Sterile Pyuria
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Pyuria is defined as the presence of leukocytes in the urine and suggests that inflammation exists in the urinary tract. Polymorphonuclear leukocytes are the predominant cell type in urinary tract infections. Monocytes, lymphocytes and eosinophils suggest interstitial nephritis. Inflammation of the adjacent structure of prostate and urethra can also cause sterile pyuria. Noninfectious systemic diseases, structural/abnormalities of the urinary tract, and adverse effects of drugs can also produce sterile pyuria (Table 1). One common cause of sterile pyuria is that of a chronic indwelling foley catheter which may cause bladder wall irritation and subsequent low grade pyuria.

Infectious diseases with sterile pyuria include microorganisms not detected by standard bacteriological media including Mycobacterium tuberculosis, fungi, viruses (herpesviruses, adenoviruses, varicella-zoster virus), leptospirosis, brucellosis, and parasites (Schistosomiasis). Fastidious bacteria such as Hemophilus influenzae will also not be detected by routine cultures. Systemic fungal infection such as Cryptococcus neoformans, Blastomyces dermatitidis or Coccidioides immitis involving the prostate or epididymitis can cause sterile pyuria in the urine. Urinary tract infection treated with antibiotics may show pyuria for up to a week following discontinuation of the antibiotics. A perinephric abscess may lead to subsequent sterile pyuria.

Systemic causes of sterile pyuria include diabetic nephropathy and sickle cell disease with papillary necrosis, sarcoidosis with granulomatous nephritis, Kawasaki disease with urethral involvement, systemic lupus erythematosus with tubulointerstitial nephritis, reactive arthritis, and cyanotic congenital heart disease with glomerular and tubular dysfunction.

Structural and physiological causes of sterile pyuria include polycystic kidney disease, vesicourethral reflux, hydronephrosis, stones, retained foreign body, post transurethral resection prostate, genitourinary trauma, extreme dehydration, and hyperchloremic metabolic acidosis. Intrinsic urinary tract pathology leading to sterile pyuria include papillary necrosis secondary to obstructive uropathy, tubulointerstitial nephritis, glomerulonephritis, interstitial cystitis, renal transplant rejection, and urinary tract tumors.

Many drugs have been associated with interstitial nephritis (Table2). Medication groups most commonly implicated in drug-induced interstitial nephritis include NSAIDS and antibiotics. Antibiotics cause acute interstitial/tubulointerstitial nephritis through two different mechanisms: a drug induced hypersensitivity process and direct action due to drug accumulation. Hypersensitivity can occur from allergic interstitial nephritis secondary to an immunocomplex allergic reaction (beta-lactams, rifampin, vancomycin), and granulomatous interstitial nephritis secondary to a cell mediated allergic reaction.
(ciprofloxacin, penicillin). The triad of rash, fever, and eosinophilia are most commonly seen in beta-lactam associated acute interstitial nephritis. Anti-staphylococcal penicillin’s such as naftilin or oxacillin are the most common culprit. The urinalysis with acute interstitial nephritis typically shows leukocyte casts in addition to leukocytes. Eosinophiluria is suggestive of acute interstitial nephritis.
Table 1. Differential Diagnosis of Sterile Pyuria

**Contamination during collection**
- Vaginal secretions
- Foreskin secretions

**Infectious Diseases**
- Urethritis
- Tuberculosis and other mycobacterial infections
- Viral cystitis (herpes, adenoviruses, varicella-zoster)
- Leptospirosis
- *Hemophilus influenzae*
- Brucellosis
- Urinary schistosomiasis
- Systemic fungal infections
- Partially treated urinary tract infections

**Infections of structures adjacent to the urinary tract**
- Appendicitis
- Diverticulitis
- Prostatitis
- Perinephric Abscess

**Noninfectious Diseases**
**Systemic Causes**
- Diabetic nephropathy
- Sickle cell disease nephropathy
- Sarcoidosis
- Kawasaki disease
- Reactive Arthritis
- Systemic lupus erythematosus
- Cyanotic congenital heart disease

**Structural and Physiologic Causes**
- Polycystic kidney disease
- Vesicourethral reflex
- Nephrocalcinosis/urolithiasis
- Retained foreign body
- Transurethral resection prostate
- Hydronephrosis
- Genitourinary trauma
- Extreme dehydration
- Hyperchloremic metabolic acidosis

**Intrinsc Urinary Tract Pathology**
- Papillary necrosis
- Obstructive uropathy
- Tubulointerstitial diseases
  - Interstitial nephritis
  - Renal transplant rejection
- Glomerulonephritis
- Interstitial cystitis
- Renal/ureteral/bladder tumors

(Modified from Kunin CM, Urinary Tract Infections, Williams and Wilkins, 5th edition, 1997)
Table 2. Drug-related Cause of Sterile Pyuria

Drug-induced tubulointerstitial nephritis
- NSAIDS
- Antibiotics
  - Beta-lactams, sulfonamides, rifampicin, tetracyclines, isoniazid, ciprofloxacin, polymyxin, ethambutol, erythromycin, vancomycin, acyclovir, indinavir
- Diuretics
  - Thiazides, furosemide, clorthialidone, triamterene
- Anticonvulsants
  - Carbamazepine, phenytoin, phenobarbital, diazepam
- Hypouricaemics
  - Allopurinol, sulfinpyrazone
- Others
  - Lithium, omeprazole, cimetidine, aspirin, clofibrate, captopril, aldomet, azathioprine

Tubular dysfunction
- Toluene

Papillary necrosis
- NSAIDS

Cystitis
- Cyclophosphamide, NSAIDS, danazol, allopurinol, tranilast (anti-allergic drug)

NSAIDS: Non-Steroidal Anti-Inflammatory Drugs
Reading List


