IN THE NAME OF GOD

I and renal stone

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Introduction

- Nephrolithiasis is known to be a medical condition characterized by high prevalence all over the world .

- During the last decades, the incidence of nephrolithiasis is rising in both genders ,with resulting increased economic burden for health systems.

- **Calcium stones** are the **most common** type of renal stone.

- Cystine, struvite, and pure uric acid are less common but have high recurrence rates.

renal stones

- ✓ Calcium oxalate (75%–90%) is the most frequent component of calculi
- ✓ uric acid (5%–20%)
- ✓ calcium phosphate (6%–13%)
- ✓ struvite (2%–15%)
- ✓ apatite (1%)
- ✓ cystine (0.5%–1%)

Risk factors

intrinsic or extrinsic factors

- **The former** one includes age, gender, ethnic and familial backgrounds.

- **the latter** group consists of climate and environment, lifestyle and dietary habits, occupation and education level.

The **most important factors**, determining the prevalence, incidence, recurrence rates and constituent of calculi, are climate and dietary habits.

Risk factors you can control

- **How much fluid you drink**. The most common cause of kidney stones.
- **Your diet**. Diets **high in protein, sodium, and oxalate-rich foods**, increase your risk for kidney stones.
- **Overweight**. This can cause both insulin resistance and increased **calcium** in the urine, which can result in a greater risk for kidney stones.
- **Medicine**., such as **acetazolamide** and **indinavir** triamterene ,**topiramat**; sulfanamides ;penicillin;cephalosporin;quinolones ;nitrofurantoin and rarely **ACE inhibitor** can cause kidney stones to form.

Risk factors you cannot control

- **Age and gender**
  - Men between the ages of **30 and 50** are most likely to get **kidney** stones.
  - Postmenopausal women with low estrogen levels have an increased risk for kidney stones.
- **A family history of kidney stones.**

- **A personal history of frequent urinary tract infections.**

- **Other diseases or conditions**, such as **Crohn's disease**, **hyperparathyroidism**, **or gout.**

- **Intestinal surgery or gastric bypass surgery,** lead to **hyperoxaluria and hypocitraturia.**

Urinary calculi promoters & inhibitors

- **Urinary calculi promoters:** Calcium, sodium, oxalate, **uric acid**, urate and cystine.

- **Urinary calculi inhibitors:** Magnesium, potassium, pyrophosphate, **citrate,** glycosamino glycans kidney proteins such as nephrocalcin, osteopontin, tamm-horsfall protein, muco-protein, uropontin, crystal matrix protein, renal lithostathine, urinary prothrombin fragment 1, and calgranulin.

"Citrate is the main complexer for calcium ions in the urinary track"

