Keep Calm: It is only renal failure

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Aim

Acute Kidney Injury (AKI)

vs

Chronic Kidney Disease (CKD).

Top tips to aid care for these people.

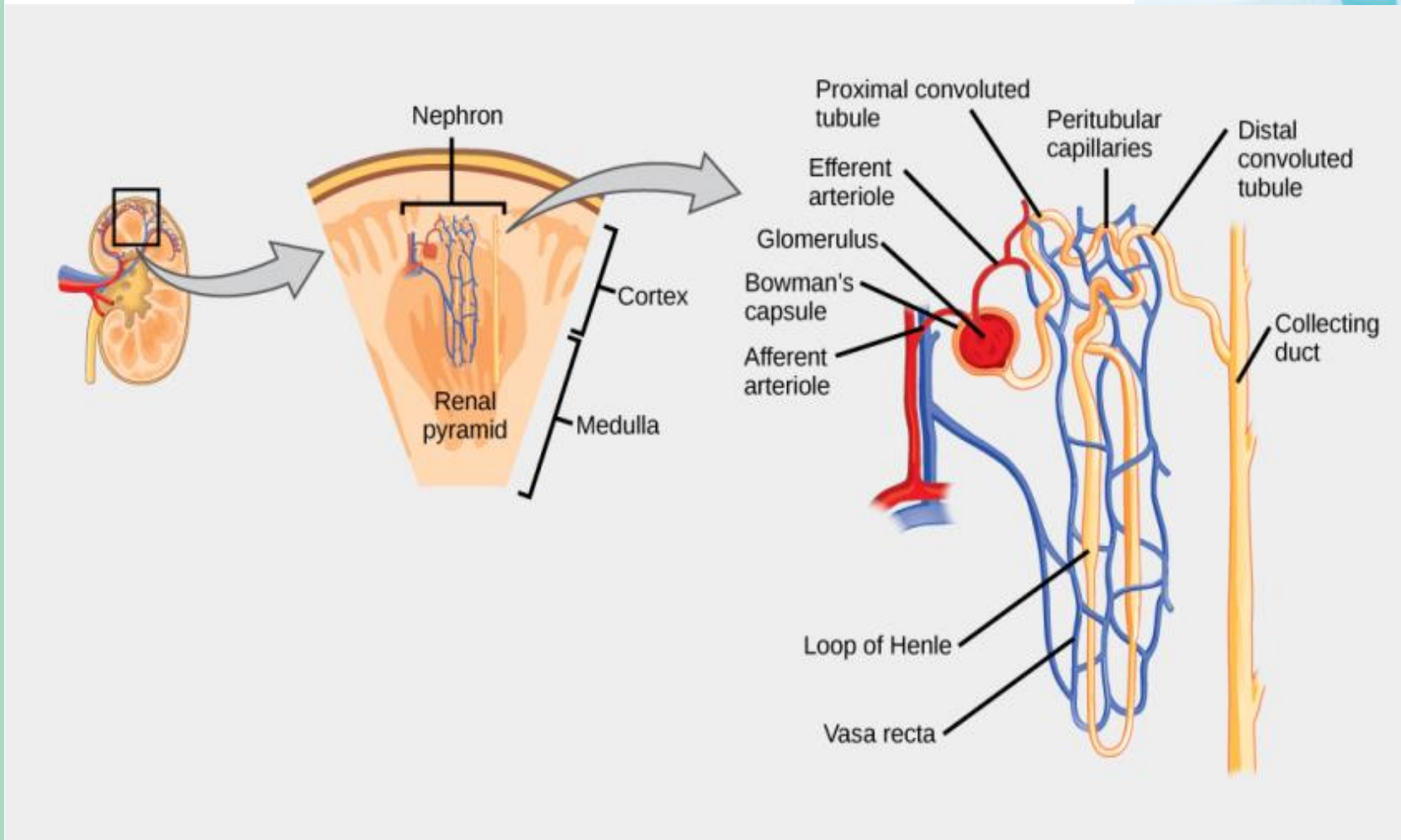
Learning Outcomes:

- Functions of the kidney
- Measuring kidney function
- Tests and Investigations
- AKI
- CKD
- Top tips on drug dosing!

What Do the Kidneys Do?

