Birmingham Children's Hospital NHS
NHS Foundation Trust

AKI: more than NICE

David V Milford

World Kidney Day

14 March 2013

Kidneys for Life: Stop Acute Kidney Injury

www.worldkidneyday.org


International Society of Nephrology (ISN) Gateway - The ISN Website - Windows Internet Explorer provided by Birmingham Children
http://www.theisn.org/itemid-666
Bing
Favorites
Web Slice Gallery
Health Informatics - Repo...
International Society of Nephrology (ISN) Gatewa...
Page
Safety
Tools
International Society of Nephrology
Advancing Nephrology Around the World
Select Language
ISN Member Login
search...
Follow Us:
Home
About ISN
Membership
News
Programs
Regions
Topics
Initiatives
Publications
Education
Events
0by25
Zero preventable deaths from AKI by 2025
Register now for the Global Snapshot on AKI
0by25 is endorsed by:
Advancing Nephrology Around the World
Click image to see more
1 2 3 4 5 6 7 8
KI
ISN
ISN Programs
Kidney International
News
Blog
Corporate Members
Join the Nephrology 2015 course in Boston
in Events
Friday, 03 October 2014
Internet | Protected Mode: Off
100%
20:16
05/10/2014

AKI is recognised by…

- inability to maintain homeostasis or aspects of renal function:

  fluid balance

  Na+/K+

  acid-base

- How does it manifest - Acute v Chronic

- In critical illness usually acute or acute on chronic

Acute Kidney Injury

- Pre-renal - normal tubular and glomerular function; GFR is depressed by compromised renal perfusion (potentially reversible/transient).
- Intrinsic - diseases of the glomerulus or tubule; secondary to ischaemia or toxic agents/drugs (may be treatable)
- Post(obstructive) - increase in tubular pressure decreases filtration driving force (potentially reversible/transient).
- Acute on chronic – acute decline in function superimposed on pre-existing CKD, may or may not be reversible

Consequences of AKI

- Increased morbidity
- Increased mortality
- Increased cost of health care
- Increased patient/family stress
- Risk of CKD

NCEPOD report published in 2009 (excluding children)

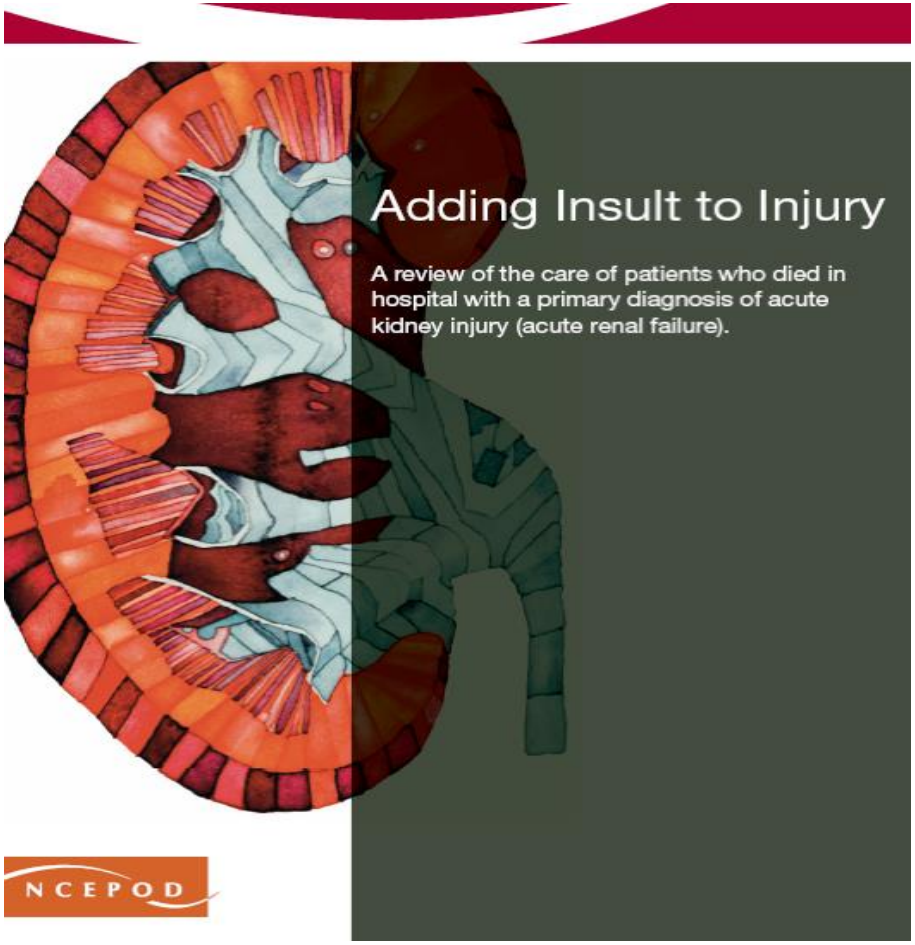
Poor assessment of risk for AKI in acute illness

