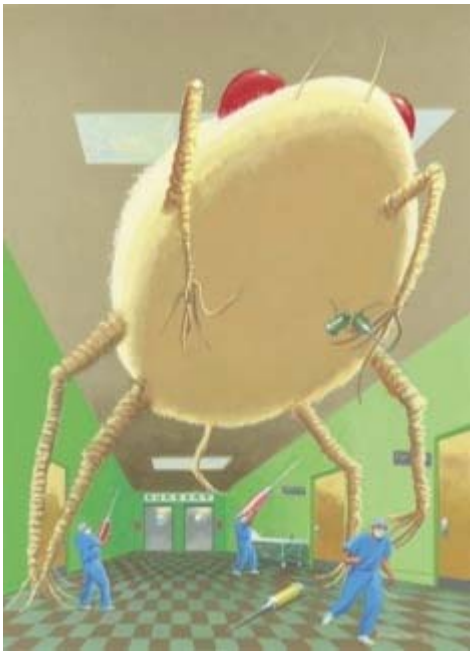
MEDICAL DISPATCH

SUPERBUGS

The new generation of resistant infections is almost impossible to treat.

by Jerome Groopman

AUGUST 11, 2008



Doctors fear that dangerous bacteria may become entrenched in hospitals

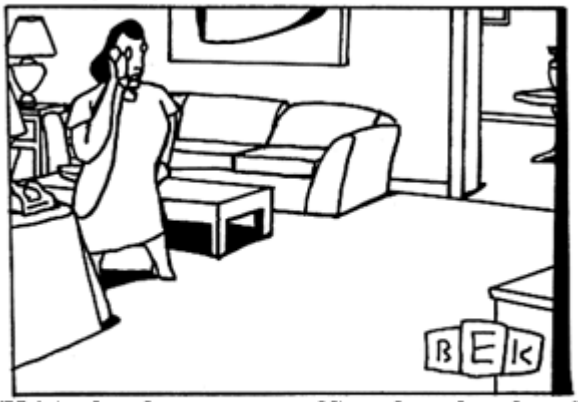
In August, 2000, Dr. Roger Wetherbee, an infectious-disease expert at New York University's Tisch Hospital, received a disturbing call from the hospital's microbiology laboratory. At the time, Wetherbee was in charge of handling outbreaks of dangerous microbes in the hospital, and the laboratory had isolated a bacterium called *Klebsiella pneumoniae* from a patient in an intensive-care unit. "It was literally resistant to every meaningful antibiotic that we had," Wetherbee recalled recently. The microbe was sensitive only to a drug called colistin, which had been developed decades earlier and largely abandoned as a systemic treatment, because it can severely damage the kidneys. "So we had this report, and I looked at it and said to myself, 'My God, this is an organism that basically we can't treat.' "

Klebsiella is in a class of bacteria called gram-negative, based on its failure to pick up the dye in a Gram's stain test. (Gram-positive organisms, which include *Streptococcus* and *Staphylococcus* , have a different cellular structure.) It inhabits both humans and animals and can survive in water and on inanimate objects. We can carry it on our skin and in our noses and throats, but it is most often found in our stool, and fecal contamination on the hands of caregivers is the most frequent source of infection among patients. Healthy people can harbor *Klebsiella* to no detrimental effect; those with debilitating conditions, like liver disease or severe diabetes, or those recovering from major surgery, are most likely to fall ill. The bacterium is oval in shape, resembling a TicTac, and has a thick, sugar-filled outer coat, which makes it difficult for white blood cells to engulf and destroy it. Fimbria—fine, hairlike extensions that enable *Klebsiella* to adhere to the lining of the throat, trachea, and bronchi—project from the bacteria's surface; the attached microbes can travel deep into our lungs, where they destroy the delicate alveoli, the air sacs that allow us to obtain oxygen. The resulting hemorrhage produces a blood-filled sputum, nicknamed "currant jelly." *Klebsiella* can also attach to the urinary tract and infect the kidneys. When the bacteria enter the bloodstream, they release a fatty substance

known as an endotoxin, which injures the lining of the blood vessels and can cause fatal shock.

