Hematuria, Stones and Tumours

UBC Urology
Overview of Hematuria

**Objectives:**

1. Take a relevant history from a patient with gross hematuria.

2. Order relevant laboratory and radiologic tests for a patient with gross hematuria.

3. Know who to refer to a urologist for further evaluation.
Case #1

55 year old male with two days of gross hematuria.

What are the 4 general causes of gross hematuria in an adult?
Case #1 – Causes of Hematuria

1. Infections
2. Stones
3. Tumours
4. Trauma

Other conditions are uncommon;
- pseudoheamaturia (ingestion of beets, red dyes, laxatives)
- glomerulonephritis, hemoglobinuria, myoglobinuria
- congenital AV malformations in the kidneys
- GU endometriosis
Case #1

55 year old male with two days of gross hematuria.

What questions should you ask this patient?
Hematuria History

Localizing signs/symptoms
- flank/abdominal pain vs. voiding symptoms
- Initial vs. terminal vs. total hematuria

Systemic condition
- Bleeding elsewhere (nosebleeds, hematochezia)
- Fever, chills, weight loss
Hematuria History

Risk Factors

• Smoking
• Occupation (eg. painter, hairdresser)
• Medications (eg.: warfarin)
• Trauma
• Previous stones, malignancy, infections
Case #1 – Take Home Messages

1. Gross, painless hematuria is a malignancy until proven otherwise.
2. Stones, infections and trauma are rarely asymptomatic and are suspected from the history.
3. Anticoagulation and systemic coagulopathy are not sufficient explanation for gross hematuria.
Case #1

55 year old male with two days of gross hematuria.

What laboratory test should you order for this patient?
Case #1 – Lab Tests

- Urinalysis
- Urine culture
- WBC, Hgb, Platelets
- INR
- Creatinine
Glomerulonephritis may present as gross hematuria but urine microscopy will typically show “crenated” RBCs, RBC casts, granular casts and the dipstick will show heavy proteinuria.
Case #1

55 year old male with two days of gross hematuria.

What radiologic test(s) should you order for this patient?
Intravenous pyelogram (IVP)

Historic relevance only – not routinely used

**Pro**
- Good for detecting anything (stone or cancer) within the collecting system (especially ureter/renal pelvis).

**Con**
- Will miss small renal tumours.
- IV contrast allergy.
- IV contrast nephrotoxicity.
- Expensive.
- Radiation.
Ultrasound

Pro
- Good for renal tumours, stones within the kidney and hydronephrosis.
- Inexpensive.
- Safe.

Con
- Will miss ureteral stones, ureteral tumours and most small or flat bladder tumours, small renal tumours.
- May not differentiate blood clot from tumour in bladder or renal pelvis.
- No functional information.
CT - IVP

**Pro**
- Non-contrast CT for patients with renal colic.
- Most sensitive for detecting any GU pathology
  - Accurate staging of renal/ureteric tumours and renal trauma.
- May demonstrate other disorders (eg.: abd. aneurysm).
- First choice for patients with gross hematuria.

**Con**
- Adverse reaction to IV contrast (allergy and nephrotoxicity).
- Expensive.
- Radiation exposure.
Case #1 – Test Results

- Urinalysis: >100 RBC/hpf
- No UTI
- Normal creatinine (and other labs)
- Normal CT-IVP
Case #1

55 year old male with two days of gross hematuria.

Should this patient be referred to a Urologist?
Case #1 - Referral

YES !!!

- Gross hematuria in an adult (almost) always warrants cystoscopy
- Forgo cystoscopy only if risk of the procedure is greater than the risk of missing a bladder tumour
- Referral for gross hematuria is always appropriate!!!
Cystoscopy and retrograde pyelogram
Retrograde Pyelogram
Case #1 - Cystoscopy

- Cystoscopy is done as an outpatient, usually with local anaesthetic and no sedation.
- The procedure only takes a few minutes.
- Risk of cystitis after procedure.
Microhematuria

• Definition:
  – >3 RBC/hpf on 2 out of 3 UA

• Etiology:
  – Same as gross hematuria; less likely malignancy

• Work-up:
  – Renal U/S recommended for upper tract (or CT-IVP in higher risk patient)
  – No cysto if no risk factors
  – 3 year surveillance if negative work-up
Urinary Cytology

- Recommended for evaluation of gross or microhematuria
- Random urine sample but not first morning sample
- Can detect high grade carcinoma in situ or other high grade lesions that are easily missed on upper tract studies and cystoscopy
Summary - Hematuria

• Painless/asymptomatic gross hematuria is a malignancy until proven otherwise.

