Chapter 1

Getting a Handle on the True Nature of Bacteria

In This Chapter

- Exploring the discovery of bacteria and their role in health
- Looking at the connection between bacteria and brain development
- Investigating bacteria's role in mood and anxiety

The United States, the world leader in so many other areas of health and medical science, is considered an "emerging market" in the development and use of probiotics; such supplements are far more popular in Europe and Asia, and probiotic-rich foods (see Chapter 11) are staples in many cultures around the globe.

Interestingly, according to the National Health Interview Survey conducted by the National Institutes of Health's National Center for Complementary and Alternative Medicine (`http://nccam.nih.gov`), Americans use probiotics for their children, but not for themselves. Certainly, children can benefit from probiotics (see Chapter 8), but research indicates that probiotics are appropriate for grown-ups too. Even healthy adults can help maintain their good health by taking probiotics.

As in other countries, yogurt manufacturers in the United States have long touted the benefits of live cultures of bacteria in their products. More recently, companies like Dannon have begun aggressively marketing yogurt and its friendly bacteria as a way to regulate your digestive system — and they back up their claims by financing or conducting clinical studies.

The National Center for Complementary and Alternative Medicine also has made probiotic research a high priority for funding projects. The center supports research on using probiotics to alleviate or prevent various gastrointestinal disorders in infants and children; treating and preventing antibiotic-related diarrhea (see Chapter 4); and improving the efficacy of flu vaccines.

Government and privately funded research is turning up lots of evidence that probiotics can do more than regulate your digestive system. I provide information on various health applications for specific probiotic strains throughout this book. But researchers also are uncovering fascinating links between the bacteria in your digestive system and your brain's development, as well as mental health issues like anxiety and depression, which I discuss later in this chapter. First, though, the next section provides a brief overview of the theories and discoveries about bacteria's role in sickness and health.

Exploring the History of Bacteria Theories and Practices

Centuries before the invention of the microscope enabled researchers to observe living organisms that are invisible to the naked eye, some scientists theorized that tiny creatures spread disease among animals and humans. Ancient Hindu texts, for example, refer to living agents as causing disease. In 36 BC Marcus Terentius Varro warned against building homes and farms near swamps because such areas breed "certain minute creatures, which cannot be seen by the eyes, which enter the body through the mouth and nose and there cause serious diseases."

Even so, conventional wisdom discounted the idea that organisms like bacteria, or germs, caused illness. The prevalent theory was that disease generated spontaneously. Even Anton van Leeuwenhoek, considered the father of microbiology, didn't connect the organisms he saw under his microscope with disease. And the idea that human contact could transmit harmful microorganisms met with massive resistance among the medical and scientific communities.

In the following sections, I provide a brief overview of how the germ theory of disease developed and the history of using probiotics, or good bacteria, to promote good health.

Understanding germ theory

Although it forms the basis of medical treatment and hygiene practices today, *germ theory* — the idea that microorganisms are responsible for causing and spreading illness — was quite controversial for centuries. Before the invention of the microscope, most people (including most doctors and scientists) believed that disease either arose spontaneously or was spread through "bad air," or *miasma*.

Ignaz Semmelweis, a Hungarian obstetrician working at a Vienna hospital in 1847, noticed that when doctors and medical students attended births, new mothers were far more likely to die of *puerperal* fever, commonly known as childbed fever, than women who delivered their babies at home with the aid of a midwife. Semmelweis observed that doctors and medical students at the hospital often delivered babies right after performing autopsies, and he insisted that doctors wash their hands in a chlorinated solution before examining pregnant women. This elementary technique lowered the childbed fever death rate at the hospital from nearly 1 in 5 to about 1 in 50.

English physician John Snow added evidence supporting the germ theory when he traced the origins of a cholera outbreak in London in the 1850s. Snow noticed that the homes of people affected by the outbreak all got their water from the same pump, and he identified that water as the mechanism for spreading the disease.

In the 1860s, Louis Pasteur conducted experiments that proved that living organisms in freshly boiled broth came from outside the broth rather than spontaneously generating within it. A decade later, Joseph Lister (for whom the Listerine brand mouthwash is named) developed procedures for sterilizing surgical instruments and wounds in hospitals.

Although some physicians and scientists proposed some version of germ theory for centuries, the idea didn't gain wide acceptance until the late 19th century, when Robert Koch demonstrated that anthrax was caused by specific bacteria.

Since then, germ theory has led to development of antibiotics and hygiene standards, and it remains a foundational element of both modern medicine and microbiology.

Discovering probiotics' benefits

For more than a century, germ theory (see the preceding section) focused on the idea that bacteria caused disease. In fact, many common bacteria do cause illness in humans and animals, but many others are harmless, and still others are actually beneficial. Beneficial bacteria today are known as probiotics.

Years ago, scientists believed that human beings and the bacteria in their bodies had a *commensal* relationship — meaning that they exist together without harming each other. Advances in medicine helped to clarify that this relationship is *mutualistic;* that is, both your body and the bacteria in it benefit from each other.

