Hematuria Pearls: Tell Me Something I Don't Already Know!

73rd McGill Annual Refresher Course for Family Physicians

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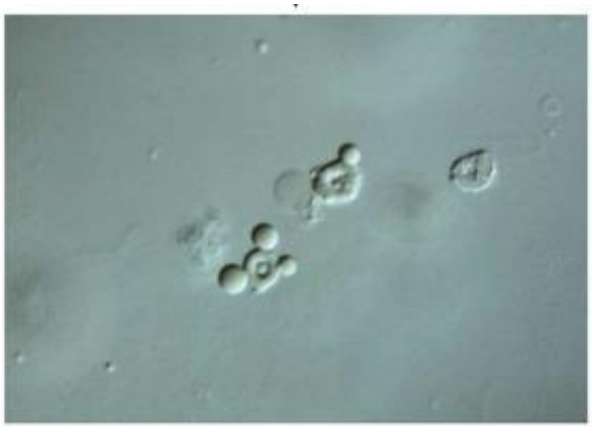
Conflicts

- None

Objectives

- To discuss presentation and workup of glomerular causes of hematuria
- Some pearls from each diagnosis
- Some urologic stuff
- Tying it all together



38 year old man applying for life insurance

- Microscopic hematuria
- Repeat it x2, still there
- Now what?

- History
- Physical (BP, edema)
- Labs: chem 7, CBC, Urine culture/ STD screen
- Abdo ultrasound or CT
- Urine microscopy
- **Urine protein/Cr (U P/Cr)** and **albumin/Cr ratio (A/Cr)**

Renal Labs

Urine

- [x] Analyse d'urine / Urinalysis
- [x] Albumine/Créatinine ratio (U mALB)
- [ ] U Bêta-HCG (U HCG qual)
- [ ] U Créatinine
- [ ] U Culture *

(*Contenant stérile séparé/ Separate sterile container)

- [ ] U Électrolytes (Cl, K, Na) & Créatinine
- [ ] U Osmolalité /Osmolality
- [ ] _____

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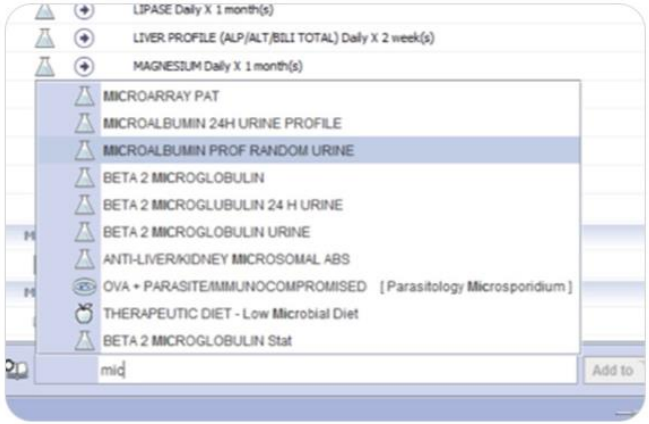
INDS-115 @pod_tina · 2022-06-17

Asking for a Nephrology consult without a urinalysis, urine P/Cr A/Cr or UNa is like asking for a Respirology consult without a CXR, a Cardio consult without an ECG/ trops, or for a Neuro consult without a head CT



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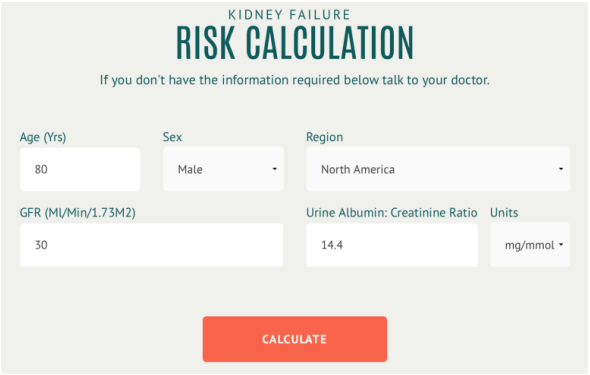
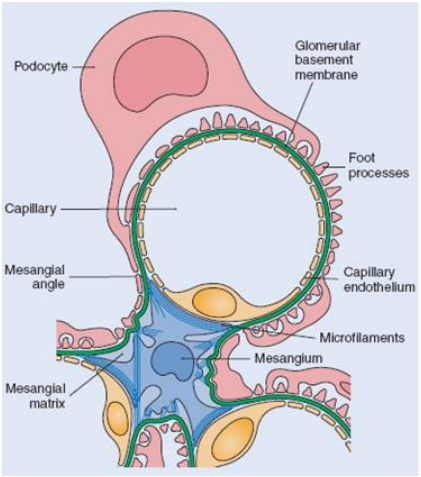
Urine Protein Interpretation

