

FUNGAL URINARY TRACT INFECTION

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QUESTIONS

1. Is fungal urinary tract infection common in hospitalized patients?

2. What are the risk factors?

3. What is the treatment?

DEFINITION

- Funguria: The presence of fungus species in the urine.



PATHOGENESIS (1)

1 - CANDIDA SPECIES:

Table 1 <i>Candida</i> species causing candiduria and urinary tract infections	
Species	Comments
<i>Candida albicans</i>	<u>Most common</u> colonizing and infecting species (50%–70% in most series); most strains fluconazole susceptible
<i>Candida glabrata</i>	Second or third most common species (10%–35%, depends on geography); most common in older adults, uncommon in children; most strains fluconazole resistant
<i>Candida tropicalis</i>	Second or third most common species (10%–35%, depends on geography); most strains fluconazole susceptible
<i>Candida parapsilosis</i>	Uncommon in urine (1%–7%); common cause of central line-associated candidemia and neonatal candidiasis; most strains fluconazole susceptible
<i>Candida krusei</i>	Uncommon in urine (1%–2%); innately fluconazole resistant

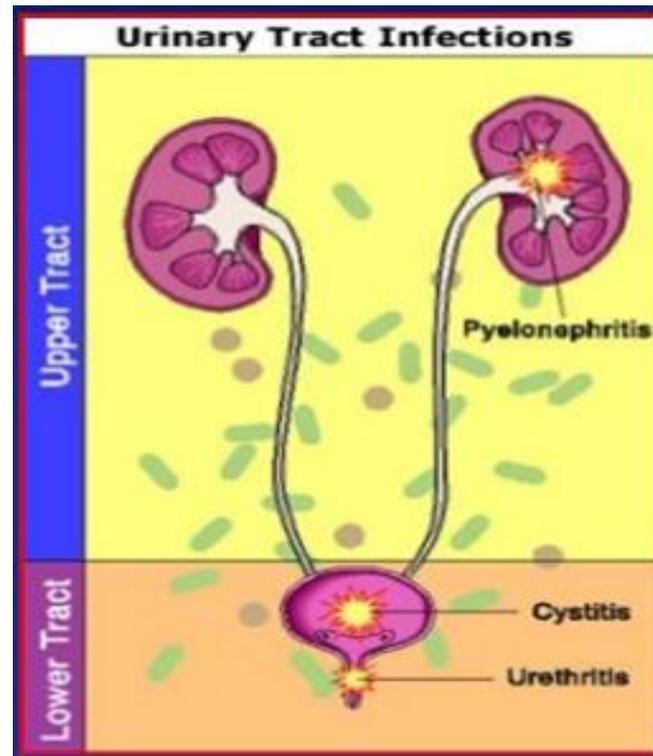
PATHOGENESIS (2)

2- NON CANDIDA FUNGAL INFECTION:

- *Aspergillus* species
- *Fusarium* species
- *Trichosporon* species
- Mucorales (eg, *Rhizopus*, *Mucor* species)
- Dematiaceous molds
- *Cryptococcus neoformans*
- Dimorphic fungi (eg, *Histoplasma capsulatum*, *Coccidioides* species, *Blastomyces dermatitidis*, *Paracoccidioides brasiliensis*, *Sporothrix schenckii*, and *Penicillium marneffeii*)

