A microscopic solution - The best gut bugs to lose weight

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Rob Knight used to be paunchy. He was about 80 pounds overweight, in fact, when he and his girlfriend Amanda took a trip to Peru in 2008. The couple backpacked up the Inca Trail to the Amazon, where they were beset by a nasty bout of diarrhoea. They seemed to recover, then it flared up again, and both took the same antibiotic to get rid of the bug.

When they returned home, the couple resumed their usual diet and exercise, except Knight started losing weight—a lot of it. Over the next few months he dropped nearly six stone (84 pounds) and effortlessly went from obese to a healthy body weight. While he was downsizing his trousers, Amanda lost no weight at all.

“I believe the difference was related to a radical change in my microbes,” Knight relates in his book, *Follow Your Gut* (Simon & Schuster, 2015). “We each responded differently to the same disease and the same course of treatment.”

It’s an educated guess. Knight, a professor at the University of California at San Diego, is an expert on human microbes, tiny single-celled organisms including bacteria and viruses. He is also co-founder of the American Gut Project, a crowd-funded endeavour that has begun to chart all those microbes residing in and on the human body. (British Gut is the UK counterpart with the same objective.)

Thanks to new DNA-sequencing technologies, scientists are able to explore what is turning out to be a vastly greater microscopic world within humans than they ever imagined. And their first glimpses are revealing that the microscopic life forms inside us are astonishingly numerous and diverse.

Our bodies comprise around 10 trillion human cells, for example, but there are about 100 trillion microbes in our ears, eyes, noses, belly buttons and especially our guts. It turns out that these microbes—collectively known as our ‘microbiota’—and their millions of genes—the ‘microbiome’—are far more important than medical textbooks have acknowledged.

Indeed, while doctors continue to cavalierly prescribe antibiotics in record numbers, a huge body of research is proving that the microbes they are attacking are crucial to our health, regulating our immune systems and preventing disease, digesting our food, manufacturing vitamins and affecting everything from our mental health to our weight.

Microbesity

The microbiome and its impact on obesity is one of the fastest moving areas of study, perhaps because it is one of the fastest growing epidemics of our time and linked to myriad other soaring health conditions, including heart disease, diabetes, cancer, musculoskeletal diseases, depression, anxiety and decreased life expectancy. It is estimated that obesity already costs the National Health Service (NHS) upwards of £5 billion per year and, last year, a public-health study revealed that by their eleventh year, a third of British school children are already overweight or obese.1

It's a problem that is rapidly engulfing the underdeveloped nations too. Worldwide, one in three adults is overweight and one in 10 is obese. The estimated 2.3 billion tubby people on the planet are more than the population of China, the US and all of Europe combined—and growing.2

We all know people who struggle to lose weight; no matter how much they starve themselves or how many hours they spend at the gym, they just can't shed all of the excess. And there are those people who seem able to eat nothing but junk and stay skinny. While dietitians and doctors have focused on calorie-counting, new research is revealing our battle with the bulge may have a lot to do with the types of organisms dominating our microbiome, described as one of our body's largest organs, weighing almost as much as our brain.

In a case study reported last year, a woman undergoing a faecal microbiota transplant to fight a superbug bacterial infection in her gut suddenly gained a "tremendous" amount of weight.3 She was suffering from a *Clostridium difficile* superbug infection, which was resistant to multiple courses of antibiotics. In the US, at least 10,000 people die annually from antibiotic-resistant *C. difficile*, often following from the use of broad-spectrum antibiotics, when 'good' bacteria are battered and their guts are overwhelmed by the pathogen, causing severe diarrhoea and sometimes fatal sepsis. It has been shown that transferring a faecal sample from a healthy individual (containing their gut microbes) can restore the balance of gut bacteria and conquer the disease—sometimes within hours. The NHS adopted the procedure in 2014.

In this woman's case, she opted for a faecal transplant from her 16-year-old daughter, who was healthy but heavy at 140 pounds. It worked and she was cured of the infection, but within 16 months, she had inexplicably gained 34 pounds and was tipping the scales at 170, though she had never been overweight before. Three years later, despite diet and exercise, she weighed 177 pounds and her daughter's weight had climbed to 170.

Some resident of her daughter's microbiome must have made both women obese, the doctors concluded, and they recommended that overweight people be excluded from faecal donations.

A gut guesstimate

Now, scientists can predict with 90-per-cent accuracy if a person is overweight just by looking at their gut microbes. Often the ratio of certain phyla of bacteria, say Firmicutes to Bacteroidetes, is high, but not always. As you don't need to look at a person's microbes to see if they're overweight, the real challenge is determining exactly what microbes are causing the trouble and how to fix it.

"My lab and others haven't been able yet to design a microbe community that actually slims down a mouse (or a person), although that's certainly the goal," says Knight. "But in yet-unpublished research, other groups have reported using antibiotics to target the bacteria that proliferate on a high-fat diet, successfully slimming down the mice, even if they ate unhealthily."

