

Urinary Tract Infection (UTI)

Factsheet

What is a urinary tract infection (UTI)?

A urinary tract infection (UTI) is an infection occurring anywhere in the urinary tract-from the kidneys to the urethra. A lower UTI involves the bladder and anything below, like the urethra and prostate. Infections of the bladder are sometimes called cystitis. An upper UTI involves the urinary system above the bladder, such as the ureters and kidneys (kidney infection or pyelonephritis).



What causes a UTI?

It was once thought that urine is sterile, but the normal bladder in fact hosts a urinary microbiome (urobiome)—a community of microorganisms such as fungi, bacteria and viruses. It is now understood that a UTI can occur when the normal urobiome is taken over by a urinary pathogen (a diseasecausing bacteria) or when the urobiome becomes out of balance.1-4

Historically it was assumed, and many doctors still believe, that a UTI is the result of bacteria such as E.coli entering the 'sterile' urinary tract via the bowel, usually through sexual intercourse or personal hygiene habits. However, the discovery of the urobiome in 2014 is leading to a more accurate and useful understanding of bladder health and disease, including the many different pathogens that can cause infection and why infection occurs in some people and not others.

Who is likely to get a UTI?

Women are the most impacted by UTI, with 1 in 2 women having a UTI in their lifetime, compared to 1 in 20 men.5 However, UTI also affects babies, children, men and especially elderly people.

There is a common belief that women are more prone to UTIs due to the length and positioning of their urethra. However, research supporting this theory is difficult to find.

UTIs are common in otherwise healthy adult women, but there are some stages of life and some medical conditions that can increase their likelihood. These include pregnancy, menopause/ post-menopause, diabetes, conditions causing immunosuppression, physical injuries impacting the spine/pelvis and conditions requiring catheterisation.6









UTI symptoms

Symptoms of an acute UTI can include bladder/lower abdominal pain and/ or pressure, painful urination (dysuria), urgency, abnormal frequency of urination, lower back pain, urethral pain/spasms/burning, feeling tired, weak, confused or shaky (more common in the elderly) and sometimes cloudy, smelly or even blood-filled urine.

If left untreated, the bacteria causing the infection can travel upwards and affect the kidneys. Symptoms of a kidney infection include typical UTI symptoms, along with chills, fever and flank pain/ pressure. In the worst case, bacteria can then enter the blood stream, resulting in life-threatening septic shock. This is rare but extremely serious.

Commonly used UTI tests are unreliable and have high failure rates.

UTI diagnosis

A UTI is usually diagnosed by a doctor who tests your urine sample for signs of infection with a dipstick at the clinic, and/or sends a sample to a laboratory to test for bacteria. In some states, a pharmacist can diagnose a UTI by asking about your symptoms and your UTI history.

Even though commonly used UTI tests are considered 'gold standard', research has shown they are unreliable and have high failure rates.

Urinary dipstick

Dipsticks are often the first diagnostic tool GPs use to confirm or rule out a UTI. These tests are designed to quickly identify signs of infection, such as white blood cells (leucocytes or pus cells), blood, pH levels and nitrites. They can be useful in confirming a clearly positive acute UTI; however, research has found they are highly insensitive and unreliable and should never be used to rule out an infection.7



Urine culture (MSU)

After your GP listens to your symptoms and tests your urine with a dipstick, they will probably send a mid-stream urine sample (MSU) to the laboratory to see which bacteria is causing your UTI. The laboratory will try to grow the bacteria on a culture plate to help the doctor decide on the right antibiotic. Either a technician or a machine will conduct a urinalysis, where a small amount of urine is examined under a microscope to check for other signs of infection, such as white blood cells, red blood cells and epithelial cells. These readings will be used alongside the MSU culture results to determine if there is an infection.

