Treatment of the Infected Stone

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KEYWORDS

- Struvite • Calcium carbonate apatite • Staghorn • Obstructive pyelonephritis • Kidney stones
- Urinary tract infection

KEY POINTS

- Infection stones result from urease-producing bacteria and are struvite and/or calcium carbonate apatite in composition.
- Optimal management of infection stones is complete stone removal, and failure to achieve complete stone clearance results in a high recurrence rate.
- Obstructive pyelonephritis is a urologic emergency and can result in urosepsis and death.
- Emergent decompression with retrograde ureteral stent placement or percutaneous nephrostomy tube (PCNT) placement and broad-spectrum antibiotics are imperative to treating patients with obstructive pyelonephritis.

INTRODUCTION

An infected kidney stone can refer to stones that form because of urinary tract infections (UTIs) with urease-producing bacteria, secondarily infected stones of any composition, or stones obstructing the urinary tract leading to pyelonephritis. Most commonly, kidney stones that form secondary to urease-producing bacteria are composed of struvite or calcium carbonate apatite, and presentation is frequently incidental and generally nonemergent. Secondarily infected metabolic stones have also been described. These stones are frequently colonized with non–urease-producing bacteria and often have discordant culture results compared with the lower urinary tract. Obstructive pyelonephritis secondary to urinary tract calculi is considered a urologic emergency, and immediate treatment is indicated to avoid serious complications, including urosepsis and death. Given the difference in pathophysiology and treatment approach, these entities are discussed separately.

Infection Stones

Infection stones are most commonly composed of magnesium ammonium phosphate (ie, struvite) and/or calcium carbonate apatite. These stones result from chronic infections with urease-producing bacterial pathogens and frequently form large branched stones known as staghorn calculi. The incidence of infection stones has overall decreased during the last 30 years, likely due to improved medical care. They are more common in women (10%–11% vs 4% in men) and elderly patients.[1,2] The pathogenesis of struvite and calcium carbonate apatite stone formation is presented in **Fig. 1**.[3,4] Urease from bacteria splits urea into ammonia and carbon dioxide. Ammonia reacts with water to become ammonium and hydroxide ions, which creates an alkaline milieu. In this alkaline environment, the ammonium combines with magnesium, phosphate, and water to create magnesium ammonium phosphate stones. The carbon dioxide eventually breaks down to carbonate, which combines with calcium and phosphate to

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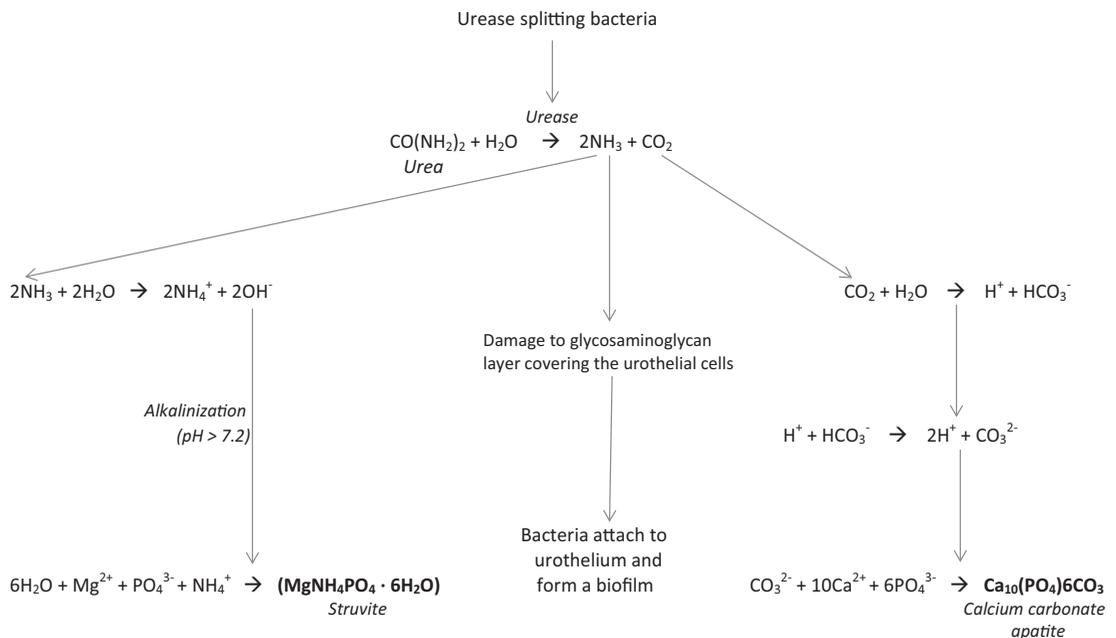* Corresponding author. Department of Urologic Surgery, Administrative Office, A-1302 Medical Center North, Vanderbilt University Medical Center, Nashville, TN 37232-2765.
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Fig. 1. Pathogenesis of infection stones. Urease from bacteria splits urea (ie, carbamide) into ammonia and carbon dioxide. The ammonia combines with water to produce ammonium and hydroxide. Hydroxide results in an alkalosis of the urine leading to the formation of magnesium ammonium phosphate (ie, struvite). The ammonia also damages the glycosaminoglycan layer causing urothelial damage, allowing the bacteria to attach to the urothelium and form a biofilm. Carbon dioxide complexes with water to form bicarbonate and then carbonate. Carbonate combines with calcium and phosphate forming calcium carbonate apatite.