• Trauma, infections and stones are suspected based on the history.

• US or CT-IVP plus cystoscopy are appropriate in most patients with hematuria.
Objectives:
1. Provide differential diagnosis for solid renal mass.
2. Describe the evaluation of a patient with a suspected renal cell carcinoma.
Case #2

55 year old male with gross, painless hematuria.

Differential diagnosis?
Solid renal mass – Differential diagnosis

Malignant - primary
• Renal cell carcinoma
• Transitional cell carcinoma

Benign
• Oncocytoma
• Angiomyolipoma
• Abscess
• Pseudotumour (dromedary hump, hypertrophied column of Bertin, compensatory hypertrophy, etc…)

Malignant – secondary
• Metastasis
• Lymphoma
Fat within the mass is diagnostic of angiomyolipoma (-10 to -100 Hounsfield units)
Case #2

55 year old male with hematuria and a solid renal mass.

What further tests are required before deciding on treatment?
Case #2 – Metastatic Evaluation

- Ca++, Alk. Phos.
- LFT’s
- CXR
- review CT scan for:
  1. local extension of tumour (eg. adrenal invasion)
  2. regional lymphadenopathy
  3. renal vein or IVC thrombus
  4. liver mets
  5. size/function of the opposite kidney
Case #2

If the serum Ca^{++} is elevated, what is likely cause?
Case #2 – Paraneoplastic Syndromes

renin - hypertension
PTH-like peptide - hypercalcemia*
erythropoietin - polycythemia

abnormal liver function (Stauffer Syndrome)

(*hypercalcemia can also be caused by bone metastases)
Case #2

Treatment for locally confined renal cell carcinoma?
Radical vs. Partial Nephrectomy
Indications for Partial Nephrectomy

**Mandatory indication**
- solitary kidney
- bilateral tumours
- Hereditary syndromes (esp. von Hippel-Lindau syndrome)
- pre-existing renal impairment

**Elective indication**
- implies contralateral kidney is intact and functioning
- any small renal mass (< 4 cm diameter)
- especially if underlying disease such as HTN/DM
- trend toward partial for any tumor up to 7cm and larger tumors if technically feasible
Radiofrequency (RFA) vs. Cryoablation
Renal Cell Carcinoma Histology

Clear cell 75-80%

Papillary 7-14%

Chromophobe 5-8%

Sarcomatoid / Others 1-2%
Renal Cell Carcinoma Staging

- **T1** less than 7 cm
  - T1a <4cm
  - T1b 4-7 cm
- **T2** >7cm but confined to kidney
- **T3** extends beyond kidney
  - T3a adipose/adrenal
  - T3b renal vein, IVC below diaphragm
  - T3c IVC above diaphragm
- **T4** invades neighbouring organ/side wall
RCC Survival

Five year disease-specific survival

T1  95%
T2  90%
T3a 60%
T3b, c 25% (if completely resected)
T4  20%
N+  10% – 20%
M1  0%
NEPHRECTOMY FOLLOWED BY INTERFERON ALFA-2b COMPARED WITH INTERFERON ALFA-2b ALONE FOR METASTATIC RENAL-CELL CANCER

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Targeted Therapy

- Tyrosine kinase (esp. VEGFR) inhibitors:
  - sunitinib
  - sorafenib
  - pazopanib
  - axitinib

- Anti-VEGF-mAb:
  - bevacizumab

- mTOR inhibitors:
  - temsirolimus
  - everolimus
Summary – Solid Renal Mass

• 70-90% likelihood of being renal cell carcinoma, depending on size
• Usually no biopsy – move straight to surgical intervention
• Try to preserve nephrons = partial nephrectomy
• Many new therapies improve survival of patients with metastatic renal cell carcinoma
Objectives:

1. State 3 risk factors for transitional cell carcinoma of the bladder

2. State the treatment options for superficial and invasive TCC of the bladder
55 year old male with gross painless hematuria and a normal renal ultrasound. Cystoscopy shows this:
Case #3

What are the risk factors for transitional cell carcinoma of the bladder?
Risk factors for TCC

- **smoking** (R.R. 4X that of non-smokers)
- occupational exposure to aniline dyes, aromatic amines (eg.: textile manufacturing, dry cleaning, painting)
- previous exposure to cyclophosphamide (eg.: chemotherapy for lymphoma)
- previous radiotherapy (eg.: treatment of carcinoma of the cervix)
Case #3

Next steps?
Case #3

Any patient with bladder tumour requires CT-IVP – preferably before biopsy of tumor – to assess kidneys, ureters, local extension, regional adenopathy and intra-abdominal metastases.
Case #3

- Transurethral resection of bladder tumor (TURBT) in operating room.
- Resection includes underlying detrusor muscle for optimal pathologic examination.
Case #3

How do you stage bladder tumours?
Non-muscle invasive bladder cancer (NMIBC)

Muscle invasive bladder cancer (MIBC)
Case #3

What treatments may be given for non-invasive TCC of the bladder after transurethral resection?
Indications for Intravesical Therapy

- any high grade tumour
- any lamina propria invasion (stage T1)
- carcinoma-in-situ
- multi-focal tumours
- rapid recurrence after initial resection
- (unable to completely resect transurethrally)
Intravesical Therapy

• Bacille Calmette-Guerin (BCG)
  - Only agent to demonstrate decreased rate of progression in non-invasive bladder cancer
  - Requires induction and maintenance (36 months)

• Mitomycin
  - Especially effective as single dose after TURBT
  - Reduces short-term recurrence rate (within 2 years)

• Thiotepa (historical only)
  - Increased systemic toxicity due to small molecular weight – therefore used only infrequently
Case #3

What are the indications for radical cystectomy for TCC of the bladder?
Indications for Radical Cystectomy

Curative
- muscle invasive TCC (≥T2)
- CIS or high-grade Ta/T1 that fails intravesical therapy
- extensive non-invasive tumours that cannot be resected

Palliative
- control of hemorrhage in metastatic disease
- extremely rare
Case #3

What do you do with the kidneys and ureters once the bladder is out?
Urinary Diversion – Ileal conduit

Pro
- simplest to create
- lowest risk of peri-operative complications
- lowest risk of longer term metabolic complications

Con
- abdominal stoma ("bag")
- incontinence
Indiana Pouch

- continent but must use catheters
- abdominal stoma but no collection bag
- higher risk of surgical and post-operative complications
- higher risk of metabolic complications
Orthotopic Neobladder

- continent and can void
- 20% nocturnal incontinence
- 1-2% need for self-catheterization (higher in women)
- higher risk of surgical and post-operative complications
- higher risk of metabolic complications
- cannot be done if urethrectomy required
Chemotherapy for Bladder Cancer

- Gemcitabine/cisplatin most commonly used, although best evidence for MVAC (methotrexate/vinblastine/adriamycin/cisplatin)
- 60% response rate in metastatic disease – but rarely durable
- 5% survival benefit at 5 years when given before cystectomy (neoadjuvant)
- Questionable benefit after cystectomy (adjuvant)
TCC of the Upper Tract

- “filling defect” seen on retrograde pyelogram

- If opposite kidney is normal and there is no metastatic disease then treatment is a radical nephroureterectomy

- Can attempt endoscopic management if low volume and low stage/grade (need good biopsy)
Kidney Stones

Objectives:
1. Give a differential diagnosis for acute flank pain including two life-threatening conditions
2. Describe the laboratory and radiologic evaluation of a patient with renal colic
3. Know 4 different kinds of kidney stones and the risk factors for stone formation
4. Know 3 indications for emergency drainage of an obstructed kidney
Case #4

55 year old man with microscopic hematuria and acute flank pain.