- Metabolic control of the body
- Removal of waste
- Removal of drugs
- Removal of fluid
- Hormones that control BP
- Produces active vitamin D
- Maintains healthy bones
- Red blood cell production

20% of cardiac output
180 Litres of fluid



Measuring Kidney Function

Estimated GFR (eGFR)

- Reported by most labs alongside Creatinine
- Gives renal capacity if BSA 1.73m^2
- MDRD or CKD-EPI (NICE & UK Kidney Association recommend using this equation)
- Used by labs for reporting CKD staging

Creatinine Clearance (CrCl)

- Most drug dosages are based on this equation
- Which weight to use…….

$$\text{CrCl (ml/min)} = \frac{F \times (140 - \text{age}) \times \text{wt (kg)}}{\text{serum creatinine (µmol/L)}}$$

F = 1.04 Female & 1.23 male

When do we NOT measure or estimate Kidney Function?

For people receiving dialysis!

What is Acute Kidney Injury?

- a **significant deterioration in renal function** occurring over **hours or days,**

- clinically manifesting as an abrupt and sustained **rise in serum urea and creatinine**

KDIGO acute kidney injury stages.

Stage	Serum creatinine	Urine output
1	1.5–1.9 times baseline OR ⩾0.3 mg/dl (⩾26.5 µmol/l) increase	<0.5 ml/kg/h for 6–12 hours
2	2.0–2.9 times baseline	<0.5 ml/kg/h for ⩾12 hours
3	3.0 times baseline OR Increase in serum creatinine to ⩾4.0 mg/dl (⩾353.6 µmol/l) OR Initiation of renal replacement therapy OR, In patients <18 years, decrease in eGFR to <35 ml/min per 1.73 m^2	<0.3 ml/kg/h for ⩾24 hours OR Anuria for ⩾12 hours

https://www.thinkkidneys.nhs.uk/

Acute Kidney Injury

Pre-renal 80%

– inadequate perfusion

Intrinsic Renal Failure **10%**

– vascular, glomerular, tubular, interstitial

Post-renal **10%**

– obstruction (bladder outflow or ureteric obstruction)

Approx 2/3rds of cases begin in the community

A history of AKI:

- reduces life expectancy
- Increases risk of CVD
- Increases risk of poor quality of life

Early recognition – prevents up to 30% of deaths due to AKI

Prognosis – consequences are important even for mild cases. The kidney remembers!

Complications – due to kidney being unable to maintain fluid, electrolyte and acid-base balance.

NICE guideline [NG148]

