Cysts and Stones

Dr. Caroline Stigant

CKD Symposium

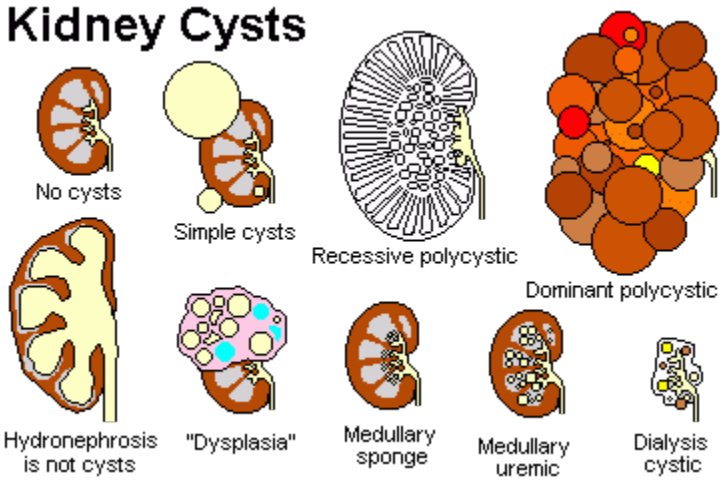
November 29, 2014

OBJECTIVES

- Learn how to manage patients with single and multiple cystic conditions of the kidney (diet / lifestyle, blood pressure, imaging, follow-up, drug therapy)
- Learn what types of kidney stones can form and prevalence of each
- Learn how to prescribe effective preventive therapy for different stone types

CYST CLASSIFICATION – DISTRIBUTION / SIZE / NUMBER

- Simple cysts
- Complex cysts
- PCKD
  - Autosomal recessive
  - Autosomal dominant
- Acquired renal cystic disease
- Medullary Sponge Kidney
- Medullary Cystic disease ('Autosomal Dominant Interstitial Kidney Disease')
- Other
  - von Hippel Lindau
  - Tuberous sclerosis



SIMPLE CYSTS

- Incidence:
  - Varies by population, age (highest in older males)
  - < 1% below age 30; 30% above 70
    - Bilateral in 9% > 70 years
- Histopathology:
  - Single epithelial cell layer, clear or straw coloured fluid within resembling plasma
- Significance:
  - ? None
  - Some case series association with hyperfiltration, mild renal impairment, hypertension, albuminuria *Rule AD et al. AJKD 2012;59(5):611*
  - Complications rare: Renin-induced hypertension, infection, bleeding (gross hematuria +/- flank pain), obstruction
- No follow-up imaging necessary

COMPLEX CYSTS

Bosniak Renal Cyst Classification System

I - **Simple cyst** with a hairline-thin wall.
- No septa, calcifications, or solid components.
- Water attenuation, no enhancement.

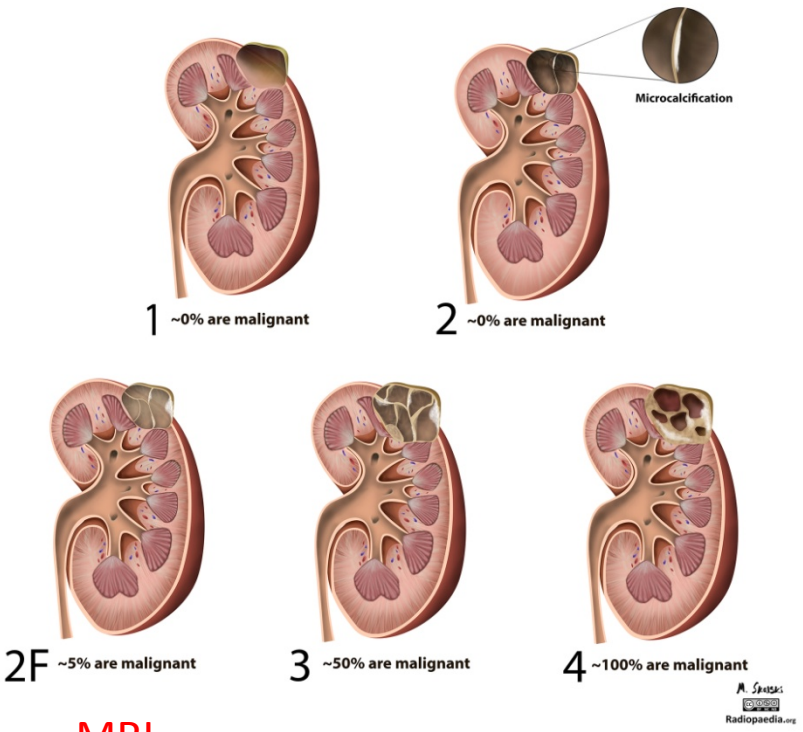
II - **Septa**: few hairline-thin in which not measurable enhancement may be appreciated.
- **Calcification**: fine or a short segment of slightly thickened may be present in the wall or septa.
- **High-attenuation**: uniform in lesions (< 3cm) that are sharply marginated and do not enhance.

