INTERPRETING LABORATORY RESULTS

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Today

Interpreting laboratory tests:

- Kidney – CKD, AKI, K
- Liver
- Thyroid
- Common pitfalls
- Interactive cases

The Kidney

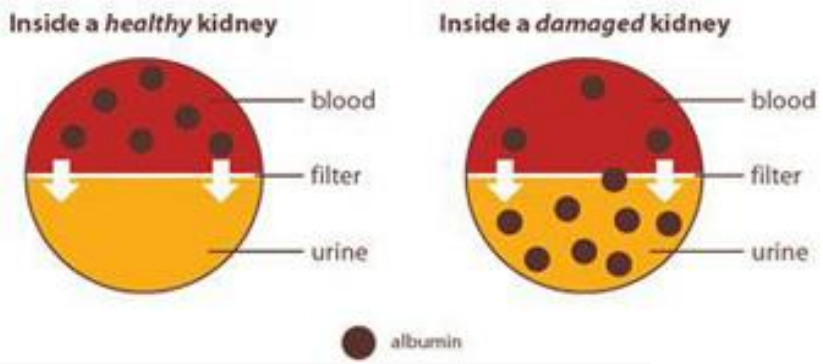
64, M, Hypertension, CKD screen, no previous results

UREA AND ELECTROLYTES			Sex M	Age 64 years
Na	140	mmol/L	(134-145)	
K	4.5	mmol/L	(3.6-5.0)	
Urea	2.5	mmol/L	(1.7-7.1)	
Creatinine	114 H	umol/L	(59-104)	
eGFR	58	mL/min/1.73m²		

Does this patient have CKD?

What would you do next?

Testing for CKD



Who should be tested for CKD

1.1.27 Monitor GFR at least annually in people prescribed drugs known to be nephrotoxic, such as calcineurin inhibitors (for example, cyclosporin or tacrolimus), lithium and non-steroidal anti-inflammatory drugs (NSAIDs). **[2008, amended 2014]**

1.1.28 Offer testing for CKD using eGFRcreatinine and ACR to people with any of the following risk factors:

- diabetes
- hypertension
- acute kidney injury (see recommendation 1.3.9)
- cardiovascular disease (ischaemic heart disease, chronic heart failure, peripheral vascular disease or cerebral vascular disease)
- structural renal tract disease, recurrent renal calculi or prostatic hypertrophy
- multisystem diseases with potential kidney involvement – for example, systemic lupus erythematosus
- family history of end-stage kidney disease (GFR category G5) or hereditary kidney disease
- opportunistic detection of haematuria. **[new 2014]**

NICE National Institute for Health and Care Excellence

National CKD audit

64, M, Hypertension, CKD screen, 2 weeks later

UREA AND ELECTROLYTES Sex M Age 64 years

Na	134	mmol/L	(134-145)
K	4.5	mmol/L	(3.6-5.0)
Urea	2.5	mmol/L	(1.7-7.1)
Creatinine	112 H	umol/L	(59-104)
eGFR	60	mL/min/1.73m²	

Urine Albumin/Creatinine Ratio

Urine Albumin	34.0	mg/L
Urine Creatinine	9.8	mmol/L
Urine Albumin/Creatinine Ratio	3.5	mg/mmol

Does this patient have clinical proteinuria?

Does this patient have CKD?

What would you do next?

Definition of CKD

CKD is defined as abnormalities of kidney structure or function, present for >3 months, with implications for health. (*Not Graded*)

Criteria for CKD (either of the following present for >3 months)	
Markers of kidney damage (one or more)	Albuminuria (AER ≥30 mg/24 hours; ACR ≥30 mg/g [≥3 mg/mmol]) Urine sediment abnormalities Electrolyte and other abnormalities due to tubular disorders Abnormalities detected by histology Structural abnormalities detected by imaging History of kidney transplantation
Decreased GFR	GFR <60 ml/min/1.73 m^2 (GFR categories G3a–G5)

Abbreviations: CKD, chronic kidney disease; GFR, glomerular filtration rate.

KIDNEY DISEASE · IMPROVING GLOBAL OUTCOMES ®
KDIGO

NICE National Institute for Health and Care Excellence

64, M, Hypertension, 4 months later

UREA AND ELECTROLYTES Sex M Age 64 years

Na	140	mmol/L	(134-145)
K	4.5	mmol/L	(3.6-5.0)
Urea	2.5	mmol/L	(1.7-7.1)
Creatinine	114 H	umol/L	(59-104)
eGFR	58	mL/min/1.73m²	

Sample collection time 16:00pm

Urine Albumin/Creatinine Ratio

Urine Albumin	36.0	mg/L
Urine Creatinine	7.2	mmol/L
Urine Albumin/Creatinine Ratio	5.0	mg/mmol

Does this patient have proteinuria?

Does this patient have CKD?

Why is this important?

Why is the detection of CKD important?

It may be clinically silent until an advanced stage and early detection enables you to:

1. Identify and treat reversible causes of CKD

2. Avoid/slow the complications of CKD including:

- Progression to ESRF
- Risk of AKI
- Metabolic and endocrine complications
- Risk of drug toxicity and complications from intravascular radiocontrast administration, surgery etc
- Risk of CVD
- Risk of other common conditions affecting the elderly including infections, frailty and cognitive impairment

3. Prepare people for the possibility of ESRF (dialysis/renal transplant)

WHAT DO THE GUIDELINES TELL US ? (1)

Chronic Kidney Disease – Assessment and management NICE CG 182, 2014

- Diagnostic investigations ✓
- Pharmacotherapy
- Self-management
- Acute Kidney Injury

WHAT DO THE GUIDELINES TELL US? (2)

NICE Chronic Kidney Disease – Assessment and management: CG 182, 2014

- e.GFR calculation: CKD-EPI versus MDRD (4 variable)
- ACR and proteinuria
- Cystatin C versus creatinine

e.GFR: MDRD versus CKD-EPI

- Both use 4 variables: creatinine, age, gender, race but different equations (limitations of creatinine based equations still apply)
- NICE recommends CKD-EPI
  - improved accuracy (NB >75 yrs)
  - identifies people at greater risk of adverse outcome from CKD
  - Reduces the overall prevalence of CKD diagnosed by an e.GFR of <60 mL/min
- No equation works equally well in all populations
- CKD should not be diagnosed if e.GFR is between 45-60 mls/min by either MDRD or EPI if no other marker of CKD

64, M, Hypertension, recap

UREA AND ELECTROLYTES Sex M Age 64 years

Na		140	mmol/L	(134-145)
K		4.5	mmol/L	(3.6-5.0)
Urea		2.5	mmol/L	(1.7-7.1)
Creatinine		114 H	umol/L	(59-104)
eGFR	(CKD-EPI)	58	mL/min/1.73m²	
eGFR (MDRD)		56	mL/min/1.73m²	

Urine Albumin/Creatinine Ratio

Urine Albumin	36.0	mg/L
Urine Creatinine	7.2	mmol/L
Urine Albumin/Creatinine Ratio	5.0	mg/mmol

Sample collection time 16:00pm

The following are true

This patient is likely to have CKD

CKD can not be excluded at this point

Urine ACR should be repeated on an EMU sample

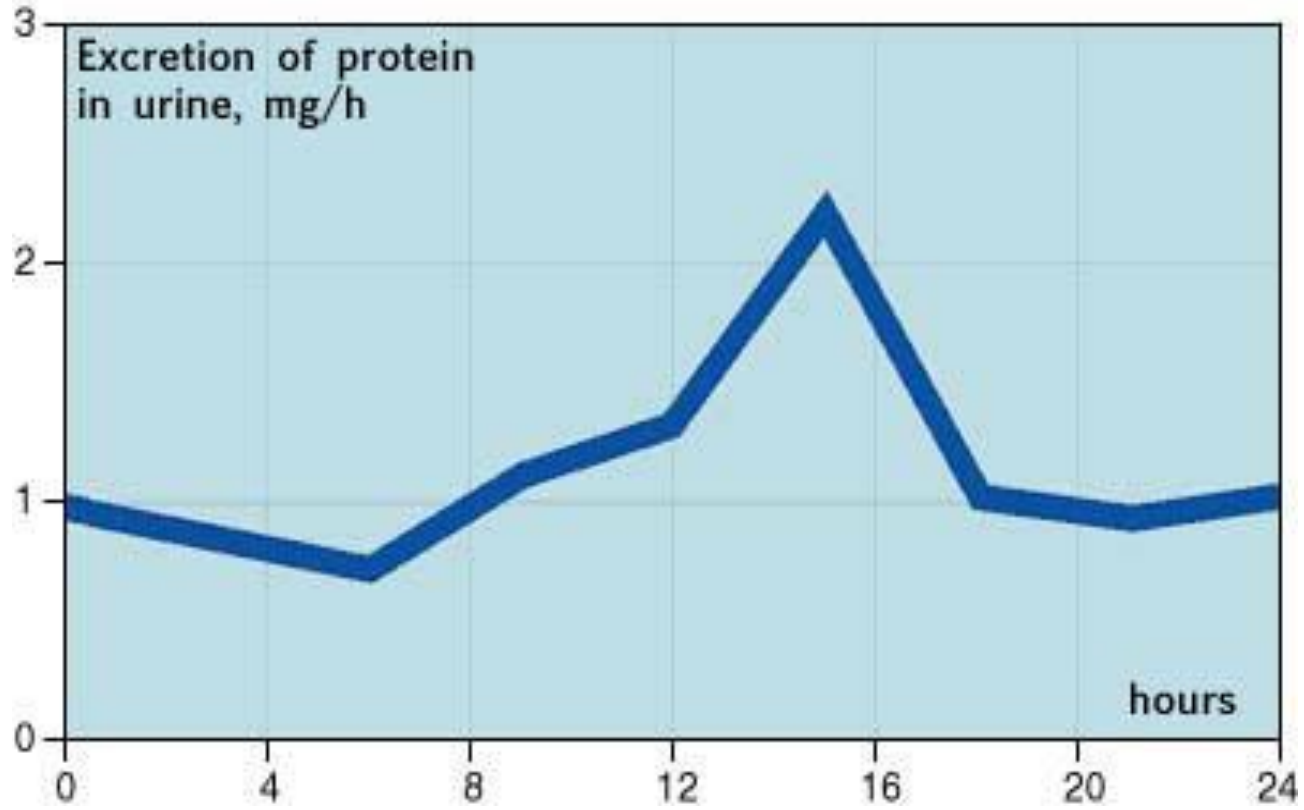
ACR and proteinuria (1)

- NICE recommends use of urine ACR rather than PCR because it has greater sensitivity than PCR for low levels of proteinuria
- Normal mean value of urine albumin loss = 10 mg/24 hours (1mg/mmol)
- Clinical proteinuria defined as urinary albumin loss ≥ 30mg/24 hours = ACR≥ 3mg/mmol *assumes average daily urinary creatinine loss of around 10 mmol*
- For quantification and monitoring of established proteinuria (ACR>70 mg/mmol), PCR can be used as an alternative

ACR pitfalls (1)

- Biological variation of ACR is high with lower variation for ACR on EMU (36%)
- NICE recommends *repeat urine ACR on EMU after 3 months if initial ACR 3-70 mg/mmol to check if abnormality persists*
- If initial ACR >70 mg/mmol, repeat sample need not be tested

Daily time course of protein excretion in urine



ACR pitfalls (2)

- Urine creatinine corrects for dilution (and confirms urine!) However, influenced by muscle mass.

✓High muscle mass - > underestimation of ACR

✓Low muscle mass - > overestimation of ACR

- Interpret results with patient's muscle mass in mind rather than dutifully observing a single COV

- If in doubt, arrange timed collection

56, M, Spina bifida, recurrent UTI ,EMU

EMU - collected at 08:00 am

Urine Albumin/Creatinine Ratio

Urine Albumin	9.0	mg/L
Urine Creatinine	1.5	mmol/L
Urine Albumin/Creatinine Ratio	6.0	mg/mmol

The following are true:

- Urine is probably very dilute
- This patient has clinical proteinuria
- Repeat EMU ACR should be organised after 3 months
- A timed urine collection for albumin excretion should be considered

64, M, Hypertension, repeat EMU ACR

UREA AND ELECTROLYTES Sex M Age 64 years

Na	140	mmol/L	(134-145)
K	4.5	mmol/L	(3.6-5.0)
Urea	2.5	mmol/L	(1.7-7.1)
Creatinine	114 H	umol/L	(59-104)
eGFR (CKD-EPI)	58	mL/min/1.73m²	

Urine Albumin/Creatinine Ratio

Urine Albumin	22.0	mg/L
Urine Creatinine	20.7	mmol/L
Urine Albumin/Creatinine Ratio	1.1	mg/mmol

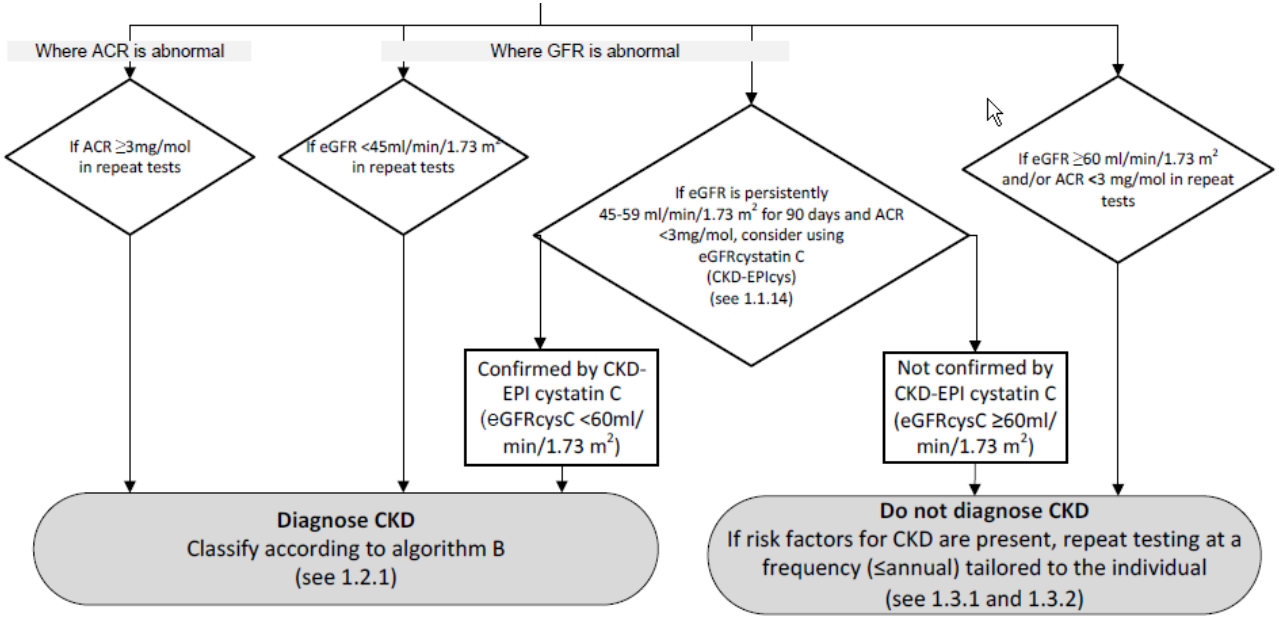
EMU collected at 07:00 am

The following are true:

- This patient is likely to have CKD
- This patient does not have clinical proteinuria
- e.GFR Cystatin C measurement should be considered at this point

NICE, CG 182 recommendations

- Consider e.GFR Cystatin C at initial diagnosis to confirm or rule out CKD in people with:
  - e.GFR creatinine 45–59 ml/min/1.73 m^2 for at least 90 days **and**
  - no proteinuria (ACR stage 1) or other marker of kidney disease



Abbreviations: ACR = albumin creatinine ratio; AKI = acute kidney injury; CKD = chronic kidney disease; CKD-EPI= chronic kidney disease epidemiology collaboration); eGFR = estimated glomerular filtration rate; G5=eGFR<15ml/min/1.73m²

Cystatin C (1)

- An (expensive) alternative to creatinine

- **? a superior marker of GFR**

  Levels chiefly determined by GFR:

  - Unaffected by age, gender, muscle mass
  - Unaffected by most drugs, infection, diet

- Useful where creatinine is not appropriate:

  e.g. Extremes of muscle mass

Cystatin C (2)

Caution:

- Affected by (uncontrolled) thyroid disease
- Data suggests that Cystatin C may be affected by many factors other than GFR
- Cystatin C is not yet routinely available nationally as yet
- Needs to be commissioned if used

64, M, Hypertension, Cystatin C

UREA AND ELECTROLYTES Sex M Age 64 years

Na	136	mmol/L	(134-145)
K	4.7	mmol/L	(3.6-5.0)
Urea	2.5	mmol/L	(1.7-7.1)
Creatinine	114 H	umol/L	(59-104)
eGFR	58	mL/min/1.73m²	

NOTE: From 18th July eGFR will be calculated using a new formula (CKD-EPI)

e.GFR Cystatin C = 57 mls/min/1.73 m^2

Urine Albumin/Creatinine Ratio

Urine Albumin	22.0	mg/L
Urine Creatinine	20.7	mmol/L
Urine Albumin/Creatinine Ratio	1.1	mg/mmol

EMU collected at 07:00 am

Final diagnosis: CKD (READ coded)
Started on CCB
Staging?
Frequency of monitoring?