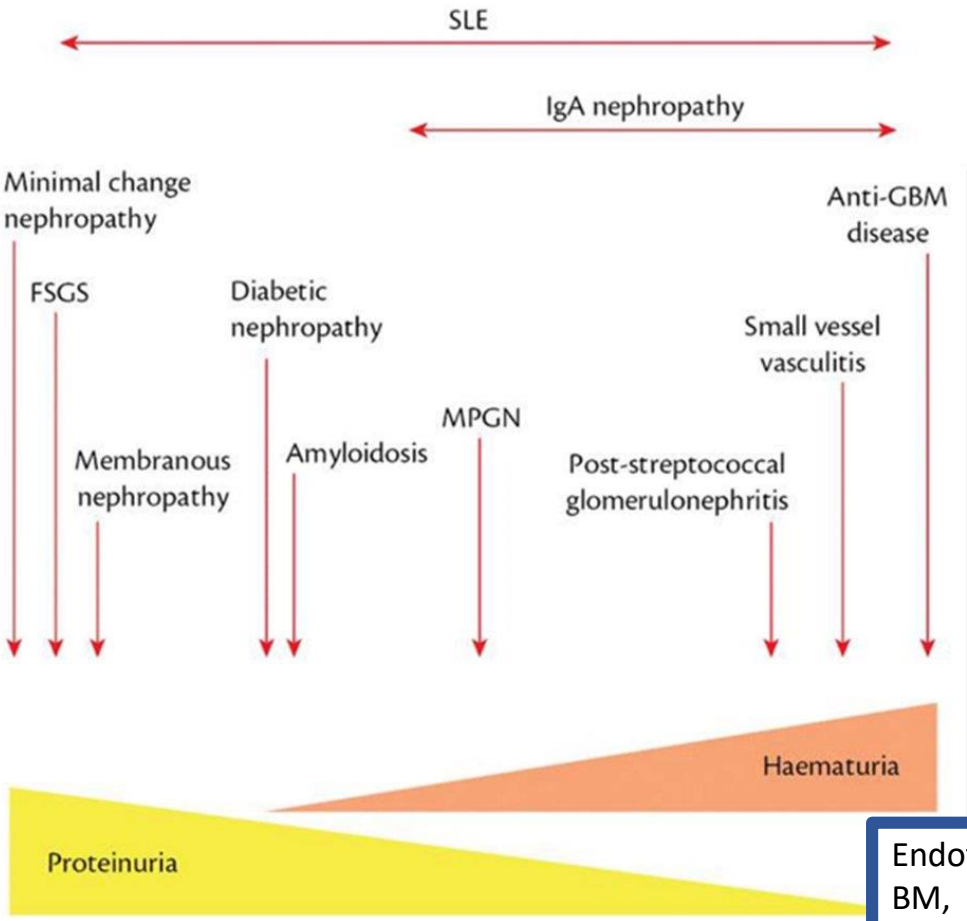


- Urine albumin/Cr (A/Cr): answers the question: is the endothelium healthy?
  - < 1.9 mmol/mg - yes it is
  - >1.9 no it might not be
  - Prognosis of kidney disease- A/Cr is used to calculate risk of progression of renal disease to dialysis in 2 or 5 years in the kidney failure risk equation: kidneyfailurerisk.com

