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The inside story of the microbiome

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Scientists have grasped the importance of the microbiome just as modern lifestyles are ravaging it

Cross-sections of some of the fruit and vegetables that make for a healthy microbiome, as captured by magnetic resonance imaging (MRI)

The Diet Myth: The Real Science Behind What We Eat, by Tim Spector, *Weidenfeld & Nicolson, RRP£14.99, 320 pages*

Follow Your Gut: The Enormous Impact of Tiny Microbes, by Rob Knight with Brendan Buhler, *Simon & Schuster, RRP£7.99/RRP$16.99, 128 pages*

Gut: The Inside Story of Our Body's Most Underrated Organ, by Giulia Enders, *Scribe RRP£14.99/Greystone Books RRP$17.95, 272 pages*

What is the greatest advance in scientific understanding of the human body so far this century? With due respect to the progress made in human genetics, oncology and neuroscience, my answer is appreciation of the microbiome: the vast population of microbes that live within all of us and play a vital role in our health and wellbeing.

Although microbiologists have known for many decades that everyone hosts resident bacteria, beneficial and malign, their diversity and biological significance are only now becoming clear as scientists deploy new techniques of molecular biology to probe the microbiome. A healthy adult is made up of about 10tn human cells; microbial cells are smaller but there are 10 times more of them, weighing in at 3lb in total, roughly the same as the brain.

Recent research shows that the hundreds of microbial species populating this teeming inner world play essential roles in the most fundamental processes of our lives, from digestion to immune response and even behaviour. Imbalances in the microbiome, caused by aspects of the modern lifestyle such as medication, sanitation and diet, have been linked with diseases from obesity and diabetes to asthma and eczema.

The microbiome is fertile territory for popular publishing, combining as it does exciting and fast-paced science with medical self-help — how to adjust your own microbiome for a healthier life. The three titles reviewed here are good examples of this new biomedical genre. All focus on the gut, where the bulk of our bacteria live and work, while looking, too, at the significant populations inhabiting mouth, skin, genitals and other parts of the human body. And all three are models of clear, accessible and entertaining science writing by active researchers.

Tim Spector, author of *The Diet Myth*, is professor of genetic epidemiology at King's College London — and famous for leading the Twins UK team that compares identical and non-identical twins to untangle the genetic and environmental influences on disease and physical appearance. He also leads the British Gut Project and is currently using DNA sequencing to study the microbiomes of 5,000 twins. Spector's book is the most comprehensive of the three, with dietary advice detailing what is known about the impact on the microbiome of different categories of food ingredient (fats, proteins, carbohydrates, fibre, vitamins and sweeteners) as well as alcohol, caffeine, antibiotics and other drugs.

Rob Knight, who wrote *Follow Your Gut* with science journalist Brendan Buhler, is another high-profile author: a professor of paediatrics, and computer science and engineering, at the University of California, San Diego, and co-founder of the American Gut Project. His book is relatively concise but still manages to pack in colourful stories.

Giulia Enders, the author of *Gut*, is a young medical researcher working on her doctorate at Frankfurt's Institute for Microbiology. Her book was originally published last year in German as Darm mit Charme ("Charming Bowels") and the text retains a charming freshness in David Shaw's translation, leavened further with some sweetly naive illustrations by the author's sister, Jill Enders.

The key point made by all three books is that you cannot maintain a healthy diet if you ignore the impact of food and drink on your gut microbes, which are essential intermediaries in the digestive process. Indeed, Spector claims that examining the DNA of our microbiome is much better for predicting obesity than looking at human genes.

The average American child goes through 17 courses of antibiotic, most of them unnecessary

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Over millions of years we have evolved together with microbes for

mutual survival, yet recently this fine-tuning and selection has gone wrong. Studies comparing urban Americans and Europeans with people living in the Amazon rainforest or rural Papua New Guinea, enjoying rich and varied diets and without antibiotics, show how much microbial diversity has been lost in the industrialised world.

We are endowed with a microbiome at birth. A baby born in the conventional way is swarming with millions of microbes by the time she emerges from her mother, as Spector puts it. The first dose consists of vaginal bacteria from the birth canal. “Then because of their close proximity and the pressure on all the body’s sphincters, a light mixture of urinary and faecal microbes are sprinkled onto her face and hands, followed by a different set of microbes covering the rest of her body as a result of rubbing against the skin of her mother’s legs.”

All three authors point out the microbial deprivation suffered by babies born by caesarean section, who cannot pick up bacteria in the same natural way. Caesarean births are associated with higher rates of a broad range of diseases associated with the microbiome, according to Knight. Spector quotes a study showing that C-section birth increases the risk of obesity by 20 per cent. And Enders blames her own caesarean delivery and her mother’s inability to breastfeed her — maternal milk provides another good dose of bacteria — for the multiplicity of health problems she suffered during childhood.

