The Atlantic

Are Antibiotics Making People Larger?

Overuse of the drugs seems to make us gain weight—even when we don't take them.

A demonstrator feeds mock antibiotics to chicken puppets during a protest denouncing industrial farming in Berlin.
Thomas Peter / Reuters

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Doctors in Newport, Rhode Island, had to change one of their policies last year because they inadvertently made a young woman obese. At least, because they believe they possibly did.

A few months beforehand, the 32-year-old mother, who had never before

been obese, had developed a vaginal infection. She took an antibiotic and, as expected, the infection went away. But shortly after, the woman's stomach began to ache. A test of her stool found the presence of a lethal toxin.

We've long known that taking an antibiotic can inadvertently lead to another infection. In this case, it was an overgrowth of the bacterium *Clostridium difficile* in the woman's colon. *C. difficile* is an opportunist that can exist in harmony with the other bacteria in our guts; it's only when that ecosystem is disrupted that *C. difficile* takes over and becomes deadly. It releases a toxin (which is actually a relative of the toxin sold as Botox, or *Clostridium botulinum* toxin) that causes a person's bowels to decay and expand and rupture, and the person dies. Last year in the U.S. alone, *C. difficile* killed 15,000 people. Most of the cases were precipitated by treatment with an antibiotic.

To escape this fate, the Rhode Island woman began treatment to kill the *C. difficile*, with another antibiotic. She also tested positive for another bacterial infection of the stomach, *Helicobacter pylori*. So the doctors treated her with two additional antibiotics. Despite all of this, her condition deteriorated.

In a last-ditch attempt to restore balance to her intestinal flora, her doctors recommended a fecal transplant, the technical term for the vogue medical procedure that is simply putting one person's feces into another person. The idea is that the transplanted feces will populate the sick person's bowels with a healthy bacterial population. At the request of the patient, the Newport doctors did not use a "professional" stool donor, but instead utilized the excreta of the woman's 16-year-old daughter.

The transplant was a success, in that the woman's symptoms went away. The bacterial ecosystem finally appeared to be restored to some kind of order. But they also seemed to have brought something else along. The woman's daughter was obese, and in the months after the transplant, the patient

gained 34 pounds, qualifying her as obese for the first time in her life.

"This case serves as a note of caution," her gastroenterologists later wrote a medical-journal report. "We recommend selecting non-overweight [fecal] donors."

Antibiotics in manure that seep into soil have been detected in carrots, lettuce, and green onions.

Of course, many things could have caused her weight gain. Treatment of *Helicobacter pylori*, the bacteria that causes most ulcers, is itself associated with weight gain. Infectious-disease specialists at Massachusetts General Hospital Elizabeth Hohmann and Ana Weil noted at the time that "it is possible and perhaps even likely that the weight gain in the case reported was influenced not only by microbial communities transmitted during [fecal transplant], but also by genetic factors."

In a randomized controlled trial of the reverse scenario, where overweight people with metabolic syndrome underwent fecal transplants from lean donors, recipients showed improvement in their degrees of insulin resistance. Taken together with other research on the effects of gut microbes on body weight and metabolism, Hohmann and Weill concluded in the same journal: "These studies take the concept of 'you are what you eat' to breathtaking new heights and certainly should stimulate further study!"

Of course, most people who are overweight have not had a fecal transplant. Most people will never need a fecal transplant. But the idea that a person can essentially *contract* obesity because of a change in gut microbes is at once exciting and unnerving—because exposure to microbe-altering drugs in day-to-day life has become almost inevitable. This month, the U.S. Food and Drug Administration quietly released a report that said over the past year,

antibiotics sold annually for use in food animals increased to 33,860,000 pounds.