Acute kidney injury: prevention, detection and management

18 December 2019

Identify - acute illness & at risk

Investigate - serum creatinine vs baseline

Prevent - iodinated contrast agents

Perform - urine dipstick testing & act on abnormal results

Review meds - stop nephrotoxic medications

No identified cause - urgent ultrasound of the urinary tract

Nephrology Referral - AKI stage 3/diagnosis may need specialist treatment

NHS University Hospitals Plymouth NHS Trust

sam THE SOCIETY FOR ACUTE MEDICINE

2·6 ROUNDUP

In Acute Kidney Injury (AKI) if the creatinine jumps by 26 do ROUNDUP

R epeat U+Es
Daily U+E's whilst in AKI

O bstruction ruled out
Examine/bladder scan. US if no improvement

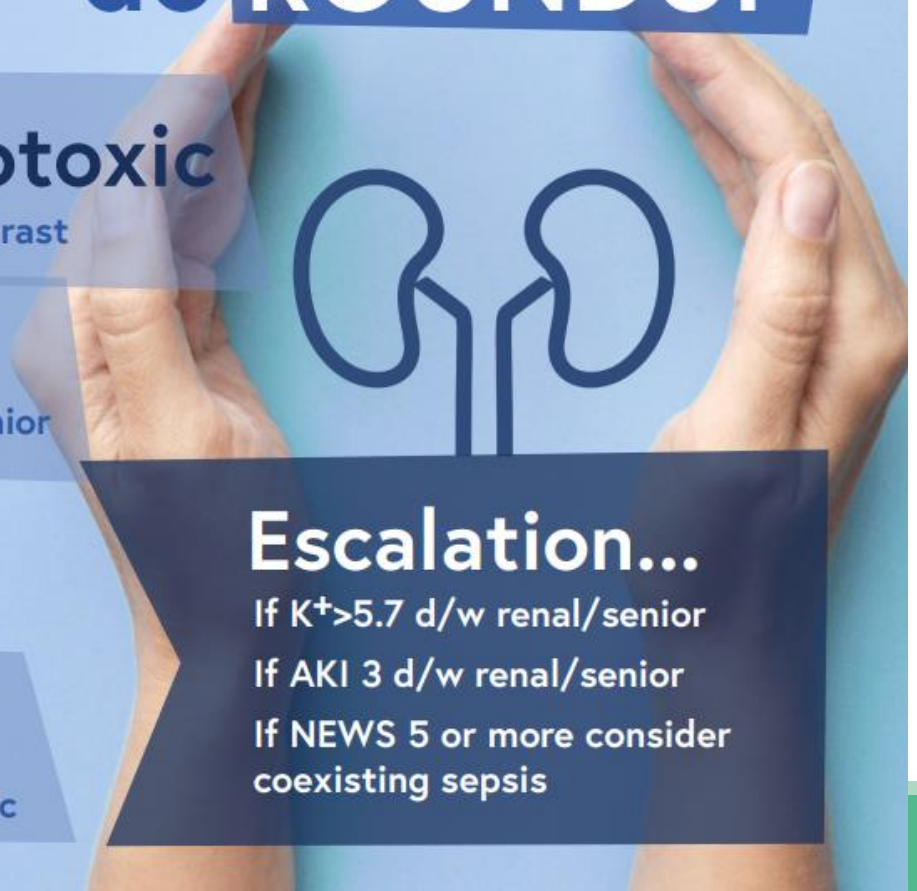
U rinalysis - dip urine
If blood/protein – send for urine PCR

N ephrosensitive/Nephrotoxic
...meds suspended. Hold ACEi/NSAID/diuretics/contrast

D ry or wet ?
Consider rehydration. If fluid overload d/w renal/senior

U rinary output
Fluid balance chart

P rescriptions reviewed
Dose adjustments of antibiotics/opiates/clexane, etc



Escalation...

If K^+>5.7 d/w renal/senior

If AKI 3 d/w renal/senior

If NEWS 5 or more consider coexisting sepsis

What is Chronic Kidney Disease?

- a progressive decline in the glomerular filtration rate (GFR) for at least 3 months.
- Stages are based on GFR and albuminuria.

NICE guideline [NG203] August 2021

Shrinking and scarring **with CKD** once renal function < 30ml/min/1.72m^2

Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012

GFR categories (ml/min per 1.73 m^2) Description and range			Persistent albuminuria categories Description and range		
			A1	A2	A3
			Normal to mildly increased	Moderately increased	Severely increased
			<30 mg/g <3 mg/mmol	30–300 mg/g 3–30 mg/mmol	>300 mg/g >30 mg/mmol
G1	Normal or high	≥90			
G2	Mildly decreased	60–89			
G3a	Mildly to moderately decreased	45–59			
G3b	Moderately to severely decreased	30–44			
G4	Severely decreased	15–29			
G5	Kidney failure	<15			

Green, low risk (if no other markers of kidney disease, no CKD); yellow, moderately increased risk; orange, high risk; red, very high risk.

Chronic Kidney Disease –
permanent damage

Diabetic nephropathy

Hypertensive nephrosclerosis

Glomerulonephritis (inc lupus and vasculitis)

