Candida Urinary Tract Infections—Treatment

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In many instances a report from the clinical laboratory indicating candiduria represents colonization or procurement contamination of the specimen and not invasive candidiasis. Even if infection of the urinary tract by Candida species can be confirmed, antifungal therapy is not always warranted. Further investigation may reveal predisposing factors, which if corrected or treated, result in the resolution of the infection. For those with symptomatic urinary tract infections (UTIs), the choice of antifungal agent will depend upon the clinical status of the patient, the site of infection, and the pharmacokinetics and pharmacodynamics of the agent. Because of its safety, achievement of high concentrations in the urine, and availability in both an oral and intravenous formulation, fluconazole is preferred for the treatment of Candida UTIs. Flucytosine is concentrated in urine and has broad activity against Candida spp, but its use requires caution because of toxicity. Low-dose amphotericin B may be useful for Candida UTIs in selected patients. The role of echinocandins and azoles that do not achieve measurable concentrations in the urine is not clear. Small case series note some success, but failures have also occurred. Irrigation of the bladder with antifungal agents has limited utility. However, with fungus balls, irrigation of the renal pelvis through a nephrostomy tube can be useful in combination with systemic antifungal agents.

The presence of candiduria represents a therapeutic challenge for a physician because the patients in whom it may be encountered range from asymptomatic and ambulatory to desperately ill. Accordingly, a classification scheme might permit an orderly approach to management. It is logical to group the patients whose urine has yielded Candida species as follows: (1) those with asymptomatic candiduria (previously healthy patients); (2) those with asymptomatic candiduria (pre-disposed outpatients); (3) those with asymptomatic candiduria (pre-disposed inpatients); (4) those with symptomatic candiduria (cystitis, pyelonephritis, prostatitis, epididymo-orchitis, or urinary tract fungus balls); and (5) clinically unstable patients with candiduria. An algorithm summarizing an approach to the management of these groups of patients with candiduria is provided in Figures 1 and 2.

ASYMPTOMATIC CANDIDURIA, PREVIOUSLY HEALTHY PATIENT

The presence of candiduria should be verified with a second, clean-voided urine culture. Many times it is found that the first culture was contaminated, especially in samples from female patients. Once the presence of candiduria is confirmed, a careful history and physical examination and screening laboratory studies to look for symptoms or signs of predisposing factors (Table 1) are essential because occult diabetes mellitus, genitourinary structural abnormalities, diminished renal function, and metabolic abnormalities may be discovered [1–3]. If no explanation for candiduria is found, a follow-up examination of the urine is generally all that is necessary because candiduria can be expected to resolve within weeks to months without therapeutic intervention in the vast majority of individuals [4].
ASYMPTOMATIC CANDIDURIA, PREDISPOSED OUTPATIENT

The management of outpatients who have candiduria and who have a predisposing condition is more complicated because yeast in the urine may reflect an invasive infection that requires an antifungal agent for cure. The presence of candiduria can also be a marker for a process that requires urgent intervention, such as the treatment of a urologic abnormality and associated obstruction. Imaging of the kidneys and collecting system as a baseline in patients with diabetes mellitus or repeating imaging studies in those with known abnormalities of the kidney and collecting system is recommended so that the appropriate treatment can be given.

Antifungal therapy can be avoided in most instances because the long-term consequences of candiduria are generally benign, even among predisposed patients [5]. For example, yeast in the urine of an asymptomatic, elderly, diabetic patient with heavy glycosuria may well disappear with tighter control of serum glucose levels. Candiduria that complicates antibiotic therapy frequently resolves shortly after antibiotics are stopped. If benign prostatic hyperplasia and mild obstruction have resulted in asymptomatic candiduria, a peripherally acting α-adrenergic blocking agent may be all that is required for resolution. Close follow-up of such predisposed patients is prudent.

