UROLOGIC STONE DISEASE

THE FIRST EPISODE OF URINARY CALCULI FOR MEN OCCURS AT ~30, RANGE 20-50. FIRST OCCURRENCE IS RARE AFTER 60

WOMEN DEVELOP STONES IN BIMODAL DISTRIBUTION →around 35 and 55

CHILDREN <16 ACCOUNT FOR 7% OF CASES → MOST COMMON CAUSE IN PAEDIATRICS ARE METABOLIC ABNORMALITIES (50%), UROLOGIC ANOMALIES (20%) AND INFECTION (15%) → IMMOBILISATION STONES IN 5%

PATHOPHYSIOLOGY:

- Stone formation is a multistep process that includes:
  - Supersaturation of the urine with urinary solutes
  - Lack of inhibitor substances
  - Urinary stasis
- Increasing the amount of solvent (urine) and decreasing the amount of solute (e.g. calcium, uric acid) can aid in prevention
- Urinary inhibitors such as citrate, magnesium, uromodulin → can prevent crystal precipitation and stone formation
- Free flow of urine can help increase the amount of solvent and wash away crystals
- STASIS can result from:
  - Neurogenic bladder
  - Anatomic anomalies
  - Presence of foreign bodies (e.g. suture)
- ~75-80% of all calculi are COMPOSED OF CALCIUM:
  - Oxalate, phosphate or both
  - Calcium excretion is elevated in conditions that include:
    - Hyperparathyroidism
    - Absorptive and renal hypercalciuria
    - Immobilisation syndrome
  - Oxalate secretion is enhanced in IBD, those with small bowel resection
- 10-15% of stones are STRUVITE (magnesium-ammonium phosphate):
  - These stones are associated with infection by UREA-SPLITTING ORGANISMS
  - Most common cause of STAGHORN CALCULI → form a cast of the renal pelvis
  - Urea-splitting organisms include → proteus, klebsiella, staph
  - Antibiotic penetration into staghorn calculi is poor → potential for urosepsis exists as long as these remain → surgical intervention recommended
- URIC ACID STONES → 10% of urolithiasis
  - ~25% OF PATIENTS WITH GOUT WILL DEVELOP KIDNEY STONE AND THEY OCCUR ~1% PER YEAR AFTER THE FIRST ATTACK

    - Urate stones are RADIOLUCENT
- CYSTINE STONES ARE RARE
- Some medications predispose to stones:
    - Protease inhibitor → INDINAVIR → associated with 4-10% incidence of symptomatic urolithiasis
    - Carbonic anhydrase inhibitors
    - Triamterene
    - Laxative abuse
- With appropriate evaluation, 90% of stones can have cause identified and 85% of calcium oxalate stones can be prevented

Table 97-1 Risk Factors for the Development of Urinary Calculi

Risk Factor	Mechanisms
Bowel disease	Promotes low urine volume; acidic urine depletes available citrate (inhibitor); hyperoxaluria
Excess dietary meat	Creates acidic urinary milieu, depletes available citrate (inhibitor); promotes hyperuricosuria
Excess dietary oxalate	Promotes hyperoxaluria
Excess dietary sodium	Promotes hypercalciuria
Family history	Genetic predisposition
Insulin resistance	Ammonia mishandling; alters pH of urine
Gout	Promotes hyperuricosuria
Low urine volume	Allows solute to supersaturate
Obesity	May promote hypercalciuria; dietary discretions above
Primary hyperparathyroidism	Creates persistent hypercalciuria
Prolonged immobilization	Bone turnover creates hypercalciuria
Renal tubular acidosis (type 1)	Alkaline urine promotes calcium phosphate supersaturation; loss of citrate (inhibitor)

- Pain associated with kidney stones is due to OBSTRUCTION OF A HOLLOW VISCOUS ORGAN (URETER) and SUBSEQUENT HYDRONEPHROSIS CREATING PRESSURE AGAINST GEROTA FASCIA → causing flank pain
    - A migrating, but non-obstructive stone also causes pain
- If unrelieved, irreversible renal damage occurs within 3 weeks with complete obstruction
    - During acute obstruction, most patients have no rise in serum creatinine because the unobstructed kidney functions at up to 185% of its baseline capacity
    - A rise in creatinine in acute obstruction suggests a solitary kidney or preexisting renal disease such that the unobstructed kidney is unable to compensate completely
- The PROBABILITY OF SPONTANEOUS PASSAGE OF STONES IS DETERMINED BY:
    - Size
    - Shape
    - Location
    - Degree of ureteral obstruction