What is the differential diagnosis?
Differential diagnosis of renal colic

- abdominal aortic dissection
- abdominal aortic aneurysm rupture
- cholecystitis
- biliary colic
- appendicitis
- diverticulitis
- duodenal ulcer
- viral gastroenteritis
- inflammatory bowel disease
- splenic infarct
- acute lumbar disc herniation
- herpes zoster

- acute pancreatitis
- renal abscess
- pyelonephritis
- acute glomerulonephritis
- renal vein thrombosis
- renal infarct
- ectopic pregnancy
- pelvic inflammatory disease
- Fitz-Hugh-Curtis syndrome
- torsion/rupture of ovarian cyst
- endometriosis
“Wait a minute here, Mr. Crumbley. . . . Maybe it isn’t kidney stones after all.”
Case #4

55 year old male with microscopic hematuria and renal colic.

Diagnostic evaluation?
Radiologic evaluation of renal colic

KUB

- “kidneys, ureters, bladder”
- plain X-ray of the abdomen
- 85% of stones are visible
- no information regarding obstruction
Radiologic evaluation of renal colic

CT-KUB

- no contrast
- fast, inexpensive
- imaging modality of choice
- visualizes other abdominal/retroperitoneal structures
- obstruction inferred by hydronephrosis

Stone in intramural ureter
Case #4

Where are ureteric stones likely to be seen in a patient with renal colic?
3 Physiologic Narrowings

- Ureteropelvic junction
- Crossing of iliac artery (midureter)
- Ureterovesical junction
Case #4

55 year old male with microscopic hematuria and renal colic.

How likely is a 4 mm stone at the right UVJ likely to pass spontaneously?

An 8 mm stone at the right UPJ?
Spontaneous Passage of a Ureteral Stone

In uncomplicated cases, spontaneous passage of the stone is safest; the likelihood of spontaneous passage is dependent on the size of the stone:

<table>
<thead>
<tr>
<th>size</th>
<th>likelihood</th>
</tr>
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<tbody>
<tr>
<td>≤ 4 mm</td>
<td>90%</td>
</tr>
<tr>
<td>5 mm – 7 mm</td>
<td>50%</td>
</tr>
<tr>
<td>≥ 8 mm</td>
<td>20%</td>
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</tbody>
</table>
55 year old male with microscopic hematuria and renal colic.

What other lab tests do you need before making treatment decisions?
Lab Tests

- CBC (? elevated WBC ?)
- Creatinine (? impaired renal function ?)
- Urine microscopy (? bacteriuria or pyuria or↑pH ?)

- Ca++, uric acid, PO₄⁻⁻ are often ordered but these will not influence the acute management
Case #4

55 year old male with microscopic hematuria and renal colic.

What are the indications for immediate drainage of an obstructed kidney?

When can you leave a kidney obstructed to allow for spontaneous passage of a stone?
Immediate Referral to a Urologist

- **obstructed ureter plus fever, chills, bacteriuria or elevated WBC** (risk of urosepsis – may be life-threatening)
- obstructions ureter in an insulin-dependent diabetic (risk of papillary necrosis or emphysematous pyelonephritis)
- solitary kidney
- pre-existing renal disease
- significant co-morbid conditions (congestive heart failure, pregnant …)
Case #4

Name 4 different kinds of kidney stones and the factors that predispose to stone formation?
Types of Stones

**Calcium Oxalate**

- most common stone
- most common predisposing factors:
  1. dietary hyperoxaluria (chocolate, nuts, tea, strawberries, peanut butter, cabbage or excessive restriction of dietary calcium)
  2. hypercalciuria (absorptive; inherited condition)
  3. dietary hypercalciuria due to excess dietary sodium or meat proteins
Types of Stones

**Calcium Phosphate**
- second most common stone
- often seen in patients with metabolic abnormalities:
  1. primary hyperparathyroidism
  2. distal renal tubular acidosis
  3. hypercalcemia due to malignancy or sarcoid
Types of Stones