Nephrolithiasis: Evaluation

History and Physical Examination

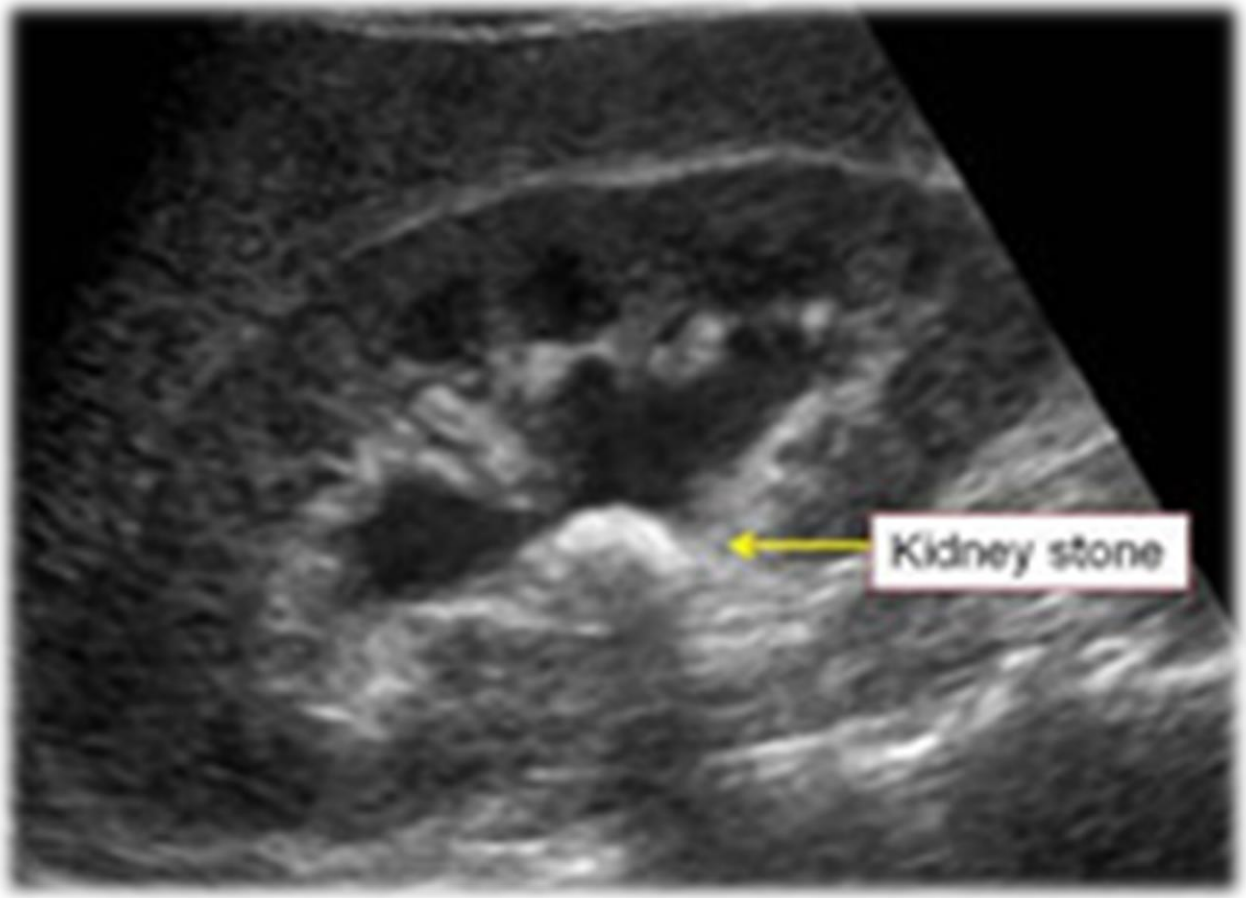
- Total number of stones
- Any evidence of residual stones
- The number and types of procedures
- Previous preventive treatments
- Family history
- Related medical illnesses
- Diet &medications

Radiologic Evaluation

Ultrasonography

- **US** has a **sensitivity of 24%** and a **specificity of 90%.**
- US can **only image the kidney and the proximal ureter**, and may also miss stones **smaller than 3 mm** in diameter.
- US is **preferred in pregnant women** with suspected calculi to minimize radiation exposure.
- Due to the high rate of false-negative results, if nephrolithiasis is not confirmed in pregnant women, and if symptoms suggestive of renal calculi persist, **single-shot IVP should be performed.**

Ultrasonography



Plain radiograph of the kidney, ureter and bladder

- KUB has a sensitivity that ranges from 45–60% in the evaluation of acute flank pain.
- KUB cannot visualise radiolucent stones (10–20% of stones), thus limiting the value of plain radiography.
- KUB may suffice for assessing the size, shape, and location of urinary calculi in some patients.

