Upper Urinary Tract Infections

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Purpose

The purpose of this course is to describe the pathophysiology, risk factors, types of infections, symptoms, and treatment of upper urinary tract infections and to explain diagnostic procedures.

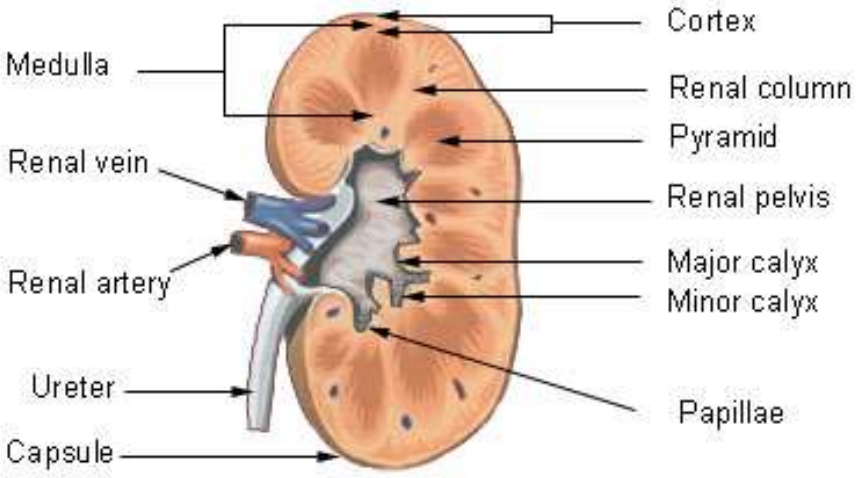
Goals

Upon completion of this course, the healthcare provider should be able to:

- Describe the anatomy of the kidney.
- List at least 4 pathogenic agents often associated with acute pyelonephritis.
- Describe at least 5 common symptoms of acute pyelonephritis as well as age-related differences in symptoms.
- Discuss treatment options for acute pyelonephritis.
- Discuss the causes of chronic pyelonephritis.
- Discuss at least 3 complications associated with chronic pyelonephritis.
- Discuss treatment options for chronic pyelonephritis.
- Discuss the difference between renal abscess and perirenal abscess.
- Describe at least 4 risk factors for development of renal abscesses.
- Discuss treatment options for renal and perirenal abscesses.
- Discuss normal and abnormal urinalysis results.
- Discuss normal and abnormal renal function tests.
- Describe at least 6 different diagnostic procedures.

Introduction

Frontal section through the Kidney



The kidneys are located on either side of the vertebral column at T-12 to L3. Typically, an adult kidney is about 5 inches long and weighs 4 to 6 ounces. Kidneys are enclosed in a fibrous membrane called the capsule and surrounded by fat and connective tissue. Ureters and vessels enter through the hilus, which opens to the kidney pelvis. The outer layer of the kidney is the cortex and the inner layer, the medulla, which consists of a number of pyramids separated by renal columns. The pyramid apices are the papillae, through which urine passes into the minor and major calyces and into the pelvis and ureters.

The functional unit of the kidney is the nephron (about 1 million in each kidney). About 25 to 30% of the cardiac output (1200 ml) flows through the kidneys each minute. The primary function of the kidneys is to filter blood and maintain internal homeostasis. Upper urinary infections can impair this function. Because the blood flows through the kidney, bacteria in the kidneys can be readily transmitted into the blood, so upper urinary tract infections pose considerable risk of developing systemic infections.

The urinary tract comprises the kidneys, ureters, bladder, and urethra. Urinary tract infections (UTIs), caused by pathogenic microorganisms invading the urinary tract are classified as lower UTIs if they affect the bladder (cystitis) or urethra (urethritis) while upper urinary tract infections affect the kidney. **[See CE course: Lower Urinary Tract Infections.]** Upper urinary tract infections include acute and chronic pyelonephritis, renal abscess, and perirenal abscess.

Upper UTIs can develop from invasion per the ureters from an ascending lower urinary tract infection or from a systemic infection spread by the blood to the kidneys. Because static urine provides a good medium for bacterial growth, obstruction from tumors, calculi, strictures, and benign prostatic hypertrophy can increase the risk of infection. Additionally, an incompetent ureterovesical valve may allow reflux of urine from the bladder into the kidneys.

