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A way to end recurrent urinary tract infections? Study with mice gives hope

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Millions of people worldwide – mostly women – suffer from recurrent urinary tract infections (UTIs) that seriously degrade their health and quality of life. Antibiotics treat individual infections, but preventing recurrent ones largely has been unattainable because of the way bacteria lodge in the inner layers of the bladder and quietly hide from drugs that can kill them.

In new studies with mice, however, researchers led by University of Utah microbiologists have shown that when chitosan, an FDA-approved compound for pharmaceutical, agricultural and other uses, is given in conjunction with antibiotics, it assists the bladder in ridding itself of "reservoir" populations of bacteria that live in its deeper layers and potentially cause recurrent infections. If the effectiveness of chitosan (ky-ta-san) against reservoir populations of bacteria could be confirmed in people, the compound might one day serve to augment antibiotic treatments of recurrent UTIs, according to Matthew Blango, Ph.D., a U of U postdoctoral researcher and first author on the study that appeared Tuesday, March 25, 2014, online in the journal *PLOS ONE*.

"Antibiotics don't do a good job of getting rid of reservoir populations," Blango says. "But when augmented with chitosan, there was a significant reduction in the level of bacteria in mouse bladders."

Matthew Mulvey, Ph.D., U of U professor of pathology senior author on the study. Elizabeth M. Ott, Ph.D., also a U postdoctoral fellow, is a co-author along with two researchers from the University of Ljubljana,

Slovenia.

UTIs are responsible for nearly 10 million health care office visits, 1.5 million hospitalizations and $1 billion in costs annually in the United States, according to the National Kidney Foundation. The infections are more common in women, with one in five getting at least one UTI during her lifetime. Unfortunately, after the first infection, some people will get a second, third and fourth or more UTIs, with each successive infection making them more susceptible to recurrent episodes.

The urinary tract comprises the kidneys, bladder, uretha and ureters. UTIs are caused primarily by bacteria known as uropathogenic *Escherichia coli* (UPEC), which originate in the bowel but move into the urinary tract. UPEC often are susceptible to antibiotics, but they also have the ability to pass through the surface lining in the bladder and permeate into deeper layers of cells and tissue where they lie dormant and invulnerable to drugs. Periodically, though, UPEC bacteria replicate in the tissues, which may cause recurrent UTI flare-ups in people.

To destroy reservoir populations of UPEC, Blango, Mulvey and their colleagues infused mouse bladders with chitosan for 20 minutes, during which time the compound worked to exfoliate large cells lining the surface of the bladders. The exfoliation of cells did not harm the deeper layers of the mouse bladders but caused dormant reservoirs of UPEC to move toward the surface of the bladders and divide and replicate, making them susceptible to antibiotics.

The researchers followed up the chitosan by giving the mice a one-week course of fluoroquinolones, an antibiotic class commonly used to treat UTIs. A week later, when they checked the level of UPEC in the mouse bladders, Blango and his colleagues found the reservoir populations of the bacteria for the most part were gone.

"Effectively, there were no bacteria in the bladder," Blango says.

The mouse bladders also regenerated the surface lining of exfoliated cells in about a week.

The results in mice don't mean that people with recurrent UTIs can or should start taking chitosan with antibiotics. Large-scale trials with people would be needed to verify the efficacy of the compound in humans. Blango's and Mulvey's colleagues in Slovania are looking into that prospect, while the U of U researchers are interested in refining and improving the results in mice.

More information: dx.plos.org/10.1371/journal.pone.0093327

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