As with dipsticks, the urine culture test is shown to miss a large proportion of infections.8-15

See more about UTI tests here: www.chronicutiaustralia.org.au /uti-testing









When a UTI keeps coming back or won't go away

The biggest risk factor of developing another UTI is having had an initial UTI. For women, after experiencing a first UTI, a quarter will have a recurrence within six months. If someone has a history of one or more UTIs, the risk of a recurrence in the same year rises to 70 percent.16

Recurrent UTI

People with more than two cultureproven (positive) UTIs in six months, or more than three positive UTIs in one year, are generally diagnosed as having recurrent UTI.

For women, after experiencing a first UTI, one in four will have a recurrence within six months.

Chronic UTI

People with ongoing or intermittent UTI symptoms may be suffering from a chronic UTI. A chronic UTI can develop when bacteria evading the immune system or antibiotic attack burrow into the bladder and/or urethral lining (uroepithelium), where they safely hide away from further attack. There they can remain dormant for long periods. 17-30

It is common in chronic UTI for standard UTI test results to be reported as 'negative' or to receive a mix of 'positive' and 'negative' test results. This unfortunately leads to further investigations and misdiagnoses of other conditions to explain the symptoms.

While chronic UTI can be challenging to diagnose and treat using existing medical guidelines, it is important to remember that all forms of UTI are treatable and there is no need to put up with ongoing pain and other distressing symptoms.

In 2023, the National Health Service (NHS) in the United Kingdom added chronic UTI to its website's UTI health information page for consumers. You can read more here: www.nhs.uk/ conditions/urinary-tract-infections-utis

You can read more about chronic UTI here: www.chronicutiaustralia.org.au/ chronic-uti/what-is-chronic-uti



Asymptomatic bacteriuria

Asymptomatic bacteriuria (ASB) is when a urine culture grows bacteria in a person who has no UTI symptoms. Doctors are less inclined to treat ASB in many patient groups now that it is understood urine cultures can grow harmless bacteria found in the urobiome.









UTI treatment

Uncomplicated acute UTI

Researchers have found that for around a third of women who develop an uncomplicated acute UTI, the infection may resolve spontaneously.31 This means they can manage symptoms at home by doing things like increasing fluid intake and taking ibuprofen, and their symptoms will resolve over a week to 10 days.

However, for the majority who do require antibiotic treatment for a UTI, in Australia this will most likely be a short course of first-line antibiotics, such as trimethoprim 300 mg orally at night for three days or nitrofurantoin 100 mg, six-hourly for five days. Many doctors and patients are unaware that between one quarter to one third of women have UTIs that fail treatment and they will require followup medical treatment to fully clear the infection and resolve symptoms. 32-34

Recurrent UTI

Existing treatment guidelines for recurrent UTI include a trial of longterm prophylaxis (a daily low-dose antibiotic to 'keep urine sterile'), selfstart therapy (where the patient is given a script for a short-course antibiotic, to be used when they develop UTI symptoms) or post-intercourse prophylaxis (taking a 'once off' antibiotic after sex to prevent a UTI developing).35

Chronic UTI

Currently, the only scientifically backed treatment for chronic UTI requires a constant level of full dose, firstgeneration antibiotic in the urine, supported by a urinary antiseptic

(methenamine hippurate, also known as Hiprex), over a protracted period until symptoms clear.³⁶ The treatment approach prevents embedded bacteria from escaping, reinfecting and colonising new cells that line the bladder/urinary tract. The treatment period for chronic UTI varies between patients. UK research has shown that the mean (average) treatment length following a specific protocol was 383 days.38

If you suspect you could have a chronic UTI, please learn as much as you can about chronic UTI at www. chronicutiaustralia.org.au and share the information with a supportive and trusted doctor who may help treat your infection appropriately. There are currently no clinics in Australia specialising in diagnosing and treating this form of UTI.