Staging of CKD

- CKD should be classified based on cause, GFR category and proteinuria category
- ACR (kidney damage) given the same importance as GFR (kidney function) in estimating severity of CKD
- This is because risk of adverse outcomes e.g. progression to ESRF, AKI, all cause mortality and cardiovascular events increase with decreasing GFR **and** increasing ACR
- The combination of increased ACR and decreased GFR multiply the risk of adverse outcomes

CKD classification

Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012

Numbers in boxes are a guide to frequency of monitoring as recommended by NICE

GFR categories (ml/min per 1.73 m²) 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	1 if CKD	1	≥1
	G2	Mildly decreased	60–89	1 if CKD	1	≥1
	G3a	Mildly to moderately decreased	45–59	1	1	2
	G3b	Moderately to severely decreased	30–44	≤2	2	≥2
	G4	Severely decreased	15–29	2	2	3
	G5	Kidney failure	<15	4	≥4	≥4

INCREASING RISK

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

INCREASING RISK

Basic actions in CKD

Non-renal lab monitoring:

- Hb: G3b onwards
- Ca/PO4/PTH: G4 onwards

Referral:

- G4 onwards
- A3 + haematuria or ACR > 70 mg/mol
- >25% fall in GFR or
- >15 mls fall in 12 months

64, M, Hypertension – BP 170/96 on CCB

- Compliance checked
- Combination therapy commenced with Perindopril
- Target BP <140/90
- UE rechecked after 10/7

UREA AND ELECTROLYTES Sex M Age 64 years

Na	134	mmol/L	(134-145)
K	5.1 H	mmol/L	(3.6-5.0)
Urea	2.5	mmol/L	(1.7-7.1)
Creatinine	122 H	umol/L	(59-104)
eGFR	54	mL/min/1.73m²	

NOTE: From 18th July eGFR will be calculated using a new formula (CKD-EPI)

- 2/12 later, BP = 135/85

NICE, CG182 : RAS meds in CKD

- Care starting in pts with [K^+] > 5 mmol/L
- After **starting** or **increasing dose**, check U&E after 7-14 days
- Accept:
  - Drop in eGFR of <25%
  - Increase in Creat of < 30%

But, if any change, needs re-check after 1-2 weeks to ensure stability

- Stop if K ≥ 6 mmol/L and other drugs known to promote HyperK have been discontinued

64, M, hypertension, CCB, ACE, statin, acutely unwell

- Productive cough and DIB for 5/7
- Off food and drink, not passing as much urine as usual
- O/E orientated TPP, T=37.6 BP = 110/60, RR=13, sats = 97%, HR=90
- Antibiotics started
- Decision made to treat at home initially

64, M, hypertension, CCB, ACE, statin, acutely unwell

CHEMISTRY - Blood

UREA AND ELECTROLYTES Sex M Age 64 years

Na	136	mmol/L	(134-145)
K	5.0	mmol/L	(3.6-5.0)
Urea	12.5 H	mmol/L	(1.7-7.1)
Creatinine	179 H	umol/L	(59-104)
eGFR	34	mL/min/1.73m²	

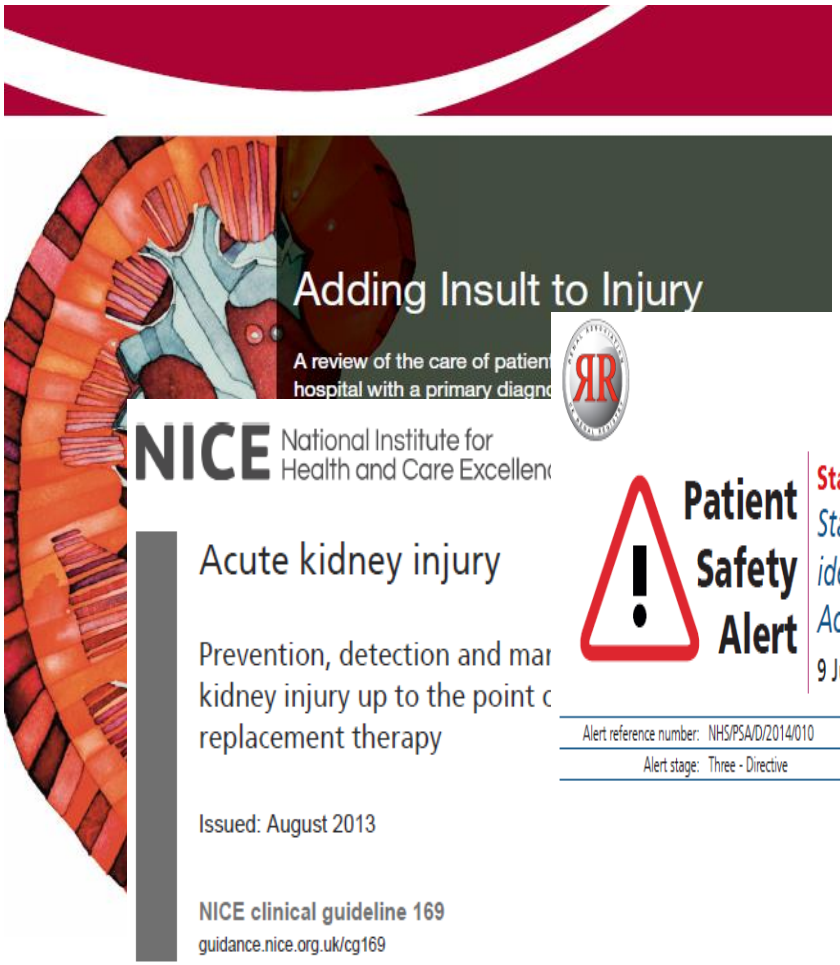
NOTE: From 18th July eGFR will be calculated using a new formula (CKD-EPI)

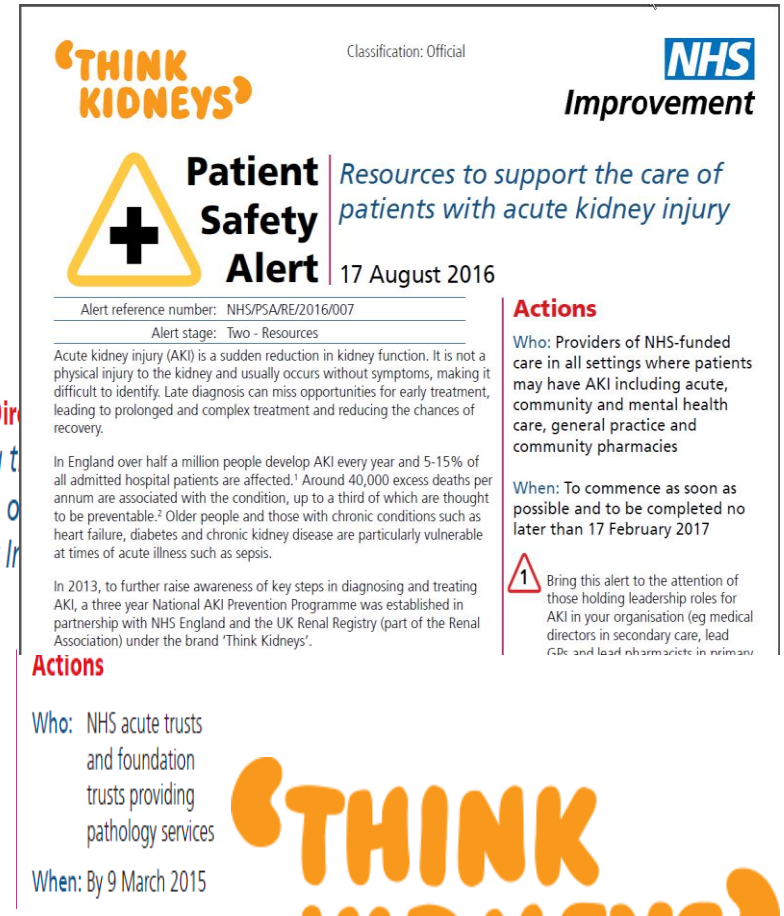
AKI Warning Stage	1 H	(<0)
Clinical Comment	Consider drugs that may be harmful to kidneys, obstruction, hydration and infection.	

The following are true

1. The AKI alert is likely to be false positive, no further action is required
2. The AKI alert is likely to be a true positive, this patient should be reviewed within 24 hours
3. Only the ACEi should be stopped temporarily
4. Both the ACEi and CCB should be stopped temporarily
5. The patient should be admitted immediately
6. If confirmed, the AKI episode should be READ coded
7. This patient should be followed up for progression of CKD

AKI is high on the agenda



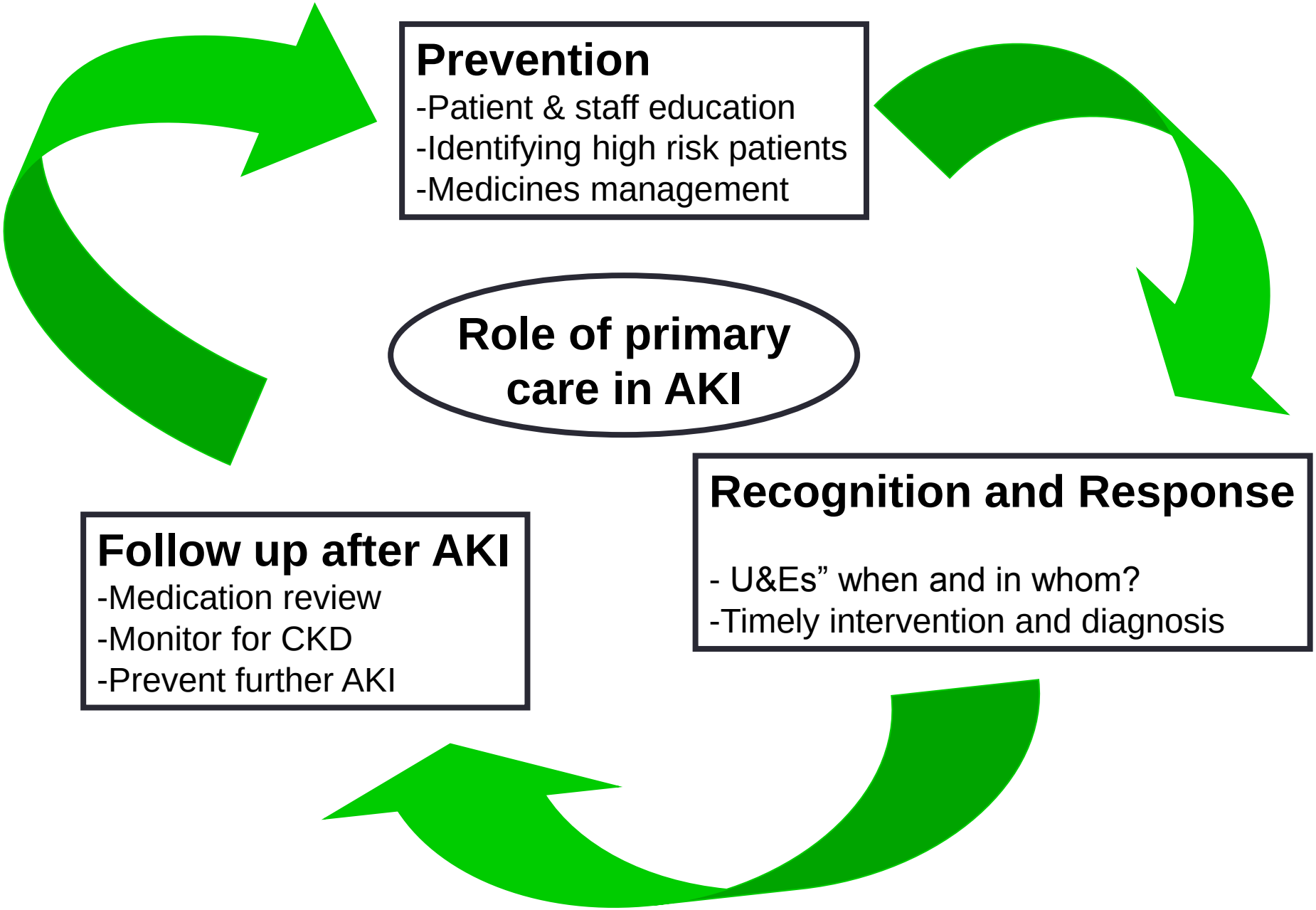


Acute Kidney Injury (AKI)

- Acute kidney injury (previously known as acute renal failure) covers a wide spectrum of injury to the kidneys, not just kidney failure
- Arises from a rapid fall in renal function over hours or days resulting in increases in serum urea and creatinine levels, electrolyte disturbance and metabolic acidosis.
- Urine output can be preserved but is often decreased and time=nephrons…

AKI – setting the scene

- About 20% of all adult emergency admissions to hospital develop some degree of AKI
- About 25% of those will die
- Many of the cases will start in the community
- Between 20% and 30% of cases of AKI are preventable. Prevention could save up to 12,000 lives each year
- NHS costs related to AKI are between £434 and £620 million per year


Prevention
-Patient & staff education
-Identifying high risk patients
-Medicines management
Role of primary care in AKI
Recognition and Response
- U&Es" when and in whom?
-Timely intervention and diagnosis
Follow up after AKI
-Medication review
-Monitor for CKD
-Prevent further AKI