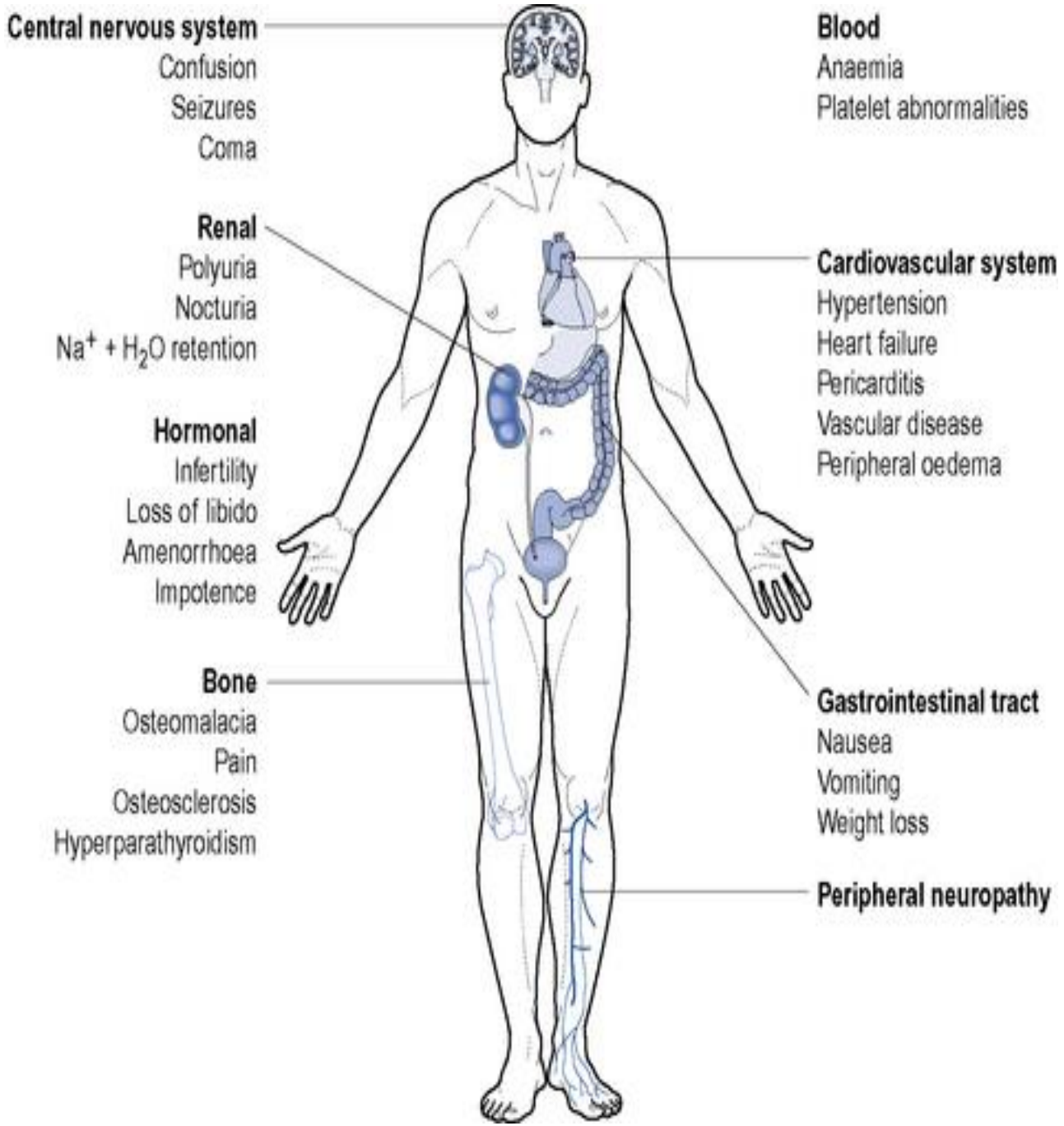
Interstitial nephritis

Polycystic Kidney Disease

Pyelonephritis

Many new drugs available and coming along to treat diseases

Treat symptoms eg itch



Hypertension

Blood pressure control

- slows the progression of CKD
- reduces cardiovascular morbidity and mortality.

- Consider use of potassium binders to allow dose titration of ACEi / ARB

Targets (for all stages of CKD)

BP <140/90

Lower target BP <130/80 if:

- Macroalbuminuria (ACR>70 or PCR>100)
- or Diabetes
- Polycystic Kidney Disease

ACE inhibitor OR ARB

- Diabetic Nephropathy or Proteinuria
- Not both (MHRA guidance)

Transplant recipient

- Calcium antagonist (advised by transplant team)

CARDIOVASCULAR Morbidity

- Diabetes
- Steroid resistant nephrotic syndrome
- Transplantation
- Vasculitis
- Ciclosporin / sirolimus

CARDIOVASCULAR DISEASE

the leading cause of morbidity and mortality in the CKD population

CVD mortality risk (compared to without CKD) is:

- Doubled for people with CKD stages G3a
- Tripled for people with CKD stage G4

Atherosclerosis increases linearly once eGFR decreases to less than 60 mL/min/1.73 m^2

