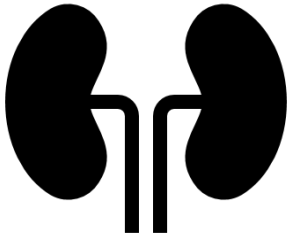
Kidney Cysts and Stones

CKD CME



CKD EDUCATION

• ONLINE CME FOR PRIMARY CARE •

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BCRenal

Disclosures

I have no disclosures to declare

I have no relationships with commercial interests

I have no conflicts of interest to report

I will discuss the off-label use of some medications

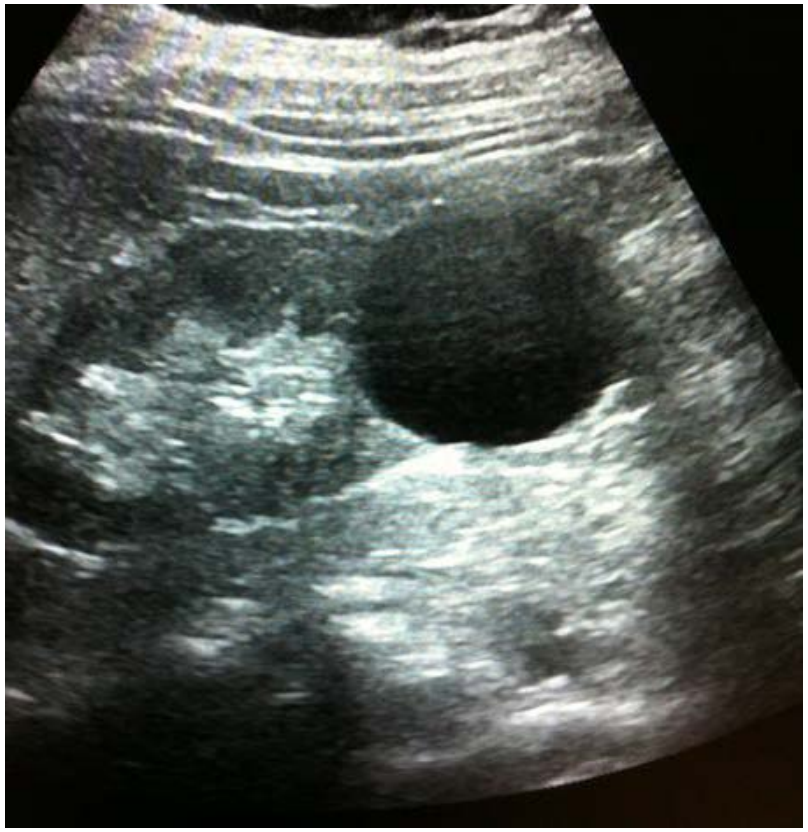
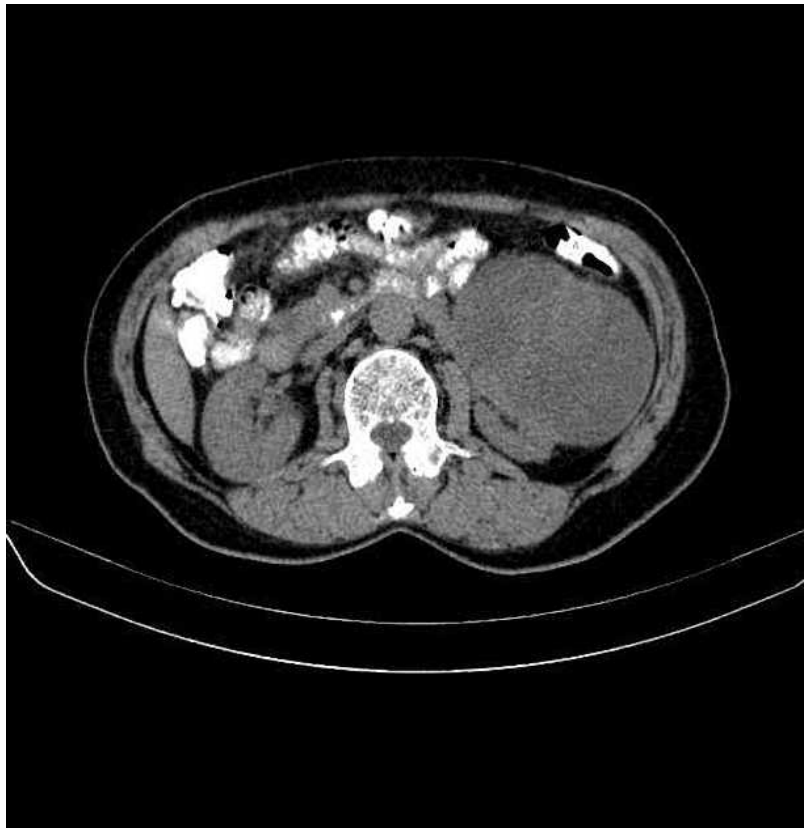
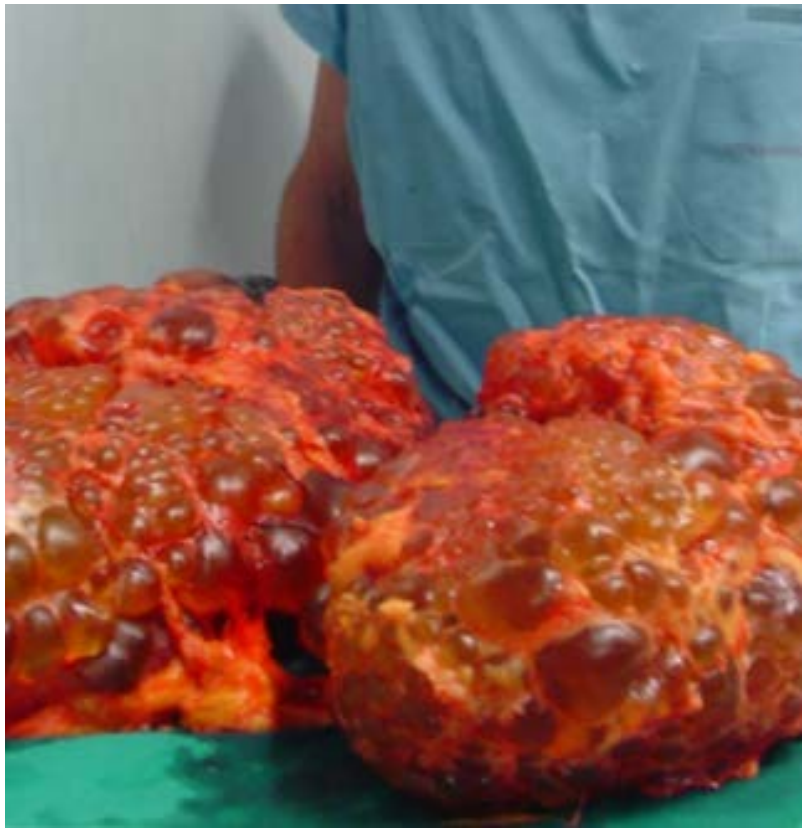
I am not a urologist so this talk will be from the medical perspective