AKI Risk factors: adults

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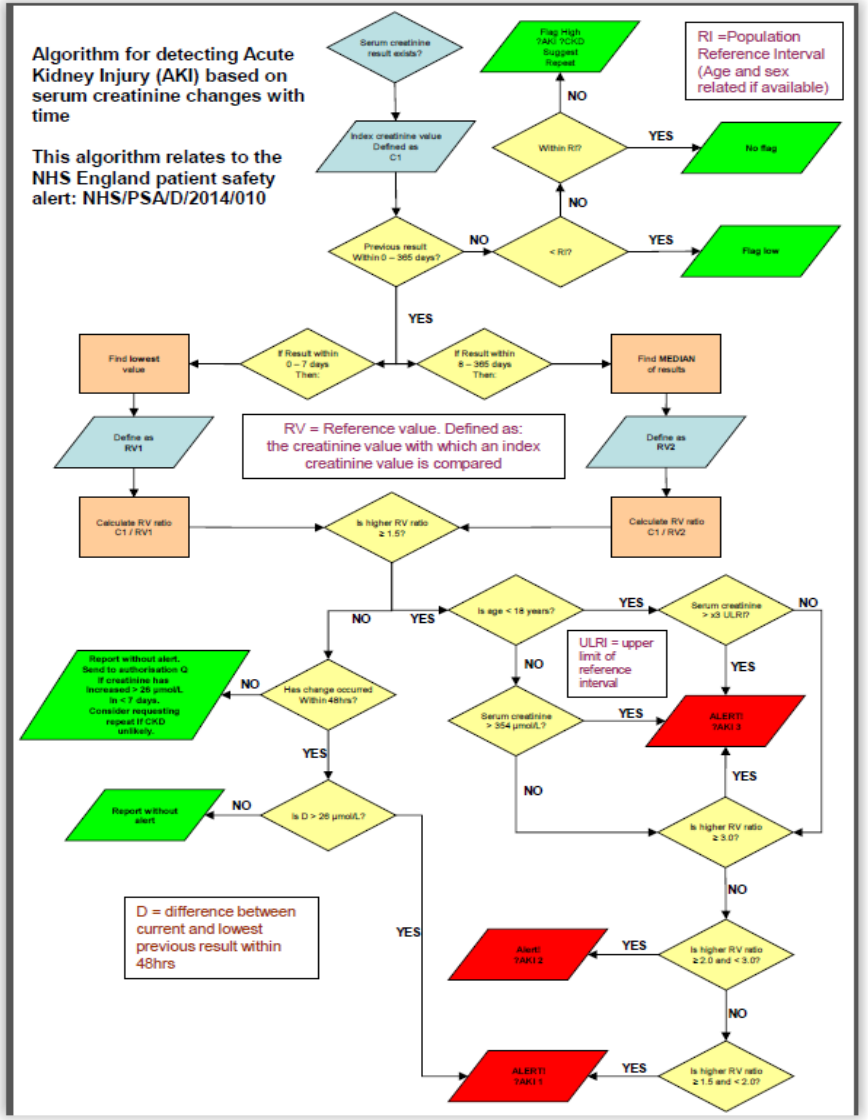
Patient specific

- **Chronic kidney disease (or history of)**
- Age 65 years or over
- Diabetes
- Heart failure
- Liver disease
- Limited access to fluids, e.g. via neurological impairment

Situation specific

- **Hypovolaemia**
- Sepsis
- Use of drugs with nephrotoxic potential (for example, NSAIDs, ACE inhibitors)
- Symptoms or history of urological obstruction
- Use of iodinated contrast agents within past week
- Oliguria
- Deteriorating early warning scores

AKI Detection



Stage 1

- Rise in creatinine of 1-1.9 x baseline*
- Increase in creatinine ≥26 µmol/L within 48 hours

Stage 2

- Rise in creatinine of 2-2.9 x baseline*

Stage 3

- Creatinine ≥ 3 x baseline*
- Creatinine > 354 µmol/L and >1.5 x baseline*

Detection → **Alerts**

False alarms

- For true AKI, SCr change known **or presumed to have occurred** within preceding 7 days
- If no recent SCr then clinical context vital to decide if SCr rise is likely to be ‘acute’ (and thus consistent with ‘acute kidney injury’). Consider repeat U+E’s within 48-72 hours
- Risk of False positive - CKD & previous SCr nearly 12/12 ago, Trimethoprim Rx, recent pregnancy
- Risk of False negative: patients with recurrent AKI preceding year - > spuriously high baseline

Table 2: Recognising and Responding to Acute Kidney Injury for Adults in Primary Care*

"Think" Cause	"Think" Medication#	"Think" Fluids	"Think" Review¥
History of acute Illness? • Think Sepsis • Think Hypotension Intrinsic kidney disease? (E.g. vasculitis) • Think Urinalysis Urinary tract obstruction?	Any medication which could **exacerbate** AKI? Consider withholding: • NSAIDs • Diuretics • Antihypertensive medication Any medication which may **accumulate** and cause harm during AKI? Any **new** medication that may **cause** AKI?(E.g. drug induced tubulo-interstitial nephritis)	What is the patient's volume status? If hypovolemia present: • When did patient last pass urine? • Can the patient increase fluid intake? • Is admission for IV fluid replacement and monitoring required? Does the patient have and/or need carer support?	Does the patient need acute admission? If not, when will you review? Have you ensured handover?¥

*Refer to main guidance document – Responding to AKI Warning Stage Test Results in Primary Care

Refer to medicines optimisation toolkit for primary care http://www.thinkkidneys.nhs.uk/aki/medicines-optimisation-for-aki

¥ Refer to overarching principles in communication of diagnostic test results https://www.england.nhs.uk/patientsafety/discharge

The table is a guide to support recognition and response to AKI in primary care
The table does not apply to children and young people (<18 years) or patients receiving end of life care

Table1. Acute Kidney Injury: Recommended response times to AKI Warning Stage Test Results for Adults in Primary Care

AKI Warning Stage Test Result Confirm or refute automated AKI Test Result by comparing patient's current creatinine **within clinical context** against baseline creatinine	**Clinical Context Within Which Blood Test Taken#** If clinical context is unknown, then assume high pre-test probability until proven otherwise	
	LOW Pre-test Probability of AKI Stable Clinical Context	**HIGH Pre-test Probability of AKI** Context of Acute Illness
AKI Warning Stage 1 Current creatinine ≥1.5 x baseline level (or creatinine rise >26 mol/L 48 hrs)	**Consider clinical review ≤ 72 hours of e-alert*** **If AKI confirmed** → manage as per table 2	**Consider clinical review ≤ 24 hours of e-alert*** **Likely Stage 1 AKI** → manage as per table 2
AKI Warning Stage 2 Current creatinine ≥2 x baseline level	**Consider clinical review ≤ 24 hours of e-alert*** **If AKI confirmed** → manage as per table 2	**Consider clinical review ≤ 6 hours of e-alert*** **Likely Stage 2 AKI** → manage as per table 2
AKI Warning Stage 3 Current creatinine ≥3 x baseline level (or creatinine 1.5 x baseline and >354 mol/L)	**Consider clinical review ≤ 6 hours of e-alert*** **If AKI confirmed** → consider admission	**Consider Immediate Admission*** Likely Stage 3 AKI

#Clinical Context

Why was the blood test taken?

- Routine chronic disease monitoring
- Drug monitoring
- Assessment of acute illness

Creatinine rise within stable clinical context may reflect unstable CKD instead of AKI, especially if longer time period between current and baseline creatinine.

***AKI Risk Factors/Clinical Features Prompting Earlier Review**

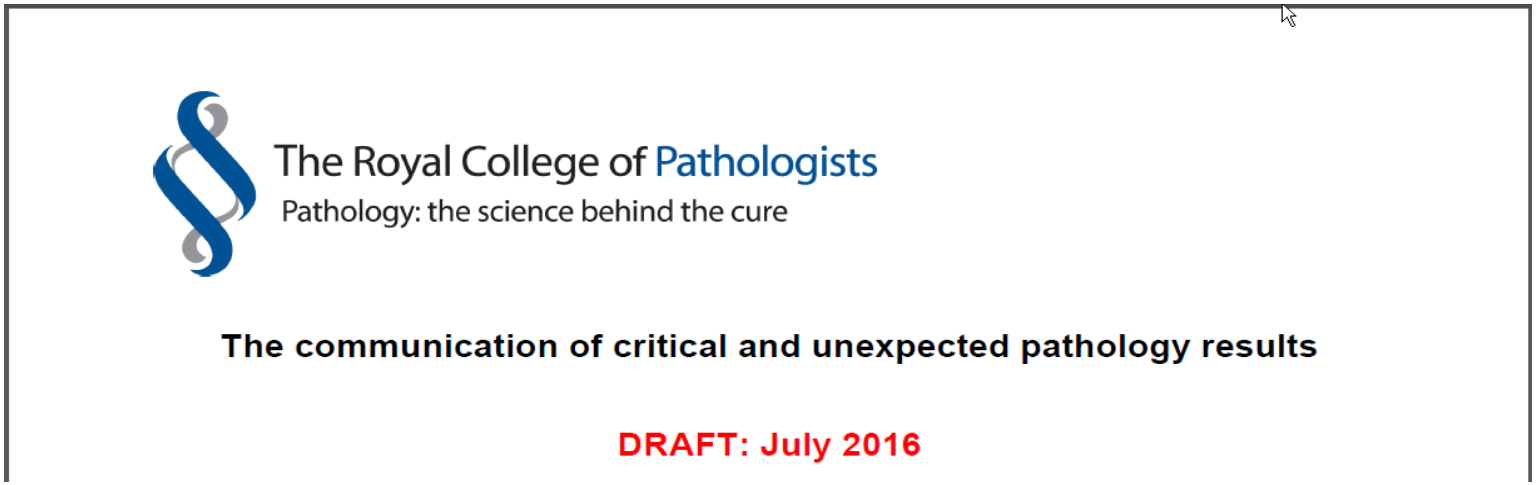
- Poor oral intake/urine output
- Evidence of hyperkalaemia, especially if moderate(K+ 6.0-6.4) or severe (K+ ≥ 6.5)¥
- Known history of CKD stages 4 & 5 or history of kidney transplant
- Deficient Immunity
- Frail with co-morbidities (CKD, diabetes, heart failure, liver disease, neurological or cognitive impairment)
- Past history of AKI
- Suspected intrinsic kidney disease
- Suspected urinary tract obstruction

¥ UK Renal Association Clinical Practice Guidelines (2014) recommends emergency assessment and treatment of severe hyperkalaemia (K+≥6.5mmol/l) – click here
Refer to main guidance document – Responding to AKI Warning Stage Test Results for Adults in Primary Care

The table is a guide to support an initial response to an AKI Warning Stage Test Result but clinical judgement must prevail.
The table does not apply to children and young people (<18 years) or patients receiving end of life care.

Laboratory timeliness of communication to primary care (including OOH)

- Agreed that AKI 3 should be “interruptive communication”
- Debate about AKI 1 & 2 and importance of potassium level in determining urgency
- Steer obtained by RAND consensus process which included a broad range of GPs but RCPath guidance definitive and currently awaited



64, M, Hypertension, 4 months post AKI

UREA AND ELECTROLYTES Sex M Age 64 years

Na	138	mmol/L	(134-145)
K	3.9	mmol/L	(3.6-5.0)
Urea	2.5	mmol/L	(1.7-7.1)
Creatinine	176 H	umol/L	(59-104)
eGFR	34	mL/min/1.73m²	

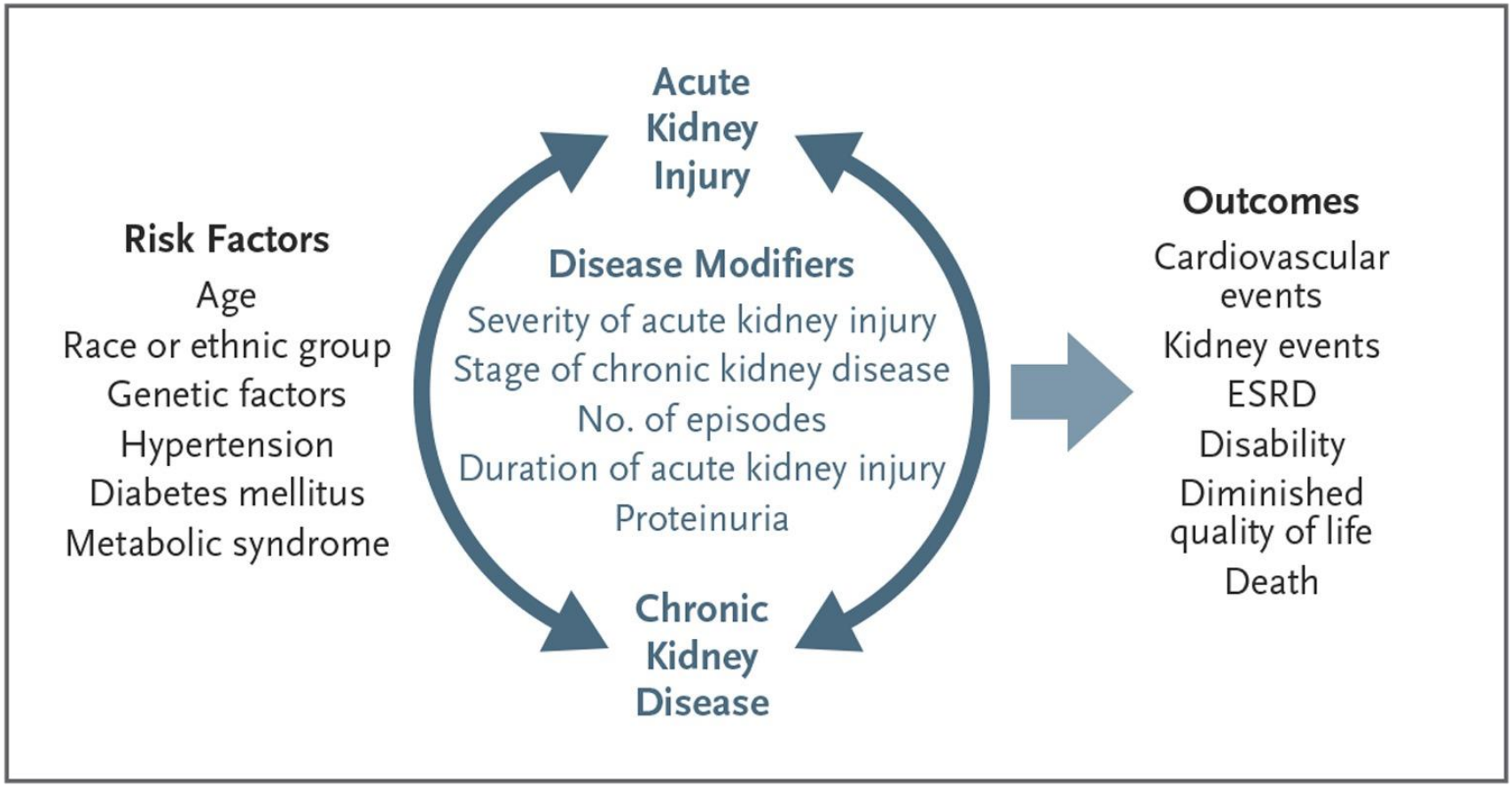
NOTE: From 18th July eGFR will be calculated using a new formula (CKD-EPI)

EMU - collected at 7am

Urine Albumin/Creatinine Ratio

Urine Albumin	46.0	mg/L
Urine Creatinine	19.4	mmol/L
Urine Albumin/Creatinine Ratio	2.4	mg/mmol

Acute Kidney Injury and Chronic Kidney Disease as an Interconnected Syndrome



Chawla LS et al. N Engl J Med 2014;371:58-66

The NEW ENGLAND JOURNAL of MEDICINE

NICE CG182 - AKI

- 1.3.9 Monitor people for the development or progression of CKD for at least 2–3 years after acute kidney injury, even if serum creatinine has returned to baseline. [new 2014]
- 1.3.10 Advise people who have had acute kidney injury that they are at increased risk of CKD developing or progressing. [new 2014]

NICE National Institute for Health and Care Excellence

Further resources

www.thinkkidneys.nhs.uk/aki/resources/primary-care/

Resources for Primary Care

As acute kidney injury warning stage test results for adults begin to be received electronically in primary care, Think Kidneys has developed a range of resources specifically for primary care.