- Most common sites of obstruction:
    - PELVI-URETERAL JUNCTION (PUJ)
    - PELVIC BRIM
    - VESICOURETERIC JUNCTION (VUJ) → this is the most constrictive site of the ureter due to the muscular coat of the bladder
- BASED ON SIZE ALONE:
    - 98% of stones <5mm will pass within 4 weeks without intervention
    - 60% of stones 5-7mm
    - 39% stones >7mm will pass within 4 weeks
    - A measured stone on CT is 88% of actual size

CLINICAL FEATURES:

- CLASSIC SYMPTOM COMPLEX IS:
    - Acute onset of crampy, intermittent pain that originates in the flank and radiates to the groin
    - Pain is visceral in nature
- Patients may demonstrate rebound tenderness (29%), guarding (61%) and rigidity (8%)
- Pain is accompanied by N+V in 50%
- The adrenergic response to pain can result in tachycardia, hypertension and diaphoresis
- Haematuria is present in ~85%, whereas only 30% have gross haematuria
- The location of the pain correlates somewhat with the location:
    - Upper ureter → flank
    - Mid-ureter → lower anterior quadrant of abdomen
    - Distal → groin
- Stones in VUJ can mimic a UTI by causing frequency, urgency and dysuria in 3-24% cases
- Overall → 20-30% of children may have only painless haematuria with urologic stone disease
- HISTORY SHOULD ASCERTAIN:
    - Risk factors for stone development
    - Risk factors for poor stone-related outcome

Table 97-2 Important Historical Features for Poor Outcome with Stone
Renal function at risk
Diabetes
Hypertension
Renal insufficiency
Single kidney
Horseshoe kidney
Transplanted kidney
History of difficulty with stones
Extractions
Stents
Ureterostomy tubes
Lithotripsy
Symptoms of infection
Fever
Hypotension
Systemic illness
Urinary tract infection

- Risk factors for mimickers:
  - AAA → stones do not usually present in men older than 60 and DO NOT CAUSE HYPOTENSION UNLESS THE PATIENT IS SEPTIC. Renal colic is the most common misdiagnosis given to patients with ruptured AAA
  - RENAL ARTERY THROMBOSIS → need to think about it, as early on, no change will be seen as no contrast is given in standard CT KUB

DIAGNOSIS:

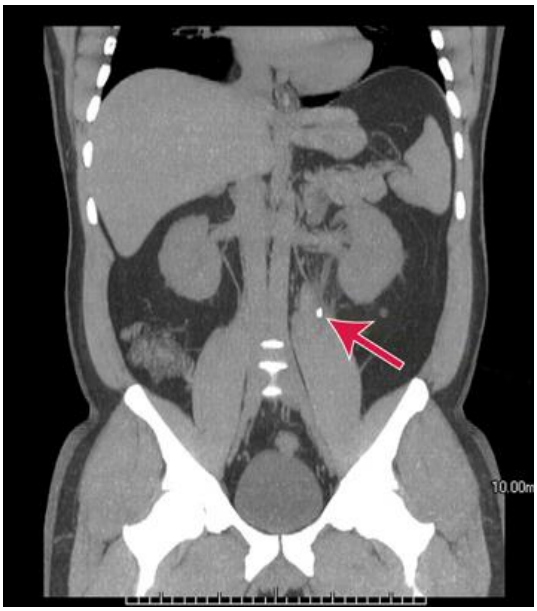
- Diagnosis is clinically suspected, supported with presence of haematuria and imaging confirms the diagnosis with certainty
- LAB EVALUATION:
  - Centres on evaluation for infection, kidney dysfunction and possibility of pregnancy (i.e. consider ectopic and risk of imaging)
  - HAEMATURIA → either its presence or absence can mislead clinicians:
    - 10-15% of patients with nephrolithiasis WILL HAVE NO HAEMATURIA
    - In contrast, of patients with flank pain and haematuria → 24% HAVE NO RADIOGRAPHIC EVIDENCE OF URETEROLITHIASIS
  - Check renal function
  - Unless febrile or systemically ill → FBC does not add much as many patients will have stress demargination and adrenergic response
  - Other tests → Calcium and uric acid → may help aid in diagnosis of the cause of the stone
- IMAGING:
  - Confirms presence of ureteral stone, rules out other diagnoses, defines stone location and assists with management if the stone fails to pass
  - In patients for whom the physician had a high pretest probability, CT showed a stone in only 80% and an alternative diagnosis was revealed in 33%