Although the best advice for parents is to opt for natural childbirth and breastfeeding, an emergency may make a C-section unavoidable — which is what happened to Knight’s partner Amanda. “Our daughter was born via an unplanned caesarean section, and I was holding her 20 minutes later,” he writes. “But today’s medical technology doesn’t supply everything. When it came to her microbes, we took matters into our own hands and swabbed her with samples from Amanda’s vagina. Our baby needed those microbes.” A clinical trial of this process, now called “vaginal inoculation”, has started in Puerto Rico.

The microbiome grows and diversifies further during early childhood, picking up beneficial bacteria from the environment. Here we encounter the “hygiene hypothesis”, first formulated in the 1980s to explain the exploding epidemic of autoimmune and allergic disorders such as asthma and eczema. In its original form the hypothesis proposed that the young immune system needs “training” through exposure to diverse bacterial and viral pathogens; problems emerge in excessively clean modern homes that fail to provide sufficient immunological challenges.

The current version of the hygiene hypothesis focuses more on the essential role that the microbiome plays in our immune defences. As Enders points out, about 80 per cent of the human immune system is located in the gut. It has to be extremely careful to suppress its defensive instincts and allow the many beneficial bacteria to live there in peace, while recognising dangerous elements in the crowd and weeding them out.

All of which requires careful training through exposure to multiple

microbes, good and bad, Spector explains. Gut microbes communicate with the human immune system through so-called regulatory T-cells, or Treg cells, in the intestinal walls. High Treg levels are generally healthy because they damp down excessive activity in the immune system.

Evidence to support the hygiene hypothesis is growing fast. For instance, Erika von Mutius of Dr von Hauner Children's Hospital in Munich, a pioneer in this field, has shown that exposure to farming in early life reduces substantially the risk of allergies and asthma — and some of this effect can be explained by children's contact with farm animals and unpasteurised raw milk.

"In general," says Knight, "exposure to diverse microbes, whether through older siblings, pets, or livestock — or through good old-fashioned playing outdoors — seems to help, even if scientists are still sorting out the specific microbes involved. It may be that diversity itself is most important."

Enders goes further. "Disinfectants have no place in a normal household," she writes. "The aim of cleaning . . . should be to reduce bacteria numbers, but not to eliminate them. Even harmful bacteria can be good for us when the immune system uses them for training — a couple of thousand salmonella bacteria in the kitchen sink provide our immune system with the opportunity to do a little sightseeing. Salmonella become dangerous only when they turn up in greater numbers."

Needless to say, all these authors advise against antibiotics unless you need them to fight a serious drug-sensitive infection, because the side-effects of killing beneficial bacteria alongside the pathogens can also be serious. Yet the average American child goes through 17 courses of antibiotic before reaching adulthood, most of them unnecessary, according to Spector.

How, then, can people restore their ravaged microbiomes? Besides eating a varied diet rich in fruit, vegetables and nuts, taking probiotics and prebiotics may help. To illustrate the difference between these two easily confused categories, Knight invites us to think of our microbiome as a lawn. Prebiotics are like fertilisers; they are mostly soluble vegetable and fruit fibres that can be fermented by bacteria in the large intestine to provide essential nutrients. Foods rich in prebiotics include artichokes, chicory, leeks and celeriac.

Taking probiotics is more like reseeding an unhealthy lawn with desirable grasses. Probiotics, often referred to as "good bacteria" or "helpful bacteria", are typically yoghurt-based foods or drinks containing a few species of live microbes. Although taking these will do you no harm, there is not much convincing evidence of their benefit from well-conducted clinical trials. As Spector says, this is probably because we all have different microbiomes to start with; without knowing which microbes to replace, it is a lottery whether particular yoghurt concoctions will work for you. In the future it may be possible to tailor probiotics for people to compensate for their individual microbial deficits.

A more drastic option, which Knight compares with ripping out a weed-infested lawn and laying down fresh turf, is to have a faecal or stool transplant from someone with a healthy microbiome. This procedure has proven remarkably successful in curing people who are seriously ill with Clostridium difficile infection and have very abnormal gut microbes. Research is now under way to extend faecal transplants to other disorders.

If you want to discover the health or otherwise of your own microbiome, this is now possible through the British Gut Project or American Gut Project, in return for a contribution to their research funds (a minimum £75 for UK residents). Just Google them to discover how to proceed.

But bear in mind Knight's cautionary words: "Much of the news you hear about disease in the microbiome can be confusing, contradictory, or sometimes overhyped . . . This complexity is worth keeping in mind anytime you hear sweeping claims about it or simple fixes for a variety of its ailments."

Although the authors of these three books are enthusiastic practitioners of microbiome research, they stop short of making excessive claims. The revelation that each of us depends on our individual living world, with far more inhabitants than there are people on earth, is surely sensational enough.

Clive Cookson is the FT's science editor

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