IIF - **Septa**:multiple hairline-thin in which not measurable enhancement of septum or wall is appreciated.
- **Minimal thickening of wall or septa**, which may contain calcification, that may be thick and nodular, but no measurable contrast enhancement.
- No enhancing soft-tissue components.
- **Intrarenal:** totally intrarenal nonenhancing high-attenuating renal lesions; these lesions are generally well marginated.

III - **Measurable enhancement**
Cystic mass with thickened irregular or smooth walls or septa in which measurable enhancement is present

IV - **Enhancing soft-tissue components**
Clearly malignant cystic masses that can have all of the criteria of category III but also contain distinct enhancing soft-tissue components independent of the wall or septa

Bosniak classification of renal cysts

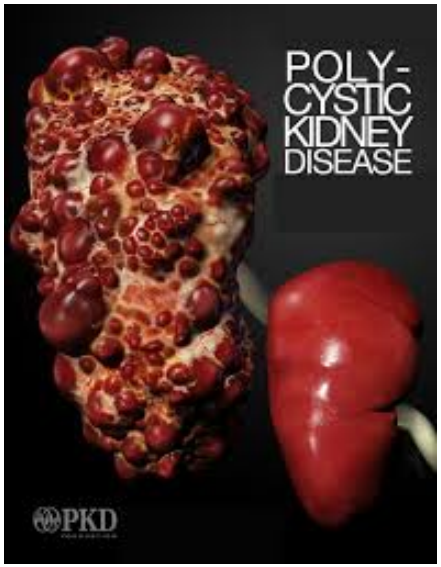


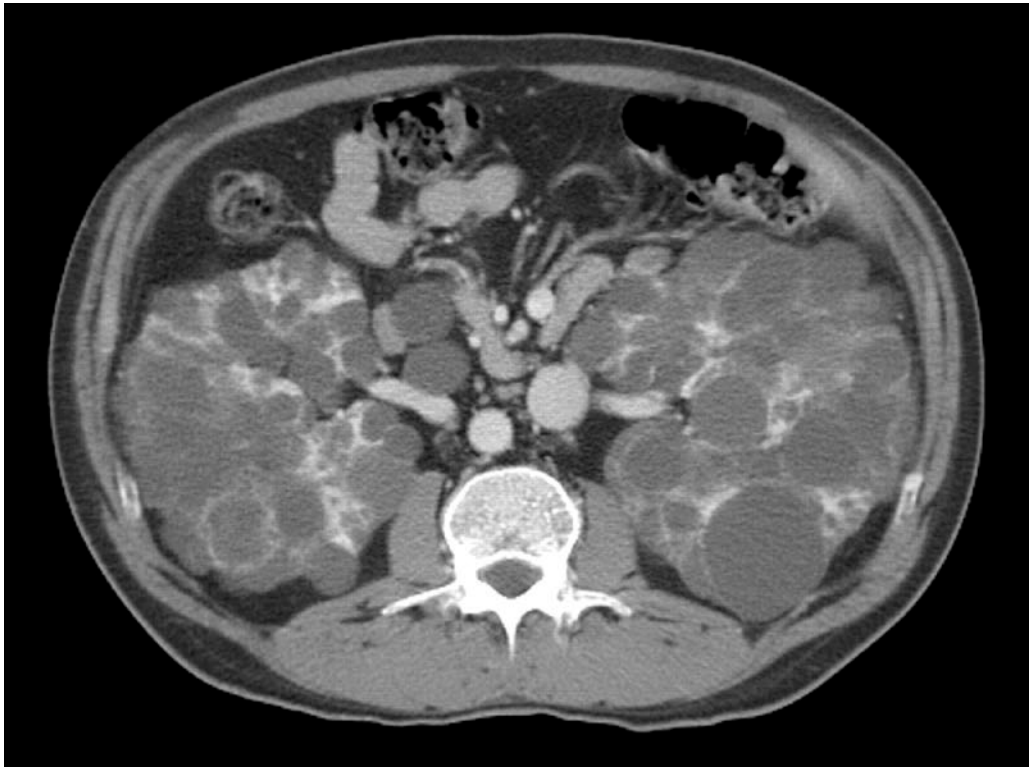
MRI
Observe

Most offered surgery

Resect

POLYCYSTIC KIDNEY DISEASE





Cyst criteria for diagnosis if family history **known**:

- 15-39: 3+ cysts unilateral or bilateral
- 40-59: 2+ cysts per kidney
- 60+: 4+ cysts per kidney

If family history **unknown**: no definite number for unequivocal diagnosis, but 10+ per kidney 'strongly suspect'

Pei Y et al. JASN 2009;20(1):25

PCKD - FEATURES

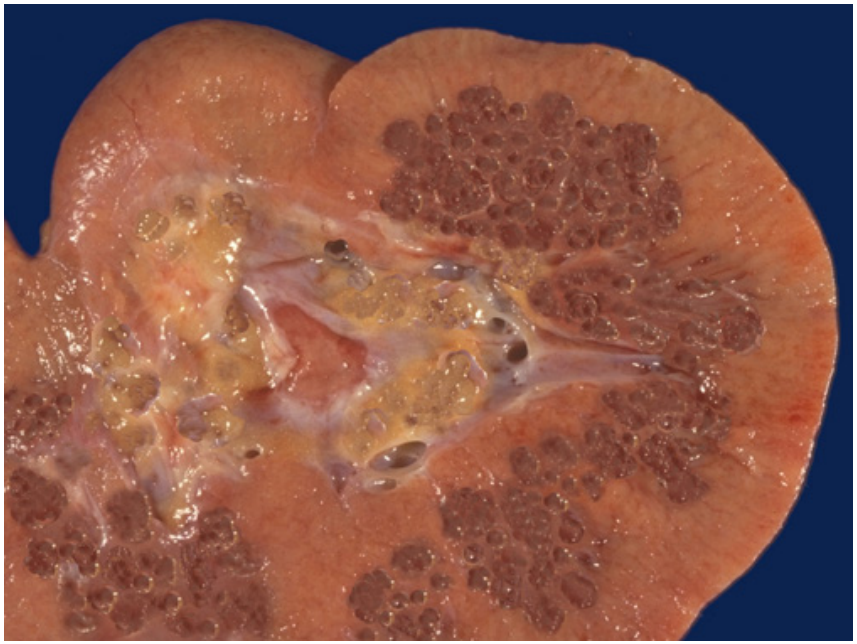
- Incidence: 1/400
- Renal +/- liver (about 50%) +/- pancreatic cysts
- Cyst complications
  - Bleeding (gross hematuria +/- flank pain), infection, renin-induced hypertension, obstruction, stones
- Mass effects
  - Fullness/bloating, early satiety; transplant considerations
- Hypertension
  - Renin-induced
  - Renal parenchymal
- Extra-renal manifestations:
  - Intracranial aneurysm (incidence 5% < 30 yrs, 20% >60 yrs)
  - Inguinal hernia
  - Cardiac valvular: Mitral valve prolapse >> AR
  - AAA – possibly higher risk
  - Renal Cell Carcinoma- possibly higher risk
- Renal Failure

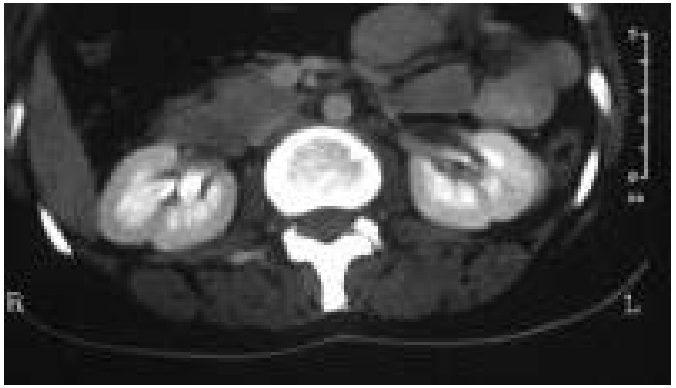
Chapman AB et al NEJM 1992;327(13):916)

PCKD – RENAL FAILURE

- Incidence ESRD 6 PMP; ?majority with PCKD
- Comprise 5-10% of prevalent HD patients in Canada
- Once renal function drops, rate -5 mL/min/year *Torres et al. KI 2009;76(2):149*
- Higher risk of ESRD if:
  - Pt factors: Genetics (PCKD1 >> PCKD2), male, low birth weight
  - Clinical factors – HTN:
    - GFR > 60, age < 50 aim BP 95/60 – 110/70, choose ACE inhibitor *(Schrier R et al, NEJM Nov 2014)*
    - GFR 25-60, aim BP 110/70 – 130/80, choose ACE inhibitor *(Torres V et al, NEJM Nov 2014)*
  - Imaging factors: Nephromegaly
  - Laboratory factors: albuminuria, hyperuricemia, increased urine sodium excretion, increased plasma copeptin level (surrogate for vasopressin)
- Treatment
  - Diet / lifestyle: ? Protein restriction; low Na; fluids > 3L/day, avoid caffeine
  - BP control: ACE inhibitors 1st line; BP target
  - ? mTOR inhibitors, somatostatin, vasopressin receptor antagonists
  - Rarely nephrectomy required

MEDULLARY SPONGE KIDNEY





NEPHROLITHIASIS – A PAINFUL PROBLEM!