**Uric Acid**

- radiolucent on KUB but visualized on CT-KUB
- predisposing factors:
  - persistently acidic urine
  - low urine volumes (eg. from chronic diarrhea, excess sweating, inadequate fluid intake)
  - gout (hyperuricemia)
  - excess dietary purine (meat)
  - chemotherapy for lymphoma, leukemia
Types of Stones

**Struvite (infection stones)**

- magnesium, calcium and ammonium phosphate
- urine pH > 8.0, therefore will only form in the presence of urease-secreting bacteria
- tend to form large stones or staghorn stones
- urease-secreting bacteria include Proteus, Klebsiella, Providentia, Pseudomonas and Staph. aureus – but *not* E. coli
Relief of Obstruction

Ureteric stents

- can be placed retrograde via cystoscopy or antegrade via nephrostomy
- indwelling “double-J” stents remain in place due to coiling of the ends in the renal pelvis and bladder
Relief of Obstruction

Percutaneous Nephrostomy

• temporary drainage into an external collecting bag
• inserted by radiologist under local anaesthetic
Describe three standard surgical therapies for renal and ureteral stones.
Extracorporeal Shock Wave Lithotripsy (ESWL)

• stone is localized by x-ray (or u/s)
• patient and shockhead are positioned so that stone is at the focal point of the focused shock waves
• repeated shock waves gradually fragment the stone
• fragments are passed in the urine
Extracorporeal Shock Wave Lithotripsy (ESWL)
Holmium Laser Lithotripsy of a Ureteric Stone
Treatment of a Large Stone

Staghorn stone

- ESWL will fragment the stone but the large stone burden is not likely to pass spontaneously
- stones over 20 mm in diameter are better treated with PNL
Percutaneous Nephrolithotripsy
Testicular Tumors

Objectives

1. Differential diagnosis of a scrotal mass
   - Caveat: recognize testicular torsion!
2. Classify testicular tumors
3. Treatment of testicular malignancies
Case #5

28 year old man with a right scrotal mass.

Evaluation?
History

- onset
- pain
- firmness
- history of undescended testis
- urethral discharge
- STDs
- LUTS
Physical Exam

- location of mass (testis, epididymis, scrotum)
- reduces in supine position?
- is mass tender?
- transillumination?

What test is next?
Diagnostic Tests

Urinalysis

- pyuria with epididymitis

Ultrasound

- sensitive and specific for testicular tumour
Scrotal Mass - Differential Diagnosis

- hydrocoele
- spermatocoele
- varicocoele
- epididymitis/orchitis
- inguinal hernia
- testicular tumor
- paratesticular tumour (i.e.: adenomatoid tumour or cystadenoma of the epididymis)
Hydrocoele

- fluid within tunica vaginalis
- called “communicating hydrocoele” if *processus vaginalis* is patent
- typically painless
- transilluminates
- cannot palpate testicle
- no treatment required unless for cosmetic reasons
Spermatocoele

- cystic dilatation (aneurysm) of epididymal tubule
- transilluminates
- painless
- can palpate body of testicle separate from the mass
- no treatment required unless for cosmetic reasons
Varicocoele

- varicosities of pampiniform plexus
- 90% on left side
- seen in 15% of post-pubertal male population
- typically asymptomatic but may cause “achiness”
- increases in size with valsala or standing position.
- associated with male factor infertility but most men with varicocoeles can expect normal fertility.
- surgical or angiographic correction of the varicocoele results in improvement in semen parameters (number, motility, morphology) in 70% to 90% of cases
Varicocoele
Right Varicocele

Not a normal variant – must consider retroperitoneal mass/tumor with obstruction of flow in right gonadal vein.
In adolescents and young men, with no history of trauma, the possibilities include:

- Testicular Torsion
- Torsion of the Appendix Testis
- Epididymitis

Testicular torsion and torsion of the appendix testis are extremely uncommon in men >40 yrs.
“Acute Scrotum”

History: associated voiding symptoms or fever? (suggesting infection)

Physical examination:
- “lie” of the testicle (high-riding in torsion), cremasteric reflex (absent in torsion), Prehn’s sign (relief of pain on lifting or supporting the scrotum – suggests epididymitis).