form calcium carbonate apatite stones. The most common urease-producing bacterial pathogens are *Proteus* spp, *Klebsiella* spp, *Providencia* spp, *Morganella morganni*, and *Staphylococcus aureus*.[5,6] Infection stones are commonly asymptomatic or present with UTIs, flank or abdominal pain, fevers, gross hematuria, or less commonly with sepsis or renal insufficiency.[7] Patients with indwelling catheters, neurogenic bladder, and urinary diversion have the highest risk of developing infection stones due to chronic bacterial colonization. The natural history of these stones is associated with progressive morbidity and mortality, with the 10-year mortality rate reported at 28% with nonsurgical management versus 7% with surgical treatment.[8]

Secondarily infected stones, which are nonstruvite and non–calcium carbonate apatite stones associated with infection, have been described.[9] In a series of 125 patients undergoing percutaneous nephrolithotomy (PCNL), de Cógáin and colleagues[9] found that 24 (23%) of 106 patients with nonstruvite stones had positive stone cultures. A history of neurogenic bladder was associated with positive stone culture in both patients with infected nonstruvite and struvite stones in this series. Non–urease-producing bacteria, including *Escherichia coli* and *Enterococcus* spp, are the predominant

organisms colonizing these metabolic stones.[9,10] Whether these stones form and become secondarily infected or whether these stones result from a nidus of infection that propagates stone formation is unclear. Theories for how bacteria could be a nidus for nonstruvite and non–calcium carbonate apatite stones include kidney cell injury and inflammation potentiating crystal retention, alteration of the microenvironment by bacterial metabolic activity, or biofilm that acts as a matrix for stone growth.[9] In general, sending a sample for stone culture should be considered for all patients undergoing PCNL to help target antibiotic therapy in the event of a postoperative infection. Patients should make appropriate dietary modifications and receive specific medical therapy based on metabolic studies to prevent recurrent urolithiasis. Further studies are necessary to elucidate the exact role and clinical significance of bacteria in these stones.

Obstructive Pyelonephritis

Pyelonephritis is an infection of the kidney with typical presentation including but not limited to fever, flank pain, and irritative lower urinary tract symptoms. Obstructive pyelonephritis is a complicated UTI and considered a urologic emergency because of the significant risk of morbidity and

mortality.[11–13] Borofsky and colleagues[12] identified 1712 patients from the Nationwide Inpatient Sample between 2007 and 2009 who had ureteral calculi and sepsis and found a 19% rate of mortality if decompression was not performed versus 9% for those who underwent surgical decompression. Ureteral stones are responsible for approximately two-thirds of the occurrences of obstructive pyelonephritis.[14]

PATIENT EVALUATION OVERVIEW
Infection Stones

Patients with infection stones typically do not present with acute colic and instead are found incidentally or due to complaints of vague abdominal or back pain, recurrent UTIs, and/or gross hematuria.[7] Box 1 provides a summary of the initial evaluation of these patients. A focused history and physical examination should be performed.

A urinalysis (UA) may show an alkaline pH (>7.0) and evidence of an infection, including leukocyte esterase, white blood cells (WBCs), nitrite, and blood. Magnesium ammonium phosphate crystals (which are coffin shaped) may also be noted on the UA of a patient with infection stones. Urine culture should be done, and is likely to grow a urease-producing bacteria. A basic metabolic panel is used to assess kidney function, as infectious staghorn calculi have a high risk of causing renal insufficiency.[8] Hematocrit, platelet count, and coagulation panel values are necessary for surgical planning.

