



Women & Urinary Tract Infections

HOW UTIs CAN AFFECT BRAIN HEALTH

Nan was sharp as a tack, well into her 90s. She seemed to forget nothing and no one," said Dana Dinerman, an editor who lives in New Jersey. "I'd often wonder how she kept track of all the little details about so many people. She'd always follow up on everything going on in my family's life and remembered to ask about my friends, too."

But one time, Dinerman noticed her grandmother was confused about things that didn't usually trip her up. "I wondered if she was showing early symptoms of Alzheimer's disease, as her father had it," she said.

Dinerman was surprised to learn her grandmother's confusion was caused by a urinary tract infection (UTI), as she had not mentioned any other symptoms. "It was a relief when she returned to her usual self after the UTI resolved."

Mind Over Matter® spoke with leading experts and rounded up the latest evidence on how UTIs affect brain health, the importance of accurate diagnosis and treatment, challenges with existing treatments, and an innovative sublingual vaccine that holds promise for reducing the number of recurrent infections. [➔](#)

UTIs IN WOMEN

Most UTIs are infections of the bladder and the urethra, the tube that carries urine from the bladder to outside the body. UTIs are caused by bacteria that enter via the urethra and spread in the cells lining these parts of the lower urinary system. One of the main culprits is *Escherichia coli* (E. coli), which is commonly found in the gastrointestinal tract.

UTIs are a leading cause of bacterial infections in women.

MORE THAN 50% OF WOMEN WILL HAVE A UTI IN THEIR LIFETIME, AND FIVE TO 10% OF WOMEN WILL SUFFER FROM RECURRENT UTIs, DEFINED AS THREE OR MORE IN A YEAR OR TWO OR MORE WITHIN SIX MONTHS.

If a UTI extends higher up from the bladder, it can cause a kidney infection, which can be severe, but that only happens in about one out of 30 cases, according to the American Urological Association.

Women are more likely to develop UTIs than men for several reasons. Anatomically speaking, women have shorter urethras. Sexual intercourse and the use of contraceptive spermicides and diaphragms are additional risk factors. In post-menopausal women, lower estrogen levels thin the cells lining the urinary tract, increasing the susceptibility to infection.

According to Dr. Kalpana Gupta, Chief of the Section of Infectious Diseases at the Veterans Administration Boston Healthcare System and Professor of Medicine at the Chobanian and Avedisian School of Medicine,

“IT’S OFTEN INCORRECTLY ASSUMED WOMEN ARE AT FAULT FOR CONTRACTING UTIs, AND IT’S SO UNFORTUNATE THIS STIGMA EXISTS. I’VE HAD WOMEN TELL ME THEY BATHE BEFORE AND AFTER INTERCOURSE IN AN ATTEMPT TO ‘STAY CLEAN.’

But UTIs are not due to women being “unclean” or doing things incorrectly, like wiping in the wrong direction or the way they have sex. Bacteria are always present on and in our bodies. UTIs occur when certain bacteria colonize and spread in the mucosal lining of the urinary tract. Wiping differently or bathing more often does not make a difference.”

Common UTI symptoms may include a burning sensation when urinating, a persistent, strong urge to pee, passing cloudy, red, bright-pink or cola-coloured urine, and pain in the centre of the pelvis and around the pubic bone area.

OLDER WOMEN DEVELOPING A UTI MAY NOT HAVE ANY OF THE MORE COMMON SYMPTOMS.

Instead, they may experience delirium, low blood pressure, an irregularly elevated heart rate, or fever. If they also have dementia as a pre-existing condition, the UTI may cause heightened confusion and agitation without them realizing why or being able to tell others they’re not feeling well.

HOW UTIs AFFECT THE BRAIN

It’s no wonder Dinerman was concerned about her grandmother’s unexpected forgetfulness, because it’s not widely known that UTIs can affect the brain in older women.

“Having an infection can certainly affect cognition, especially in older individuals, but dementia and delirium are two different syndromes,” said Dr. Gupta. “Delirium is a sudden onset of confusion that waxes and wanes and typically lasts a few hours or days. Dementia is a much slower and ongoing process related to a neurodegenerative disease, such as Alzheimer’s or Parkinson’s disease, that doesn’t resolve and occurs over many years.”

Symptoms of delirium may include delusions, hallucinations, altered mood, dramatically reduced responsiveness, or paradoxically, increased agitation and hypervigilance. Old age, frailty, and existing cognitive impairment can raise the risk of experiencing delirium when an additional stressor, like an infection, gets added to the mix.