The links below will provide members of the multidisciplinary team caring for people with, or at risk of AKI with information and guidance on how to respond. The aim is to improve safety and outcomes for patients.

Introduction to AKI

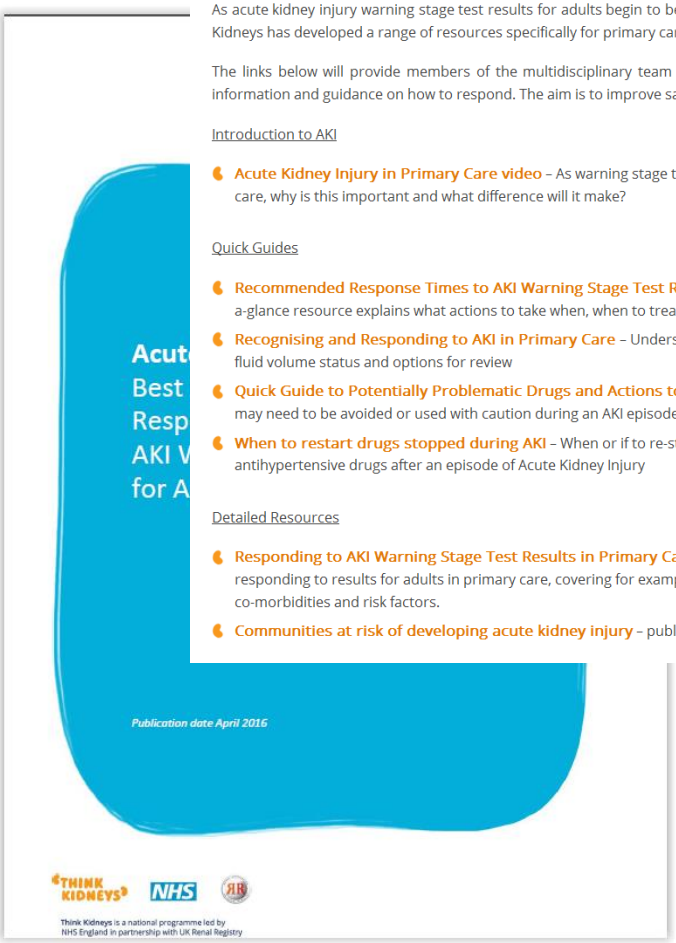
- **Acute Kidney Injury in Primary Care video** – As warning stage test results for AKI are received in primary care, why is this important and what difference will it make?

Quick Guides

- **Recommended Response Times to AKI Warning Stage Test Results for Adults in Primary Care** – This at-a-glance resource explains what actions to take when, when to treat or when to refer
- **Recognising and Responding to AKI in Primary Care** – Understanding cause, possible medication factors, fluid volume status and options for review
- **Quick Guide to Potentially Problematic Drugs and Actions to Take in Primary Care** – Which medications may need to be avoided or used with caution during an AKI episode
- **When to restart drugs stopped during AKI** – When or if to re-start ACEI, ARB, diuretics and other antihypertensive drugs after an episode of Acute Kidney Injury

Detailed Resources

- **Responding to AKI Warning Stage Test Results in Primary Care** – Highlighting key factors to consider when responding to results for adults in primary care, covering for example the stages of AKI, history of acute illness, co-morbidities and risk factors.
- **Communities at risk of developing acute kidney injury** – publication detailing those most at risk of AKI

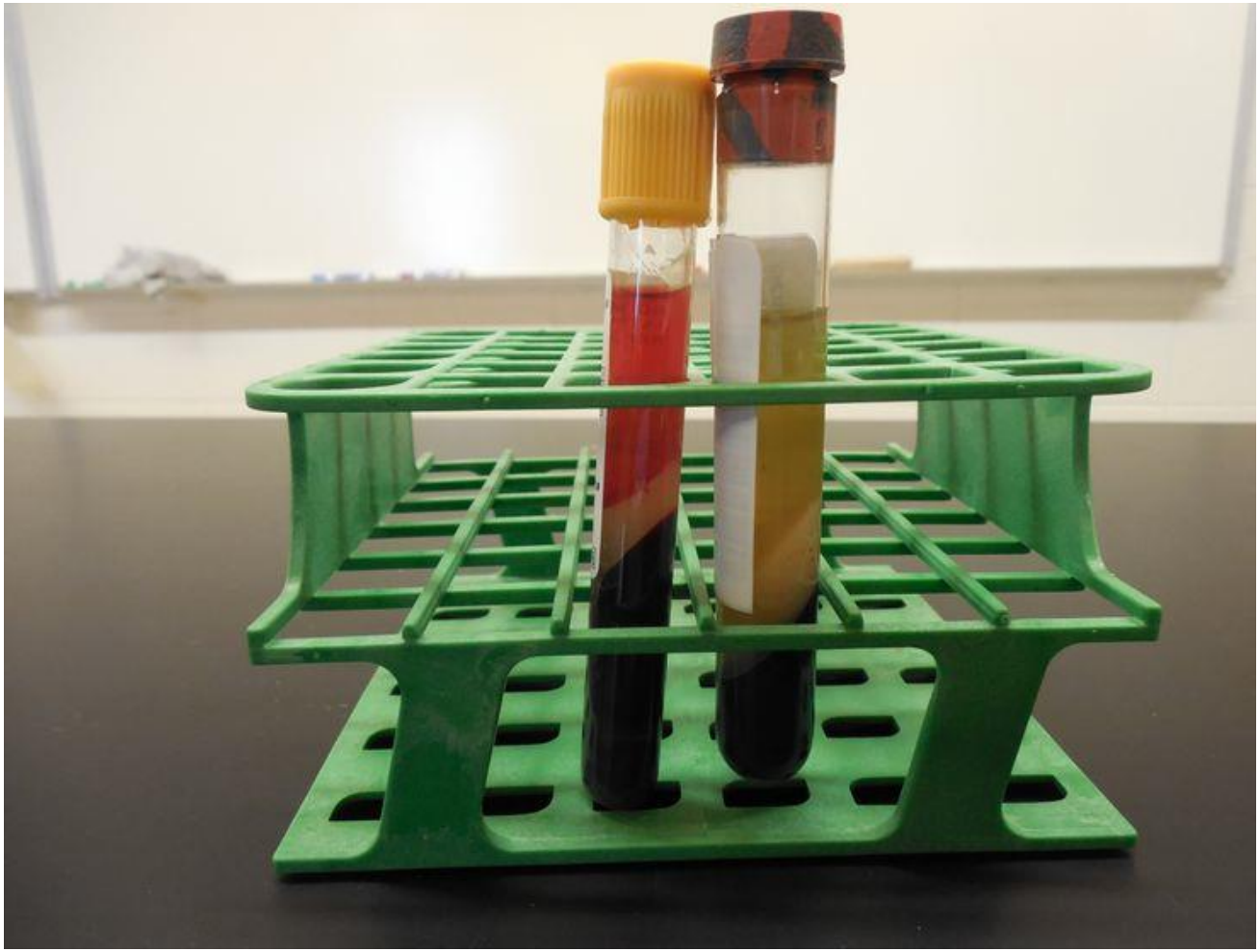


AKI module June 2016

Interpreting renal function tests - take home points

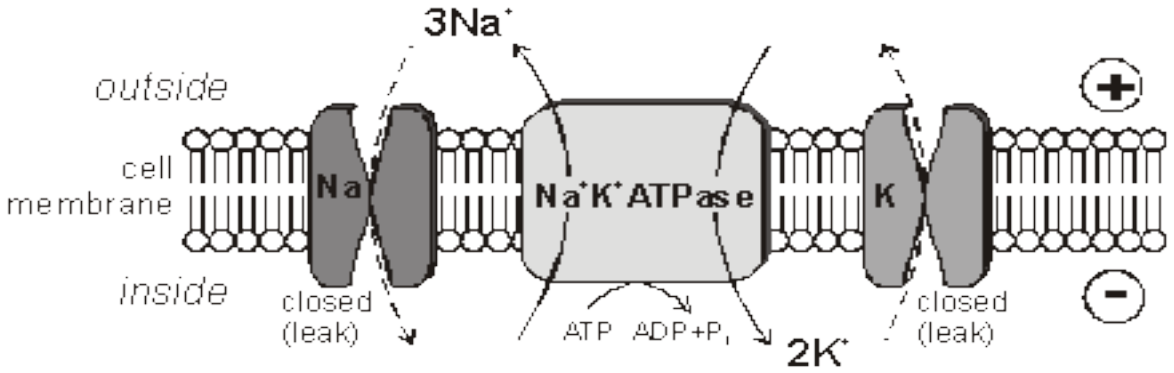
- There is a strong international & national focus on improving the accuracy and early detection of patients with CKD
- Get clear on how to diagnose CKD and the limitations of the diagnostic tools at your disposal
- AKI is common, harmful, costly and often preventable. In around 2/3 admissions, it starts in the community
- Know how to **Risk assess, Recognise and Respond**
- AKI and CKD have a bidirectional relationship. If a patient has had AKI – look for CKD and if a patient has CKD – watch out for AKI!

Potassium conundrums



Why worry about hyperkalaemia in primary care?

- Severe hyperkalemia carries the risk of a cardiac event and should be treated as a medical emergency – 1st presentation may be VF arrest
- BUT pseudohyperkalaemia is a frequent problem in samples from primary care and is a source of avoidable referrals/admissions
- Distinguishing spurious from true abnormalities is therefore critical



59, female, FH ESRD, routine UE's check

CHEMISTRY - Blood

UREA AND ELECTROLYTES Sex F Age 59 years

Na	134	mmol/L	(134-145)
K	6.4 H	mmol/L	(3.6-5.0)
Urea	4.2	mmol/L	(1.7-7.1)
Creatinine	101 H	umol/L	(45-84)
eGFR	52	mL/min/1.73m²	

POTASSIUM COMMENT:
Result has been checked.

6/12 ago

UREA AND ELECTROLYTES Sex F Age 59 years

Na	135	mmol/L	(134-145)
K	5.7 H	mmol/L	(3.6-5.0)
Urea	4.9	mmol/L	(1.7-7.1)
Creatinine	92 H	umol/L	(45-84)
eGFR	56	mL/min/1.73m²	

Your next step would be…

1. No action necessary – probably delayed separation
2. Ring patient, check drug history and advise stop any OTC NSAIDS/herbal remedies and arrange repeat UE's next day
3. Arrange urgent 12 lead ECG
4. Send to A+E for urgent repeat U+E's same day
5. 'Blue light' admission by ambulance
6. Urgent referral to nephrology
7. The laboratory should be contacted and the result discussed

A raised potassium arriving at the surgery

More likely to be true

- CKD
- Diabetes
- Significant change in renal function from previous
- Metabolic acidosis
- Acutely unwell
- Elderly
- Relevant drugs

Drugs to think about in hyperkalaemia

- **Drugs that limit renal K+ excretion** *e.g. ACEi, ARB, Spironolactone, Amiloride, Non selective beta blockers*
- **Nephrotoxic drugs** *e.g. NSAIDS*
- **K+ containing drugs** *e.g. certain laxatives – Movicol, Kleen prep, Fybogel*
- **K+ supplements** *e.g. KCl 'Losalt'*

J R Coll Physicians Edinb 2013; 43:246–51

A raised potassium arriving at the surgery

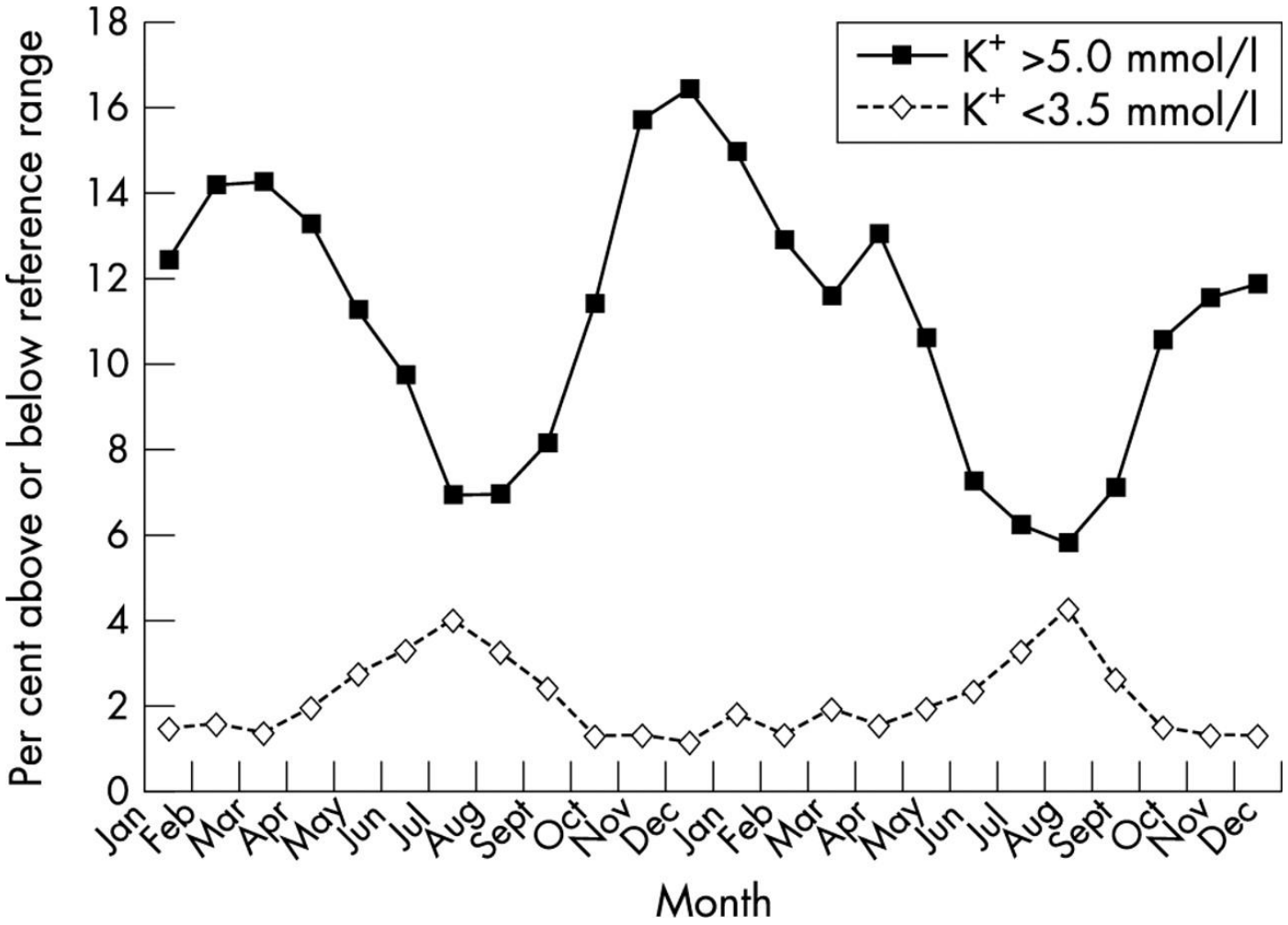
More likely to be true

- Diabetes
- CKD
- Significant change in renal function from previous
- Metabolic acidosis
- Relevant drugs
- Acutely unwell
- Elderly

More likely to be spurious

- Normal renal function
- Normal serum bicarbonate
- No relevant drugs
- Haemolysed sample
- Long time getting to lab
- Raised WBC/platelets
- EDTA contamination
- Season!

