Antibiotic resistance is a public-health crisis with potentially devastating effects. Here's what researchers are doing to solve this problem—and what you need to know about protecting yourself.

BY JOANA LOURENÇO

THE RISE OF THE SUPERBUG

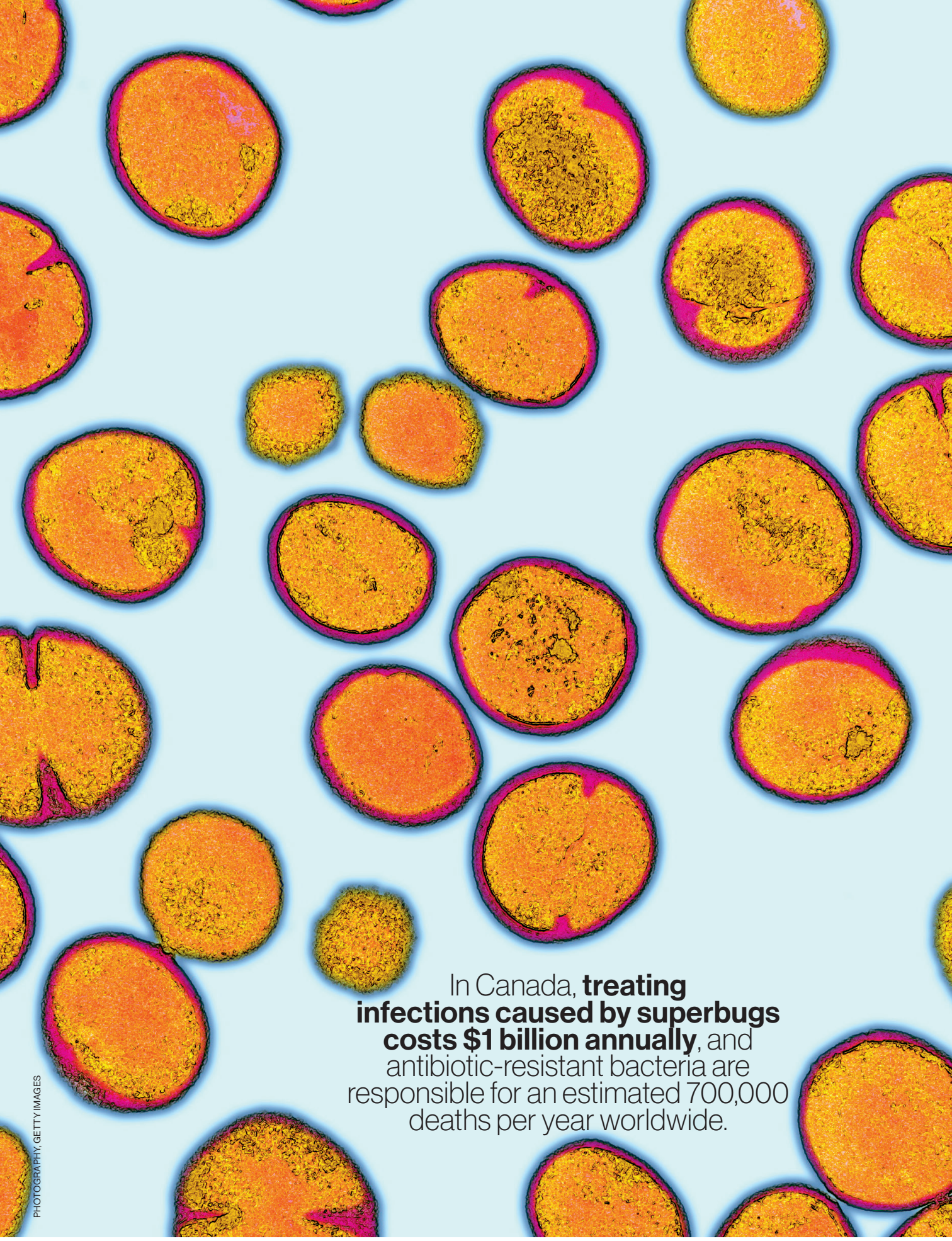
WHEN TERESA ZURBERG fell on a nail while building a new fence four years ago, she worried about tetanus, and maybe scarring. She went to the hospital, where doctors gave her oral antibiotics. But when sepsis (also referred to as blood poisoning, an extreme—and rare—reaction to an infection) set in and she was prescribed more medication, the incident led to one of the most harrowing experiences of her life.

