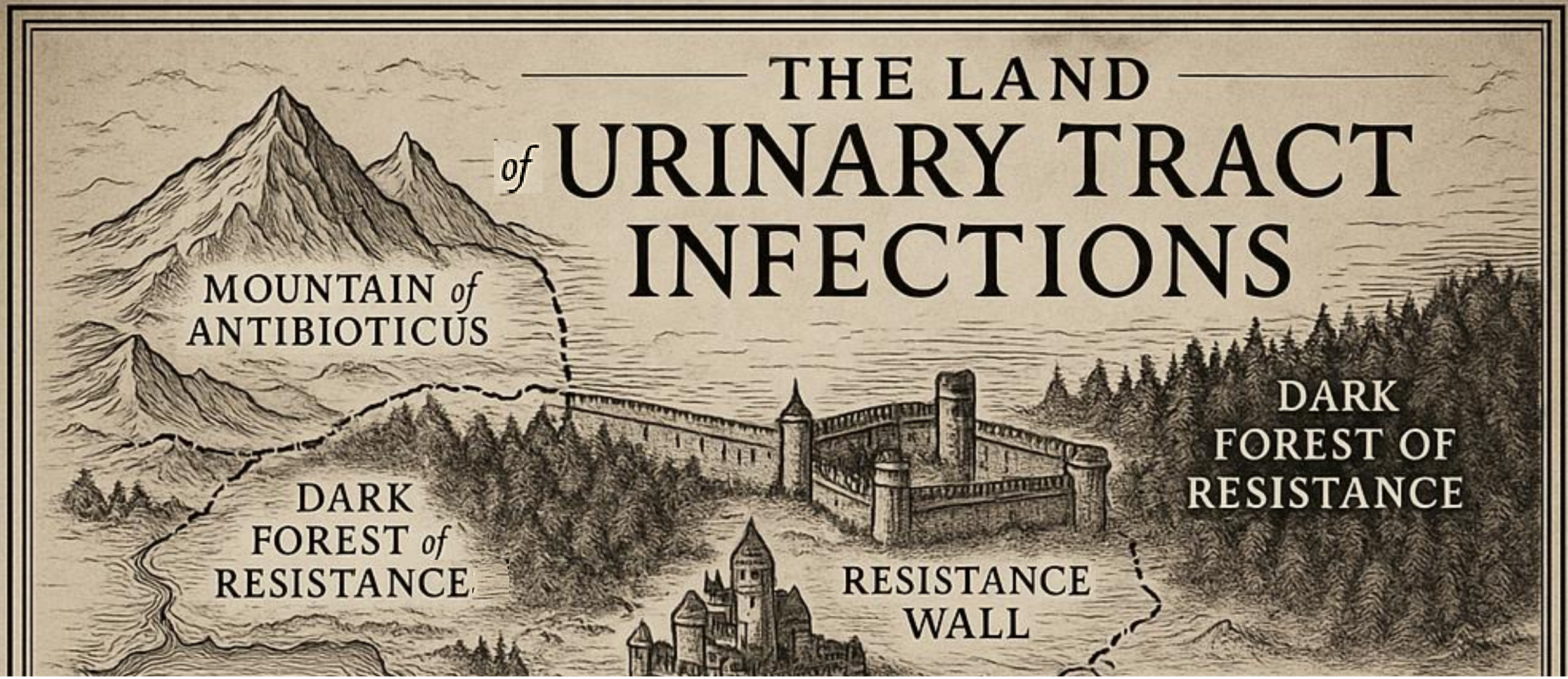

Dre Laura Cordes Lourenço
Médecin interne en recherche clinique
Service des maladies infectieuses
Séminaire des praticiens du 27.11.2025

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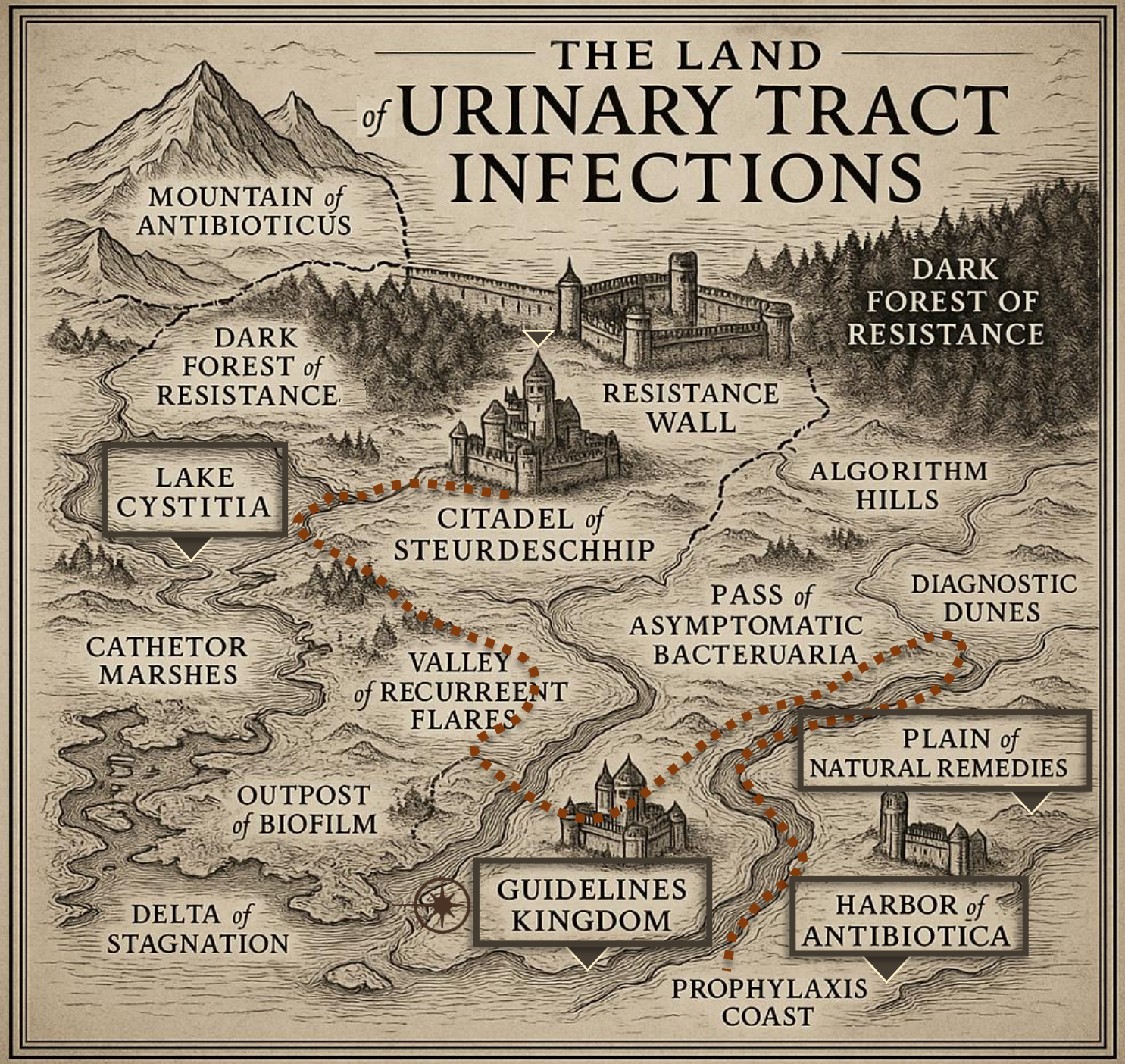
THE LAND
of URINARY TRACT INFECTIONS
MOUNTAIN of ANTIBIOTICUS
DARK FOREST of RESISTANCE
DARK FOREST OF RESISTANCE
RESISTANCE WALL
LAKE CYSTITIA
ALGORITHM HILLS
CITADEL of STEURDESCHHIP
PASS of ASYMPTOMATIC BACTERUARIA
DIAGNOSTIC DUNES
CATHETOR MARSHES
VALLEY of RECURREENT FLARES
PLAIN of NATURAL REMEDIES
OUTPOST of BIOFILM
GUIDELINES KINGDOM
HARBOR of ANTIBIOTICA
DELTA of STAGNATION
PROPHYLAXIS COAST