Box 1
Initial evaluation of patients with suspicion for infection stones

History
- Symptoms
  - Flank pain, abdominal pain, fevers, chills, gross hematuria
  - LUTS: dysuria, hematuria, urgency, frequency
- Urologic history
  - UTI, pyelonephritis
  - Urolithiasis
  - Urinary diversion and/or neurogenic bladder
  - Anatomic abnormalities (UPJO, strictures)
  - Chronic indwelling catheters, SPT or CIC
  - Urethral strictures
  - Prior urologic surgeries
- Anticoagulation or antiplatelet therapy (and if these can be held)

Physical examination
- Fever/hypothermia, vital signs
- CVAT, abdominal/suprapubic tenderness
- Musculoskeletal deformities

Laboratory tests
- UA and urine culture
- BMP, CBC, coagulation panel
- ± Blood cultures (if presenting acutely with fever/concern for sepsis)

Radiology
- Noncontrast CT scan (gold standard)
- KUB and/or renal US (best used for follow-up)
- ± Renogram

Abbreviations: BMP, basic metabolic panel; CBC, complete blood count; CIC, clean intermittent catheterization; CT, computed tomography; CVAT, costovertebral angle tenderness; KUB, kidney ureter bladder radiography; LUTS, lower urinary tract symptoms; SPT, suprapubic tube; UA, urinalysis; UPJO, ureteropelvic junction obstruction; US, ultrasonography; UTI, urinary tract infection.

Imaging with noncontrast computerized tomography (CT) is the gold standard for both diagnosis and surgical planning. Kidney, ureter, and bladder radiography and/or renal ultrasonography (US) may be used for follow-up. A renogram should be performed if poor function is suspected in the affected kidney.

Obstructive Pyelonephritis

Initial evaluation of patients presenting with obstructive pyelonephritis most frequently begins in the emergency room (ER). **Box 2** provides a summary of the initial evaluation of these patients. A focused history and physical examination should be performed, with careful attention paid to vital signs and hemodynamic stability. Findings of poor performance status and a history of paralysis in patients with obstructive pyelonephritis should alert the medical practitioner to an increased risk for sepsis.[13] The use of anticoagulation or antiplatelet therapy must be assessed. For patients with paralysis and contractures, physical examination should also assess mobility of the patient's lower body and the ability to place them in lithotomy position for cystoscopy. Patients with severe lower extremity contractures that prohibit cystoscopic access may require PCNTs for decompression.

UA may show signs of infection, with positivity for leukocyte esterase, WBCs, blood, and nitrite; however, a negative UA result does not rule out infection. The urine proximal to an obstructing stone may be infected, whereas the voided urine

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Box 2
Initial evaluation of patients with obstructive pyelonephritis

History
- Symptoms
  - Flank pain, abdominal pain, nausea, vomiting, fevers, chills
  - LUTS: dysuria, hematuria, urgency, frequency
- Urologic history
  - UTI, pyelonephritis
  - Urolithiasis
  - Anatomic abnormalities (UPJO, strictures)
  - Urologic surgeries
- Past history of malignancy, irradiation, abdominal surgeries (risks for ureteral obstruction)
- Risk factors for infection (DM, HIV/AIDS, performance status, paralysis, other immunocompromised states)
- Anticoagulation or antiplatelet therapy

Physical examination
- Fever/hypothermia, hemodynamic stability
- CVAT, abdominal pain/suprapubic pain

Laboratory tests
- UA, CBC, BMP, ± albumin, ± CRP
- Voided urine culture and blood culture at presentation
- Urine culture from the kidney(s) at the time of decompression

Radiology
- Noncontrast CT abdomen and pelvis
- Ultrasonography (can consider as first line if patient is stable and there is low suspicion for stone) ± KUB

Abbreviations: AIDS, acquired immune deficiency syndrome; BMP, basic metabolic panel; CBC, complete blood count; CRP, c-reactive protein; CVAT, costovertebral angle tenderness; DM, diabetes mellitus; HIV, human immunodeficiency virus; KUB, kidney ureter bladder radiography; LUTS, lower urinary tract symptoms; UPJO, ureteropelvic junction obstruction.

distal to this may be sterile. Glucosuria should alert the clinician to poorly controlled or undiagnosed diabetes mellitus. The practitioner should be aware that patients with thrombocytopenia[13,15,16] and low serum albumin levels[13,15] are at an increased risk of developing septic shock and should be monitored appropriately. Urine and blood cultures should be sent on presentation, and a urine culture from the kidney(s) should be obtained at the time of decompression. Although some series have found C-reactive protein (CRP) levels helpful in distinguishing between infected and sterile hydronephrosis[17] as well as for identifying those patients who will develop urosepsis,[13] the utility of CRP in the management of obstructive pyelonephritis is unclear.

Imaging is required to differentiate nonobstructive from obstructive pyelonephritis. Although US can detect hydronephrosis and has the advantage of avoiding ionizing radiation, it is user dependent, limited by body habitus, and frequently suboptimal in identifying the specific source of ureteral obstruction. Some advocate for bedside US in the ER to screen for hydronephrosis before CT scan to avoid radiation and unnecessary costs.[18] US performed in the ER has a reported sensitivity of 80% and specificity of 83%.[19] A bedside US by the ER physician may be reasonable as an initial evaluation for ureteral obstruction in a stable patient. Ultimately, however, a CT scan should be obtained to confirm the diagnosis and clearly characterize the cause of obstruction, which affects the choice of decompression procedure as well as guides future definitive surgical therapy.