Tisch Hospital has four intensive-care units, all in the east wing on the fifteenth floor, and at the time of the outbreak there were thirty-two intensive-care beds. The I.C.U.s were built in 1961, and although the equipment had been modernized over the years, the units had otherwise remained relatively unchanged: the beds were close to each other, with I.V. pumps and respirators between them, and doctors and nursing staff were shared among the various I.C.U.s. This was an ideal environment for a highly infectious bacterium.

It was the first major outbreak of this multidrug-resistant strain of *Klebsiella* in the United States, and Wetherbee was concerned that the bacterium had become so well adapted in the I.C.U. that it could not be killed with the usual ammonia and phenol disinfectants. Only bleach seemed able to destroy it. Wetherbee and his team instructed doctors, nurses, and custodial staff to perform meticulous hand washing, and had them wear gowns and gloves when attending to infected patients. He instituted strict protocols to insure that gloves were changed and hands vigorously disinfected after handling the tubing on each patient's ventilator. Spray bottles with bleach solutions were installed in the I.C.U.s, and surfaces and equipment were cleaned several times a day. Nevertheless, in the ensuing months *Klebsiella* infected more than a dozen patients.



"He's in the other room, grumbling about the culture."

In late autumn of 2000, in addition to pneumonia patients began contracting urinary-tract and bloodstream infections from *Klebsiella*. The latter are often lethal, since once *Klebsiella* infects the bloodstream it can spread to every organ in the body. Wetherbee reviewed procedures in the I.C.U. again and discovered that the Foley catheters, used to drain urine from the bladder, had become a common source of contamination; when emptying the urine bags, staff members inadvertently splashed infected urine onto their gloves and onto nearby machinery. "They were very effectively moving the organism from one bed to the next," Wetherbee said. He ordered all the I.C.U.s to be decontaminated; the patients were temporarily moved out, supplies discarded, curtains changed, and each room was cleaned from floor to ceiling with a bleach solution. Even so, of the thirty-four patients with infections that year, nearly half died. The outbreak subsided in October, 2003, after even more stringent procedures for decontamination and hygiene were instituted: patients kept in isolation, and staff and visitors required to wear gloves, masks, and gowns at all times.

"My basic premise," Wetherbee said, "is that you take a capable microörganism like *Klebsiella* and you put it through the gruelling test of being exposed to a broad spectrum of antibiotics and it will eventually defeat your efforts, as this one did." Although Tisch Hospital has not had another outbreak, the bacteria appeared soon after at several hospitals in Brooklyn and one in Queens. When I spoke to infectious-disease experts this spring, I was told that the resistant *Klebsiella* had also appeared at Mt. Sinai Medical Center, in Manhattan, and in hospitals in New Jersey, Pennsylvania, Cleveland, and St. Louis.

Of the so-called superbugs—those bacteria that have developed immunity to a wide number of antibiotics—the methicillin-resistant *Staphylococcus aureus*, or MRSA, is the most well known. Dr. Robert Moellering, a professor at Harvard Medical School, a past president of the Infectious Diseases Society of America, and a leading expert on antibiotic resistance, pointed out that MRSA, like *Klebsiella*, originally occurred in I.C.U.s, especially among patients who had undergone major surgery. "Until about ten years ago," Moellering told me, "virtually all cases of MRSA were either in hospitals or nursing homes. In the hospital setting, they cause wound infections after surgery, pneumonias, and bloodstream infections from indwelling catheters. But they can cause a variety of other infections, all the way to bacterial meningitis." The first deaths from MRSA in community settings, reported at the end of the nineteen-nineties, were among children in North Dakota and Minnesota. "And then it started showing up in men who have sex with men," Moellering said. "Soon, it began to be spread in prisons among the prisoners. Now we see it in a whole bunch of other populations." An outbreak among the St. Louis Rams football team, passed on through shared equipment, particularly