One double-blind, randomized, placebo-controlled trial seriously challenged the wisdom of treating asymptomatic candiduria. In a study designed to test the efficacy of fluconazole in asymptomatic or minimally symptomatic candiduria, Sobel and colleagues found that fluconazole was superior to placebo in eradicating *Candida* from the urine in both catheterized and uncatheterized patients in the short term [6]. However, 2 weeks after discontinuation of the study drug or placebo, candiduria had recurred in 40% of the catheterized subjects and 30% of those without a bladder catheter. None of these mostly elderly, female patients with multiple comorbid conditions developed candidemia. Ironically, this drug trial demonstrated not only the lack of long-term efficacy but the futility of treating the majority of predisposed but asymptomatic patients even with an agent with optimal pharmacokinetics for the kidney and collecting system.

ASYMPTOMATIC CANDIDURIA, PREDISPOSED INPATIENT

In an era of increasing acuity of illness among hospitalized patients, many are predisposed to candiduria for 1 or more reasons and are unaware of or unable to complain of any associated symptoms. This is especially true if an indwelling bladder catheter is present and the patient is being cared for in an intensive care unit (ICU). Hospitalized patients who have an indwelling bladder catheter are at risk of acquiring yeast in the urine. Platt and colleagues reported that 26.5% of all catheter-associated UTIs (defined as the recovery of $>10^5$ organisms per
mililiter) were due to Candida species [7]. However, the authors provided no distinction of infection from colonization of the catheterized urinary tract among the patients, and no conclusions about the need for therapy can be assumed from these data. Indeed, candiduria in this setting most likely represents colonization of the bladder and catheter by Candida spp.

The possibility of disseminated candidiasis should be considered in all hospitalized patients with candiduria, especially in patients in the ICU. Candidemia is common in this setting, and 46%–80% of persons with candidemia will have accompanying candiduria [8–10]. Moreover, Candida spp are the fourth most common isolates from blood cultures among hospitalized patients [11]. Despite these observations, candidemia is encountered in <5% of patients in most ICUs [12–16]. Thus, most patients with candiduria probably do not have disseminated infection.

Since many patients in the ICU have an indwelling bladder catheter to monitor urine output, when candiduria is found, changing or removing the catheter can be anticipated to clear the candiduria in 20%–40% of individuals [6]. When possible, discontinuing antibiotics that are no longer necessary and treating other predisposing conditions simultaneously should also be done. If candiduria fails to resolve despite these measures, a more deep-seated infection should be suspected, and imaging of the kidneys and collecting system is indicated. Such studies may reveal renal abscess, fungus ball, or other urologic abnormality accounting for the persistent funguria and that may require an invasive procedure for management.

Antifungal treatment of candiduria in an inpatient should be reserved for those patients who have solid clinical evidence of infection of the kidney or collecting system or disseminated candidiasis [6, 17]. Until reliable methods for detecting invasive candidiasis in predisposed patients become available, antifungal agents will continue to be used empirically and, many times, inappropriately in this setting. This is unfortunate because for many of these individuals, control or elimination of predisposing factors likely would have resolved candiduria [4, 5, 18].

**SYMPTOMATIC CANDIDURIA, CYSTITIS, PYELONEPHRITIS, PROSTATITIS, EPIDIDYMO-ORCHITIS, and URINARY TRACT FUNGUS BALLS**

**Cystitis**

Assuming that predisposing factors have been eliminated or managed to the extent possible, the in vitro activity and pharmacokinetics of fluconazole make it the drug of choice for cystitis due to most species of Candida, with the exception of resistant Candida glabrata, Candida krusei, and other less common resistant yeasts. A dose of 200–400 mg orally, daily, for 2 weeks should be adequate because fluconazole, which is highly water soluble, is primarily excreted into the urine as active drug [19–21]. Expected concentrations in urine exceed the minimal inhibitory concentration (MIC) not only for susceptible yeasts (MIC, ≤8 μg/mL) but also for organisms that are susceptible but dose-dependent (MIC, 16–32 μg/mL) and sometimes even

![Algorithm for the management of symptomatic candiduria.](cid:2011:52 (Suppl 6) S459)
Table 1. Predisposing Factors for Candiduria and Candida Urinary Tract Infections