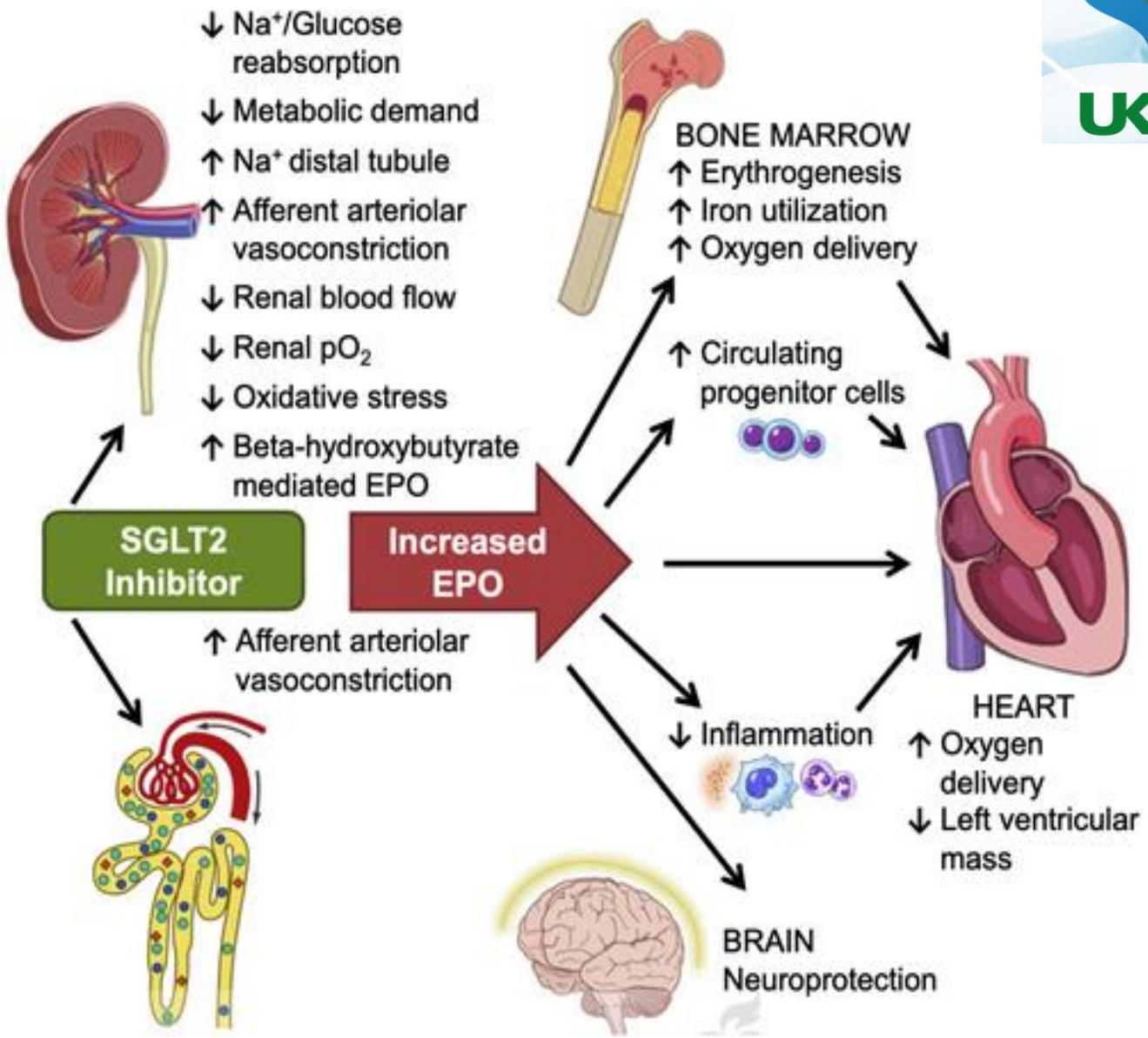
Hyperlipidaemia treatment in CKD is based on CVD risk.

SGLT2 inhibitors

- Dapagliflozin
- Empagliflozin

MRAs

- Finerenone



Renal Anaemia – new medication available

Dietary

Iron absorption

Blood loss

Reduced and impaired erythropoiesis

Exclude OTHER causes of anaemia BEFORE treating with:

- Iron (oral vs IV)
- Erythropoietin (via secondary care)
- HIF HB inhibitors (via secondary care)

to maintain Hb 100 -120g/ litre

Pain Control in Renal Impairment

ONE of the most common and distressing symptoms for people with chronic kidney disease (CKD).

Use the analgesic ladder.

Start low and go slow

- ✓ Paracetamol
- ✓ Tramadol low dose 50mg tds
- ✓ Strong opioids - oxycodone OR fentanyl

Prevent constipation

Opioid sparing – **again start low and go slow**

- ✓ Amitriptyline,
- ✓ Gabapentin
- ✓ Pregabalin

Risk of AKI……..

