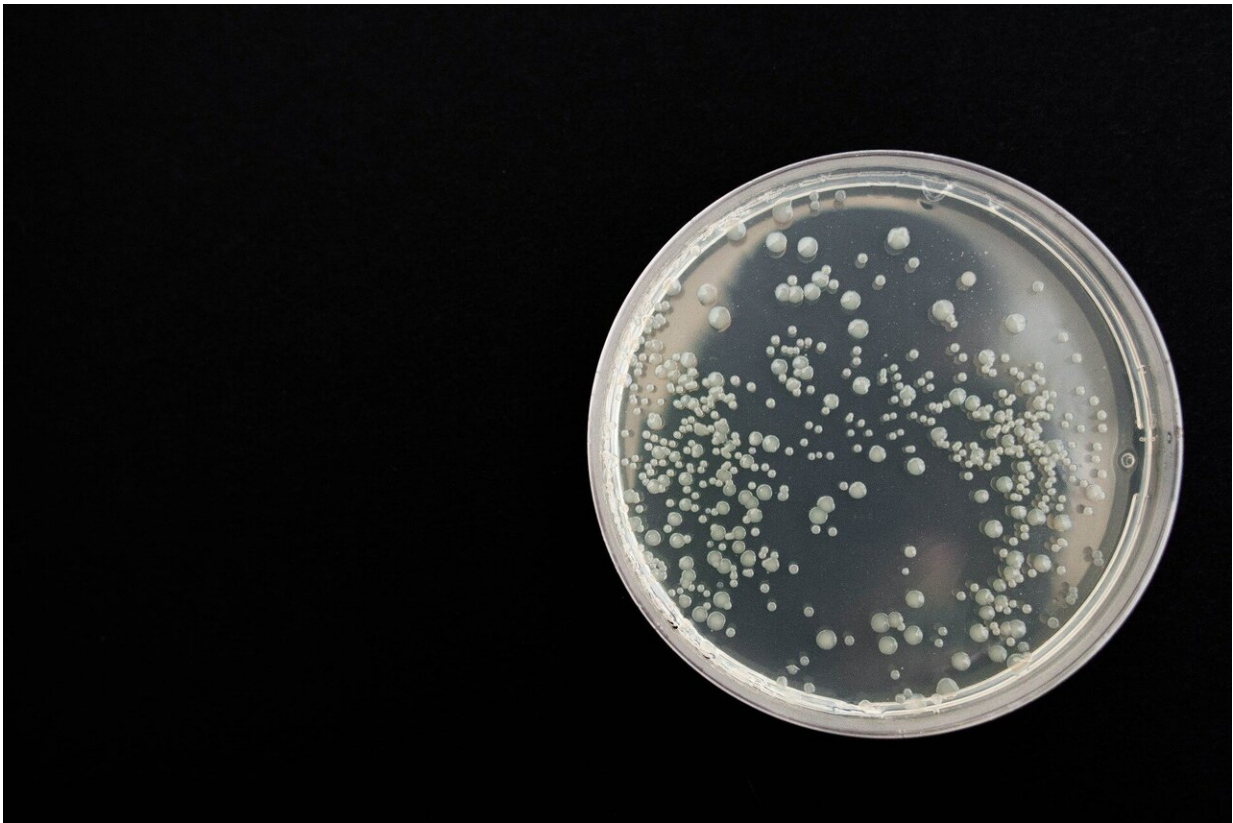


# Study shows promising approach for the prevention and cure of gonorrhea in women

March 10 2020

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In research recently published in *mBio*, researchers from the Abigail Wexner Research Institute (AWRI) at Nationwide Children's Hospital and Griffith University's Institute for Glycomics have discovered non-

antibiotic (host-targeted) therapies for the effective treatment of *Neisseria gonorrhoeae* infections by repurposing existing drugs.

Gonorrhoea is the second most commonly reported sexually transmitted infection (STI). The Centers for Disease Control and Prevention estimates that approximately 1.14 million new gonococcal infections occur in the United States each year. Gonorrhea is now a major public health threat, with alarming increases in incidence over the past five years (67% in the U.S. and 80% in Australia).