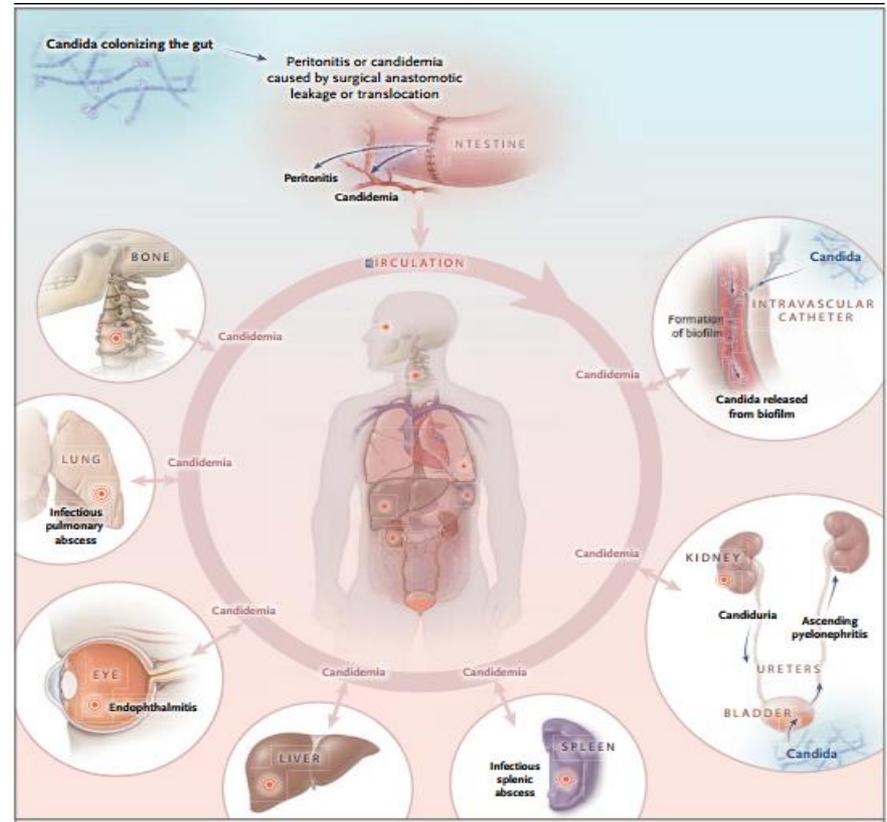
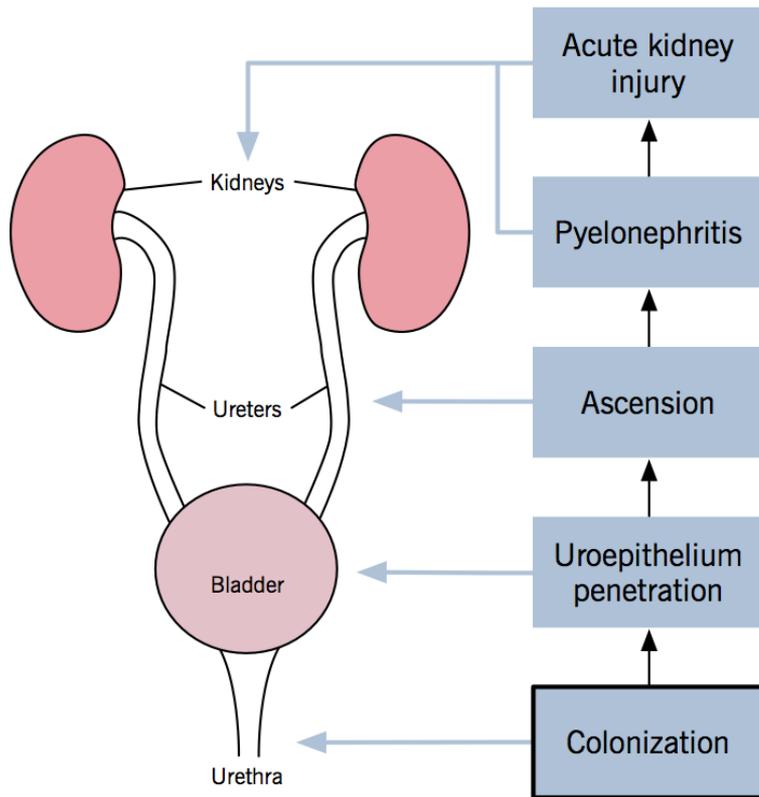
CLASSIFICATION

- Upper UTI fungal infection: pyelonephritis
- Lower UTI fungal infection: cystitis
- → Different treatment



PATHOPHYSIOLOGY

Pathogenesis of urinary tract infection



Ascend the urinary tract from a focus of candidal colonization at or near the urethra (retrograde infection)

Candida species enter the upper urinary tract from the bloodstream (antegrade infection)

FUNGUS BALL

- Patients with fungal tract infection can develop fungus balls that consist of masses of hyphae.
- Fungus balls can grow to a large size and lead to obstruction of the collecting system → surgical intervention or percutaneous drainage is required.

PREDISPOSING FACTORS

Table 1. Predisposing Factors for Candiduria and *Candida* Urinary Tract Infections

Diabetes mellitus	Renal transplantation
Extremes of age	Instrumentation of the urinary tract
Female sex	Concomitant bacteriuria
Prolonged hospitalization	Congenital abnormalities of the urinary tract
ICU admission	Structural abnormalities of the urinary tract
Broad-spectrum antibiotics	Indwelling urinary tract devices
Bladder dysfunction	Bladder stones
Urinary stasis	
Nephrolithiasis	

EPIDEMIOLOGY

- Common event in hospitalized patients.
- A European observational study: *Candida* was the third most common organism isolated from urine in hospitalized patients [1]
- Yeast-related UTIs:[2]
 - Healthy newborns: rare.
 - Neonatal, pediatric ICUs, premature infants: common

[1] Clin Microbiol Infect. 2001 Oct;7(10):523-31.