SCIENTISTS DON’T KNOW YET EXACTLY HOW A BACTERIAL INFECTION IN THE URINARY TRACT CAUSES DELIRIUM IN OLDER ADULTS.

One hypothesis is that increasing age makes the brain more susceptible to circulating inflammatory substances the body produces in response to infections.

UTIs negatively affect brain health in younger women, too. “Families, friends, and bosses at work tend to think UTIs are a nuisance easily treated with antibiotics,” said Dr. J. Curtis Nickel, professor emeritus in the Department of Urology at Queen’s University, clinician scientist at Kingston General Health Research Institute in Kingston, Ontario, and former Canada Research Chair in Urologic Pain and Inflammation, Tier 1.

“THE TRUTH IS RECURRENT UTIs HAVE A SIGNIFICANT NEGATIVE IMPACT NOT ONLY ON WOMEN’S PHYSICAL HEALTH, BUT ALSO ON THEIR MENTAL HEALTH, CAUSING ANXIETY, DEPRESSION, AND STRESS.

Recurrent UTIs reduce women's quality of life, self-esteem, ability to work or perform daily activities, and the quality of social relationships, according to a large review of the published literature.

The analysis, published in March 2022 in the journal *GMS Infectious Diseases*, also found that one-third of women with recurrent UTIs experienced them very often or often after sexual intercourse, and more than half reported their sexual relations were negatively influenced as a result.

ACCURATE DIAGNOSIS IS ESSENTIAL

An accurate diagnosis matters for both delirium and UTIs. For individuals experiencing delirium, pinpointing the cause is essential because episodes can have long-term negative consequences on brain health. Delirium can also accelerate cognitive decline in individuals living with Alzheimer's disease.

The United Kingdom National Health Service shows UTIs at the top of their list of common causes of delirium in older adults and individuals with dementia. They also include a stroke or mini-stroke, low blood sugar level in people with diabetes, head injury, taking drugs, carbon monoxide poisoning, a severe asthma attack, and epileptic seizures as other potential causes.

WHEN IT COMES TO DIAGNOSING A UTI, ACCURACY IS ESSENTIAL FOR DETERMINING THE BEST TREATMENT APPROACH.

HELPFUL TIPS FOR PREVENTING UTIs

The Mayo Clinic recommends the following tips for lowering your risk of developing a UTI:

- ▶ **drink plenty of fluids, especially water, to dilute your urine and lower the concentration of bacteria in your bladder;**
- ▶ **empty your bladder often.** It's normal to pee four to eight times daily;
- ▶ **urinate soon after sex.** Voiding after intercourse removes some of the bacteria close to your urethra opening; and
- ▶ **drink cranberry juice.** A recently updated meta-analysis published in the *Cochrane Database of Systematic Reviews* in April 2023 found that cranberry juice or capsules probably reduced symptomatic, confirmed UTIs in women with a history of recurrent UTIs by 26%.

A test-strip urinalysis done at the doctor's office or at home only provides a yes-no answer on whether white blood cells are present. Only a urine culture test performed by a medical lab can identify the specific strains and bacterial species causing a UTI, enabling your healthcare provider to prescribe the right antibiotic to clear the infection.

You may be surprised to learn that cloudy, discoloured, or foul-smelling urine does not necessarily indicate the presence of an infection. In fact, there are public health campaigns with the tagline "Symptom-free pee, LET IT BE," encouraging healthcare providers not to prescribe antibiotics indiscriminately.

CHALLENGES WITH EXISTING TREATMENTS

Since the discovery of penicillin in 1928, antibiotics have cured many infectious diseases, prevented many postoperative infections, and saved countless lives. But globally, antibiotic drug development has slowed to a crawl, and at the same time, more bacteria are becoming superbugs, developing multiple ways to resist the antibiotics we have left.

Many women are prescribed antibiotics when they have bacteria in their urine without symptoms, known as asymptomatic bacteriuria, according to an extensive review of the published medical literature by researchers at the California Institute of Behavioral Neurosciences & Psychology.

The authors noted this practice increases the risk of antibiotic resistance and also accelerates the development of delirium. Their review was published in December 2022 in the journal *Cureus*.

Keep in mind that about one-third of women recover from uncomplicated UTIs without antibiotics. But UTI symptoms, such as fiery pain on urination, can be exceedingly uncomfortable while waiting a day or two for urine culture test results to come back.

As a result, many women with UTI symptoms are prescribed the wrong antibiotic, such as a broad-spectrum drug, when a targeted drug better matched to the bacterial strain would be more effective.

A recent study published in *Open Forum Infectious Diseases* found that almost half of about 670,000 women diagnosed with uncomplicated UTIs were prescribed an inappropriate antibiotic, and more than 75% were prescribed antibiotics for a longer period than necessary.

