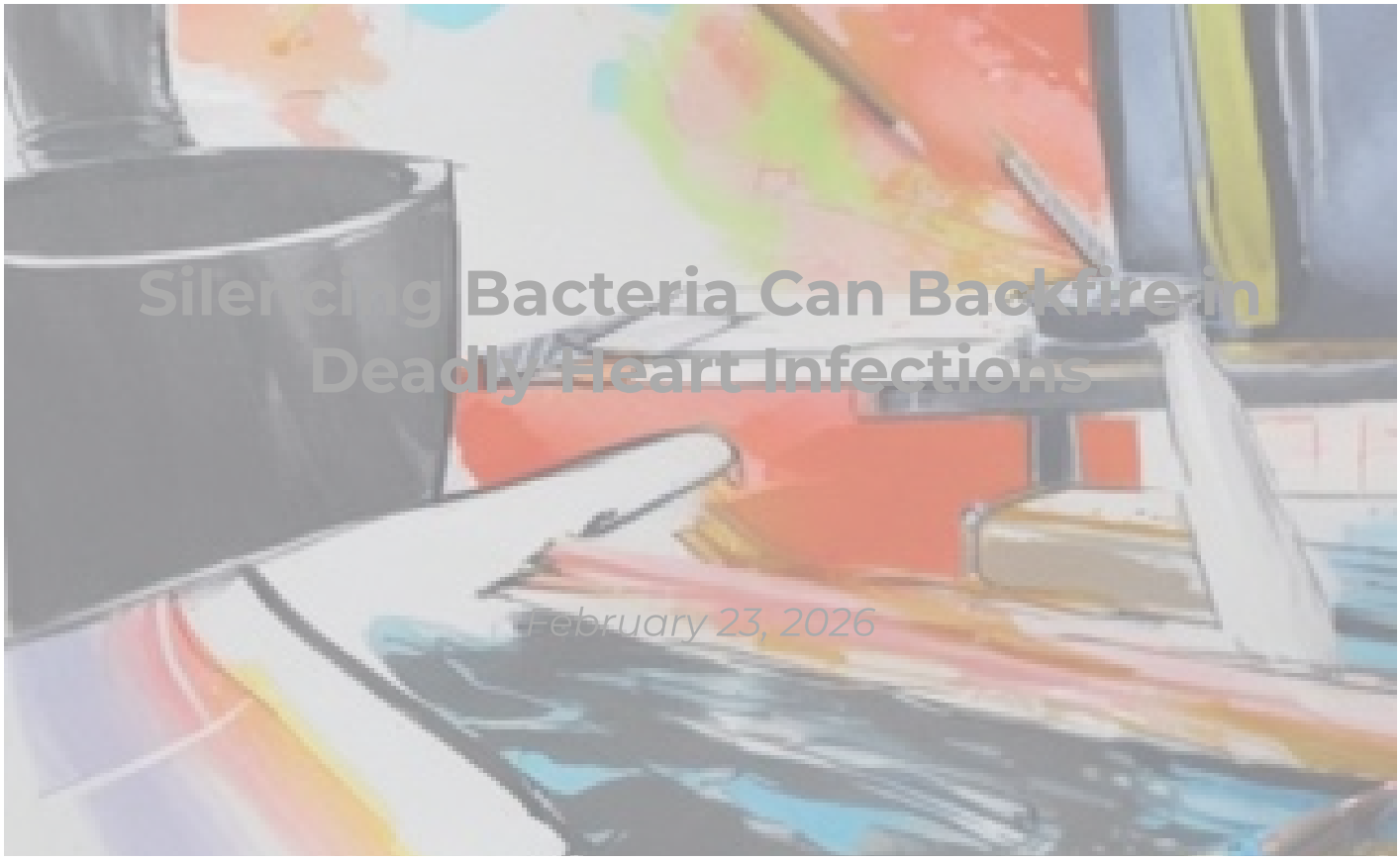

Silencing Bacteria Can Backfire in Deadly Heart Infections

February 23, 2026

> *A new study from the University of Geneva and NTU Singapore finds that shutting down bacterial communication in a dangerous heart infection can actually make the disease worse. The work challenges a major drug-*

> *development strategy and points to the need for smarter, more targeted therapies.*

The University Network

Blocking how bacteria “talk” to each other has long been seen as a promising way to disarm dangerous infections without fueling antibiotic resistance. But new research from the University of Geneva (UNIGE) and Nanyang Technological University, Singapore (NTU Singapore) suggests that, at least for a serious heart infection, silencing bacterial communication can backfire.

In experiments and patient samples focused on infectious endocarditis, a life-threatening infection of the heart’s inner lining and valves, scientists found that disrupting bacterial signaling in the pathogen *Enterococcus faecalis* can lead to larger, tougher biofilms and worse clinical outcomes.

