most people do not take the threat of untreatable, drug-resistant bacteria seriously. This lack of public understanding of the seriousness of the situation causes consumers in situations that are not immediately life-threatening to undervalue antibiotics – they are unwilling to pay more for new treatments for old bugs, despite the substantial R&D costs that go into producing dugs that the bacteria are not resistant to. In fact, at the time of discovery, the average net value of a new antibiotic for the developer today is a loss of $50 million.[8]

What's Being Done About It?

The slowdown in production of new and effective antibiotics is a clear public health threat. The FDA and Congress have both taken steps to address the problem, but most promising responses have unsurprisingly come from the free market.

Government Response

The FDA has released guidance directing farmers raising animals for consumption to alter their use of antibiotics that are approved for human use. The FDA is asking these farmers to voluntarily limit their use of antibiotics to therapeutic purposes under the oversight of a licensed veterinarian.[9] Though this guidance is voluntary, it appears that most livestock operations are willing to comply.[10] This is an important step in minimizing the opportunities bacteria have to develop resistances to drugs that are important to human health.

In 2012, Congress passed the Food and Drug Administration Safety and Innovation Act (S. 3187), which among other provisions, included the Generating Antibiotic Incentives Now (GAIN) Act.[11] The GAIN Act allows for more antibiotics that treat serious and life threatening infections to have an extended five-year exclusivity period beyond that of other drugs.[12] This law attempts to counterbalance the disincentives of a long FDA approval process and low returns on R&D investment, but may also drive up the price of these drugs by preventing competition from generic manufacturers. Nonetheless, the scientific reality is that antibiotics are still liable to lose their effectiveness (and therefore value) over time.

Congress is also currently considering the Promise for Antibiotics and Therapeutics for Health (PATH) Act to minimize the negative effects of the long FDA approval proves.[13] If enacted, this bill would allow for an expedited approval pathway for antibiotics for use in narrowly defined patient populations with serious, specific illnesses and an unmet need for treatment. These developers would later be able to apply for an expanded approval and the drug could be used off label if appropriate.

Private Sector Response

The response to the vacuum in antibiotic production has been most impressive in the private sector. The rise in new tests and specialized firms can both prevent and meet the need for new drugs.

The development of rapid diagnostics and changes in technology of Laboratory Developed Tests can provide health care providers with accurate diagnoses quicker.[14] By providing a diagnosis in hours rather than days, better diagnostic tests can enable the use of antibiotics before an infection has time to spread. It will also help reduce misuse of antibiotics.[15] These benefits will help slow the development of drug-resistant strains of infectious bacteria.

Specialized drug development firms and academic institutions with outside grant funding that focus exclusively on the development of antibiotics have largely replaced major pharmaceutical companies in the field.[16] With no other drugs on the market, small firms can focus exclusively on R&D. Once a drug has been developed, firms may apply for FDA fast-track approval for small, targeted populations of the sickest patients.[17] If successful, this business model encourages the sale of the patent to large drug companies with the resources to manufacture the drug on a large scale, and follow through on the full FDA approval process. By eliminating manufacturing and trial costs, small developers can generate a modest profit developing otherwise profitless antibiotics.[18]

[1] http://www.healthline.com/health/antibiotics/why-pipeline-running-dry