Dr. Gupta has spent more than a decade investigating how 

to optimize treatment and prevention strategies for UTIs in women. In 2010, she was Chair of the Infectious Diseases Society of America (IDSA) UTI Guideline Update Committee, and is a current member of the IDSA committee working on an update in progress.

“Our research has shown the presence of healthy flora is essential for keeping infection at bay in the mucosa lining of the urethra and bladder,” said Dr. Gupta.

“ANTIBIOTICS WIPE OUT HEALTHY FLORA THROUGHOUT YOUR BODY, INCLUDING YOUR INTESTINE, VAGINA, AND URINARY TRACT, INCREASING THE RISK OF FUTURE UTIs.

“Each individual’s flora is distinct, so access to historical urine culture results can be incredibly helpful for choosing the best antibiotic if results are not available yet for a present episode, especially if patients change healthcare providers,” said Dr Gupta.

“Women should keep track of their UTI history, including symptoms, lab culture results, antibiotics prescribed and whether the medications resolved their infections.”

RESEARCHERS CONTINUE INVESTIGATING WAYS TO OPTIMIZE ANTIBIOTIC TREATMENTS FOR UTIs WHILE LESSENING THE RISKS OF COMMON, UNWANTED SIDE EFFECTS, SUCH AS HEADACHES AND GASTROINTESTINAL UPSET.

For example, Dr. Gupta led a study that found five days of nitrofurantoin (Macrobid), a common drug for treating UTIs, was as effective as three days of trimethoprim-sulfamethoxazole (Bactrim), the gold standard treatment at the time.

“The IDSA treatment guidelines now recommend five days of Macrobid instead of seven, which greatly benefits patients. They experience fewer side effects and get back to what they need to do sooner,” she said.

As a final plot twist, be aware that many antibiotics are associated with delirium, according to a recent study. Researchers at the University of South Carolina and the University of Texas at Austin analyzed 15 years of records in the reported adverse events database collected by the United States Food and Drug Administration (FDA).

They found statistically higher rates of delirium were reported with the use of 16 common antibiotics, some of which are prescribed for treating UTIs. Their study was published in *Drugs Real World Outcomes* in March 2022.

A NOVEL VACCINE

An innovative vaccine for reducing the number of recurrent UTIs in women is already approved and available for use under special access programs in 26 countries, such as Spain, the U.K., and New Zealand - but not yet in North America.

Known as Uromune, the vaccine is sprayed under the tongue. It contains inactivated strains of four bacterial species that most commonly cause UTIs - *E. coli*, *Klebsiella pneumoniae*, *Enterococcus faecalis*, and *Proteus vulgaris*.

THE VACCINE ENCOURAGES THE BODY TO BUILD IMMUNITY AGAINST THESE BACTERIA IN THE MUCOSAL LINING OF THE URINARY TRACT WITHOUT GASTRIC SIDE EFFECTS AND WITHOUT WIPING OUT HEALTHY FLORA IN THE GUT, URINARY TRACT, OR OTHER AREAS OF THE BODY.

Dr. Nickel recently led the first North American clinical trial of Uromune in Kingston and Toronto. A total of 67 women ages 18 to 80 who experienced more than three UTIs in the previous year participated in the study between 2019 and 2022. They used the vaccine twice daily for three months, and researchers followed them for an additional nine months.

Uromune significantly reduced the average number of UTIs for the group from 6.8 to 1.7 per year - a 75% reduction - and 40% of women in the study had zero UTIs in the nine-month follow-up period.

The results, published in October 2023 in the *Canadian Urological Association Journal*, demonstrated that the vaccine is safe and effective for reducing recurrent UTIs in women. The vaccine manufacturer has applied for approval in Canada, and time will tell whether the company files for FDA approval in the United States.

Dr. Nickel, who has no financial interest in the company that makes Uromune, said,

“AN ANTIBIOTIC-FREE, EFFECTIVE TREATMENT FOR REDUCING RECURRENT UTIs WOULD CERTAINLY BE A WELCOME RELIEF TO MANY WOMEN WHO SUFFER IN SILENCE.

The science of preventing, diagnosing, and treating UTIs continues to evolve. In the meantime, be aware of how they can affect your physical and mental health. If you or a loved one experiences sudden unexplained confusion, like Dinerman’s grandmother, seek medical attention right away. You should also consult your healthcare provider if you or a loved one have UTI symptoms to discuss the pros and cons of the best treatment options with a view to minimizing the inappropriate use of antibiotics. 🌐