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Sugar boosters could lead to cheap, effective treatments for chronic bacterial infections

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James Collins, a pioneering researcher in the new field of systems biology and a MacArthur Genius, says: "You know the old saying: 'a spoonful of sugar makes the medicine go down?' This is more like 'a spoonful of sugar makes the medicine work.'

Dr. Collins, a professor of Biomedical Engineering at Boston University who is also a Howard Hughes Medical Institute investigator and a core faculty member of the Wyss Institute for Biologically Inspired Engineering at Harvard University, is talking about his recent development of an effective, low-cost – and surprising – way to treat chronic bacterial infections, such as staph, strep, tuberculosis, and infections of the urinary tract.

He and his team of scientists discovered that a simple compound – sugar – dramatically boosts the effectiveness of first-line antibiotics. Their findings appear in the May 12 issue of *Nature*.

Dr. Collins, 45, who is also a founder of the new field of synthetic biology, has a personal interest in this research. His 71 year old mother, Eileen Collins, was hospitalized several times in recent years with recurrent bouts of a serious staph infection. Doctors treated her with multiple intravenous antibiotics and still the infection could not be killed. It was his mother's suffering that added urgency to Dr. Collins' research. (While Mrs. Collins is not symptomatic at the moment, she is still on antibiotics).

In addition, his own undergraduate track career at the College of the Holy Cross years ago was cut short by a persistent staph infection. Despite repeated doses of erythromycin, the infection continued to sap his energy and he was unable to compete in his event – the mile -- during his junior and senior years.

Chronic and recurrent infections are typically caused by bacterial 'persisters' – a small subpopulation of bacteria that manage to survive an antibiotic onslaught by essentially shutting down and metabolically going into hibernation.

As a result, the patient initially appears to be fully recovered, but over the course of weeks or months, the persisters return to life, often stronger and more aggressive than ever before, and the patient relapses.

Bacterial persistence is a major obstacle in the successful treatment of infectious diseases. It can stretch illnesses out over months, cause infections to spread to kidneys and other organs, and send treatment costs soaring. Given its adverse clinical and public health impact, bacterial persistence has become a growing area of research.

Yet to date, no treatment directly targets bacterial persisters.

Unlike antibiotic-resistant bacteria, whose ability to withstand drug treatments is based on genetic mutations fostered by exposure to drug treatment, persisters are genetically identical to the other members of their bacterial community. What separates them from the pack is their ability to switch into power-save mode.

Dr. Collins' research team has now discovered an inexpensive and effective way to rouse these bacterial sleepers, using a simple weapon – sugar – to stimulate them into an active state in which they are just as vulnerable to antibiotics as the others in their community.

Dr. Collins' approach consists of adding sugar to the antibiotic. The sugar acts as a stimulant, essentially turning on normal bacterial responses, such as dying when confronted by a killer antibiotic.

Using this strategy on E. coli bacteria, a common cause of urinary tract infections, the team was able to eliminate 99.9 per cent of the persisters within just two hours - compared to no effect without sugar. The approach was similarly effective in killing Staphylococcus aureus bacteria, which cause sometimes deadly staph infections.

"Our goal was to improve the effectiveness of existing antibiotics, rather than invent new ones, which can be a long and costly process," says Collins' Boston University colleague, Kyle Allison, who was the first author on the study.

The findings have the potential to improve the lives of untold numbers of people who struggle with nagging infections, while also reducing healthcare costs substantially.

The most significant impact of this research could be on TB, a chronic bacterial infection that affects the lungs and causes more deaths than any other infections disease. The World Health Organization reports that approximately 4,700 people die from TB every day. An initial course of treatment typically takes five to nine months. Collins and Allison will next investigate whether sugar additives can improve the efficacy of TB drugs.

Provided by Boston University