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<th>Predisposing Factors</th>
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<tr>
<td>Diabetes mellitus</td>
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<td>Renal transplantation</td>
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<td>Extremes of age</td>
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<td>Instrumentation of the urinary tract</td>
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<td>Female sex</td>
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<td>Concurrent bacteriuria</td>
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<td>Prolonged hospitalization</td>
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<td>Congenital abnormalities of the urinary tract</td>
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<td>Intensive care unit admission</td>
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<td>Structural abnormalities of the urinary tract</td>
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<td>Broad-spectrum antibiotics</td>
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<td>Indwelling urinary tract devices</td>
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<td>Bladder dysfunction</td>
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<td>Urinary stasis</td>
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<td>Nephrolithias</td>
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those that are resistant (MIC, \( \geq 64 \mu g/mL \)) [22]. Such levels can be achieved because the drug is concentrated in the urine, yielding urine levels \( >100 \mu g/mL \), which is 10-fold the simultaneous plasma levels. Given its safety profile and efficacy, fluconazole is clearly the agent of choice for the initial treatment of most patients with symptomatic Candida cystitis.

Other azoles that could serve as alternative choices for resistant isolates are not useful for cystitis because of minimal excretion of the active compound into the urine (itraconazole concentration, \(<1\%\); voriconazole concentration, \(<5\\%\); posaconazole concentration, \(<1\%)\) [23–26]. For patients who are allergic to fluconazole or for those in whom therapy clearly fails despite maximum doses and optimal management of urologic abnormalities and other predisposing conditions, other agents such as oral flucytosine and parenteral amphotericin B (AmB) or local AmB bladder instillations may be necessary.

Candida isolates are usually susceptible to flucytosine (<1.25 \( \mu g/mL \)), and this agent is concentrated in urine to levels of \( >30 \mu g/mL \) [27, 28]. Approximately 25% of Candida albicans isolates are resistant to flucytosine, but most C. glabrata isolates are susceptible [29]. Eradication of Candida bladder infections with flucytosine can be expected in \(~70\%) of symptomatic individuals [30], but the duration of therapy has not been established. Generally, therapy is given for only 7–10 d because resistance develops quickly when this agent is used alone for an extended period. A dose of 25 mg/kg every 6 h is recommended, with adjustment of the dose or dosing interval in patients with renal insufficiency. Treatment with flucytosine is limited by toxicity and has been associated with detectable serum levels of 5-fluorouracil [31]. As expected, normal tissues with a high rate of cellular turnover, such as the bone marrow and gastrointestinal mucosa, are vulnerable [32]. Frequent complete blood cell counts and close monitoring of patients for rash, diarrhea, or other gastrointestinal complaints are essential. Hepatotoxicity has also been associated with flucytosine treatment in up to 41% of patients, warranting monitoring of liver-associated enzyme levels, but the mechanism by which liver injury occurs is not known [33].

The toxicity of AmB would seem to militate against the use of this agent for cystitis. However, in an occasional patient with a refractory infection or unusually severe symptoms, AmB should be considered. C. albicans isolates are susceptible to AmB concentrations ranging from \( 0.05–1 \mu g/mL \), and the MIC for most other Candida species ranges between \( 0.25 \) and \( 3 \mu g/mL \) [34, 35]. Although reports of AmB-resistant strains exist, the phenomenon is rare and has been most often observed among non-C. albicans organisms, such as Candida lusitaniae [36, 37].

The dose and duration of treatment have not been established, but animal studies have revealed pharmacokinetic features of AmB that allow the compound to be used in humans with greater safety and increased cost-efficacy. Craven and colleagues previously demonstrated in dogs that a single intravenous dose of AmB was followed by prolonged urinary excretion [38]. Urine concentrations exceeded MICs reported for most Candida species for days to weeks following a single 1-mg/kg dose. Pilot studies substantiated the feasibility of this approach in humans [39, 40]. Reports of the results in 35 patients with persistent candiduria are available, including the results of a randomized, controlled, comparative trial that showed that single-dose AmB was more cost-efficacious than other modalities of treatment [41]. The studies showed a success rate of 72% in eradicating yeast from the urine with a single intravenous dose of AmB, suggesting that the delayed urinary excretion of AmB might be used to advantage in Candida cystitis as well as other forms of refractory Candida UTIs.