affected the team's linemen; artificial turf, which causes skin abrasions that are prone to infection, exacerbated the problem. Other outbreaks were reported among insular religious groups in rural New York; Hurricane Katrina evacuees; and illegal tattoo recipients. "And now it's basically everybody," Moellering said. The deadly toxin produced by the strain of MRSA found in U.S. communities, Panton-Valentine leukocidin, is thought to destroy the membranes of white blood cells, damaging the body's primary defense against the microbe. In 2006, the Centers for Disease Control and Prevention recorded some nineteen thousand deaths and a hundred and five thousand infections from MRSA.

Unlike resistant forms of *Klebsiella* and other gram-negative bacteria, however, MRSA can be treated. "There are about a dozen new antibiotics coming on the market in the next couple of years," Moellering noted. "But there are no good drugs coming along for these gram-negatives." *Klebsiella* and similarly classified bacteria, including *Acinetobacter*, *Enterobacter*, and *Pseudomonas*, have an extra cellular envelope that MRSA lacks, and that hampers the entry of large molecules like antibiotic drugs. "The *Klebsiella* that caused particular trouble in New York are spreading out," Moellering told me. "They have very high mortality rates. They are sort of the doomsday-scenario bugs."

In 1968, Moellering travelled to Malaita, in the Solomon Islands. "I was really interested to see whether we could find an antibiotic-resistant population of bacteria in a place that had never seen antibiotics," Moellering said. The natives practiced head-hunting and cannibalism, and were isolated as much by conflict as by the island's dense jungle. Moellering identified microbes there that were resistant to the antibiotics streptomycin and tetracycline, which were then in use in the West but had never been introduced clinically on Malaita. Later studies found resistant bacteria in many other isolated indigenous human populations, as well as in natural reservoirs like aquifers.

Before the development of antibiotics, the threat of infection was urgent: until 1936, pneumonia was the No. 1 cause of death in the United States, and amputation was sometimes the only cure for infected wounds. The introduction of sulfa drugs, in the nineteen-thirties, and penicillin, in the nineteen-forties, suddenly made many bacterial infections curable. As a result, doctors prescribed the drugs widely—often for sore throats, sinus congestion, and coughs that were due not to bacteria but to viruses. In response, bacteria quickly developed resistance to the most common antibiotics. The public assumed that the pharmaceutical industry and researchers in academic hospitals would continue to identify effective new treatments, and for many years they did. In the nineteen-eighties, a class of drugs called carbapenems was developed to combat gram-negative organisms like *Klebsiella*, *Pseudomonas*, and *Acinetobacter*. "They were, at the time, thought to be drugs of last resort, because they had activity against a whole variety of multiply-resistant gram-negative bacteria that were already floating around," Moellering said. Many hospitals put the drugs "on reserve," but an apparent cure-all was too tempting for some physicians, and the tight stewardship slowly broke down. Inevitably, mutant, resistant microbes flourished, and even the carbapenems' effectiveness waned.

Now microbes are appearing far outside their environmental niches. *Acinetobacter* thrives in warm, humid climates, like Honduras, as well as in parts of Iraq, and is normally found in soil. An article published in the military magazine *Proceedings* in February reported that more than two hundred and fifty patients at U.S. military hospitals were infected with a highly resistant strain of *Acinetobacter* between 2003 and 2005, with seven deaths as of June, 2006, linked to "*Acinetobacter*-related complications." In 2004, about thirty per cent of all patients returning from Iraq and Afghanistan tested positive for the bacteria. "It's a big problem, and it's contaminated the evacuation facilities in Germany and a lot of the V.A. hospitals in the United States where these soldiers have been brought," Moellering said. Patients evacuated to Stockholm from Thailand after the 2004 tsunami were often infected with resistant gram-negative microbes, including a strain of *Acinetobacter* that was resistant even to colistin, the antibiotic used, to variable effect, in the outbreak at Tisch Hospital. The practice of "clinical tourism," in which patients travel long distances for more advanced or more affordable medical centers, may introduce resistant microbes into hospitals where they had not existed before.