The concept that some bacteria may promote health rather than harm it was born in the early 20th century when Russian scientist Eli Metchnikoff hypothesized that eating fermented milk products contributed to the long life span of Bulgarian peasants. He concluded that fermented milk helped to "seed" the intestine with friendly bacteria, which suppressed the growth of harmful bacteria.

Metchnikoff believed that lactic acid bacteria in milk contributed to the Bulgarian peasants' general health and long lives, and he was the first scientist to propose using these bacteria to prevent and treat certain illnesses. He also was the first to suggest that it's possible to modify the gut flora by replacing harmful bacteria with useful microorganisms, later winning a Nobel Prize for his work.

Every society has consumed some type of fermented food on a daily basis, and anthropologists theorize this practice dates from prehistoric times. As a food staple, cow's milk dates back at least 9,000 years, and some Central Asian people drank horse milk long before cows were domesticated. They stored milk in bladders made of animal intestines, and the microorganisms from the bladders fermented the milk into yogurt.

Marco Polo: Probiotics pioneer

Thirteenth-century explorer and tradesman Marco Polo, the first European to travel deep into the interior of China and Mongolia, mentioned *kefir*, a fermented milk drink, and its "magical properties," in his travel journals. Some historians think kefir may have contributed to the high survival rate among Marco Polo's sailors at a time when many seamen died of intestinal disorders.

Kefir is one of the oldest known fermented milk products, but it wasn't generally known outside the Caucasus region (at the border between Europe and Asia) until the 19th century. To learn more about kefir's interesting history, visit `www.kefir.biz/history.htm`.

Food historians note that yogurt was widely consumed in Central Asia, India, and the Middle East for thousands of years. Indian texts dating from around 6000 BC refer to the health benefits of milk and milk products, and modern Indian cuisine includes more than 700 kinds of yogurt and cheese products. As exploration opened up trade between Asia and Europe, yogurt and other fermented dairy products made their way into Europe and eventually to the New World. (See the nearby sidebar, "Marco Polo: Probiotics pioneer.")

Fermented milks are the best example of early probiotics. Milk turns sour in hot climates, so — especially in the days before refrigeration — many people deliberately fermented milk to make curd, or yogurt. Today, the same curd or yogurt is made in a controlled environment by adding live cultures such as *Lactobacillus acidophilus* or *Lactobacillus bulgaricus*.

Bacteria are categorized using Latin nomenclature that identifies genus and species. So *Lactobacillus* means a bacterium that produces lactic (or milk) acid, and *acidophilus* means the bacterium is a species that survives well in acid environments, such as your stomach.

Looking at Bacteria and the Brain

Recent research into how various bacteria interact with and affect systems outside the digestive tract has turned up intriguing connections between the brain and the gut.

For example, researchers at The Sage Colleges in Troy, New York, found that mice fed with a harmless strain of soil bacteria learned a new maze twice as fast as mice who weren't given the bacteria, and the bacteria-fed mice exhibited fewer signs of anxiety, such as grooming and searching (see "Controlling Mood and Anxiety" later in this chapter).

Meanwhile, a collaborative study between scientists at Karolinska Institutet in Sweden and the Genome Institute of Singapore indicates that gut bacteria may play a critical role in brain development, which influences adult behavior. The researchers compared behavior and *gene expression* — the way information in genes is translated and used to communicate with cells — between mice raised with normal gut bacteria and *germ-free* mice, which had no gut bacteria.

The germ-free mice were more active and exhibited more risky behaviors than the normal mice. When the germ-free mice were exposed to normal bacteria very early in life, their behavior as adults was closer to that of normal adult mice. But exposing the germ-free mice to these bacteria as adults had no effect on their behavior, indicating that bacteria play an important role in early brain development. In fact, the researchers identified significant differences in gene expression and signaling pathways between the two groups of mice; these differences involved learning, memory, and motor control.

The research team was careful to note that their findings apply only to mice, and it's too early to say whether gut bacteria play a similar role in human brain development. However, these findings open up intriguing possibilities for discovering just how big a role gut bacteria play in human physical development. (To understand why researchers use mice and other organisms to study human development and disease, see the nearby sidebar, "Of mice and humans.")

Of mice and humans

Researchers in many fields routinely experiment on mice before they develop clinical trials for humans because, biologically speaking, humans and mice have a lot in common. Cells in humans and mice (as well as fruit flies, yeasts, and many other animals and organisms) have a distinct nucleus encased in a membrane, and several genes are interchangeable between species.

Bacteria differ from humans, mice, and other organisms in that their cells don't have a compartmentalized nucleus. Instead, bacterial cells have a less-defined *nucleoid region* that contains their DNA.

Mouse models of human diseases give researchers important insights into how diseases develop and progress, as well as the molecular and genetic pathways involved. When scientists develop new drugs or therapies, they first test them on mice and other lab animals before moving onto clinical trials to assess their safety and effectiveness in humans.

Controlling Mood and Anxiety

Researchers also are investigating the relationship between bacteria in your digestive system and psychological issues, such as depression, stress, and anxiety. These connections also have implications for your immune system.