PHARMACOLOGIC TREATMENT OPTIONS
Infection Stones

Infection stones are optimally managed surgically with the goal of complete stone clearance. After surgery, pharmacologic preventative measures can be considered, including acidification of the urine, inhibition of urease, chemolysis via topical application, and suppressive antibiotic therapy. Medical therapy alone can also be considered for those unable to undergo surgery. Crystallization of infection stones occurs at a pH greater than 7.0 to 7.2. Acidification of the urine to less than pH 6.5 can greatly increase the solubility of this type of infection stone. Urinary acidification with ascorbic acid, ammonium chloride, ammonium sulfate, ammonium nitrite, and L-methionine has been reported.[6,20] L-Methionine is an oral medication that is metabolized to sulfate and hydrogen ions.[21] In vitro studies using L-methionine have shown excellent ability to dissolve infection stones,[22] and older in vivo series have shown

favorable urinary acidification.[23] Contemporary in vivo studies are needed to assess for safety and efficacy. Urinary acidification is rarely implemented today.

Acetohydroxamic acid (AHA) is an oral agent that acts as a urease inhibitor. AHA was initially described in the 1960s and is the only US Food and Drug Administration (FDA)-approved urease inhibitor.[24] Hydroxyurea was also investigated as an oral urease inhibitor but was found to be inferior to AHA.[25] AHA works well because it achieves high levels in the urine and can penetrate bacterial cell walls. Randomized and placebo-controlled studies have proved AHA's ability to significantly reduce stone growth; however, it does not decrease existing stone burden.[26–28] Griffith and colleagues[26] in a randomized, double-blind, placebo-controlled trial of AHA in 210 patients with spinal cord injury reported a significant decrease in stone growth for those receiving AHA versus placebo (33% and 60%, respectively). However, many patients experience psychoneurologic, hematologic, and gastrointestinal side effects, with 22% unable to tolerate AHA.[27,29] The presence of renal insufficiency increases the risk of toxicity and results in decreased efficacy. Thus, AHA is contraindicated for patients with a creatinine level greater than 2.5 mg/dL^2. It is also contraindicated in pregnant women and women of childbearing age who are not using birth control. The American Urological Association (AUA) guidelines state that AHA may be offered only after surgical options have been exhausted for patients with residual or recurrent struvite stones.[30] They also encourage the use of AHA in patients with abnormal lower urinary tracts (ie, neurogenic bladder or urinary diversion) and struvite and/or calcium carbonate apatite stones because of the high risk for recurrent stone formation.[31]

Topical chemolysis and dissolution with Renacidin irrigant (10% hemiacidrin) or Suby G solution (3.2% citric acid) into the collecting system has also been described.[32–34] In the 1960s, 6 patients died after treatment with Renacidin, which led to the ban of this irrigant by the FDA. Further investigation found that these deaths were related to administration of the irrigant under high pressure resulting in pyelovenous back flow, systemic absorption, urosepsis, and subsequent death.[35] Dissolution therapy for infection stones via PCNTs, ureteral stents, and/or access sheaths is now considered safe and effective as long as it is performed in the setting of sterile urine, with prophylactic antibiotics and at low renal pelvic pressures.[34] Postoperative application is limited for multiple reasons including the need to know the stone composition before administration,

difficulty maintaining a low-pressure system, need for constant nursing care, need for replacement/exchange of ureteral stents and nephrostomy tubes when they become obstructed, and need for prolonged hospitalization. For those patients with infection stones who are not cured with surgical stone removal, dissolution therapy can be considered and is currently approved by the FDA for use in this setting.

In theory, the eradication of urease-producing bacteria in the urinary tract with antibiotics should halt the formation of infection stones, and older series have even reported that infection stones may dissolve in sterile urine[36,37]; however, antibiotics do not penetrate infection stones. Ultimately, surgical removal is required to achieve sterility. There are anecdotal reports of decreased recurrence of infection stones by placing patients on suppressive antibiotic therapy for several months after surgical stone removal, but there are no series in the literature studying this approach. With increasing rates of antimicrobial resistance, evidence is needed to justify the use of prolonged antimicrobial therapy in this patient population. Another suggested approach is to check a urine culture every month for 3 months after surgical removal of infection stones and treat as needed.[38] Further studies are necessary to clearly state the role of suppressive antibiotics after surgical removal of infection stones.