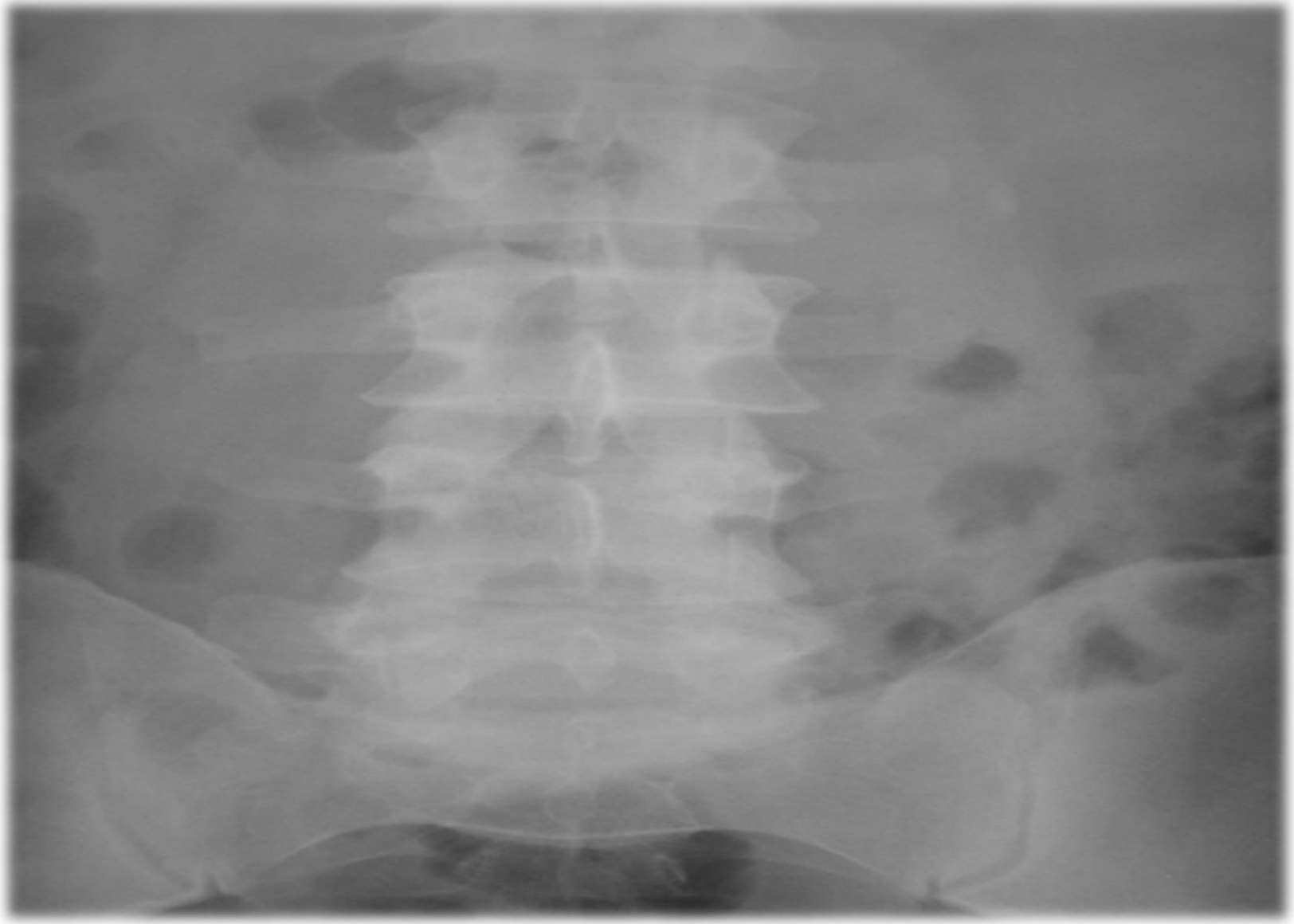


Figure 1 Patient presented with left loin pain. Kidney, ureter and bladder (KUB) *x* ray showing 7 mm radiopaque stone laying lateral to the tip of transverse process of L2.

Intravenous urography

- IVU has a detection rate as high as 70–90% it can only visualise radiopaque stones (80–90% of stones).

- **Some undesirable aspects of IVU:** radiation exposure, risk of nephrotoxicity, contrast reaction and the time it takes, particularly when delayed films are required.

- The reported incidence of contrast-induced renal failure is **approximately 1%**, while in the population **with pre-existing renal failure and diabetes mellitus**, the risk of contrast-induced **nephrotoxicity is 25%.**