Pyelonephritis, Acute

Acute pyelonephritis is inflammation of the renal pelvis, tubules, and interstitial tissue. While bacterial infection is the most common cause, pyelonephritis can also occur from fungi, protozoa, or viruses. Most cases of pyelonephritis occur when bacteria from a lower tract infection ascends through the ureters into the kidneys although it may result from systemic infection. Pyelonephritis may result in small cortical abscesses (sub-capsular) surrounded by areas of hyperemia.

The most common pathogenic agent is *Escherichia coli*, but other common agents include *Klebsiella, Proteus,* or Enterobacter species. If pyelonephritis develops from complicated lower urinary tract infections or systemic infections, other agents may include *Staphylococcus aureus, Pseudomonas aeruginosa* and *Acinetobacter* spp. Resistant strains are frequently encountered. Infectious agents may also include MRSA, *Enterococcus* spp. (including VRE), and *Candida spp*. Infections may be polymicrobial, especially if chronic urinary catheter or stents are present.

Risk factors are similar to those for lower urinary tract infections. Those who are pregnant, immunocompromised, or diabetic are especially at risk of developing chronic disease or other complications. Pyelonephritis can cause abscesses to form, sepsis, and kidney failure, so adequate treatment is critical. Usual diagnostic procedures include blood studies, urinalysis, and urine cultures. Urosepsis, a systemic infection, can arise from pyelonephritis. Septic shock, leading to death, can result from infection with Gram-negative organisms.

Symptoms vary widely, but people usually appear acutely ill. Pyelonephritis may be uncomplicated or complicated. Complicated infections are less responsive to treatment. If pyelonephritis arises from a lower urinary tract infection, people may exhibit a combination of lower and upper urinary tract infection symptoms:

- Dysuria and frequency.
- Hematuria.
- Flank pain and/or low back pain.

- Fever and chills.
- Costovertebral angle tenderness.
- Nausea and vomiting.

Symptoms may vary somewhat according to age:

- Infants: Change in feeding habits
- Older adults: Change in mental status.
- Young women: Symptoms consistent with lower urinary tract infection.

Treatment options

Treatment usually continues for 10 to 14 days. Commonly used antibiotic agents include:

- Ceftriaxone (Rocephin®) 1-2 g IV daily or divided doses BID.
- Tobramycin (Nebcin®) with dosage varying, beginning with 3 mg/kg IV or IM q 8 hours.
- Cephalexin (Keflex®) 250 to 1000 mg q 6 hrs. for 10 to 14 days.
- Ertapenem (Ivanz®) 1 g qd for 14 days IV or 7 days IM.

Additional treatment may include antipyretics (ibuprofen, acetaminophen) and analgesia and antispasmodics to relieve pain. In some cases, symptomless infection recurs, leading to chronic infection, so follow-up urine cultures should be done 2 weeks after completion of antibiotic therapy.

If infection persists, the patient may need to continue antibiotics for about 6 weeks. Hydration is especially important to flush the kidneys and promote healing. If patients are unable to take adequate oral fluids because of nausea and vomiting, then they may require IV fluids.