Alternative and complementary treatments

Hiprex (methenamine hippurate)

Hiprex is an old antibacterial agent that acts as a urinary antiseptic. Its main function is to clear planktonic (free floating) bacteria in the urinary tract. Therefore, it can play a supportive role and is often prescribed by chronic UTI specialists in conjunction with a protracted course of full therapeutic dose antibiotics. A 2022 British study found that methenamine hippurate (Hiprex) was non-inferior to prophylactic low-dose antibiotic therapy in helping prevent recurrence of infection and might be an appropriate alternative for women with a history of recurrent UTI.39

Hiprex can be purchased over the counter in Australia.

Hormonal treatment

When women reach peri or post menopause their estrogen levels start to decrease, and some women find they start to develop recurrent UTIs or their recurrent UTIs worsen significantly. Although the research into how hormones impact the urobiome is still in its infancy, it has been found the female hormone oestrogen may protect against UTI in postmenopausal women by improving two of the body's defence mechanisms. First, it may help trigger the production of the body's natural antimicrobial proteins in the bladder. Second, by tightening and strengthening the surface layer of the bladder cells, oestrogen may help protect the underlying cells from infection.40

Natural therapies

UTI is the second most common human bacterial infection in the world. so it is not surprising to find countless costly natural therapies on the internet claiming to cure infections. Most are not backed by clinical research and do not have authentic anecdotal support.

There is some research suggesting that a natural sugar called D-mannose may help prevent recurrent infections in some people by stopping certain bacteria from attaching to the bladder lining. 41 A modified and 'super charged' form of mannose, known as mannosides, are said to be highly efficacious in treating and preventing UTI in pre-clinical models, with more research currently underway.42













Treating a UTI at home

Researchers say that in about a third of women who develop an uncomplicated UTI, the infection may resolve by about 7-10 days without the need for antibiotics. 43 Although there is little evidence supporting over-the-counter medications for UTI, some people selftreat with urinary alkalisers, cranberry products, D-mannose or non-steroidal anti-inflammatory drugs (NSAIDs) such as Ibuprofen.44

You should listen to your body and pay attention to your symptoms and seek medical help if your symptoms are not resolving or they worsen. It is important to see a doctor or attend a hospital emergency department urgently if you experience any symptoms suggestive of a kidney infection (pyelonephritis) or sepsis, as described in the next section.



When to seek medical treatment for a UTI

If this is the first time you have had a UTI, it is a good idea to go straight to a doctor for assessment and advice.

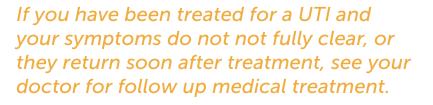
If this is not your first time and you are familiar with the signs and symptoms of a UTI, take the action you would normally take. For example, if your infection typically resolves spontaneously without medical help, do what works for you (e.g. drink water, take ibuprofen, take D-mannose). If you know your UTIs do not resolve without antibiotics, see your doctor as soon as possible.

If you have been treated for a UTI and your symptoms have not fully resolved, or they did clear and returned soon after, it is important to see your doctor to request further treatment. If your doctor insists on a urine culture to confirm your infection is still present, it is important to remind them that urine cultures have high failure rates, particularly during and soon after antibiotic treatment when the infection cultured may not meet the arbitrary threshold set for diagnosing an acute UTI.

When to seek help urgently

If your symptoms develop rapidly and you are experiencing flank pain (where your kidneys are), see a doctor or attend a hospital emergency department urgently. It is also important to seek help promptly from a doctor or a hospital emergency department if you experience any of the following symptoms:

- · Nausea or vomiting
- Rigors
- · Shivering, chills
- Muscle pain
- Feeling confused or very drowsy
- · Not passing urine all day
- Blood in the urine
- Temperature above 38°C
- Kidney pain in the back or under the ribs
- Worsening UTI symptoms
- If taking antibiotics, no improvement in UTI symptoms after 48 hours.45











Preventing UTIs

There are many different thoughts on how someone can prevent UTIs. Tips and advice from doctors, websites and well-meaning friends and family are often not backed by clinical research, and some are even scientifically disproven. However, there are anecdotal accounts that some people find some of the following actions useful:

- Urinating soon after sex.
- Increasing fluids to dilute urine (this can also have the opposite effect of weakening the natural immune response in the urine and diluting antibiotics if you are taking them).
- · Avoiding constipation.
- · Taking probiotics, cranberry products, D-mannose.
- Avoiding spermicides when having sex with or without a diaphragm.
- · Avoiding holding in urine for long periods of time.
- · Avoiding scented feminine products.