Obstructive Pyelonephritis

Obstructive pyelonephritis requires dual therapy with broad-spectrum antibiotics and emergent decompression. Selection of empiric antibiotic therapy can be complicated because of the increasing antimicrobial resistance both nationally and worldwide.[39–42] Choice of empiric antibiotic therapy can be guided by reviewing prior urine culture data, urine culture gram-staining result,[43] the hospital's antibiogram, and antimicrobial stewardship's recommendations.[44] In general, the patient should be administered broad-spectrum antibiotics to cover for common gram-negative pathogens with or without antibiotics to cover gram-positive pathogens. One series reported on their experience with obstructive pyelonephritis and found that 79% of bacterial pathogens were gram-negative rods, with *E coli* being the most common (66%) and *Enterococcus* spp making up two-thirds of the gram-positive pathogens.[44] Of the 65 patients in this series, 2 had candida in their urine specimens. Coverage for gram-positive pathogens should be initiated if the patient presents with sepsis, if gram-positive bacteria are noted on gram staining, and if the patient has a history of prior UTIs with gram-positive pathogens. Once the organisms in the urine and blood cultures are determined, the patient should be switched to a 1- to 2-week course of culture-specific antibiotics.[45]

NONPHARMACOLOGIC TREATMENT OPTIONS
Infection Stones

Dietary modifications to prevent infection stones have generally focused on reducing urinary phosphorous and magnesium levels by avoiding dietary foods and vitamin supplements high in these elements. Shorr and Carter[46] proposed a regimen in the 1940s of a low-phosphate, low-calcium diet with oral estrogens (to decrease calcium excretion) and an aluminum hydroxide gel to bind phosphate in the gut. Although studies found significant stone dissolution and reduced stone growth[46] as well as decreased stone recurrence following PCNL[47] on this regimen, the Shorr diet has been shown to result in significant metabolic abnormalities related to the aluminum hydroxide, including constipation, anorexia, lethargy, bone pain, and hypercalciuria.[48] The Shorr diet with aluminum hydroxide is not currently recommended.

Obstructive Pyelonephritis

There is no role for nonpharmacologic treatment of obstructive pyelonephritis in the acute setting. Long-term efforts to decrease recurrent nephrolithiasis and UTIs through dietary measures are indicated.

SURGICAL TREATMENT OPTIONS
Infection Stones

Surgical management with the goal of complete stone clearance is the standard of care for patients with infection stones. **Table 1** provides a summary of surgical treatment options for infection stones as recommended by AUA guidelines and reported in the literature.

For those well enough to undergo surgical intervention, the current AUA guidelines recommend PCNL monotherapy as the treatment of choice for staghorn calculi.[31] PCNL in combination with flexible ureteroscopy results in less access tracts and decreased blood loss.[59] PCNL and ureteroscopy may be performed simultaneously in the prone position with a split leg bed, avoiding time needed to reposition from dorsal lithotomy to prone.[60,61] Combination therapy for the treatment of infection stones refers to the use of PCNL with shockwave lithotripsy (SWL). Segura and colleagues[62] reported a disappointing stone free rate of 23% in their series of 16 consecutive

Table 1
Surgical approaches for infection stones

Surgery	Indication	Evidence
PCNL (± URS, ± flexible nephroscopy)	First line per AUA guidelines	Preminger et al,[31] 2005
PCNL + SWL	When calyces cannot be accessed with nephroscopy or additional access tracts	Preminger et al,[31] 2005; Merhej et al,[49] 1998
SWL monotherapy (+stent or PCNT)	Stone burden <500 mm^2 with no/minimal dilation of the collecting system	Preminger et al,[31] 2005; Lam et al,[50] 1992
URS monotherapy	May consider for partial staghorn stones in patients unable to undergo PCNL	Healy & Ogan,[51] 2007
ANL (open or lap/RAL)	PCNL failure, extremely large stones, aberrant collecting system anatomy (ie, calyceal diverticulum, infundibular stenosis), unfavorable body habitus for PCNL (ie, morbid obesity, skeletal deformities), pelvic or transplant kidneys	Preminger et al,[31] 2005; Bove et al,[52] 2012; Assimos,[53] 2001; King et al,[54] 2014; Ghani et al,[55] 2013; Giedelman et al,[56] 2012; Simforoosh et al,[57] 2008; Elbahnasy et al,[58] 2011

Abbreviations: ANL, anatrophic lithotripsy; lap, laparoscopic; RAL, robotic-assisted laparoscopic; SWL, shockwave lithotripsy; URS, ureteroscopy.