The lipid formulations of AmB were designed to decrease renal toxicity. The 3 lipid formulations that are available are less nephrotoxic but do not achieve appreciable levels in the kidneys or in urine. Efficacy in Candida cystitis would not be predicted. Indeed, failure to eradicate yeast from the urinary tract has already been reported despite the efficacy of lipid formulations of AmB in disseminated candidiasis [42].

Another approach to the treatment of Candida cystitis has been to irrigate the bladder with AmB. The dosage most commonly used is 50 mg AmB diluted in 1 L of sterile water to give a concentration of 50 \( \mu g/mL \) [43]. A dosage of 10 \( \mu g/mL \) has been noted to be less efficacious [44]. Continuous irrigation of the bladder with this suspension for 5–7 d resolves Candida cystitis in \( >90\% \) of patients [45]. However, the relapse rate after local bladder irrigation is high [46]. Unless patients with symptomatic infections require a bladder catheter for other clinical indications, it is wise to avoid bladder irrigation. Catheter-induced bacteriuria can be expected in 20%–70% of these...
individuals, which poses a serious risk in itself [47, 48]. A recent review of the evidence for the therapeutic use of bladder irrigation concluded that “the use of amphotericin B bladder irrigation is a strategy rarely needed in our present clinical armamentarium” [49, p. 1469].

However, in the unusual patient who has C. krusei or fluconazole-resistant C. glabrata cystitis, AmB bladder irrigation can sometimes prove useful [50]. This approach should be done in concert with surgical correction of urinary tract obstruction or other mechanical abnormalities. In patients who have severe cystitis noted at cystoscopy, bladder irrigation can be given in conjunction with parenteral treatment using an agent to which the organism is susceptible, usually AmB or an echinocandin.

**Pyelonephritis**

Renal parenchymal infection is generally the result of candidemia, but retrograde infection of the kidneys can occur under conditions of urinary tract obstruction, concomitant bacteriuria, or profound immunosuppression [51]. Fluconazole is the agent of choice for pyelonephritis. A dose of 400 mg daily is ordinarily given, for 2 weeks. For most patients, the oral formulation is appropriate. Fluconazole is effective for a majority of UTIs, since C. albicans accounts for 40%–65% of yeast isolates from urine and Candida tropicalis and Candida parapsilosis account for ~25%; all 3 species are susceptible to fluconazole [6, 52–56]. However, infection due to C. glabrata is now more common than that caused by C. tropicalis and C. parapsilosis in some geographic areas, accounting for ~20% of urine isolates [3, 17]. The susceptibility of C. glabrata to fluconazole is highly variable; MICs range from .25 to 256 μg/mL. The MIC90 and MIC50 for fluconazole are reported to be 16 μg/mL and 4 μg/mL, respectively [57, 58].

It should be remembered that resistant organisms are classified as such on the basis of achievable serum concentrations. Renal parenchymal levels of fluconazole are probably more relevant and have been studied. Walsh and colleagues found that tissue concentrations in the kidney ranged from 18 to 27 μg/g of tissue in rabbits given a dose of fluconazole of 25 mg/kg body weight [20]. The ratio of tissue to plasma concentrations was consistently >.8, and trough levels in tissue were >3-fold higher than those of simultaneously collected serum samples, confirming accumulation of fluconazole in the kidney. Reported urine concentrations of >100 μg/mL provide additional confidence that fluconazole should be effective in the treatment of most Candida pyelonephritis including that caused by C. glabrata and the other common non-C. albicans species [59]. However, failures of fluconazole for the treatment of C. glabrata renal infection have been reported with increasing frequency [60].

Perfect and colleagues observed that itraconazole was equivalent to fluconazole in a rabbit model of hematogenous renal parenchymal candidiasis [61]. No details were provided by the authors as to involvement or clearance of infection from the lower urinary tract by itraconazole in these animals. There are few data in humans for the use of this agent for Candida pyelonephritis, and given its low excretion into the urine, it is unlikely to be efficacious for patients with Candida UTIs.

Posaconazole has potent activity against C. albicans and a variety of non-C. albicans species, including C. glabrata and C. krusei, that are resistant to fluconazole and itraconazole [55]. Posaconazole has demonstrated efficacy in a murine model of hematogenous renal parenchymal candidiasis [62]. However, only ~10% of active drug can be recovered in urine [25, 26]. Thus, like that of itraconazole, its antifungal activity in the renal parenchyma and other deep tissue sites would be expected to be adequate, but that in the urinary collecting system would be doubtful.