2025

IDSA

Old Classifications

Uncomplicated UTI: Acute cystitis in afebrile nonpregnant premenopausal women with no diabetes and no urologic abnormalities

Acute Pyelonephritis: Acute kidney infection in women otherwise meeting the definition of uncomplicated UTI above

Complicated UTI: All other UTIs

New Classifications

Uncomplicated UTI: Infection confined to the bladder in afebrile women or men

Complicated UTI: infection beyond the bladder in women or men

- Pyelonephritis
- Febrile or bacteremic UTI
- Catheter-associated (CAUTI)
- Prostatitis* (*not covered by these guidelines)

This simplified definition no longer considers
gender, comorbidities or pregnancy as determining factors

Infectious Diseases Society of America. Complicated Urinary Tract Infections (cUTI): Clinical Guidelines for Treatment and Management. July 17, 2025. Accessed July 21, 2025.

IDSA

Communicable
by CMI Communications

Ep. 38: The 2025 IDSA Complicated UTI Guidelines

2025

« Nothing really « new », aligns with clinical practice »

New Classifications

Complicated UTI: infection beyond the bladder in women or men

- Pyelonephritis
- Febrile or bacteremic UTI
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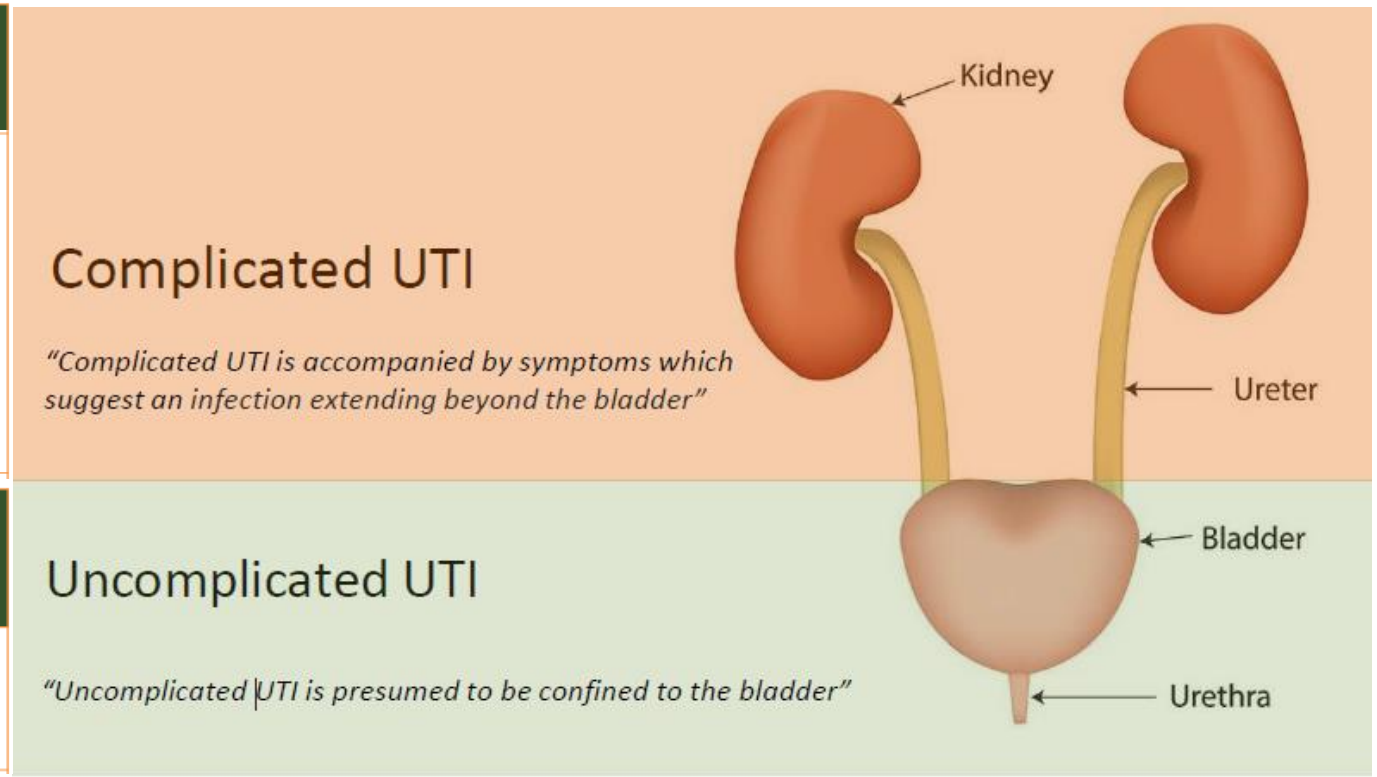
New Classifications

Uncomplicated UTI: Infection confined to the bladder in afebrile women or men



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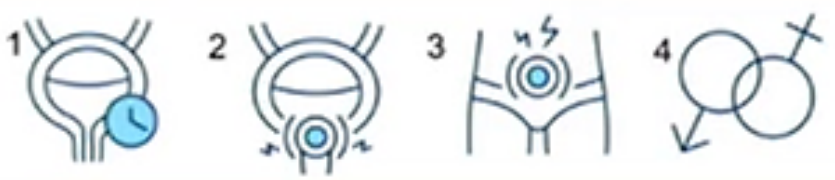
Infectious Diseases Society of America. Complicated Urinary Tract Infections (cUTI): Clinical Guidelines for Treatment and Management. July 17, 2025. Accessed July 21, 2025.