Potassium concentrations above & below the reference range



Sinclair, D et al. J Clin Pathol 2003;56:385-387

Investigations

UREA AND ELECTROLYTES — Sex F — Age 59 years

Na	136	mmol/L	(134-145)
K	6.1 H	mmol/L	(3.6-5.0)
Urea	4.2	mmol/L	(1.7-7.1)
Creatinine	101 H	umol/L	(45-84)
eGFR	52	mL/min/1.73m²	

Plasma Potassium	5.6 H	mmol/L	(3.6-5.0)

CHEMISTRY - Blood

Bicarbonate	20 L	mmol/L	(22-30)

Full blood count:

Wbc	4.8	10^9/L	(4.0-10.0)		
Rbc	5.33 H	10^{12}/L	(3.80-4.80)		
Hb	144	g/L	(120-150)		
Hct	0.445		(0.360-0.460)		
MCV	84	fL	(83-101)		
MCH	27.0	pg	(27.0-32.0)		
MCHC	324	g/L	(315-345)		
Platelets	365	10^9/L	(150-410)		
Neutrophils	2.46	10^9/L	(2.00-7.00)	Neutrophils.	51.30 %
Lymphocytes	1.61	10^9/L	(1.00-3.00)	Lymphocytes.	33.50 %
Monocytes	0.49	10^9/L	(0.20-1.00)	Monocytes.	10.30 %
Eosinophils	0.17	10^9/L	(0.02-0.50)	Eosinophils.	3.60 %
Basophils	0.06	10^9/L	(0.00-0.10)	Basophils.	1.30 %
NRBC	0.00	10^9/L			

Type 4 RTA

- Consider in any patient with persistent hyperkalaemia in whom there is no obvious cause
- Underlying issue is aldosterone deficiency or resistance and may be a consequence of drugs (e.g. NSAIDs), renal interstitial disease, diabetes
- Typically seen in patients with mild to moderate CKD (stage G2-4)
- Usually associated with mild hyperchloraemic metabolic acidosis
- May require renal dietetic support to manage hyperK +/- fludrocortisone.

Preventing Pseudo (or normo!) hyperkalaemia in primary care

- Label **DATE AND TIME** of collection of specimens
- Reduce transit time (logistics)
- Optimise storage conditions
- **ALWAYS** take the U&E's (gold top) first (vacutainer system)
- Leakage of K from platelets during clotting and centrifugation in patients with high WBC/platelets/'Leaky cells' can lead to pseudo-hyperkalaemia

Please use a **Lithium Heparin** sample (Green top) if suspected

Preventing Hyperkalaemia in Primary care

If mild (5.5-6.0) or moderate (6.1-6.4) hyperkalaemia:

- Stop NSAIDs and herbal remedies
- Consider a low K diet and avoid K supplements
- Consider prescribing a TDZ or loop diuretic
- Correct acidosis with $NaHCO_3$ in CKD

As a general rule:

- Start drugs at low doses
- Drugs interfering with the RAAS system such as NSAIDS, ACEi, ARB, Aliskaren and diuretics should be stopped during acute illness >24 hours particularly when associated with hypovolaemia and/or hypotension

84, male, lethargy and weakness

CHEMISTRY - Blood

UREA AND ELECTROLYTES Sex M Age 84 years

Na	140	mmol/L	(134-145)
K	2.8 L	mmol/L	(3.6-5.0)
Urea	6.1	mmol/L	(1.7-7.1)
Creatinine	98	umol/L	(59-104)
eGFR	61	mL/min/1.73m²	

NOTE: From 18th July eGFR will be calculated using a new formula (CKD-EPI)

eGFR (MDRD) 63 mL/min/1.73m²

Patient types ok for calculation = IAKI & OAKI
Patient Type IAKI

POTASSIUM COMMENT:
Result has been checked.

Full blood count:

Wbc	10.3 H	10^9/L	(4.0-10.0)
Rbc	4.40 L	10^{12}/L	(4.50-5.50)
Hb	152	g/L	(130-170)
Hct	0.457		(0.400-0.500)
MCV	104 H	fL	(83-101)
MCH	34.5 H	pg	(27.0-32.0)
MCHC	333	g/L	(315-345)
Platelets	209	10^9/L	(150-410)
Neutrophils	6.36	10^9/L	(2.00-7.00)
Lymphocytes	2.76	10^9/L	(1.00-3.00)
Monocytes	0.89	10^9/L	(0.20-1.00)
Eosinophils	0.27	10^9/L	(0.02-0.50)
Basophils	0.03	10^9/L	(0.00-0.10)
RDW	14.3	%CV	(10.0-16.0)

My next step would be… INTERACTIVE

1. Arrange ECG
2. Arrange further blood and urine tests
3. Start Sando-K
4. All of the above (1-3)
5. Admit for IV potassium replacement
6. Refer Nephrology
7. Likely pseudohypokalaemia – ring laboratory to discuss

An approach to hypokalaemia

- Risk stratify and admit for IV replacement if appropriate
- Initiate investigations to establish the underlying cause
- Replace the deficit
- Treat the underlying cause

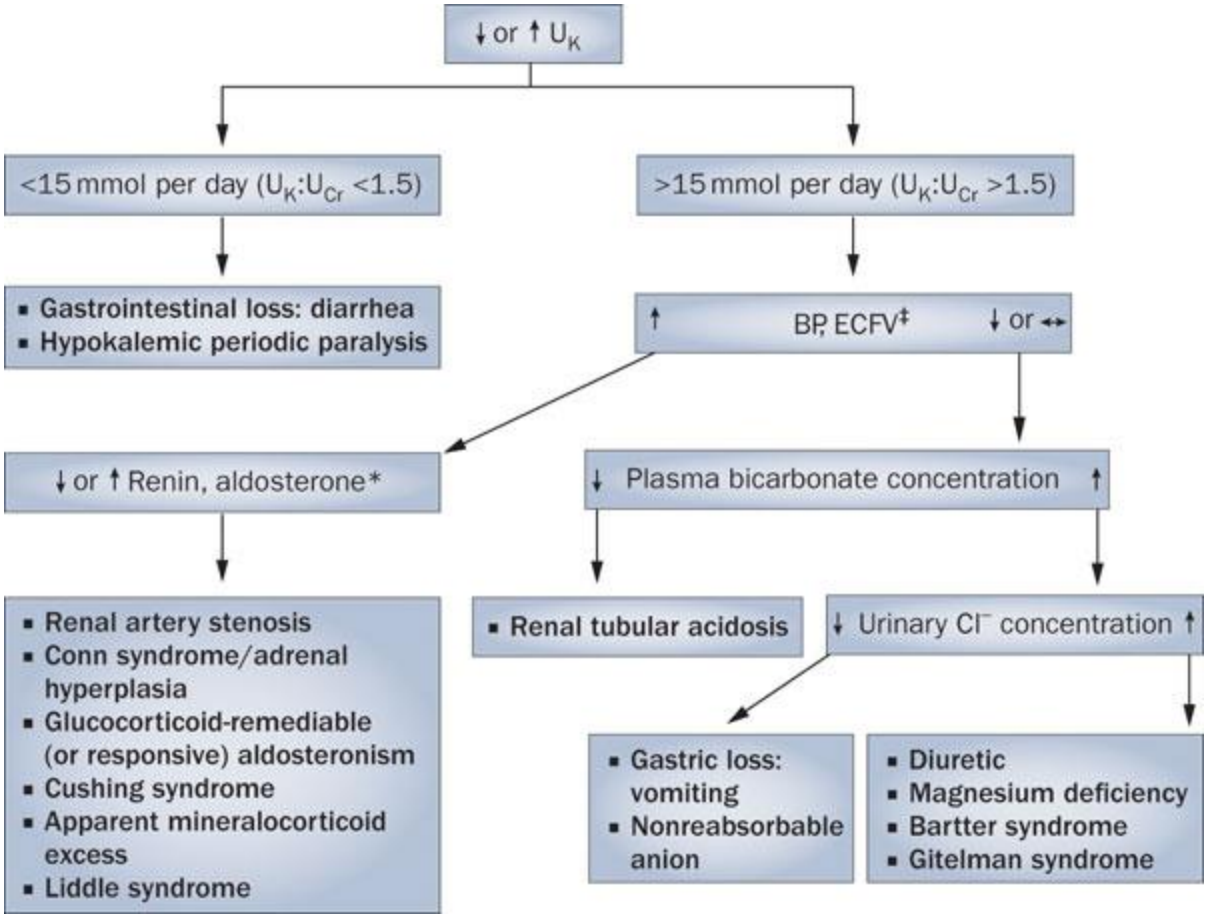
Establishing the cause of unexplained hypokalaemia

Before starting treatment

Key Questions:

- Is the K+ being lost in the urine?
- If so, is the patient hypertensive?
- What is the acid-base status?
- Is serum magnesium normal?

Figure 5 A clinical algorithm for investigating hypokalemia



Unwin, R. J. *et al.* (2011) Pathophysiology and management of hypokalemia: a clinical perspective
Nat. Rev. Nephrol. doi:10.1038/nrneph.2010.175

nature REVIEWS NEPHROLOGY

Further investigations…

CHEMISTRY - Blood

UREA AND ELECTROLYTES

Spot urine K/creatinine ratio = 9 mmol/mol

Na	139	mmol/L	
K	3.2 L	mmol/L	
Urea	4.4	mmol/L	
Creatinine	98	umol/L	(59-104)
eGFR	61	mL/min/1.73m²	

Vitamin B12	326	ng/L	(130-1100)
Serum Folate	5.0	ug/L	(2.7-15.0)

B12 interpretation	
Less Than 100ng/L	Low B12
100-129 ng/L	Borderline B12, may be due to causes other than B12 deficiency
Greater Than 130 ng/L	Normal

CHEMISTRY - Blood

Magnesium :	0.56 L	mmol/L	(0.70-0.90)

Urine Collection period	24	h	
Urine Volume	4363	mL	
Urine creatinine	3021	umol/L	
Urine creatinine output	13.2	mmol/24h	(7.0-21.0)
Urine magnesium	1.2	mmol/L	
Urine magnesium output	5.2	mmol/24h	(2.5-8.5)

Analysis performed at University College London

84, male, on Magnesium and K replacement

CHEMISTRY - Blood

UREA AND ELECTROLYTES

Na	143	mmol/L	(134-145)
K	3.5 L	mmol/L	(3.6-5.0)
Bicarbonate	35 H	mmol/L	(22-30)
Urea	6.6	mmol/L	(1.7-7.1)
Creatinine	86	umol/L	(59-104)
eGFR	77	mL/min/1.73m²	

CHEMISTRY - Blood

UREA AND ELECTROLYTES

Na	139	mmol/L	(134-145)
K	3.6	mmol/L	(3.6-5.0)
Bicarbonate	29	mmol/L	(22-30)
Urea	6.4	mmol/L	(1.7-7.1)
Creatinine	73	umol/L	(55-125)
Creatinine	98	umol/L	(59-104)
eGFR	61	mL/min/1.73m²	

Take home points - Potassium

- Pseudohyperkalaemia **is common** in samples from primary care. If concerned speak to your lab.
- A raised potassium in the absence of a significant change in renal function and a normal serum bicarbonate level is **unlikely** to be true.
- Pseudohypokalaemia is **not common** and low potassium results are **generally** true
- Clarify whether potassium is being lost via the kidneys or gut as a first step (before starting treatment)
- Always think Mg in treatment resistant hypokalaemia

Interpreting abnormal LFT's (ALFT's)

Why are ALFT's important?

Liver disease…

- May be clinically silent even at an advanced stage
- Risk factors may not be easy to elicit
- Often picked up on the basis of abnormal LFT's in otherwise well patients
- Most liver disease is preventable or treatable if diagnosed at a sufficiently early stage that lifestyle changes and treatments can make a difference

An approach to ALFT's

Aim to answer 3 key questions:

1.Is liver disease present?

2. What is the aetiology?

3. What is the severity?

50, female, health care worker, T2DM on Metformin, Ramipril and Simvastatin

CHEMISTRY - Blood

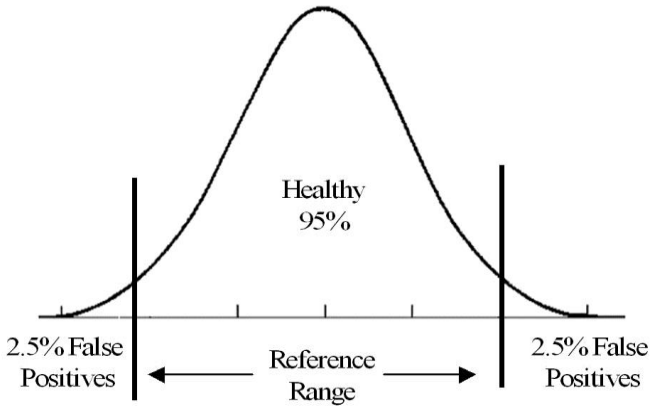
LIVER FUNCTION TEST			
Tot.Bilirubin	10	umol/L	(0-22)
Total Protein	67	g/L	(63-82)
Albumin	40	g/L	(35-50)
Globulin	26	g/L	(21-35)
Alk. Phosph.	76	U/L	(38-126)
ALT	71 H	U/L	(0-50)

CHEMISTRY - Blood

GGT	143 H	U/L	(0-60)

Likeliest cause of raised ALT…

1. Probably spurious - just repeat
2. Probably normal
3. ALT from non-hepatic source
4. Medication related
5. Diet related
6. NAFLD
7. Alcohol
8. Viral hepatitis



Is Liver disease present? Risk assessment

- Medication history (current and previous) including OTC drugs
- A personal history of autoimmune disease(s)
- A Family history of liver disease of any variety
- An assessment of risk for blood borne viruses
- An assessment of risk of NAFLD
- An assessment of harmful or hazardous alcohol intake

An approach to ALFT's

Aim to answer 3 key questions:

1 Is liver disease present?

2. **What is the aetiology?**

3. What is the severity?

Skelly et al J Hepatol (2001)

354 consecutive cases of transaminase >2N , unexplained

• NASH	34%
• NAFL	32%
• Crypt. Hepatitis	9%
• Drugs	8%
• Normal	6%
• Alcohol	3%
• Immune (CAH, PBC)	3%
• Granulomas	2%
• Others (H/C, Wilsons)	2%

Suspecting NAFLD (1)