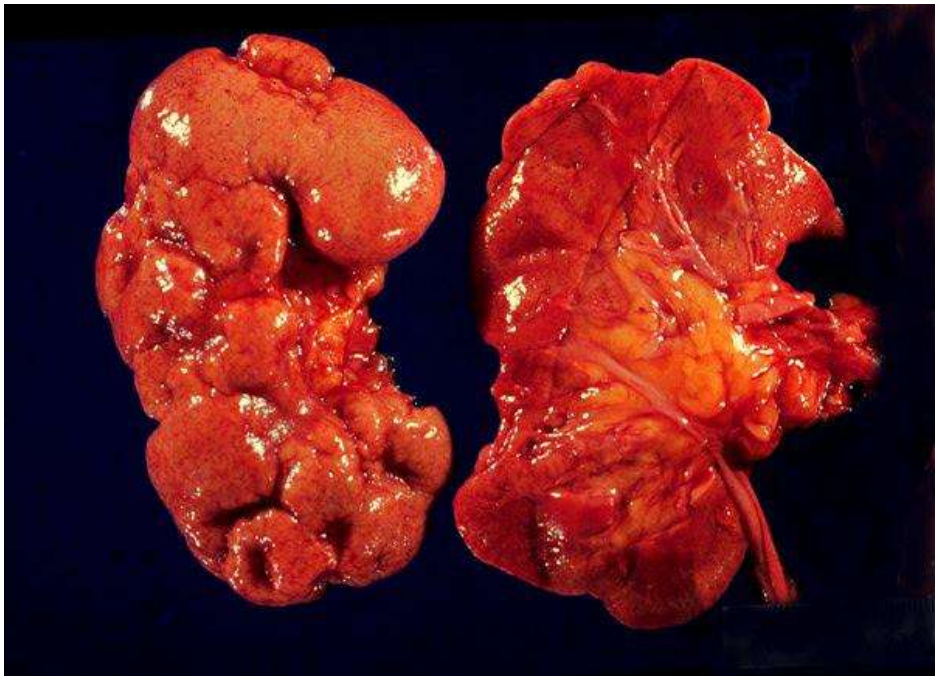
Women who develop acute pyelonephritis during pregnancy are usually hospitalized for 2 to 3 days for IV antibiotic therapy and then continue with oral antibiotics after they become afebrile and show improvement in condition.

Pyelonephritis, Chronic

The primary problem with chronic pyelonephritis is that people are often essentially symptomless unless an exacerbation occurs. People may have non-specific symptoms of poor appetite, fatigue, general malaise, polyuria, excess thirst, and weight loss. Children may exhibit failure to thrive.

Chronic pyelonephritis usually results from recurrent bouts of infection but it may occur without a history of infection. Chronic pyelonephritis most often occurs in those with anatomic abnormalities, such as obstructions or vesicoureteral reflux. Because of this, chronic pyelonephritis is more common in infants and young children (<2 years) than in older children or adults.

The chronic infection causes fibrous, irregular scarring and damage to the kidney, resulting in eventual kidney failure and end-stage renal disease (ESRD) from loss of nephrons if both kidneys are involved. The kidneys shrink and become misshapen. Other complications include hypertension and kidney stones (resulting from chronic infection with urea-splitting organisms).



Diagnostic procedures include IV urograms, voiding cystourethrogram (VCUG), renal scan, ultrasound, cystoscopy, CT scan, and renal biopsy. Kidney function is assessed through creatinine clearance, blood urea nitrogen, and creatinine levels. Urine cultures determine if bacteria is present in the urine.

Treatment options Long-term prophylaxis with antibiotics may reduce scarring related to chronic bouts of infection although careful monitoring is necessary as some drugs may be toxic to kidneys with impaired functioning. Usually patients are encouraged to have 3 to 4 L of fluid intake daily in order to flush the kidneys.

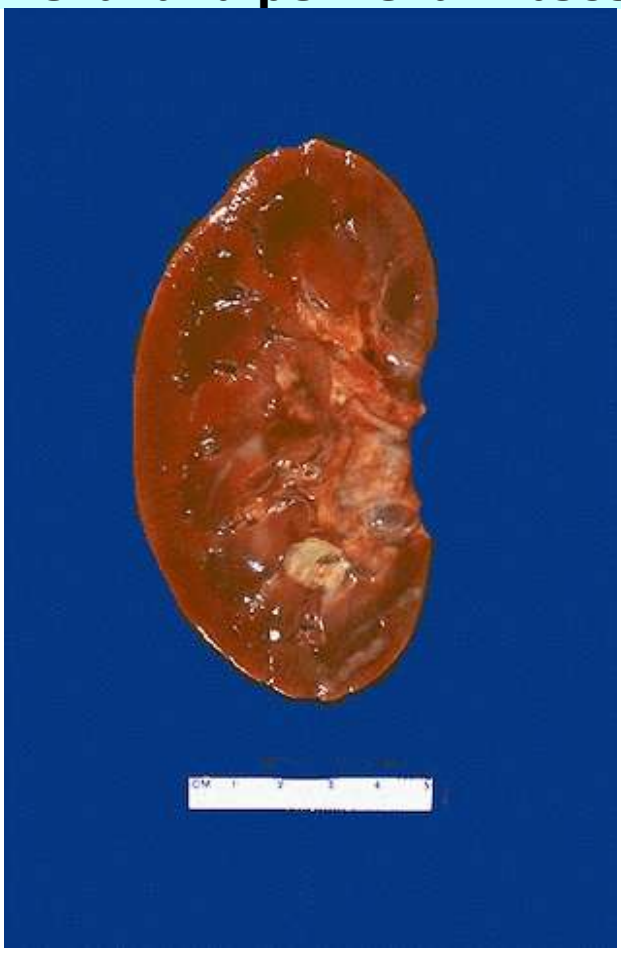
Treatment may vary somewhat depending upon the degree of damage to the kidneys. Oral antibiotics include:

- Amoxicillin 500 mg q 8 hrs. (125 mg q 8 hr. for children).
- Cephalexin (Keflex®) 500 mg QID (25-50 mg/kg/d in 4 doses for children).
- TMP 160 mg/SMZ 800 mg BID (8-12 mg/kg/d TMP in 2 doses).
- Nitrofurantoin 50-100 mg q HS (adult only).

Other treatments include:

- Protein restriction.
- ACE inhibitors for hypertension.

Renal and perirenal Abscess



Renal or perirenal abscess is caused by systemic spread of infection to the kidney or from ascending urinary tract infections. In renal abscess, lobar necrosis occurs and purulent material develops in an enclosed cavity. Cortical abscesses result from *Staphylococcus* aureus in about

90% of cases and almost always result from systemic infection. Infection can spread from multiple skin abscesses, such as may occur with intravenous drug users.

Corticomedullary abscesses usually develop from ascending UTIs:

- Acute focal bacterial nephritis/pyelonephritis: Well-localized kidney infection.
- Emphysematous pyelonephritis: Necrotizing type of nephritis.
- Xanthogranulomatous pyelonephritis: Chronic infection associated with renal calculus.

Cortical abscesses are more common in males (75%), but cortico-medullary abscesses occur equally in males and females. Renal abscesses occur more frequently than perirenal. In perirenal abscess, the purulent material forms from perirenal fat necrosis. In many cases, perirenal abscesses develop from a corticomedullary abscess that ruptures the capsule.

Risk factors include recurrent UTIs, renal calculi, urologic procedures (ureteroscopy), vesicoureteral reflux, and diabetes. Patients with abscesses typically develop non-specific symptoms or symptoms consistent with cystitis or pyelonephritis, so patients may be misdiagnosed. Typical symptoms include:

- Fever and chills.
- Dysuria.
- Frequency.
- Hematuria.
- Abdominal and/or flank pain.
- Weight loss.
- General malaise.

Diagnosis results from increased white count, urine culture and sensitivities, x-ray, ultrasound, and CT scan. In some cases, a palpable mass may be evident. Renal or perirenal abscess should be considered if patients show no response to antibiotic therapy within 5 days.

Treatment includes percutaneous drainage of the abscess and IV antibiotics, usually for Gram-negative organisms. If diagnosis or an enclosed renal abscess is made early, IV antibiotic therapy without drainage may be adequate. Perirenal abscess requires open surgical drainage

Treatment options

If treatment occurs before serious damage to the kidney, then recovery is good; however, some have underlying chronic kidney infection and may develop renal failure. Identifying the underlying cause of the renal abscess, such as ureterovesical reflux, and treating it is essential to preventing recurrence. In severe cases, nephrectomy may be necessary.

Treatment with antibiotics varies according to the result of cultures, as treatment must be specific to the infective agent. Dosage may need to be adjusted if renal insufficiency is present. Intravenous antibiotics commonly used include:

- Piperacillin and tazobactam sodium (Zosyn®) 3.375 g IV q 6 hours. (No pediatric dose.)
- Ticarcillin and clavulanate (Timentin®) 3.1 g IV q 4-6 hours (50 mg/kg IV q 4-6 hours for children, not to exceed 3.1 g).
- Nafcillin (Nafcil®) 102 g IV q 4 hours. (No pediatric dose.)
- Ceftazidime (Fortaz®) 1-2 g IV/IM q 8 to 12 hours (30-50 mg/kg IV q 8 hours for children).
- Cefepime (Maxipime®) 2 g IV q 12 hours. (No pediatric dose.)
- Ciprofloxacin (Cipro®) 400 mg q 12 hours or 500 mg po q 12 hours. (No pediatric dose.)
- Levofloxacin (Levaquin®) 250-500 mg/day. (No pediatric dose.)
- Gentamicin 2 mg/kg initially followed by 1.7 mg/kg IV/IM q 8 hours (2-2.5 mg/kg IV/IM q 8 hours for children).
- Amikacin (Amikin®) 7.5 mg/kg IV/IM q 8 hours for adults and children.
- Tobramycin (Nebcin®) 2 mg/kg followed by 1.7 mg/kg IV/IM q 8 hours (2-2.5 mg IV/IM q 8 hours).