Mitigating Potential Bias

I will let you know when discussing off-label medication use

Objectives

1. To review the approach to renal cysts found on imaging
2. To discuss the management of renal cysts and need for specialist referral
3. To briefly review the management of polycystic kidney disease
4. To discuss the different types of kidney stones and expected course
5. To review lifestyle and medical options for recurrent kidney stone prevention

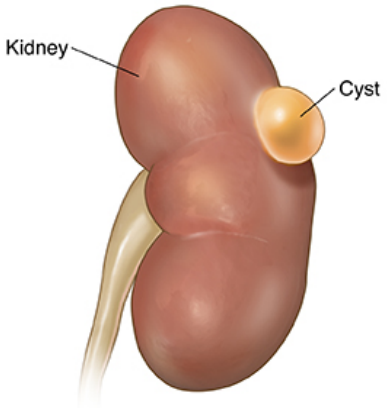




Renal Cysts

Renal Cysts

- Cysts are typically classified by distribution, size and number
- Classification
  - Simple cysts
  - Complex cysts (Bosniak classification)
  - Polycystic kidney disease (ADPKD, ARPKD)
  - Acquired renal cysts
  - Medullary Sponge Kidney
  - Unusual conditions associated with renal cysts:
    - Medullary Cystic Disease (aka autosomal dominant interstitial kidney disease)
    - Von Hippel Lindau
    - Tuberous Sclerosis
    - Nephronophthisis

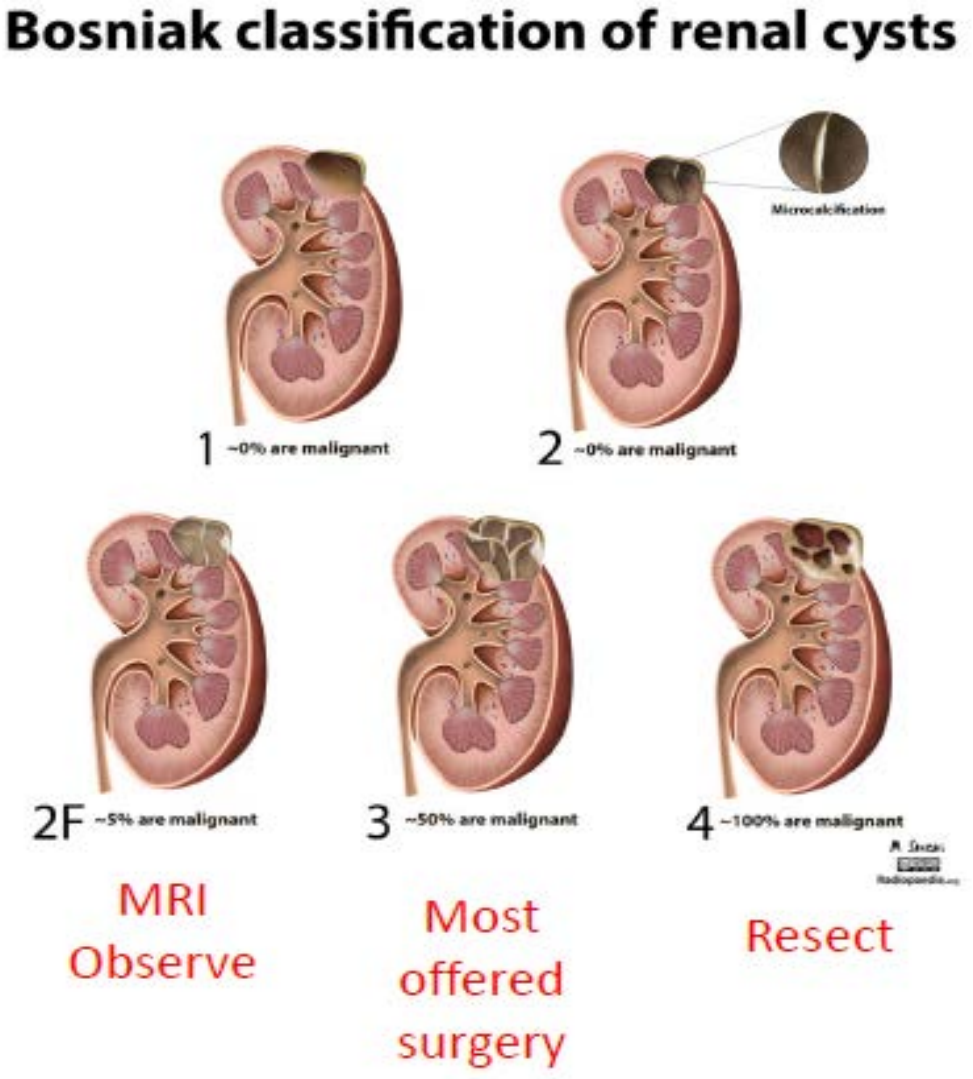
Simple Cysts



- Incidence varies by population, age (highest in older males)
  - < 1% below age 30; 30% above 70 Bilateral in 9% > 70 years
  - Very common incidental finding in older patients on routine imaging
  - Simple cysts may be solitary or multiple and bilateral – if see bilateral cysts in younger people think PKD!
- Clinical presentation:
  - Typically produce NO signs or symptoms (rarely rupture or cause pain/hematuria etc.)
  - Unless obstruction is present, simple renal cysts do not compromise renal function
- Significance
  - ? None - Inconsistent association w/ hyperfiltration, mild renal impairment, HTN, albuminuria
- **No follow-up imaging necessary if radiologist determines it's a simple cyst** (i.e. no complex features)
  - Goal is to accurately distinguishing simple renal cysts from complex renal cysts associated with inc risk of malignancy → if radiology report is unclear or poor-quality images may need to repeated for this reason or CT ordered if lesion equivocal

Complex Cysts

- Classified with the Bosniak Renal Cyst Classification, I to IV
  - Classification based on contrast CT (CT Renal Mass protocol) but ultrasound alone okay for simple cysts
- Class II (not IIF) may warrant repeat imaging in 6-12 months to ensure stability and that it is not a IIF
- Comparison of previous imaging helpful to radiologists – try to use same clinic/hospital site
- It is important that patients with Bosniak cysts IIF and above be referred to **Urology** for monitoring
  - No indication for nephrology referral if normal GFR
- MRI can often be helpful for indeterminant lesions
  - or for those with renal impairment where we want to avoid contrast

