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URINARY TRACT INFECTIONS (UTIS) (DIAGNOSIS, TREATMENT AND MANAGING RECURRENT UTIS)

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- Nothing to disclose

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- Nothing to disclose

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CLINICAL DISCLOSURE – OUTDATED IDSA GUIDELINES

Uncomplicated Cystitis and Pyelonephritis (UTI) (Archived)

Published CID, 3/1/2011

Clinical Infectious Diseases, Volume 52, Issue 5, 1 March 2011, Pages e103–e120, https://doi.org/10.1093/cid/ciq257
Published:01 March 2011

This guideline is currently being updated.

Uncomplicated cystitis and Pyelonephritis (UTI). Uncomplicated Cystitis and Pyelonephritis (UTI). (n.d.). Retrieved from https://www.idsociety.org/practice-guideline/uncomplicated-cystitis-and-pyelonephritis-uti/

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THANK YOU

- Thank you, Dr. Lisa Speiser, and Dr. Robert Orenstein for sharing their slides some of which I utilized here.

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LEARNING OBJECTIVES

- **Review diagnosis of Urinary Tract Infection.**
- **Recurrent UTIs**
- **Therapy options**

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EPIDEMIOLOGY- SOME NUMBERS

One of the most common bacterial illnesses

- Over 50% of women get UTI and it is recurrent in 30-44%
- 50% will have a 3rd episode if they had 2 episodes in the last 6 months
- Cause over 400,000 hospitalizations
- 40 % of hospital acquired infections
- 2nd most common indication for antibiotics prescribing – 15%
- Women have one in three lifetime chances of developing a UTI – that's 50 times more than for men
- Acquire resistant bacteria once treated and those can persist for up to 12 months

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ON THE OTHER HAND,

- Very frequently misdiagnosed and mistreated.
- Up to 50% of women with lower urinary tract “ symptoms” do not have UTIs.
- 15-30% of men and 25-50% of women have **asymptomatic bacteremia**

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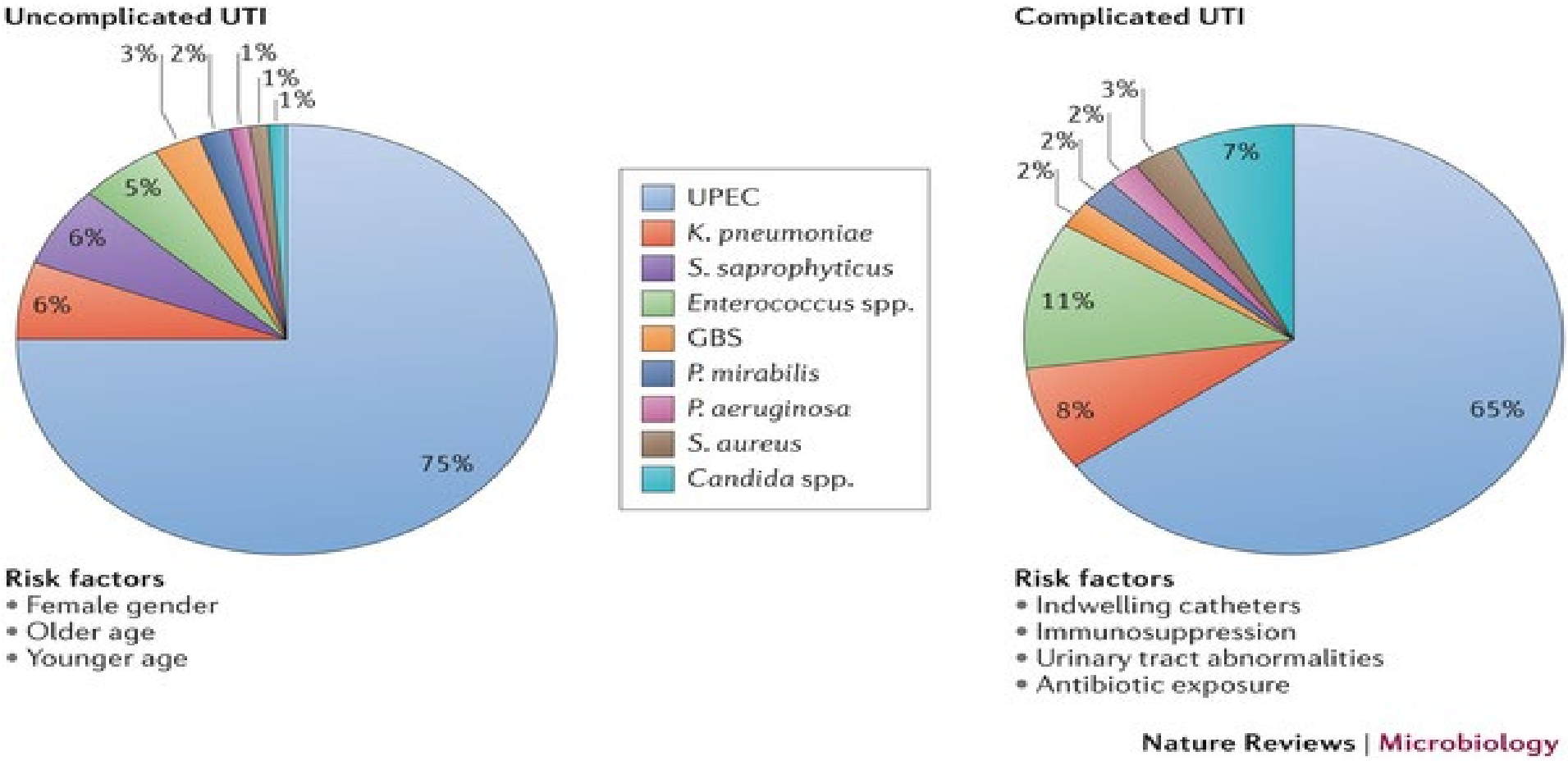
MICROBIOLOGY OF UTI