2025

- Localized infection →cystitis
- Inflammation of the bladder
- Does not elicit a systemic inflammatory respo
  – Fever and other systemic signs and symptoms are **absent**

- Classic symptoms:

1. Frequency (pollakurie)
2. Urgency (‘urgenturies’)
3. Suprapubic tenderness or pressure
   Dysuria (pain or burning on urination)
4. Applies to all sexes

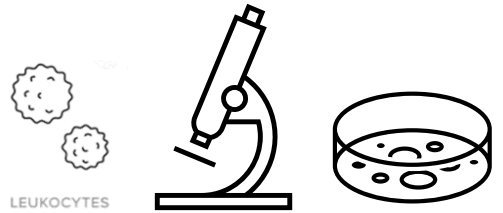


Risk factors may be present and should be addressed !

- Signs (not sensitive or specific)
  - Cloudy urine
  - Pink urine (hematuria)

- Pyuria (>10 WBC /hpf)
  and
- Bacteriuria (≥ 10^2 cfu/ml)

→are insufficient to diagnose UTI



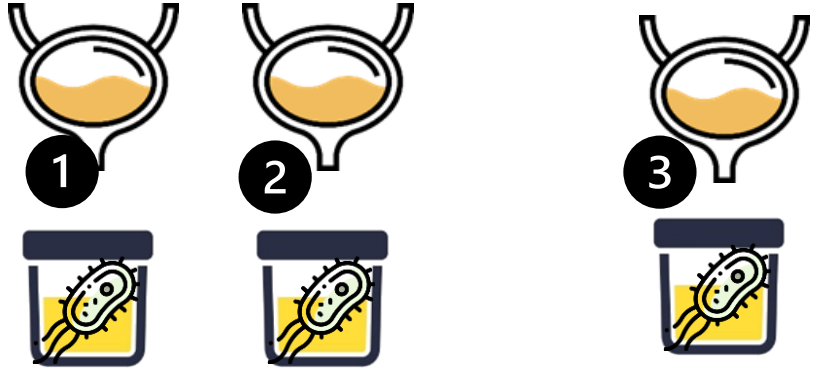
Huttner, Bielicki, Haidar. Chapter 36, Brenner & Rector’s THE KIDNEY,12th edition (in press)

ALL ARBITRARY DEFINITIONS !

Gupta et al 2017

Recurrent UTI (Gupta et al 2017)

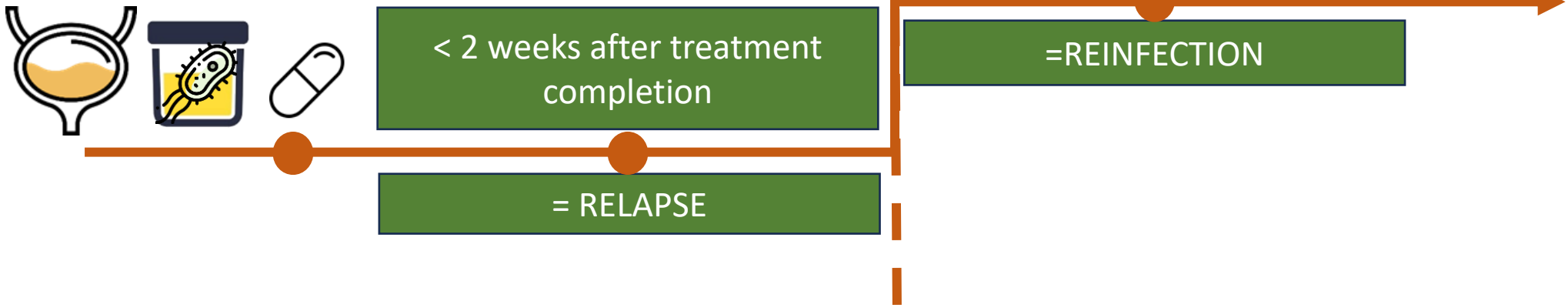
= Suspected or microbiologically confirmed UTI



≥2 times in 6 months

or ≥3 times in 12 months

If the recurrence occurs:



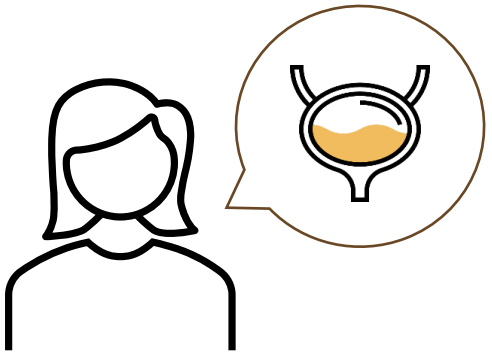
RISK FACTORS

THE HOST		
AGE/GENDER	**URINARY TRACT ABNOMALITIES**	**COMORBIDITIES**
Infants / Geriatric	Anatomic or functional abnormalities	Diabetes
Male Prostatic involvment	Post void residual volume	Neurological
Female Pregnancy	Vesicoureteral reflux	Immuno-compromised
BEHAVIOUR	Obstruction at any site of urinary tract	
Sexual intercourse Spermicide use	**Endogenous :** • Stones • Organ prolapsus	
	Exogenous: • Recent instrumentation • Indwelling catheters, stents • Foreign body	

*ESBL: extended-spectrum beta-lactamase

Raz R et al. Clin Infect Dis. 2000;30(1):152-156
Finer et al. Lancet Infect Dis. 2004;4(10):631-635

ONCE UPON A TIME AT THE UTI CLINIC



- 28-yo woman, no past medical history
- First job as teacher
- «My bladder is on fire, my dipstick is positive!»

- You need more history before making any decision
- You prescribe «pill-in-the-pocket» for her current symptoms
- You prescribe post-coital nitrofurantoin as prophylaxis
- You encourage her to seek psychotherapy (stress impacts the immune system)
- You prescribe ciprofloxacin for her current UTI
- Repeat urinalysis prior to treatment

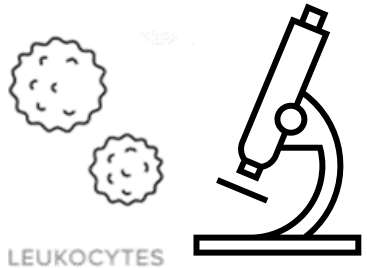
It always happens after sex!

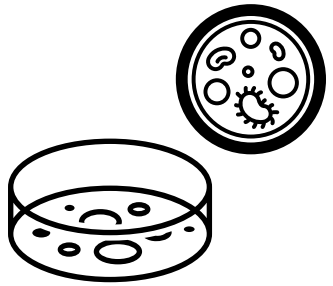
MESSAGE N°1: DIAGNOSIS IS CLINICAL !