- Urine protein/Cr is a surrogate for 24 hour urine collection and protein quantification and answers the question: is this a glomerulonephritis? > 3 g/g yes! It is a GN

Presence of glomerular hematuria is determined by the location of pathology

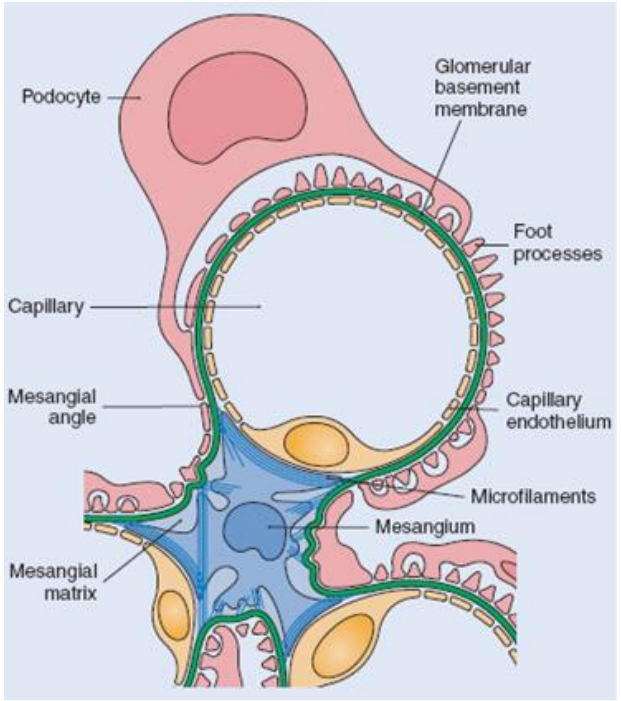




Podocyte

Endothelium, BM, mesangial proliferation

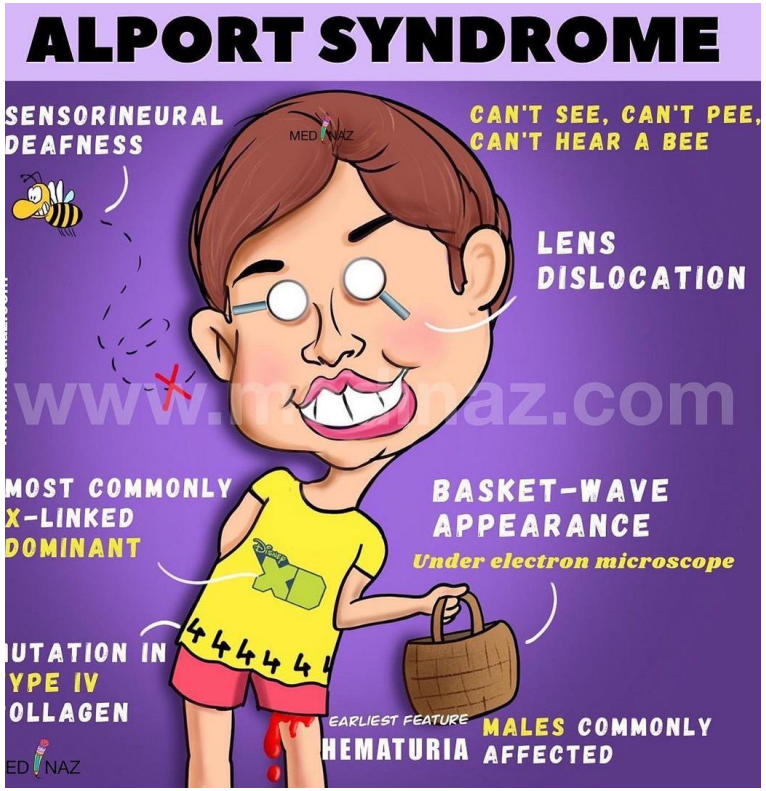
Hematuria - Thin Basement Membrane Disease



- 1% of population
- Thin GBM, EM diagnosis, type 4 collagen
- Family history of hematuria in 30-50% (AD), no kidney failure in family.
- Urinary protein excretion and BP are typically normal
- If abnormal, may be unrecognized Alports
- In nephrology IN GENERAL usually no biopsy if normal Cr and < 1 g/g proteinuria, we watch and wait, yearly U PCR, ACR measures
- Is conception with another individual with isolated hematuria being planned?

