Like us, some bacteria age, although scientists long believed they couldn’t. Theoretical studies suggest that unequal division is the prerequisite for aging, and a new study of an asymmetrically dividing bacterium backs the argument. Starvation also provokes aging in some bugs, causing them to start producing proteins that are vulnerable to oxidative damage. Deprived bacteria deploy defenses against oxidation that are similar to those in worms and higher organisms. Bacteria’s ability to survive brutal conditions might clue scientists in to ways to make our own cells resist aging.

Hollywood stars have thrown their fame behind campaigns to save charismatic creatures such as dolphins and tigers. But you don’t see celebrities speaking up for bacteria. It’s no wonder that bugs don’t appeal to the swanky set. Bacteria live in the worst neighborhoods: scalding hot springs, decaying carcasses, camels’ intestines. Instead of lunching at Spago or skiing at Aspen, they spend their meager lives stewing in pus or nibbling somebody’s gums. Yet some species of bacteria can pull off a trick that would make Botox-shooting Hollywood starlets gape with envy: They are immune to aging and potentially immortal.

Until recently, scientists believed that all bacteria were ageless, but the thinking on this point has grown more subtle. Now researchers know that some bugs do get old. They are trying to define the evolutionary and environmental conditions that allow bacterial aging, and they are demonstrating the process in the lab. Although the field of bacterial aging remains small, the microbes’ lightning reproduction rate, simplicity, and hardiness in extreme habitats have enticed a range of researchers, from evolutionary biologists keen to understand the origin of aging to physicists who want to learn why things fall apart.

Their work is starting to make a mark. A study published last week detected aging in dividing bacteria, something once thought impossible. Other researchers have been working out details of how bacteria endure long periods of starvation that provoke senescence. The results, some scientists argue, might even provide clues about how our own cells age and how to fight the decay.

Symmetry Yields Immortality

The argument that bacteria are ageless dates back at least to the 1950s and 1960s, when researchers such as Peter Medawar, George C. Williams, and W. D. Hamilton were building the framework for the evolutionary theory of aging (see “Aging Research Grows Up†”). According to the theory, organisms deteriorate over time because natural selection slacks off with age. Natural selection can’t weed out mutations that cause damage late in life, because most of an organism’s reproduction lies in the past. The bacterial style of multiplication exempts these creatures from aging, Williams wrote, because they lack distinct body cells and sex cells. Bacteria and other asexual microorganisms not only pass on their genes to the next generation, they pass on themselves. For example, a cell xeroxes its DNA and stockpiles proteins and other contents, then division parcels out the old and the new equally between the two cells. In effect, each product is an offspring with full potential life span and fertility. So for bacteria, natural selection doesn’t weaken with age, and it favors creatures that resist decay. Otherwise, newly minted cells would inherit broken-down proteins and battered DNA—the equivalent of kids being born with creaky knees, bad backs, and hardened arteries.

Most researchers followed Williams’s lead and assumed that bacteria escape aging, says Martin Ackermann, an evolutionary biologist at the University of California, San Diego, who is exploring the conditions that promote senescence (see Ackermann Science Article†). However, in 1993 evolutionary biologist Linda Partridge, then at Edinburgh University in the U.K., and her colleague Nicholas Barton extended and clarified Williams’s argument. Bugs could grow old, they wrote, if parent cells differed from their offspring. They contended that asymmetry between the generations, not the distinction between body and sex cells, is necessary for aging in any organism. For example, if one cell emerges from division newer than the other—perhaps by nabbing a larger portion of the fresh proteins—the species should age. Supporting the idea, other studies have documented senescence in single-celled eukaryotes with asymmetric division but no sex cells. Ackermann decided to find out whether bacteria senesce too.

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† sageke.sciencemag.org/cgi/content/abstract/sageke;2003/25/or9

‡ sageke.sciencemag.org/cgi/content/full/sageke;2001/1/oa1

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Like Mother, Unlike Daughter

Ackermann, Stephen Stearns of Yale University, and Urs Jenal of the University of Basel in Switzerland tested for aging in a bacterium called Caulobacter crescentus, which starts life as a free-swimming “swarmer cell.” After motoring around for a spell, the bacterium glues itself to a surface and starts extruding new swarmers. Ackermann and colleagues monitored the reproduction of attached bacteria. After 300 hours, offspring output had fallen by about half, suggesting that the bugs were weakening with age. The study, the first to demonstrate aging in dividing bacteria, supports the importance of asymmetry for senescence, says Ackermann. Mother cells don’t hand down the stalk that anchors them to a solid support—and they might retain some of their cellular innards as well.

Although Caulobacter’s stalk elongates over time, the researchers detected no physical deterioration with increasing age—no bacterial equivalent of gray hair and wrinkles. Ackermann plans to track the allocation of proteins in mother and offspring cells to determine whether the fresh cells get more newly made molecules. Such measurements might help answer questions such as how much asymmetry is necessary for aging to evolve.

Caulobacter’s life cycle is unusual, but many other species split asymmetrically, Ackermann says. “People are realizing that bacteria are much more structured than they thought.” Even in Escherichia coli, some proteins pile up near the pole and aren’t divvied up equally between the two cells, he notes. What’s more, many kinds of bacteria assumed to have symmetrical division probably don’t—no one has checked carefully, he says. That possibility means that many more species of bacteria might fall victim to aging.