"I lost 20 pounds in five days," says Teresa, now 45. "It was terrible; I couldn't eat, and I had to go to the bathroom every 20 minutes. On top of everything, I had a bad reaction to one of the drugs—it felt like my head was being attacked by fire ants."

While she didn't know it at the time, the Maple Ridge, B.C., native was in the throes of a *C. difficile* infection. *Clostridium difficile* is a nasty bacterium that can damage the colon and cause severe diarrhea; in some cases, the reaction is fatal. These bacteria can live on surfaces contaminated by feces, where they may be picked up and enter the body through hand-to-mouth contact. (The bugs are also found naturally in the digestive system of a small percentage of adults, where they're usually harmless.) *C. difficile* bacteria are increasingly resistant to some antibiotics; when they're allowed to multiply—usually after a high dose of drugs is administered—they can cause a severe infection. That's what happened to Teresa.

"I was on so many antibiotics, they killed off the good bacteria in my gut and let the bad bacteria take over," she explains. "In my case, [that bacteria] was *C. difficile*."

Some strains of bacteria (like *C. difficile* or E. coli) can develop genetic mutations that allow them to survive an antibiotic. Others start out as naturally occurring bacteria in the environment—in soil or water—and in our bodies; these bacteria don't wreak havoc until something alters them. In both cases, antibiotics play a big role: They may disrupt bacteria cells, causing mutations. The drugs don't just target the bugs that are making you ill; they also get rid of healthy, normal bacteria in the body, which creates an opportunity for trouble-makers to take roost. With time, these tough bugs may dodge various treatments. In other words, they become superbugs.



In Canada, **treating infections caused by superbugs costs $1 billion annually**, and antibiotic-resistant bacteria are responsible for an estimated 700,000 deaths per year worldwide.

PHOTOGRAPHY: GETTY IMAGES

Antibiotic-resistant bacteria are on the rise around the world. And, while some people are more at risk (babies and the elderly, for example), no one is immune. Before becoming ill, Teresa was a fit, healthy 42-year-old who worked as a canine handler and a cardiology technologist after years spent as an army medic. If it can happen to her, it can happen to you.

WHAT'S TO BLAME?

The development of antibiotics nearly a century ago was revolutionary. Finally, harmful, even deadly, bacteria could be controlled and destroyed. But instead of seeing antibiotics as a precious resource, we've taken their effectiveness for granted—and that's what's getting us into trouble.

Today, when people get a bacterial infection, it's assumed they can be cured with a brief course of antibiotics. The expectation of a quick fix for even mild infections has led to overprescribing, one of the contributing factors of antibiotic resistance. So has the demand for drugs when the cause is not bacterial—we've all been told the flu virus doesn't respond to antibiotics, which is also true for many ear and sinus infections—but this is something patients don't always want to hear.

The misuse of antibiotics in hospitals is another major issue. "The problem is that we often start patients on antibiotics when we don't need to. We use drugs that are broad-spectrum—they cover more germs than they need to—and we continue therapy for too long," says Dr. Andrew Morris, a professor of medicine at the University of Toronto and medical director of the antimicrobial stewardship program at the Sinai Health System-University Health Network in Toronto.

