AUSTRALIA & NEW ZEALAND GENERAL MEDICINE UPDATE

2 common renal causes of AKI when the urine is bland

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Definition of AKI

Definition is based on either

- An increase in serum creatinine (SCr) above baseline levels OR
- A fall in urine output

KDIGO guidelines

- Increase in SCr by > 0.3 mg/dl (26.5µmol/l) within 48 hours or >50% in 7 days
- Urine volume < 0.5 ml/kg/h for 6 hours

AKIN guidelines

- Increase in serum creatinine of ≥0.3 mg/dL (26.5µmol/l) or ≥50% within 48 hours
- Urine output of <0.5 mL/kg/hour for >6 hours

‘KDIGO’ staging of AKI severity

Stage	Creatinine change over baseline	Oliguria criteria
1	Increase in serum creatinine to 1.5 to 1.9 times baseline OR increase in serum creatinine by ≥0.3 mg/dL (≥26.5 micromol/L)	<0.5mL/kg/hr for 6-12 hours
2	Increase in serum creatinine to 2.0 to 2.9 times baseline	<0.5mL/kg/hr for >12 hours
3	Increase in serum creatinine to 3.0 times baseline OR Increase in serum creatinine to ≥4.0 mg/dL (354 µmol/L) OR Initiation of RRT	<0.3mL/kg/hr for > 24 hours or anuria for 12 hours

Prognosis of AKI in the elderly

- Data from US Renal Data System (USRDS):

  - Patients > 67 years old were 6.7 times more likely to develop ESRD by 2 years after discharge

  - Patients with known CKD had a 41-fold increase in the risk of ESRD

- Dialysis-requiring AKI independently associated with 28-fold increase in the risk of developing stage 4 or 5 CKD and more than a twofold increased risk of death

'Acute kidney injury increases risk of ESRD among elderly'AUIshani A, Xue JL, Himmelfarb J, Eggers PW, Kimmel PL, Molitoris BA, Collins AJ ;J Am Soc Nephrol. 2009;20(1):223. Epub 2008 Nov 19

'Dialysis-requiring acute renal failure increases the risk of progressive chronic kidney disease' Lo LJ, Go AS, Chertow GM, McCulloch CE, Fan D, Ordoñez JD, Hsu CY; Kidney Int. 2009;76(8):893. Epub 2009 Jul 29.

Causes of AKI in hospitalised patients

- Acute tubular necrosis (ATN) – 45 percent
- Prerenal disease – 21 percent
- Acute superimposed on CKD – 13 percent (due to ATN or prerenal disease)
- Urinary tract obstruction – 10 percent (most often older men with prostatic disease)
- Glomerulonephritis or vasculitis – 4 percent
- **Acute intertitial nephritis (AIN) – 2 percent**
- **Atheroemboli – 1 percent**

Note: Prerenal causes lead to 70% of community AKI

Urine evaluation in AKI

- Urine dipstick: **Extremely valuable bedside investigation**; haematuria and/or proteinuria (and no suspicion of urinary infection or stones or tumour) points towards intrinsic glomerulonephritis or renal vasculitis

- Send urine for dysmorphic red blood cells and RBC casts if haematuria seen (with no evidence of UTI, stones or anatomical lesions on USG/CT)

- 4+ proteinuria with hypoalbuminemia and oedema points towards nephrotic syndrome (though nephrotic syndrome usually does not present with AKI)

Acute Interstitial Nephritis (AIN)

- Characterised histologically by inflammatory infiltrate in the renal interstitium (glomeruli normal)
- Majority caused by drugs *(with antibiotics responsible for half of these cases)*
- Patients often asymptomatic with rise in serum creatinine 3 to 5 days following drug exposure (can be after weeks or months)
- Often a diagnosis of exclusion along with h/o recent drug exposure
- Actual incidence is probably higher than 2% as most patients do not have biopsy and there is increasing use of PPI/antibiotics/diuretics