Because it is a fluconazole congener with excellent activity against most fluconazole-resistant Candida species, voriconazole might be considered the “heir apparent” for Candida UTIs refractory to fluconazole therapy. The efficacy of voriconazole in renal parenchymal candidiasis was found to be superior to that of either AmB or fluconazole in an animal model of hematogenous C. krusei infection, establishing its potential in eradicating Candida species from the kidney [63]. Unfortunately, urine voriconazole levels are low, with <5% of active drug excreted, and its usefulness in Candida UTIs is minimal [24].

Candida renal parenchymal infections as a component of disseminated candidiasis in various experimental models have been readily cleared with the echinocandins caspofungin, anidulafungin, and micafungin [64–68]. Given the high frequency of renal involvement in humans with disseminated candidiasis, efficacy of the echinocandins in pyelonephritis could be expected. However, all the echinocandins are extensively metabolized, and very little active drug can be recovered in the urine [69]. Therefore, eradication of Candida in the vascularized cortex and interstitium of the kidney by echinocandins is more likely than in the collecting system, and clinical experience is minimal [68]. In a retrospective review of data from the caspofungin database, this agent was found to be efficacious in 3 patients who had Candida pyelonephritis of ascending origin and in whom other antifungal therapy had failed [70].

The favorable pharmacokinetics of flucytosine in the urinary tract [28] and proven efficacy in a variety of forms of urinary tract candidiasis make it a consideration for patients who are able to take oral medications and for whom fluconazole cannot be used [27]. A dose of 25 mg/kg every 6 h with adjustment for renal insufficiency is standard. Since in some instances prolonged treatment may be required, the potentially serious toxicity of the compound mandates close follow-up of patients, and in these cases, this agent should be given with another antifungal agent, such as amphotericin B, to avoid the development of
resistance [32]. Particular attention needs to be given to bone marrow depression when both flucytosine and AmB are given together.

AmB deoxycholate has demonstrated efficacy in virtually all forms of invasive candidiasis and remains the choice of some clinicians for systemic and severe forms of urinary tract candidiasis in seriously ill patients. However, the lipid formulations of AmB should not be used for treating renal candidiasis. The reduced nephrotoxicity of these agents suggests that their tissue penetration in the renal parenchyma is reduced. Decreased clearance of renal foci of C. albicans in leukopenic mice has been demonstrated when liposomal AmB was compared with AmB deoxycholate, and failure to eradicate Candida from the urinary tract has been reported in humans [42, 71].

**Treatment in Patients With Renal Failure**

Given the above therapeutic considerations for the management of Candida cystitis and pyelonephritis, the concomitant presence of renal insufficiency will affect the selection and dosing of antifungal compounds and most probably impact therapy outcome as well. It was shown in one study that the likelihood of eradicating Candida from the urinary tract with fluconazole was inversely proportional to the degree of renal impairment [6]. A study of the pharmacokinetics of fluconazole in pediatric patients with renal failure demonstrated that the drug was almost completely cleared by peritoneal dialysis, making it likely that urine concentrations of the compound would most likely be subtherapeutic in this patient population [72]. However, urine levels were not measured in those patients who were still producing urine. In a single report in the literature documenting urine concentrations of fluconazole in patients with renal disease, Debruyne and Rycckelynck administered fluconazole orally or intraperitoneally to 3 groups, each with 5 patients, who were receiving continuous ambulatory peritoneal dialysis (CAPD): group 1 received an oral dose of 100 mg; groups 2 and 3 received 50 mg or 150 mg, respectively, in the dialysis bag [73]. These investigators then measured fluconazole levels in urine, dialysate, and serum at intervals for 144 h. The mean urine fluconazole concentrations 48 h following the 100-mg oral dose ranged from 1.8 to 1.9 µg/mL. During the 96 h following the 50-mg intraperitoneal dose, mean urine concentrations of fluconazole ranged from 1.15 to 0.66 µg/mL. Following the 150-mg intraperitoneal dose, the mean urine concentrations ranged from 2.2 and 1.4 µg/mL (as estimated from the graph) for the same time period. The focus of this publication was the therapeutic potential of fluconazole in peritoneal fluid during CAPD for Candida peritonitis and not candiduria. Nevertheless, the study demonstrates that a measurable amount of fluconazole continues to be excreted in urine for days in some patients with end-stage renal disease after relatively small doses. The authors gave no information about the causes of renal failure in the 15 patients. Therefore, it is possible that the pharmacokinetics of fluconazole could vary widely among patients with diseased kidneys with respect to urine concentrations.