Presence of new-onset frequency, dysuria, and urgency
in absence of vaginal discharge and pain

→positive predictive value (PPV) of 90%

Bent et al. JAMA. 2002;287(20):2701-2710
Nicolle. Urol Clin North Am. 2008;35(1):1-12





MESSAGE N°2:

Unless you suspect infection with a resistant bacterium and need pathogen identification with antibiogram

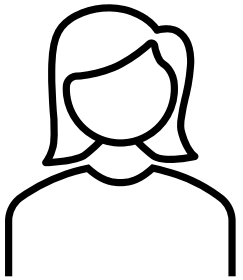
→**Empiric** therapy is given (don't do or wait for culture)…
It's *Escherichia coli* up to 85% of the time!

Urinalysis and culture are indicated
→Any recurrent UTI (resistant organisms?)
→Suspected upper UTI (pyelonephritis)

Culture is not necessary:
In the absence of symptoms/signs
After antimicrobial treatment for "control"

Huttner, Hasse, Galperine, Kronenberg. Swiss UTI guidelines (www.ssi.guidelines.ch) 2018-2024

Next Patient



- 55-yo woman with rheumatoid arthritis
- One UTI every few years since her 20s
- And now she has this, again! 3-4 in the past 6 months!!
- Each UTI treated with various antibiotics

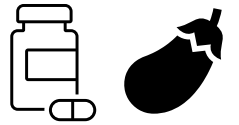
- You need more history before making any decision
- You prescribe nitrofurantoin for her current symptoms
- You prescribe daily nitrofurantoin as prophylaxis
- You refer her for a urologic work-up

She has been receiving upadacitinib (JKI) for 6 months

UTI is a side effect find the cause

Not every patient needs a urologic work-up right away

Start with the medication list (non-invasive)
Take a sexual history
Look for modifiable risk factors !



Autoimmune disorders, malignancies…
But also osteoporosis, asthma, hypercholesterolemia!

- Monoclonal antibodies, janus kinase inhibitors, etc.…
  - 100 mABs approved, 500 names assigned

- Other medications increasing risk for UTI:

Sodium-glucose-transport inhbitors (SGTI)
Antihistamines, anti-cholinergics, anti-psychotics
→Retention of urine

Identify modifiable risk factors for recurrence

EXAMPLES (NON EXHAUSTIVE)	WHY	STRATEGY
Limited mobility	suboptimal voiding/stasis	Not always possible! Urinating “twice in a row” (10-15 seconds in between)
Constipation Fecal incontinence		Regulate bowel movement
Daily activities (retention++)		Avoid urine retention
Menopause	Vaginal atrophy Reduced lactobacilli Higher pH	Moisturizer (Bepanthen unguent) Topical oestrogen cream
Stress	Probably downregulates mucosal immunity	Stress management

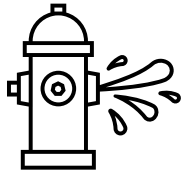
UTI is a side effect find the cause

Not every patient needs a urologic work-up right away

Start with the medication list (non-invasive)
Take a sexual history
Look for modifiable risk factors !

If non-contributory, proceed to urologic work-up

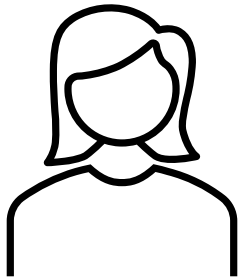
- Renal stones



- Urinary incontinence

- Urinary retention
  - Detrusor underactivity
  - Bladder outlet obstruction
    (urethral sphincter hyperactivity)
  - Etc.

Her last antibiogram in her pocket!



	Escherichia coli	*Enterococcus faecium*
amoxicilline	R	R
amoxicilline-clavulanate	R	R
cefuroxime	R	R
ceftriaxone	R	R
vancomycine	R	S
imipénème	S	R
ertapénème	S	R
norfloxacine	R	R
ciprofloxacine	R	R
co-trimoxazole	R	R
nitrofurantoïne	R	R
fosfomycine	R	R

- She’s looking at you expectantly.
- You:

a. Repeat the urine culture and ask her to come back in 2 days

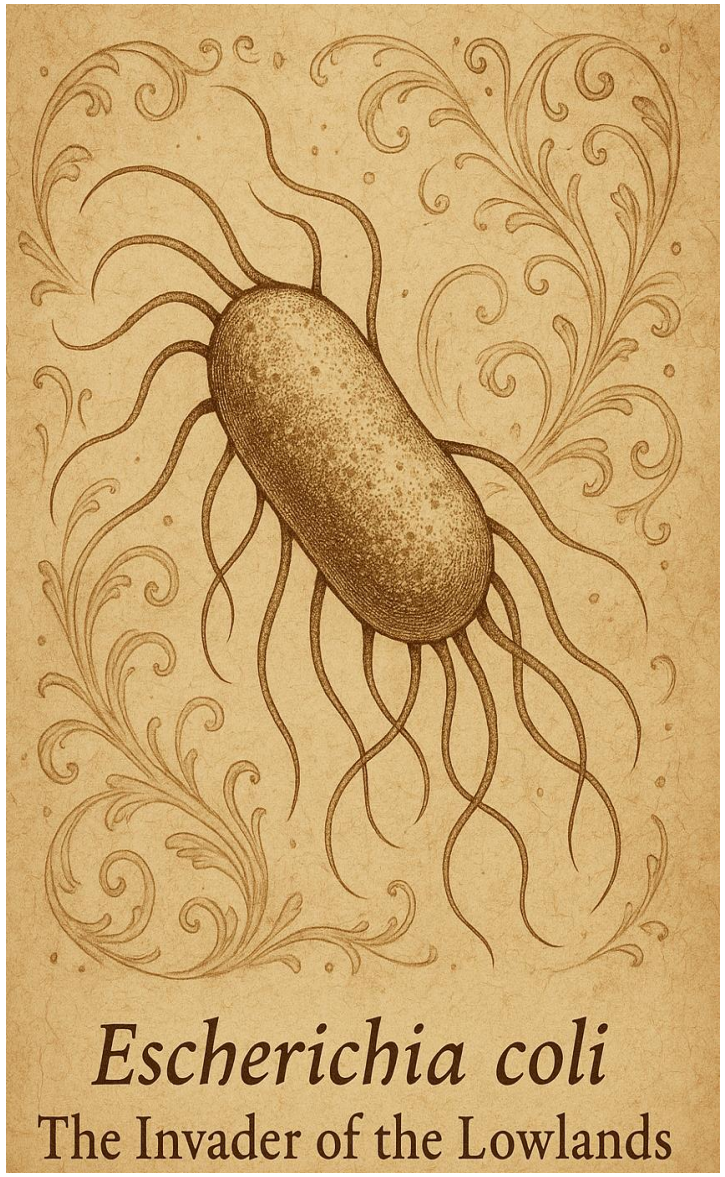
b. Organize at home i.v. vancomycin and ertapenem therapy

c. Organize at home i.v. ertapenem therapy 

d. Prescribe symptomatic therapy with ibuprofen 

e. Call the infectious disease specialist 

There can be more than one right answer!