patients undergoing PCNL followed by SWL. Based on this study, the current AUA guidelines state that if SWL is to be performed with PCNL, PCNL should be the first modality used to treat these patients as well as the last because clearance of all fragments after SWL is unlikely.[31] SWL may be used in cases in which residual stones cannot be treated with flexible nephroscopy or via another access tract. However, in general, flexible nephroscopy and ureteroscopy obviates SWL for inaccessible calyces.[31] Although older series have found SWL monotherapy with stent or PCNT acceptable treatment of smaller stone burden (<500 mm^2) with no or minimal dilation of the renal collecting system, most urologists who treat complex stone disease still perform PCNL in this cohort.[50] Open surgery with anatrophic nephrolithotomy (ANL) is not appropriate for most patients with infection or staghorn stones per the AUA guidelines, although it may be considered for cases in which the stone is not expected to be removed by a reasonable number of less invasive procedures. Although open stone removal results in stone free rates similar to those of PCNL, this approach is associated with increased morbidity, convalescence period, hospital stay, narcotic requirement, and complications.[63] A minimally invasive alternative to open ANL is laparoscopic and robotic ANL, which have recently been described.[54–57]

In preparation for surgery, a noncontrast CT scan is obtained to delineate the anatomy and guide the surgical approach. A renogram should be obtained if there is concern for a poorly functioning renal unit, and nephrectomy considered if poor function is confirmed and the contralateral kidney is normal.

Patients with suspected infection stones are at increased risk for infectious complications after PCNL. Preplacement of PCNT allows for drainage, aspiration, and culture of stagnant and infected urine. By administering a course of antibiotics based on this pelvic urine culture, some have shown a decreased rate of postoperative bacteremia, systemic inflammatory response syndrome (SIRS), and sepsis,[64,65] which is likely because stone culture results correlates more closely with renal pelvic than bladder culture results.[66] In a retrospective review of 219 patients, Benson and colleagues[64] reported a 6% rate of SIRS/sepsis at the time of PCNL in those undergoing concurrent PCNT placement versus none in those undergoing preplaced PCNT.

If bladder urine culture results are positive, patients undergoing stone treatment without preplaced PCNT should be treated with a course of preoperative antibiotics with the goal of sterilizing the urine. For those patients without positive results on preoperative urine culture, current AUA guidelines recommend limiting perioperative

antibiotics to less than 24 hours except for those patients with external urinary catheters present before surgery, with risk factors (ie, advanced age, anatomic abnormalities of the urinary tract, poor nutritional status, tobacco use, chronic corticosteroid use, immunodeficiency, or prolonged hospitalization), or with bacteriuria.[67] However, several series have shown significant reduction in postoperative sepsis by administering all patients undergoing PCNL a prophylactic course of antibiotics.[68,69] Mariappan and colleagues[69] found that 52 patients who had dilated collecting systems, stone burden greater than 2 cm, and no confounding factors predisposing to UTIs who received a 1-week course of ciprofloxacin before PCNL had a 3-fold lower risk of postoperative UTI and SIRS than 46 patients who received standard perioperative antibiotics on the day of surgery. Bag and colleagues[68] prospectively randomized 101 patients with greater than 2.5-cm kidney stones and/or hydronephrosis with sterile preoperative urine cultures to a 7-day course of nitrofurantoin versus no antibiotics before PCNL and found a statistically significant lower rate of postoperative SIRS (19% vs 49%), endotoxemia (18% vs 42%), positive result on kidney urine culture (0% vs 10%), and positive result on stone culture (8% vs 30%) in the arm receiving nitrofurantoin. Although these 2 small series support a week of preoperative antibiotics before PCNL, larger, prospective, randomized studies are underway to better elucidate the risks and benefits of empiric antibiotics used in this setting.

Given the known discordance between results of bladder urine culture and stone culture, strong consideration should be given to sending a sample for stone culture to help target antibiotic therapy if the patient develops a postoperative infection. Multiple series have examined the relationship between results of preoperative urine culture from the bladder and kidney stone culture and found poor correlation between the two.[70,71] One series by Eswara and colleagues[70] reported on 328 consecutive patients who underwent stone surgery and found for those 11 patients who developed sepsis, readmission urine culture result correlated with stone culture result in 64% of cases and with preoperative urine culture result in only 9% of cases (P = .02). A stone culture at the time of surgery may be helpful to guide antibiotic therapy in the setting of postoperative UTI and/or urosepsis.

Obstructive Pyelonephritis

Although older series may support withholding emergency decompression in patients with fever and obstructing urolithiasis,[72] it is clear that decompression with retrograde ureteral stent placement or PCNT is imperative to decrease morbidity and mortality.[12] Some have theorized that ureteral stent placement is inferior to PCNT because of the risk of exacerbating infection via stone manipulation and by providing suboptimal drainage compared with a larger-caliber nephrostomy tube. Pearle and colleagues[73] randomized 42 consecutive patients with obstructing ureteral stones and clinical evidence of infection to drainage with PCNT or retrograde ureteral stent placement and found that neither modality was superior in promoting rapid recovery after drainage, although ureteral stent placement was found to be more than twice as costly as PCNT ($1137 vs $2401). The only benefit of PCNT versus ureteral stent placement in this setting was found as a secondary end point from a series out of Syria, which reported that patients who underwent decompression with PCNT required shorter antibiotic courses than those managed with stents.[74]