Nature Reviews Microbiology 13, 269-284 (2015)

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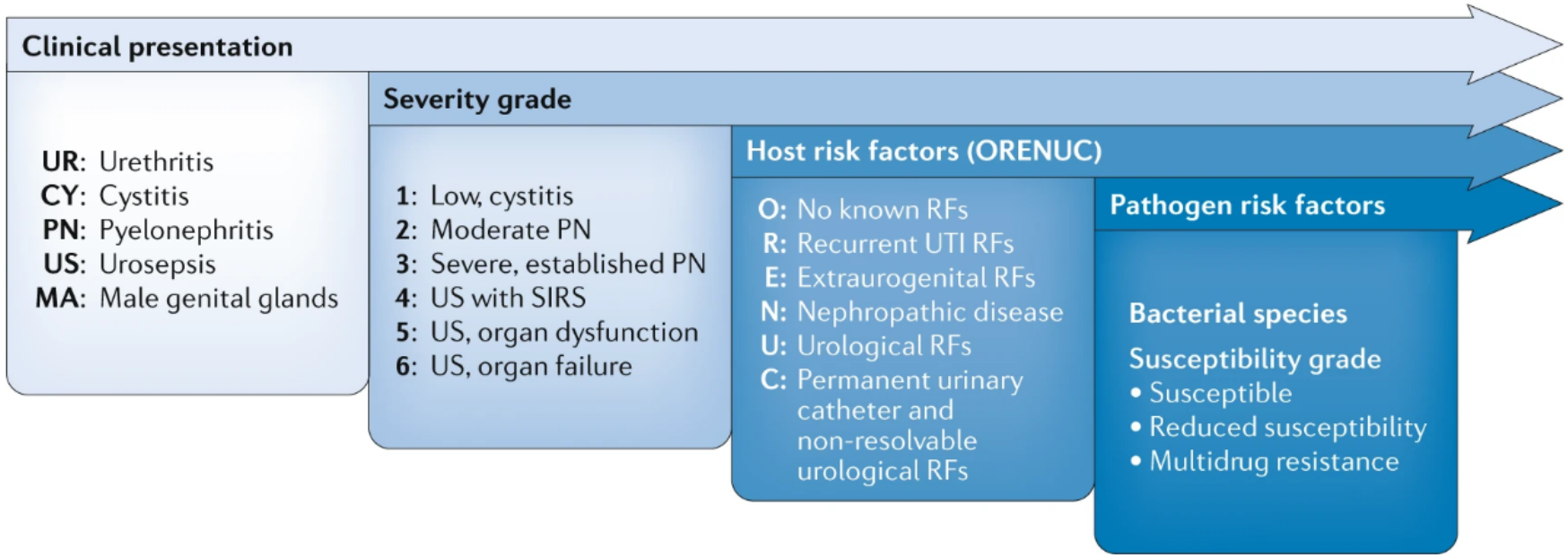
EUROPEAN SECTION OF INFECTIONS IN UROLOGY (ESIU) – CLASSIFICATION OF UTI

Fig. 2: The European Section of Infections in Urology classification of UTIs.

From: Epidemiology, definition and treatment of complicated urinary tract infections



The classification and severity assessment[27] involves evaluation of the clinical presentations (that is, identifying the focus of infection), grading the severity of the infection (which is related to both location of the infection, symptom severity and severity of functional impairment), and identification of host and pathogen risk factors (RFs). SIRS, systemic inflammatory response syndrome. Reprinted with permission from ref.[27], European Association of Urology.