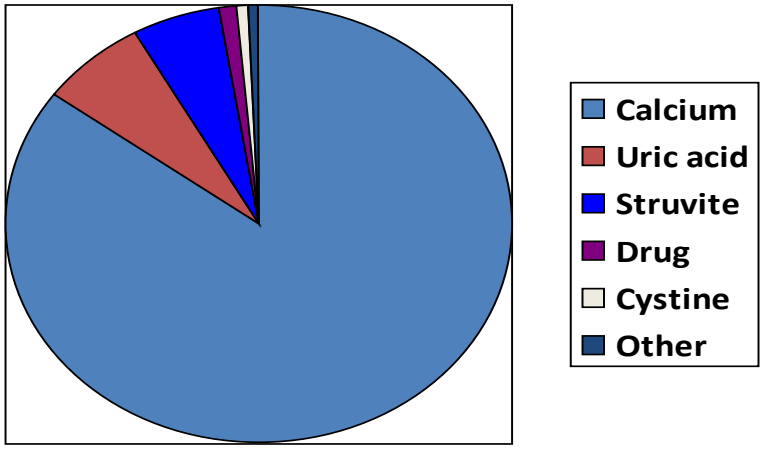
- Affects approx 10% of adults
  - Slight male predominance
- Incidence varies geographically
- Approx 50% have one or more recurrence at 10 years
  - Detailed evaluation generally performed for recurrent stone formers
- Can cause significant morbidity
- Rare cause of end-stage kidney failure

PATHOPHYSIOLOGY

- Supersaturation
- Stasis
- Structural abnormality

TYPES OF STONES

- **Calcium**
  - Calcium oxalate
  - Calcium phosphate
- **Uric acid**
- **Struvite 'staghorn'**
  - Magnesium ammonium phosphate
- **Drug-related**
  - Creation of metabolic environment favouring stone formation
  - Crystallization of drug itself when supersaturated in urine
- Rare Stone Disorders:
  - APRT Deficiency, Dent Disease, **Cystinuria,** Primary hyperoxaluria



HOW CAN I TELL WHAT TYPE OF STONE MY PATIENT HAS?

- **History**
  - Age, comorbidities, medications, family history, occupation / environment, prior kidney or GI surgery
- **Physical**
  - Urinalysis
    - presence of crystals
- **Lab testing**
  - Serum: creatinine, bicarbonate, calcium, PTH, glucose/HgA1c, uric acid
  - Urine (24 hr): calcium, uric acid, oxalate, sodium, citrate
  - Urine pH: uric acid crystals form in acidic uric, calcium phosphate crystals form in alkaline urine, urine is alkaline with struvite stones
- **Imaging**:
  - Radiolucent (uric acid stones) vs opaque (most other stones)
  - ? Nephrocalcinosis
- **Stone Analysis**

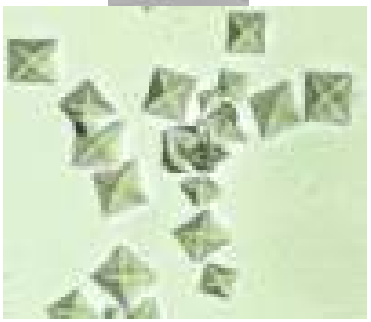
SELECTED MEDICATIONS

- Change urine pH or composition:
  - Vitamin C
  - Vitamin D
  - Calcium (ie. $CaCO_3$)
  - Diuretics: carbonic anhydrase inhibitors, loop diuretics, other (common OTC herbal remedies)

- Drug precipitates:
  - Antimicrobials: acyclovir, amoxicillin, ampicillin, ceftriaxone, ciprofloxacin, sulfamethoxazole
    - Protease inhibitors: indinavir
  - Guaifenesin
  - Triamterene
  - Methotrexate

CALCIUM OXALATE

- Most common (80-85%)
- Presumed diagnosis unless atypical features
- Higher incidence:
  - Post (partial) bowel resection
  - High dose Vitamin C
  - Family history
- Hypercalciuria not necessary
- Hyperoxaluria not necessary



