Agenda

I. Epidemiology and risk factors
II. Pathophysiology
III. The Radiologist’s Predicament
IV. History of Nephrolithiasis Imaging Modalities
V. Summary of Clinical Protocol
Epidemiology

- 12% of the US population will have a urinary tract stone at some point in their lifetime
  - Peak incidence 30-50 years old
- 2-3% of population will experience acute renal colic
  - 40% to 50% recur within 5 years
  - 50% to 60% recur within 10 years
  - 75% recur within 20 to 30 years.

- Adults: Incidence in men 3X that in women
- Children: Incidence males = females
Contributing Factors

herits Heredity (RTA, cystinuria)

Geography

- High incidence in: US, Britain, Scandinavia, northern India and Pakistan, Mediterranean countries, northern Australia, central Europe, and China.
- Low incidence in: Central and South America and most of Africa.

Decreased H₂O intake and urinary output in people predisposed to stone formation

Diet which can increase urinary excretion of stone forming substances

Sedentary life style

Affluence
Mechanism of Stone Formation

ロー Related to the solubility product constant:

If $A_{(aq)} + B_{(aq)} \rightarrow AB_{(s)}$ then $[A][B] = K_{sp}$

ロー Calculation is more complicated in urine than in H$_2$O, but similar principles apply

↪ If $A \times B > K_{sp}$ then precipitate forms

ロー Once a crystal forms, it can act as a nidus for more precipitate formation as long as the solution continues to be supersaturated
Stone Composition

Most consist of 95% crystalline material and 5% non-crystalline matrix.

- Matrix material consists of protein, cellular debris, and other organic materials.

Most stones have only one or two crystalline components.

75% of urinary calculi contain calcium oxalate, calcium phosphate, or both.

Struvite containing stones are seen in pts with chronic urea splitting organism infections.
Stone Size and Obstruction

 générations of medical students learn to quote the figure of 2 mm, as the size below which the stone is expected to pass spontaneously.

 This number is based on plain film and IVU assessment

 CT has demonstrated stones 1 mm or less that have resulted in obstruction\(^1\)

\(^1\)Radiologic Clinics North America - 1999 Sep; 37(5): 911-52
Common Sites of Obstruction

Three sites predominate where the ureter narrows in diameter:

1) The ureteropelvic junction (UPJ)
2) Iliac vessels bifurcation
3) The ureterovesical junction (UVJ)
Stone Site and Obstruction

Some stones will spontaneously pass

- Varies depending on location

A study by Morse and Resnick in which 60% of stones passed spontaneously showed:

- 22% for proximal ureteral stones,
- 46% for midureteral stones,
- 71% for distal ureteral stones.

(These authors did not distinguish between distal ureteral stones and stones at the UVJ).
The Radiologists’ Predicament

One cold evening, the night float radiologist is viewing films from ED...

Our Patient presented with Left flank/lower quadrant pain
The Radiologists’ Predicament

The Differential for that is long. What do I need to look for?
# DDX for LLQ/Flank Pain

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Possible findings on KUB</th>
</tr>
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<tbody>
<tr>
<td>Ovarian Torsion</td>
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<tr>
<td>Ovarian cyst</td>
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<td>Ectopic Pregnancy</td>
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</tr>
<tr>
<td>Diverticulitis</td>
<td>Wall thickening</td>
</tr>
<tr>
<td>Renal Stones</td>
<td>Radiopaque stone in area of ureter</td>
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For Completeness, let’s review DDX for RLQ/Flank Pain

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Possible findings on KUB</th>
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<tbody>
<tr>
<td>Appendicitis</td>
<td>Appendicolith</td>
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<tr>
<td>Ovarian Torsion</td>
<td>none</td>
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<tr>
<td>Ectopic Pregnancy</td>
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</tr>
<tr>
<td>Ovarian cyst</td>
<td>none</td>
</tr>
<tr>
<td>Right Sided Divertics</td>
<td>wall thickening</td>
</tr>
<tr>
<td>Typhlitis</td>
<td>Cecal thickening</td>
</tr>
<tr>
<td>Renal Stones</td>
<td>Radiopaque stone in area of ureter</td>
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</tbody>
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Menu of Tests

- Abdominal and pelvic ultrasound
- Abdominal and pelvic CT
- Abdominal and pelvic MRI
- IVU
- Barium GI studies
The Most Appropriate Test

- In some women, and all pregnant women and children US is usually ordered first
- In men a CT scan is often the first and definitive test
- Our patient is a 47 year old male, so a CT was obtained
Abdominal CT Scan
Abdominal CT Scan

Without IV Contrast

- Liver
- Pancreas
- Spleen
- Calcified Stone in Left Kidney (Not responsible for obstruction)
- Right Kidney
- IVC
- Left Kidney