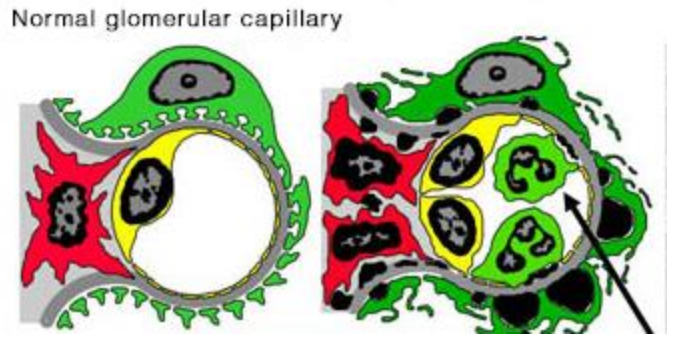
Alport syndrome

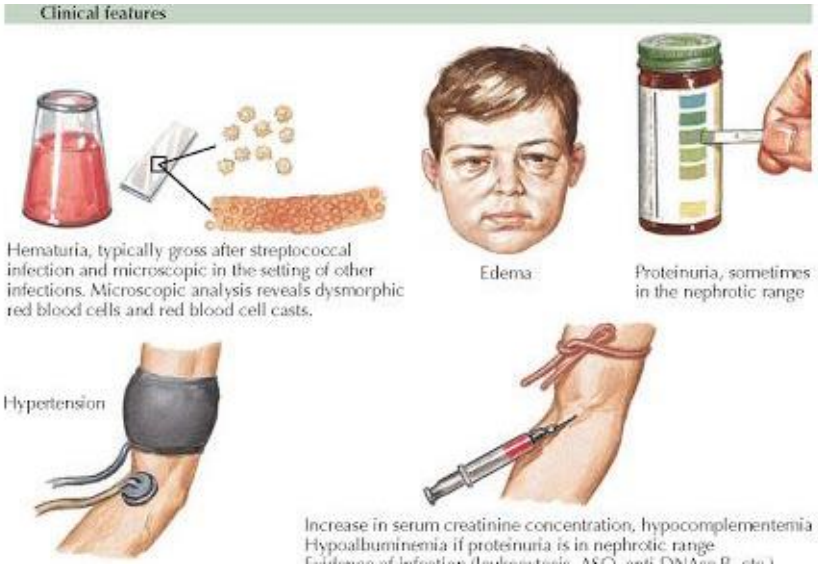
- Collagen 4 mutation - alpha-5 chain
- X-linked in the majority 85-90%. All of these are male → dialysis
- 10-15% have autosomal recessive – male or female and the same disease manifestations as X linked
- Females carriers- one mutated X. Almost all have some degree of hematuria, and a minority develop kidney failure (Lyonization of one X in each cell is variable)



Post-streptococcal glomerulonephritis

- Gross hematuria in 30 - 50% with acute tea, cola-colored, **post**pharyngitic (2-6 weeks post infection)
- Hypertension, edema, AKI
- Labs: High ASO titres, low C3
- Throat or skin (impetigo) infections
- Many bacterial and viral causes as well
- Immune complex deposit outside the capillaries
- Ages: 3-12 then > 60 years old
- Recovery usual by 2 months but often PERSISTENT hematuria post e.g. 1 year