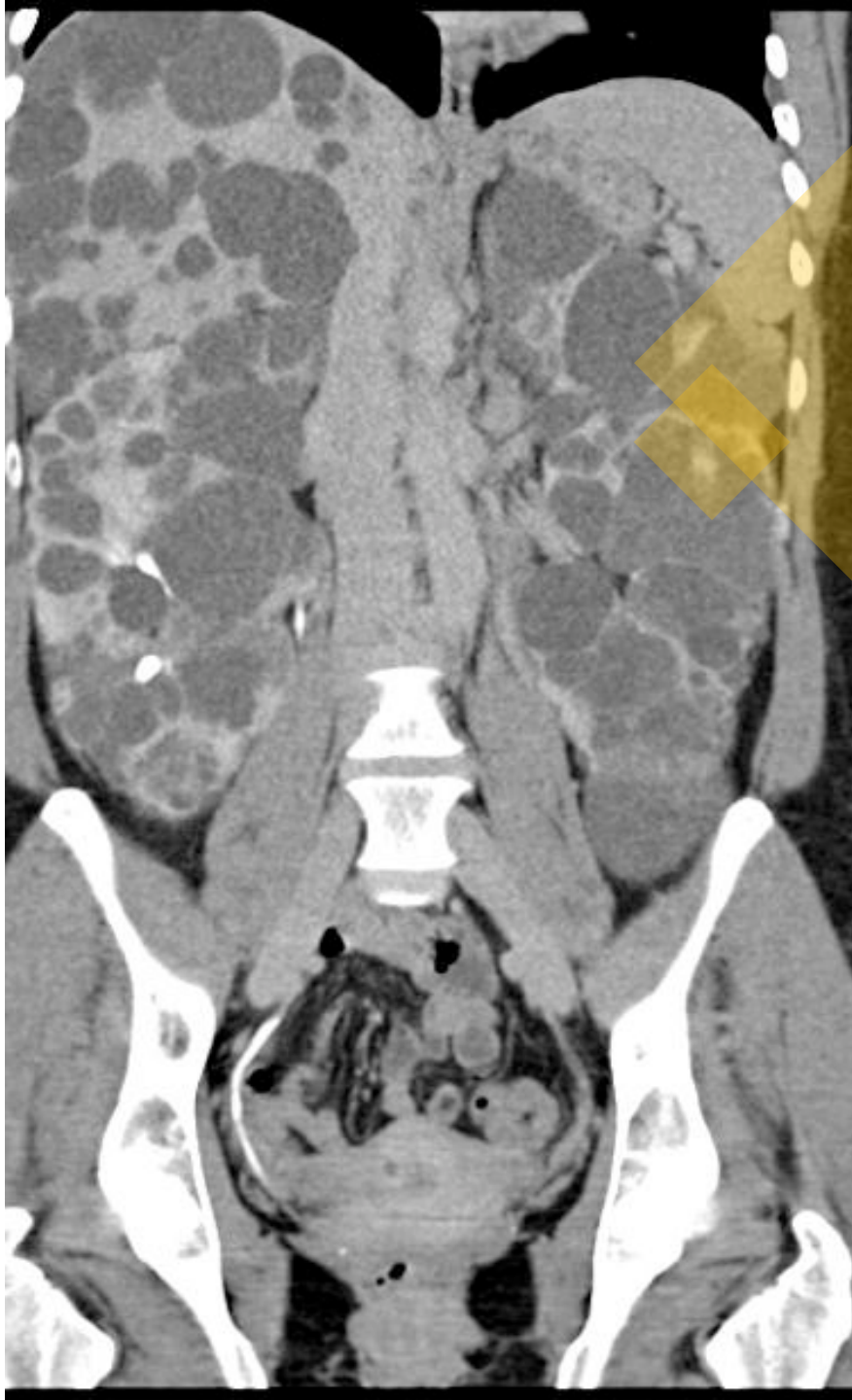


Definition of Bosniak classification of cystic renal masses by CT scanning

Category I - Simple benign cyst with the following features:
Hairline thin wall.
Density less than 20 Hounsfield units (similar to water).
Does not contain septa, calcification, or solid components.
Does not enhance.
Category II - Cystic lesions with the following features:
A few hairline thin septa.
"Perceived" enhancement may be present. There is no measurable enhancement.
Uniformly high attenuation lesions <3 cm that are well marginated and do not enhance fall into this category.
Category IIF - Minimally complicated cysts that do not neatly fall into category II. These lesions are generally well marginated but have some suspicious features that require follow-up:
Multiple hairline thin septa or minimal smooth thickening of the wall or septa.
"Perceived" enhancement of septa or wall may be present.
Thick and nodular calcification of the wall or septa, but no measurable contrast enhancement is present.
Totally intrarenal, nonenhancing, high attenuation lesions >3 cm in diameter fall into this category.
Category III - True indeterminate cystic masses that typically undergo surgical evaluation, although many lesions are benign. These lesions show the following:
Thickened irregular or smooth walls or septa in which measurable enhancement is present.
Category IV - These mostly malignant lesions have the following features:
All category III criteria.
Enhancing soft-tissue components adjacent to, but independent of, the wall or septum.

Polycystic Kidney Disease

- Genetic disorder - multiple bilateral renal cysts associated with renal, extra-renal manifestations and risk of ESRD
  - Can be autosomal dominant (most common) or autosomal recessive
  - 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
- Hypertension
- 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



PKD Ultrasound Cyst criteria

Table 4: Ultrasound Criteria for Diagnosis of ADPKD[11]

AGE (YEARS)	PKD1	PKD2	UNKNOWN ADPKD GENE TYPE
15-30	≥3 cysts* PPV, 100% SEN, 94.3%	PPV, 100% SEN, 69.5%	PPV, 100% SEN, 81.7%
30-39	≥3 cysts* PPV, 100% SEN, 96.6%	PPV, 100% SEN, 94.9%	PPV, 100% SEN, 95.5%
40-59	≥2 cysts in each kidney PPV, 100% SEN, 92.6%	PPV, 100% SEN, 88.8%	PPV, 100% SEN, 90%

Table 5: Ultrasound Criteria for Exclusion of ADPKD[11]

AGE (YEARS)	PKD1	PKD2	UNKNOWN ADPKD GENE TYPE
15-30	No renal cysts seen NPV, 99.1% SPEC, 97.6%	NPV, 83.5% SPEC, 96.6%	NPV, 90.8% SPEC, 97.1%
30-39	No renal cysts seen NPV, 100% SPEC, 96%	NPV, 96.8% SPEC, 93.8%	NPV, 98.3% SPEC, 94.8%
40-59	No renal cysts seen NPV, 100% SPEC, 93.9%	NPV, 100% SPEC, 93.7%	NPV, 100% SPEC, 93.9%