Classic uropathogen list:

✓ Escherichia coli

✓ Klebsiella spp.

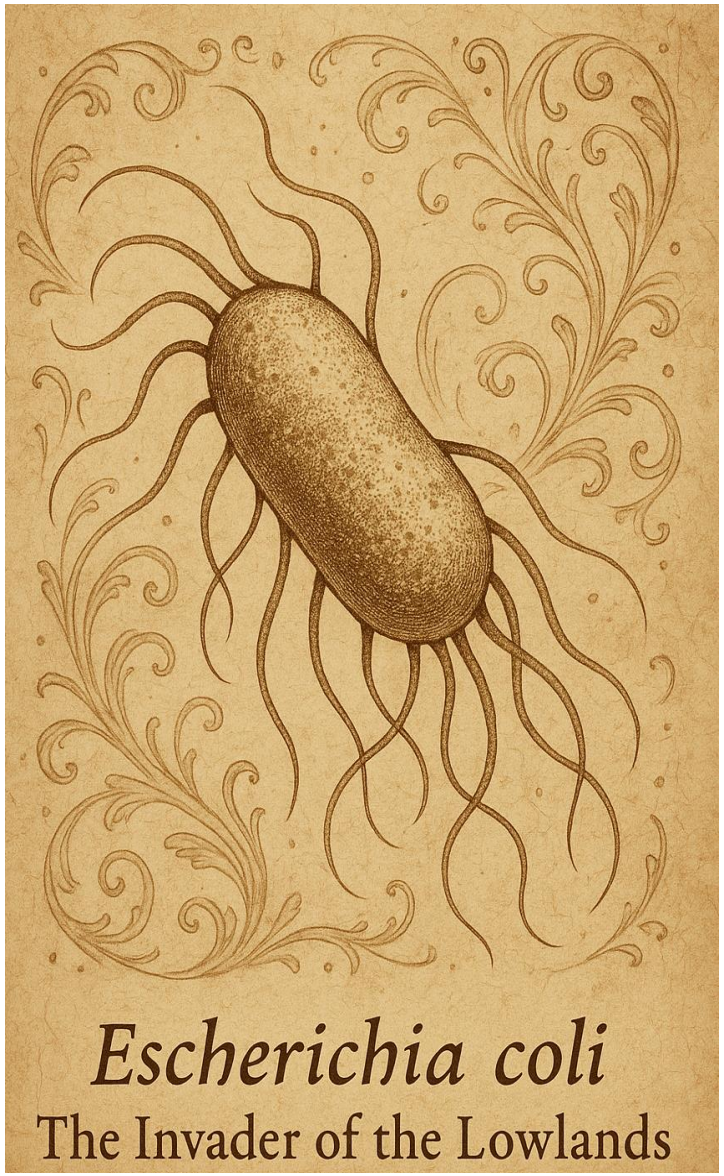
? Enterococcus spp.

✓ *Proteus* spp.

✓ Enterobacter spp.

? Staphylococcus saprophyticus

Escherichia coli is still the main culprit in UTI (85% of cases)



- Most *E. coli* is not pathogenic but beneficial!
  - ~200 serotypes, only about **30** are **uropathogenic**
  - **Flagellae** give it an advantage for mobility
  - **Pili** allow it to adhere to uroepithelial cells

Some strains can form intracellular bacterial communities (IBC)

- Usually clonal
- Biofilm-*like*
- Act as a reservoir
- Avoid immune clearance and resist antibiotic therapy
- Presence of IBC increases the odds of recurrent UTI by 3.3 (95%CI 1.3–9)

Battistuzzi et al. BMC Evol Biol 2004;4:44;
Lukjancenko O et al. Microb Ecol 2010;60(4):708-20;
Mulvey MA, et al. Infect Immun. 2001; 69:4572–4579.

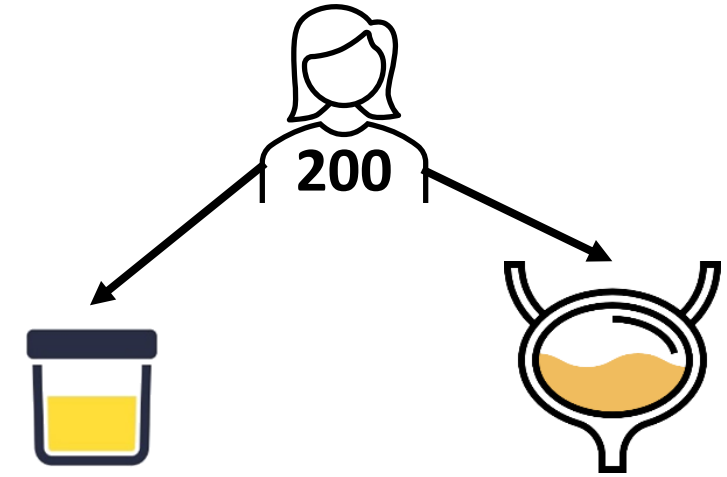
One single-center study to change our minds

Voided Midstream Urine Culture and Acute Cystitis in Premenopausal Women

Thomas M. Hooton, M.D., Pacita L. Roberts, M.S., Marsha E. Cox, B.S., and Ann E. Stapleton, M.D.

N= 200 women with uncomplicated acute UTI

2 cultures collected:



Midstream urine culture

Culture by catheterization ("straight cath")

Which organisms were really in the bladder?
Which were likely contaminants along the way?