Although ureteral stent placement and PCNT have both been shown to be effective methods of decompression, in some circumstances one method is indicated over the other (Table 2). The presence of hemodynamic instability may limit

Table 2
Mode of decompression considerations for obstructive pyelonephritis

Favoring Ureteral Stent	Favoring PCNT
• Interventional radiologist unavailable • Failed PCNT attempt • Uncorrected coagulopathy • Minimal hydronephrosis • Unfavorable anatomy for percutaneous access	• Urologist unavailable • Failed ureteral stent attempt • Difficult retrograde access (ie, urinary diversion, renal transplant) • Inability to access the bladder (ie, urethral stricture, lower extremity contractures) • Steinstrasse and/or large stone burden • Concern for impacted ureteral stone • Inability to tolerate general anesthesia

the use of general anesthesia. Although most urologists place ureteral stents under general anesthesia, several series have shown that retrograde ureteral stent placement under local anesthesia is safe and effective, with less than 10% rate of failure.[75–77] A retrospective review of 119 primary ureteral stent placements reported by Sivalingam and colleagues[75] compared 46 cases undergoing stent placement with local anesthesia with 73 cases with general anesthesia and found no statistical difference in placement failure (1.3% for those under general anesthesia vs 8.7% for those under local anesthesia, $P = .07$) and no complications in either group. However, the cost was 4-fold greater in the group undergoing stent placement with general anesthesia ($30,060 vs $7700).

When attempting ureteral stent placement under local anesthesia, the authors recommend the use of lidocaine jelly and a flexible cystoscope for improved patient tolerance. Patient consent should be obtained for both procedures before being sedated or undergoing anesthesia in the event that the first attempt at decompression fails. This method prevents delay in implementing a secondary procedure that may be time sensitive and life saving.

At the time of decompression, a kidney urine culture should be done. Given the risk of urosepsis after decompression, patients should be observed in a monitored setting such as an intensive care unit. A Foley catheter is also recommended for maximum decompression of the urinary collecting system. After a 1- to 2-week course of culture-specific antibiotics, the patient can be scheduled for definitive stone treatment.[45]

TREATMENT RESISTANCE/COMPLICATIONS
Infection Stones

Patients with infection stones undergoing surgical stone removal are at increased risk of adverse events compared with those undergoing surgery for metabolic stones. Higher rates of infectious and bleeding complications are likely related to bacterial colonization of the stones and chronic inflammation related to persistent infection. Thus, although one would expect similar rates of urinary extravasation (7%), renal pelvis perforation (3%), colonic injury (0.2%–0.8%), and pleural injury (0%–3%) for all patients undergoing PCNL, those with infection stones are likely to experience higher rates of infectious and bleeding complications than the following rates that are typically reported: bleeding (8%), blood transfusion (6%–17%), fever (11%–32%), and sepsis (0.3%–5%).[78,79]

Similarly, although complications for all comers undergoing SWL includes bacteriuria (8%–24%), bacteremia (14%), sepsis (<1–3%), steinstrasse (3%), perinephric hematomas (20%–25%), symptomatic perinephric hematoma (<1%), and gastrointestinal tract injury (2%), patients undergoing SWL for infection stones have even higher risks of these postoperative infectious adverse events.[80–83] Some have even shown that performing SWL in the setting of a staghorn stone with a positive urine culture result and urinary obstruction increases the risk of postoperative sepsis.[83] Similarly, if an infection stone is treated ureteroscopically either because a more invasive approach could not be safely performed or because there was low suspicion for infection stone at the time of surgical planning, these patients are at higher risk for postoperative infectious complications and especially sepsis related to increased intrarenal pressures secondary to irrigation. Use of a ureteral access sheath at the time of ureteroscopy may decrease intrarenal pressures and risks of postoperative systemic infection. Otherwise these patients are at similar risks to other patients undergoing ureteroscopy for urolithiasis, including risks of bleeding (0.3%–2%), stricture (0.5%–3%), ureteral perforation (0%–15%), extravasation (<1%), ureteral avulsion (<0.5%), and steinstrasse (rare).[84] Open ANL is now rarely performed given the development and success of minimally invasive techniques and the morbidity related to this procedure, including the risk of serious complications such as pneumothorax, pulmonary embolism, wound infection, acute tubular necrosis, rhabdomyolysis, hemorrhage, vascular injuries, and urinoma.[53] Of the small series publishing their outcomes of robotic and laparoscopic ANL, reported complications include gross hematuria requiring continuous bladder irrigation, blood transfusion, splenic injury necessitating splenectomy, and vascular fistula.[54,56,85]