Meanwhile, antibiotic use in agricultural industries has grown rapidly. "Seventy per cent of the antibiotics administered in America end up in agriculture," Michael Pollan, a professor of journalism at Berkeley and the author of "In Defense of Food: An Eater's Manifesto," told me. "The drugs are not used to cure sick animals but to prevent them from getting sick, because we crowd them together under filthy circumstances. These are perfect environments for disease. And we also have found, for reasons that I don't think we entirely understand, that administering low levels of antibiotics to animals speeds their growth." The theory is that by killing intestinal bacteria the competition for energy is reduced, so that the animal absorbs more energy from the food and therefore grows faster. The Food and Drug Administration, which is often criticized for its lack of attention to the risks of widespread use of antibiotics, offers

recommended, non-binding guidelines for these drugs but has rarely withdrawn approval for their application. A spokesman for the Center for Veterinary Medicine at the F.D.A. told me that the center "believes that prudent drug-use principles are essential to the control of antimicrobial resistance." A study by David L. Smith, Jonathan Dushoff, and J. Glenn Morris, published by *PLoS Medicine*, from the *Public Library of Science*, in 2005, noted that the transmission of resistant bacteria from animal to human populations is difficult to measure, but that "antibiotics and antibiotic-resistant bacteria (ARB) are found in the air and soil around farms, in surface and ground water, in wild-animal populations, and on retail meat and poultry. ARB are carried into the kitchen on contaminated meat and poultry, where other foods are cross-contaminated because of common unsafe handling practices." The researchers developed a mathematical model that suggested that the impact of the transmission of these bacteria from agriculture may be more significant than that of hospital transmissions. "The problem is that we have created the perfect environment in which to breed superbugs that are antibiotic-resistant," Pollan told me. "We've created a petri dish in our factory farms for the evolution of dangerous pathogens."

Ten years ago, the Institute of Medicine of the National Academy of Sciences, in Washington, D.C., assessed the economic impact of resistant microbes in the United States at up to five billion dollars, and experts now believe the figure to be much higher. In July, 2004, the Infectious Diseases Society of America released a white paper, "Bad Bugs, No Drugs: As Antibiotic Discovery Stagnates . . . A Public Health Crisis Brews," citing 2002 C.D.C. data showing that, of that year's estimated ninety thousand deaths annually in U.S. hospitals owing to bacterial infection, more than seventy per cent had been caused by organisms that were resistant to at least one of the drugs commonly used to treat them. Drawing on these data, collected mostly from hospitals in large urban areas which are affiliated with medical schools, the Centers for Disease Control and Prevention found more than a hundred thousand cases of gram-negative antibiotic-resistant bacteria. No precise numbers for all infections, including those outside hospitals, have been calculated, but the C.D.C. also reported that, among gram-negative hospital-acquired infections, about twenty per cent were resistant to state-of-the-art drugs.

In April, I visited Dr. Stuart Levy, at Tufts University School of Medicine. Levy is a researcher-physician who has made key discoveries about how bacteria become resistant to antibiotics. In addition to the natural cell envelope of *Klebsiella*, Levy outlined three primary changes in bacteria that make them resistant to antibiotics. Each change involves either a mutation in the bacterium's own DNA or the importation of mutated DNA from another. (Bacteria can exchange DNA in the form of plasmids, molecules that are shared by the microbes and allow them to survive inhibitory antibiotics.) First, the bacteria may acquire an enzyme that can either act like a pair of scissors, cutting the drug into an inactive form, or modify the drug's chemical structure, so that it is rendered impotent. Thirty years ago, Levy discovered a second change: pumps inside the bacteria that could spit out the antibiotic once it had passed through the cell wall. His first reports were met with profound skepticism, but now, Levy told me, "most people would say that efflux is the most common form of bacterial resistance to antibiotics." The third change involves mutations that alter the inner contents of the microbe, so that the antibiotic can no longer inactivate its target.