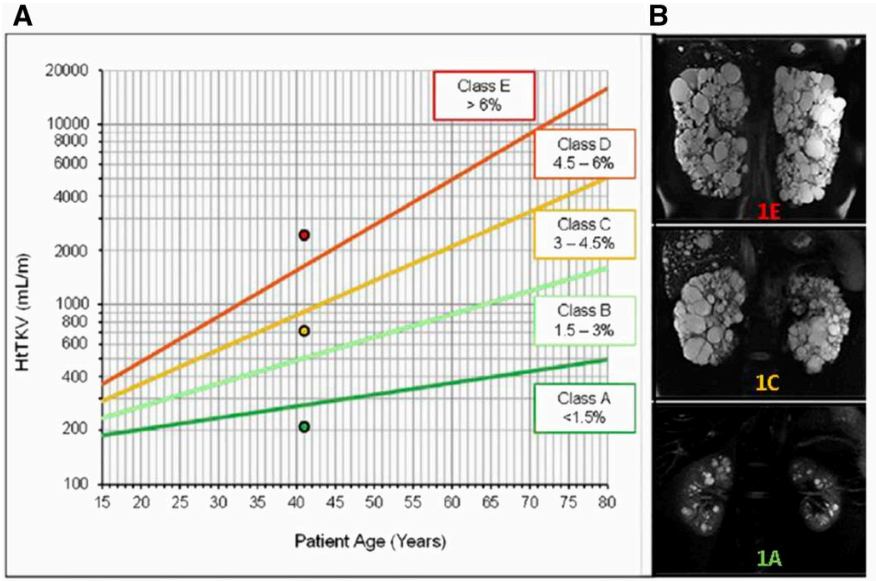
Positive predictive values for ultrasound diagnosis of ADPKD are quite good at all ages but negative predictive values are poor at young ages

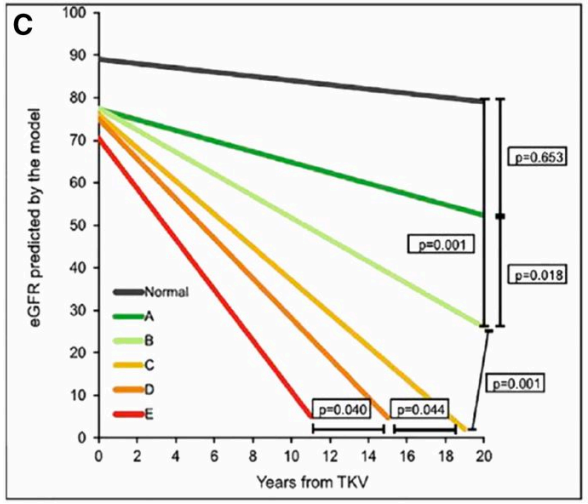
If screening is performed early in life, it is important to recognize that a negative test does not definitively rule out the disease

In such an individual, testing should be repeated later in life

PKD Renal Failure

- Comprise 5-10% of prevalent HD patients in Canada
- Once renal function drops can drop at a rate -5 mL/min/year
- Higher risk of ESRD if:
  - Pt factors: Genetics (PCKD1 >> PCKD2), male, low birth weight
  - Clinical factors – HTN, Kidney size (measured as total kidney volume)
    - Rate of cyst growth and size at a given age – Mayo classification increasingly important factor
  - Laboratory factors: albuminuria, hyperuricemia, increased urine sodium excretion
- Note: Early cysts with normal kidney size NOT associated with drop in GFR → in this case consider alternate causes of CKD





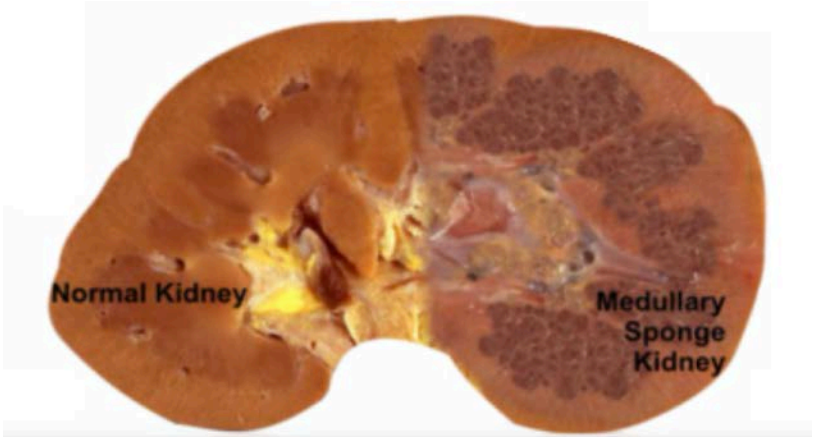
	Estimated eGFR slope (ml/min/SA per year)	
	Male	*Female*
Class 1A	-0.23	0.03
Class 1B	-1.33	-1.13
Class 1C	-2.36	-2.43
Class 1D	-3.48	-3.29
Class 1E	-4.78	-4.58

PKD Treatment

- Treatment Diet / lifestyle:
  - Protein restriction
  - Low Na diet
  - Fluids > 2.5 - 3L/day (suppress ADH), avoid caffeine
- BP control:
  - ACE inhibitors/ARBs 1st line
  - If age < 50 with eGFR > 60 and no significant CV morbidities should target blood pressure of **≤ 110/75 mm Hg** (as measured by home blood pressure monitoring – HALT PKD Trial)
  - If age > 50 than **<130/80 mm Hg**
- Tolvaptan (V2 vasopressin receptor antagonist)
  - Only disease specific therapy available at this time with evidence for slowing disease progression in high risk groups (age 18-65, GFR >25 and high risk for progression)
  - Main side effects nocturia/polyuria/polydipsia – risk of liver enzyme abnormality → close monitoring required
  - $$$ but now covered by Pharmacare/BC Renal
- Role for early referral to nephrology as many therapies likely to have larger benefit if started early (many therapies in pipeline)

Medullary Sponge Kidney

- Congenital disorder characterized by malformation of terminal collecting ducts in pericalyceal region of renal pyramids → collecting duct dilatation associated with formation of both small microscopic and large medullary cysts that are often diffuse but don't involve cortex
- <1% population, often found on work up for kidney stones or incidental
- Can be associated with:
  - Recurrent UTIs
  - Hematuria
  - Nephrolithiasis
  - Chronic pain (with or without stone)
  - Urine concentrating defect (polyuria)
- CKD risk is low overall
- Management is largely supportive
  - Stone prevention
  - Pain management