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Abdominal CT Scan

Without IV Contrast

- Gallbladder
- Colon with stool
- Right Kidney
- IVC
- Liver
- Descending Colon
- Aorta
- Dilated collecting system
- Left Kidney
- Perinephric stranding

No Stones Observed
Pelvic CT Scan

Without IV Contrast

- Bladder
- Phleboliths
- Uretovesicular Junction (UVJ)

No Stones Observed
IV Contrast Enhanced Abdominal CT Scan

No Stones Observed

Left Kidney
Right Kidney
Liver
Gallbladder
Aorta
IVC
Stranding
Summary of CT Findings

☒ Delayed excretion and dilation of the renal pelvis and collecting system are c/w acute renal obstruction.
☒ Still no stone was visualized?! 
☒ Almost all stones should be seen on unenhanced helical CT.
Plain Film following Abdominal CT
Plain Film following Abdominal CT

- Right Kidney
- Right ureter
- Bladder
- Left Kidney (enlarged, poorly functioning)
Findings

Findings are consistent with left renal obstruction but again the site of obstruction was not seen.
Sonography

Let’s review the ultrasound appearance of renal obstruction
Sonography

RIGHT KIDNEY
Sonography

Legend
NL Right Kidney
Fat ****

NORMAL RIGHT KIDNEY
Sonography
Sonography

Legend
Liver
Gallstones
Fat ***
Gallbladder
Kidney

[Image of a sonogram with annotations]

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Sonography

HYDRONEPHROTIC LEFT KIDNEY
Sonography

Legend
- Dilated Collecting System (DC)
- Kidney (∨)
- Fat (***)

DC
Sonography

Bladder

Prostate
The Appropriate Test

 DECLARE An IVU and an Ultrasound were not indicated in this patient, as the CT scan coupled with the history made the diagnosis. So what was the history?
Back to the History

❑ The Radiologist, attending ER Doc and medical student met to review the imaging results. The Radiologist and ER Doc smiled knowingly.

❑ They suggested the medical student talk with the patient about his medical history, research nephrolithiasis on the web and then report why no stone was visualized.

❑ Here’s what the medical student found…. 
Patient History

 зр PG is a 47 year old HIV+ male who has recently started taking Indinavir.

☞ His doctor asked him to drink at least 1.5 liters of fluid everyday, but he is too busy at work to comply

☞ He began experiencing left flank/LLQ pain approximately 12 hours ago which became intolerable.
History of Imaging Nephrolithiasis

First image of renal calculus:

- April 1896 by John Macintyre
- Just a few months after Roentgen’s discovery of x-rays
- Gained support quickly

Orton in 1908 publishes on the diagnostic dilemma of the misdiagnosis of a phlebolith as renal calculus
Attempts to visualize the ureters

- Tuffier (1896) - 1st opacification of the ureter on radiograph
  - inserted a metal wire into a ureteral catheter
  - radiopaque ureteral catheters were developed to diagnose ureteral stones. Other means of outlining the ureters on radiographs were soon attempted.

- Wittek (1903) - used air, but it did not gain popularity.

- Voelcker and von Lichtenberg (1905) - 1st liquid contrast agent
  - a colloidal suspension of silver (Collargol) instilled into the bladder.
  - 1906 same MDs opacified the entire collecting system
  - 1st technique of retrograde pyelogram
  - Collargol deemed responsible for several cases of renal damage and even some deaths
Attempts to visualize the ureters

❖ Cameron (1918) - 1st iodine-containing contrast material
  ↳ Solution of sodium and potassium iodide
  ↳ became the agent of choice for retrograde pyelography
  ↳ Retrograde pyelography, however, was still less than ideal given that cystoscopy and instrumentation were required.

❖ Weld (1919) reports a contralateral pyelogram in the contralateral kidney in patients undergoing unilateral retrograde pyelography.
  ↳ Assumed to be due to absorption of the contrast material into the circulation where it was filtered and excreted by both kidneys.

❖ Osborne (1923) - first use of IV sodium iodide to achieve a bilateral pyelogram
  ↳ Poor quality and consistency of images obtained in this manner.
Attempts to visualize the ureters

- “Modern” intravenous urography (IVU)
  - Swick (1929) - iodinated pyridine compound (Selectan)
  - Contrast agent of choice for the next 20 years.

- Iodinated benzoic Acid derivatives used in 1952
  - Much safer than pyridine-based agents

- Nonionic agents introduced - 1980s
For almost a century after Macintyre’s initial finding, the plain radiograph was felt to be the diagnostic imaging of choice for nephrolithiasis.