Urinalysis and urine culture should be done in all cases (pyuria suggests epididymitis)
Testicular Torsion

- Typically 12 to 18 years of age.
- Presents with acute onset of severe scrotal pain and swelling not associated with trauma.
- Physical exam should include cremasteric reflex and differentiate epididymis from testicle.
- Urinalysis should be normal (pyuria suggests epididymitis)
- Ultrasound with Doppler is most helpful ancillary test.
- The most common misdiagnoses are torsion of the testicular appendix and epididymitis.
Testicular Torsion

normal Doppler signal in right testicle and absent signal in left testicle
Epididymitis

- Doppler signal is increased with inflammation
- thickened epididymis visualized
Epididymitis

- Men < 35 years of age – chlamydia, gonorrhea (STD)
- Men > 35 years of age – coliforms (UTI)

- Diagnosis often made by physical exam, but pain and swelling in advanced cases make the exam less helpful.
- Complications include abscess formation, testicular infarction and infertility.
- Treatment is 4 weeks of antibiotics with rest, ice, NSAIDs.
Torsion of Appendix Testis
Testicular Cancer

Special features:

- It occurs in young men who are otherwise in good health
- Even widely metastatic disease is potentially curable with multimodal chemotherapy
Testicular Tumours Classification

A. **Primary**
   1. **Germ cell tumours**
      - seminomatous
      - non-seminomatous
   2. **Non-germ cell tumours**
      - Leydig cell tumour
      - Sertoli cell tumour

B. **Secondary (lymphoma/leukemia)**
Classification of Testicular Germ Cell Tumours

- Seminoma (classic/spermatocytic/anaplastic)
- Non-seminoma
  - Embryonal Carcinoma
  - Teratocarcinoma = immature teratoma
  - Choriocarcinoma
  - Yolk Sac Tumour (most common form in children)
  - Teratoma (benign but can metastasize and grow)
Usual presentation is a painless intratesticular mass discovered on self-examination.

Typical age at diagnosis is 15 to 35 years, although smaller clusters of cases occur during infancy and over 60 years of age.
Self - Examination

Self – examination should be taught to young men.

They need to be shown the difference between the testicle and the epididymis.

They need to report any hard or suspicious lesions immediately.
Tumour Markers

• β-HCG – produced by choriocarcinoma and in limited quantities by seminoma. Serum $T_{1/2} = 24$ hrs.

• α-fetoprotein – produced by yolk sac tumours, embryonal carcinoma and teratocarcinoma. Never found in patient with pure seminoma. Serum $T_{1/2} = 3 – 5$ days.

• LDH – correlates with tumour volume
Radical Orchiectomy

Testicle with the tunica vaginalis and spermatic cord are delivered through an inguinal incision.

Scrotal incisions or biopsies should never be done.

Check markers again after orchiectomy.
Testicular Cancer - Metastasis

• Predictable pattern of spread:
  – Retroperitoneal lymph nodes first (along spermatic vessels towards hilum of kidney)
  – Lung metastases second
  – Other organs after lungs

• Every patient requires CT-abd/pelvis, and either CXR or chest CT
Retroperitoneal Lymphadenopathy

Large retroperitoneal mass in patient with right testicular NSGCT
Testicular Cancer - Management

• Organ-confined, no mets (“clinical stage I”)
  – Active surveillance by far most commonly practiced strategy
  – Sometimes chemo/XRT/RPLND

• Metastatic (stage II and III)
  – Almost every patient gets chemo (rarely XRT for seminoma)
  – NSGCT patients often require subsequent RPLND and resection of chest masses
Testicular Cancer - Management

• Differences for seminoma and NSGCT
  – both exquisitely sensitive to chemotherapy
    • BEP or EP x 3-4 cycles
  – seminoma also responsive to XRT
    • but rarely used because of potential toxicity
  – post-chemotherapy retroperitoneal lymph node dissection rarely used for seminoma, but performed for every residual mass >1 cm in NSGCT (risk of teratoma)
Retroperitoneal Lymph Node Dissection