The study, published in *Nature Communications*, challenges what one outside expert, Matthaios Papadimitriou-Olivgeris, called “the prevailing paradigm that quorum-sensing inhibition is uniformly beneficial in bacterial infections.” It also highlights how complex bacterial behavior can be inside the human body, and why one-size-fits-all approaches to new anti-infection drugs may be risky.

Infectious endocarditis is a medical emergency that often requires weeks of intravenous antibiotics and sometimes surgery to repair or replace damaged heart valves. Bacteria such as *Enterococcus faecalis* can latch onto valve surfaces and build biofilms — dense, slimy communities that are notoriously hard for antibiotics and immune cells to penetrate.

To coordinate this collective behavior, many bacteria use a system called quorum sensing. They release and detect small chemical signals that tell them how many neighbors are nearby, then switch on group behaviors like biofilm formation or toxin production once they reach a critical density.

Because quorum sensing controls virulence in many pathogens, drug developers have been exploring quorum-sensing inhibitors as a way to “disarm” bacteria without killing them outright, which could reduce the pressure that drives antibiotic resistance.

The new work from UNIGE and NTU's Singapore Centre for Environmental Life Sciences and Engineering (SCELSE) shows that, in the context of heart valve infections caused by *Enterococcus faecalis*, that strategy can have the opposite effect.

Using devices that mimic the intense blood flow over heart valves, combined with an animal model of cardiac infection, the researchers discovered that the physical forces inside the heart already interfere with bacterial communication during the earliest stages of infection.

"On the surface of heart valves, bacteria are exposed to intense blood flow," lead author Haris Antypas, a senior research fellow at SCELSE, said in a news release. "This flow disrupts the chemical signals bacteria use to communicate, effectively shutting down quorum sensing."

As the infection progresses, bacteria burrow deeper into the clumps of tissue and microbes known as vegetations, where they are more sheltered from the bloodstream. In this protected environment, quorum sensing normally switches on and acts as a kind of brake, limiting runaway biofilm growth.

But when the team studied strains of *Enterococcus faecalis* that completely lacked quorum sensing, they found that this natural brake was gone. In animal models, these strains formed larger, more resilient biofilms on heart valves, tolerated antibiotics better and caused more severe disease.

The researchers traced this effect to at least two biological changes. First, the bacteria produced fewer proteases, enzymes that break down proteins and can help remodel their surroundings. Second, they shifted their metabolism in ways that allowed them to tap into nutrients from the host more efficiently, fueling persistent growth inside the heart.

To see whether this phenomenon mattered in real-world patients, the team analyzed *Enterococcus faecalis* isolates from people with infectious endocarditis in the United States and Switzerland. Nearly half of the clinical samples lacked a functioning quorum-sensing system.

"These are not rare mutants," Antypas added. "They are common in patients, and our data suggest they may actively contribute to poorer clinical outcomes."

Those cases were associated with longer-lasting bacteremia — bacteria remaining in the bloodstream despite active antibiotic treatment — a sign of stubborn, hard-to-clear infection.

Taken together, the findings suggest that, at least for *Enterococcus faecalis* infective endocarditis, inhibiting quorum sensing is not a safe bet.

“Our results show that in infectious endocarditis, inhibiting quorum sensing can actually harm the patient by promoting biofilm growth,” added senior author Kimberly Kline, a professor in the Department of Microbiology and Molecular Medicine at UNIGE’s Faculty of Medicine and a visiting academic at SCELSE. “Understanding when and where bacterial communication helps or harms the patient will be essential for designing smarter therapies.”

In an independent commentary, Papadimitriou-Olivgeris, a senior physician and privat-docent at the Service of Infectious Diseases at Lausanne University Hospital, emphasized how the work complicates current drug-development efforts.

“In *Enterococcus faecalis* infective endocarditis, absence of the *Enterococcus faecalis system regulator (Fsr)* quorum-sensing system leads to enhanced biofilm formation, metabolic adaptation, and increased antibiotic tolerance, resulting in prolonged bacteraemia in patients, an effect that was also recapitulated in experimental strains with targeted *fsr* deletion,” he said in the news release**.**

“While quorum-sensing inhibition is actively pursued as an anti-virulence strategy for several pathogens, these results underscore the need for caution when considering anti-quorum-sensing approaches in *E. faecalis* infective endocarditis, where such interventions may paradoxically worsen disease outcomes,” he added.

For students and early-career scientists, the study is a reminder that biological systems often behave differently in the body than they do in a petri dish. A strategy that looks promising in one pathogen or one type of infection can be harmful in another.

The work also underscores the importance of context in designing the next generation of anti-infective therapies. Rather than assuming that blocking bacterial communication is always helpful, researchers will

need to map out when quorum sensing restrains disease and when it drives it.

Future studies are likely to explore how these findings apply to other bacteria and infection sites, and whether it is possible to fine-tune quorum-sensing interventions so they help the host instead of the pathogen. For patients with infectious endocarditis, the hope is that a deeper understanding of bacterial behavior on heart valves will eventually lead to treatments that are both more precise and more effective.

Source: Nanyang Technological University, Singapore