Hooton et al. N Engl J Med 2013;369:1883-91

One single-center study to change our minds

Voided Midstream Urine Culture and Acute Cystitis in Premenopausal Women

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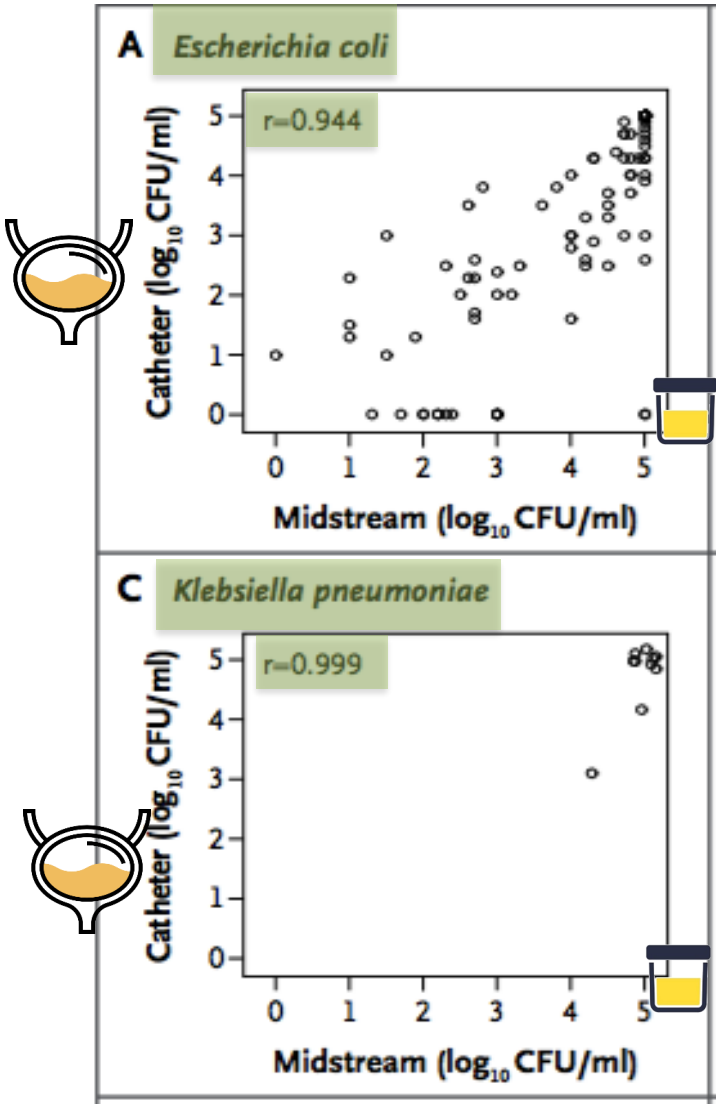


Often a contaminant

Enterococcus!

…but Enterococcus can still be *occasionally* pathogenic (foreign-body material)

MESSAGE 3:
What happens in a culture may not always be relevant *in vivo!*

Hooton et al. N Engl J Med 2013;369:1883-91

UP TO DATE ANTIBIOTIC STRATEGIES

	DAYS	1	2	3	4	5
SSI 2019		**Delayed prescription «PILL IN THE POCKET»**				
		Nitrofurantoin 100 mg 3x/j *				
		TMP-SMX 960 mg 2x/j				
USA/EU 2025		**Delayed prescription «PILL IN THE POCKET»**				
		Nitrofurantoin 100 mg 3x/j				

SSI: Société Suisse d'Infectiologie
TMP-SMX: co-trimoxazole

Huttner et al., JAMA 2018 doi:10.1001/jama.2018.3627
Martischang et al., PLoS One 2021 https://doi.org/10.1371/journal.pone.0256464

JAMA | Original Investigation

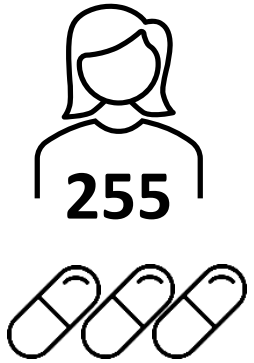
Effect of 5-Day Nitrofurantoin vs Single-Dose Fosfomycin on Clinical Resolution of Uncomplicated Lower Urinary Tract Infection in Women

A Randomized Clinical Trial

Nitrofurantoin vs fosfomycin

for lower urinary tract infection

RCT, open label, analyst blinded, multicenter, 2018
N = 513 non pregnant women with symptomatic UTI and positive dipstick (leuco and nitrites +) median age 44 years [IQR 31-64]



Nitrofurantoin
100 mg TID 5 days

VS

Fosfomycin
3g QD

Clinical and microbiological response at 28 days

CLINICAL SUCCESS	**70% (171/244)**	**58%** (139/241)
MICROBIO SUCCESS	74% (129/175)	63% (103/163)

Significantly greater likelihood of clinical and microbiologic resolution at 28 days after therapy completion.

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Huttner et al., JAMA 2018 doi:10.1001/jama.2018.3627

MESSAGE N°7
Ntrofurantoin is infinitely non-inferior

- *E. coli* does not easily become resistant to this drug

<1% resistance in Swiss strains (ANRESIS.CH)

- Collateral damage (resistance selection)

→appears **minimal**

- Serious toxicity (pulmonary >hepatic fibrosis)

→ **rare (1/100'000 50 cases in litterature)**

  - Occurs exclusively with long-term (prophylactic) nitrofurantoin
  - Is reversible if recognized quickly
  - Patient education

Willmann et al., BMC Biology 2019 https://doi.org/10.1186/s12915-019-0692-y
Stewardson et al, CMI 2018 https://doi.org/10.1016/j.cmi.2017.12.026

MESSAGE N°8

Ciprofloxacin and co-trimoxazole should be reserved (when possible) for upper UTI

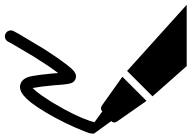
- Ciprofloxacin and co-trimoxazole: clinically superior
- Strong, rapid clinical response
- They penetrate renal tissue

• But *E. coli* and other uropathogens become quickly **resistant** (point-mutation)

• Collateral damage is **considerable**!

Willmann et al., BMC Biology 2019 https://doi.org/10.1186/s12915-019-0692-y
Stewardson et al, CMI 2018 https://doi.org/10.1016/j.cmi.2017.12.026

“DELAYED ANTIBIOTIC THERAPY” HOW DOES IT WORK?



“En reserve”

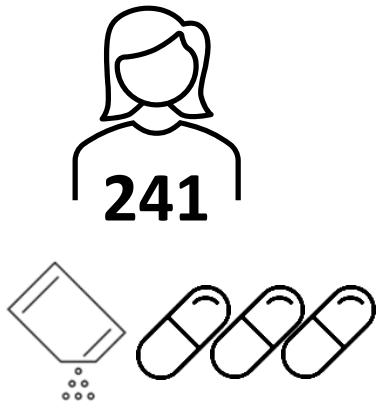
- Write a prescription for **5 days of nitrofurantoin 3x 100 mg** (first-line) in case of lower UTI symptoms
  - Second-line can be: fosfomycin 1x 3g po or 1x 3g /48h
- The patient keeps it ‘in her pocket’ and decides when she should take it
- Ask her to wait 2-3 days before taking the antibiotic if possible
- Encourage her to drink even more water at first symptoms and to take ibuprofen for symptomatic relief
- No need for repeat visits to the doctor, waiting for culture results, etc.
- Renewable !

Evidence for delayed antibiotic therapy

aka ‘Pill in the pocket’

Ibuprofen versus fosfomycin for uncomplicated urinary tract infection in women: randomised controlled trial

N= 494 women with uncomplicated UTI aged median age 36 (IQR 24-50)



VS

Ibuprofen
3x 400 mg daily for 3 days
+ 1 placebo sachet

Fosfomycin
Singe-dose 3g for 3 days
+ placebo tablets

- 67% of women recovered fully without antibiotics
- Symptoms lasted 1 day longer in the ibuprofen group

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Gagyor et al. BMJ 2015 ;351:h6544 doi: 10.1136/bmj.h6544

How many progressed to pyelonephritis ??