Obstructive Pyelonephritis

Patients with obstructive pyelonephritis are at risk to develop urosepsis and its sequelae, including acute kidney injury and death. Mortality rates for patients with obstructive pyelonephritis and sepsis are reported at 9% for those undergoing surgical decompression and 19% for those without decompression.[12] Potential complications related to nephrostomy tube placement include bleeding, although severe bleeding requiring transfusion is rare (1%–3%); liver, splenic, or pleural injury (0.1%–0.3%); and rarely colonic or small-bowel injury.[86,87] Ureteral stent placement can be complicated by ureteral perforation and malposition requiring another procedure for decompression. In addition, ureteral stents can cause

significant bother specifically related to urinary symptoms. Quality of life has been shown to be superior for patients with ureteral stones managed with PCNTs than for those with ureteral stents.[74,88]

EVALUATION OF OUTCOMES AND LONG-TERM RECOMMENDATIONS
Infection Stones

PCNL monotherapy stone free rates range from 82% to 93%.[50,89] Lower stone free rates have been reported with SWL and PCNL combination therapy ranging from 67% to 78% even when PCNL is last.[49,50] Lam and colleagues[50] report a stone free rate of 92% for renal stones less than 500 mm^2 that were in a nondilated collecting system treated with SWL monotherapy in a series of 12 patients. Stone free rates after open ANL are reported to be high, ranging from 80% to 100%.[90,91] Stone free rates after pure laparoscopic ANL are reported at 80% to 88%,[85,92] whereas early experience with the robotic-assisted laparoscopic approach reports fairly low stone free rates at 29% to 33%.[54,55]

The presence of residual stone fragments in patients with infection stones composed of struvite and/or calcium carbonate apatite significantly increases the risk of stone recurrence, with a 0% to 10% recurrence rate for those who are stone free postoperatively versus 40% to 85% in the setting of residual stone fragments.[20,29] Patients who are rendered stone free have a lower rate of postoperative UTI (38%) versus those with residual fragments (64%).[29]

After surgery, preventative measures may be helpful including dietary modifications as previously described in the nonpharmacologic section and urinary acidification and urease inhibitors as described in the pharmacologic section of this article. Sterilization of the urine with antibiotics may help decrease stone recurrence, as persistent infection is known to increase the risk of stone recurrence. However, there is not much more than anecdotal evidence of this approach in the literature, and the best regimen in terms of antibiotic selection, duration, and dosing is unknown. Antibiotic use in this setting can be even more complicated when stone and/or renal pelvic urine cultures resistance patterns show no oral options. For those patients with secondarily infected metabolic stones, a full metabolic workup with a 24-hour urine study should be performed. Metabolic evaluation may also be beneficial in patients with infection stones given the findings of a recent series comparing postoperative stone events in patients with struvite stones with and without metabolic evaluation and directed medical therapy. In this series, 39 patients with pure and mixed struvite stones who underwent metabolic evaluation and directed treatment had significantly less stone events postoperatively compared with 17 patients with pure struvite stones and no metabolic workup or management.[93]

Obstructive Pyelonephritis

Vahlensieck and colleagues[14] reported on their experience with 57 patients treated for obstructive pyelonephritis during a 5-year period and found that 32% go on to have recurrent UTIs and 11% experience recurrent obstructive pyelonephritis over a 5-year follow-up period. For those patients with recurrent UTIs and no obvious cause that can be definitively treated (ie, incomplete bladder emptying secondary to benign prostatic hypertrophy), prophylactic antibiotics may be beneficial. Metabolic evaluation is recommended even in patients with first-time stone formation who have a history of obstructive pyelonephritis given the potential risk of sepsis with future stone events.

SUMMARY/DISCUSSION
Infection Stones

Infection stones are struvite and/or calcium carbonate apatite in composition and occur as a result of UTI with urease-producing bacteria. Surgery with the aim of complete stone removal is the mainstay of treatment. PCNL is the treatment of choice for most patients with large infection stones per AUA guidelines. In certain circumstances, other surgical approaches including combination therapy for SWL with PCNL, SWL monotherapy, ureteroscopy, and open and laparoscopic/robotic approaches may be appropriate. A course of preoperative antibiotics has been shown to decrease the rate of SIRS/sepsis after PCNL. Nonsurgical approaches with dietary measures, urease inhibitors, and dissolution therapy may be useful adjuncts to surgical intervention or as a primary treatment of those who are medically unfit to undergo a surgical procedure.

Obstructive Pyelonephritis

Obstructing ureteral stones with concurrent UTI is a urologic emergency and requires immediate decompression, broad-spectrum antibiotics, and close monitoring for urosepsis. Obstructive pyelonephritis with sepsis without decompression has a 19% mortality rate. PCNT and retrograde ureteral stenting are both adequate for decompression. Long-term interventions to prevent recurrent infections and stones is useful given the high rate of recurrent UTIs and 10% risk of recurrent obstructive pyelonephritis in these patients.

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