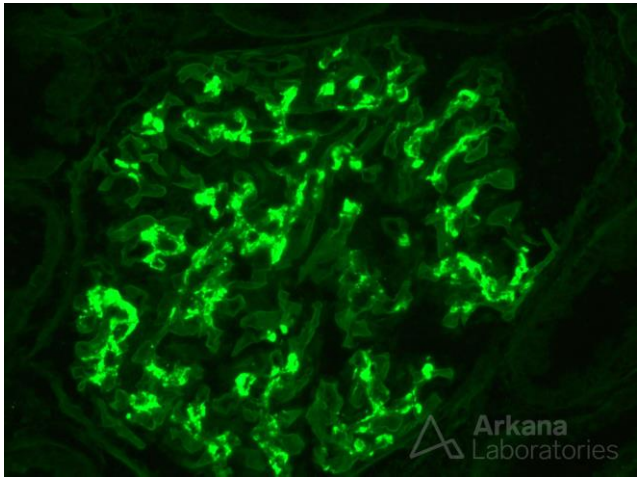


IgA nephropathy

- 20-30% with gross hematuria
- Onset of hematuria is shortly after respiratory infection - timing of IgA is 1-3 days post (vs. 2 weeks after in post strep)
- Don’t measuring serum IgA -useless in making diagnosis
- Kidney biopsy? Only if increased Cr, U P/Cr > 1 g/g.

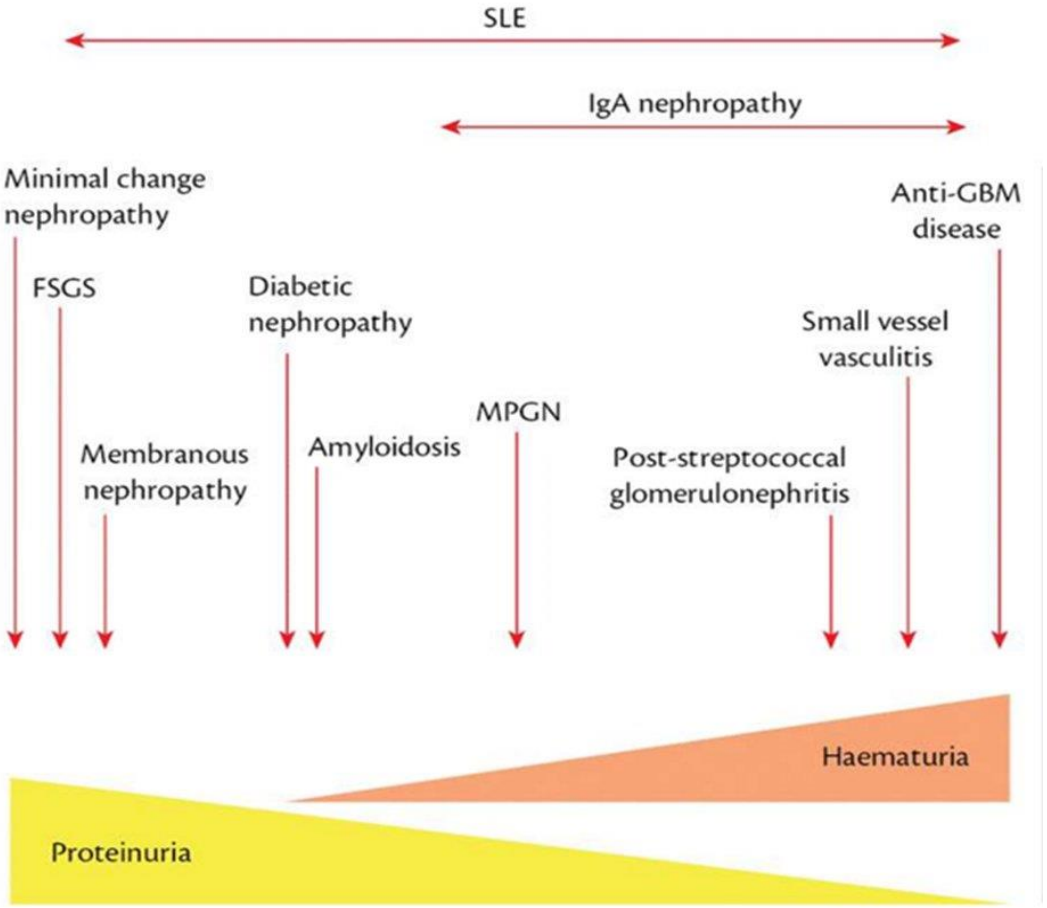
- If normal Cr and U P/Cr < 1 g/g we follow (e.g. q 6-12 months with UA, U P/Cr, serum Cr, BP) and reconsider for bx if the disease makes a move