URIC ACID STONES

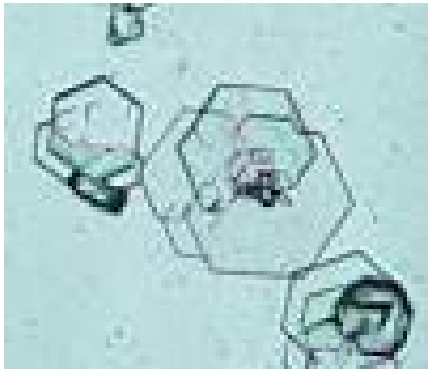
- Reasonably common
- Risk factors:
  - Gout
  - Chronic diarrhea
  - Obesity
  - Metabolic syndrome / DM
  - Malignancy
- Not seen on plain X-ray
- Hyperuricosuria common

STRUVITE STONES

- Magnesium ammonium phosphate + calcium carbonate
- Formed in infected upper urinary tract:
  - Females, neurogenic bladder, urinary diversion
  - Can grow quickly so often present late
    - UTI symptoms, flank pain, gross hematuria
    - pH > 7
- Antibiotics and surgical removal required

CYSTINE STONES

- Cystinuria 1/7000 live births
  - Reduced renal absorption cystine (plus ornithine, lysine, arginine)
- +/- Family history
- Often presents in childhood
- Can form staghorn calculi
- Less radiopaque than calcium stones



WHAT PROVEN TREATMENTS ARE THERE?

- Increasing fluid intake
- Thiazide diuretic (reduces urine calcium)
- Allopurinol (reduces urine uric acid)
- Citrate (raises urine citrate / raises urine pH)

OTHER TREATMENTS

- Diet
- Oral calcium (oxalate binding)
- Disease-specific
  - ie. captopril or penicillamine for cystinuria
- Analgesia
- Alpha blockers (relax smooth muscle tone of ureters to help stone pass / relieve colic)
- Lithotripsy
- Surgical
  - Endoscopic
  - Percutaneous
  - Open
- MEDICAL THERAPY DOES NOT DISSOLVE STONES

DIET - SUMMARY

Diet Parameter	Goal (daily)
Fluid	Enough for urine output > 2.5 L
Sodium	< 2000 mg, possibly lower
Calcium	800-1200 mg (NOT restricted!)
Oxalate	40-50 mg
Citrate	? Specific target
Protein	< 6 oz
Vitamin C	< 1000 mg

Case 1 - Patient AS

- 34 F 4 year history of recurrent nephrolithiasis, onset with renal colic at age 26 when pregnant
  - Every 6 months, then monthly severe colic
  - Stone obstruction twice (9mm, 1.2cm); bilateral ureteric obstruction with urosepsis
  - Ureteric stents placed on multiple occasions
- No family history
- CT-KUB consistent with medullary sponge kidneys; multiple bilateral calculi up to 3 mm in size

AS - continued

- Normal serum biochemistry
- Stone analysis: calcium oxalate
- Urinalysis: pH 6.5, RBC 40-100/hpf
- 24 hr urine:
  - Volume 3.7 L
  - Calcium 5.2 (2.2-6.5 mmol/d)
  - Oxalate 344 (40-340 umol/d)
  - Citrate 4.44 (0.7-4.9 mmol/d)
  - Sodium 207 (40-220 mmol/d)
  - Uric acid 3.4 (1-3.8 mmol/d)

AS – follow-up 3 years later…

- Therapy:
  - HCTZ 12.5 mg po BID
  - Potassium citrate 50 mEq po TID
  - Prazosin 1 mg po OD
  - Cipro 500 mg po OD
  - Endoscopic stone extraction & laser lithotripsy x2
- Urine pH 8.5
- Urine volume still high, biochemistry still normal
- Right hydronephrosis with multiple impacted ureteric stones – currently awaiting surgery

Case 2 – Patient WM

- 32 F of Chinese descent, presented with creatinine 106 on routine lab testing
  - U/S: nephrocalcinosis, bilateral hydronephrosis, cortical thinning
  - CT: staghorn calculi bilaterally, multiple intrarenal stones
- Extensive surgery / subsequent surgeries
- Pregnancy with nephrolithiasis complicating
- Urine amino acid electrophoresis: urine cystine excretion 4x normal
- Increased fluids, diet control, and K citrate

OBJECTIVES REVISITED

- Learn how to manage patients with single and multiple cystic conditions of the kidney (diet / lifestyle, blood pressure, imaging, follow-up, drug therapy)
- Learn what types of kidney stones can form and prevalence of each
- Learn how to prescribe effective preventive therapy for different stone types