Alzheimer’s disease, atherosclerosis, and other diseases of aging might share something with sinus infections and flu. According to preliminary research, all stem from bacterial or viral attacks. Circumstantial evidence points to the lung-attacking bacterium Chlamydia pneumoniae, the herpes simplex I virus, and other germs. Although supporters of the hypothesis have amassed suggestive data, many researchers remain skeptical. However, advocates argue that we might have to accept weaker-than-usual evidence because the diseases kill so many people.

Since the discovery of Alzheimer’s disease (AD) a century ago, researchers have puzzled over the cause of the brain-ravaging illness, investigating everything from nutrient deficiencies to the aluminum in cooking pans. But if an unorthodox hypothesis proves correct, the culprit in AD was right under our noses all the time—or even inside them. A growing stack of papers implicates bacteria and viruses in many of old age’s scourges, including atherosclerosis, AD, and some cancers. The evidence for microbial involvement so far is inconclusive. But this year’s Nobel Prize in physiology or medicine recognizes investigators who demonstrated that one condition long thought to be non-infectious—ulcers—results from bacterial attack. Moreover, because the baby boomers are entering the prime years for chronic illnesses, researchers should be aware that microbes might foment some of these diseases, says microbiologist Ronald Luftig of Louisiana State University Medical Center in New Orleans. Establishing a link between bugs and sickness could be a boon for patients, says Luftig, co-author of an American Society for Microbiology report published earlier this year on the microbial hypothesis. Doctors might be able to launch their arsenal of pathogen-fighting weapons at some dreaded illnesses of old age. However, certain bugs are so elusive that scientists might never build an ironclad case against them.

Assertions that bacteria and viruses underlie chronic illnesses aren’t new. They date back almost to the discovery that germs cause disease, says evolutionary biologist Paul Ewald of the University of Louisville in Kentucky. Microbiologists gathered the first evidence linking infections to atherosclerosis and ulcers in the late 1800s, and some New York City hospitals were treating ulcers with antibiotics in the 1940s, he says.

One reason the idea fell out of favor, Ewald notes in his 2002 book Plague Time, is that smoldering chronic diseases don’t resemble the raging infections such as flu that doctors were familiar with. Some negative findings also sowed doubt. For example, a 1954 study that found no trace of microbes in stomach mucus from nearly 1200 people seemed to torpedo the notion that bacteria are the wrongdoers in ulcers. Later papers criticized the author for failing to use the most sensitive stain to test for the responsible germ. Nonetheless, the work was influential, and the idea sank out of sight.

It resurfaced in Perth, Australia, in the early 1980s. Robin Warren and Barry Marshall of the Royal Perth Hospital spied a corkscrew-shaped bug—later dubbed Helicobacter pylori—in tissue samples from patients suffering from gastritis, an inflammation of the stomach and small intestine that can lead to ulcers. Doctors had previously blamed the painful and sometimes lethal irritations on excess acid induced by stress, bad diet, and other causes. Although the Australian group garnered plenty of epidemiological support, finding the microbes in almost all subjects with ulcers, some derring-do sealed the argument. Skeptics claimed that the bacteria couldn’t withstand stomach acid, so Marshall chugged a solution of H. pylori. Within 5 days, he was agonizing through a fierce case of gastritis. The researchers later showed that the combination of antibiotics and the H. pylori–killing compound bismuth banished ulcers nearly 80% of the time. The work earned Warren and Marshall the Nobel Prize this year. “Their winning represents a meaningful recognition of the veracity of the idea that infection may be

Culprit or bystander? Chlamydia pneumoniae bacteria (red) inhabit a cell within arterial plaque.
chronic diseases; they are killing over half of us.”

—Paul Ewald

Skeptic goes further, contending that the C. pneumoniae and herpessviruses in the brains of some AD patients might have nothing to do with the malady. They could be bystanders that find damaged tissues congenital but cause no illness. Skeptics also note that several studies have failed to find microbes in samples from AD patients. A further limitation, Mattson adds, is that researchers have uncovered little about how the bugs could spur diseases such as AD.

Hold on, says Ewald. Amassing definitive data that C. pneumoniae and other germs incite chronic scourges won’t be possible. For more than a century, microbiologists have relied on a set of rules known as Koch’s postulates to establish that a particular microbe causes a disease. Researchers need to isolate the bug from a disease victim, rear it in the lab, and then trigger the illness by exposing a lab animal to it. However, many of the suspects in chronic disease distort isolation and won’t grow in culture, making those steps in the protocol impossible. Even finding the microbes can be difficult, Ewald says, because our methods for flushing out furtive pathogens such as C. pneumoniae, which takes refuge inside body cells, are limited. Moreover, some pathogens might serve as “triggers” for the disease, says Balin. They could ignite illness, possibly by unleashing inflammation, which can progress even if the bacteria or viruses later disappear. Such a lag between infection and illness occurs in Reiter syndrome, a type of arthritis that usually erupts weeks or months after a bacterial attack on the digestive or urinary systems. Researchers discovered the link because in some patients, joint problems begin while more typical symptoms of an infection remain.

Better techniques for detecting pathogens might solve some of these problems. But researchers should be willing to bend Koch’s postulates, Ewald argues. They have done so in the past, he says. For instance, scientists accepted that the hepatitis C virus instigates liver cancer without confirmation from animal studies.

Fighting Back

The price of waiting for stronger evidence is too high, says Ewald. Chronic illnesses “are the most important diseases; they are killing over half of us.” If we tentatively agree that viruses and bacteria are culpable, we can deploy our anti-infection weapons to battle the bugs. For example, he notes, such acceptance would allow doctors to use antibiotics against AD without being censured for providing inadequate care. They can be now, he says, because unlike drugs such as memantine, antibiotics are not approved for treating AD. Dosing everybody with antibiotics would be counterproductive because it would trigger resistance to the compounds. However, if more young patients with lung infections sought treatment with antibiotics, doctors might be able to squelch C. pneumoniae before it sets up house in the body, says Balin.
This preventive approach could be the best hope for stemming chronic illnesses with antibiotics. The compounds don’t appear to reverse cardiovascular disease, as a Journal of the American Medical Association report concluded earlier this year. The paper weighed results from 11 studies that tested the effectiveness of antibiotics against atherosclerosis and concluded that the drugs don’t help. That finding shows that antibiotics can’t reverse decades of arterial damage, but they might still thwart it if taken earlier in life, Balin says.

Our best defenses, several researchers agree, would be vaccines against C. pneumoniae and other nasties. Because vaccines aren’t profitable for companies, governments would have to undertake their development, says Mattson. The shots could help keep our arteries clear and our brains sound as we get older. And that development wouldn’t be anything to sneeze at.

Mitch Leslie, a science writer in Portland, Oregon, plans to stop snorting C. pneumoniae.

References