MESSAGE 5:

Patients with untreated cystitis progress to pyelonephritis only rarely:

Ibuprofen: 5/241 (2%)

Fosfomycin :1/243 (<1%)

Diclofenac: 6/133 (5%)

Gagyor et al. BMJ 2015 ;351:h6544 doi: 10.1136/bmj.h6544
Kronenberg et al, BMJ 2017;359:j4784 http://dx.doi.org/10.1136/bmj.j4784

Evidence for delayed antibiotic therapy

('Pill in the pocket')

Who should not try delayed antibiotic therapy?

- A patient with a history of pyelonephritis
- A deeply immunosuppressed patient (Including *poorly controlled* diabetes mellitus)
- A patient with symptoms for ≥5 days
- A patient who is not able to be a partner in her care
- Men
- Elderly women (?)

Huttner et al., JAMA 2018 doi:10.1001/jama.2018.3627
Martischang et al., PLoS One 2021 https://doi.org/10.1371/journal.pone.0256464

Nitrofurantoin prophylaxis options

100 mg 1x/j

Nitrofurantoin 100 mg po every evening is probably the best option

- Efficacy →well established in multiple RCT – 50% risk of UTI compared to placebo
- Ecologic impact → minimal
- Side effects→ gastro-intestinal (nausea)

Nitrofurantoin 50 mg daily is probably as good as 100 mg daily for recurrent UTI → as many UTI in both groups (15%) at 12 months from observational data

Nitrofurantoin 50mg is not available everywhere in CH → France

In sexually active women when UTIs follow sexual activity
→try post-coital antibiotic prophylaxis!
→ 1-2h after sex

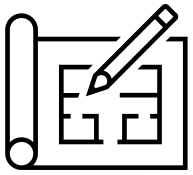
Huttner, Verhaegh, Harbarth et al. J Antimicrob Chemother 2015; 70:2456-64
Muller, Verhaegh, Harbarth et al. Clin Microbiol Infect 23 (2017); 355e362
Ten Doesschate et al, Clin Microbiol Infect 2022 https://doi.org/10.1016/j.cmi.2021.05.048

Nitrofurantoin prophylaxis

100 mg 1x/j

Breakthrough UTI can still happen (nobody is perfect)

- Not systematically a sign of resistance
- Apply “pill in the pocket strategy”
- Resume prophylaxis after UTI episode
- If fever→ seek medical advice
- If persistence of symptoms→ perform urinalysis



How long?

- Long term prophylaxis can mean anything from 3m to 5y
- Reevaluate every 3 months
- Plan to stop treatment – shared decision-making

Antibiotic sparing strategies

Dilution and flushing out bacteria

Target bacterial adhesion

Microbiota altering treatment

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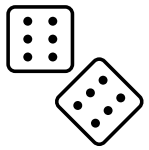
Write a prescription for water, too!

≥2.5L H20/j

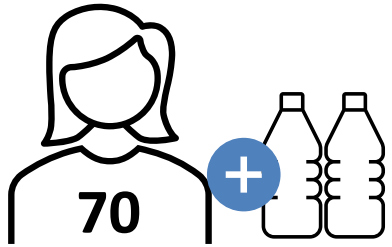
JAMA Internal Medicine | Original Investigation

Effect of Increased Daily Water Intake in Premenopausal Women With Recurrent Urinary Tract Infections

A Randomized Clinical Trial

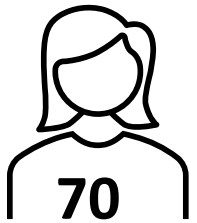


RCT, open-label, single center, 2018
N = 140 premenopausal with recurrent UTI, less than 1.5L intake
Follow-up 12 months



+1.5L extra/day

VS



No change in daily habits

- **Half as many UTIs in the water group**
  1.7 vs. 3.2 mean cystitis episodes, *P* < .001
- Half as many antibiotic days
- 1.9 vs. 3.6 antibiotic courses, *P* < .001

Increased water intake at first symptoms may help ‘clear’ infection (may!)

More data needed!

Hooton et al. *JAMA Intern Med*. 2018;178(11):1509-1515

Antibiotic sparing strategies

Target bacterial adhesion

- Cranberry is not better than placebo ?
- Rationale: proanthocyanidins; acidify urine and reduce bacterial adhesion/prevent fimbrial expression

- No evidence yet that cranberry juice resolves (or shortens) active UTI
  - Most research is on prevention
  - No data on duration, preparation and dose

EAU: although the efficacy of cranberry products is unclear, the panel consensus says:

«Clinicians may recommmend them for rUTI prevention in women who are informed of the weak evidence base due to their favorable benefit to harm ratio.»

Antibiotic sparing strategies

Target bacterial adhesion

D-mannose: monosaccharide isomer of glucose

Rational: mimics uroepithelial receptors to competitively bind to bacterial surface ligands

One large, well-designed, investigator-initiated placebo-controlled trial→**D-mannose had no effect on UTI recurrence**

Hôpitaux Universitaires Genève

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JAMA Internal Medicine RCT, double-blind, single center, 2024

RCT: D-Mannose for Prevention of Recurrent Urinary Tract Infection Among Women

POPULATION

598 Women

~600

Women ≥18 y with recurrent urinary tract infection (UTI)

Mean (range) age, 58 (18-93) y

INTERVENTION

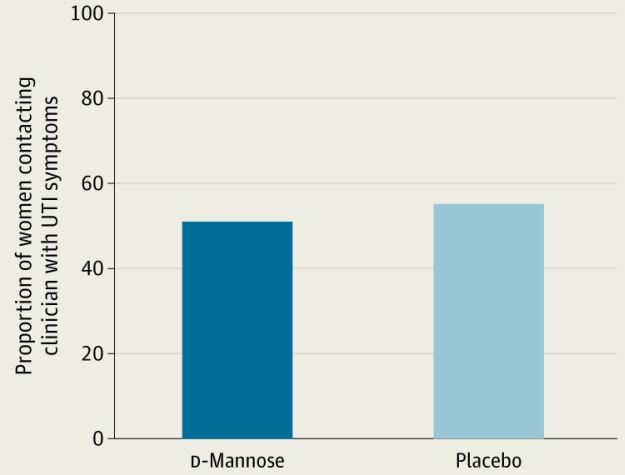
598 Individuals

303 D-Mannose prophylaxis
2 g Daily of D-mannose powder

295 Placebo prophylaxis
Daily similar-volume scoop of fructose powder

FINDINGS

The proportion of women contacting ambulatory care with a clinically suspected UTI was not statistically different between the 2 groups



D-Mannose prophylaxis: 150 of 294 women (51.0%)
Placebo prophylaxis: 161 of 289 women (55.7%)
Unadjusted risk difference, −5%; 95% CI, −13% to 3%; *P* = .26

SETTINGS / LOCATIONS

99 General practices in England and Wales

PRIMARY OUTCOME

Proportion of women contacting ambulatory care with a clinically suspected UTI within 6 mo of study entry

Recurrence: 55% of controls vs 51% with D-mannose

Hayward G, Mort S, Hay AD, et al. *JAMA Intern Med.* 2024;184(6):619–628

Antibiotic sparing strategies

Microbiota altering treatment

- Probiotics (*Lactobacillus spp*.)
- Rationale: vaginal flora regeneration to prevent cystitis. Lactobacilli release bactericidal peptides and hydrogen peroxide.

