A New Way to KILL INFECTIONS

Mark Offerhaus, Chief Executive of the Dutch firm Micreos, talks about the company's antibiotic alternative that uses endolysins.

Antibiotic resistance is increasingly becoming a serious global threat to public health and is the cause of many common infections, including those affecting the urinary tract, lungs, and bloodstream. The impact of these infections is felt globally. Furthermore, a high percentage of hospital-acquired infections is caused by highly resistant bacteria, such as methicillin-resistant *Staphylococcus aureus* (MRSA).

Each year in the United States, at least 2 million people become infected with bacteria that are resistant to antibiotics and at least 23,000 people die each year as a direct result of these infections, according to the Centers for Disease Control.

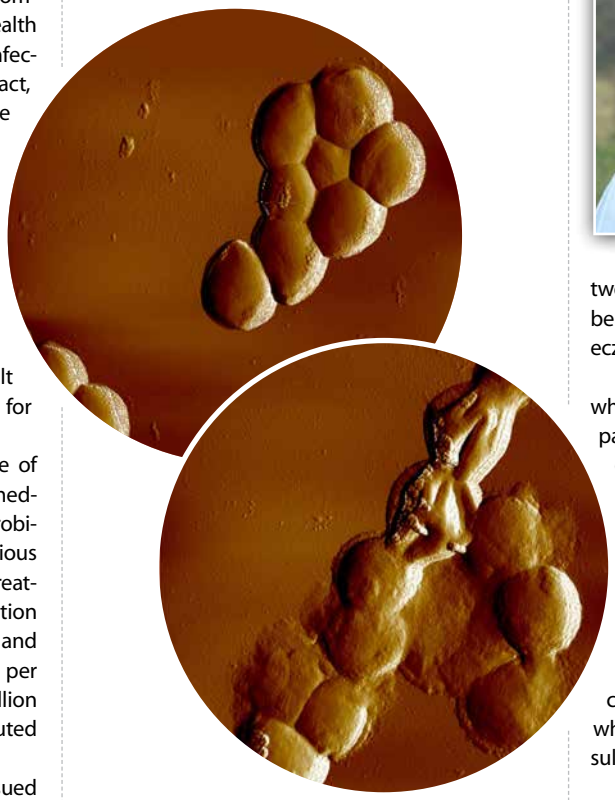
In 2009, the Alliance for the Prudent Use of Antibiotics (APUA) conducted a study of the medical and societal costs attributable to antimicrobial-resistant infections (ARI). In its Clinical Infectious Diseases report, the medical costs for ARI treatment, including those associated with duration of hospital stay, comorbidities, ICU, surgery, and mortality ranged from $18,588 to $29,069 per patient. The team extrapolated that $10.7 billion to $15.0 billion in societal costs can be attributed to antibiotic resistance.

In September 2014, President Obama issued an executive order authorizing the establishment of a task force to work to help detect, prevent, and control antibiotic-resistant infections.

The Dutch company Micreos has developed an alternative to antibiotics — Staphefekt — that is infection-specific and thwarts bacteria's mechanism for mutating. Staphefekt SA.100 specifically targets *Staphylococcus aureus,* including strains, such as MRSA, that are resistant to antibiotics. Thanks to its targeting mechanism, it leaves beneficial bacteria unharmed, which is especially important for longer-term use.

Staphefekt uses endolysins, which are bacteria-killing enzymes that originate from bacteriophages (phages), bacterial viruses. In nature, phages use bacteria to replicate. In this sense, phages can be regarded as bacteria's natural enemies.

"In order to replicate, phages attach to the particular bacterial species to which they are linked after which their DNA is drawn into the bacteria," says Mark Offerhaus, chief executive of Micreos.



These photos show living MRSA bacteria before and two minutes after exposure to Staphefekt.

Now inside the bacteria, the phage DNA commands the bacteria to reproduce new phages.

"Over billions of years of coevolution of phages and bacteria, the phages have found a foolproof way to exit from the bacterial host," he says. "They do this by releasing endolysins, which puncture bacterial cell wall to release the progeny phages into the environment."

Mr. Offerhaus says the specificity of this technology makes it an ideal tool to target bacterial infections.

"Phages are selective, and can reproduce only in specific bacteria," he says. "Antibiotics, such as penicillin, do not distinguish between different species of bacteria. We now realize that the vast majority of the bacteria in our gut and on our skin are beneficial to how the body functions. By eliminating all bacteria without distinguishing between the bad and the beneficial ones, we seem to be creating a lot of new health problems, such as eczema and Crohn's disease."

Mark Offerhaus

Researchers are beginning to understand that while antibiotics are powerful weapons against pathogens, they are indiscriminate, killing the good bacteria along with the bad.

For example, some antibiotics have been known to disrupt the bacteria that can keep other serious infections at bay, such as the *Clostridium difficile* (C. diff) infection. In the colon, there are numerous bacteria that prevent *C. diff* spores from becoming active. When antibiotics kill normal bacteria in the colon, they allow *C. diff* to populate the void, which then produces two toxins. These toxins result in the pooling of white blood cells in the colon.

Staphefekt was launched in 2013 in the Netherlands under the Gladskin brand for people with skin conditions with an infectious component, such as acne, eczema, rosacea, and skin irritation. In November 2014 the company launched in Europe Staphefekt XDR.300, a liquid solution for topical use against *Staphylococcus aureus*, including MRSA.

Mr. Offerhaus says Micreos will now approach the U.S. market and plans to meet with U.S. regulators to discuss the fastest entry possibilities.

To drive the development of the technology and explore new applications, Micreos has established the Staphefekt Open Source Collaboration program. As part of this program, Micreos will make Staphefekt available to researchers who wish to explore new application areas. The company's primary areas of interest include treatment of MRSA skin- and soft tissue infections, wound treatment, and biofilm formation on implants.

"We want people to benefit from our technology as soon as possible so we are making Staphefekt available for free to researchers," Mr. Offerhaus says. PV