[2] Clinical Infectious Diseases 2011;52(S6):S433–S436

Table 2 Micro-organisms isolated in urine (>1%)

EU countries (n = 224)		Non-EU countries (n = 116)		Total (n = 340)	
<i>Escherichia coli</i> *	79 (35.3%)	<i>Escherichia coli</i> *	25 (21.6%)	<i>Escherichia coli</i>	104 (30.6%)
<i>Enterococcus sp.</i>	34 (15.2%)	<i>Pseudomonas aeruginosa</i> *	16 (13.8%)	<i>Enterococcus sp.</i>	48 (14.1%)
<i>Candida sp.</i>	29 (12.9%)	<i>Candida sp.</i>	15 (12.9%)	<i>Candida sp.</i>	44 (12.9%)
<i>Klebsiella sp.</i>	22 (9.8%)	<i>Enterococcus sp.</i>	14 (12.1%)	<i>Klebsiella sp.</i>	34 (10%)
<i>Proteus sp.</i>	15 (6.7%)	<i>Klebsiella sp.</i>	12 (10.3%)	<i>Pseudomonas aeruginosa</i>	28 (8.2%)
<i>Pseudomonas aeruginosa</i> *	12 (5.4%)	<i>Proteus sp.</i>	10 (8.6%)	<i>Proteus sp.</i>	25 (7.4%)
<i>Enterobacter sp.</i>	10 (4.5%)	<i>Staphylococcus aureus</i>	5 (4.3%)	<i>Enterobacter sp.</i>	14 (4.1%)
<i>Staphylococcus aureus</i>	7 (3.1%)	<i>Enterobacter sp.</i>	4 (3.4%)	<i>Staphylococcus aureus</i>	12 (3.5%)
<i>Citrobacter sp.</i>	6 (2.7%)	CNS	4 (3.4%)	CNS	7 (2.1%)
<i>Morganella sp.</i>	3 (1.3%)	<i>Acinetobacter sp.</i>	3 (2.6%)	<i>Citrobacter sp.</i>	9 (2.6%)
CNS	3 (1.3%)	<i>Citrobacter sp.</i>	3 (2.6%)		

* $P < 0.05$.

CNS, coagulase-negative staphylococci.

DIAGNOSIS

URINALYSIS -URINE CULTURE - MICROSCOPY

- Urinalysis and culture of urine: initial laboratory studies that should be performed.
- **NOT** provides much help in distinguishing colonization from infection.[1]
- The techniques routinely used in most clinical laboratories for the detection of bacteria will also detect yeasts in urine. The exception is *C. glabrata*.
- **Quantitation** has **not proved** useful in the diagnosis of Candida UTIs.[2]

[1] Infect Dis Clin N Am 28 (2014) 61–74.

[2]Clinical Infectious Diseases 2011;52(S6):S452–S456

IMAGES STUDY

Ultrasound

- Portability and safety → initial study
- Hydronephrosis
- Fungus balls

IVP (intravenous pyelogram) = UIV

- Hydronephrosis,
- A focal mass in the collecting system, or a
- Nonfunctioning kidney.

CT

MRI

DMSA



FIGURE 3. Intravenous urography: large filling defect of the renal pelvis due to partially radiolucent material.