The above tips appear to help only some people in certain circumstances. If you do not find them useful, it is not your fault and it does not mean you are doing anything wrong.



Future UTI diagnosis and treatments

Bladder/urinary tract research has been severely overlooked and underfunded throughout history. Since the discovery of the urobiome, however, interest has grown among research teams around the world. This is leading to an expanding knowledge base, with research into new diagnostic methods, better antibiotic therapies and nonantibiotic therapies being explored.

Here are some exciting treatments currently being researched:

- New nanoparticle technology that administers an antibiotic directly into the bladder where it can penetrate uropathogens protected by biofilm and/or hiding inside the cells that line the bladder.
- · Vaccination against select urinary pathogens and to boost the natural immune response.
- Bacteriophage therapy (using viruses to attack pathogenic bacteria).
- Probiotics to return the urobiome to a healthy, balanced state.
- Super-strength mannosides to stop bacteria like E.coli from attaching in the bladder wall.

Research is currently underway looking for new diagnostic methods and better treatments for UTI.









More information

www.chronicutiaustralia.org.au

Produced by Chronic UTI Australia (Inc.)

Version 1, February 2024

This UTI factsheet, and other materials on our website, is made available for information purposes only and does not constitute medical or other personal or professional advice or instruction. The information has been researched and compiled by volunteers who do not have medical training/ qualifications. Chronic UTI Australia (Inc) shares information available in the public domain in respect of urinary tract infection which, based on the reasonable opinion of its volunteers, it considers to be from a reliable or authoritative source. Should you require more information or medical help, please consult your doctor.

References

- The New World of the Urinary Microbiota in Women www.pubmed.ncbi.nlm.nih.gov/26003055/
- Urine is Not Sterile: Use of Enhanced Urine Culture Techniques to Detect Resident Bacterial Flora in the Adult Female Bladder, www.ncbi.nlm.nih.gov/pmc/articles/PMC3957746
- The female urinary microbiota, urinary health and common urinary disorders, www.pubmed.ncbi.nlm.nih.gov/28217699/
- Bladder Biome Project 2023 Live Q&A with Alan Wolfe, www.youtube.com/watch?v=ZR0llaM2QhQ (last viewed February 2024)
- Foxman, B. (2003), Epidemiology of urinary tract infections: Incidence, morbidity, and economic costs. Disease-a-Month, 49(2), 53-70. doi: 10.1016/S0011-5029(03)90000-9 www.ncbi.nlm.nih.gov/pubmed/12601337
- Foxman, B. (2003), Epidemiology of urinary tract infections: Incidence, morbidity, and economic costs. Disease-a-Month, 49(2), 53-70. doi: 10.1016/S0011-5029(03)90000-9 www.ncbi.nlm.nih.gov/pubmed/12601337
- Hurlbut TA 3rd & Littenberg B: The diagnostic accuracy of rapid dipstick tests to predict urinary tract infection. Am J Clin Pathol 1991; 96: 582
- Stamm WE. Recent developments in the diagnosis and treatment of urinary tract infections www.ncbi.nlm.nih.gov/pmc/articles/ PMC1274066