Drug Dosing in Patients with Renal Impairment and During RRT

Molecular weight

half-life

percentage protein-binding,

volume of distribution.

www.renaldrugdatabase.org

Speak to your Local Renal Pharmacist who will provide Advice and Support

Reduce dose by:

- decreasing the dose
- or by increasing the dosing interval,
- or sometimes by a combination of both.

- Type of Renal replacement therapy affects dosing.

- Clearance MAY be altered by different machines.

Tertiary Nephrology Services

To prepare for and provide

renal replacement therapy

(including transplant)

Haemodialysis

- In-hospital / satellite unit 3 x week, 3-4 hours
- Home HD

Peritoneal Dialysis

- Automated Peritoneal Dialysis
- Continuous Ambulatory Peritoneal Dialysis

Care with Medicine Dosing and Timing

- Antibiotics

Transplantation

1. **Tacrolimus (or ciclosporin)**

NOT interchangeable MUST be prescribed by BRAND

e.g. Adoport (bd), Prograf (bd), Advagraf (od), Envarsus (od)

Consider drug interactions DO NOT give clarithromycin

2. **Mycophenolate mofetil / Mycophenolic acid**
3. **Prednisolone**

Case studies

Background- Case 1

- Following COVID-19 we have seen an increased use of DOACs
- More complex scenarios
- Inappropriate scenarios (MHRA alert metallic valves)
- Unclear documentation for anticoagulant indication
- MHRA alert June 2020 -risk of major bleeding with DOACs
- Highlights importance of the right dose
- Always use CrCl for dosing (MHRA 2018)

Case 1-AKI

72 year old male, 60kg

NH resident

P/C: unwell, fever, drowsy

Impression: Urosepsis

PMH: MI, HTN, BPH, dementia, CKD stage 3/4

Hospital discharge with thrombophlebitis 6 weeks ago haematology plan anticoagulate 3/12

Meds on admission:

Aspirin75mg od

Edoxaban 30mg od

Bisoprolol 2.5mg bd

Tamsulosin 400microg od

Atorvastatin 20mg od

Furosemide 40mg om

Continued….

- Results on admission:

	On admission	Baseline
Creatinine	691	180
Urea	25	8
Sodium	156	138
Potassium	5.6	4.2
C-G CrCl	7	28
SARS-Cov2 PCR	+	
Urine sample	E-coli	
BP	100/60mmHg	130/80mmHg

Plan

- IV gentamicin + IV tazocin
- IV fluids
- No obvious COVID chest symptoms, no oxygen requirements

Initial thoughts

	On admission	Baseline
Creatinine	691	180
Urea	25	8
Sodium	156	138
Potassium	5.6	4.2
C-G CrCl	7	28
SARS-Cov2 PCR	+	
Urine sample	E-coli	
BP	100/60mmHg	130/80mmHg

Meds on admission:

Aspirin 75mg od

Edoxaban 30mg od

Bisoprolol 2.5mg bd

Tamsulosin 400microg od

Atorvastatin 20mg od

Furosemide 40mg om

What happened?

- Furosemide was stopped
- Edoxaban crossed off for a 3 days
- Edoxaban was then re-started after 3 days (CrCl 10ml/min note AKI)
- Request to order edoxaban over weekend-day 6 admission, 3rd ward
- Day 6 CrCl was 15ml/min but dehydrated, low BP on IV fluids
- What would you do?

What happened?

?Over/Under coagulated
?Need therapeutic anticoagulation
(Additional risk factors COVID , immobile, sepsis)

Entry in notes – discuss with haematology

Switched to therapeutic LMWH

Needs discharge plan

Still eligible for DOAC?
Or short course of LMWH to complete the course? Need monitoring with this?

Anticoagulation in AKI

It was appropriate to stop edoxaban on admission

Needed a plan or patient at risk of VTE or a bleeding event

All patients with severe AKI switch to LMWH

In early AKI watch creatinine trends –may need dose adjustment or therapy review

CrCl not accurate in AKI

Russo et 2021 found increased death from bleeding in hospitalised COVID patients with AKI ? Overdose of anticoagulants

What if……

- Patient had been 140kg?

- If the patient had an above knee amputation?