TREATMENT – ASYMPTOMATIC CANDIDURIA

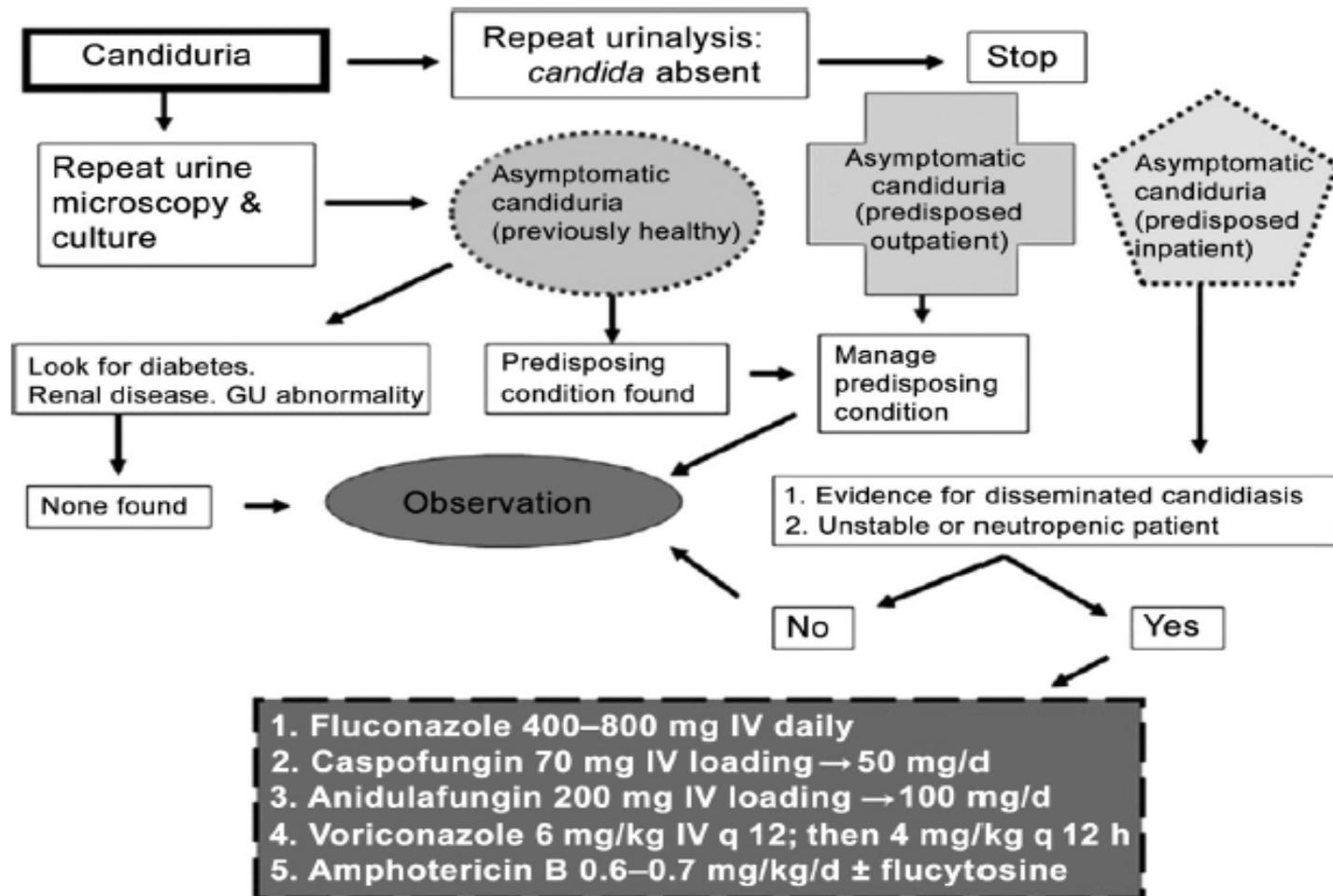


Fig. 1. Algorithm for the management of asymptomatic candiduria. IV, intravenous. (From Fisher JF, Sobel JD, Kauffman CA, et al. *Candida* urinary tract infections—treatment. Clin Infect Dis 2011;52(Suppl 6):S458; with permission.)

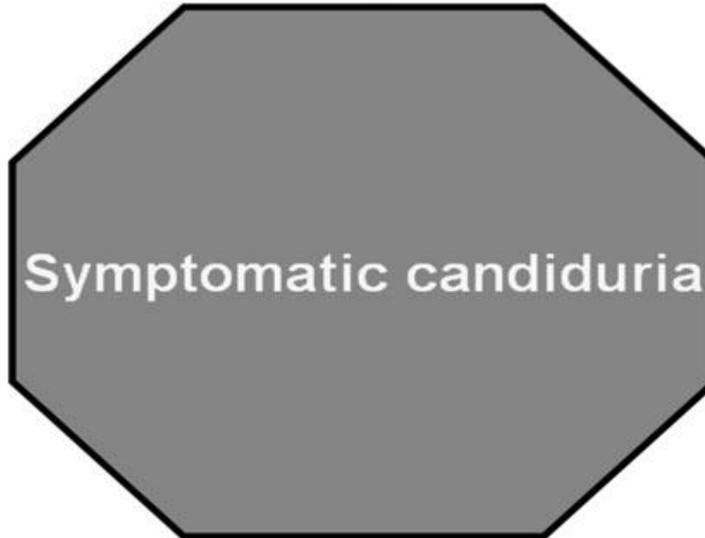
TREATMENT – SYMPTOMATIC CANDIDURIA

cystitis, pyelonephritis:

1. fluconazole 400mg po x 2-4 wks
2. flucytosine 25mg/kg po qid x 2-4 wks
3. AmB 0.3-1mg/kg iv 1 or more doses

prostatitis, epididymo-orchitis:

1. fluconazole 400mg po x 4 wks
2. surgical drainage



fungus ball:

1. fluconazole 400mg po x 4 wks
2. flucytosine 25mg/kg po qid x 2-4 wks
3. AmB 0.3-1mg/kg iv 1 or more doses
4. surgical drainage

Table 3

Treatment of *Candida* urinary tract infections, with dosages for adult patients with normal kidney function

Indication	First-Line Treatment	Alternative Options for Resistant <i>Candida</i> Species
Asymptomatic candiduria in very low birth weight neonates or neutropenic patients	Treat for disseminated candidiasis: fluconazole, 400 mg qd × 2 wk	AmB, 0.5–1.0 mg/kg/d × 2 wk
Asymptomatic candiduria in patient about to undergo urological procedure	Fluconazole, 200–400 mg qd periprocedure	AmB, 0.3–0.6 mg/kg/d periprocedure
Cystitis	Fluconazole, 200 mg qd × 2 wk	AmB, 0.3–0.6 mg/kg/d × 1–7 d; 5-FC, 25 mg/kg tid × 7–10 d
Pyelonephritis	Fluconazole, 200–400 mg qd × 2 wk	AmB, 0.5–0.7 mg/kg/d × 2 wk; 5-FC, 25 mg/kg tid × 2 wk; or both AmB and 5-FC × 2 wk
Renal infection—hematogenous spread	Treat for disseminated candidiasis: fluconazole, 400 mg qd × 2 wk	AmB, 0.5–1.0 mg/kg/d × 2 wk
Fungus ball (bladder, ureter, or kidney)	Fluconazole, 200–400 mg qd until resolved; surgical removal	Local instillation of AmB an effective adjunct

Abbreviations: 5-FC, flucytosine; AmB, amphotericin B deoxycholate; qd, every day; tid, 3 times a day.

Treatment – Non candida fungal urinary tract disease

Pathogens	Pathophysiology	Treatment	
Aspergillosis:	Genitourinary infections Prostatic infection	Amphotericin B (0.5–1 mg/kg/d) 3 months	–Drainage of abscesses –Nephrectomy
Cryptococcus	Disseminated disease.	Fluconazole (up to 600 mg/d).	
Blastomycosis	Epididymitis and prostatitis	IV amphotericin B with total dosage of 1 to 2 g	
Mucormycosis	Renal infection Systemic infection:	Amphotericin B therapy (>1 g total dose) Immunosuppression	Nephrectomy
Coccidiomycosis	Epididymis, testis, prostate, and kidney	IV amphotericin B total dose of 500–2500 mg).	Serologic antibody testing
Histoplasmosis	Disseminated disease (HIV/AIDS).	IV amphotericin B (>2000 mg total dose) + itraconazole (200 mg x 12 weeks)	

SUMMARY

- Funguria is common in hospitalized patients and is generally benign.
- Risk factors for candiduria include urinary tract drainage devices, prior antibiotic therapy, diabetes, urinary tract pathology, and malignancy
- Most patients with candiduria are asymptomatic, which rarely requires antifungal therapy.
- For symptomatic patients, fluconazole is the mainstay of therapy.



HAPPY NEW YEAR

REFERENCES

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2. Sobel JD, Fisher JF, Kauffman CA, et al. Candida urinary tract infections—epidemiology. *Clin Infect Dis* 2011;52(suppl 6):S433–6.
3. Fisher JF, Sobel JD, Kauffman CA, et al. Candida urinary tract infections—treatment. *Clin Infect Dis* 2011;52(supply 6):S457–66.
4. Kauffman CA. Diagnosis and management of fungal urinary tract infection. *Infect Dis Clin North Am* 2014; 28(1):61–74.
5. *N Engl J Med* 2015;373:1445-56.