Scientists have learned a lot about how the different systems in your body communicate with each other, but they're far from fully understanding the complexities of that communication. The idea that gut bacteria play a role in systemic communications is relatively new, and most studies have so far been done only in mice or rats, not in humans. However, these studies open up fascinating possibilities for treating a host of physical and psychological issues.

In the following sections, you discover how stress can impact your immune system by changing the composition of your gut bacteria, as well as the potential links between probiotic bacteria and mood and anxiety.

Stressing out your immune system

Medical researchers have long known that stress depresses immune function, but only recently have they linked stress to changes in gut bacteria. (See Chapters 2 and 3 for more on how good bacteria help your immune system function properly.)

Collaborating researchers at Ohio State University and Texas Tech University discovered that exposure to stress changes the composition, diversity, and raw numbers of bacteria in the gut. Fewer kinds of good bacteria live in the digestive system of stressed subjects, and harmful bacteria proliferate.

This early research indicates that stress or psychological pressure has a significant impact on gut bacteria populations, which in turn affects immune function. This connection may explain why certain diseases, such as inflammatory bowel disease (see Chapter 4) and asthma, often seem to get worse during periods of unusual stress.

Other research indicates that gut bacteria may play a role in stimulating behavior that benefits immune function. When you're sick, you usually feel sluggish and perhaps even depressed; you don't move as quickly or as much as you do when you're healthy. This lack of physical and mental energy may be an immune system response that helps speed recovery. Studies in mice indicate that certain bacteria have a calming effect on behavior, similar to your own lethargic demeanor during sickness.

Exploring the brain-bacteria link

What if the next generation of antidepressants came in the form of foods like yogurt? Scientists are discovering more every day about the link between your brain chemistry and the bacteria in your gut — and yogurt laced with antidepressant bacteria is one possible therapy that may arise from this research.

To understand how gut bacteria impact brain chemistry, researchers in Ireland fed mice a broth containing *Lactobacillus rhamnosus JB-1*, a strain of good bacteria that lives naturally in your digestive tract. The researchers then compared the mice's behavior and brain chemistry to those of mice that were fed plain broth.

Brain cells have *receptors* that receive and respond to chemical signals from other cells. One of these chemicals, a neurotransmitter called *gamma-aminobutyric acid*, or GABA, inhibits activity in the central nervous system and regulates several physiological and psychological processes in the brain. In people who suffer from depression, certain GABA receptor components are decreased; when you suffer from stress or anxiety, certain GABA receptor components are increased.

In the bacteria-fed mice, the GABA receptor components associated with depression were higher, while the receptor components associated with stress and anxiety were lower. The results indicate that the bacteria helped maintain normal brain chemistry.

In addition, the bacteria-fed mice exhibited much less behavior associated with stress, anxiety, and depression, and levels of stress hormones were significantly lower when the bacteria-fed mice were exposed to stressful situations like mazes.

Just as important as learning that this particular bacteria strain influences the same neurochemicals that antidepressants and anti-anxiety medications target is figuring out how the brain and gut bacteria communicate. The *vagus nerve* connects the brain with the digestive system, and the researchers in this study confirmed that the *Lactobacillus* strain used this same pathway to exchange information with the brain. When researchers cut the vagus nerve in the bacteria-fed mice, the bacteria's impact was lost; neither the mice's behavior nor GABA receptor levels changed.

Changing behavior by changing gut bacteria

Canadian researchers have demonstrated a link between gut bacteria and behavior in mice, which may have implications for treating behavioral disorders in humans.

The researchers used germ-free mice and colonized their digestive tracts with bacteria from mice with different behavioral patterns to see whether the bacteria influenced the mice's behavior. Germ-free mice whose genetic background favored passive behavior were given bacteria from mice with

more exploratory behaviors, and genetically active mice were given bacteria from mice with passive backgrounds.

The results of the experiments showed that the different bacteria compositions changed the mice's predicted behavior patterns. Mice with passive genetic backgrounds became more active and daring, while mice with active backgrounds became more passive.

This research indicates that any disruption to the gut bacteria — whether from illness, antibiotics, or other factors — can have a significant impact on behavior. And because certain digestive ailments, such as irritable bowel syndrome, are associated with behavioral disorders, probiotics may have therapeutic potential for restoring normal gut bacteria and alleviating gastrointestinal problems.

One small French study seems to indicate that what happens in mice and rats can happen in humans too. In a 30-day trial, 55 healthy men and women were randomly assigned to take either a daily probiotic supplement consisting of *Lactobacillus helveticus R0052* and *Bifidobacterium longum R0175*, or a placebo. Participants filled out questionnaires before and after treatment to assess their mood, stress levels, and coping skills; in addition, researchers measured stress hormone levels in participants' urine.

Compared with the placebo group, the probiotic group had lower levels of urinary stress hormones and reported less depression, anger, and hostility, and the kind of worry that can lead to physical symptoms.

The research into the connection between probiotics and physical and mental health is both encouraging and exciting. However, all the research to date indicates that only certain specific strains of good bacteria confer these specific health benefits. So don't count on eating today's live-culture yogurts to treat your depression or anxiety symptoms; chances are, the products on the shelves aren't properly formulated for such specific therapeutic uses. Much more research is needed to discover exactly which probiotic strains are most beneficial.