

► **Combating
Drug Resistance**



Dr. Roger Pomerantz

ROGER POMERANTZ, M.D., Senior VP and Head of Infectious Disease Research at Merck, talks about why antimicrobial resistance is a major global concern.

➔ **PV: How big of a problem is antimicrobial resistance?**

POMERANTZ: For the first time since the antibiotic era started in the 1930s, there are organisms in America, Europe, and the rest of the world, that are resistant to all known antimicrobials. At Merck, we consider this a state of emergency — a global antimicrobial resistance emergency — fueled by a significant unmet medical need for safe and effective antimicrobial treatments.

One reason resistance has become a major issue is the overuse of antibiotics — and this is not limited to the developed world. In some parts of the world, antibiotics are available over the counter. In the United States, patients can get antibiotics too easily and for infections that are not caused by bacteria. In addition, antibiotics are put in animal feed, which eventually migrates into the water supply and can ultimately change antibiotic resistance patterns. Finally, unless an organism can be eradicated, we are usually chasing that organism's resistance. With new antibiotics, even when used properly, there will be an increase in resistance slowly over time.

Good stewardship to manage the appropriate use of antibiotics by healthcare providers and patients can help to slow the development of resistance and prolong the efficacy of current antibiotics.

➔ **PV: Why is this an issue for someone who may only get a simple infection once or twice a year?**

POMERANTZ: Anytime antibiotics are used inappropriately or patients stop treatment before taking all of the recommended doses it adds to the resistance problem and furthers overall antibiotic resistance in the environment. This also continues to make it harder for us to develop new medicines. On a single patient level, if we don't develop medicines to manage the simple infections that someone might get once or twice a year, eventually these will become not so simple.

Staphylococcus aureus (Staph), for example, has become increasingly resistant. In the 1940s, Staph infections could be treated with penicillin. Because of resistance, this hasn't been possible for many decades now, and further resistance to methicillin-like drugs has led to methicillin-resistant staph aureus (MRSA). Certain Gram-negative organisms, such as E. coli or Pseudomonas, are another group of organisms that have developed increasingly difficult-to-treat, resistant mechanisms. Then there are what I like to call "Andromeda strains," or super resistant organisms for which we haven't yet found an effective antibiotic treatment.

➔ **PV: Can antibiotic resistance be resolved?**

POMERANTZ: Bacteria are simple organisms, but very good at getting around different pressures. Only by eradicating the actual organism itself will we be able to declare victory.

At Merck, we have a program — Study Monitoring Antimicrobial Resistance Trends (SMART) — that is a worldwide surveillance study for intra-abdominal infections. We monitor and collect data, on a global and longitudinal basis, on the level of in vitro susceptibility to intra-abdominal bacteria from clinical institutions, teaching hospitals, and community hospitals.

We can then continually monitor antimicrobial resistance patterns in hospitals, which allows researchers to make good choices when they have to decide on an empirical therapy before they actually know the organism's sensitivity, which is often the case with sick patients in the hospital.

This information will help us to develop better medicines in the future and it helps inform physicians about how microbial flora are changing even before we may notice the differences.

➔ **PV: What product in Merck's pipeline do you think is most promising for resistant bacteria?**

POMERANTZ: We have data on a new beta-lac-

tamase inhibitor, which acts by stopping certain resistant organisms from inhibiting beta lactams. With this approach we are trying to make other antibiotics in the penicillin class more resistant to an organism's mutation. With a beta-lactamase inhibitor we can turn back the microbial clock so that medicines can function in a way they haven't been able to for many years.

We also have several drugs called carbapenems that are part of a group of antibiotics related to penicillin. Carbapenems are still useful for difficult-to-treat infections, but more and more organisms are developing resistance to them. **PV**

ANTIMICROBIAL QUICK FACTS

- » Increasing use of antimicrobials in humans, animals, and agriculture has resulted in many microbes developing resistance to these previously powerful drugs.
- » Many infectious diseases are increasingly difficult to treat because of antimicrobial-resistant organisms, including HIV infection, staphylococcal infection, tuberculosis, influenza, gonorrhea, and candida infection
- » Between 5% and 10% of all hospital patients develop an infection, leading to an increase of about \$5 billion in annual U.S. healthcare costs.
- » About 90,000 of these patients die each year as a result of their infections, up from 13,300 patient deaths in 1992.

Source: National Institute of Allergy and Infectious Disease. For more information, visit niaid.nih.gov.




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