This was supported by many reports throughout the years quoting excellent sensitivity values.
The Plain Radiograph

Many studies reported the sensitivity of the plain radiograph to be quite high:

- 1932 – 89% of stones radiopaque (Twinem)
- 1933 – 90% of stones radiopaque (Ravich)
- 1962 – 90% of stones radiopaque (Herring)
- The 5th edition of *Brenner and Rector’s The Kidney* quotes 85% are radiopaque
The Plain Radiograph

- Other studies reported less impressive numbers
  - 1985 62% radiopaque (Roth)
  - 1991 58% radiopaque (Mutgi)

- Problem with all of the studies:
  - Used recovery of stones by the patient or a positive IVU to make a diagnosis of ureterolithiasis.
  - This is not proof that the calcific density seen on the abdominal radiograph was the stone.
The Plain Radiograph

The final answer on sensitivity:

- CT used as a gold standard to confirm the precise location of calcific densities seen on plain radiography (Levine et al)
- Sensitivity of 59% for detecting ureteral calculi (95% CI for this value being 49% to 70%).
- Films viewed three times (twice blinded and once unblinded)
## Stone composition and its appearance on plain radiograph

<table>
<thead>
<tr>
<th>Stone Composition</th>
<th>Appearance on Radiograph</th>
</tr>
</thead>
<tbody>
<tr>
<td>✡ Calcium phosphate</td>
<td>✡ Most radiodense</td>
</tr>
<tr>
<td>✡ Calcium oxalate</td>
<td>✡ &lt; Calcium phosphate</td>
</tr>
<tr>
<td>✡ Struvite</td>
<td>✡ &lt; Calcium oxalate</td>
</tr>
<tr>
<td>✡ Cystine</td>
<td>✡ Mildly radiodense</td>
</tr>
<tr>
<td>✡ Uric acid</td>
<td>✡ Radiolucent</td>
</tr>
<tr>
<td>✡ matrix stones</td>
<td>✡ Radiolucent</td>
</tr>
<tr>
<td>✡ Indinivar</td>
<td>✡ Radiolucent</td>
</tr>
</tbody>
</table>
Other Factors that Determine Visibility on Radiograph

- Peak kilovoltage used:
  - low kilovoltage (peak) technique (60 to 70 kVp) is ideal, but this may not be possible especially with obese patients

- Presence of overlying bowel contents or bone.

- Size of the stone
  - generally must be $\geq 2$ mm to be seen on plain radiographs
Visibility on Radiograph

¬ Bottom line:

❖ if a calcific density is seen along the anatomic course of the ureters on a plain radiograph, it cannot be definitively said to be in the ureter, because the ureter cannot be directly visualized.

❖ However, if the patient’s clinical presentation suggests urolithiasis this calcification mandates a renal work up.
Advantages of IVU

☑ Can usually diagnose ureteral obstruction
☑ Can image radiolucent stones
☑ Gives Rough estimate of renal function based on timing of opacification with contrast.
IVU

♀ Signs of obstruction include

♂ a delayed nephrogram
♂ delayed pyelogram
♂ dilatation of the collecting system,

♀ No literature that these findings correlate with true physiologic parameters, treatment outcome, or degree of residual renal impairment s/p obstruction.
Disadvantages of IVU

- IV iodinated contrast material - risk of adverse reactions
  - GI: nausea, vomiting
  - CP: bronchospasm, hypotension
  - CNS: seizures
  - Other: nephrotoxicity, urticaria, anaphylactoid reactions
- Indirect findings may be absent (acute partial obstruction).
- Multiple radiographs may be needed to determine level of obstruction leading to an increased dose of radiation.
- Cannot diagnoses nonrenal causes of flank pain.
IVU: Pyelogram Phase
IVU: Pyelogram Phase

Right Calyx

Left Calyx

Bladder
Sonography

US can detect

- dilatation of the collecting system
- changes in renal blood flow
- altered urine flow through the ureteral orifices in the bladder that may accompany obstruction.
- Stones may be visualized as an echogenic focus with or without acoustic shadowing.
  - Stones within the ureter generally **CANNOT** be seen with US
Advantages of Sonography

- Patient is not exposed to radiation
- Stone visualization is not dependent on their composition
- Quick, inexpensive study
Disadvantages of Sonography

✧ Size of stones cannot be accurately measured.
✧ Diagnosis rests on indirect signs of obstruction, which may be unreliable.
   ➔ Delay of ≥ 24 hours s/p onset of obstruction for collecting system dilatation and altered blood flow.
   ➔ Forniceal rupture with decompression of the pelvocalyceal system will yield ambiguous results.
   ➔ Therefore, high rate of false-negative US studies.
✧ Can be hard to image extra-ureteral causes of obstruction
CT as a modality to image ureteral calculi