- Administration reduced UTI episodes
  Small investigator-initiated, randomized, placebo-controlled trial, oral and vaginal lactobacilli

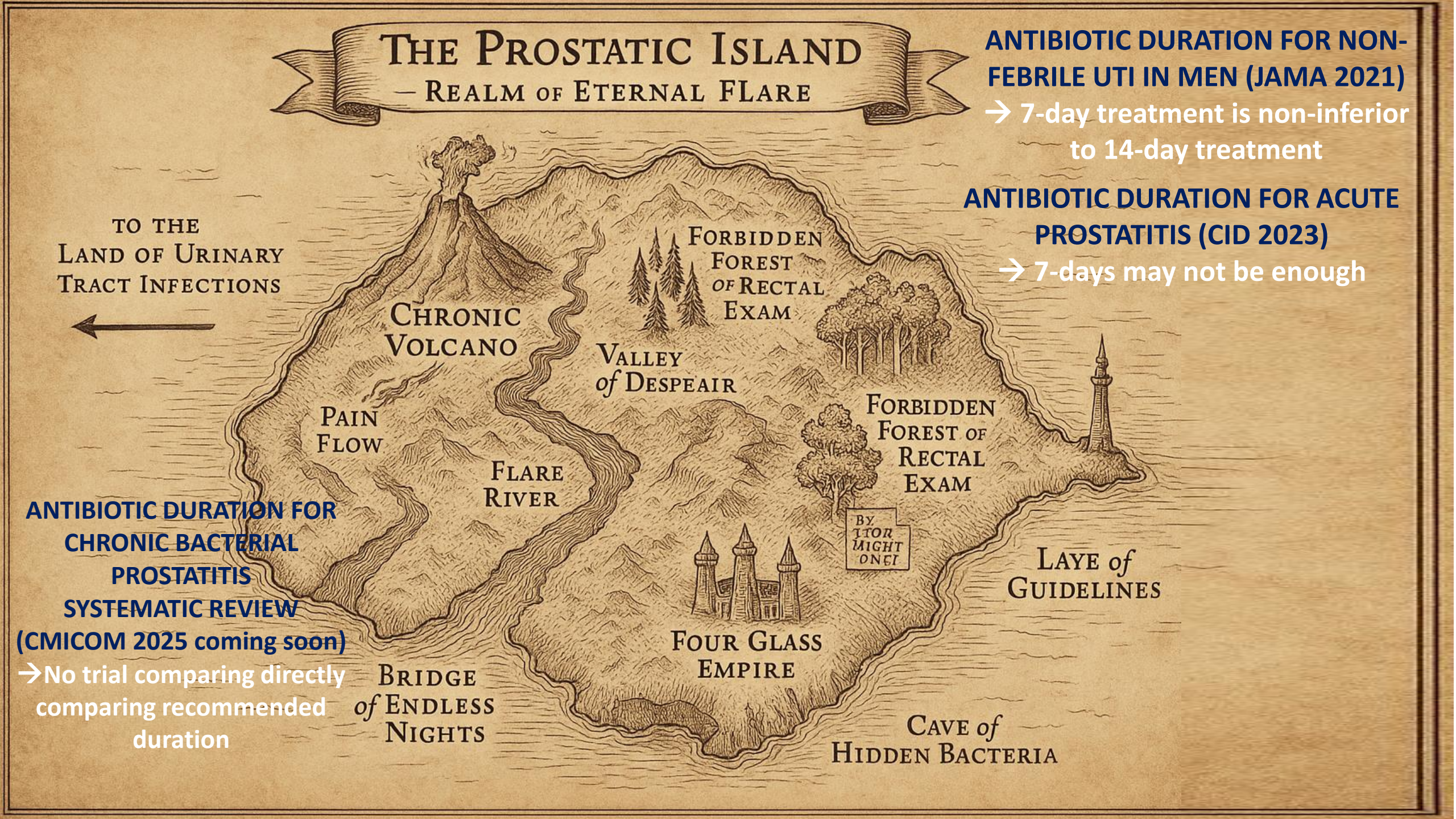
EAU 2025:
«The current evidence is insufficient and of too low quality to provide specific recommendation on the administration route, optimal dosage or duration»

Some thoughts

- UTI are incredibly complicated

- Heterogeneity of UTI population:
- Men, elderly, diabetic patients, immunocompromised patients, pregnant women, neurogenic bladder…

- Optimal management is not uniform across different patient groups
- Consensus based standard definitions



ANTIBIOTIC DURATION FOR NON-FEBRILE UTI IN MEN (JAMA 2021)

→ 7-day treatment is non-inferior to 14-day treatment

ANTIBIOTIC DURATION FOR ACUTE PROSTATITIS (CID 2023)

→ 7-days may not be enough

ANTIBIOTIC DURATION FOR CHRONIC BACTERIAL PROSTATITIS SYSTEMATIC REVIEW (CMICOM 2025 coming soon)

→No trial comparing directly comparing recommended duration

Key messages

And

Ressources

- Not every cystitis needs an antibiotic
- ‘Pill-in-the-pocket’ may work for recurrent cystitis
- Enterococci & Strep group B are rarely uropathogens
- Fosfomycin at a single-dose is inferior to other antibiotics
- Patient education is key !

Schweizerische Gesellschaft für Infektiologie
Swiss Society for Infectious Diseases
Société Suisse d'Infectiologie

IDSA

European Association of Urology

Firstline

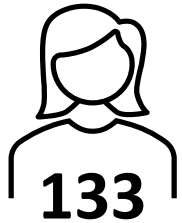
& Pre Angela Huttner

Evidence for delayed antibiotic therapy

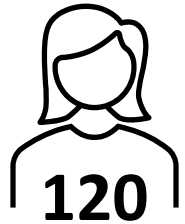
aka ‘Pill in the pocket’

Symptomatic treatment of uncomplicated lower urinary tract infections in the ambulatory setting: randomised, double blind trial

N= 253 with uncomplicated UTI, age 18-70yo, multicentric, 2017



VS



Diclofenac
3x 75 mg daily for 3 days

Norfloxacin
400 mg daily for 3 days

Median time until resolution	4 days	2 days

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Kronenberg et al, BMJ 2017;359:j4784 doi.org/10.1136/bmj.j4784