

## Staph can lurk deep within nose

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Scientists at the Stanford University School of Medicine have revealed that formerly overlooked sites deep inside the nose may be reservoirs for *Staphylococcus aureus*, a major bacterial cause of disease.

The results of the study will be published Dec. 11 in *Cell Host & Microbe*.

The Stanford investigators further found an inverse relationship between the presence of *S. aureus* at these sites and that of a different bacterial species, *Corynebacterium pseudodiphtheriticum*, suggesting that the two organisms compete with each other and that *C. pseudodiphtheriticum*—or some molecular product it excretes—may prove useful in countering *S. aureus* infections.

"About one-third of all people are persistent *S. aureus* carriers, another third are occasional carriers and a remaining third don't seem to carry *S. aureus* at all," said David Relman, MD, the Thomas C. and Joan M. Merigan Professor and a professor of medicine and of microbiology and immunology. Relman, who is also chief of the infectious <u>disease</u> section at Veterans Affairs Palo Alto Health Care System, was the study's senior author. The lead author was Miling Yan, PhD, a graduate student in Relman's lab at the time the experiments were performed.

"The nose has been long known to be a primary reservoir of *S. aureus*," Relman said. The bug also abounds on the skin, with a special affinity for the armpits and groin. The vast majority of the time, however, it does little or no harm. (If it's doing any good, no one has figured out yet



what that is, Relman added.)

But if the skin is compromised by, for example, a wound or a medical incision or catheter placement, *S. aureus* can get into the bloodstream and cause serious and even life-threatening problems such as sepsis, pneumonia or infection of heart valves. Close to half of all *S. aureus* strains are resistant to a family of antibiotics that includes methicillin. In 2011, more than 80,000 severe methicillin-resistant *S. aureus* infections, as well as more than 11,000 related deaths, occurred in the United States alone, along with a much higher number of less-severe infections.

"Not everyone who carries *S. aureus* gets sick," Relman said. "When they're out walking the streets and otherwise healthy, attempts to rid them of their *S. aureus* are not necessary, and even sometimes futile. But once a carrier enters a hospital with an underlying illness or a weakened immune system or a high likelihood of undergoing skin-penetrating procedures, *S. aureus* carriage is a major liability."

Rigorous and somewhat tedious regimens for eliminating *S. aureus* residing on people's skin or in their noses do exist, but it's typically a matter of weeks or months before the bacteria repopulate those who are susceptible. The new study offers a possible reason why this is the case.

The scientists recruited 12 healthy subjects and brought them to a Stanford ear, nose and throat clinic run by study co-author Peter Hwang, MD, professor of otolaryngology. Employing special instrumentation to allow them to guide tiny swabs to precise locations within the nose, they took samples from three specific areas. The first location—and far and away the most well-studied because it's much more accessible—was the anterior naris, a relatively dry skin-like patch of tissue located near the nostril. The second was the middle meatus—a warmer, wetter, mucusproducing fold found about midway up the nasal cavity. And the third was the sphenoethmoidal recess, situated deep within the cavity near the



roof of the nose and, like the middle meatus, warm, wet and mucosal.

The researchers found that the presence or absence of *S. aureus* at one nasal site typically correlated with its presence or absence at the other two. An implication: If a person's anterior naris is carrying the bacteria, the upper mucosal areas probably are, too. This could be why efforts to banish *S. aureus* have so often proved short-lived. Focusing efforts largely on the bacteria in the anterior naris, which current decolonization procedures do, leaves deeper <u>reservoirs</u> intact.

Relman's team learned three other things, as well. First, the relative abundance of *S. aureus* was inversely related to that of another bacterial species, *C. pseudodiphtheriticum*. When one was present at high levels, the other was present at low levels or absent. One of the study's co-authors, Sunje Pamp, PhD, a research associate in Relman's lab, put the two <u>bacterial species</u> on an agar plate to scrutinize this relationship further, and found that *C. pseudodiphtheriticum* strongly blocked the growth of *S. aureus*.

The researchers suspect that something *C. pseudodiphtheticum* produces and secretes—perhaps a protein, or possibly a small molecule—is responsible for *S. aureus*' failure to thrive. If such a substance could be identified, Pamp said, it could provide clues to the development of new compounds to prevent or treat *S. aureus* infections.

Second, the microbial communities in those patients who harbor *S*. *aureus* differed in other ways from those in patients who don't. This could mean that *S*. *aureus* alters its environment to make it more or less hospitable to various other microbes. Or it could mean that different microbial communities are more or less hospitable to colonization by *S*. *aureus*. If the latter is the case, it may be possible to predict, based on their resident nasal microbes, which patients are most likely to be at high risk of a *S*. *aureus* infection—even if they're not currently carrying



it—and monitor and treat them accordingly. Those patients found to be at lower risk could be spared such procedures.

Third, in the middle meatus and the sphenoethmoidal recess—the two deeper, wetter mucosal regions of the <u>nose</u>—microbial communities were similar to each another, but quite distinct from the one inhabiting the more accessible and better-studied outer site, the anterior naris. This suggests that currently routine methods of sampling the nasal cavity for microbe-research purposes may be yielding skewed results.

## Provided by Stanford University Medical Center

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