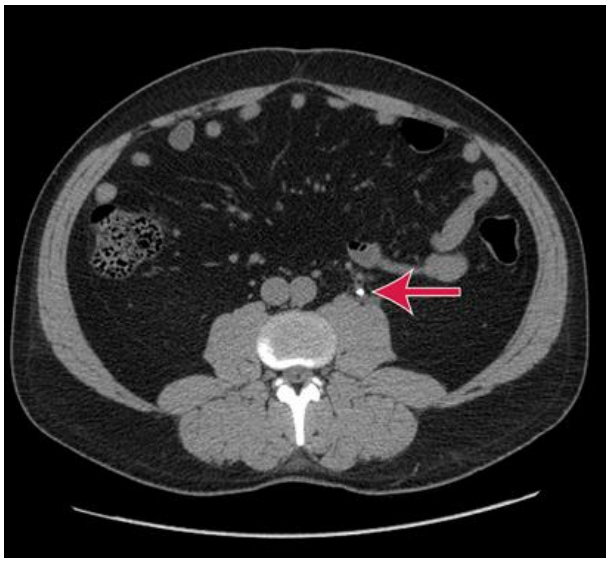
- CURRENT ADVICE IS TO SCAN ON FIRST PRESENTATION OF RENAL COLIC
- As for patients with recurrent renal colic, the need for imaging hinges on:
  - Did the patient have a complication with previous stones?
  - Is the diagnosis in question (?drug seeker, age >50)
  - What is the patient's previous radiation load

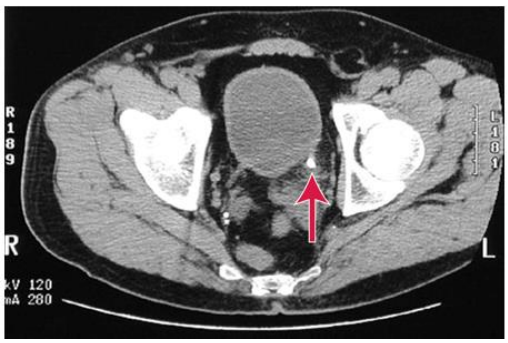
Table 97-3 Ancillary Tests in Urologic Stone Disease

Test	Sensitivity (%)	Specificity (%)	LR+	LR−	Comments
Noncontrast CT	94–97	96–99	24–×	0.02–0.04	Advantages: speed, no RCM, detects other diagnoses
					Disadvantages: radiation, no evaluation of renal function
IV urogram	64–90	94–100	15–×	0.11–0.15	Advantage: evaluates renal function
					Disadvantage: RCM (allergy, nephrotoxicity, metformin)
US	63–85	79–100	10–×	0.10–0.34	Advantages: pregnancy, no RCM, no radiation, no known side effects
					Disadvantages: insensitive in middle third of the ureter, may miss smaller stones (<5 mm)
Plain abdominal radiograph	29–58	69–74	1.9–2.0	0.58–0.64	Advantage: may be used to follow stones
					Disadvantage: poor sensitivity and specificity

