Evolutionary war between microorganisms affecting human health, biologist says

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Bashey-Visser's research focuses on an insect-killing nematode in the genus *Steinernema*. Credit: Cole Beeler

Health experts have warned for years that the overuse of antibiotics is creating "superbugs" able to resist drugs treating infection.

But now scientists at Indiana University and elsewhere are finding evidence that an invisible war between microorganisms may also be catching humans in the crossfire.

This conflict is discussed in a recent article from IU biologist Farrah Bashey-Visser in the journal *Philosophical Transactions of the Royal Society B: Biological Sciences*.

"Bacteria aren't just evolving to resist new drugs, they are also constantly evolving due to competition with other microorganisms," said Bashey-Visser, an assistant scientist in the IU Bloomington College of Arts and Sciences' Department of Biology.

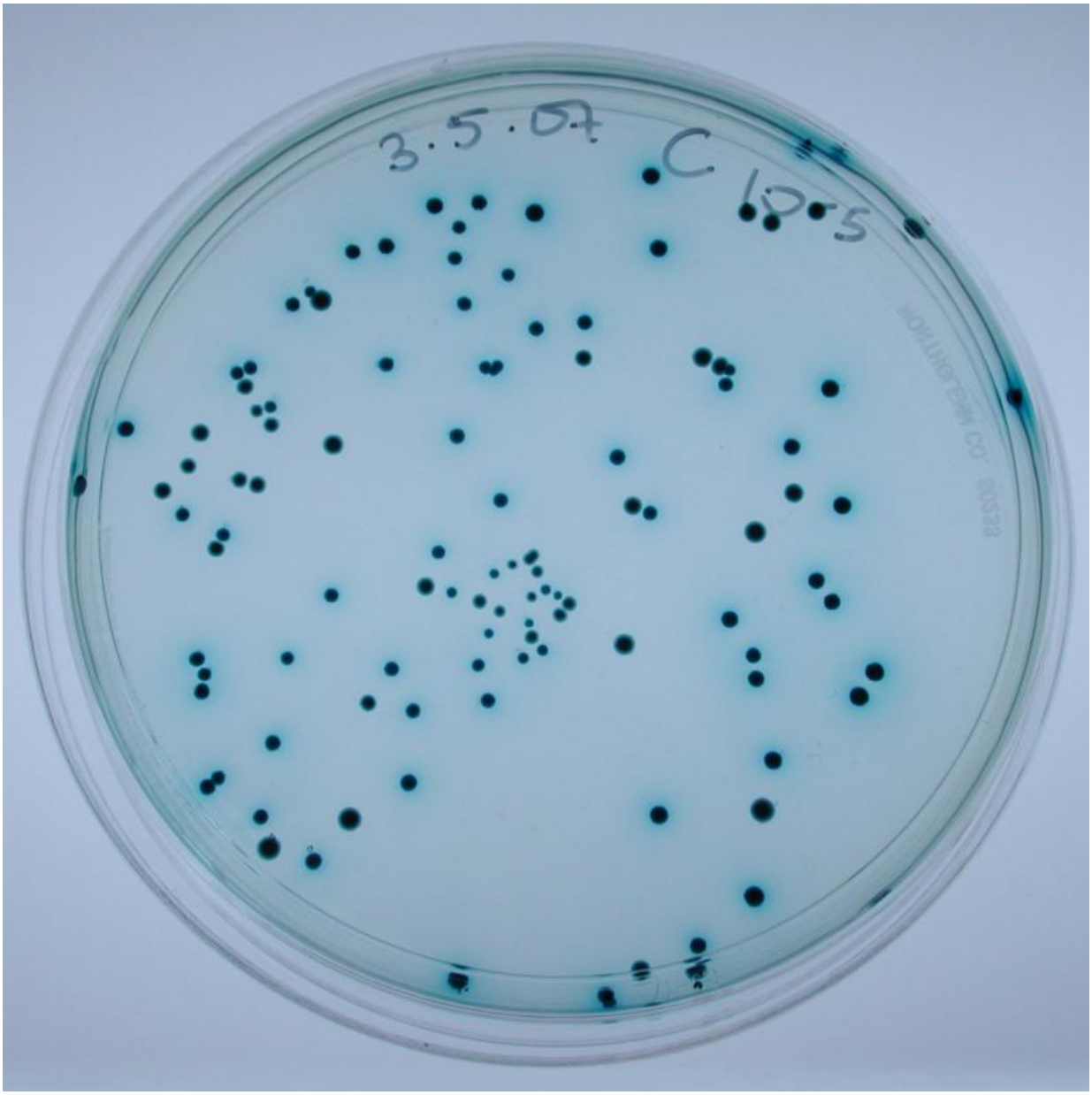
The result is that humans can be left trying to play catch-up.