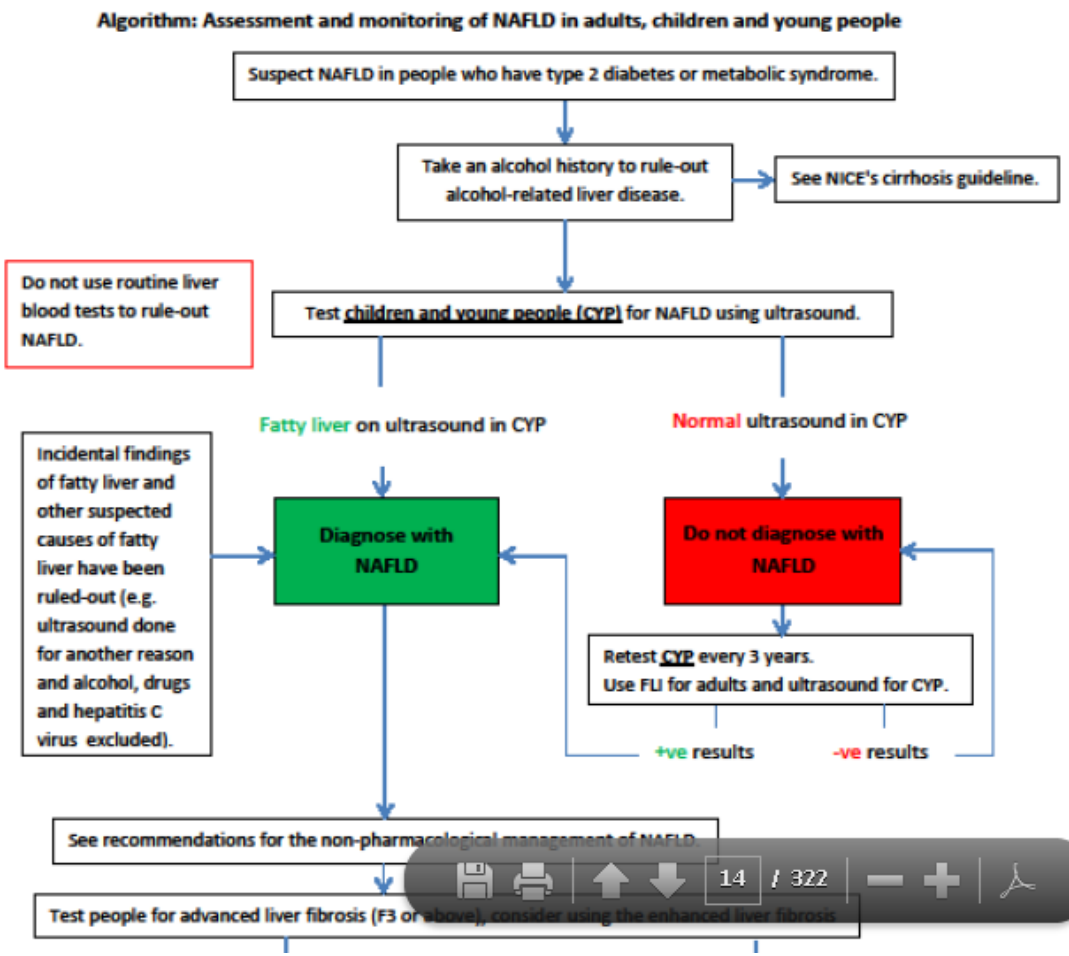
- Many patients with NAFLD remain undiagnosed and recognising those at risk is the first step
- Clinicians over-rely on ALFT's to identify patients with NAFLD so patients with significant liver disease can be overlooked potentially missing opportunities for intervention
- Although NAFLD is a very common cause of ALFT's , majority (>70%) have normal LFT's

Suspecting NAFLD (2)

- **Metabolic syndrome** (54%)
- **T2DM** (53%)
- BMI >30 (46%)
- Triglycerides > 1.7 mmol/L (46%)
- Low HDL (36%) Men < 1.03 mmol/L Women < 1.29 mmol/L
- Wide waist circumference (36%) Men ≥ 102 cm Women; ≥ 88cm

NICE guidance NG49 2016

Diagnosing NAFLD (1)



Diagnosing NAFLD (2)

'…For people with ALFT's and either suspected or confirmed NAFLD, alternative causes must be excluded with a detailed drug history and laboratory tests of:

- Chronic viral hepatitis (HBVsAg +HCV serology)
- Autoimmune liver disease (ANA/AMA/SMA/LKM1 antibodies/Immunoglobulins – Ig A, IgG, IgM)
- Treatable metabolic disease (HFE, Wilson's, Coeliac disease and Alpha-1-antitrypsin deficiency)

Results of investigations

- No relevant Family History
- AUDIT questionnaire – No harmful or hazardous drinking
- Risk factors for BBV and NAFLD
- Liver screen: Ferritin = 467 ug/L (24-300)
- USS Liver –Fatty liver

Diagnosis ?

Investigating raised ferritin in primary care (1)

No Iron Overload (90%)

- Liver disease
- Alcohol excess
- Acute/chronic inflammation
- Infections
- Malignancy
- Metabolic syndrome

Iron Overload (10%)

- *Primary:* Hereditary Haemochromatosis
- *Secondary:* repeated blood transfusions or IV iron infusions, Inherited or Acquired Chronic Anaemia with inefficient erythropoiesis,

  Thalassaemia, PCT

Investigating raised ferritin in primary care (2)

- Clinical assessment and check FBC, UE, LFT's and CRP
- Check 9am fasting transferrin saturation (TFS) - if normal excludes iron overload, suggests reactive cause
- Do not check TFS during acute illness/raised CRP as serum iron is a negative acute phase reactant and may misleadingly decrease TFS
- Unexplained ferritin >1000 mg/L warrant referral
- Mild increases (500-1000 ug/L); no overload (normal TFS), trial of lifestyle interventions may be appropriate but seek hepatology advice

Case 5 – Results of investigations

- No relevant Family History
- AUDIT questionnaire – No harmful or hazardous drinking
- Risk factors for BBV and NAFLD
- Liver screen: Ferritin = 467 ug/L (24-300)
- USS Liver –Fatty liver
- Normal FBC and CRP
- **9am fasting TFS = 39% (<45%)**

Diagnosis ?

An approach to ALFT's

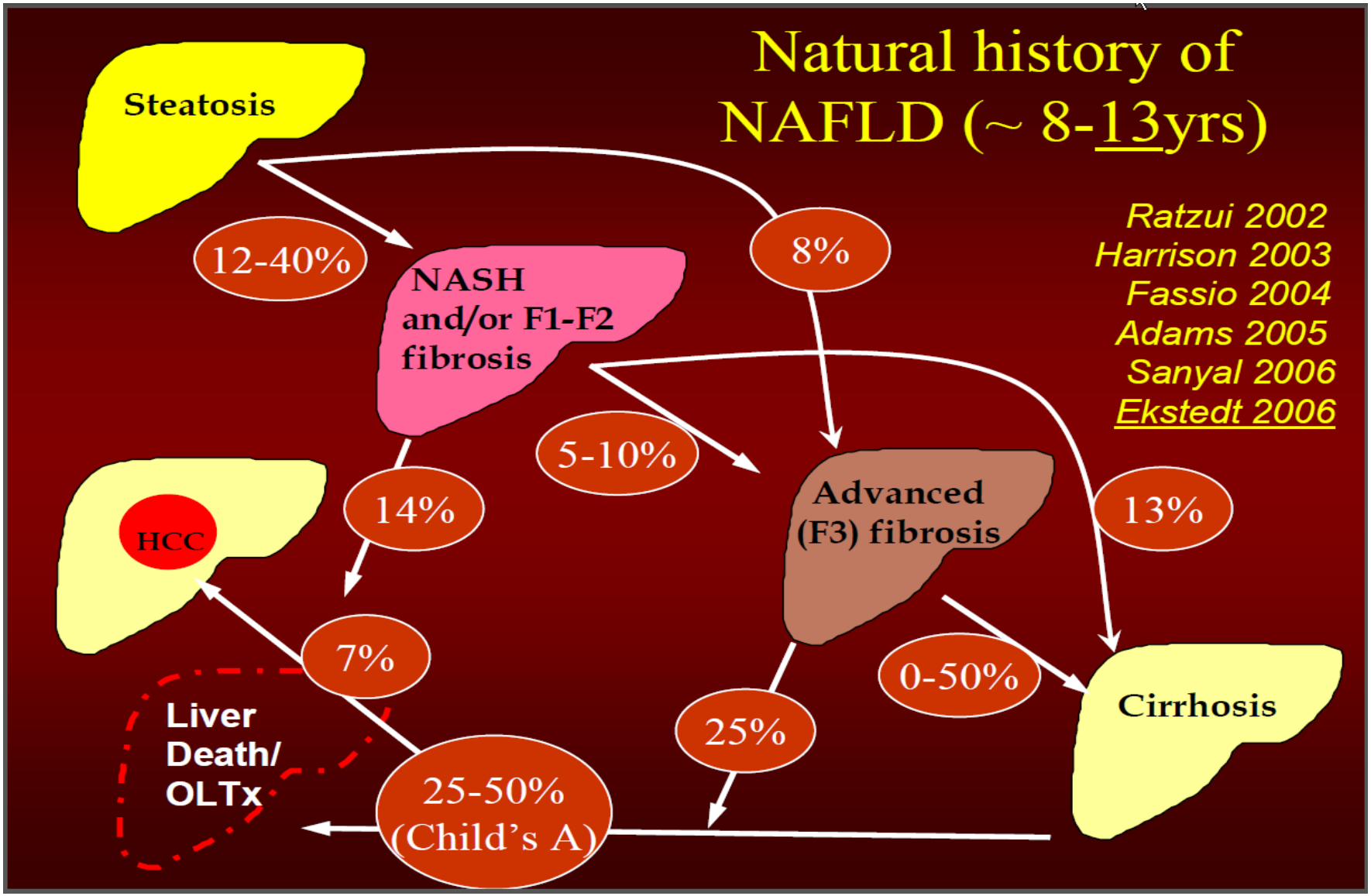
Aim to answer 3 key questions:

1.Is liver disease present?

2. What is the aetiology?

3. **What is the severity?**

Natural History of NAFLD



Case 5 – Assessment of severity

Key questions:

- Does this patient have advanced fibrosis/cirrhosis?

Examination:

- No peripheral stigmata of advanced liver disease
- No splenomegaly
- No hypoalbuminaemia or thrombocytopenia

Assessment of severity

- Liver biopsy - gold standard BUT invasive and limited resource
- Non-invasive tools commonly used to risk stratify patients with NAFLD

Aim: to perform a non-invasive ‘staging fibrosis’ to identify patients with advanced fibrosis who are at risk of liver related complications

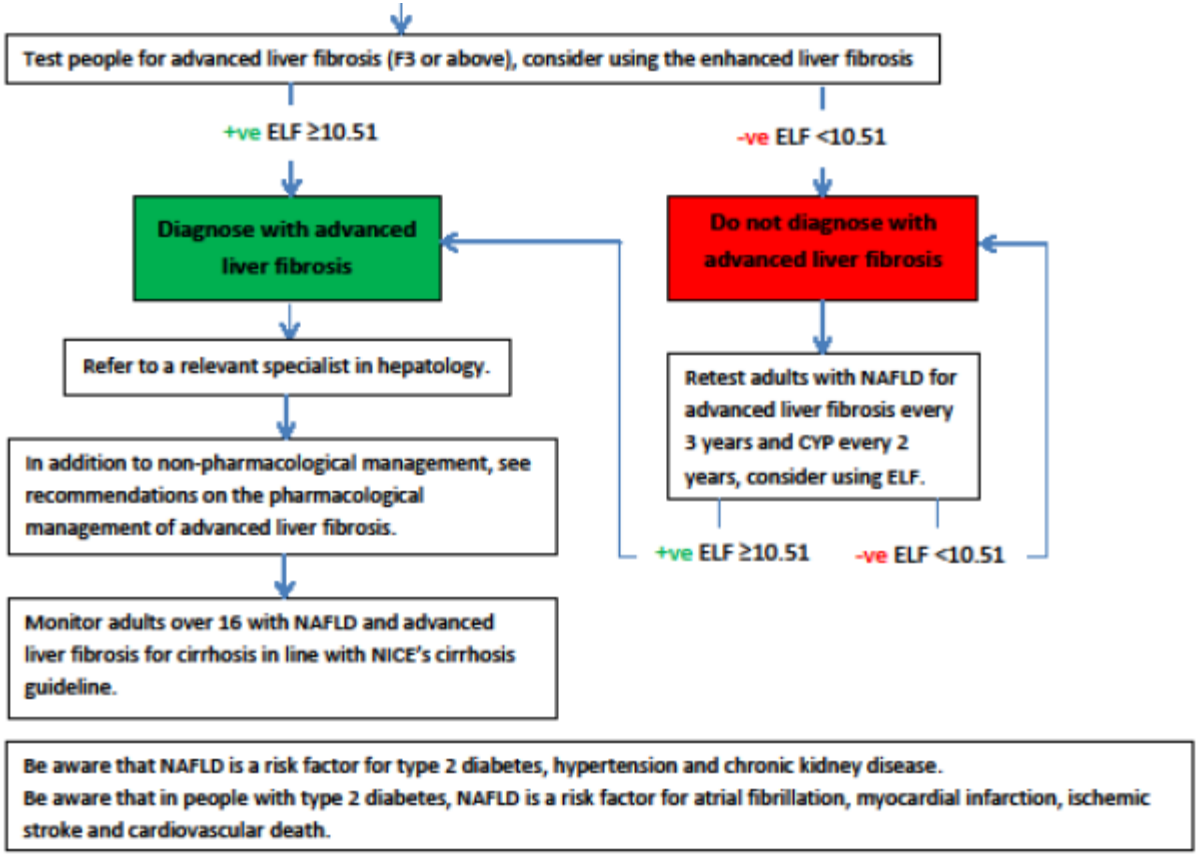
Non-invasive tools – current armory

Markers of liver fibrosis

- *Fibroscan (Transient elastography)*
- *NAFLD fibrosis score, Fib-4 score, AST/ALT ratio,* ***ELF***

NICE guidance recommends ELF score in primary care

NICE NG49 NAFLD 07/16



National Institute for Health and Care Excellence 2016

17 year old girl with abdominal pain

CHEMISTRY - Blood

LIVER FUNCTION TEST

Tot.Bilirubin	47 H	umol/L	(0-22)
Total Protein	77	g/L	(63-82)
Albumin	50	g/L	(35-50)
Globulin	27	g/L	(21-35)
Alk. Phosph.	130	U/L	(89-365)
ALT	6	U/L	(0-50)

Date Collected	31/08/2016	30/08/2016	22/04/2016
Time Collected	14:40	08:30	11:00
Episode	1661215106	1661208963	1660694652
	Ref1	Ref2	Ref3
CHEMISTRY - Blood			
Direct Bilirub	8	-	-
Na	-	142	142
K	-	4.3	5.2 H
Urea	-	3.0	5.1
Creatinine	-	77	73
Total Bilirubi	47 H	81 H	45 H
Total Protein	-	77	73
Albumin	-	50	46
Globulin	-	27	27
ALT	-	6	11
GGT	-	12	11
Alk. Phosph.	-	130	129

Date Collected	30/08/2016	22/04/2016
Time Collected	11:57	11:00
Episode	1661208963	1660694652
	Ref4	Ref5
HAEMATOLOGY		
Hb	168	157
Wbc	8.5	5.3
Rbc	5.47	5.09
Hct	0.498	0.450
MCV	91	88
MCH	30.7	30.8
Platelets	293	252
Neutrophils	6.44	2.93
Lymphocytes	1.42	1.54
Monocytes	0.58	0.49
Eosinophils	0.02	0.28
Basophils	0.04	0.06

My next step would be …

1. Do nothing – unlikely to be of significance
2. Repeat LFT's and request 'Direct Bilirubin'
3. Dipstick urine
4. Repeat LFT's with FBC on a fasting sample
5. Repeat LFT's with FBC, blood film, reticulocytes, haptoglobin and LDH
6. Repeat LFT's and request GGT
7. All steps 2-6

17 year old girl with abdominal pain

CHEMISTRY - Blood

Total Bilirubin	47 H	umol/L	(0-22)
Direct Bilirubin	8	umol/L	

Date Collected	30/08/2016	22/04/2016
Time Collected	11:57	11:00
Episode	1661208963	1660694652
	Ref4	Ref5
HAEMATOLOGY		
Hb	168	157
Wbc	8.5	5.3
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Hct	0.498	0.450
MCV	91	88
MCH	30.7	30.8
Platelets	293	252
Neutrophils	6.44	2.93
Lymphocytes	1.42	1.54
Monocytes	0.58	0.49
Eosinophils	0.02	0.28
Basophils	0.04	0.06

