Nephrolithiasis is a clinical condition characterized by the presence of stones in the kidney. Calcium oxalate stones are the most common stones. Clinical presentation is with acute flank pain. Non-contrast CT is the investigation of choice in nephrolithiasis and can diagnose all types of stones. Management depends on the location and size of the stone. Smaller stones have a greater chance to pass spontaneously, while stones larger than 5 mm need surgical management with percutaneous nephrolithotomy, extracorporeal lithotripsy, or open surgery.

Definition of Nephrolithiasis

Nephrolithiasis - The Kidney Stone
Nephrolithiasis, also called kidney stone or renal calculus, is a condition in which stones are formed within the nephrons.

It occurs due to supersaturation and crystallization of inorganic and organic phosphates and acids.

Epidemiology

Nephrolithiasis as a Common Disorder

Nephrolithiasis is one of the most common urological disorders, with roughly 2 million patients present annually on an outpatient basis with a stone disease in the United States. It has a prevalence of 12% in males and 7% in females. The recurrence rate is estimated to be 52% at 10 years after the first episode.

Classification – Types of Stones

Calcium Stones

Calcium stones form the major part of all the stones. The types of calcium stones are:

- Calcium oxalate stones (most common, forming 70-80% of stones)
- Calcium phosphate stones (~15% of stones)

Magnesium Ammonium Phosphate Stones (Struvite Stones)

Struvite stones, also called triple phosphate stones, are commonly associated with urinary tract infections by the urease-producing bacteria (Proteus). These are more common in females than in males, because there is an increased predisposition of urinary tract infection in females. When a stone is large, branched that fills all or part of the renal pelvis, it is called staghorn calculus.
Uric Acid Stones

These are characteristically seen in patients with hyperuricemia either due to excessive uric acid production or under-secretion of uric acid.

Cystine Stones

Cystine stones are seen in patients who have a defective amino acid transporter in the proximal tubule with decreased reabsorption of cystine. It leads to the increased concentration of cystine in the urine (cystinuria), resulting in a formation of pathognomonic hexagonal-shaped stones.

Pathophysiology and Risk Factors

Supersaturation and crystallization are the two primary factors responsible for stone formation. Multiple risk factors have been identified that promote nephrolithiasis. They
have been divided into urinary, dietary, and non-dietary risk factors.

**Urinary Factors**

- **Urine pH:** It affects the likelihood of kidney stone formation. An acidic urine favors uric acid precipitation, while an alkaline urine (as may be seen with urinary tract infections and renal tubular acidosis) promotes calcium phosphate stone formation.
- **Hypercalciuria:** Increased urinary calcium excretion promotes nephrolithiasis. The hypercalciuria may be due to an increase in intestinal absorption, bone resorption or renal loss.
- **Hyperoxaluria:** Increased urinary oxalate excretion promotes nephrolithiasis by binding to calcium and forming insoluble calcium oxalate stones.
- **Hypocitraturia:** An under-secretion of urinary stone inhibitors, for instance, citrate, promotes nephrolithiasis. The citrate normally combines with calcium forming soluble complexes, making calcium unavailable to bind to oxalate.
- **Low urine volume:** Decreased urinary volume increases the risk of nephrolithiasis due to supersaturation and precipitation of crystals.

**Dietary Factors**

- **Calcium:** A higher calcium dietary intake is associated with a lower incidence of kidney stones. Normally, intestinal calcium binds to the oxalates and prevents the absorption of oxalates into the circulation. Decreased calcium leads to an increased absorption of oxalates, which further predisposes calcium oxalate stones.
- **Oxalate:** A higher oxalate intake increases urinary oxalate excretion and increases the risk of nephrolithiasis.
- **Protein:** Higher animal protein is related to higher urine calcium excretion and lower urine citrate excretion, both favoring stone formation.
- **Decreased fluid intake** increases the risk of nephrolithiasis. It is recommended to have at least 8-10 glasses of pure water daily.

**Non-dietary**

- **Family history:** A positive family history increases the risk of stone formation by 2.5 times than general population.
- **Systemic disorders:** Nephrolithiasis is associated with multiple systemic disorders, for instance, primary hyperparathyroidism, renal tubular acidosis, Crohn's disease and gout.
- **Environmental factors:** Higher temperatures and increased fluid loss in sweating without adequate fluid intake promotes stone formation due to lower urine volume.

