Urolithiasis

by:

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Introduction:.

Urinary calculi are the third most common affliction of the urinary tract, next to urinary tract infections and pathologic conditions of the prostate.

Etiology

- Depends on urinary pH, ionic strength, solute concentration, and complexation
- The greater the concentration of 2 ions, the more likely they are to precipitate, a specific point termed the

solubility product (Ksp). Concentrations above this point are metastable and are capable of initiating crystal growth and heterogeneous nucleation . As solutions become more concentrated, the activity product eventually reaches the **formation product** (Kfp)

- Complexation influences the availability of specific ions. For instance, sodium complexes with oxalate and decreases its free ionic form, while sulfates can complex with calcium .

- Other substances found in the urinary tract including magnesium, citrate, pyrophosphate, and a variety of trace metals. These inhibitors may act at the active crystal growth sites or as inhibitors in solution (as with citrate).

Theories to explain urinary stone disease are incomplete

The nucleation theory =

stones originate from crystals or foreign bodies immersed in supersaturated urine.

Against it is Stones do not always form in patients who are hyperexcretors or who are at risk for dehydration.

many stone formers' 24-hour urine collections are completely normal.

- The crystal inhibitor theory
- calculi form owing to the absence or low concentration of natural stone inhibitors, (magnesium, citrate, pyrophosphate).

- This theory does not have absolute validity since many people lacking such inhibitors

  may never form stones, and others with an abundance of inhibitors may, paradoxically, form them

- The theory of mass precipitation or intranephronic calculosis suggests that the distal tubules or collecting ducts, or both
- The fixed particle theory postulates that formed crystals are somehow retained within cells or beneath tubular epithelium.

COMPONENT of stone

crystalline component

steps of crystal formation are

nucleation, -growth, and -aggregation

- Nucleation initiates the stone process and may be induced by a variety of substances, including proteinaceous matrix, crystals, foreign bodies, and other particulate tissues.
- Heterogeneous nucleation (epitaxy), requires less energy and in less saturated urine, is a common theme in stone formation , crystal of one type thereby serves as a nidus for the nucleation of another type with a similar crystal lattice.

eg. uric acid crystals initiating calcium oxalate formation.

MATRIX COMPONENT

- It is composed predominantly of protein, with small amounts of hexose and hexosamine.
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The role of matrix in the initiation of ordinary urinary stones as well as matrix stones is unknown.

It may serve as a nidus for crystal aggregation or as a glue

Urinary Ions

A. CALCIUM

- major ion in urinary crystals , over 95% of the calcium is reabsorbed
- Diuretic medications may exert a hypocalciuric. Many factors influence availability of calcium in solution, including complexation with citrate, phosphate, and sulfate .
- An increase in monosodium urates and a decrease in urinary pH further interfere with this complexation and therefore promote crystal aggregation.

B. OXALATE

- Oxalate is a normal waste product of metabolism and is relatively insoluble , principal precursors of oxalate are glycine and ascorbic acid
- 10–15% of oxalate found in the urine originates from the diet .
- Once absorbed from the small bowel, oxalate is excreted almost exclusively by the proximal tubule ,
- The calcium within the bowel lumen is an important factor influencing the amount of oxalate that is absorbed. Small changes in oxalate levels in the urine can have a dramatic impact on the supersaturation of calcium oxalate .
- Hyperoxaluria may develop in inflammatory bowel disease, smallbowel resection, and bowel bypass. Renal calculi develop in 5–10% of patients with these conditions.

C. PHOSPHATE

- complexes with calcium in urine , related to the amount of dietary phosphate (especially in meats, dairy products, and vegetables). Parathyroid hormone inhibits this reabsorption

D. URIC ACID

- Uric acid is the by-product of purine metabolism , The pKa of uric acid is 5.75. Undissociated uric acid predominates with pH values less than this. Elevated pH values increase urate, which is soluble.
- Pure uric acid crystals and calculi are typically radiolucent.
- They are visible on noncontrast CT images.