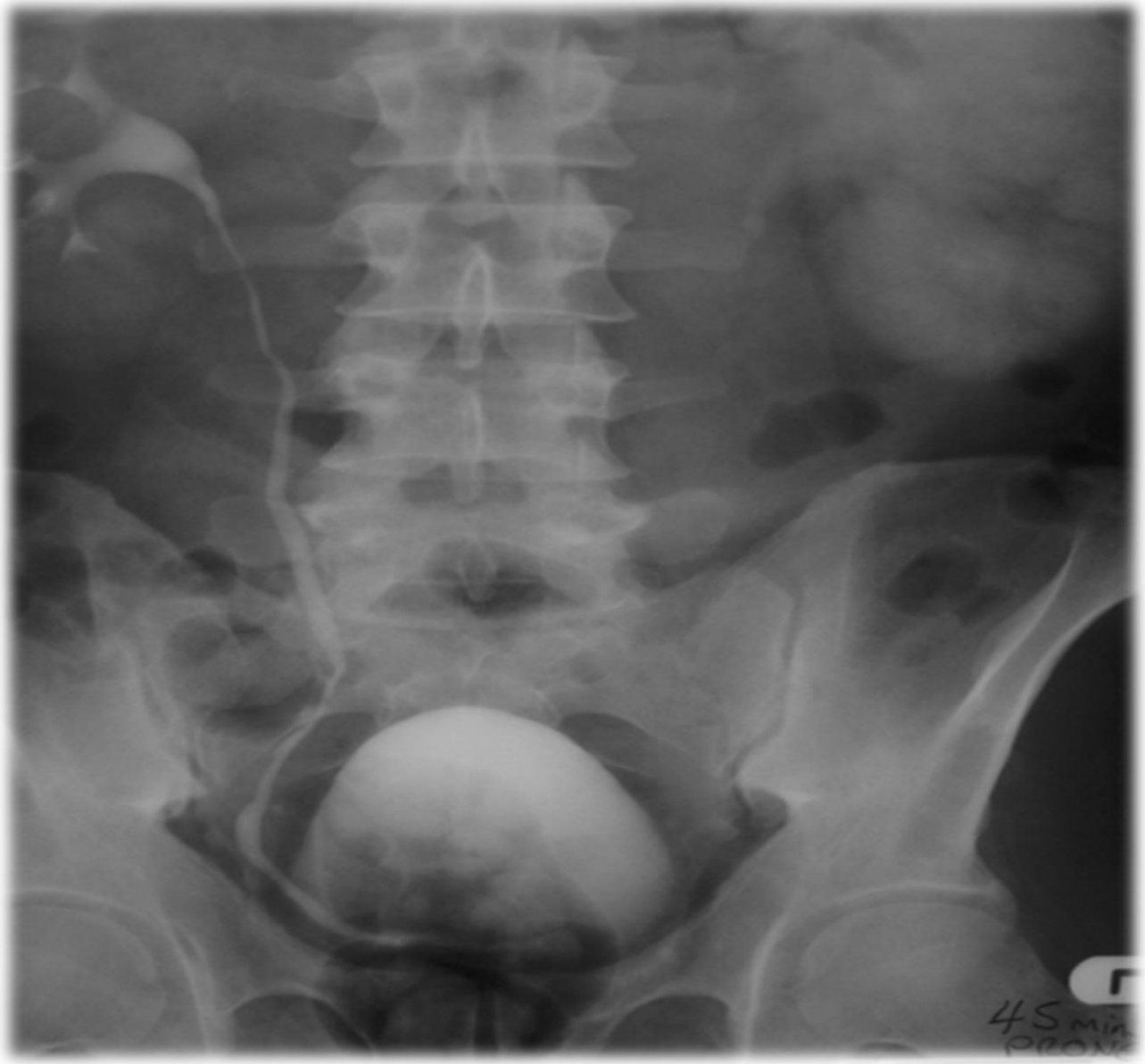
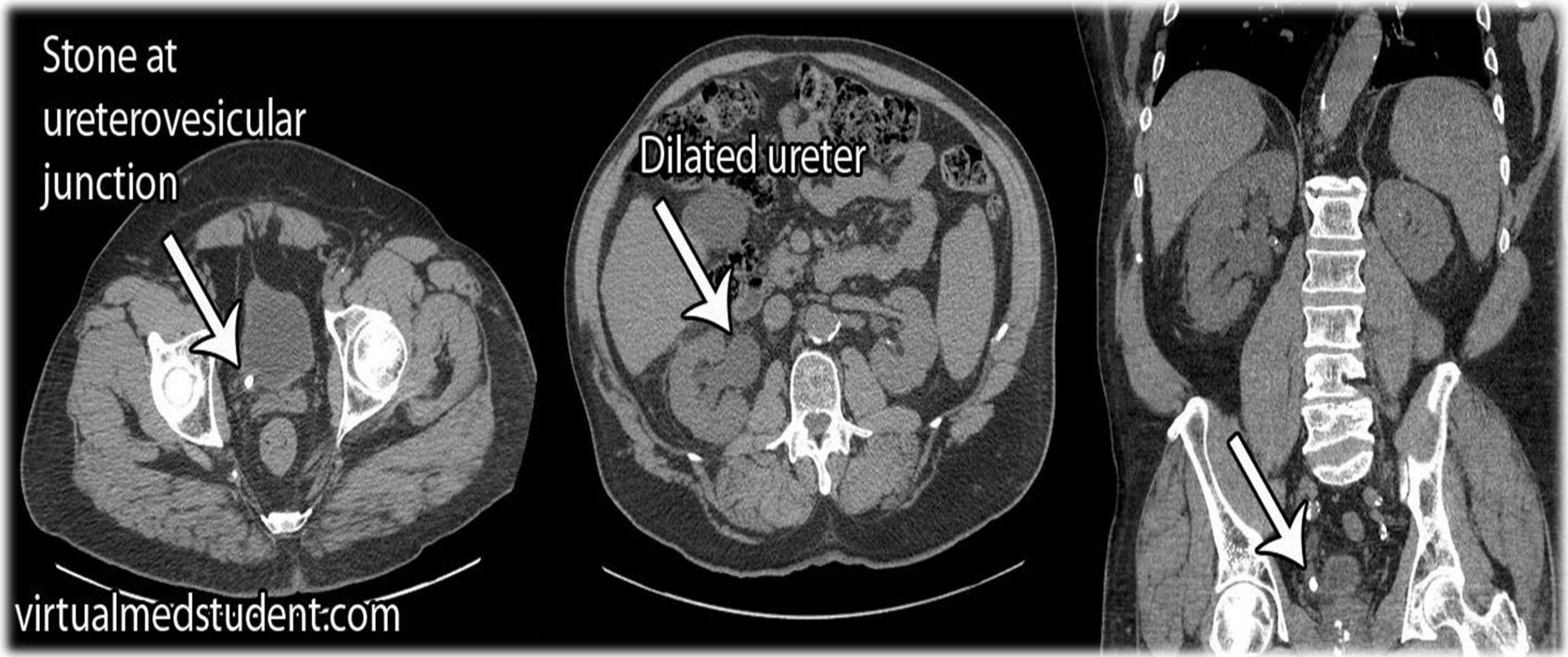