**Clinical Features**

**Abdominal pain** is the presenting feature of the nephrolithiasis. The pain can be moderate to severe in intensity, colicky and paroxysmal in nature, often associated with nausea and vomiting. The location of pain is dependent on the site of obstruction. The presence of flank pain, radiating to the groin, is due to the presence of a stone in the lower ureter, while the presence of constant flank pain indicates the presence of a stone at the upper ureter or at ureteropelvic junction. The patients are usually
restless and agitated.

Diagnosis & Laboratory Investigations

Urine Examination

The microscopic urine examination may show **characteristic crystals** that are formed as a result of supersaturation of the inorganic salts present in the urine.

- **Calcium stones:** Enveloped or dumbbell shaped oxalate crystals
- **Struvite stones:** Coffin lid crystals
- **Uric acid stones:** Rhomboid or rosette shaped stones are seen
- **Cystine stones:** Hexagonal stones

**Urine dipstick test** helps in etiologic differentiations by checking the pH, erythrocytes, leukocytes, bacteria, and protein.

The urine **cyanide-nitroprusside test** is positive for identification of **cystinuria**.

Radiological Investigations

1. **Plain X-ray:** Most of the renal stones are radio-opaque and can be seen on plain abdominal X-ray. The notable exception is the uric acid stones that are radiolucent.
2. **Ultrasound:** It helps in the identification of the renal stones and accompanying **hydronephrosis**.
CT scan: A non-contrast CT scan is the investigation of choice in the diagnosis of the nephrolithiasis. It helps in the diagnosis of all kind of stones (including radiolucent uric acid stones), along with the accurate size and location.

Stone Analysis

The urine analysis of the stones is recommended to know about the stone type and address the risk factors accordingly.

Treatment of Nephrolithiasis

Acute pain management involves the administration of NSAIDs and opioids. The anti-emetics drugs are also given.

The specific treatment depends on the extent, nature, and location of the stone. It usually involves a combined medical and surgical approach.

Generally, smaller stones, less than 5 mm, have an increased chance of responding to the medical treatment and most of these stones pass spontaneously in the urine, whereas stones more than 5 mm have a less chance of falling spontaneously.

Medical therapy

Medical therapy involves wait-and-watch, increased fluid intake and urine alkalinization. The oral alpha adrenergic blocker can be administered if the stone is small and located in the lower ureter. These drugs decrease the tone of the urethral muscle and facilitate the smooth passage of the small stone.

In uric acid stones, medical treatment also includes administration of xanthine oxidase inhibitors, while in cysteine stones, a low methionine diet is advised.

Surgical Management

- Extracorporeal shock wave lithotripsy (ESWL): It is a non-invasive method in which targeted high-frequency ultrasound shock waves are used from outside of the body to break a kidney stone into small fragments. These
fragments then pass easily through the urinary tract and out from the body.  
- **Percutaneous nephrolithotomy** (PCNL): It is a minimally-invasive surgery in which kidney stones are removed by making a small incision through the skin. This method is used for the stones that are easily approached, located near the pelvic region, and are more than 2 cm in size.

- **Open Surgery**

Administration of antibiotics is required to cover the acute infection and maintenance of sterile tract.

**Prognosis**

The majority of stones pass spontaneously. There is an increased chance of recurrence in patients with nephrolithiasis. Increased fluid intake along with metabolic evaluation is recommended in these patients.

Hospitalization is required in conditions where an obstruction due to kidney stone is associated with urinary tract infection. Emergent surgical drainage is required in the presence of urosepsis and pyelonephritis.

**Review Questions**

The solutions are located below the sources.

1. **What are the most characteristic features of the cystine stones?**
   - A. Envelope or dumbbell shaped crystals
   - B. Coffin lid crystals
   - C. Rhomboid or rosette shaped stones
   - D. Hexagonal stones
   - E. Conical crystals

2. **Which of the following is the investigation of choice for the diagnosis of nephrolithiasis?**
   - A. CT scan
   - B. Ultrasound
   - C. Plain X-ray
   - D. Stone analysis
   - E. Acoustic microscopy

3. **The composition of struvite stones is...**
   - A. ...magnesium ammonium phosphate
   - B. ...calcium only
   - C. ...calcium oxalate
   - D. ...phosphate only
   - E. ...uric acid

**References**


Diagnosis and acute management of suspected nephrolithiasis in adults via upToDate.com

Cystine stones via upToDate.com

Uric acid nephrolithiasis via upToDate.com

Correct answers: 1D, 2A, 3A

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