- Tarnished Gold—the 'Standard' Urine Culture: Reassessing the Characteristics of a Criterion Standard for Detecting Urinary Microbes www.frontiersin.org/articles/10.3389/ fruro.2023.1206046/full
- 10 Bacteriuria in the Catheterized Patient. What Quantitative Level of Bacteriuria is Relevant? <u>www.pubmed.ncbi.nlm.nih.gov/6749229</u>
- 11 Diagnosis of Bacteriuria in Men: Specimen Collection and Culture Interpretation, www.pubmed.ncbi.nlm.nih.gov/3559288/
- 12 Reassessment of Routine Midstream Culture in Diagnosis of Urinary Tract Infection, www.jcm.asm.org/content/early/2018/12/10/ JCM.01452-18
- 13 The Clinical Urine Culture: Enhanced Techniques Improve Detection of Clinically Relevant Microorganisms www.jcm.asm.org/ content/54/5/1216
- 14 Voided Midstream Urine Culture and Acute Cystitis in Premenopausal Women, www.pubmed.ncbi.nlm.nih. gov/24224622/
- 15 Urine Trouble: Should we think Differently about UTI? www.link.springer.com/article/10.1007%2Fs00192-017-3528-8
- 16 Betsy, F. (2010). The epidemiology of urinary tract infection. Nature Reviews Urology, 7(12), 653. doi: 10.1038/nrurol.2010.190 www.ncbi.nlm.nih.gov/pubmed/21139641
- 17 www.ncbi.nlm.nih.gov/pmc/articles/PMC132990/
- 18 Spectrum of Bacterial Colonization Associated with Urothelial Cells from Patients with Chronic Lower Urinary Tract Symptoms, www.ncbi.nlm.nih.gov/pmc/articles/PMC3697662
- 19 Differentiation and Developmental Pathways of Uropathogenic Escherichia coli in Urinary Tract Pathogenesis', www.pnas.org/ content/pnas/101/5/1333.full.pdf
- 20 Major Breakthrough for Chronic UTI Sufferers Set to Improve Testing and Treatment of Condition, www.inews.co.uk/ news/chronic-uti-recognised-nice-first-time-breakthroughsufferers-2330102
- 21 Importance of Biofilms in Urinary Tract Infections: New Therapeutic Approaches, www.downloads.hindawi.com/ archive/2014/543974.pdf
- 22 Detection of Intracellular Bacterial Communities in Human Urinary Tract Infection, www.journals.plos.org/plosmedicine/ article?id=10.1371/journal.pmed.0040329
- 23 Intracellular Bacterial Communities: A Potential Etiology for Chronic Lower Urinary Tract Symptoms, www.ncbi.nlm.nih. gov/pmc/articles/PMC4617679/?fbclid=IwAR1bEw86dVbhFYIHREPhz6c1xrxSqDBWUgLuvV-HDjbF3Ez7gY8tWXvmMs
- 24 Bacterial Persister Cell Formation and Dormancy, www.ncbi.nlm.nih.gov/pmc/articles/PMC3837759
- 25 A Human Urothelial Microtissue Model Reveals Shared Colonization and Survival Strategies between Uropathogens and Commensals', www.science.org/doi/full/10.1126/sciadv.adi9834