Wagenlehner, F.M.E., Bjerklund Johansen, T.E., Cai, T. *et al.* Epidemiology, definition and treatment of complicated urinary tract infections. *Nat Rev Urol* **17**, 586–600 (2020). https://doi.org/10.1038/s41585-020-0362-4

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UTI – SYMPTOMS

Diagnosis primarily via urine analysis and culture

Acute simple cystitis	Upper urinary tract infection/pyelonephritis
Dysuria, frequency, urgency,	Fever
Frequency	Back pain
Urgency	Nausea/vomiting
Suprapubic pain	Abdominal pain
-+ hematuria	+- cystitis

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RECURRENT UTIS

- Occur in at least 20% of women with uncomplicated UTI
- 2 or > episodes in 6 months or 3 or > in a year
- Relapse:
  - If current infection is caused by same pathogen as the initial UTI and occurs within 2 weeks of completion of treatment for the original infection
- Re-infection:
  - more than 2 weeks after treatment, even if the uropathogen is the same as the original
  - If current infection is caused by a different strain than initial UTI

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RECURRENT UTIS

- If the initial urine culture is suspected to be a contamination, then you must repeat or collect via urine catheterization.
- Suspect contamination when you see:

1. Epithelia cells
2. Mucus
3. Mixed bacterial and fungal culture results

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RECURRENT UTI: RISK FACTORS

- Spermicidal products
- Sexual activity
- Urologic factors
  - Urinary incontinence
  - Presence of cystocele
  - Post-voiding residual urine
- Genetic factors
  - Increased susceptibility to vaginal colonization with uropathogens

BMJ 2013;346:f3140

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IS IT RECURRENT UTI

UTI likely

- Women with symptoms and consistent urine analysis and cultures
- Women with signs and symptoms with variable culture results

Another issue?

- Women with symptoms, pyuria, hematuria with negative cultures
- Women with signs and symptoms and normal urine
- Women with persistent symptoms after therapy for UTI with negative cultures

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APPROACH TO PATIENTS WITH “ RECURRENT UTIS”

- Are they symptomatic or this is based on positive surveillance culture?
- If true recurrence, were they treated with proper drug, dosage and duration?
- Could it be noninfectious complaint?

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OTHER LUTS CAUSING CONDITIONS

- Noninfectious interstitial cystitis
- Bladder malignancy
- Urethral strictures
- Sexually transmitted infections (STIs)
- Bacterial Vaginosis
- Neurological dysfunction//abnormalities
- Atrophic vaginitis
- Foreign body

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WORK UP/ QUESTIONS, EXAM AND MORE

- Complete history
  - Bowel issues, prior abdominal and pelvis surgeries
  - Sexual activity
  - Other gynecological issues
  - Use of contraception and what type?
  - Drug allergies – antibiotics

- Physical and pelvic exam

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RED FLAGS IN RECURRENT UTIS

- Hematuria – especially persistent
- Persistent pain
- GU system stones
- Pelvic radiation
- Anatomic abnormalities like fistulas
- Pelvic malignancies
- Spinal cord/neurological illnesses
- Obstructive symptoms
- Immunosuppression

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IMAGING IN RECURRENT UTI

- No need for **routine** cystoscopy and upper tract imaging, reserve for red flagged patients, failure to improve or suspected malignancy in which cystoscopy can be diagnostic.
- Imaging (ultrasound) when you suspect obstruction.
- Remember fever takes a while to resolve in pyelonephritis. Imaging only if fever fails to resolve after 72 hours of “ appropriate” antibiotic therapy.
- I would have low threshold for imaging in pyelonephritis in diabetic patients at risk for complicated infections.

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WHO EARNS THE LABEL “ COMPLICATED”?

Complicated UTIs
Male sex
Uncontrolled Diabetes Mellitus
Immunocompromised patients
Structurally or functionally abnormal urinary tract
Hospital acquired infections
Presence of indwelling catheters
Pregnancy

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MANAGEMENT OF RECURRENT UTI

- Obtain urine analysis and culture **for each symptomatic episode** before starting antibiotics. Self-starting therapy can be reasonable for some.