And there's also the livestock issue. "Antibiotics are used to treat infections in animals, just like they are in humans, and that's extremely important," explains Dr. Michael Mulvey, chief of antimicrobial resistance and nosocomial infections at the Public Health Agency of Canada's national microbiology laboratory in Winnipeg. "But some farming practices [also] use antibiotics in very low doses in the feed or water to promote the growth of animals and fatten them up. [Doing this] leads to antibiotic resistance in bacteria, and that's potentially where some of the problems emerge." Indeed, in a recent report for the World Health Organization, researchers at the University of Calgary concluded that there's a direct link between use of antibiotics in animals and drug resistance. That doesn't mean superbugs are in your food supply; according to the Canadian Food Inspection Agency, antibiotic levels in meat are rarely found to be above the maximum levels set by Health Canada. And antibiotic-resistant bacteria aren't passed on to humans through cooked or pasteurized animal products, such as meat and milk, since those processes kill bacteria. Instead, it's more about overuse. The more bacteria are exposed to an antibiotic, the more likely they are to develop resistance. Then, when humans are subjected to those bacteria—sometimes through animal waste contaminating lakes and rivers where we get drinking water or as a result of safety failures in our food supply—we don't have any weapons to fight them.

WHY PANIC NOW?

The World Health Organization recently called the rise of superbugs a "global emergency"; in September 2016, the United Nations held a General Assembly devoted to the "fundamental long-term threat" of drug-resistant bacteria. (This is especially telling, considering it's only the fourth time in UN history that it has held a high-level meeting for a health issue.)

But we've known about antibiotic resistance for decades. Take penicillin, for instance: Discovered in 1928, it was being used to treat serious infections by the 1940s. By the '50s, there was such widespread resistance that "many of the advances of the prior decade were threatened," according to an article published in 2015 in *Pharmacy and Therapeutics*. Other hostile bacteria quickly emerged—the first cases of methicillin-resistant *Staphylococcus aureus*, a bacterium that's a common cause of infections in some hospitals, began to pop up in the 1960s.

How to Protect Yourself

While you can't completely shield yourself from drug-resistant infections, there are four simple steps you can take to lower your risk.

WASH YOUR HANDS

They have their uses, but alcohol-based hand sanitizers can't replace good old hand washing. They don't kill *C. difficile*, for example, but soap and water will.

GET THE FLU VACCINE

The influenza virus weakens the immune system, which has the side-effect of making you more vulnerable to other bugs. Getting the vaccine every year is your best shot at preventing the flu.

BE CAREFUL WHEN HANDLING RAW MEAT

Though the risk of contracting superbugs from food is extremely low, make sure to wash countertops, hands and utensils with soap and water after contact with raw meat.

TAKE ANTIBIOTICS ONLY WHEN ABSOLUTELY NECESSARY

We don't think of these drugs as precious resources, but they are. (See The New Antibiotic Rules, page 73, for more info.)

ILLUSTRATIONS, THINKSTOCK

So why the renewed worry? It all comes down to our tools. We're running out of antibiotics, and as our arsenal becomes depleted, the germs are becoming more and more resistant. Last year, news broke that MCR-1, a newly discovered gene that makes bacteria immune to colistin—one of our last-resort antibiotics—has been found in humans and beef in Canada. And the family of bacteria called carbapenem-resistant *Enterobacteriaceae* (CRE) is increasingly troubling experts. Germs in this group, like E. coli and *Klebsiella*, are normal residents of our gut flora—but they have a genetic mutation that predisposes them to antibiotic resistance. Earlier this year, a Nevada woman died of an infection caused by a CRE strain that couldn't be treated with any of the 26 antibiotics currently available in the U.S. These bugs have also been found in Europe, China and, yes, Canada.

RUNNING OUT OF OPTIONS

It's tempting to think of these superbug infections as rare and the stuff of science-fiction movies. However, there's a genuine concern for the future availability of remedies for everyday illnesses. "There is a real risk that there could be no antibiotics left to treat some common infections," warns Dr. Mulvey. Certain strains of gonorrhea, tuberculosis, pneumonia and urinary tract infections (80 percent of which are caused by E. coli) have already become immune to the drugs that worked years ago.