Haemodialysis patient

- 65 year old male
- Type 2 diabetes- on dialysis
- ACS 6 months ago
- Longstanding spinal stenosis not amenable to surgery
- Asked to review due to pain issues, recent admission was opioid toxic

Haemodialysis patient

Morphgesic(morphine) MR 20mg bd (was 120mg MR bd at time of opioid toxicity)

Gabapentin 100mg bd

Amitriptyline 10mg nocte was stopped post-ACS

Lanthanum 750mg tds

Paracetamol 1g qds

Atorvastatin 80mg nocte

Aspirin 75mg daily

Clopidogrel 75mg daily

Omeprazole 20mg daily

Furosemide 160mg bd (still passes some urine)

How are you?

- Agonising pain
- Not sleeping
- No longer mobile with crutches
- Son working unable to take him out in wheelchair- isolated
- Low mood
- Irritable- falling out wife
- Fatigued
- Not been able to get hold of GP– no-one has addressed his pain in the last few months
- Terrible itch (not mentioned until questioned as evident)

Pain relief options in dialysis

- Tried oxycodone with no response
- Fentanyl had made him aggressive
- Wasn't overly keen on a patch
- Converted and switched to hydromorphone (+50% current dose) with breakthrough
- Referred to palliative care/pain team for input

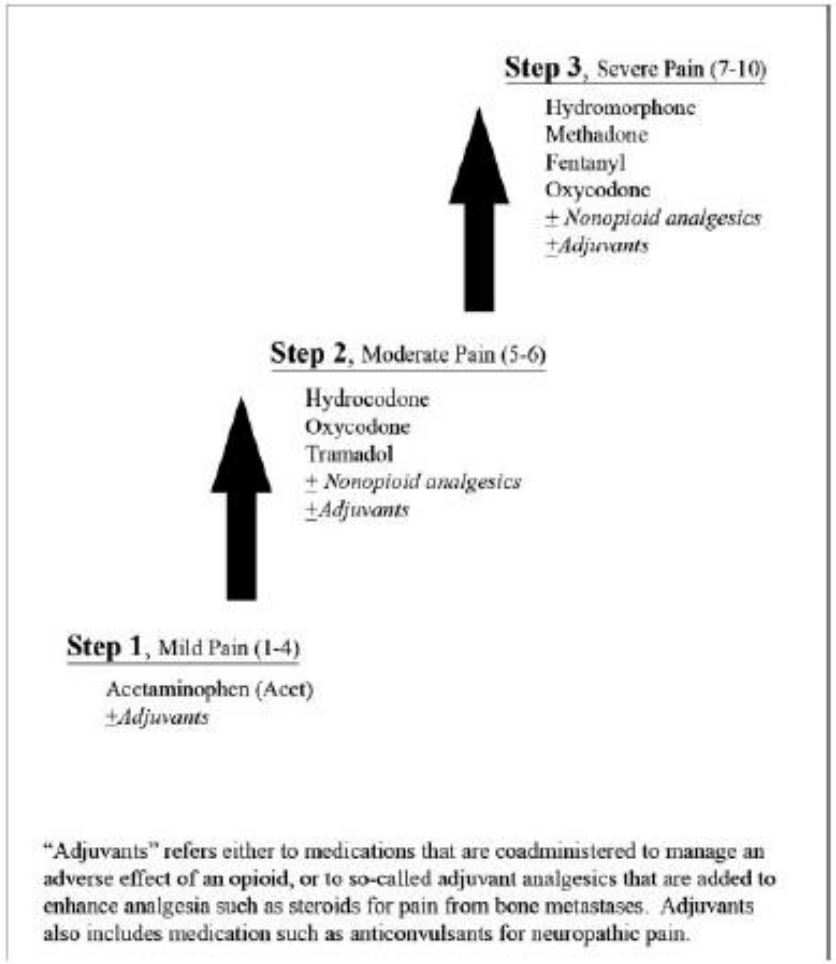


Figure 1. The World Health Organization three-step analgesic ladder modified to exclude drugs unsafe in renal failure. Pa-

Efficacy of the World Health Organization Analgesic Ladder to Treat Pain in End-Stage Renal Disease
Ahmad S. Barakzoy, Alvin H. Moss
JASN Nov 2006, 17 (11) 3198-3203; DOI: 10.1681/ASN.2006050477

Any questions?

Further learning

NICE CKD & AKI Guidelines
National Renal Pharmacy Group (RPG)
&
UK Kidney Association (UKKA)
Centre for Pharmacy Post-Graduate Education (CPPE)