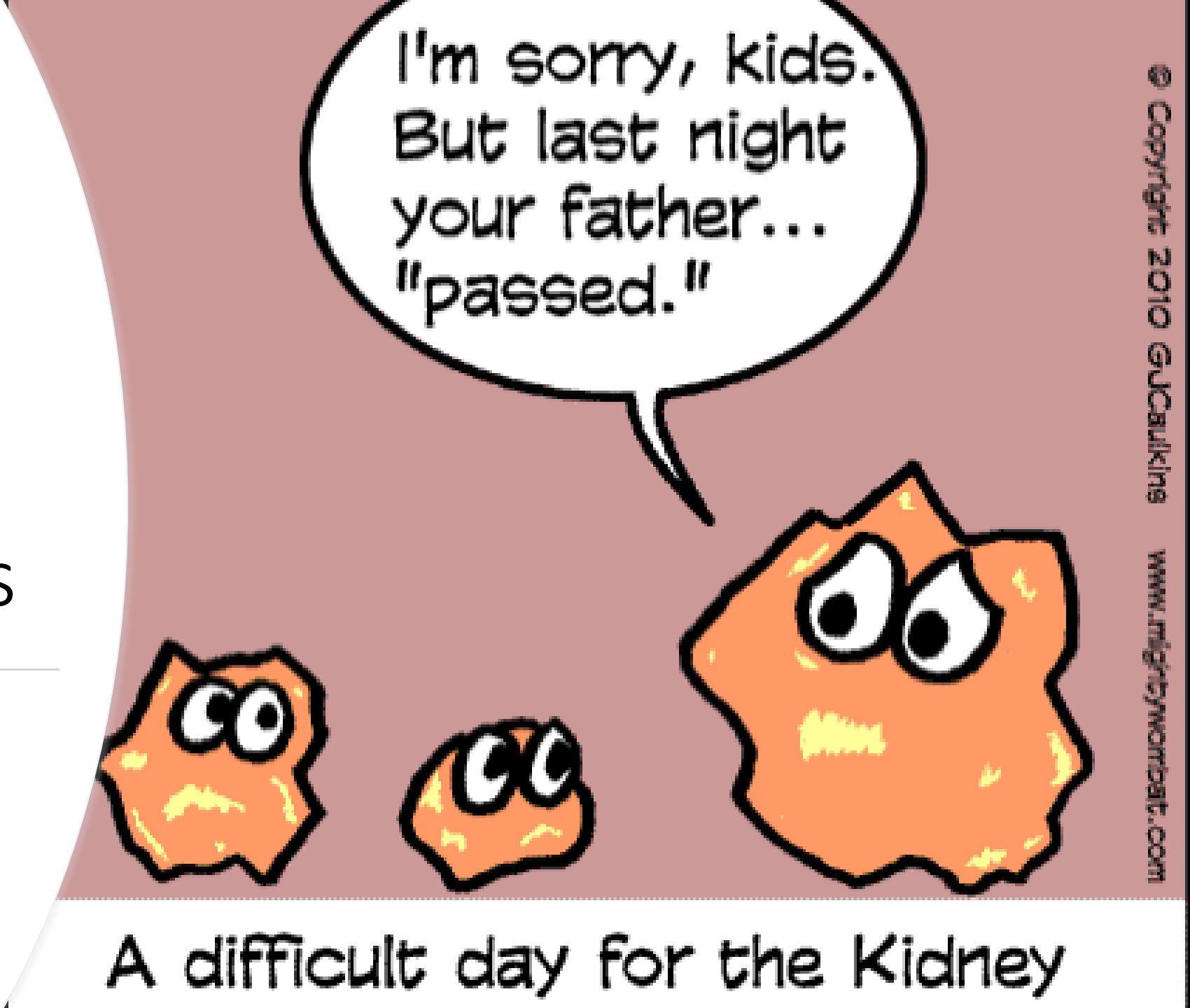
Other Rare Cystic Disorders

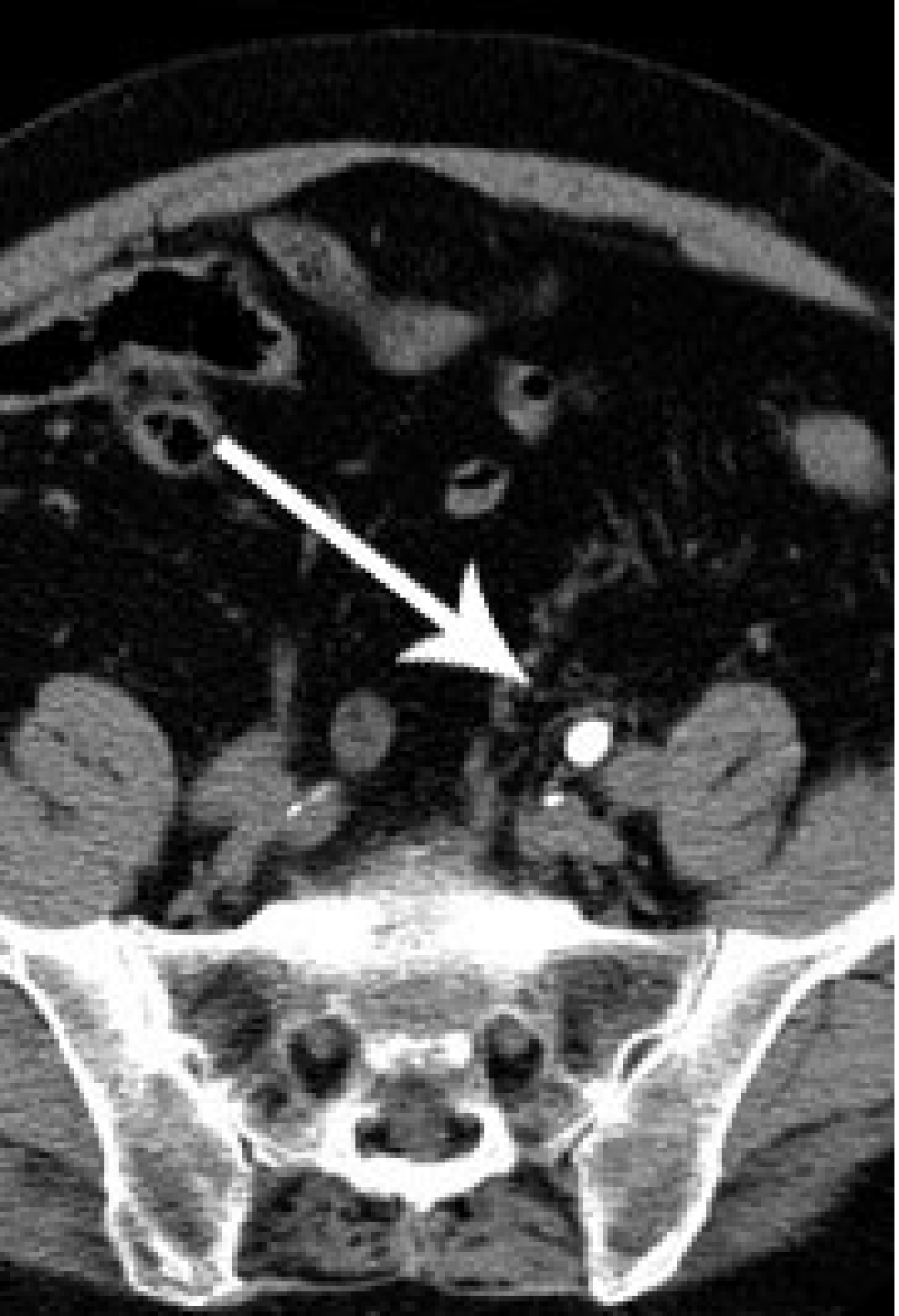
- Medullary Cystic Kidney disease
- Von Hippel Lindau
  - Renal cysts and RCC in addition to other benign and malignant tumors
- Tuberous Sclerosis
  - Associated with angiomyolipomas of the kidney (AMLs) which if large are associated with potentially life threatning bleeding
  - May require surgery, IR embolization or medical therapy with mTOR inhibitors
  - Suspect TS if see AMLs especially bilateral with +Fx or neurologic/dermatologic maninfestations
- Nephronophthisis
  - Pediatric diagnosis, ESRD by age 20

Renal Cysts: When to refer?