Figure 2 Patient after administration of intravenous contrast medium, showing left nephrogram and contrast coming down to the level of the stone

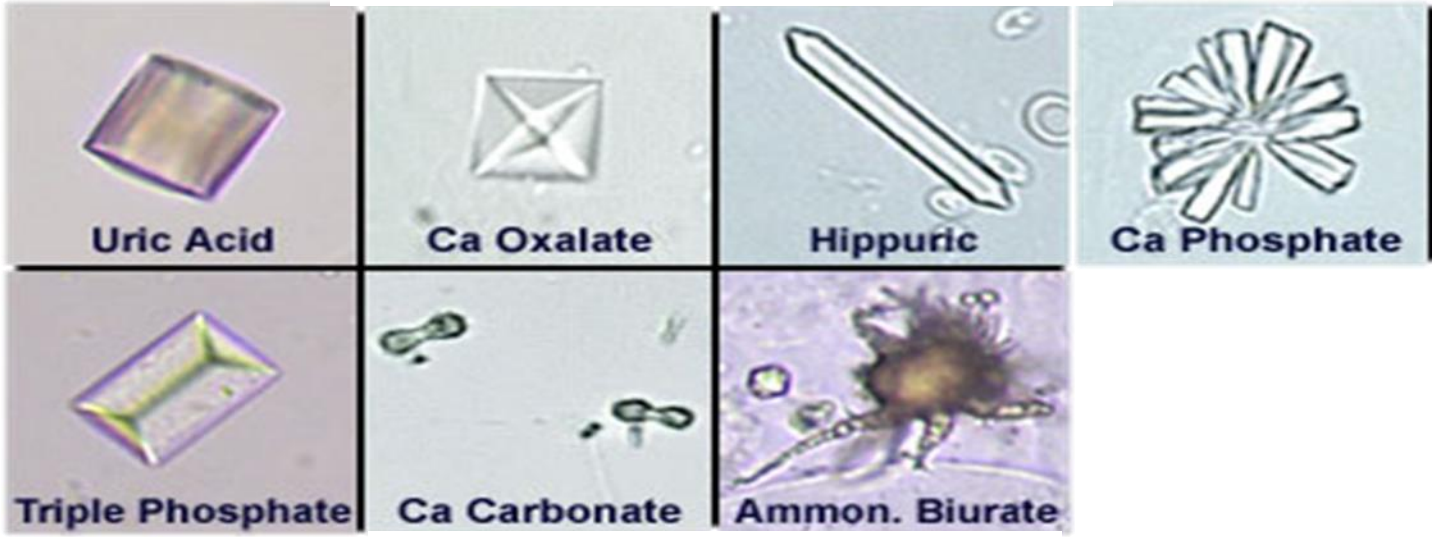
Non-contrast enhanced computed tomography