Diagnostic procedures

A wide range of diagnostic procedures is used with upper urinary tract infections. The initial tests for pyelonephritis are the urinalysis and urine cultures, but if the infection does not respond to treatment or recurs or complications occur, then further testing is indicated to determine the underlying cause and progress of kidney disease.

Urinalysis	
Color	Pale yellow/ amber and darkens when urine is concentrated or other substances (such as blood or bile) or present.
Appearance	Clear but may be slightly cloudy.
Odor	Slight. Bacteria may give urine a foul smell, depending

	upon the organism. Some foods, such as asparagus, change odor.
Specific gravity	1.015 to 1.025. Determines kidney's ability to concentrate urinary solutes. SpGr compares the weight of urine (in particles) in comparison to distilled water. High fluid intake lowers the SpGr and low intake raises it. In kidney disease, SpGr often does not vary. SpGr may increase if protein levels increase or if there is fever, vomiting, or dehydration.
pH	Usually ranges 4.5 to 8 with average of 5 to 6. Medications, such as Mandelamine, some foods, such as cranberries, and Vitamin C may make urine acid (<7 pH). Alkaline urine (>7) occurs with bacteriuria, urinary tract infections, as well as kidney and respiratory diseases.
Sediment	Red cell casts from acute infections, broad casts from kidney disorders, and white cell casts from pyelonephritis. Leukocytes > 10 per ml^3 are present with urinary tract infections. Crystals should not be present.
Glucose, ketones, protein, blood, bilirubin, and nitrate	Negative. Urine glucose may increase with infection (with normal blood glucose). Frank blood may be caused by some parasites and diseases but also by drugs, smoking, excessive exercise, and menstrual fluids. Increased red blood cells may result from lower urinary tract infections.
Urobilinogen	0.1-1.0 units.

Urine culture and sensitivities Culture and sensitivities are done to identify infective agents and determine which antibiotics they are sensitive to. Results should show <10,000 organisms/ml of urine. Results of >10,000 are considered evidence of infection. However, care must be taken when obtaining a urine sample because bacteria found in the urine sample may result from pathogenic microorganisms or contamination from skin or improper handling. Urinary cultures are positive for urine infection if the organism is found on Gram stain and if two urine cultures isolate the same organism with >102 colonies/ml of urine in catheterized specimens or <105 colonies/ml of urine with patients receiving appropriate antibiotics.

Blood cultures If bacteremia is suspected, then blood cultures are warranted to determine the infective agent and

initiate therapy before sepsis occurs.

Renal function studies	
Specific gravity	1.015-1.025.
Osmolality (urine)	350-900mOsm/kg/24 hours. Osmolality measures the concentration or dilution of the number of electrolytes or other molecules per kg/urine. Osmolality increases with dehydration; osmolality decreases with fluid retention. Urine is dilute and the osmolality is fixed with kidney disease.
Osmolality (serum)	275-295 mOsm/kg.
Uric acid	Male 4.4 to 7.6, Female 2.3 to 6.6. Levels increase with renal failure.
Creatinine clearance (24-hour)	Male 85 to 125 mL/min/1.73 m^2, Female 75 to 115 mL/min/1.73 m^2. Evaluates the amount of blood cleared of creatinine in 1 minute. Approximates the glomerular filtration rate.
Serum creatinine	0.6-1.2mg/dL. Increases with impaired renal function, urinary tract obstruction, and nephritis. Level should remain stable with normal functioning.
Urine creatinine	Male 14 to 26 mg/kg/24 hr., Female 11 to 20 mg/kg/24 hr.
Blood urea nitrogen (BUN)	7-8 mg/dL (8-20 mg/dL >age 60). Increase indicates impaired renal function, as urea is end product of protein metabolism.
BUN/creatinine ratio	10:1. Increases with hypovolemia. With intrinsic kidney disease, the ratio is normal, but the BUN and creatinine are increased.