- Any patient with suspected PKD should be referred to **Nephrology** even if renal function is normal
- Patients with complex renal cysts with possibility of malignancy i.e. Bosniak Class IIF and above should be referred to **Urology**
- Simple cysts do not require referral or follow up imaging
- Other unusual causes may have interdisciplinary involvement
  - AML management in TS – urology +/-nephrology
  - Medullary sponge kidney – urology (stone) +/- nephrology
  - Pediatric conditions

Nephrolithiasis





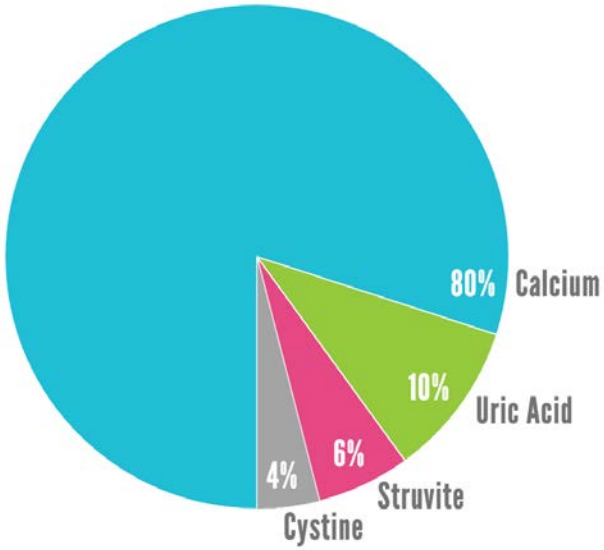
Nephrolithiasis

- Affects approximately 10% of adults
- Slight male predominance
- Incidence varies geographically
- Approximately 50% have one or more recurrence at 10 years
- Can cause significant morbidity
- Rare cause of end-stage kidney failure

Pathophysiology of Kidney Stone Formation

- Supersaturation
  - Increased amount of crystal forming substances such as calcium, uric acid, oxalate relative to urine volume (concentration)
- Stasis
  - Urinary flow low or bladder outlet obstruction (bladder stones)
- Decreased amount of “inhibitors” in urine that normally prevent supersaturation and crystal formation
  - i.e. citrate
- Structural abnormalities and infection can also play a role

Types of Stones



- **Calcium** – majority of kidney stones are calcium stones
  - Calcium oxalate
  - Calcium phosphate
- **Uric acid**
- **Struvite 'staghorn'** –Magnesium ammonium phosphate
  - Infection related
- **Drug-related**
  - Creation of metabolic environment favouring stone formation ex. Vitamin C, carbonic anhydrase inhibitors, loop diuretics, topirimate
  - Crystallization of drug itself when supersaturated in urine ex. acyclovir, ciprofloxacin, ARVs (indinavir) guaifenesin, Triamterene, Methotrexate
- **Rare Stone Disorders**
  - APRT Deficiency, Dent Disease, Cystinuria, primary hyperoxaluria

How can I tell what type of kidney stone my patient has?

- **History**
  - Age, comorbidities, medications, family history, occupation/environment, prior kidney or GI surgery, s/sx of UTI
- **Lab testing**
  - Serum: creatinine, bicarbonate, calcium, PTH, glucose/HgA1c, uric acid
  - Urine (24 hr): calcium, uric acid, oxalate, sodium, citrate – **see later, not needed for all**
  - Urine pH: uric acid crystals form in acidic uric, calcium phosphate crystals form in alkaline urine, urine is alkaline with struvite stones
  - Urinalysis presence of crystals (note: calcium oxalate crystals are common in concentrated urine and don't necessarily indicate presence of stones)
- **Imaging**: Radiolucent (uric acid stones) vs opaque (most other stones)
- **Stone Analysis**

Calcium Stones

- **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
- **Calcium phosphate**
  - Form in alkaline urine
  - Associated conditions: distal renal tubular acidosis, primary hyperparathyroidism, chronic urinary tract infection, hypercalciuria, and/or hyperphosphaturia.
  - May see mix of calcium oxalate and calcium phosphate stones

Uric Acid Stones

- Reasonably common, risk factors include:
  - Gout
  - Chronic diarrhea
  - Obesity
  - Metabolic syndrome / DM
  - Malignancy
- Form in acidic urine
- Not seen on plain X-ray
- Hyperuricosuria common but not found in all

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 of cystine (plus ornithine, lysine, arginine)
- +/- Family history
- Often presents in childhood
- Can form staghorn calculi
- Less radiopaque than calcium stones

Kidney Stones: When to refer?

- All obstructive stones should be referred urgently to urology
- Symptomatic stones should always be referred
- Patients with solitary kidney and any stone should be referred to urology
- Small incidental stones seen on renal ultrasound should ideally be confirmed on CT KUB or KUB x-ray (especially if <4 mm) prior to referral to urology
- All kidney stones need basic work up and dietary advice
  - Even first time stone pts should have a basic evaluation including a urinalysis ± culture, serum electrolytes, serum Ca and creatinine

Patients requiring a more in-depth evaluation

- Patients with recurrent kidney stones should be referred to urology +/- nephrology
  - These patients require a more detailed metabolic work up – additional BW and 24 hour urine
  - These patients may require medications in addition to more tailored dietary advice
  - Stone clinics in place at VGH and SMH (?other sites) run by nephrology with dietician support for recurrent stone formers
    - Multidisciplinary stone clinics have been shown to reduce stone recurrence rates

- Children (<18 years of age)
- Bilateral or multiple stones
- Recurrent stones (having had two or more kidney stone episodes in the past)
- Non-calcium stones (e.g., uric acid, cystine)
- Pure calcium phosphate stones
- Any complicated stone episode that resulted in a severe (if even temporary) acute kidney injury, sepsis, hospitalization, or complicated hospital admission
- Any stone requiring percutaneous nephrolithotomy treatment
- Stones in the setting of a solitary (anatomical or functional) kidney
- Patients with renal insufficiency
- History of kidney stones and systemic disease that increases the risk of kidney stones (e.g., gout, osteoporosis, bowel disorders, hyperparathyroidism, renal tubular acidosis, etc.)
- Occupation where public safety is at risk (e.g., pilots, air traffic controller, police officer, military personnel, firemen)