But a number of researchers suspect that, because hundreds of species of microbes inhabit the human gut, the microbial patterns of obesity may be highly individualized and also difficult to target without doing collateral damage to other significant species.

Also, it is increasingly likely that an antibiotic approach to disease may have got us into the fat problem to begin with. Being doused with antibiotics in early life similar to the frequent treatments children are prescribed predisposes male mice to obesity earlier than it does female mice, who tend to put on weight around mid-life, though both are affected permanently. And specifically using amoxicillin and tylosin, the most widely prescribed antibiotics for children, was found to measurably diminish the diversity in their bug populations—that is, the number of different species present in the gut—just as a pesticide might kill birds as collateral damage when targeting unwanted pathogens.

In a breakthrough mouse study (see box, page 34), with amoxicillin use, the bug profile usually

recovered with time, but for tylosin, it did not. Just as most occupations are fairly evenly distributed in human populations in peacetime while soldiers are disproportionately represented in wartime, "Tylosin treatment gave us the wartime equivalent, with low [microbe] evenness," says Martin Blaser, author of *Missing Microbes* (Henry Holt and Co., 2014). In microbiology terms, it's called 'dysbiosis' when certain types of organisms and/or the chemicals they produce predominate.

Blaser and his colleagues then looked at a British study, the Avon Longitudinal Study of Parents and Children, which followed 14,500 children from 1991 and found, unsurprisingly, that those who received antibiotics in the first six months of life became fatter (see box, page 34).4

A 2014 American study found that 69 per cent of children were prescribed antibiotics when under age two, and they were more likely to be obese in later childhood.5

The myth that antibiotics are totally safe is hard to uproot, however. Despite reports that they are prescribed in error about two-thirds of the time and that superbugs are emerging as a result of overprescription, British GPs increased their antibiotic prescriptions by 6 per cent between 2010 and 2013. And that's not counting our antibiotic exposure from the foods we eat every day.

Agriculture is still the biggest consumer of antibiotics,6 so unless we're eating organic and antibiotic-free, we're exposed to the drugs every time we eat meat, eggs and farmed fish.

Other factors, such as increased caesarean deliveries, have also been implicated in the weight-gain epidemic. C-section delivery is associated with an increased body mass in childhood and adolescence, and scientists think that babies delivered surgically could be deprived of some key metabolism-regulating microbes that, in natural childbirth, are acquired in the birth canal.7

Researchers have barely begun to examine how all chemicals, food additives, vaccines and other prescriptions alter the microbiome, and affect obesity and other diseases.

Can we manipulate our microbes?

There is encouraging research emerging that our microbiomes, which are constantly shifting, dynamic living ecosystems, can be altered by the food we eat. When we feast, our microbes feast. Just as when one organism is wiped out from a food chain in the wild and the whole food chain is altered, so it seems that we can deliberately starve some species in our gut and cultivate 'good' bugs that shift us to a healthy weight.

A 2014 study by Harvard University scientists found that volunteers eating a diet of mostly meat and cheese rapidly developed a very different microbiome composition from those eating a plant-based vegan diet. Within days, the animal-eaters' microbiome shifted, showing a marked increase in the activity of species such as *Bilophila wadsworthia*, which is associated with inflammatory bowel and heart disease.8

A 2015 follow-up mouse study confirmed that diet trumps genes in shaping the microbes, so if you think you're predestined to be overweight because your mother was overweight, you're very likely wrong.9

"The food you eat clearly affects the composition of the bacterial communities in your gut—high-fat, low-fibre diets are associated with a very different microbial profile than low-fat, high-fibre diets and that microbial composition can, in turn, influence whether or not you end up gaining weight," says gastroenterologist Robynne Chutkan in her book, *The Microbiome Solution* (Avery, 2015).

Yet 'high-fat' is a bit misleading because, apparently, all fats are not equal. The experimental fat mice were all fed a high-saturated-fat diet to get that way. A 2011 study by Harvard University researchers found that high-fat potato chips were the food most associated with weight gain, whereas other high-fat foods like yoghurt and nuts were associated with weight loss.10

The upshot: avoid inflammatory saturated fats, and consume healthy omega-3 fats found in nuts, seeds and oily fish.

The fibre connection

When he was 17 years old in 1977, Gerard Mullin tipped the scales at a whopping 293 pounds. He was depressed and discouraged. But later that year, Mullin was inspired by the boxing movie *Rocky* and determined to do something about it. He tried a number of fad diets that didn't help much, but when he stumbled on a book about increasing fibre to lose weight, he started eating oat bran every day, cutting out red meat and adding in yoghurt.

"In no time I was dropping weight and feeling fantastic," Mullin recounts in his book, *The Gut Balance Revolution* (Rodale Books, 2014). When the first 50 pounds were gone, he started running and lifting weights, and he was on his way to ultimately shedding more than 120 pounds. He kept it off and went on to become a leading integrative gastroenterologist at Johns Hopkins Hospital,

inspiring others in the epidemic battle against the bulge.