- **E. SODIUM**
- sodium plays an important role in regulating the crystallization of calcium salts in urine. and may play a role in initiating crystal development and aggregation
- High dietary sodium intake increases urinary calcium excretion
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- **F. CITRATE**
- A deficiency commonly is associated with stone formation in those with chronic diarrhea or renal tubular acidosis type I (distal tubular defect) and in patients undergoing chronic thiazide therapy. Estrogen increases citrate excretion

- **G. MAGNESIUM**
- deficiency is associated with an increased incidence of urinary stone disease calcium oxalate ,
- Magnesium is a component of struvite calculi , magnesium exerts its effect is undefined. supplements do not protect against stone formation in normal people

- **H. SULFATE**
- prevent urinary calculi complex with calcium

- **OTHER URINARY STONE INHIBITORS**
- glycosaminoglycans, pyrophosphates, and uropontin , preventing urine crystal formation + Fluoride

Stone Varieties

- **CALCIUM CALCULI**
- Eighty to eighty-five percent of all urinary stones are calcareous. most commonly due to
- elevated urinary calcium,
- elevated urinary uric acid,
- elevated urinary oxalate,
- or a decreased level of urinary citrate.

- **1. Absorptive hypercalciuric nephrolithiasis—** intake averages 900–1000 mg/ day. one-third is absorbed by the small bowel (jejunum) , and of that portion 150–200 mg is obligatorily excreted in the urine.
- Absorptive hypercalciuria is due to increased calcium absorption leading to increased calcium filtered from the glomerulus & suppression of parathyroid hormone, leading to decreased tubular reabsorption of calcium, end with hypercalciuria (>4 mg/kg).
- Cellulose phosphate must be taken with meals to be available when calcium is ingested , Hydrochlorothiazides are an alternative treatment for **type I** absorptive hypercalciuria**,** limited long-term efficacy **Type II** absorptive hypercalciuria is dietary dependent and is a common cause of urinary stone disease. There is no specific medical therapy **Type III** absorptive hypercalciuria is secondary to a phosphate renal leak

- **2. Resorptive hypercalciuric nephrolithiasis—**
- obvious primary hyperparathyroidism
- **3. Renal-induced hypercalciuric nephrolithiasis—**
- due to an intrinsic renal tubular defect in calcium excretion, patients have *an elevated fasting
- urinary calcium level,* normal serum calcium level, and an *elevated parathyroid hormone level. treated with hydrochlorothiazides. Unlike their role in type I absorptive hypercalciuria, in this setting hydrochlorothiazides have a durable long-term effect.

- **4. Hyperuricosuric calcium nephrolithiasis—**
- excessive dietary intake of purines or an increase in endogenous uric acid production
- Patients have *elevated urinary uric acid levels (>600 mg/24 h in women and >750 mg/24 h in men)
- and **consistently have a urinary pH >5.5. The urinary pH helps to differentiate hyperuricosuric calcium from hyperuricosuric uric acid stone formation. changing their diet.
- Allopurinol

- **5. Hyperoxaluric calcium nephrolithiasis**
- due to increased urinary oxalate levels (>40 mg/24 h) as in patients with inflammatory bowel disease or other chronic diarrheal states that result in severe dehydration
- Enteric hyperoxaluric calcium nephrolithiasis is successfully treated with oral calcium
- Primary hyperoxaluria is a rare hereditary disease. It is associated with calcium oxalate renal calculi, nephrocalcinosis, and other distant deposits of oxalate, culminating in progressive renal failure and eventual death. Oxalate crystal deposits develop rapidly in transplanted kidneys.
- Combined liver and renal transplantation has cured this previously fatal rare disease

- **6. Hypocitraturic calcium nephrolithiasis**
- Increased metabolic demands on the mitochondria of renal cells decrease the excretion of citrate. Such conditions include intracellular metabolic cidosis, hypokalemia (as with thiazide therapy), fasting, hypomagnesemia, androgens, gluconeogenesis, **it** complexes with calcium, thereby decreasing the ionic calcium concentration
- Six to eight glasses of lemonade can increase urinary citrate excretion by approximately 150 mg/24 h and thus either limit or eliminate the need for pharmacologic citrate supplementation.