Down and Out in Stationary Phase

Drill sergeants and football coaches like to tout the benefits of hardship, but in some bacteria, adversity can provoke aging. Food scarcity is probably the norm in nature, according to many researchers. “We are biased by the fact that we can grow bacteria in the lab and they double every 20 minutes,” says microbial geneticist Steven Finkel of the University of Southern California (USC) in Los Angeles. “In the wild, they starve and have to maintain and repair themselves.” Some bacteria respond to desperate times by encasing themselves to form spores; others try to tough it out by slowing their metabolism and curtailing reproduction—entering what’s called stationary phase.

A bacterium in stationary phase slowly declines, a process that resembles aging in other organisms, says microbiologist Thomas Nyström of Göteborg University in Sweden. Over time, its membrane frays and it eventually loses the ability to divide. The similarity to aging goes deeper. In a study published 5 years ago, Nyström and colleague Sam Dukan showed that, like graying worms and flies, E. coli in stationary phase accumulate proteins marred by reactive oxygen species (ROS), destructive products of metabolism (see “The Two Faces of Oxygen”†). “The cells have a problem with oxidative management,” Nyström says.

Like human cells, bacteria fight back by pouring out proteins that combat stress—more than 40 in all, including the oxidant-squelching enzymes superoxide dismutase (SOD) and catalase. A molecule known as σ disperses the defense system by hastening production of the protective proteins. It directs the enzyme that copies DNA into RNA to genes that code for the stress fighters. Nyström points out the similarity of this system to the stress response in nematodes, in which a single protein, called daf-16, helps crank up production of antistress defenses. Although bacteria and worms don’t use the same proteins to control their stress response—σ and daf-16 are not related by sequence similarity—they use the same strategy of designating a single protein to turn on many genes, he says.

Nyström’s studies have revealed a new source of aging-related oxidative damage in bacteria that might also wound eukaryotic cells. Stationary phase E. coli fill with scarred proteins, but the obvious explanations for the increase—that ROS output rises or oxidant defenses stumble—are wrong, he says. Instead, the bacteria pump out more faulty proteins that are vulnerable to oxidants. Starvation makes the protein-manufacturing machinery more error prone, he says. It’s possible that the same sloppiness is a source of damaged proteins in old eukaryotes.

The Survival Artists

Bacteria endure conditions even harsher than starvation: radiation, extreme heat, acid, freezing. “Bacteria can live ridiculously long periods of time under very nasty conditions,” says Finkel. He argues that by understanding the basis for their hardness, we might better understand how our cells stay spruce—or fail to—as we age. For example, the rugged species Deinococcus radiodurans shrugs off a blast of radiation 3000 times the lethal dose for a person. Deinococcus endures because it deploys enzymes that glue its shattered DNA back together. Researchers have found that the human versions of these repair enzymes go awry in some cases of colon cancer. Looking for similar connections, Finkel is starting a project to study how bacteria control buildup of advanced glycation end products (AGEs), sticky modifications that can mar proteins and DNA and that play a role in atherosclerosis, loss of skin elasticity, and Alzheimer’s disease. He hopes to learn how the bugs fend off AGEs and what allows AGEs to finally start accumulating.

Bacteria might also reveal some general rules about why cells persist or fall apart, says Mark Goulian of the University of Pennsylvania in Philadelphia. A physicist with a passion for microbes, Goulian is interested in why things break. Living things look as if they aren’t built to last, he says. “When you think about cells, it’s amazing that they function at all.” He has just begun experiments to determine what makes some bacteria outlast others. “It will probably turn out that what life is all about is stopping errors.”

A Bacterial Takeover?

Bacteria offer many benefits for researchers studying aging. They are more prolific than the Osmonds. Many species boast sequenced genomes, and scientists know their biochemistry in detail. If bacteria start to reveal secrets of human aging, will they usurp yeast as the premier microbial model of senescence? Valter Longo, a molecular biologist at USC who has studied aging in bacteria and yeast, doesn’t think so. Because of their swift reproduction, bacteria are ideal for evolutionary studies, and they will

† sageke.sciencemag.org/cgi/content/full/sageke;2001/1/oa5

‡ sageke.sciencemag.org/cgi/content/full/sageke;2003/25/ns5
help round out our understanding of the mechanisms of aging, he says. But they won’t replace yeast, says Longo, because they are too different from us. “I think yeast covers most of what bacteria cover, and it connects better to higher organisms.”

Even if bacteria colonize only a corner in labs that study aging, researchers will have plenty to ponder. For instance, evolutionary theory still holds that symmetrically dividing bacteria should be immortal. Researchers don’t know how these bugs could retain their immaculate condition, although they have some ideas. What might keep fast-dividing bacteria from aging is their rapid reproduction, says Nyström. They are continually remaking themselves, rebuilding their DNA and pumping out new proteins, and the fresh cell components swamp any that have incurred damage. “Rapid growth does a lot of wonders for a cell,” he says.

Bacteria are only distant kin to humans. However, aging provokes similar damage to their cells and ours, and they deploy some of the same defenses, such as antioxidant enzymes. We might be able swipe some of their survival strategies, which natural selection has honed over billions of years, to fortify our own cells against the grim reaper. Who knows, someday the work might even give age-conscious Hollywood actors an alternative to Botox and plastic surgery.

Mitch Leslie writes from Albuquerque, New Mexico. He has recently grown to appreciate his asymmetry.

References