Sticky antibiotic provides glue for successful treatment

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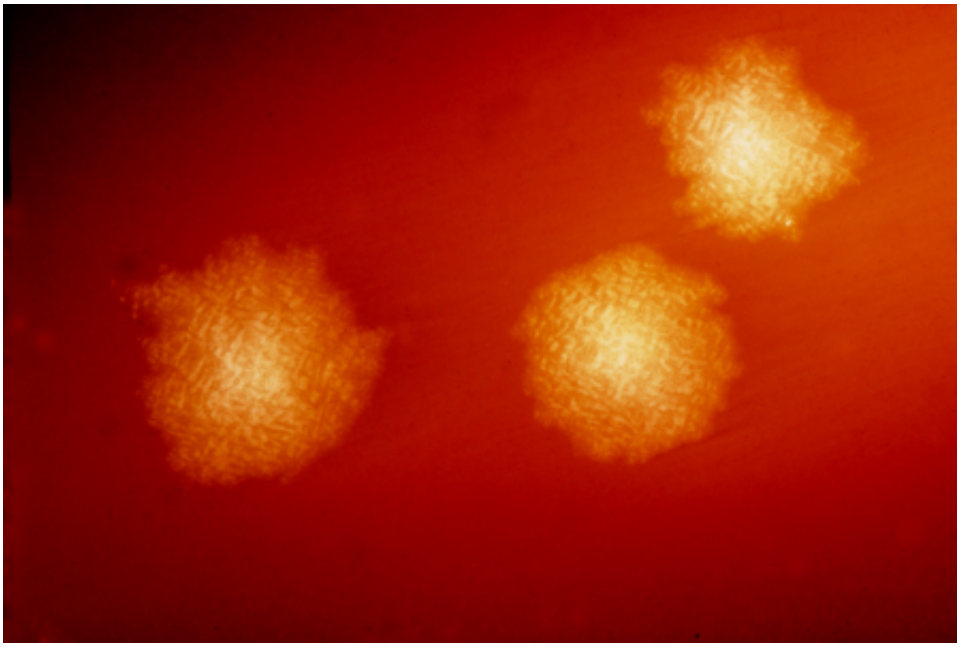

This photograph depicts Clostridium difficile colonies after 48hrs growth on a blood agar plate; Magnified 4.8X. C. difficile, an anaerobic gram-positive rod, is the most frequently identified cause of antibiotic-associated diarrhea (AAD). It accounts for approximately 15–25% of all episodes of AAD. Credit: CDC

Researchers have found how an antibiotic used to treat a debilitating gut infection stays put inside the body giving it time to effectively treat the problem, a discovery that will pave the way for the development of more effective antibiotic treatments to fight superbugs.

PE (pseudomembranous colitis) is a debilitating inflammation of the colon caused by infection with the microbe *Clostridium difficile* (and sometimes Staphylococcus aureus). The sugar- or carbohydrate-containing antibiotic known as vancomycin is taken by mouth to kill the infecting microbe.

To be effective, vancomycin needs to stay in the GI tract (gut) close to where it is needed and not be diluted away or lost through the lining of the gut and into the bloodstream. A multi-disciplinary team of scientists at the Universities of Nottingham and Leeds have now shown this 'staying put' mechanism is precisely what happens and that it can occur in an unexpected way.

Forming a formidable barrier

The research, published today in *Scientific Reports* shows that protein-carbohydrate molecules of the gut called mucins provide a formidable barrier helping to prevent the drug escaping using a unique mechanism of formation of large molecular complexes or clumps. The antibiotic and mucins join together to form a mucoadhesive complex, likely trapping the antibiotic within large complexes. It is the trapped vancomycin which the scientists believe may lead to delayed transit of the antibiotic leading to prolonged exposure of the antibiotic to the infectious *C. difficile*.

Dr. Mary Phillips-Jones, Associate Professor in Polymer & Microbial Biophysics at the University of Nottingham led the research, she said: "Vancomycin is a precious 'last-line' antibiotic in the clinician's arsenal of therapies to fight several important pathogens including MRSA, pneumonia, as well as *C. difficile*. The clumping effect with gut mucins revealed in our study not only gives new information about what may happen when the antibiotic is given orally, but might also provide new insights into its behaviour when infused into patients suffering from

other life-threatening infections."

The findings also fit with other studies which show that oral vancomycin produces high levels of vancomycin resistance amongst some gut bacteria (VRE), contributing to the generation of antimicrobial resistance (a serious concern); the clumping/ complexation phenomenon may therefore provide the first explanation of a mechanism by which this VRE generation occurs. But the benefits of taking oral vancomycin at the right time and when appropriate still outweigh any negative generation of antimicrobial resistance, and the study highlights that it is wise to take vancomycin when your GP advises it is good to do so.

Dr. Stephen Harding, Professor of Applied Biochemistry at the University of Nottingham added: "The antibiotic vancomycin is a truly remarkable molecule—a drug with its own mucoadhesive or sticky property which slows its transit through the gut right down giving maximum therapeutic effect and minimizing unused vancomycin being returned to the environment. If scientists are going to win the fight against anti-microbial resistance, joint institutional and interdisciplinary approaches like this successful one are going to prove crucial."

Provided by University of Nottingham