- Meanwhile: ACEi ACEi ACEi ACEi



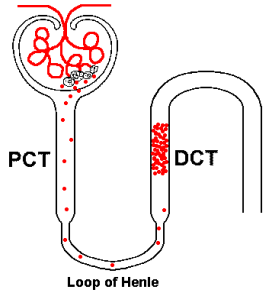
Nephritic syndrome- RPGN

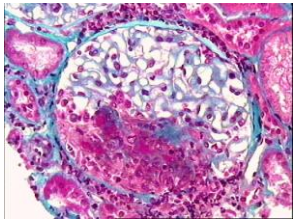
- Lupus (class 4)
- Pauci immune (ANCA vasculitis)
- Anti-GBM
- IgA nephropathy

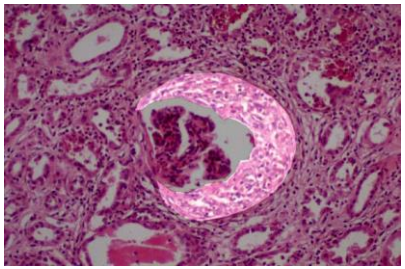


RPGN = Rapidly Progressive Glomerulonephritis

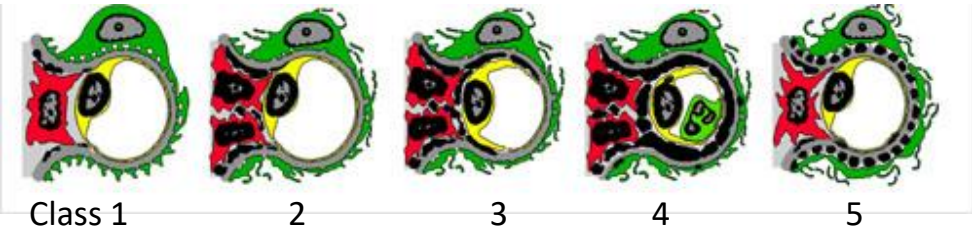
- Patient is unwell, edema, hematuria with rapidly rising Cr 80 $\rightarrow$ 400 μmol/L in days-weeks. RBC casts.
- Biopsy: crescents: proliferation of the epithelial cells of Bowman's capsule
- Page nephrology on call to discuss case, send to ER with copy of old labs, need to be seen that same day







Lupus nephritis



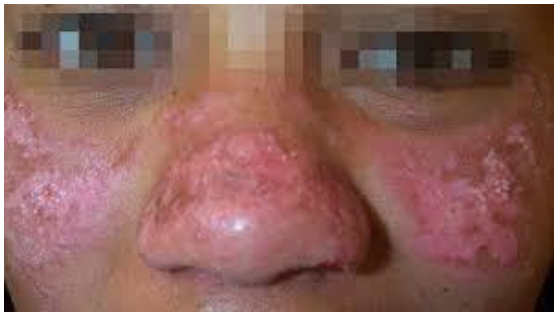
- Microscopic hematuria is almost always present, but never in isolation- ALWAYS with proteinuria (U P/Cr)
- 25-50% have abnormalities of urine or renal function early in their course, although up to 60% of adults and 80% of children may develop renal abnormalities later
- Anti dsDNA and anti-Smith are strongly associated with nephritis
- anti-Smith is highly specific, but present only in ~30% with nephritis, more in Afro-Caribbean patients than in Caucasians. Treatment may eliminate anti-dsDNA antibodies from the circulation, while ANA positivity remains
- Class IV is the most common LN and has the worst prognosis
- 6-19% ESRD

Serology positive Lupus without nephritis

- 7-30% have LN at SLE diagnosis, and 30-50% develop LN after SLE diagnosis, most within 5 years

- After 10 years about 70% of Lupus patients will have some renal involvement

- Higher likelihood of Lupus Neprhitis in AA and Hispanic populations



Autosomal Dominant Polycystic Kidney Disease

- Features: hematuria, proteinuria 0.5 – 1 g/day, HTN, infection, stones.