That's a 22 percent increase since five years prior (which was the first time the amount was even measured). Usage also increased in 2014 alone, despite several prominent food producers and restaurants like Whole Foods and Chipotle swearing off antibiotic-raised animal products. Most of those antibiotics are "medically important," meaning they are used in humans to treat diseases. But a majority of antibiotics are not absorbed by the animal, just excreted. So even those that are not medically important manage to find their ways into soil and water as they become part of the 18 gallons of manure that every cow produces every day.

Antibiotics in manure that seep into soil have been detected in carrots, lettuce, and green onions. Some antibiotics remain active for months after passing through the animal and are detectable in rivers miles from their use; a study of a river in Colorado found several antibiotics everywhere except for "a pristine site in the mountains before the river had encountered urban or agricultural landscapes." Antibiotic overuse turned the Hudson River into a breeding ground for drug-resistant bacteria.

Antibiotics do, of course, save many lives in the appropriate medical context. But in animals, antibiotics are rarely given to treat illness. They are given blindly to entire populations to prevent possible infections—which is never indicated medically. Even less medically warranted—actually contrary to the interest of the animal—antibiotics are given as appetite and growth stimulants. In the 1950s, shortly after the advent of modern antibiotics, ranchers noticed that cattle that were treated for infections would put on weight. Because ranchers are paid by the pound, rather than by the number of cattle sold, the idea had appeal. By the 1970s, blanket administration of antibiotics to promote growth became common practice.

Because people so enjoy eating meat and cheese for various reasons—note the 76 million Facebook users who will watch when *Buzzfeed* posts a video of a pepperoni grilled-cheese sandwich or the 108 million who watch the bacon-wrapped grilled-cheese sandwich—animals must be quickly grown to great sizes in order to accommodate the demand for meat that will serve a planet of 7 billion humans. As that number approaches 8 and then 9 billion, the need for antibiotics in meat production will be only greater. And despite the fact that ranchers have known for decades that antibiotics cause their animals to gain weight, the idea that this has a similar effect on people is somehow just now seeping into the heads of everyone else.

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Only in the last few years have we begun to understand the extent of the effects of the microbes inside us on our health—or, rather, as being a part of our health. As the microbiologists Rob DeSalle and Susan Perkins write in their new book *Welcome to the Microbiome*, "It's not the microbes that cause problems with our health, but rather disruptions in the natural ecology of our bodies that lead to illness. It is only when the co-evolved ecological balance of our body's cells with the trillions of microbes living in and on us is thrown out of whack that pathogenicity [disease] arises."

This may be the first time that the word *pathogenicity* has been used in the same sentence as *whack*. Scientists are still figuring out how to talk about all of this. It was only recently that DNA-sequencing technology allowed them to learn that there are indeed trillions of microbes inside each of us, and that in the absence of pathogenicity, the microbiome keeps us healthy every minute of every day, playing significant roles in digestion and assembly of nutrients and vitamins.

The idea is only very recently hitting mass audiences. If you've ridden a subway in New York this month, you've seen an ad for a new exhibit about

the microbiome at the American Museum of Natural History called "The Secret World Inside You." DeSalle and Perkins are the curators. Of all things bodily that could belong in a natural history museum, the microbiome makes the most obvious case for itself. The species that live inside us are older than humans by millennia. Dinosaurs had microbiomes. And our internal ecosystems—the ecosystems that we *are*—have been dramatically affected by the food and drugs we put into the natural world and, directly or indirectly, back into ourselves.

One of the first people Perkins took through the exhibit was a student of hers from Berlin. "When she learned that 70 percent of the antibiotics in the U.S. go to farm animals," Perkins recalled, "she said she's never eating American meat again."

The German student was apparently unaware that antibiotics are widely used in German agriculture, too.

Antibiotic Use by Country

Review on Antimicrobial Resistance

In May, though, the German government announced an aggressive reduction strategy. Denmark and the Netherlands have successfully reduced antibiotic use dramatically in the past five years. Meanwhile, the use of antibiotics in the U.S. and most other countries continues to increase. Congress did recently vote to increase spending on antibiotic resistance, but none of that money went to the Department of Agriculture. If worldwide use continues at the current rate, by 2030 there will be 211 million pounds of antibiotics going into livestock every year—creating resistant bacteria and bleeding into soil, water, and the food system.