"I now realize that I'd developed a way of eating that restricted foods that promote inflammation and spike blood sugar and fat-forming insulin," says Mullin. "I was also supporting the growth of friendly bacteria in my gut with prebiotic fibre-rich foods and live yoghurt cultures . . . this may be the key reason the diet worked."

Mullin's weight-loss programme included a 30-day high-protein, low-carbohydrate, 'reboot' diet that eliminates gluten, all sugars except stevia and most dairy foods, and radically reduces other short-chain carbs and sugary foods that bacteria love called FODMAPs (fermentable oligo-, di- and monosaccharides, and polyols). Initially, even foods that are good for weight loss, such as fibre and beans, are restricted to starve out the bacteria and 'till the soil'. Eventually, it incorporates a broad range of high-quality lean meats, eggs, fish, artisanal hard cheeses, non-sugary fruits and vegetables such as blueberries, plums and green vegetables, and some grains, and so resembles a Mediterranean diet.

For Mullin, there is one ingredient more important than all those he lays out in his book to lose weight: perseverance. "No single pill or supplement will allow you to burn away fat for the long term if you don't change what you eat and how you live," he says.

Mullin has a *Rocky* movie poster hanging on his office wall to remind him how to deal with life's knockdowns and the real reason he lost 120 pounds. "Rocky represents the kind of mind and heart I believe it takes to succeed in the world and be healthy," he says. "You have to be a fighter. Life will knock you down. But it's not about how many times you get knocked down, it's about how many times you get back up.

"As Rocky said, 'That's how winning's done'."

Of mice and men

When microbes from fat mice are transplanted into normal-sized mice that have been raised in a sterile environment and have no gut bacteria of their own, they quickly grow fat too. It doesn't matter if the germ-donor fat mice are fat because they were fed a high-fat diet to make them fat or they have a genetic mutation that makes them fat. And scientists have determined that it's the bacteria in the stool, not viruses or some other component, that seem to be inducing the change

from skinny to fat.

In a related study, when microbes from obese humans were transplanted into germ-free mice, they too became obese.

Microbiome-enhancing superfoods

Here are some of the microbiome-enhancing superfoods Gerard Mullin (see page 34) advocates for weight loss.

Apples. Scientists at the School of Food Science at Washington State University studied the gut microbiome profiles of obese and lean lab rats before and after they ate apples, and found that every variety of apple they tested had the ability to normalize the imbalanced gut flora of obese rats. The tart green Granny Smith, highest in the non-digestible fibres that gut flora thrive on, showed the greatest benefit.1

Cinnamon. This spice is a zero-calorie fat-burning powerhouse. One US Department of Agriculture (USDA) study showed that just ¼ tsp of cinnamon daily lowers blood sugar, cholesterol, triglycerides and low-density lipoprotein (LDL) cholesterol in type 2 diabetics.2 It also blocks glucose absorption and enhances the uptake of sugar in the blood by insulin. Other research has shown that it slows stomach-emptying to reduce after-meal blood sugar spikes.3 Plus, cinnamon has antimicrobial properties that work against a number of pathogenic gut microbes.4

Chia seeds. Loaded with antioxidants, anti-inflammatory omega-3 fats, high-quality protein and plant nutrients, these little seeds used to be best known in the West for growing chia pets. But research has shown they can prevent cardiovascular disease and diabetes, and lower blood fats.5 Include them in smoothies, salads, soups and more for a crunchy, low-sugar filler. They're also a high-fibre treat for 'good' gut microbes.

Wild salmon. Salmon is packed with omega-3 healthy fats that improve insulin sensitivity and help to burn fat and prevent heart disease. Mullin says that wild salmon have a much higher ratio of beneficial fats than farmed fish, which are also frequently doused with antibiotics and fed genetically modified corn and soy. Salmon in the wild are also less contaminated with toxic chemicals like dioxins and polychlorinated biphenyls (PCBs).6

Whey protein. Mullin favours this super protein because it has the highest concentration of

branched-chain amino acids, especially leucine, which preserves fat-burning muscle for lean metabolism,7 and suppresses appetite.8 It's casein- and lactose-free, so it should be tolerated by most people sensitive to dairy, and chock-full of immune-regulating glycomacropeptides and beta-glucans, shown to heal the gut lining and cool inflammation.9

Are antibiotics the culprit?

Martin Blaser, director of the Human Microbiome Program at New York University, began to wonder a few years ago why antibiotics given to farm animals made them fat. Since the 1940s, farmers have been dousing their livestock feed with a steady stream of low-dose (subtherapeutic) antibiotics to promote rapid weight gain.

They found that no matter what antibiotic they used, it worked. And the earlier they began feeding their chickens, cows and pigs antibiotics, the fatter they grew, so the practice flourished on farms globally without a thought to safety. After all, doctors were prescribing the stuff in much higher doses to infants.

The idea that the explosive use of antibiotics in children might also be linked to the rising tide of human obesity led Blaser to his team's groundbreaking mouse studies, which have demonstrated that exposure to low-dose antibiotics in infancy changes their gut microbes, predisposing them to obesity for the rest of their lives.