The pepperoni pizza hypothesis

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What's the worst that could happen after eating a slice of pepperoni pizza? A little heartburn, for most people.

But for up to a million women in the U.S., enjoying that piece of pizza has painful consequences. They have a chronic bladder condition that causes pelvic pain. Spicy food -- as well as citrus, caffeine, tomatoes and alcohol-- can cause a flare in their symptoms and intensify the pain. It was thought that the spike in their symptoms was triggered when digesting the foods produced chemicals in the urine that irritated the bladder.

However, researchers from Northwestern University's Feinberg School of Medicine believe the symptoms -- pain and an urgent need to frequently urinate -- are actually being provoked by a surprise perpetrator. Applying their recent animal study to humans, the scientists believe the colon, irritated by the spicy food, is to blame.

Their idea opens up new treatment possibilities for "painful bladder syndrome," or interstitial cystitis, a condition that primarily affects women (only 10 percent of sufferers are men.) During a flare up, the pelvic pain is so intense some women administer anesthetic lidocaine directly into their bladders via a catheter to get relief. Patients typically also feel an urgent need to urinate up to 50 times a day and are afraid to leave their homes in case they can't find a bathroom.

"This disease has a devastating effect on people's lives," said David Klumpp, principal investigator and assistant professor of urology at the

Feinberg School. "It affects people's relationships with family and friends." Klumpp said some women who suffer from this become so depressed, they attempt suicide.

Klumpp worked with Charles Rudick, a postdoctoral fellow at the Feinberg School, on the paper, which was published in the September issue of *Nature Clinical Practice Urology*.

The Northwestern researchers believe the colon's central role in the pain is caused by the wiring of pelvic organ nerves. Nerves from this region -- the bladder, colon and prostate -- are bunched together like telephone wires and plug into the same region of the spinal cord near the tailbone.

People with interstitial cystitis have bladder nerves that are constantly transmitting pain signals to the spinal cord: a steady beep, beep, beep.

But when the colon is irritated by pepperoni pizza or another type of food, colon nerves also send a pain signal to the same area on the spinal chord. This new signal is the tipping point. It ratchets up the pain message to a chorus of BEEPEEPBEEPBEEP!

"It was known that there was cross talk between organs, but until now no one had applied the idea to how pain signals affect this real world disease, how the convergence of these two information streams could make these bladder symptoms worse," said Klumpp, who also is an assistant professor of microbiology-immunology at the Feinberg School.

The new model suggests the bladder pain can be treated rectally with an anesthetic in a suppository or gel. Another possibility is an anesthetic patch applied to pelvic skin. Studies in back pain show anesthetic patches applied to the skin can reduce back pain, Klumpp said.

"We imagine a similar kind of patch might be used to relieve pelvic pain,

which might be the best solution of all," he noted.

Klumpp's concept is based on a 2007 study in which he showed that delivering red pepper into the colon of a mouse with pre-existing pelvic pain caused the pain to worsen. When he then delivered lidocaine into the mouse colon, "it knocked down pain just as effectively as if we put it in the bladder," Klumpp said.

"We likened it to what happens to humans," Klumpp noted. "Pepperoni pizza does nothing to most people other than heartburn, but when you give it to a person with an inflamed bladder, that will cause their symptoms to flare because the nerves from the bladder and bowel are converging on the same part of the spinal cord."

Source: Northwestern University