In-depth evaluation

For those patients where an in-depth evaluation is indicated, the workup should include serum and 24-hour urine tests, as well as a thorough dietary history. These tests should include:

a) Serum:
- Creatinine, sodium, potassium, chloride, calcium, albumin, uric acid, bicarbonate
- Parathyroid hormone (PTH) level if serum calcium is high normal or abnormally elevated
- Vitamin D if low normal serum calcium or elevated serum PTH

b) 24-hour urine collection:
- Volume, creatinine, calcium, sodium, potassium, oxalate, citrate, uric acid, magnesium
- Cystine if suspect cystine stone or if the stone analysis is cystine

c) Spot urine:
- Urine pH
- Urinalysis
- Specific gravity

What proven treatments are there?

- **Increasing fluid intake** – recommend 2.5 - 3L per day
  - Most important factor to prevent recurrent stones!
  - Goal is a urine output of 2.5 L per day or more (higher in cystine stones)
- **Citrate** (raises urine citrate / raises urine pH)
  - Can be supplement (potassium citrate) or dietary (lemon contrate/water)
- **Thiazide diuretic** (reduces urine calcium)
  - Seems to be useful even if not hypercalciuria in those with calcium based stones
- **Allopurinol** (reduces urine uric acid)

Other Dietary Advice

- Dietary calcium → Do not restrict!
  - Need to make sure dietary calcium is sufficient (Recommended 1000-1200/day)
  - Usually avoid calcium supplements (exceptions: mealtime calcium in certain pts with calcium oxalate stones)
- Low sodium diet <1.5 - 2g/day
  - Low sodium diet reduces hypercalciuria
- Oxalate restriction
  - Limited evidence that this works
- Protein
  - Avoid excess protein intake and high purine foods if uric acid stones
- Avoid excessive Vitamin C intake
  - <1000 mg/day
- Diet high in fruits and vegetables (may be driven by citrate intake)

Other treatments for stone prevention

- Oral calcium (oxalate binding) with meals
- Sodium bicarbonate
- Disease-specific therapy i.e. penicillamine for cystinuria, antibiotics for struvite

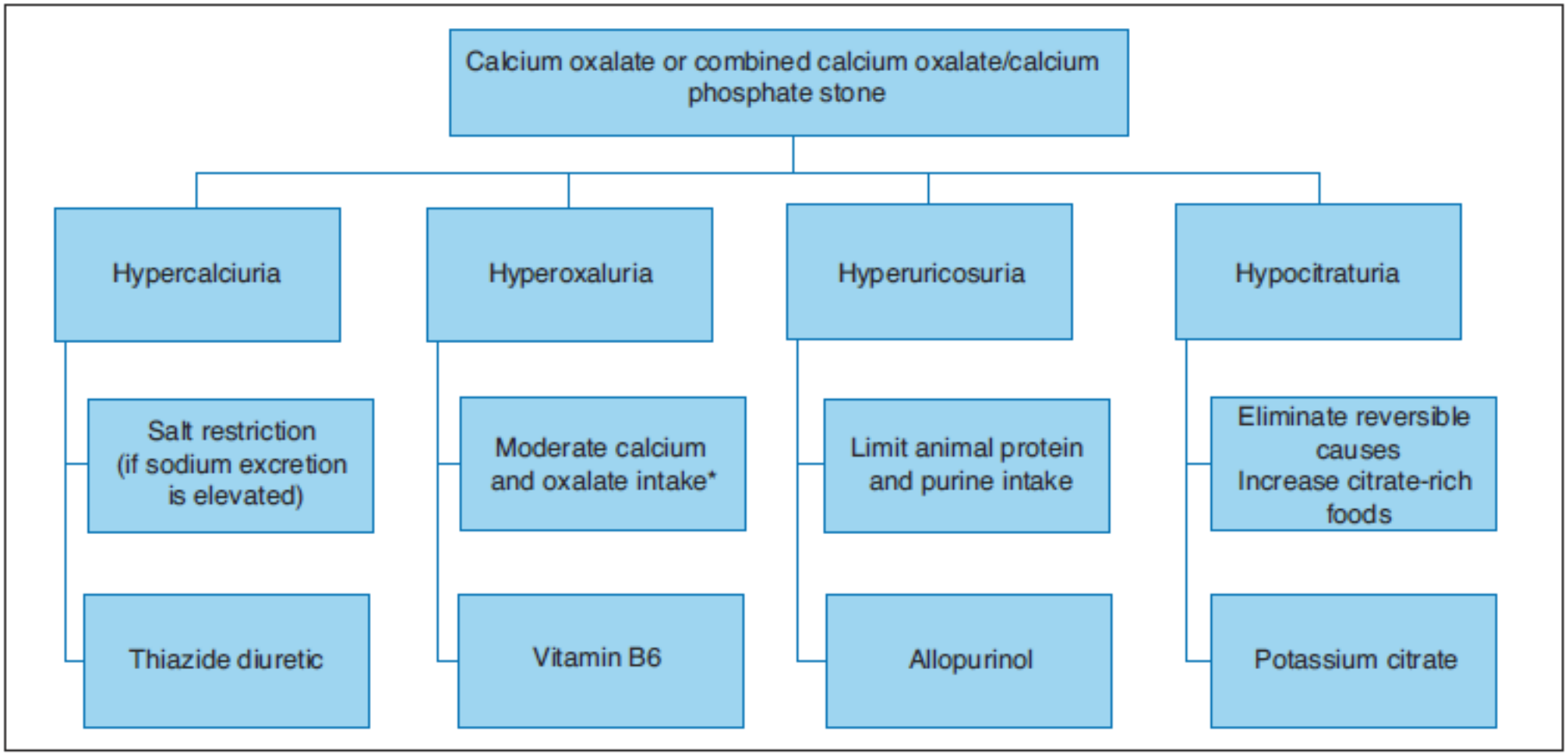


Fig. 1. Specific dietary and medical treatments for patients with calcium oxalate or mixed calcium oxalate/calcium phosphate stones.*Calcium intake 1200 mg daily (with meals), moderation of foods high in oxalate, pair oxalate and calcium-containing foods.