Additional studies focusing on urine concentrations of fluconazole in patients with renal failure could prove to be extremely useful since many predisposed individuals with candiduria have impaired kidney function. Studies correlating urine concentrations of fluconazole with clinical outcome of Candida cystitis and pyelonephritis in patients with varying degrees of renal impairment would be of interest but to our knowledge have not been done. Consequently, fluconazole dosing in patients with marginal kidney function must be chosen empirically with the expectation that concentration of the azole in the nephron and subsequent urine levels will be reduced. While lowering the dose of fluconazole for a decreased creatinine clearance may be appropriate for systemic infection, such a change may lead to failure of therapy in Candida UTIs. Hence, we believe that, in general, patients with symptomatic candiduria should be given at least 400 mg of fluconazole daily regardless of renal function in an attempt to achieve therapeutic urine concentrations. An oral 400-mg dose should produce a peak serum concentration of ~9 µg/mL at steady state, whereas an intravenous dose yields a mean level of 16.7 µg/mL [74, 75]. In light of the efficacy and tolerability of high-dose fluconazole in cryptococcal meningitis and other severe fungal infections in daily doses of up to 1,600 mg with peak concentrations above 50 µg/mL, adverse events should be minimal [76–79]. Nevertheless, careful monitoring of hepatic function during therapy is indicated.

**Prostatitis**

Because Candida prostatitis is uncommon, approaches to therapy have been derived from individual case reports over the past 25 years and not from randomized clinical trials. Over this period, new antifungal agents have been introduced, none of which have been adequately studied in this unusual form of candidiasis. Wise recently summarized the approach to the diagnosis and treatment of Candida prostatitis [80]. He and his coauthor suggested that fungal prostatitis should be treated with incision and drainage of any abscess that is present or resection of prostate tissue in addition to antifungal agents. Most case reports have emphasized the role of surgery in conjunction with an antifungal agent for the treatment of Candida prostatitis [80, 81].

AmB has been the antifungal agent most commonly used [80, 82], but fluconazole has also been given successfully [83]. Levels of fluconazole in prostatic tissue and prostatic fluid in both humans and experimental animals are 29%–89% that of serum concentrations [84–86]. In a study by Finley and colleagues, peak and trough serum levels were measured in 8 patients with benign prostatic hyperplasia who were scheduled to undergo elective transurethral prostate resection [84]. The participants
The majority of infections were caused by *C. albicans* for the treatment of 147 patients with *Candida* prostatitis. Dimitrakov and Rawadi compared fluconazole and itraconazole to make a circumstantial case for daily doses of the azole of 400 mg on the first day. Prostate tissue concentrations were then obtained 12–15 h after the last dose. Mean (± SD) peak and trough serum levels for the patients were 6.5 ± .7 and 5.2 ± .6 μg/mL, respectively, and the mean (± SD) serum concentration at the time of surgery was 6.6 ± .7 μg/mL. Prostate tissue levels at surgery were 1.9 ± .3 μg/g, or 29% of the mean serum concentration. These data suggest that the drug does not accumulate in the prostate and perhaps the concentrations achieved will not be sufficient to eradicate some strains of *C. albicans* and many non-*C. albicans* species. However, none of these patients had acute *Candida* prostatitis, in which inflammation might result in better penetration of fluconazole. Nevertheless, the data make a circumstantial case for daily doses of the azole of >200 mg to treat proven *Candida* prostatitis.