- You may start with non antibiotics approaches:
  - Follow alone
  - Increase hydration
  - Pyridium
- **20-47% of young women will have their symptoms resolve**

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ASYMPTOMATIC BACTERURIA

- Do not routinely perform surveillance.
- We do not treat ASB (very few exceptions)

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ANTIBIOTICS

- Know your local antibiograms
- Usual reasonable first lines: Nitrofurantoin (only for lower tract), Fosfomycin, TMP-SMX.
- **As short of a course as possible** (no more than 7days, 5 days even better)
- MDRO and no oral options, use IV, but can also do short , less than 7 days

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TO IDENTIFY WHY

- Avoid repeated antibiotics without getting new cultures
- Repeat urine testing is key
- More expanded work up for:

1. Complicated
2. Uncomplicated with atypical features
3. Non-responders
4. Red flags

- Try both: antibiotics and non antibiotics measures (many products)

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THE DO'S AND DON'TS

DO	DON'T	Consider
History, exam, pelvic exam	Routine cystoscopy or upper tract imaging	
Check and document all positive cultures		Some patients may benefit for empiric therapy
Use first line antibiotics		Consider short course of cultures directed IV therapy for MDRO's with no oral options
Short courses	Treat asymptomatic bacteruria	
Repeat urine culture only if symptoms persist after therapy	Perform post treatment test of cure if no symptoms	Antibiotics prophylaxis for some after risk vs benefit discussion
Vaginal estrogen		

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PREVENTION

- Hydration , more than 1.5 liters per day
- Reduce vaginal colonization: no spermicides, replete vaginal estrogen, oral and vaginal probiotics
- Prevent pathogen entry to bladder (evaluate any catheter, do you need one?, use intermittent cath instead)
- Correct local functional or structural dysfunction
- Void after sex
- No spermicides
- Methenamine (to be discussed)

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ANTIBIOTICS PROPHYLAXIS

- They help if right indication (7x less likely to get UTI)
- Continuous low dose or post coital (in appropriate cases)
- Effect subsides when stopped
- Always review risks vs. benefits vs. alternatives
- Offer in 3-6 months increments , always assess to stop
- No benefits of rotation of agents
- If develop UTI on prophylaxis: check urine culture, consider a change or methenamine

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ANTIBIOTICS FOR PROPHYLAXIS

- Nitrofurantoin – 50-100 mg/d
  - Avoid w/ CrCl<45
  - Check CBC, BMP and LFTs q3-6 bmo
  - Counsel re: lung fibrosis and hepatic fibrosis, neuropathy
  - If develop resistance – stop
- Trimethoprim 100 mg qhs
  - Avoid CrCl<15; be aware of TMP impact on K
- Fosfomycin 3 g q10 days
- Cephalexin 125 mg/d
- Cefaclor 250 mg/d

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NON-ANTIBIOTICS FOR PROPHYLAXIS

- Cranberry tablets or juice
- Oral or vaginal probiotics
- Increase Water intake
- D-Mannose
- Methenamine

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METHENAMINE (CAN BE USED INSTEAD)

- The ALTAR trial
- Randomized open label, non inferiority trial
- Eight centers in the UK, recruiting from June 2016 to June 2018
- Random assignment (1:1) to receive antibiotic prophylaxis or methenamine hippurate for 12 months. Treatment allocation was not masked and crossover between arms was allowed
- Methenamine vs (Nitro/TMP/cephalexin)
- Non inferior and slight less resistance.

Harding, C., Mossop, H., Homer, T., Chadwick, T., King, W., Carnell, S., ... & Ali, A. (2022). Alternative to prophylactic antibiotics for the treatment of recurrent urinary tract infections in women: multicentre, open label, randomised, non-inferiority trial. *bmj*, *376*.

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ESTROGEN

- It reduces future risk for recurrent cystitis in peri and post-menopausal women
- Multiple formulations available

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RECURRENT UTI WITH COMPLICATING RISK FACTORS

- Sometimes they need initial broad-spectrum therapy if ill
- Obtaining urine cultures is even more crucial as high risk of resistance
- May need urological consultation

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PARENTERAL THERAPIES FOR MDRO CUTI

- **Few oral options for cystitis 2/2 MDRO**
- **ID consultation**
  - Ertapenem (ESBL)
  - Ceftazidime Avibactam (AmpC, ESBL, KPC, OXA48)
  - Ceftolozane-Tazobactam (Pseudomonas, ESBLS, KPC)
  - Imipenem-relebactam KPC
  - Meropenem Vaborbactam (KPC)
  - Cefiderocol, Aztreonam + Avycaz (MBL's)
  - Plazomicin (CBP-Resistant)
  - Cefiderocol (Acinetobacter inc OXA, MDR P aeruginosa)

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WRAP UP

- Urinary tract infections are very common
- Women are more affected
- Recurrent UTI vs. noninfectious LUTS constitute a big portion of why patients are seen in the ID clinic
- Infectious and noninfectious measures are crucial
- Obtaining good urine cultures is crucial especially for recurrent UTIs
- The rise of resistance is a significant concern
- Think the shortest course recommended when prescribing antibiotics
- Vaginal Estrogen is a big deal
- Utilize Methenamine

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THANK YOU

- Happy to answer questions