In the past, when bacteria became resistant to antibiotics, there was an easy fix: Scientists would develop new drugs. But we can no longer rely on this strategy—since 2010, only three new antimicrobials have been approved for use in Canada. Why so few? The reasons are multifold: First, there are regulatory challenges, as government agencies require complex clinical trials involving hundreds and even thousands of patients. But that's not the only challenge. "At the end of the day, the science is really hard," says Dr. Gerard Wright, a professor of biochemistry and director of the Michael G. DeGroote Institute for Infectious Disease Research at McMaster University in Hamilton. "We've picked all the low-hanging fruit—the easy-to-find antibiotics."

In fact, that's part of the explanation for the last piece of the puzzle: There are fewer pharmaceutical companies actively developing new drugs. "There's no cogent business case for manufacturing antibiotics," explains Dr. Morris. "They're relatively cheap, used for a very short period of time and there's the risk of resistance. A drug company will not want to make a drug that becomes obsolete before the patent even expires."

LOOKING FOR SOLUTIONS

Searching out new antibiotics isn't the only way scientists are working to combat superbugs. Researchers worldwide, including Dr. Wright, are working on a promising new area of discovery: understanding resistance itself. "We've done a lot of work to figure out where resistance comes from and how it evolves," he says. If researchers can learn how to stop bacteria from becoming immune to the effects of antibiotics, our arsenal of infection-fighting drugs is suddenly not so depleted, after all. But you can't beat evolution, so you need to find a compound that blocks resistance and use it in combination with antibiotics, Dr. Wright explains. "The idea is that if we get rid of resistance, the drugs will work."

Dr. Wright and other scientists have shown that it's possible to keep antibiotic resistance at bay by using cocktails of drugs—combinations of old antibiotics with new resistance inhibitors. To find these inhibitors, as well as any potential new antibiotics, Dr. Wright and his team are screening hundreds of thousands of bacteria and fungi samples taken from soil across Canada. (Bacteria from soil are the source of most existing antibiotics.) "We've collected dirt from every province and territory, from the tip of southern Ontario to Nunavut," he says. "I've even collected soil samples from my own backyard."

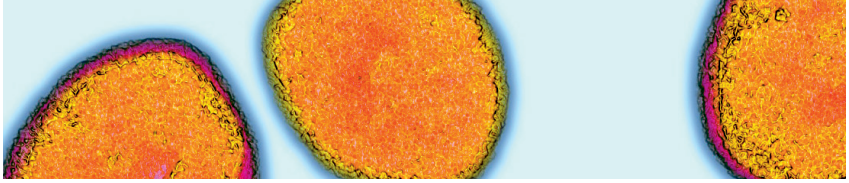
Though it may sound like a science-fair experiment, Dr. Wright's lab has had some real breakthroughs. For example, some superbugs have mutated to produce an enzyme called NDM-1, which makes them resistant to almost all antibiotics—even the last-resort ones. But one of Dr. Wright's soil samples, taken from Kejimkujik National Park in Nova Scotia, yielded *Aspergillus* fungus, which produces a chemical compound that disarms NDM-1, blocking resistance. The lab is now studying how this compound works in animals, with the hope that it will have the same type of superbug-inhibiting effect.

Dr. Wright, who currently holds a Canada Research Chair in molecular studies of antibiotics, credits support at the federal and provincial levels, as well as from private donors. Other government agencies are also stepping up to address the issue. "The Public Health Agency of Canada [PHAC] has a fairly comprehensive surveillance program in over 60 hospitals across Canada, where we're specifically monitoring the superbugs," says Dr. Mulvey. The agency runs programs that look for antibiotic resistance throughout the food chain, collecting data on farms, at abbatoirs and at the grocery store in several Canadian regions. It also keeps watch on what's happening in other countries, in order to be able to rapidly detect emerging types of resistance if they arrive in Canada.