- **B. NONCALCIUM CALCULI**
- **Struvite—** composed of magnesium, ammonium, and phosphate (MAP).
- Most commonly in women and may recur rapidly , presented as renal staghorn calculi and rarely present as ureteral stones except after surgical intervention
- **urea-splitting organisms, including *Proteus*, *Pseudomonas*, *Providencia*, *Klebsiella*, *staphylococci*, and *Mycoplasma*. *cause*** high ammonium concentration results in an alkaline urinary pH. above 7.2 (normal urinary pH is 5.85). Massive diuresis does not prevent struvite calculi. Stone removal is therapeutic. Long-term management is optimized with the removal of all foreign bodies
- Hemiacidrin (Renacidin) irrigations should be used with caution if at all

- **2. Uric acid—**
- usually found in men , Patients with gout, myeloproliferative diseases, or rapid weight loss, and those treated for malignant conditions with cytotoxic drugs have a high incidence of uric acid lithiasis Most patients with uric acid calculi, however, do not have hyperuricemia , Patients present with a urinary pH consistently <5.5, in contrast to patients with hyperuricosuric calcium nephrolithiasis, who have a urinary pH >5.5. As the urinary pH increases above the dissociation constant pKa of 5.75, it dissociates into a relatively soluble urate ion.
- Treatment is a urine *volume >2 L/day and a urinary pH >6. *Reducing dietary purines
- *allopurinol also helps reduce uric acid excretion. *Alkalinization (with oral sodium bicarbonate, potassium bicarbonate, potassium citrate, or intravenous one-sixth normal sodium lactate) may dissolve calculi and is dependent on the stone surface area. Stone fragments after lithotripsy have a dramatically increased surface area and will dissolve more rapidly. Dissolution proceeds at approximately 1 cm of stone (as seen on KUB) per month, with compliant alkalinization.

- **3. Cystine—**
- Inborn error of metabolism resulting in abnormal intestinal (small bowel) mucosal absorption and renal tubular absorption of dibasic amino acids, including cystine, ornithine, lysine, and arginine.
- Autosomal recessive fashion , heterozygous 10 times more Homozygous expression , The solubility of cystine is pH-dependent, with a pK of approximately 8.1,
- Urinalysis frequently reveals hexagonal crystals. Stone analysis confirms the diagnosis. They may present as single, multiple, or staghorn stones. The
- X-ray faintly opaque, ground-glass, smooth-edged stone,
- Medical therapy includes *high fluid intake (>3 L/day) and urinary *alkalinization , keep their pH values >7.5 . *Glutamine, ascorbic acid, and captopril are effective in some patients. Penicillamine can reduce urinary cystine levels, Mercaptopropionylglycine (Thiola), 300– 1200 mg in divided doses, forms a soluble complex with cystine and can reduce stone formation
- Surgical treatment is similar to that for other stones except that most stones are recalcitrant to extracorporeal
- (outside the body) shock wave lithotripsy (ESWL).

- **4. Xanthine—**

- secondary to a congenital deficiency of xanthine oxidase. That cause oxidation of hypoxanthine to xanthine and of xanthine to uric acid It is of interest that allopurinol,used to treat hyperuricosuric calcium nephrolithiasis and uric acid lithiasis, produces iatrogenic xanthinuria however, there are no case reports of xanthine stone formation resulting from allopurinol treatment. The stones are radiolucent and are tannish yellow in color.
- High fluid intake and urinary alkalinization are required for prophylaxis

- **Indinavir—**
- Protease inhibitors are a popular and effective treatment in patients with acquired immunodeficiency syndrome. Indinavir calculi are the only urinary stones to be radiolucent on noncontrast CT scans. Temporary cessation of the medication with intravenous hydration frequently allows these stones to pass.
- **6. Rare—**
- Silicate stones are very rare and are usually associated with long-term use of antacids containing silica.
- Triamterene stones are radiolucent and have been identified with an increased frequency. They are associated with antihypertensive medications containing triamterene,
- such as Dyazide.
- fake urinary stone, with specks of paint or other obvious curiosities. Such patients have Munchausen syndrome, and the diagnosis is difficult and made by exclusion.