Global studies have shown how quickly these bacteria can develop and spread. "This has been a problem in Mediterranean Europe that started about ten years ago," Dr. Christian Giske told me. Giske is a clinical microbiologist at Karolinska University Hospital, in Stockholm, who, with researchers in Israel and Denmark, recently reported on the worldwide spread of resistant gram-negative bacteria. He continued, "It started to get really serious during the last five or six years and has become really dramatic in Greece." A decade ago, only a few microbes in Southern Europe had multidrug resistance; now some fifty to sixty per cent of hospital-acquired infections are resistant.

Giske and his colleagues found that infection with a resistant strain of *Pseudomonas* increased, twofold to fivefold, a patient's risk of dying, and increased about twofold the patient's hospital stay. Like other experts in the field, Giske's team was concerned about the lack of new antibiotics being developed to combat gram-negative bacteria. "There are now a growing number of reports of cases of infections caused by gram-negative organisms for which no adequate therapeutic options exist," Giske and his colleagues wrote. "This return to the preantibiotic era has become a reality in many parts of the world."

Doctors and researchers fear that these bacteria may become entrenched in hospitals, threatening any patient who has significant health issues. "Anytime you hear about some kid getting snatched, you want to find something in that story that will convince you that that family is different from yours," Dr. Louis Rice, an expert in antibiotic resistance at

Louis Stokes Cleveland VA Medical Center, told me. “But the problem is that any of us could be an I.C.U. patient tomorrow. It’s not easy to convey this to people if it’s not immediately a threat. You don’t want to think about it. But it’s actually anybody who goes into a hospital. This is scary stuff.” Rice mentioned that he had a mild sinusitis and was hoping it would not need to be treated, because taking an antibiotic could change the balance of microbes in his body and make it easier for him to contract a pathogenic organism while doing his rounds at the hospital.

Genetic elements in the bacteria that promote resistance may also move into other, more easily contracted bugs. Moellering pointed out that, while *Klebsiella* seems best adapted to hospital settings, and poses the greatest risk to patients, other gram-negative bacteria—specifically *E. coli*, which is a frequent cause of urinary-tract infection in otherwise healthy people—have recently picked up the genes from *Klebsiella* which promote resistance to antibiotics.

In the past, large pharmaceutical companies were the primary sources of antibiotic research. But many of these companies have abandoned the field. “Eli Lilly and Company developed the first cephalosporins,” Moellering told me, referring to familiar drugs like Keflex. “They developed a huge number of important anti-microbial agents. They had incredible chemistry and incredible research facilities, and, unfortunately, they have completely pulled out of it now. After Squibb merged with Bristol-Myers, they closed their antibacterial program,” he said, as did Abbott, which developed key agents in the past treatment of gram-negative bacteria. A recent assessment of progress in the field, from U.C.L.A., concluded, “FDA approval of new antibacterial agents decreased by 56 per cent over the past 20 years (1998-2002 vs. 1983-1987),” noting that, in the researchers’ projection of future development only six of the five hundred and six drugs currently being developed were new antibacterial agents. Drug companies are looking for blockbuster therapies that must be taken daily for decades, drugs like Lipitor, for high cholesterol, or Zyprexa, for psychiatric disorders, used by millions of people and generating many billions of dollars each year. Antibiotics are used to treat infections, and are therefore prescribed only for days or weeks. (The exception is the use of antibiotics in livestock, which is both a profit-driver and a potential cause of antibiotic resistance.)