CT has the following advantages over IVU

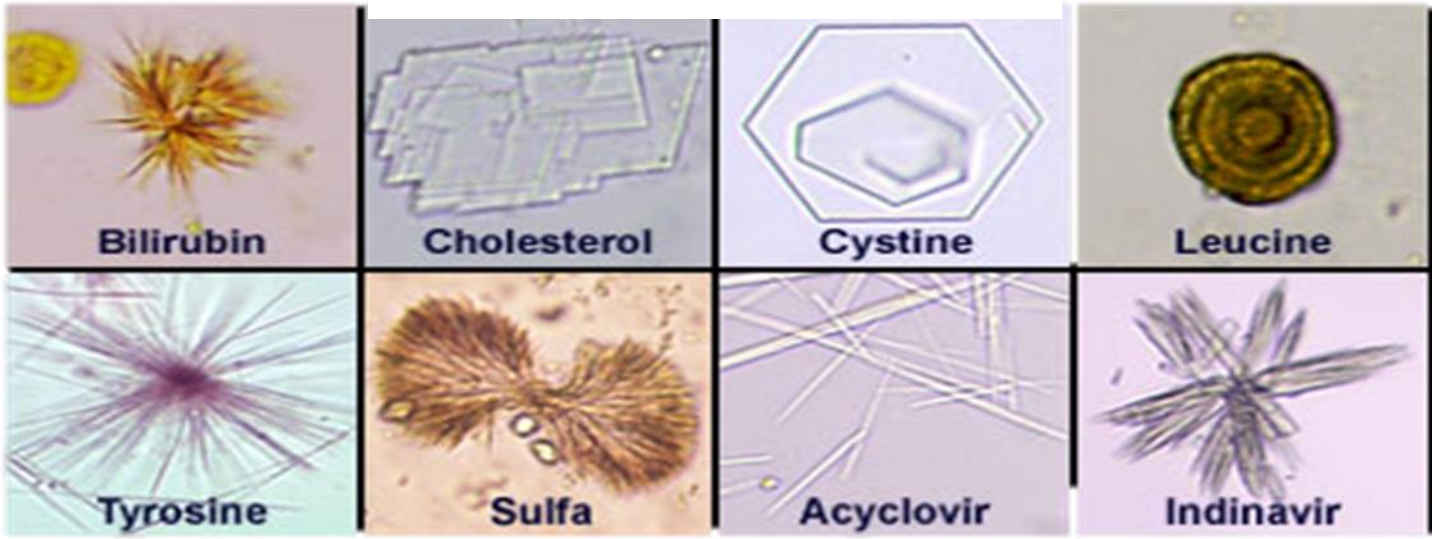
- Higher sensitivity and specificity for calculus detection.
- Not use intravenous contrast medium.
- Require a shorter examination time.
- CT can visualise **all radiopaque stones**, as well as **radiolucent** stones **such as uric acid and cystine calculi.**
- It shows the distal ureters;small stones (1 to 2 mm), and renal disorders other than stones, including hydronephrosis and intra-abdominal disorders


Stone at ureterovesicular junction
Dilated ureter
virtualmedstudent.com

Normal CRYSTALS



ABNORmal CRYSTALS



Kidney Stone Analysis

- Figure out the chemical makeup of a kidney stone
- Help guide a treatment plan to prevent more stones from forming

When a stone is available, clinicians should obtain a stone analysis at least once

- Stone composition of uric acid, cystine or struvite implicates specific metabolic or genetic abnormalities.
- knowledge of stone composition may help direct preventive measures.
- Calcium phosphate stone composition is more likely to be associated with certain medical conditions or medications, such as **RTA Type 1, primary hyperparathyroidism, medullary sponge kidney and the use of carbonic anhydrase inhibitors.**

Laboratory (Metabolic) Evaluation

- The diagnostic evaluation of a **first stone** includes a routine chemistry panel (electrolytes, creatinine, calcium, and uric acid), urinalysis, and culture.

- If the patient has high serum calcium or high urine calcium, then a parathyroid hormone level should be measured.

- All patients who have had **at least one** documented instance of a kidney stone should be informed about **24-hour urine prophylactic testing**

- The variables that should be measured in the 24-hour urine collections **are total volume, urea ,calcium, oxalate, citrate, uric acid, sodium, potassium, phosphorus, pH, and creatinine ,Cystine and magnesium**

Laboratory (Metabolic) Evaluation…

- Because individuals frequently alter their dietary habits immediately after an episode of renal colic, a patient should wait at **least six weeks** before performing 24-hour urine collections.

- **Two collections** are needed because of substantial day-to-day variability in the values; this method gives about 92% sensitivity.

Who Should Be Tested?

- ❑ significant renal failure
- ❑ high anesthetic/surgical risk factors
- ❑ multiple stones and repeated urolithiasis surgeries
- ❑ renal transplants, or solitary kidneys
- ❑ chronic diarrhea (IBS, short bowel syndrome or post gastrointestinal bypass surgery)
- ❑ all cystine stone formers
- ❑ children

Simplified Ambulatory Metabolic Evaluation and Interpretation of Urinary Parameters[a]

Random 24-Hour Urinary Profile	Expected Values (per day)	Interpretation
Total volume	≥2.5 L	Indicative of daily fluid intake (minus insensible losses); diminishes with low fluid intake, sweating, and diarrhea
pH	5.9–6.2	<5.5—increases risk of uric acid precipitation; commonly found in idiopathic uric acid stone patients, subjects with intestinal disease and diarrhea, and in those with intestinal bypass surgery >6.7— increases risk of calcium phosphate precipitation; commonly found in patients with dRTA, primary hyperparathyroidism, alkali, and carbonic anhydrase treatment >7.0–7.5— indicates urinary tract infection from urease-producing