The highly antibiotic-resistant bacteria MRSA, or methicillin-resistant Staphylococcus aureus, for example, has been shown to resist treatment in some cases due to competition with other microorganisms.

In the article, Bashey-Visser said a study recently conducted in Europe found a strain of MRSA became resistant to vancomycin after evolving within an infected host. A naturally occurring antibiotic reserved to fight the most serious infections, vancomycin was originally isolated by Eli Lilly and Co. in 1953 from soil collected by a missionary in Borneo.

The new mutant strain of MRSA in the overseas study overtook the original MRSA strain by producing a growth-inhibiting toxin. These toxins, called bacteriocins, are a common defense mechanism used by bacteria to compete against genetically similar microorganisms. However, in response to exposure to the bacteriocin, a third strain

evolved resistance to the toxin and, coincidentally, to vancomycin.



A plate with *Xenorhabdus*. Steinernema's life-cycle is dependent upon the bacteria. Credit: Farrah Bashey-Visser

This MRSA strain could resist the drug as a side effect of its evolutionary interactions within a host—a process that differs from the more typical path where antibiotic resistance arises in direct opposition to treatment.

"The more scientists understand the processes that shape the evolution of potential pathogens, the more they will be able to predict the amount of time their treatments will remain effective," Bashey-Visser said.

Physicians commonly use a "reductionist approach" to fight infections, she added. They identify the pathogen, then do whatever is the most effective to stop it.

But, while effective, this approach may also have unintended consequences.

"We're realizing more and more that harmful bacteria are just one part of our body's ecosystem, or 'microbiota,'" she said. "Broad-spectrum antibiotics can wipe out numerous beneficial bacteria species too—or worse, create an unprotected space where new species come in and wreak havoc."

Evolutionary competition among microorganisms can benefit human health too, Bashey-Visser said.

"Other studies are increasingly tracing situations where one person becomes sick while another doesn't to the presence of beneficial microorganisms," she said. "These probiotics, or 'good bacteria,' prevent infection by attacking disease-causing bacteria."

The use of less virulent bacteria to competively defeat disease-causing microorganisms is the basis of "replacement therapies," Bashey-Visser said. The process is similar to new treatments such as fecal transplants,

in which a stool sample from a donor is introduced into the gastrointestinal tract of a patient through colonoscopy, which can restore a healthy microbiota. The procedure is an increasingly common treatment for life-threatening conditions such as Clostridium difficile infection, or CDI.

According to Monika Fischer, an assistant professor of clinical medicine at the IU School of Medicine in Indianapolis who established one of the first fecal transplant programs in Indiana in 2012, doctors who perform the procedure, which colonizes patients' "gut flora" with healthy microorganisms, report a cure rate of about 90 percent.

At IU Bloomington, Bashey-Visser's research focuses on a surprisingly small species whose strange life cycle may also yield big lessons about how competition among bacteria affects biology.

The species is an insect-killing nematode in the genus Steinernema whose life cycle depends on bacteria. These roundworms, which carry a small amount of bacteria in the genus Xenorhabdus in a pouch off their intestines, cannot grow into adults until they enter an insect and release the bacteria. The bacteria helps kill and digest the insect, creating an environment in which the nematode can mature and reproduce.

"The life cycle of these tiny parasites is pretty crazy and, in many ways like our own dependence on microorganisms, wouldn't be possible without bacteria," said Bashey-Visser, whose work has revealed that competitive dynamics among the bacteria in these insects can maintain a diversity of strains within a single species.

"The more we understand these dynamics, the more we will understand about genetic diversity and preserving biodiversity," she added.

More information: *Philosophical Transactions of the Royal Society B*,

rstb.royalsocietypublishing.or … nt/370/1675/20140301

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