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At a cover price of $189.00, gastroenterologist David Johnson's new textbook *The Gut Microbiome: New Understanding and Potential Translational Applications for Disease Management* will reach many millions fewer people than *Buzzfeed*'s video extolling some "downright glorious" cheeseburger-stuffed tater tots. The first time Johnson told me his book title, I thought he was just describing the book. My next question was, "Oh, what's it called?" He repeated the title, somehow not sounding at all annoyed or confused.

Johnson is a professor of medicine and chief of gastroenterology at Eastern Virginia Medical School and the former president of the American College of Gastroenterology. He believes the microbiome holds the key to understanding the human metabolism and he thinks it will bring about profound changes in the way we approach disease prevention.

"If I take a skinny rat, and I transpose the stool from a genetically bred fat rat into the skinny rat, I can make that rat fat."

"Obesity is front and center," he said, "but also diabetes, fatty liver disease, some of the cancer pathways. The microbiome can change you very quickly. If I take a rat that is genetically bred to be a skinny rat, and I transpose the stool from a genetically bred fat rat into the skinny rat, I can make that rat fat. And the weight goes up within two weeks."

In 2014, Martin Blaser and colleagues at New York University found that steady exposure of mice to penicillin early in life predisposed them to become obese. That and similar evidence has begun to win over many scientists, including Johnson and Lee Riley, chair of the division of infectious diseases and vaccinology at the University of California, Berkeley, who comes off even more assured that the relationship is affecting humans.

"We're animals, just like food animals," Riley said "We give them antibiotics so they get fat. We are exposed to those antibiotics. It seems like a very common sense idea."

Riley has dedicated his career to studying drug-resistant infections, especially urinary tract infections and bacteria associated with food-borne illnesses like salmonella. "We've always had this idea that drug-resistant forms of bacteria often originate in food-animal reservoirs," he said. "This argument against antibiotic overuse never really got us anywhere, though."

In the meantime, he started seeing intestinal-microbiome studies that demonstrated that changes in intestinal microbiota are associated with changes in body fat in people. "So I put two and two together and said, what happened in this country in the last 20 to 30 years where you really see a surge in the obesity epidemic? Well, I don't think there has been a tremendous change in the amount of food people consume. I don't think that's the only explanation."

What Americans eat has indeed changed in recent decades. The average person eats more now than the average person of 1950, and a person can buy junk food wherever anything is sold. It's also true that many people live more sedentarily, day-to-day, than they used to. But even while the food Americans ate in the 1950s was more reasonable than it is now, it was not idyllic. White bread and American cheese and hot dogs and Spam were staples then, too. The average American now also has a gym membership of some sort. Jogging was not even a thing until the 1970s, much less Zumba, Soulcycle, or Crossfit. Millions of diet books have been sold during the rise of the obesity "epidemic" proposing every sort of diet-based solution. Despite it all, the problem has only gotten worse. Life expectancy in the U.S. has stopped increasing. Every year, the average person gets fatter.

"There must be some sort of exposure," Riley said. "Epidemics involve

common exposure. So I came up with this idea that it's probably the antibiotics in the environment."

He was far from alone in coming to that conclusion. Even though it's not something most people hear about when they're trying to lose weight, numerous scientists have recently come to believe in this hypothesis. Back in 2008, the French researcher Didier Raolt put this together in a journal article, writing bluntly, "The current obesity pandemic may be caused, in part, by antibiotic treatments."

"As those antibiotics get into animals and we consume them," Johnson said, "either we may be ingesting that antibiotic, or at least it changed the biosis of the animal. So they are effectively a different animal, another processed food."