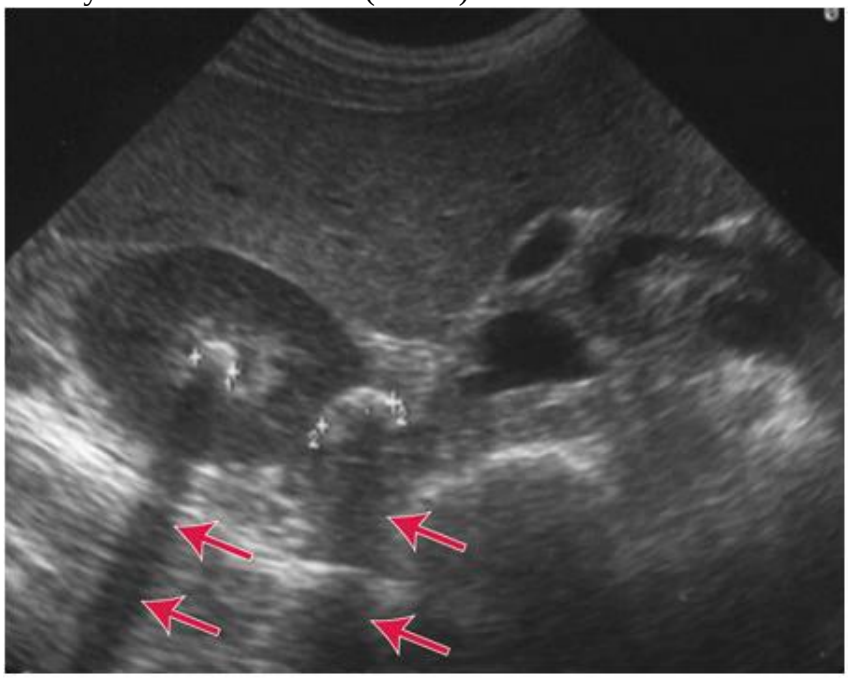
- CT:
  - Both sensitive and specific
  - Shows secondary signs of ureteral obstruction → ureteral dilation, stranding of perinephric fat, dilatation of the collecting system, renal enlargement
  - In combination, unilateral ureteral dilation and perinephric stranding is 96% for stone disease and if both are absent, NPV 93-97%







- IV UROGRAPHY:
  - Yields information about renal function and anatomy → detects calculi with modest sensitivity but excellent specificity → can be an adjunction to CT if functional information and knowledge on the degree of obstruction is required
- PLAIN ABDOMINAL RADIOGRAPHS:
  - Approximately 90% of urinary calculi are RADIOOPAQUE because calcium phosphate and oxalate have density similar to bone
  - Urate stones are essentially radiolucent as are most stones related to medications
  - Plain film is neither sensitive nor specific enough to rule in or rule out a diagnosis of ureterolithiasis → HOWEVER, ONCE THE LOCATION OF A STONE IS KNOWN ON CT, THE PROGRESSION CAN BE FOLLOWED BY PLAIN FILMS IF THE STONE IS VISIBLE
- ULTRASOUND:
  - If patients are not candidates for CT due to concerns about radiation (pregnancy and children) → US can assist
  - May miss smaller stones (<5mm) and mid-ureteric stones



US of renal pelvis showing stones

- IT IS 98% SENSITIVE FOR DETECTING **HYDRONEPHROSIS:**
  - However, of hydronephrosis diagnosed by US, up to 22% DO NOT REPRESENT OBSTRUCTION, but rather → normal anatomic variation, full bladder, renal cysts
    - Rapid crystalloid bolus can result in false positive
  - Obesity may interfere with good image acquisition
  - Advantages → noninvasive, no radiation, no known side effects

DIFFERENTIAL DIAGNOSIS:

Table 97-4 Differential Diagnoses for Ureterolithiasis	
Vascular	Aortic dissection
	Abdominal aortic aneurysm
	Renal artery embolism
	Renal vein thrombosis
	Mesenteric ischemia
Renal	Pyelonephritis
	Papillary necrosis
	Renal cell carcinoma
	Renal infarct
	Renal hemorrhage
Ureter	Blood clot
	Stricture
	Tumor (primary or metastatic)
Bladder	Tumor
	Varicose vein
	Cystitis
GI	Biliary colic
	Pancreatitis
	Perforated peptic ulcer disease
	Appendicitis
	Inguinal hernia
	Diverticulitis
	Cancer
	Bowel obstruction
Gynecologic	Ectopic pregnancy
	Pelvic inflammatory disease/tubo-ovarian abscess
	Ovarian cyst
	Ovarian torsion
	Endometriosis
GU	Testicular torsion
	Epididymitis
Other	Drug-seeking behavior
	Shingles
	Retroperitoneal hematoma/abscess/tumor

TREATMENT:

- Treatment for symptomatic nephrolithiasis in the ED includes:
  - Analgesia
  - Antiemetics
  - Antibiotics → for those with evidence of infection
  - Medical expulsion therapy → tamsulosin less in vogue, not as certain of efficacy after systematic review → more for helping in pain relief
  - IV rehydration
- Forced IV hydration results IN NO DIFFERENCE IN PAIN CONTROL OR STONE PASSAGE RATES WHEN COMPARED TO MINIMAL HYDRATION → fluids should be given to correct any fluid deficit due to vomiting or limited oral intake
- NSAIDS are primary choice of analgesics as they have a direct action on the ureter by inhibiting prostaglandins
  - Used in caution in those with GI bleeding risks and renal impairment
- Narcotics
- METOCLOPRAMIDE → in one study was shown to provide pain relief equivalent to narcotic analgesics in addition to relieving nausea
- IV antibiotic selection:
  - AMPICILLIN 2G PLUS GENTAMICIN
    - CEFEPIME/CEFTRIAXONE IF PENICILLIN ALLERGIC
    - GIVE CIPRO IF ALLERGIC TO BOTH
- ALPHA BLOCKERS (MEDICAL EXPULSION THERAPY):
  - One study showed that alpha blockers were associated with increased rate of expulsion, decreased pain and decreased time to expulsion → this study has since been challenged with advent of systematic review
  - Approximately 4% of patients will have adverse effects
  - Most utility for distal stones, where the number and density of alpha-receptors is greatest
  - TAMSULOSIN 400 MICROG DAILY FOR UP TO FOUR WEEKS

DISPOSITION AND FOLLOW UP:

- Most patients are discharged with urologic or primary care follow up

Table 97-5 Indications for Admission	
Absolute Indications for Admission	**Relative Indications for Admission**
Intractable pain or vomiting	Fever
Urosepsis	Solitary kidney or transplanted kidney without obstruction
Single or transplanted kidney with obstruction	Obstructing stone with signs of urinary infection
Acute renal failure	
Hypercalcemic crisis	Urinary extravasation
Severe medical comorbidities	Significant medical comorbidities
	Stone unlikely to pass—large stone in proximal ureter

- Because of lower rates of spontaneous passage → patients with Large (>5mm), irregular or proximal stones should be considered for admission
- Have a lower threshold for admission in those with concurrent severe underlying disease
- EMERGENT DECOMPRESSION MAY BE REQUIRED IN:
    - Solitary kidney with complete obstruction
    - Ureterolithiasis with hydronephrosis and fever
    - Urosepsis with obstruction
- URGENT UROLOGY OPINION NEEDED FOR:
    - Renal insufficiency
    - Severe underlying diseases
    - Complete obstruction or UROMA
    - Multiple ED visits
    - Stone >6mm
    - UTI without sepsis
- Discharge is appropriate in those with:
    - Smaller stones
    - In the absence of infection
    - When pain is controlled by oral analgesics
- Average time to stone passage varies aaccording to size and location → may range up to 7-20 days for stones 5-6mm in diameter
- ADVISE TO RETURN IF:
    - Fevers
    - Uncontrolled pain
    - Vomiting
- PROVIDE SCRIPT FOR ORAL OPIATE AND NSAIDS
- If the stone passes in ED, no further treatment is required
- For patients with haematuria and negative imaging studies, and no other source → outpatient urologist follow up

SPECIAL POPULATIONS/CONSIDERATIONS:

- Stones occur in 1 in 1500 pregnancies and 80-90% present in the second or third trimester
    - Presentation is the same as the nonpregnant population
    - US is imaging modality of choice
        - Problem is that 90% of pregnant patients display PHYSIOLOGIC HYDRONEPHROSIS due to ureteric compression by the gravid uterus, most often more severe on the right side
    - Radiation doses for various modalities are:
        - KUB x-ray → 0.05-0.15cGy,
        - 3 film IV pyelogram → 0.15-0.2 cGy
        - CT scan → 2.2-2.5cGy
- Children with stones need investigation for metabolic diseases and anatomic abnormality
    - Treatment is analgesia and antiemetics as stones are easier to pass in childrena than in adults
    - Medical expulsive therapy has NOT BEEN STUDIED IN KIDS
- Patients who have a known stone who return for continued pain relief:
    - Evaluate EUC for worsening renal function
    - US to evaluate for worsening obstruction
    - Movement of stone → plain film KUB
    - Evidence of infection