A HOPEFUL FUTURE

There have been some advances: Rates of methicillin-resistant *Staphylococcus aureus* infection, for example, have decreased in Canada by 25 percent since 2008. But experts believe much more needs to be done, and they're pushing for the government to invest in research and infrastructure—like the PHAC's surveillance systems or stronger regulations for the use of medicated animal feed and veterinary drugs. Dr. Morris also sees another issue: a gap in the public's knowledge and awareness of the threat of superbugs. "There are no ribbon campaigns, walkathons or bike rides for antimicrobial resistance or stewardship or anything like that, even though we rely on antibiotics for every aspect of health care," he says.

So, where will we be a decade or two from now? Dr. Wright believes we don't have a choice but to keep looking for solutions: "We simply cannot put ourselves in a situation where we're in a post-antibiotic era," he says. "Imagine how terrifyingly dangerous it would be to have open-heart surgery or ◘



a hip replacement without the ability to control infection. Antibiotics underpin almost all of modern medicine."

Teresa Zurberg would agree. To this day, the effects of her encounter with *C. difficile* still linger. She takes high-dose probiotics every day to try to undo the damage to her gut and is vigilant about the type of drugs she can use. (Any antibiotic that disrupts the balance of bacteria in her digestive system could lead to a relapse by killing off harmless bacteria, which would allow *C. difficile* bacteria to thrive.)

But her story has a silver lining. A year after her own brush with the superbug, she read about a beagle in Amsterdam who was trained to sniff out *C. difficile* in hospital patients. As a canine handler of drug- and bomb-detecting dogs, Teresa had just the right kind of animal expertise. So, she set about training her newest springer spaniel, Angus, to do the same.

Today, Angus is the only certified *C. difficile*–sniffing dog in North America, and has been on the prowl at Vancouver Coastal Health since last July. "It's an out-of-the-box approach, for sure, but the hospital has been supportive of the idea from the very beginning," says Teresa.

Angus's talent is just one of the many innovative solutions being implemented in Canada. "In this country, we have the tools and the brains," says Dr. Wright. "There are some outstanding Canadian groups with international profile working in this area, and I know that, with the right support, we can contribute to this global health problem. It's a tough row to hoe, but I'm optimistic." ●

The New Antibiotic Rules

Bombarding bugs with prescription drugs used to be the preferred method of dealing with bacterial infections, but new research says that should change. Here's the latest approach.

IF YOU'VE TAKEN a course of antibiotics recently, you've likely been told to finish all your pills—even if you start to feel better. Conventional medical wisdom says this approach helps prevent antibiotic resistance: If you don't take the full amount, there's a risk that some of the bacteria making you sick will survive and mutate into a resistant form.

However, this theory on antibiotic use is being re-evaluated. It turns out that shorter courses can sometimes be just as effective as longer ones. (There are exceptions: Those with tuberculosis or HIV, for example, need the full course.) But for infections such as sinusitis, middle-ear infections and pneumonia, your doctor may recommend a shorter course. "This is one of the greatest myths of medicine," says Dr. Andrew Morris, a University of Toronto professor and medical director of the antimicrobial stewardship program at the Sinai Health System-University Health Network in Toronto. "For 99.9 percent of the infections treated in Canada," he says, "there's no reason to believe that stopping early is harmful, and it's almost certainly beneficial."

But some of the old rules pertaining to antibiotics still hold true: Don't assume you need a prescription simply because you're sick—they won't cure viral infections like colds. Some doctors may feel pressured to prescribe an antibiotic, or they may not be sure whether you have a bacterial or viral infection, so they write out a prescription to be on the safe side. You should always ask your health-care provider whether or not you truly need an antibiotic. In many cases, a wait-and-see approach is recommended: Tell your doctor you'll fill the prescription if you don't feel better in a few days. "This has been shown repeatedly to be a beneficial way to avoid, or at least minimize, the use of antibiotics," confirms Dr. Morris.