Todd Korol / Reuters

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Only around 30 percent of antibiotics used in the United States are prescribed to treat human illness directly. So it is a smaller, but not insignificant, part of the problem that many people still think "antibiotics" means "strong medication that will cure my cold."

People exaggerate their symptoms and lie to doctors in hopes of being prescribed antibiotics. Doctors are miserly by nature and tend to withhold antibiotics, apparently, for their own amusement, the thinking must go. Or, more likely, the doctor is trying to see the forest for the trees. When you are the tree, though, and you are sick with something that's almost certainly caused by a virus (against which antibiotics can do nothing), few people care about the forest.

"People are always screaming for an antibiotic when they go to their doctor," he said. "It's cultural. To go to a doctor and come away with nothing feels like you paid money and you didn't get something."

In November, the American Academy of Pediatrics issued a strongly worded warning about the use of antibiotics in agriculture was a danger to the health of children. As *Mother Jones* put it, "The Meat Industry Is Killing Kids, Say Pediatricians." Which sounds sensational but is straightforward: The doctors note that using antibiotics to grow meat results in deadly "superbugs" that now sicken more than two million Americans every year and kill 23,000. That's in addition to $21 billion to $34 billion in medical costs (if that moves you more than the, you know, suffering children). This made minor news.

With every dose of antibiotics you take, you do damage to the microbiome. It recovers, but never to the place that it was before.

As my colleague Ed Yong pointed the week prior, which was World Antibiotic

Awareness Week (remember?), even in the face of warnings of 10 million human deaths by 2050—constituting an "apocalyptic" threat that stands to cast the world "back into the dark ages of medicine" (in the words of U.K. Prime Minister David Cameron)—almost no one seems to care about antibiotic resistance. In a study where researchers attempted to educate people about the dangers of antibiotic overuse and see which approaches were effective. They found that the interviewees were desensitized to doom-laden warnings. They dismissed them as fear mongering. As Yong recounts, "The term *superbugs* felt abstract and confusing. It made them think about swine flu or Ebola—threats that either seemed to pass with little incident, or happened to people living far away." The newly educated people, in retrospect, recommended that doctors simply tell patients: "Bacteria are getting stronger. Antibiotics won't work anymore. You could die."

That might still feel doomy. What if you told people that an antibiotic could slow their "metabolism"?

And what if that warning carried over to buying and eating food that was produced using antibiotics?

A great thing about the microbiome exhibit is that, for Perkins and colleagues, it's a sort of living experiment in education. She sees what people react to; what conceptions they come in with, and what they leave with. "This connection between the microbiome and obesity—when people start to make those connections, I've watched it. They're not happy. They seem like they might be less likely to want an antibiotic."

Perkins's own friend was sick at Thanksgiving, and her doctor told her it was just a cold, advising her to rest, drink fluids, and give it time. But, no. She told Perkins—who has devoted her professional life to the study of molecular evolutions—that she was just going to take some leftover antibiotic. And she did. "Ten minutes later she said she was feeling better," Perkins said,

exasperated. “It's like, that's impossible. That's in your head. Then she came to the exhibit last week and was freaked out.”

In a video segment at the museum, there's a bit where Stanford microbiologist Justin Sonnenburg says that with every dose of antibiotics you take, you do damage to the microbiome. It recovers, but it never recovers to the place that it was before. “That seems to really hit people hard,” Perkins said. “I think there is an understanding that antibiotics disrupt the microbiome, but it's dismissed as necessary collateral damage. And, yes, that's true if you have a real bacterial infection. But thinking, *I'm never going to get back to the place I was before. I will cause the extinction of species and taxa in my gut*—” she paused, “well, I don't think most members of the public think of it exactly like that, in those ecological terms. But the idea that every dose is doing permanent damage really resonates with people.”

I asked her if we're at a time when that feeling about antibiotics—as a harmless panacea—is going to become obsolete?

“I mean, I hope so,” she said. “I don't know. I don't have that much faith in humans, in our education. At the moment.”