“Antibiotics are the only class of drugs where all the experts, as soon as you introduce them clinically, we go out and tell everyone to try to hold it in reserve,” Rice pointed out. “If there is a new cardiology drug, every cardiologist out there is saying that everyone deserves to be on it.” In February, Rice wrote an editorial in the *Journal of Infectious Diseases* criticizing the lack of support from the National Institutes of Health; without this support, he wrote, “the big picture did not receive the attention it deserved.” Rice acknowledges that there are competing agendas. “As loud as my voice might be, there are louder voices screaming ‘AIDS,’ ” he told me. “And there are congressmen screaming ‘bioterrorism.’ ” Rice came up with the acronym ESKAPE bacteria—*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumanni, Pseudomonas aeruginosa,* and the *Entero-bacter* species—as a way of communicating the threat these microbes pose, and the Infectious Diseases Society is lobbying Congress to pass the Strategies to Address Antimicrobial Resistance Act, which would earmark funding for research on ESKAPE microbes and also set up clinical trials on how to limit infection and antibiotic resistance. Rice has also proposed studies to determine the most effective use—at what dosage, and for how long—of antibiotics for common infections like bronchitis and sinusitis.

Dr. Anthony Fauci is the director of the National Institute of Allergy and Infectious Diseases, which chairs the federal interagency working group on microbial resistance. Fauci told me that the government is acutely aware of the severity of the problem. He pointed out that the N.I.H. recently issued a call for proposals to study optimal use of antibiotics for common bacterial infections. It has also funded so-called “coöperative agreements,” including one on *Klebsiella*, to facilitate public-private partnerships where the basic research from the institute or from university laboratories can be combined with development by a pharmaceutical or a biotech company. Even so, the total funding for studying the resistance of ESKAPE microbes is about thirty-five million dollars, a fraction of the two hundred million dollars provided by the NIAID for research on antimicrobial resistance, most of which goes to malaria, t.b., and H.I.V. “The difficulty that we are faced with is that our budget has been flat for the last five years,” Fauci told me. “In real dollars, we’ve lost almost fifteen per cent purchasing power,” because of an inflation index of about three per cent for biomedical research and development.

Since September 11, 2001, significant funding has been directed toward the study of anthrax and other microbes, like the one that causes plague, which could be used as bioweapons. Although there is little concern that *Klebsiella* or *Acinetobacter* might be weaponized, the basic science of their mutation and resistance could be useful in helping us to understand these threats. Fauci hopes to make the case that funds for biodefense should be used to study the ESKAPE

bugs, but, for now, he is quick to point out the challenge posed by a lack of resources. “The problem is, it is extremely difficult to do a prospective controlled trial, because when people come into the hospital they immediately get started on some treatment, which ruins the period of study,” he said, referring to research into the treatment of common infections. “The culture of American medicine makes a study like that more difficult to execute.”

These types of studies—on how often, and for how long, antibiotics should be prescribed—are much easier to conduct in countries where medicine is largely socialized and prescriptions are tightly regulated. Recently, researchers in Israel, where most citizens receive their care through such a system, showed that refraining from empirically prescribing antibiotics during the summer months resulted in a sharp decline in ear infections caused by antibiotic-resistant microbes. (In the United States, a 1998 study estimated that fifty-five per cent of all antibiotics prescribed for respiratory infections in outpatients—22.6 million prescriptions—were unnecessary.) In Sweden, the government closely monitors all infections, and has the power to intervene as needed. “Our infection-control people have a lot of authority,” Giske said. “This is power from the legislation.” Once a resistant microbe is identified, stringent protocols are put in place, with dramatic results. Fewer than two per cent of the *staphylococci* in Sweden are MRSA, compared with sixty per cent in the United States. “Of course, it’s only around ten million people, so it’s possible to intervene because everything is smaller,” Giske said, adding, “Maybe Swedes are more used to this type of intervention and regulation.”

Stuart Levy’s laboratory occupies the eighth floor of a renovated building on Harrison Avenue in Boston’s Chinatown, across the street from Tufts Medical Center. As I passed from his office into the corridor, I detected the acrid smell of agar, which is used to grow bacteria. That day, a laboratory technician was testing specimens taken from the eyes of people with bacterial conjunctivitis who had been given an antibiotic eye drop containing fluoroquinolone. Levy was comparing the bacteria from the infected eyes with those in the noses, cheeks, and throats of the same patients. His technician held up a petri dish with a cranberry-colored agar base. The patient’s specimen was growing bacteria that were susceptible to the antibiotic; the drug had created a large oval clear zone on the plate which resembled the halo around the moon. The study investigates whether an antibiotic applied to the eye would affect bacteria in the nose and mouth as well, which might indicate that what seems to be an innocuous and limited treatment may profoundly change a wider area of the body and foster resistant microbes.