- Slow decline in GFR, multiple cysts on renal ultrasound, enlarged kidneys.
- TEMPO trial: Tolvaptan (ADH blocker) can slow progression in patients with kidney volume >750 ml (Dr. Ahsan Alam clinic RVH)

- In ADPKD progression to end-stage renal failure most commonly occurs in middle age and later. Parental history often dictates timing

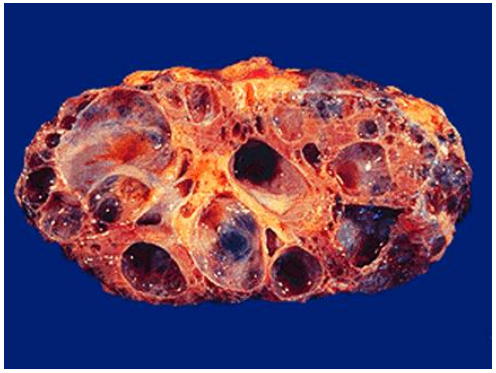
- Dialysis:

  2% @ age 40

  20-25% @ 50

  35-45% @ 60

  50-75% @ age 75

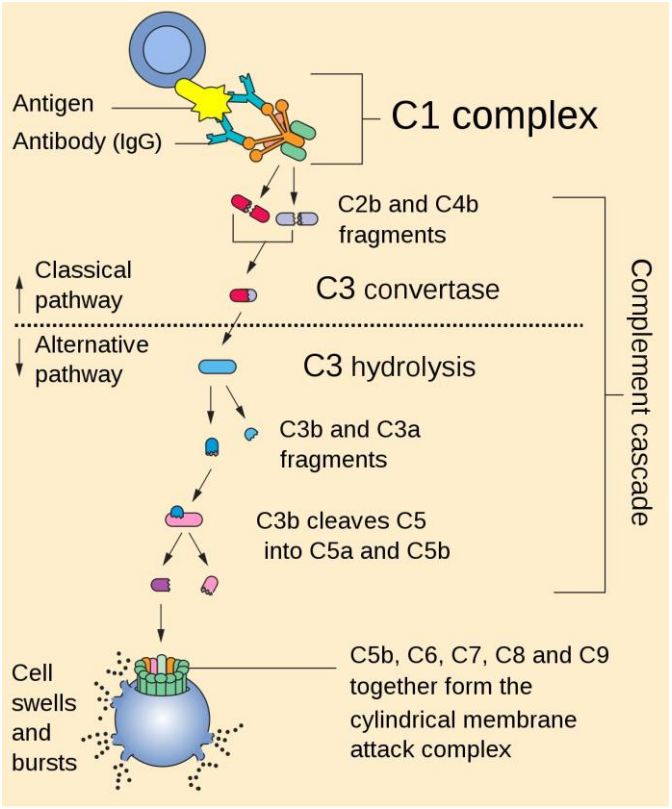


Hematuria in pregnancy

- Dipstick+ hematuria is common- 16-20% pregnant women despite careful midstream collection
- 40% are false +ve with subsequent N microscopy
- If +ve repeatedly, do urine culture, document normal Cr, screen for proteinuria, measure BP
- If no dysfunction, a comprehensive evaluation can be delayed until after pregnancy (obstetric nephrology clinic RVH)

Brown MA Am J Kidney Dis 2005;45:667-73

Paroxysmal Nocturnal Hemoglobinuria 1: 10^6



Acute Intermittent Porphyria 6: 10^6 F>M

uroporphyrinogen I synthase.

Symptoms (5 P's):

- Painful abdomen
- Port wine–colored Urine
- Polyneuropathy
- Psychological disturbances
- Precipitated by drugs (eg, Barbiturates, Oral contraceptive pills, Sulphonamides, etc.), alcohol, starvation

Aminolevulinic Acid (ALA) and Porphobilinogen (PBG) levels are substantially increased in plasma and urine, especially during acute attacks.