The disease affects both men and women, however, up to 80% of female gonococcal cervicitis is asymptomatic. When left untreated, it can lead to [pelvic inflammatory disease](#) (40% of infected women) that can result in severe long-term health implications such as infertility, adverse pregnancy outcomes and devastating neonatal complications.

The propensity of *N. gonorrhoeae* to rapidly acquire [antibiotic resistance](#) has solidified untreatable gonorrhea as a reality and, in the absence of a vaccine, has fueled interest in developing [new antibiotics](#) for gonorrhea treatment. Traditional antibiotics work by directly targeting (and killing) the bacteria and, as such, are subject to bacterial resistance mechanisms. Therefore, the development of new antibiotics that similarly target the bacterium will likely only provide a short-term solution to incurable *N. gonorrhoeae* infections.

"*N. gonorrhoeae*, the bacterium responsible for gonorrhea infections, is highly variable and exquisitely human-adapted," said study co-author Michael Jennings, Ph.D., principal research leader and deputy director at Griffith. "Its treatment evasion strategies have seen resistance develop against every antibacterial ever used to treat it. Our data strongly indicate that two, existing non-antibiotic drugs, methyldopa and carbamazepine, can be repurposed to both prevent and cure gonorrhea infection in women."

Methyldopa is a prescription medication currently used for the treatment of hypertension in pregnant women, whereas carbamazepine is used for the treatment of epilepsy.

"Carbamazepine and methyldopa work by out-competing the bacteria for binding to a specific molecule (called CR3) on the human cell surface," said study co-author Jennifer Edwards, Ph.D., principal investigator at AWRI at Nationwide Children's. "These drugs block the bacteria from binding, but they also bind in a way that is slightly different from the way the bacteria bind.

"This causes the host cell to act differently than it would when the bacteria bind," said Dr. Edwards, also an associate professor at The Ohio State University. "That is, when the drugs bind to the [host cell](#), they prime the cell to kill the bacteria. This type of host-mediated killing would not be expected to be subject to bacterial drug resistance mechanisms. We have not observed any drug resistance over sequential *N. gonorrhoeae* infections using primary human cell infection models."

*N. gonorrhoeae* infects only humans. Experimental infection of women is ethically prohibited. Animal models developed for *N. gonorrhoeae* research do not have CR3 on the mucosal surface of the female reproductive tract; however, CR3 is required for *N. gonorrhoeae* to initiate infection in women.

Therefore, the research team, led by Drs. Edwards and Jennings, used primary human cervical epithelial cells to model human cervical infection, which is the main site of [infection](#) in women. Following a single dose of methyldopa or carbamazepine, 100% clearance of *N. gonorrhoeae* occurred for cervical cells infected with multidrug-resistant ("untreatable") bacteria.

"Antibiotic resistance has emerged as one of our [greatest threats](#) to

global health," said Lauren Bakaletz, Ph.D., principal investigator and director of the Center for Microbial Pathogenesis at AWRI. "The rising incidence of multi-drug resistance demonstrated by *Neisseria gonorrhoeae* combined with recent trends of increases in the number of cases of gonorrhea worldwide have created an urgent demand for better treatment strategies, and preferably those that are not reliant on traditional antibiotics. This new study is novel, highly significant and exceptionally timely."

Mark von Itzstein, AO, director of the Institute for Glycomics, said the research team's data suggest a long-term solution to the growing problem of multidrug-resistant *Neisseria gonorrhoeae* infections.

"Given the absence of a gonococcal vaccine and the continued emergence of antibiotic-resistant and untreatable strains of *Neisseria gonorrhoeae*, this scientific finding provides a great deal of hope to millions of people around the globe who are battling this intractable disease," said von Itzstein.

**More information:** Jessica Poole et al. Repurposed Drugs That Block the Gonococcus-Complement Receptor 3 Interaction Can Prevent and Cure Gonococcal Infection of Primary Human Cervical Epithelial Cells, *mBio* (2020). [DOI: 10.1128/mBio.03046-19](https://doi.org/10.1128/mBio.03046-19)

Provided by Nationwide Children's Hospital

Citation: Study shows promising approach for the prevention and cure of gonorrhea in women (2020, March 10) retrieved 11 May 2024 from <https://medicalxpress.com/news/2020-03-approach-gonorrhea-women.html>

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