Levy has also received funding from the N.I.H. to study *Yersinia pestis*, the microbe that causes plague; the Department of Agriculture has sponsored his study of *Pseudomonas fluorescens*, a soil-based bacterium that has the potential to protect plants from microbial infection. He plans to develop it as a biocontrol agent, so that farmers can be weaned off the potent antibiotics and chemicals they use to treat their fields. “We need to treat biology with biology, not chemistry,” he said. In other studies, Levy and his team are looking at ways to render bacteria nondestructive and noninvasive, so that they might enter the body without harmful effects. This makes it necessary to identify virulence factors—which parts of the bacteria cause damage to our tissues. Levy’s laboratory is targeting a protein in gram-negative organisms called MAR, which appears to act as a master switch, turning on both virulence genes and genes that mediate resistance, like the efflux pump. In collaboration with a startup company called Paratek, of which Levy is a co-founder, his laboratory is screening novel compounds in the hope of finding a drug that blocks MAR.

Frederick Ausubel, a bacterial geneticist at the Massachusetts General Hospital, in Boston, is searching for drugs to combat bacterial virulence, using tiny animals like worms, which have intestinal cells that are similar to those in humans, and which are susceptible to lethal microbial infection. The worm that Ausubel is studying, *Caenorhabditis elegans*, is one and a half millimetres in length. “You are probably going to have to screen millions of compounds and you can’t screen millions of infected mice,” Ausubel said. “So our approach was to find an alternative host that could be infected with human pathogens which was small enough and cheap enough to be used in drug screens. What’s remarkable is that many common human pathogens, including *Staphylococcus* and *Pseudomonas*, will cause intestinal infection and kill the worms. So now you can look for a compound that cures it, that prevents the pathogen from killing the host.” Ausubel first screened some six thousand compounds by hand and found eight, none of them traditional antibiotics, that may protect the worms. He is also attempting, among other potential solutions, to find a compound that would block what is called “quorum sensing,” in which bacteria release small molecules to communicate with one another and signal when a critical mass is present. Once this quorum is reached, the bacteria turn on their virulence genes. “Bacteria don’t want to alert their host that they are there by immediately producing virulence factors which the host would recognize,” triggering the immune system, Ausubel explained. “When they reach a certain quorum, there

are too many of them for the host to do anything about it." Bonnie Bassler, a molecular biologist at Princeton University, has recently shown that it is through quorum sensing that cholera bacteria are able to accumulate in the intestines and release toxins that can be fatal; *Pseudomonas* is also known to switch on its virulence genes in response to signals from quorum sensing.

Moellering is enthusiastic but cautious about this avenue of research. "It's a great idea, but so far nobody has been able to make it work for human infections," he told me. With certain types of *staphylococci*, Moellering said, "mutations have occurred spontaneously in nature that cut down on a number of virulence factors . . . but they still cause serious infections. I'm not sure that we have a way yet to use what we know about virulence factors to develop effective antimicrobial agents. And we almost certainly will have to use these agents in combination with antibiotics." No one, Moellering said, has developed a way to disarm bacteria sufficiently to allow the human body to naturally and consistently defend against them. I asked him what we should do to combat these new superbugs. "Nobody has the answer right now," he said. "The fact of the matter is that we have found all the easy targets" for drug development. He went on, "So the only other thing we can do is continue to work on antibiotic stewardship." Meanwhile, new resistant bacteria, Moellering asserted, aren't going to go away. "We can temper things, we might be able to slow the rate of emergence of resistance, but it's unlikely that we will ever be able to conquer it." ♦

ILLUSTRATION: BRUCE MCCALL