Creatinine	15–25 mg/kg body weight (0.13–0.22 mmol/kg body weight)	Assessment of completeness of collection 15–20 mg/kg body weight (0.13–0.15 mmol/kg body weight) in females, 20–25 mg/kg body weight (0.15–0.22 mmol/kg body weight) in males; valid only in steady state of constant serum creatinine concentration with time
Sodium	100 mEq (100 mmol)	Reflects dietary sodium intake (minus extrarenal loss); much lower than dietary intake in diarrhea and with excessive sweating; high sodium intake is major cause of hypercalciuria
Potassium	40–60 mEq (100 mmol)	Reflects dietary potassium intake (minus extrarenal loss); much lower than dietary intake in diarrhea states; gauge of dietary alkali intake because most dietary potassium accompanied by organic anions
Calcium	≤250–300 mg (≤6.24–7.49 mmol)	A higher value expected in males; in states of zero balance, urinary calcium excretion is net gut absorption minus net bone deposition; secondary causes should be ruled out before making the diagnosis of idiopathic hypercalciuria

Magnesium	30–120 mg (1.23–4.94 mmol)	Low urinary magnesium detected with low magnesium intake, intestinal malabsorption (small bowel disease), and following bariatric surgery; low magnesium may increase risk of calcium stones.
Oxalate	≤45 mg (≤0.51 mmol)	Commonly encountered with intestinal disease with fat malabsorption, such as inflammatory bowel disease and following bariatric surgery; values >100 mg/day (1.14 mmol/day) suggest primary hyperoxaluria (PH); the diagnosis of PH I and PH II is further established with high urinary glycolate and L-glycerate levels.
Phosphorus	≤1100 mg (35.5 mmol)	Indicative of dietary organic and inorganic phosphorus intake and absorption; a higher

Uric acid	600–800 mg (3.57–4.76 mmol)	Hyperuricosuria is encountered with overproduction of endogenous uric acid or overindulgence of purine-rich foods such as red meat, poultry, and fish; mainly a risk factor for calcium oxalate stones when UpH is >5.5 but is a risk factor for uric acid stone when UpH < 5.5.
Sulfate	≤20 mmol	Sulfate is a marker of dietary acid intake (oxidation of sulfur-containing amino acids).
Citrate	≥320 mg (≥1.67 mmol)	Inhibitor of calcium stone formation; hypocitraturia is commonly encountered in metabolic acidosis, dRTA, chronic diarrhea, excessive protein ingestion, strenuous physical exercise, hypokalemia, intracellular acidosis, with carbonic anhydrase inhibitor drugs (e.g., acetazolamide, topiramate, zonisamide), but rarely with ACE inhibitors
Ammonium	30–40 mEq (30–40 mmol)	Ammonium is a major carrier of H^+ in the urine; its excretion corresponds with urinary sulfate (acid load); a higher ammonium-to-sulfate ratio indicates GI alkali loss.
Chloride	100 mEq (100 mmol)	Chloride varies with sodium intake.
Cystine	<30–60 mg (<0.12–0.25 mmol)	Cystine has a limited urinary solubility, at 250 mg/L.

Defining hypocitraturia

- **Hypocitraturia** usually is defined as citrate excretion of **less than 320 mg per day**
- **Severe hypocitraturia** is citrate excretion of **less than 100 mg per day**
- **mild to moderate hypocitraturia** is citrate excretion **of 100-320 mg per day**

- **optimal daily urinary citrate levels for calcium stone formers would probably range from 500-800 mg**

Hypocitraturia management

- **Potassium citrate is preferred over sodium** alkali because **sodium loading can increase urine calcium excretion**, offsetting the benefits of raising urine citrate

- Citrate treatment can **raise urine pH**, and this **may increase the risk for Ca-P stones** if urine calcium remains high and fluid intake is not maintained

Potassium citrate

- Restore normal urinary citrate (ie**, >320 mg/d** and as close to the normal mean **of 640 mg/d as possible) and to increase urinary pH to a level between 6.0 and 7.0.**

- Urinary **citrate and/or urinary pH** measurements should be **evaluated every3months**.

- Potassium citrate is available in **5- or 10-mEq tablets** (eg, Urocit-K) or as a liquid, powder, or syrup combining potassium citrate and citric acid (eg, Polycitra-K). The powder and syrup are mixed with water before ingestion.