Causes of AIN

- *Remember that any drug can cause it including your friendly PPI*

- **Drugs** (antibiotics, NSAIDs, diuretics and PPIs) – 70 to 75%
- **Infections** (streptococcus, legionella, CMV etc.) – 4 to 10%
- **Tubulointerstitial nephritis and uveitis (TINU) syndrome** – 5 to 10 %
- **Systemic disease** including sarcoidosis, Sjögren's syndrome, SLE and others – 10 to 20 %

Drugs causing AIN

- Penicillins and cephalosporins
- Sulphonamides including trimethoprim-sulfamethoxazole
- Ciprofloxacin (other quinolones less common)
- Diuretics: both loop diuretics (frusemide and bumetanide) and thiazide diuretics
- Proton pump inhibitors
- NSAIDs, including selective cyclooxygenase (COX)-2 inhibitors
- Cimetidine (only rare cases described with other H-2 blockers such as ranitidine)
- Allopurinol
- 5-aminosalicylates (e.g. mesalamine)

AIN Presentation and Diagnosis

- **Presentation**: Initially identified in the context of methicillin use when majority had the triad of rash, fever and eosinophilia

- May present from few days to months after drug exposure

- Rash – 15 %; Fever – 27 %; Eosinophilia – 23 %

- Triad of rash, fever, and eosinophilia – 10 %

- **Diagnosis:**

- History/unexplained AKI/ABSENCE of significant hematuria or proteinuria

- Urine shows white cells or white cell casts and sometimes eosinophiluria

- Renal biopsy definitive but usually not be needed

AIN Management

- Discontinuation of the potential causative agent is the mainstay
- Renal biopsy indicated if creatinine does not improve within 3-7 days of stopping offending drugs
- 2-3 months course of prednisolone for biopsy proven AIN not responding to stopping presumed offending drugs

- *Recovery of kidney function is often incomplete with:*

  -Prolonged renal failure (> three weeks)