- Has since become the gold standard and is widely used in the ED to diagnose acute ureteral obstruction.
- Specialized protocol using helical CT is referred to as a CT urogram (CTU).
Advantages of CTU

☑ May eliminate need for IV contrast
☑ Time: < 5 minutes
☑ Virtually all stones (including uric acid stones) can be readily visualized with CT
☑ Determines site and size of ureteral stones
☑ Secondary signs of obstruction allow diagnosis of recently passed stone
☑ Can diagnose other causes of acute flank pain
Accuracy of CT in determining stone size

 الشريف Neitlich et al. used spherical stone phantoms (diameters: 1 to 15 mm) & found that CT measurements had an error of 2% to 7% if the “stone” was 4 mm or greater and 6% to 12% if the diameter was less than 4 mm.*

Size is crucial to determining management!

*Presented at the annual meeting of the Society of Uroradiology, Santa Fe, New Mexico, June, 1997
Stone Visible on CT

In essence all stones are radiopaque (i.e. visualized) on CT scanning except....
Stones not visible on CT

 Worcested Indinavir (Crixovon)

- “Ahah…. That’s the protease inhibitor that PG’s on!”.
- Associated with a 4% incidence of nephrolithiasis - calculi largely contain precipitated indinivar
- Can occur in patients who never had nephrolithiasis before indinivar therapy
- Asymptomatic crystalluria occurs as well (~20%)
- Treatment: hydration and drug withdrawal. Many restart drug.

 Worcested Pure Matrix stones (uncommon)
Secondary Signs Observed on CT

1) Ureteral dilatation - very important 2° sign

- Ureter on obstructed side should have greater lumen diameter than unobstructed side at multiple levels!
- Studies report: sensitivity ~ 90%, specificity ~ 90%,
- Other causes of ureteral dilatation:
  - acute or chronic diffuse or focal pyelonephritis
  - Inflammatory processes adjacent to the ureter may can lead to decreased ureteral peristalsis both locally and diffusely, resulting in ureteral dilatation.
  - Pts who have had prior obstruction, may remain dilated
  - Extrinsic compression by an abdominal or pelvic mass
Secondary Signs Observed on CT

2) Soft tissue stranding of the perinephric fat
   - Inflammatory change or fluid in the perinephric space
   - May be most visible at the lower poles (dependent areas)
   - Specificity ~ 90%, Sensitivity ~80%
   - Relative amount of stranding may correlate with likelihood of passing the stone

3) Periureteral Stranding
   - Less common than perinephric stranding
Secondary Signs Observed on CT

4) Collecting system dilatation
   - NL prominence of the renal pelvis or an extrarenal pelvis should not be confused with dilatation
   - Harder to assess than ureteral dilatation, but specificity and sensitivity are comparable

3) Unilateral renal enlargement

4) Decreased attenuation of the obstructed kidney

5) Rim sign: edema in ureteral wall at site of stone impaction (4-24 hours s/p impaction)
In a study by Dalrymple et al, in cases where CT was negative for stone disease, it provided evidence of the following diagnoses:

- **GYN**: ovarian masses that underwent torsion or hemorrhage
- **GI**: appendicitis, diverticulitis, choledocholithiasis, Crohn's disease, pancreatitis, ventral hernia, cholecystitis
- **Cardiovascular**: leaking abdominal aortic aneurysm, renal artery aneurysm
- **Urinary tract**: pyelonephritis and bladder outlet obstruction
- **Masses**: lymphoma with hemorrhage, retroperitoneal liposarcoma, a hemorrhagic liver hemangioma, vertebral metastases, and a subserosal uterine leiomyoma
- **Other**: ruptured spleen
Summary of Clinical Protocol

Patient presents to the ED with Hx & Sx of Ureteral obstruction

Order an unenhanced helical CT

1) Stone Identified
   - Base Management on estimated size

2) No Stone seen; 2° signs of obstruction are present
   - Is patient taking Indinavir?
     - yes
     - R/O other causes of 2° signs, consult PCP and taper indinavir
     - no

3) No clear stone identified, but suspicious calcification present along ureter course
   - Obtain overlapping reconstructions at and below level of calcification

4) Indeterminate result (usually 2° to inadequate retroperitoneal fat)
   - IV contrast and rescan

5) No stone identified and no 2° signs of obstruction present
   - Exclude stone disease and work up rest of DDX

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References


Kopp J B, MD; Miller KD, MD; Mican JM, MD; et al: Crystalluria and urinary tract abnormalities associated with indinavir. Ann Internal Med. 127: 119-125, 1997.


Acknowledgments

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The End!