Potassium citrate…

- Doses of Urocit-K **greater than 100 mEq/d** should be avoided when possible. the risk of **hyperkalemia** is increased when these higher dosages are used.

- The pH change after institution of potassium citrate therapy generally is small, maintain **the pH below 7.0-7.2.**

- **At pH levels above 7.2**, the risk of calcium phosphate crystallization increases significantly.

- Citrate therapy may be **counterproductive** in patients with **infection.**

Dietary advice for single 24 h urine abnormalities.

Hypercalciuria (>6.5 and 7.5 mmol/day for women and men, respectively)
Low animal protein intake (0.8–1 g/kg/day)
Low salt intake (<5 g NaCl/day)
High intake of fruits and vegetables
Hyperoxaluria (>0.5 mmol/day)
Low dietary oxalate intake
Balanced calcium intake (1.2 g/day)/calcium supplement
Hypocitraturia (< 1.5 mmol/day)
Low animal protein intake (0.8–1 g/kg/day)
High intake of fruits and vegetables/potassium, citrate, and magnesium supplementation
Low urine pH/hyperuricosuria (>4.5 and 4.8 mmol/day for women and men, respectively)
High intake of fruits and vegetables/potassium, citrate, and magnesium supplementation
Low dietary purine intake
Low animal protein intake (0.8–1 g/kg/day)

Commonly Used Drugs in the Treatment of Hypercalciuric Calcium Nephrolithiasis

Drug	Recommended Dosage(s)	Comments
Hydrochlorothiazide	50 mg/day, 25 mg bid	A single dose is preferred because twice-daily dosage may cause nocturia, discomfort, and noncompliance.
Chlorthalidone	25 mg/day, 50 mg/day	Both dosages lower urinary calcium by the same degree; long-acting; may cause hypokalemia and secondary hypocitraturia
Indapamide	1.2 mg/day, 2.5 mg/day	This treatment may have fewer side effects than hydrochlorothiazide, including lower incidence of hypokalemia and hypotension.
Amiloride	5 mg/day	Potassium sparing; lowers urinary calcium but to a lesser degree than hydrochlorothiazide
Amiloride-hydrochlorothizide	5 mg-50 mg/day	Maintains the hypocalciuric effect of thiazide while averting the development of severe hypokalemia
Trichlormethiazide	2 mg/day, 4 mg/day	Not marketed in the United States

Medical Management of Uric Acid Stones

- oral citrate or bicarbonate therapy to increase urinary pH.

- xanthine oxidase inhibitors to decrease uric acid production if urinary uric acid excretion >800 mg/day.

Medical Management of calcium oxalate stone

- **Cholestyramine**, 2 to 4g with each meal, is even more effective as an oxalate binder, but its drawbacks include unpleasant taste and the possibility of inducing vitamin K deficiency .

- Sevelamer hydrochloride has been tried to reduce oxalate absorption, but the results are inconsistent.

- Finally, a role for other nutritional supplements, such as **vitamin B6 (pyridoxine), omega-3 fatty acids, and probiotics**, in reducing urinary oxalate excretion in **idiopathic calcium oxalate stone** formers has been suggested.

Cystine stones

- Urine dilution, alkalinization and chelating therapy have remained the cornerstone of the therapeutic approach.
- A reasonable goal is to keep the **cystine concentration under about 240 mg/L and urine pH about 7 to maintain urine cystine supersaturation lower than 1.**
- The goal almost always necessitates **more than 4L of urine volume.**
- I f the urine **pH is below 7, potassium citrate 10-20 mEq taken three times per day can be used to raise it.**
- If stones recur despite adequate hydration and alkaline urine pH, a cysteine-binding drug should be added: **D-penicillamine and tiopronin**

Follow-up

- clinicians should obtain a single **24-hour urine specimen** for stone risk factors **within 3months** of the initiation of treatment to assess response to dietary and/or medical therapy.

- After the initial follow-up, clinicians should obtain a single 24-hour urine specimen **annually or with greater frequency**, depending on stone activity, to assess patient adherence and metabolic response.

- If patients remain stone free on their treatment regimen for **an extended period of time**, discontinuation of follow-up testing may be considered

- **A one-year** imaging interval is recommended for **stable patients**, but this may be tailored based on stone activity or clinical sign;

Then **every 2-3 year** and then **every 4 year forever .**

Reference

1.Up to date 2021

2. Brenner 2020

3. Management of Kidney Stones in 2020
Andrew D. Rule, MD[1,2]; John C. Lieske, MD[1,3]; Vernon M. Pais Jr, MD[4]
JAMA. 2020

Thanks