Treatment

Intravenous hemin is more effective and should be used as first-line therapy for all acute attacks. Carbohydrate loading, usually with intravenous glucose (at least 300 g daily), may be effective in milder acute attacks of porphyria.

Suppress heme synthesis in the liver with carb loading and/or hematin, to reduce production of porphyrin precursors

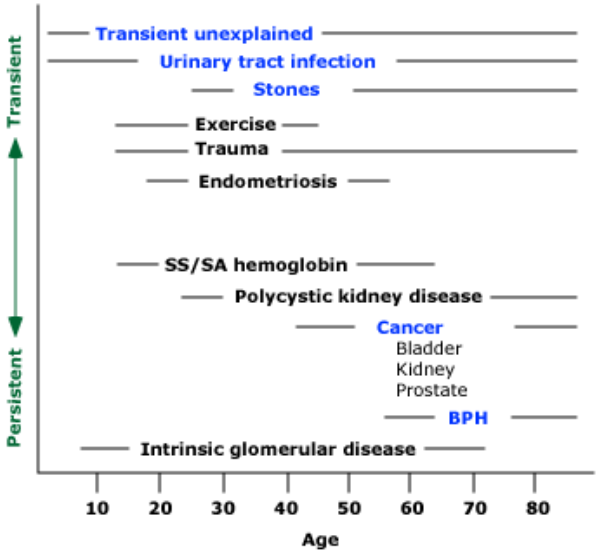
Sickle Cell Disease or Trait

- Sickling in renal medulla, tubular and nephron loss, hyperfiltration which can lead to glomerulosclerosis or FSGS
- Urine Protein/Cr ratio will distinguish the two
- Chronic kidney disease in 5-15% of which 10% will end up on dialysis
- Screening: yearly urine for UA, A/Cr, P/Cr and serum Cr

Table 2. Risk Stratification for Bladder Cancer.

High risk (one criterion raises the risk to high)
≥60 Yr of age for men and women
>30 Pack-yr of smoking
>25 Red cells per high-power field on single urinalysis
History of gross hematuria
Additional risk factors for urothelial cancer
Irritative lower urinary tract symptoms
Previous pelvic radiation therapy
Previous chemotherapy with cyclophosphamide or ifosfamide
Family history of urothelial cancer or Lynch syndrome
Occupational exposure to benzene or aromatic amines
Chronic indwelling foreign body in the urinary tract

Major causes of hematuria by age and duration



Schematic representation of the major causes of hematuria in relation to the age at which they usually occur (horizontal axis), transience or persistence (vertical axis), and frequency (blue implies more frequent).

BPH: benign prostatic hyperplasia.

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Hematuria while on anticoagulants

- In an anticoagulated AF population, gross hematuria should be considered a strong marker of potential malignancies of the urinary tract and not merely a consequence of treatment with OACs

- The probability of urinary tract cancer after hematuria is ~ 10%

- Danish nationwide registers, AF patients on OACs in 2001 - 2015. 125 063 AF patients with a median age of 74 years, majority of males (57%). The absolute risk of gross hematuria 12 months after treatment initiation increased with age ranging from 0.37%- 0.85%

38 year old man applying for life insurance

- Microscopic hematuria
- Repeat it x2, still there
- Now what?

- History – Dialysis in anyone in the family? Hematuria in anyone?
- Physical (BP, edema, rashes)
- Labs: chem 7, CBC, Urine culture/ STD screen
- Abdo ultrasound or CT
- Urine microscopy

- **Urine protein/Cr (U P/Cr) and albumin/Cr ratio (A/Cr)**

Consulting Nephrology for Hematuria

- Most hematuria is urologic
- Please do spot protein quantification: **A/Cr** and **P/CR**

- CRDS said including urine protein P/Cr or A/Cr "would be too confusing" and yet this is how nephrology triages the consults into <1 month, 1-3 months, 3-6 months etc

- If you are worrying about RPGN please page the nephrologist on call even if it's 5 pm on a Friday

Reference

- Ingelfinger JR. Hematuria in Adults. N Engl J Med. 2021 Jul 8;385(2):153-163

"Unfortunately, the urine test counted for half of the grade."