  -NSAID associated AIN

  -Substantial interstitial fibrosis/tubular atrophy on kidney biopsy

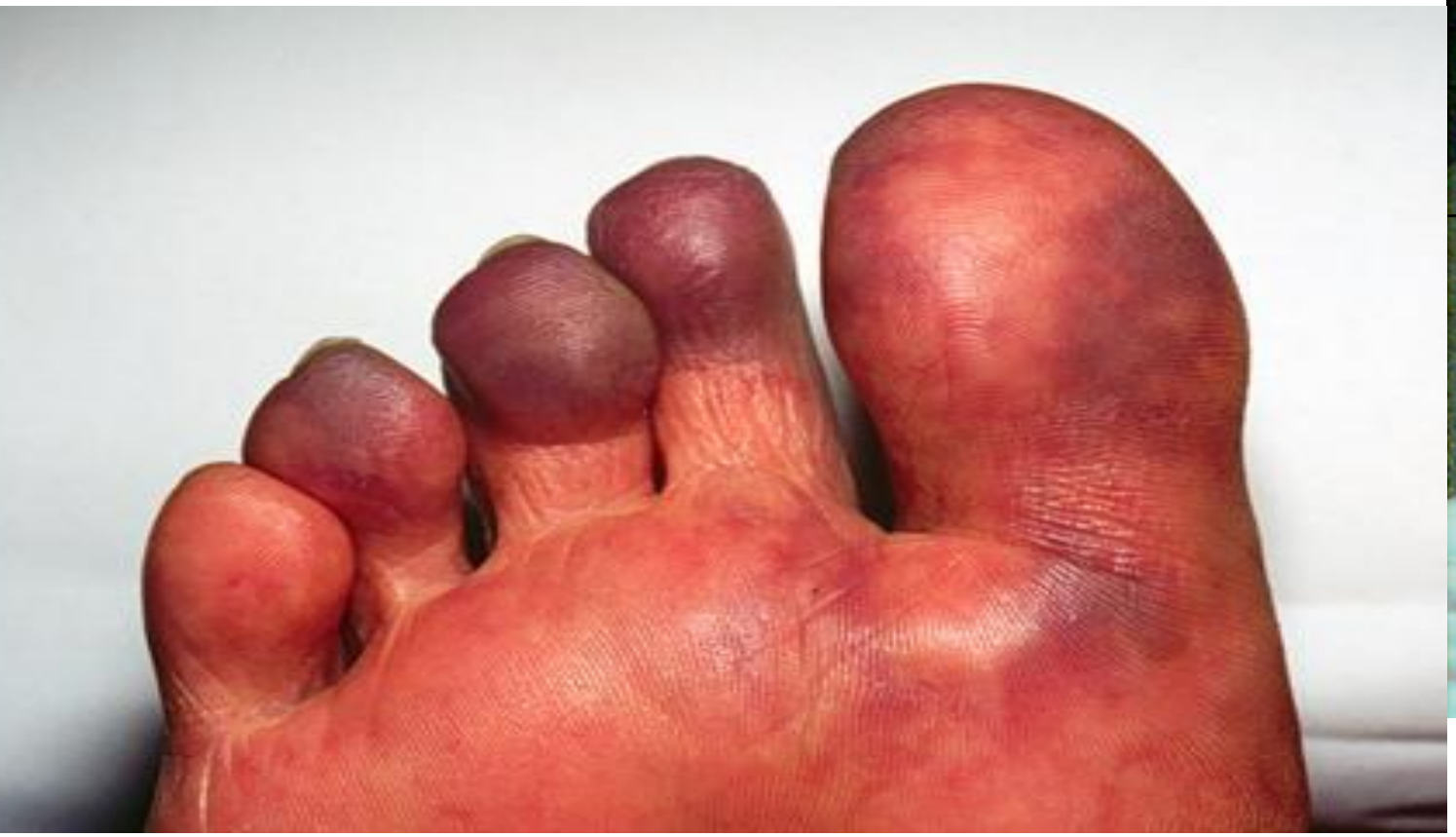
Atheroembolic Renal Disease

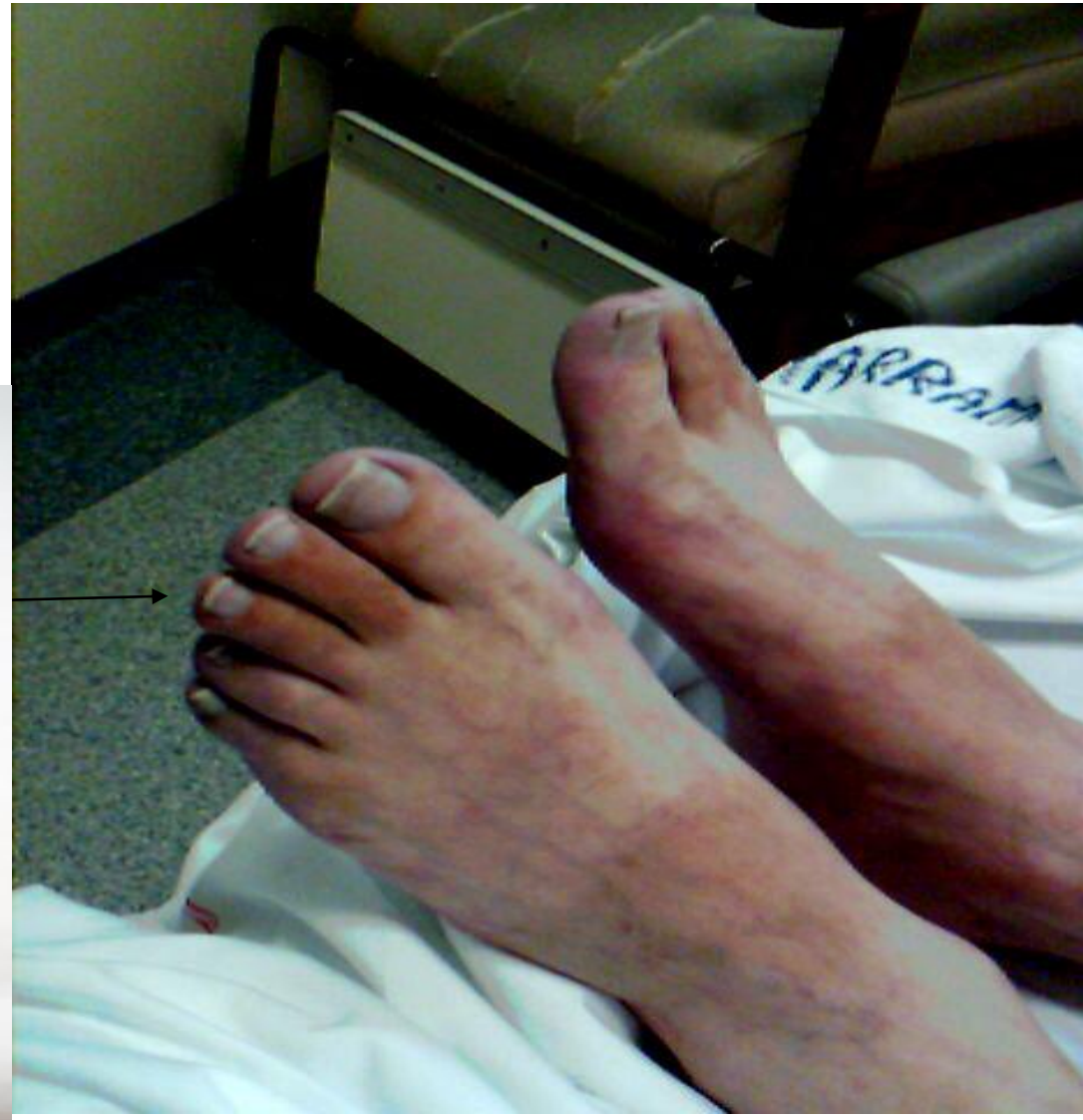
- Portions of atherosclerotic plaque break off and embolize distally, resulting in complete/partial occlusion of multiple small arteries (such as glomerular arterioles), leading to tissue or organ ischemia
- Often seen in older patients with diffuse erosive atherosclerosis
- Usually after coronary angiography or angioplasty (commonest) , renal angiography , cardiovascular surgery, thrombolytic therapy or anticoagulation

Clinical presentation

- AKI usually subacute/staggered and presents several weeks after inciting event
- Sometimes AKI rapid (within 1-2 weeks),usually in association with massive embolization
- Severe hypertension may be present
- Urine is bland
- Blue toes with normal puses, livedo reticularis, GI symptoms with pain/bleed, focal neurologic deficits, orange plaques in the retinal arterioles(Hollenhorst plaques)
- May have eosinophilia, eosinophiluria, and hypocomplementemia

Pedal Ischaemia





Diagnosis

- H/o inciting event in patient with known atheromatous condition with *no pre or post renal cause of AKI*
- Urine dipstick negative
- Often multisystem presentation as discussed in previous slide
- May have eosinophilia, eosinophiluria, and hypocomplementemia
- **Should we biopsy when we suspect this diagnosis ???**

Diagnosis

- Biopsy not required when patient present with all the following features of the classical clinical triad:
  - *A precipitating event (such as aortic or coronary angiography)*
  - *Subacute or acute kidney injury with bland urine*
  - *Typical skin findings, such as blue toe syndrome*

- Definitive diagnosis by renal biopsy showing *cleft like spaces within arteries (cholesterol ghosts)*

Management and prevention

- Supportive therapy and secondary prevention of CV disease with aggressive lipid lowering therapy
- Consider withdrawal of anticoagulation
- Avoidance or postponement of new vascular procedures if possible
- No role for glucocorticoids
- Overall prognosis poor BUT that might also be a reflection of the severity of the underlying vascular disease and other CV risk factors

Remember atheroembolic is NOT thromboembolic renal disease

- Thromboembolic renal disease usually in the setting of AF or IHD
- Complete arterial occlusion and renal infarction
- Present with flank pain, hematuria, and elevated LDH
- Management involves anticoagulation

Thank you

I don't care what day it is.
Four hours is four hours.