Numerous procedures are done to evaluate anatomy and function. Especially with chronic pyelonephritis, identifying the underlying cause of the disorder is essential to preventing further damage to the kidney.

Renal function procedures	
Intravenous pyelogram/ urograom	The IVP involves IV injection of dye followed by a series of X-rays to show the urinary structures. Bowel prep is usually done the evening prior to the procedure to empty the colon of feces and gas that may interfere with imaging. Following the procedure, the person must force fluids or receive IV fluids to flush the contrast material.

Retrograde pyelogram	The retrograde pyelogram is done per cystoscopy. Ureteral catheters are threaded through the cystoscope into the ureters and up to the kidney pelvises so dye can be injected through the catheters. This procedure may be done under anesthesia because of the discomfort involved.
Voiding cystourethrogram	The VCUG involves catheterizing the bladder and filling it with contrast material under fluoroscopy and then having the person urinate. During urination, the anatomy and physiology of the urinary system is observed. If contrast flows into the ureters and/or kidneys, this indicates vesicoureteral reflux.
Ultrasound	Ultrasound is often used initially to rule out masses and obstructions but it is less useful that CT. Ultrasound is used with VCUG to diagnose vesicoureteral reflux.
CT scan	CT scans, such as the nephrotomogram, are especially valuable to show obstructions and abscesses. The CT scan can show subtle differences in density and can be used with contrast media, so CT scans provide more information than ultrasound.
Cystoscopy	The primary purpose of the cystoscopy is to evaluate the interior of the bladder, to obtain biopsies, and remove calculi. It can also be used from the cystogram and to insert ureteral catheters.
Cystogram	Done with cystoscopy, the bladder is instilled with contrast material. This is used to evaluate anatomy and vesicoureteral reflux.
Renal scan	Radioisotopes are injected IV with radiation detector probes over the kidney. The renal scan is done to show blood flow, glomerular filtration rate, tubular function, and excretion. The scan shows the size and shape of the kidney, blood perfusion, and ability to secrete urine.
Renal biopsy	Renal biopsy may be done with CT or ultrasound guidance in order to obtain kidney tissue to determine type of disease or progress.
Renal arteriogram	Contrast material is injected directly into the renal artery per catheter inserted into femoral artery in order to visualize blood vessels in the

	kidney.

Summary

Upper urinary tract infections (UTIs) can develop from an ascending lower UTI or a systemic infection spread by the blood to the kidneys. Upper UTIs include:

- Acute pyelonephritis: Inflammation of the renal pelvis, tubules, and interstitial tissue, usually caused by bacteria. Most infections arise from ascending lower UTIs, with the most common pathogenic agent *E. coli* although a wide range of bacteria may cause infection. People appear acutely ill, with dysuria, pain, fever, chills, pain, and nausea and vomiting. Treatment with oral antibiotics for 10-14 days is usually prescribed.
- Chronic pyelonephritis: Recurrent infections that cause fibrous, irregular scarring and damage to the kidney. Chronic pyelonephritis is most common in those with anatomic abnormalities, so it occurs most often in infants and young children. Symptoms may be non-specific or similar to acute pyelonephritis. IV antibiotic therapy is indicated.
- Renal and perirenal abscesses: May result from ascending urinary tract infections or systemic infections (most common). Cortical abscesses most often result from systemic *Staphylococcus aureus* infection. Corticomedullary abscesses usually develop from ascending UTIs. Perirenal abscesses may result from corticomedullary abscess that ruptures the capsule. Symptoms are similar to pyelonephritis. Treatment may include percutaneous or open surgical drainage as well as IV antibiotics specific to causative agent.

A wide range of diagnostic procedures is used, depending on the type of infection. Common laboratory tests include urinalysis, urine culture and sensitivities, blood cultures, and renal function tests. Other procedures include IVP, retrograde pyelogram, VCUG, ultrasound, CT scan, cystoscopy, cystogram, renal scan, renal biopsy, and renal arteriogram.

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