- 26 The Clinical Implications of Bacterial Pathogenesis and Mucosal Immunity in Chronic Urinary Tract Infection, www.sciencedirect. com/science/article/pii/S1933021922017688
- 27 Bad Bugs and Beleaguered Bladders: Interplay between Uropathogenic Escherichia coli and Innate Host Defences, www.pubmed.ncbi.nlm.nih.gov/10922042
- 28 Bacterial Evasion Strategies, Urothelial Biology and New Treatments in Urinary Tract Infection, www.discovery.ucl.ac.uk/id/ eprint/10048425/1/PhD%20Thesis%20Corrected.pdf
- 29 How Chronic UTI forms, www.chronicutiaustralia.org.au/chronicuti/how-chronic-uti-forms
- 30 Cystitis Unmasked, Malone-Lee, J., (2021), tfm Publishing Limited, Shrewsbury, UK.
- 31 Uncomplicated urinary tract infection in women, BMJ 2021; 372 doi: www.doi.org/10.1136/bmj.n725, www.bmj.com/content/372/ bmj.n725
- 32 The Epidemiology of Urinary Tract Infection, www.pubmed.ncbi.nlm.nih.gov/21139641
- 33 Confronting the Urinalysis Tyrant, www.bjgplife.com/confronting-the-urinalysis-tyrant
- 34 Duration of Antibacterial Treatment for Uncomplicated Urinary Tract Infection in Women, www.pubmed.ncbi.nlm.nih.gov/15846726
- 35 <u>www.racgp.org.au/afp/2010/may/bacterial-cystitis-in-women/</u>
- 36 Recalcitrant Chronic Bladder Pain and Recurrent Cystitis but Negative Urinalysis: What Should We Do? www.link.springer.com/ article/10.1007/s00192-018-3569-7
- 37 Cross-over Data Supporting Long-term Antibiotic Treatment in Patients with Painful Lower Urinary Tract Symptoms, Pyuria and Negative Urinalysis, www.link.springer.com/article/10.1007/s00192-018-3846-5
- 38 Recalcitrant chronic bladder pain and recurrent cystitis but negative urinalysis: What should we do? 2018 www.link.springer.com/ article/10.1007/s00192-018-3569-7
- 39 Alternative to prophylactic antibiotics for the treatment of recurrent urinary tract infections in women: multicentre, open label, randomised, non-inferiority trial, 2022 www.ncbi.nlm.nih.gov/pmc/ articles/PMC8905684/
- 40 How Estrogen Fights Urinary Tract Infections, 2013 www. livescience.com/37563-uti-estrogen-menopause.html
- 41 D-mannose vs other agents for recurrent urinary tract infection prevention in adult women: a systematic review and meta-analysis, 2020 www.ncbi.nlm.nih.gov/pmc/articles/PMC7395894
- 42 Hultgren Lab, drug and vaccine development, www.hultgrenlab. wustl.edu/research/drug-and-vaccine-development/ (last accessed 25.02.2024)

- 43 www.bmj.com/content/372/bmj.n725
- 44 Uncomplicated urinary tract infection in women, 2021 www.research.bond.edu.au/files/70383621/AM_Uncomplicated_ <u>urinary_tract_infection_in_women.pdf</u>
- 45 Uncomplicated urinary tract infection in women. BMJ, 372, article n725. www.doi.org/10.1136/bmj.n725 www.research.bond.edu.au/ files/70383621/AM_Uncomplicated_urinary_tract_infection_in_ women.pdf
- 46 Novel antibiotic-loaded particles conferring eradication of deep tissue bacterial reservoirs for the treatment of chronic urinary tract infection, 2020 www.sciencedirect.com/science/article/abs/pii/ S0168365920304892?
- 47 Atocap UK, www.atocap.co.uk/ (last accessed 25.02.2024)
- 48 Dr. Abraham and Dr. Staats Receive R21 Grant for Novel UTI Vaccine Strategy, Duke University School of Medicine, Duke Pathology website, www.pathology.duke.edu/news/abraham-staats-r21grant-uti-vaccine (last accessed 25.02.2024); see also Duke University School of Medicine website www.medschool.duke.edu/ news/goodbye-utis-duke-scientists-develop-vaccine-strategyurinary-tract-infections-0
- 49 Bacteriophages of the lower urinary tract, 2019 www.nature.com/articles/s41585-019-0192-4?
- 50 Recurrent Urinary Tract Infections in Women: How Promising is the Use of Probiotics? 2017 www.sciencedirect.com/science/article/ pii/S0255085720303315
- 51 The development of probiotics for women's health, 2016 www.cdnsciencepub.com/doi/10.1139/cjm-2016-0733
- 52 Hultgren Lab, drug and vaccine development, www.hultgrenlab. wustl.edu/research/drug-and-vaccine-development/ (last accessed 25 02 2024)