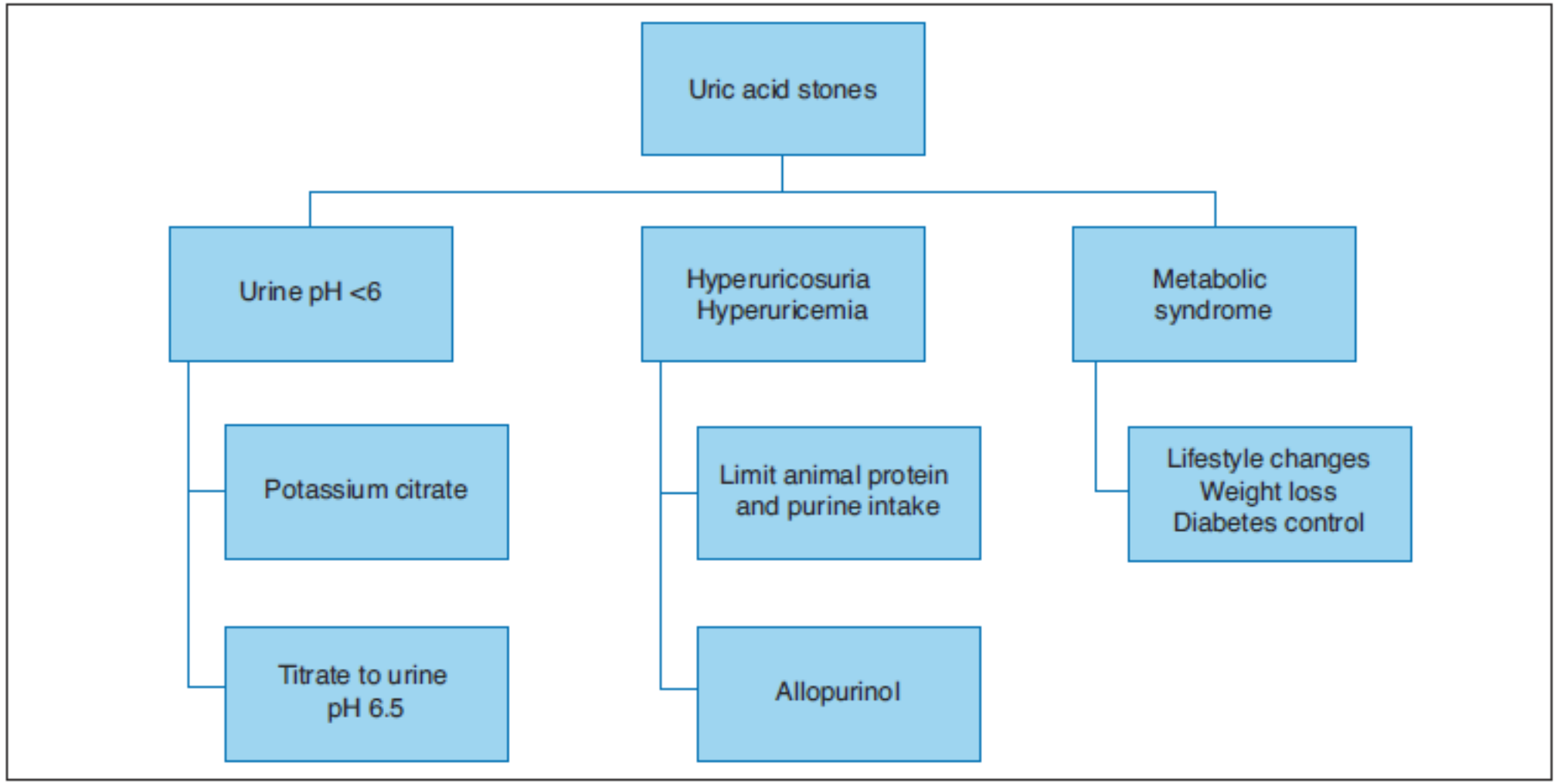


Fig. 2. Specific dietary and medical treatments for patients with uric acid stones.

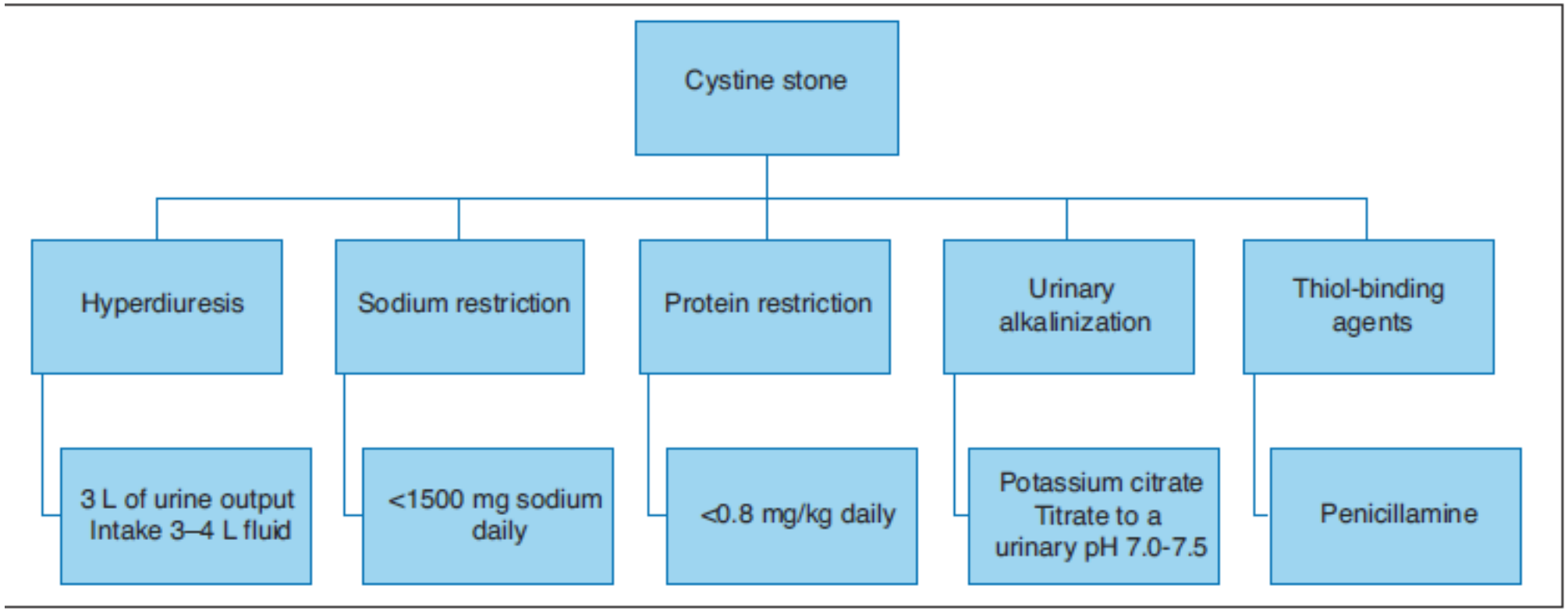


Fig. 3. Specific dietary and medical treatments for patients with cystine stones.

Questions?

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