Authorised by on 31/08/2016 at 21:03

Reticulocytes	1.0	%	(0.2-2.0)
Red blood cells	5.12	10^{12}/L	(4.50-5.50)
Reticulocytes	52.2	10^{9}/L	(50.0-100.0)
Lactate Dehydrogenase	208	U/L	(125-243)

17 year old girl with abdominal pain

CHEMISTRY - Blood

LIVER FUNCTION TEST

Tot.Bilirubin	47 H	umol/L	(0-22)
Total Protein	77	g/L	(63-82)
Albumin	50	g/L	(35-50)
Globulin	27	g/L	(21-35)
Alk. Phosph.	130	U/L	(89-365)
ALT	6	U/L	(0-50)

Date Collected	31/08/2016	30/08/2016	22/04/2016
Time Collected	14:40	08:30	11:00
Episode	1661215106	1661208963	1660694652
	Ref1	Ref2	Ref3
CHEMISTRY - Blood			
Direct Bilirub	8	-	-
Na	-	142	142
K	-	4.3	5.2 H
Urea	-	3.0	5.1
Creatinine	-	77	73
Total Bilirubi	47 H	81 H	45 H
Total Protein	-	77	73
Albumin	-	50	46
Globulin	-	27	27
ALT	-	6	11
GGT	-	12	11
Alk. Phosph.	-	130	129

Date Collected	30/08/2016	22/04/2016	
Time Collected	11:57	11:00	
Episode	1661208963	1660694652	
	Ref4	Ref5	
HAEMATOLOGY			
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Hct	0.498	0.450	
MCV	91	88	
MCH	30.7	30.8	
Platelets	293	252	
Neutrophils	6.44	2.93	
Lymphocytes	1.42	1.54	
Monocytes	0.58	0.49	
Eosinophils	0.02	0.28	
Basophils	0.04	0.06	

Investigation of isolated raised BR (1)

- A solitary raised bilirubin result (22-50 umol/L) is likely to be due to Gilbert's syndrome. Levels rise with fasting and intercurrent illness but typically no higher than 85 umol/L

- If you wish to confirm that the rise in bilirubin is unconjugated, wrap sample within usual pathology bag and request 'direct bilirubin'. Alternatively, urine dipstick should be negative for conjugated bilirubin

- Values ≤20% URL, more likely to represent statistical rather than clinical abnormality and 'DBil' measurement unreliable

- If >70% unconjugated: the patient probably has Gilbert's syndrome. You do not need to do any further tests unless you have a clinical suspicion of haemolysis (FBC, LDH, reticulocytes, Blood film)

Investigation of isolated raised BR (2)

- Values >3-4xULN: clinical disease more likely (although enzymes also likely to be raised in liver disease) and you should undertake further investigation. Consider ultrasound (conjugated >50%) or haemolysis (unconjugated >70%)

- Isolated elevations can rarely represent a conjugated hyperbilirubinaemia in the absence of liver disease -

  Dubin Johnson or Rotor syndromes:

  - rare and benign
  - present with asymptomatic jaundice in 2nd decade
  - ALP and GGT are normal (vs obstruction)

How to evaluate an isolated raised ALP in an asymptomatic patient

- Isolated raised ALP levels up to ≤20% above the ULN (typically around150 IU/L) may reflect a statistical rather than a clinical finding - repeat to establish trend
- ALP elevations usually arise from either Liver or Bone (NB intestine and placenta) and may be physiological. To identify source of raised ALP, repeat fasting with GGT
- If GGT normal, bone ALP likely and suggests increased bone turnover - check serum calcium, PO4, PTH and Vitamin D
- If GGT elevated in proportion to ALP on 2 separate occasions, liver ALP likely (but note drugs) and this suggests at least partial bile duct obstruction - check AMA, Immunoglobulins and USS Liver/GB/pancreas

How to evaluate an isolated rise in GGT in an asymptomatic patient

- Limited utility as a primary liver test
- Abused as ‘proof of alcohol abuse’ – not sensitive nor specific for alcohol excess BUT a sensitive indicator of liver disease
- No clear consensus for thresholds for action
- NICE guidance on ALFTs awaited

ALFT's - take home points

- To interpret ALFT's ask 3 Q:

1. *Is liver disease present?*
2. *What is the aetiology?*
3. *What is the severity?*

- Most common cause of ALFT's in primary care is NAFLD but do not rely on LFT's to detect this
- Most patients with NAFLD will have NAFL which is non-progressive – risk stratification using ELF in primary care now recommended to identify patients with fibrosis and cirrhosis
- An isolated raised bilirubin (22- 50 umol/L) in primary care is likely to be due to Gilbert's syndrome.

Liver screen

- Hepatitis B and C serology (HBVsAg +HCV)
- AIP and Immunoglobulins (IgA, IgG, IgM)
- Glucose and lipid profile
- Ferritin
- Alpha-1-AT
- Copper/caeruloplasmin (<60 years)
- Anti-tissue transglutaminase
- U/S evaluation liver – liver, pancreas, biliary tree
- A marker or measure of liver fibrosis

Interpreting TFT's

25, F, fatigue

THYROID PROFILE			
TSH	0.02 L	mU/L	(0.35-3.50)
FT4	12	pmol/L	(8-21)

The following are true:

- TFT's may reflect subclinical hyperthyroidism
- TFT's may reflect Non-Thyroidal Illness (NTI)
- TFT's may reflect pituitary disease
- A detailed drug history including OTC supplements should be taken
- TFT's including FT3 should be rechecked in 1-2 months
- Thyroid antibodies should be requested

25, F, fatigue ,repeat TFT's 8 weeks

CHEMISTRY - Blood

THYROID PROFILE			
TSH	0.07 L	mU/L	(0.35-3.50)
FT4	15	pmol/L	(8-21)
FT3	4.6	pmol/L	(3.8-6.0)

The following are true:

- Biochemical picture is consistent with subclinical hyperthyroidism
- There is a 1 in 2 chance that these abnormalities will spontaneously normalise
- Annual progression to overt hyperthyroidism is in the order of 5-10%
- Treatment is indicated
- If not treated, long term monitoring of TFT's is required

Sub-normal TSH, 'normal' FT4

Does the patient have subclinical hyperthyroidism?

- Exclude NTI and drug effects e.g. corticosteroids/T4
- Consider pregnancy, advanced age, pituitary disease
- Repeat full TFT's including FT3
- If biochemical picture persists may have Subclinical hyperthyroidism
- Endogenous causes include GD, TA and MNG
- Major risks are AF and osteopenia.
- Patients with suggestive symptoms, local symptoms or a large goitre, or at high risk of AF or osteoporosis may require treatment - assess on individual basis.

52,F, weight gain, poor sleep

CHEMISTRY - Blood

THYROID PROFILE			
TSH	5.96 H	mU/L	(0.35-3.50)
FT4	13	pmol/L	(8-21)

The following are true

1. TFT's may reflect non-thyroidal illness (NTI)
2. TFT's may reflect subclinical hypothyroidism
3. A 9am cortisol should be performed
4. TFT's are the most likely explanation of this patient's symptoms
5. Treatment with T4 is indicated
6. TFT's should be repeated in 3-6 months
7. Thyroid antibodies should be checked and then monitored annually

52, weight gain, poor sleep, repeat TFT's 4/12

CHEMISTRY - Blood

THYROID PROFILE			
TSH	6.49 H	mU/L	(0.35-3.50)
FT4	12	pmol/L	(8-21)

Anti-Thyroid Peroxidase Antibody

Anti-Thyroid Peroxidase Antibody	252.7 H	kU/L	(0.0-34.0)

Raised TSH (5-10 mIU/L), 'normal' FT4

Does the patient have subclinical hypothyroidism?

- Exclude NTI and drug effects e.g. heparin, aspirin
- Consider possibility of adrenal insufficiency
- Repeat TFT's in 3-6 months with thyroid antibodies
- If biochemical picture persists may have SCH

1. Positive TPO - annual TFT's or earlier if symptoms
2. Negative TPO - less frequent TFT's may be justified e.g. 3 yearly unless symptomatic

- No evidence to treat patients until TSH >10 mmol/L
- Exceptions are pregnant or actively seeking fertility

32, F, NP, on T4 planning pregnancy

CHEMISTRY - Blood

THYROID PROFILE			
TSH	5.06 H	mU/L	(0.35-3.50)

- T4 dose = 125 mcg daily for the last 5 years

My next step would be…

1. Check compliance and repeat TFT's in 6 months
2. Obtain full medication history including OTC drugs and check compliance with T4
3. Check TPO antibody status
4. Increase T4 dose to 150 mcg daily
5. Increase T4 dose to 250 mcg daily
6. Refer Endocrinology
7. Seek advice from the laboratory

32, F, NP, on T4 planning pregnancy

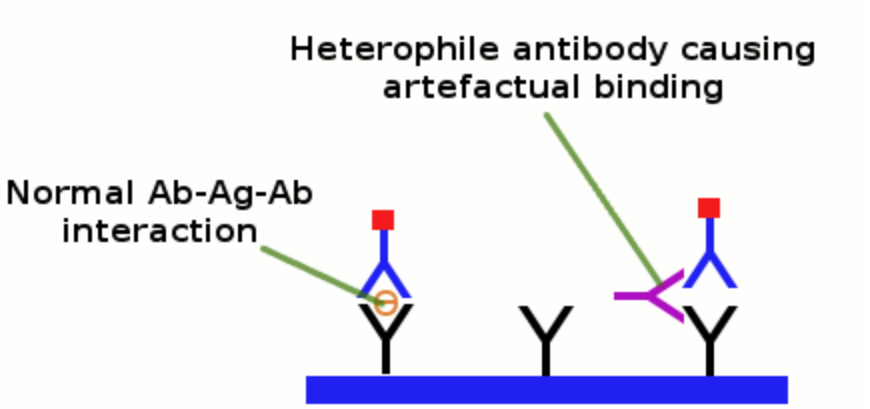
- Compliance 100%
- OTC Folic acid only
- FT4 increased to 150 mcg daily and TFT's rechecked 8/52

THYROID PROFILE			
TSH	4.96 H	mU/L	(0.35-3.50)
FT4	11	pmol/L	(8-21)

My next step would be…

1. Further repeat TFT's in 6 weeks to confirm result
2. Check TPO antibody status
3. Arrange coeliac disease screen
4. Increase T4 dose to 175 mcg daily
5. Increase T4 dose to 250 mcg daily
6. Seek advice from the laboratory
7. Refer Endocrinology

Analytical interference - immunoassay



Interpreting TFT's – take home points

- In mild (subclinical) disorders, TSH will be the most sensitive indicator of failing thyroid function, and plasma FT4 and FT3 are often normal.
- Before the diagnosis of subclinical thyroid disorders can be made, causes of an abnormal TSH other than thyroid disorders must be excluded.
- An important cause of elevated TSH is untreated adrenal insufficiency
- TPO antibody status can be useful in subclinical hypothyoidism but no need to repeat
- Think heterophilic antibody assay interference when TFT's do not make sense – discuss with laboratory

Drugs that Alter Thyroid Hormone Synthesis, Secretion and Metabolism

Decrease in TSH Secretion	Decreased Thyroid Hormone Secretion	Increased thyroid Hormone secretion	Decreased thyroidal synthesis*	Displacement of Hormone from Plasma Proteins	Impaired T4 to T3 Conversion
Dopamine Dopaminergic agents Glucocorticoids Cytokines Octreotide	Lithium Iodide Amiodarone	Iodide Amiodarone Lithium (rare)	Methimazole Carbimazole Propylthiouracil Lithium	Frusemide Fenclofenac Salicylates Mefenamic acid Carbamazepine Non-steroidal AIDs	Beta antagonists Glucocorticoids Amiodarone Propylthiouracil Iopanoic acid Radiocontrast dyes
Increase TBG, TT3, TT4	**Decrease TBG, TT3, TT4**	**Increased Hepatic Metabolism of T4**	**Impaired Absorption of Thyroxine ****	**Alter autoimmunity*****	**Modify Thyroid Hormone Action**
Oestrogens Tamoxifen Heroin Methadone Clofibrate Raloxifene	Androgens Anabolic steroids Glucocorticoids	Phenytoin Carbamazapine Barbiturates Rifampacin	Cholestyramine Cholestapol Aluminium hydroxide Ferrous sulphate Sucralfate Calcium carbonate Soy protein Proton pump inhibitors	Interleukin 1 Interferon α Interferon β TNF α	Amiodarone

*Drugs listed as causing a decrease in thyroid hormone synthesis or secretion thus leading to altered thyroid status.

** Drugs interfere with thyroid hormone absorption from the GI tract. Patients on thyroxine therapy should be advised to take their thyroxine at least 4 hours apart from these medications..

***Treatment with these cytokines have been associated with cases of transient hypothyroidism and thyrotoxicosis. These usualy resolve several months after treatment is stopped. The mechamism is unclear but the changes may be autoimmune

The other drugs listed are thought to produce abnormal thyroid function tests but patients maintain a euthyroid status. Amiodarone is an exception (see main text).

Thank-you


SHELF TO ONLY BE USED FOR EMPTIED BOXES TO BE RETURNED TO JPH/QEK
All urines now to be issued at the urine bench
MRSA BROTHS ONLY
SAMPLES FOR DEBAGGING AND REGRESTING
Yellow
BUCKET FOR BUFFER DO NOT PUT SAMPLES IN HERE (DO NOT REMOVE)

POCT testing

POCT testing pitfalls

- 54 year old SE Asian woman with recently diagnosed type 2 Diabetes Mellitus.
- Hypoglycaemic medication regime escalated over 6 months to Glicazide 160mg daily and Metformin 850mg twice daily because of a persistently raised POCT HbA1c of 69 mmol/mol (8.3%)
- Random CBG = 4.1 mmol/L

What is your next step?

Further laboratory investigations

Hb A1c	49	mmol/mol	(IFCC)

Results from large clinical trials suggest a target HbA1c close to 53 mmol/mol is clinically valuable in people with Type 1 and Type 2 diabetes under 75 years old

Glycaemic targets should take into account the individual's age, clinical condition, and hypoglycaemia risk

HAEMATOLOGY

Hb	: 117 L
Wbc	: 4.5
Rbc	: 4.86 H
Hct	: 0.363
MCV	: 75 L
MCH	: 24.1 L
Platelets	: 235
Neutrophils	: 0.96 L
Lymphocytes	: 2.89
Monocytes	: 0.43
Eosinophils	: 0.17
Basophils	: 0.05

Haemoglobinopathy Studies

Haemoglobin F	0.9	%	(0.7 - 1.3)
Haemoglobin E	22.1	%	
Peaks identified	AE		

Conclusion: Results consistent with Hb E carrier.
Hb E may be associated with microcytic hypochromic red cell indices.
Co-existing alpha thalassaemia trait cannot be excluded.
Results valid if not transfused within the last four months.

KNOW YOUR INSTRUMENTS!!

MHRA 2013 POCT TESTING 'TOP 10 TIPS'

1. **Involve your local hospital laboratory**
2. **Management:** Many people will be involved in the creation, implementation and management of POCT service. It is vital that an appropriate POCT co-ordinator is identified and a POCT committee established.
3. **Health and Safety**: Be aware of the potential health hazards associated with the handling and disposal of body fluids, sharps and waste reagents outside of a laboratory setting
4. **Training**: Training must be provided for staff who use POCT devices. Only staff whose training and competence has been established and recorded should be permitted to carry out POCT.