In a preliminary report that has never been published in full, Dimitrakov and Rawadi compared fluconazole and itraconazole for the treatment of 147 patients with *Candida* prostatitis [87]. The majority of infections were caused by *C. albicans* (48%); other species included *C. glabrata* (24%), *C. tropicalis* (19%), and *C. parapsilosis* (7%). Success of therapy with fluconazole was related to in vitro susceptibility of the isolates. More than 90% of infections resolved when the MICs were <8 μg/mL, and only 76% resolved when the MICs were ≥16 μg/mL. Resolution occurred in 81%, 50%, and 44% of itraconazole-treated subjects with MICs of <.12, .25–.5, and ≥1 μg/mL, respectively. While results are promising for both agents, data such as these should be interpreted with caution because little clinical information was provided by the authors and the data have been published thus far only in abstract form. The lower activity level of itraconazole likely reflects the lipophilic properties and poor water solubility of this agent. Prostatic secretions have a high water and minimal lipid content. The failure of itraconazole to eradicate a focus of cryptococcal prostate infection in a patient with AIDS and the persistence of *Aspergillus* prostatitis in a renal transplant recipient given itraconazole provide further anecdotal evidence that this compound is not an optimal choice for fungal prostatitis [88, 89]. No data are available regarding the penetration of voriconazole, posaconazole, or the echinocandins into prostatic tissue or secretions, and their efficacy is unknown.

In summary, successful treatment has uniformly involved surgical intervention combined with the use of AmB or fluconazole for *Candida* prostatitis [80]. There are no convincing data that itraconazole should be used. Additional studies of the appropriate dosage and duration of therapy of fluconazole and other agents are warranted.

**Epididymo-orchitis**

Treatment recommendations for *Candida* epididymo-orchitis are based entirely upon anecdotal experience from case reports [90–95]. Most patients have required surgical drainage of abscesses and/or orchietomy for cure, in conjunction with fluconazole or AmB with or without flucytosine [91–93, 95]. A single patient who responded to ketoconazole alone has been reported, but this agent is rarely used now [96].

**Fungus Balls (Bezoars and Mycetomas) of the Urinary Tract**

The location of the *Candida* fungus ball will determine the approach to therapy. Systemic treatment with AmB, with or without flucytosine, or fluconazole has been used in the majority of patients [2, 97–102]. Systemic therapy is reasonable because these luminal fungal aggregates most often result from disseminated candidiasis or deeply seated parenchymal infection. Although treatment with antifungal agents may result in spontaneous disruption and passage of the mass of hyphal filaments and debris, this is unusual [2, 103]. Almost always, an invasive procedure will need to be performed to relieve obstruction and to remove the bulk of the mass. If the urologic procedure required (eg, percutaneous nephrostomy) provides a portal of access to the renal pelvis, ureters, or bladder, local irrigation with intermittent or continuous AmB or fluconazole can be considered, but studies to determine optimal dosage and duration have not been done [97–100]. Other methods to facilitate the breakdown and passage of fungus balls have included intermittent irrigation with saline, insertion of thrombectomy devices through a percutaneous nephrostomy, percutaneous endoscopic disruption and drainage, and percutaneous irrigation with streptokinase [104–109].

**CANDIDURIA IN CLINICALLY UNSTABLE PATIENTS**

For critically ill patients, candiduria, whether symptomatic or not, should initially be regarded as a harbinger of disseminated candidiasis [10], since the kidney is the target of candidemia in ~80% of patients [8]. Indeed, the finding of yeast in the urine may be the only clue that the patient has a life-threatening infection. It follows that an astute physician will immediately consider disseminated candidiasis in such a patient and examine the optic fundi, the skin, and vascular access devices and obtain fungal blood cultures. Fortunately, most patients are not fungemic even when desperately ill, and their urinary tract is simply colonized by *Candida*, especially if an indwelling bladder catheter is present.

If the candiduric patient’s clinical condition is too unstable to permit an incremental approach to determine its cause or if clinical evidence for disseminated candidiasis is sufficiently compelling, systemic antifungal chemotherapy should be given immediately with fluconazole in a loading dose of 800 mg followed by 400 mg daily or with appropriate adjustment for renal insufficiency. An echinocandin is preferred if the patient has had recent azole exposure (caspofungin, 70-mg loading dose, then
References