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In talking about the role that antibiotics play in obesity, the burden of proof that the latter is causing the former is extremely high. The meat and dairy industries would need about as much proof as the coal industry would need to be convinced that it causes global warming. But when you have an epidemic that’s affecting one in three Americans and fueling many of the leading causes of death and medical costs—and you have a plausible mechanism that could be (partly) behind that epidemic, and it has been demonstrated in animal models—how long do you wait to act?

“The tricky thing is we can't do these experiments in humans to prove the

same causal link," Perkins said. "Except that we already are, the way we use antibiotics in the real world. The correlation is really strong."

But even looking retrospectively, all that anyone can definitively prove is a correlation. "It would be easy to draw a regression line and say *Look! Everybody who had this many doses is this much overweight,*" Perkins posited. "But to really show a mechanism for how a loss of diversity in the gut microbiome translates to obesity is tough. And we know it's not the only factor; of course it also depends on what you're eating and how much you're exercising."

"It's also very difficult to dissociate the effects of antibiotics from nutrition in a study because the more food you eat, the more antibiotics you're exposed to," Riley said. "So it's not easy to scientifically demonstrate this association. Experimentally you can do it. When you give antibiotics to animals, they gain weight. And there are all kinds of studies showing that antibiotics can be found in food and water. If someone can come up with a nice prospective study, we could do that, it's just very expensive to do, and very difficult to control human diets."

For now, Riley is an advocate for consumer incentives. Antibiotic-free meat and dairy are often more expensive, but we might be better off if they were an easy and pervasive option. Or, of course, a person could choose to eat no animal products at all, which has the highest likelihood of preventing obesity. Pescetarians, vegetarians, and especially vegans all have lower body-mass indices than carnivores. Much of the world was up in arms earlier this year when the World Health Organization said that red meat might potentially be slightly carcinogenic. What if everyone cared that much about the millions of pounds of antibiotics that go hand in hand with eating meat—and are definitely killing (and probably fattening) us in the process?

A few years ago the FDA proposed to have the animal industry do a voluntary

restriction on antibiotic use as growth promoters. That may be happening, but they still use antibiotics, they just call it preventing infection. "That's the real dilemma," Riley said. "There's a misuse of this term. As long as antibiotics aren't specifically used for growth promotion purposes, there's no rule. There's no regulation."

While meat and dairy labels now mention antibiotics, no one is actually monitoring these claims unless a product in the grocery store says "No Antibiotics, USDA Process Verified." Being labeled "Natural" says nothing about whether or not antibiotics were used. Nor does "No Hormones" (which, according to a segment on the *Today* show, apparently some people believe implies that no antibiotics were used. Antibiotics and hormones are different things.)

"The intent of the FDA was to gradually decrease the overall use of antibiotics. Apparently it's not working," said Riley. "You have two of the strongest lobbies in the world—the pharmaceutical industry and the food industry—so change is just not going to come from our government. But if people really recognize that the obesity epidemic is associated with exposure to antibiotics, I think demand for antibiotic-free food will become even greater."

So will the demand for fecal transplants, if it can be proven that certain microbial compositions can indeed help to prevent or ameliorate obesity. The mixtures of bacteria that appear to be beneficial are only beginning to be understood, but many experts have high hopes that fecal formulations could one day can be cultured and administered to improve human health in a myriad dimensions.

Until then, companies will hawk probiotics and prebiotics with little or no evidence of what direction they may be taking a person's microbiome. And every January, along with body-improvement resolutions, will welcome the

publication of an onslaught of blockbuster diet books that promise to tell you how *you* can lose weight without exercising more or eating less. As a rule, that line is always too good to be true.

If everyone were exposed to fewer antibiotics, though, that might be an exception. If people at least begin to operate under the belief that this is a real possibility, a convenient side effect might be the aversion of apocalyptic crisis.

ABOUT THE AUTHOR

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