5. Always read instructions…and be particularly aware of situations when the device should NOT be used

6. Standard Operating Protocols (SOPs) - SOPs must include the manufacturer's instructions for use

7. Assuring Quality- The analyses of quality control (QC) material can provide assurance that the system is working properly

8. Results - Results should be reviewed by appropriately qualified staff, with particular reference to the patient's history

9. Record keeping- Is essential and must include patient results, test strip lot number and operator identity

10. Maintenance - In order that devices continue to perform accurately they must be maintained according to the manufacturer's guidance.

Classification and referral for specialist assessment

Classification and referral for specialist assessment

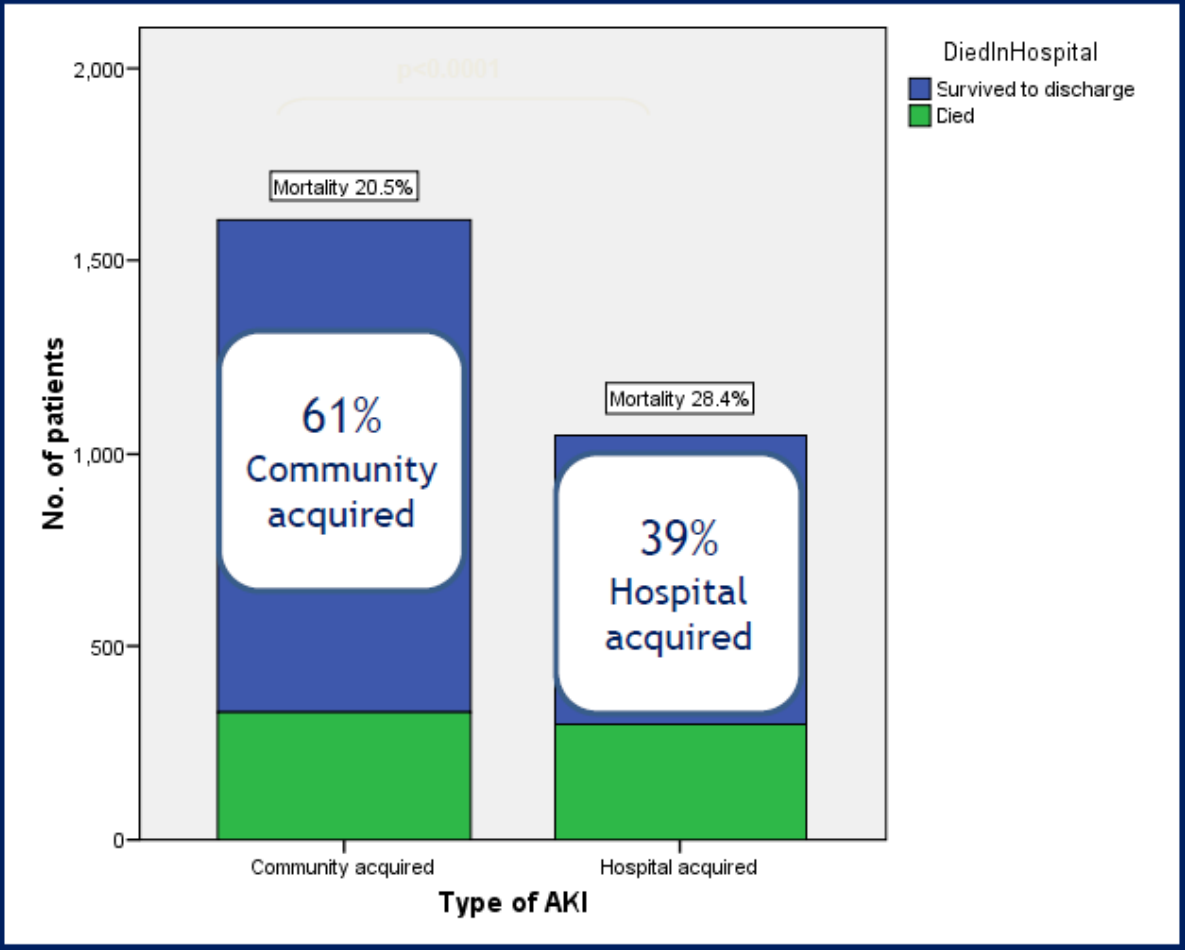
Algorithm B

GFR categories (ml/min/1.73m^2) Description and range				ACR categories (mg/mmol) Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<3	3–30	>30
	G1	Normal and high	≥90	No CKD in the absence of markers of kidney damage	Manage in primary care according to recommendations (see algorithm C) Refer for specialist assessment if the person has: - a sustained decrease in GFR of 25% or more and a change in GFR category or sustained decrease in GFR of 15 ml/min/1.73 m^2 or more within 12 months - hypertension that remains poorly controlled despite the use of at least 4 antihypertensive drugs at therapeutic doses (see also 'Hypertension' NICE clinical guideline 127) - known or suspected rare or genetic causes of CKD - suspected renal artery stenosis	Refer for specialist assessment if the person has any of the criteria in A2, or: - ACR 70 mg/mmol or more, unless known to be caused by diabetes and already appropriately treated - haematuria
	G2	Mild reduction related to normal range for a young adult	60–89			
	G3a	Mild–moderate reduction	45–59			
	G3b	Moderate–severe reduction	30–44			
	G4	Severe reduction	15–29	Refer for specialist assessment		
	G5	Kidney failure	<15			

For guidance on frequency of GFR monitoring, see recommendation 1.3.2 in the NICE guideline. For guidance on referral, see also recommendations 1.5.1 to 1.5.5

Abbreviations: ACR, albumin creatinine ratio; CKD, chronic kidney disease; GFR, glomerular filtration rate.

Working with primary care: 'Community acquired' AKI accounts for two-thirds of cases



Selby NM et al CJASN 2012; 7(4): 53

Defining AKI – causes

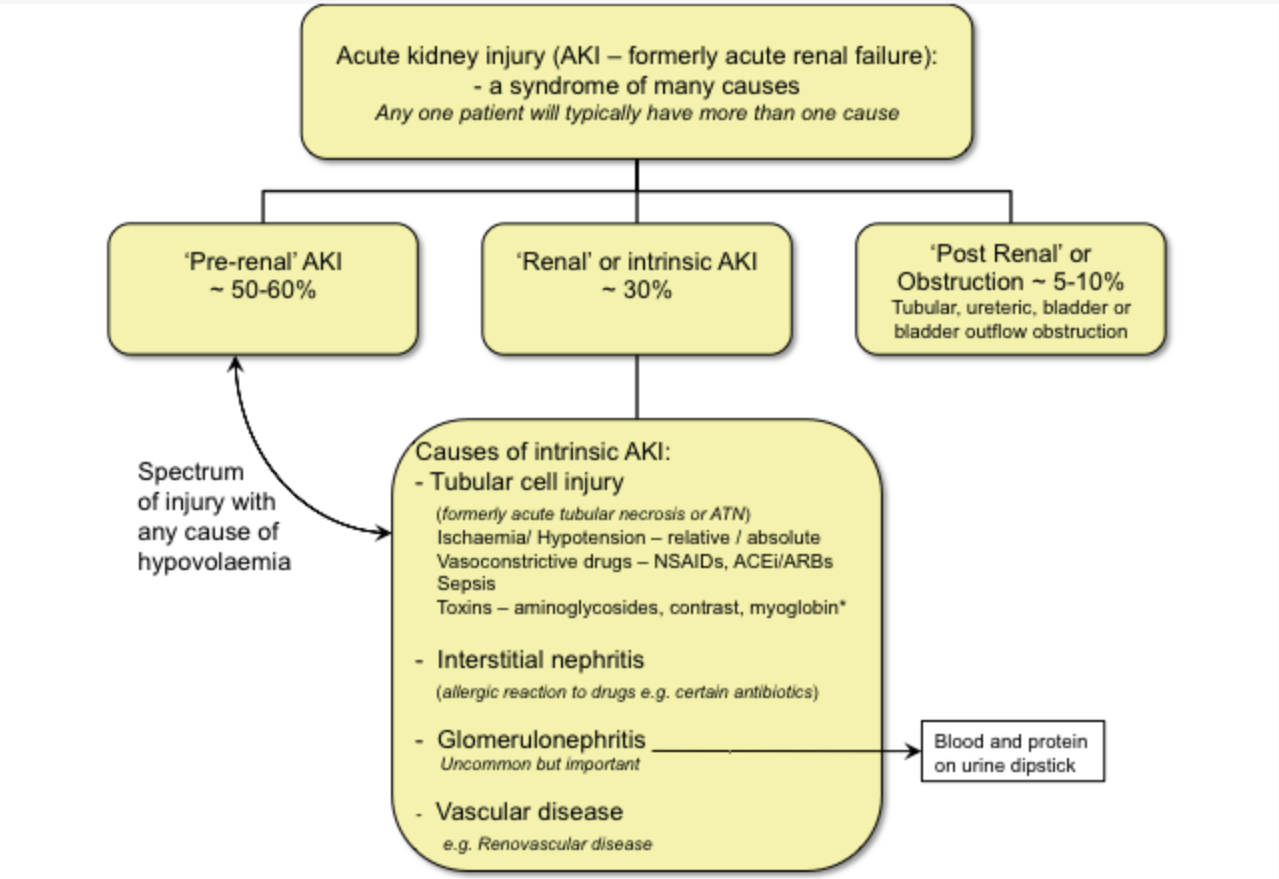


Figure 2: Causes of acute kidney injury (AKI). Note that AKI is now regarded as a spectrum of injury ranging from minimal to devastating.
NSAIDs - Non steroidal anti-inflammatory drugs; ACEi – Angiotensin converting enzyme inhibitors; ARB – Angiotensin receptor blockers; * Rhabdomyolysis

Advice / measures to prevent further episodes of AKI. Consider…

- AKI sick day rules
- Avoid long term prescription of NSAIDs where possible – especially in CKD and high risk patients
- Care with high risk combinations: ACE-i/A2RBs & NSAIDs
- Monitoring renal function after introducing certain meds, esp in high risk pts e.g. ACE-i/A2RBs, diuretics (esp. spironolactone)
- AKI care planning

'THINK KIDNEYS'

The NHS campaign to improve the care of people at risk of, or with, acute kidney injury
www.thinkkidneys.nhs.uk

Version 6: 8 July 2015

"Sick day rules" in patients at risk of Acute Kidney Injury: an Interim Position Statement from the Think Kidneys Board

Griffith K, Ashley C, Blakeman T, Fluck R, Lewington A, Selby N, Tomlinson L, Tomson C.

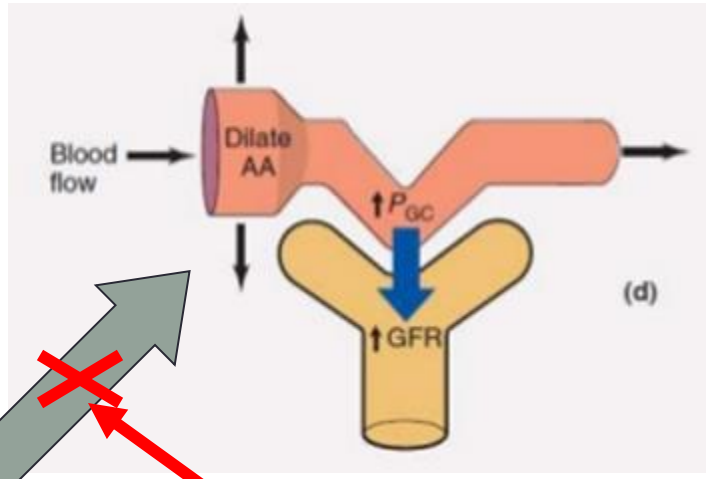
Recommended circumspection

Glomerular perfusion, drugs & AKI

- In response to reduced renal perfusion

e.g. sepsis, hypotension, hypovolaemia

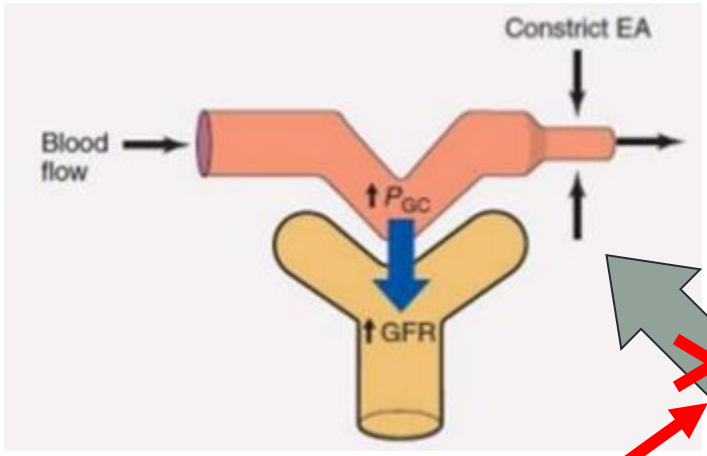
Afferent arteriolar dilation



Prostaglandin Mediated

NSAIDs

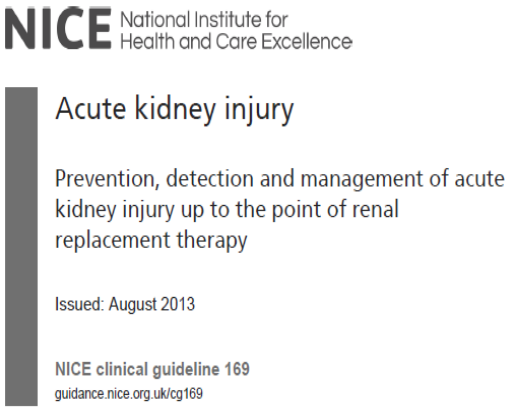
Efferent arteriolar constriction



ACEi, A2RB

Angiotensin II Mediated

Referral



- stage 3 acute kidney injury
- acute kidney injury with no clear cause
- inadequate response to treatment
- a possible diagnosis that may need specialist treatment
- (glomerulonephritis, vasculitis, interstitial nephritis, myeloma)
- complications: hyperkalaemia, fluid overload, uraemia
- prior chronic kidney disease stage 4 or 5 + added AKI (ACKD)
- a renal transplant with any AKI

Follow up after AKI: 3 things to consider

1. Has renal function recovered?

2. Review medications

3. Advice / measures to prevent further episodes of AKI

Has renal function recovered?

YES: Good!

Monitor UE's for 2-3 years even if serum creatinine has returned to baseline (& follow CKD guidelines)

NO:

- Repeat U&E in 2-4 weeks to assess for further recovery
- If still falling, keep measuring to assess new baseline
- Check U&E and ACR at **3 months** (& follow CKD guidelines)
- If significant decline in renal function, action as before (i.e. treat as further AKI)

Review medications: have medications been stopped that now need restarting?

YES:

- BP meds often stopped in AKI, usually fine to restart post discharge (if still required)
- ACE-i/A2RBs can restart once renal function stabilised – **CHECK** U&E 1 week after recommencement
- If drug implicated in AKI, update practice records to prevent further prescriptions

NO: No further action

Family history of liver disease

- Haemochromatosis
- Alpha-1-antitrypsin
- Wilson's disease
- Primary Biliary Cirrhosis
- Cystic fibrosis
- Inborn errors of metabolism e.g. LCHAD, Wolman's
- Polycystic kidney or liver disease

Risk of blood borne viruses

- Previous blood transfusion before 1991
- Some specific groups at particular risk e.g. haemophiliacs
- Injecting drug users (including those who may have ‘experimented’ even once in their youth or in the distant past!)
- People exposed to emergency treatment or trauma in Asia or Africa
- Sexual partners of infected individuals
- Immigrants or ethnic groups where Hepatitis B or C is common
- **Healthcare workers especially but not exclusively with a history of needlestick or other exposure**