

The hygiene hypothesis

It suggests lack of early exposure to infectious agents can suppress development of the immune system

BY DR. RICHARD L. GALLO
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In 1998, researchers at the University of Georgia published a paper that estimated about 5 million trillion bacterial cells reside on Earth. That's a 5 with 30 zeros. That's a lot of bacteria. Indeed, if each individual bacterium were a penny piled atop one another, it would take a trillion light-years to reach the end of the stack, which is far beyond the observable universe.

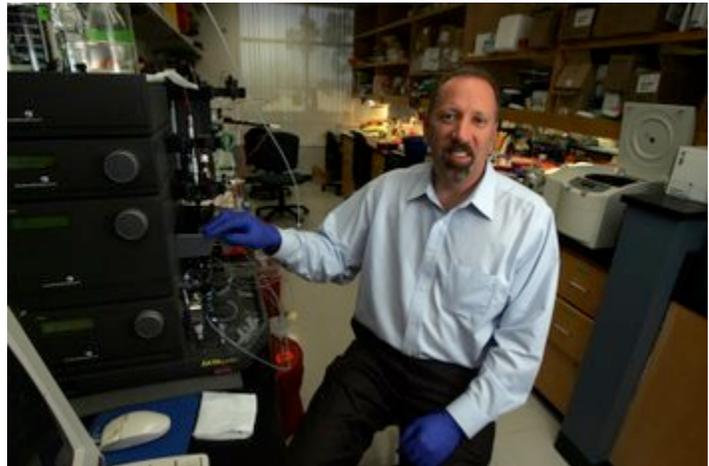
Some of these bacteria, Louis Pasteur and others duly discovered, cause disease, and so contemporary humans have long been urged, explicitly and otherwise, to fight back: Wash often. Stay clean. And don't skimp on those alcohol-based hand-sanitizing gels, foams and lotions that reportedly kill 99 percent of all germs. Odds are there's a dispenser near you right now.

But is cleanliness really next to goodness?

Maybe not. There is compelling, growing evidence that being too clean might actually be bad for your health; that it results in increased sickness and the development of chronic immunological ailments that might not occur if we all dialed back on the Dial and dispensers.

This thinking is encapsulated in an idea called "the hygiene hypothesis," which first emerged in the late-1980s. The hypothesis suggests that a lack of early childhood exposure to infectious agents and microorganisms (not just bacteria, but viruses and fungi, too) suppresses natural development of the immune system, resulting in increased susceptibility to infection and disease.

The hypothesis has been used to help explain why allergies like hay fever are less common in children from large families, even though presumably these kids are exposed to more infectious agents than those in smaller families. Epidemiologists have also noted that ailments like asthma and eczema (a kind of skin



Dr. Richard Gallo sits in his lab at the University Research Center in San Diego. Eduardo Contreras • U-T

inflammation) are more prevalent in industrialized countries where personal cleanliness is emphasized.

Though not conclusively proved, the hypothesis makes sense — at least as part of a larger explanation. Let's look at the science.

One's a crowd

If the world is fraught with bacteria, so too are you. Based solely on the average number of cells in a typical human being, we're all more inhuman than human. Bacterial cells outnumber human cells 10 to 1. Your gut, for example, is a well-known bacterial repository, home to hundreds of trillions of individual microbes (somewhere between 300 and 1,000 species), many of which beneficially assist in necessary functions like digestion and immune response. Plus, they take up space that might otherwise be occupied by nastier, disease-causing pathogens.

Your skin is similarly populated. Recent studies have identified hundreds of species, many previously unknown. One estimate calculates the total number of skin-based bacteria on the average person at roughly 1,000,000,000,000. These bacteria live in colonies, each favoring a different environmental niche. The bacteria that prefer the crook of your elbow, for example, are different from those homesteading your forearm.

Swathed in our cloaks of microbial invisibility, some questions are nonetheless obvious: How do skin bacteria survive our constant assaults with soaps and antibiotics? And why don't they make us sick more often?

In research published this year and last, my colleagues and I uncovered some of the answers. Our skin hums with constant communication and interaction between commensal or benign bacteria and skin cells. Certain species of superabundant *Staphylococcus* bacteria, for example, produce a molecule that inhibits the inflammation response (heat, redness, swelling) generated when you injure your skin. That's a good thing. Some inflammation is vital to healing, but too much can be worse than the infection.

Why do *Staphylococci* do this? It's hard to know for sure, but one possibility is that it's an evolutionary adaptation, a neat trick bacteria have developed to reduce the chances that an inflammatory response will kill them. Another possibility is that we have evolved together and count on these bacteria to help us control the skin response. In return for this microbial good deed, we reward specific bacteria with a comfortable place to live.

Recently, we discovered that a specific type of *Staphylococci* — *Staphylococcus epidermidis*, the most common bacterial species cultured from human skin — produces antimicrobial molecules that kill some other kinds of bacteria, including its cousin, *S. aureus*, a more problematic bug that causes everything from pimples and boils to deadly pneumonia, meningitis and sepsis.

S. epidermidis not only makes antimicrobials, it also instructs human skin cells to make natural antimicrobials of their own, thus serving as both warning system and mentor. The result is a balanced relationship that benefits both human hosts and our commensal bacterial buddies.

Scorched skin policy

Overuse of antibiotic soaps and hand sanitizers upsets this happy homeostasis by essentially killing all bacteria, good and bad. The consequence of this scorched skin policy is that we kill the germs that sometimes contaminate our skin and make disease transmission more difficult, but also reduce the effectiveness of our skin's antimicrobial defenses.

Wiping out all microbes means your skin is wide open to recolonization by all comers — commensals and pathogens. It may be a tossup which returns first and faster. Excessive cleanliness also removes natural oils that help keep skin supple and intact. Dry skin is more prone to cracking, which provides new entry points for bacteria and other agents. Some bacterial species that are harmless resting atop your skin are troublemakers inside it.

Of course, no one's suggesting we abandon antimicrobial soaps, gels and lotions. In some situations and circumstances, such as hospitals and health care, they are essential. Every effort must be made to reduce exposure to pathogens. More broadly, people should continue to wash their hands regularly and diligently. (There's an ongoing debate about whether daily washing beyond the wrists is necessary, but that's a different story.)

As always, nature suggests a solution, albeit one that first requires us to more fully understand the complicated relationships between microbes and our health. Rather than regularly render our skin a sort of microbial dead zone, we could develop soaps and sanitizers that are more discriminating or which include ingredients that promote the return of bacteria like *S. epidermidis* or deter the development of conditions like eczema. We do a little bit of that now with soaps and lotions that contain compounds designed to help skin retain its oils and moisture.

Someday you might slather up with something that selectively kills and fertilizes, encouraging certain microbial species to take root and call you home, thus restoring balance to our natural ecology.

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