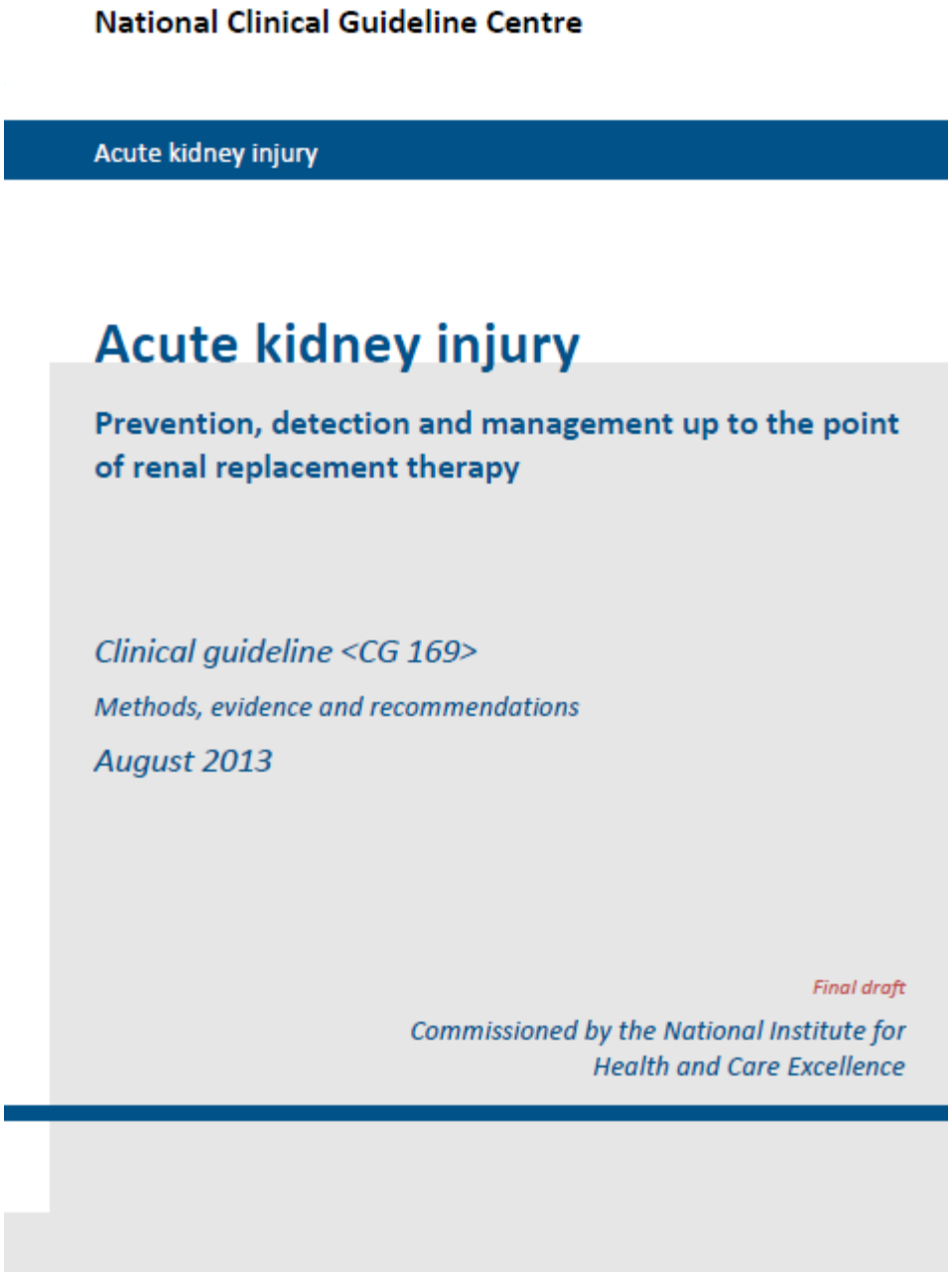
Delays in recognising AKI

Most patients with AKI are not cared for by nephrologists

Post admission AKI avoidable in 21%

‘Good’ care in <50% cases





52 Recommendations

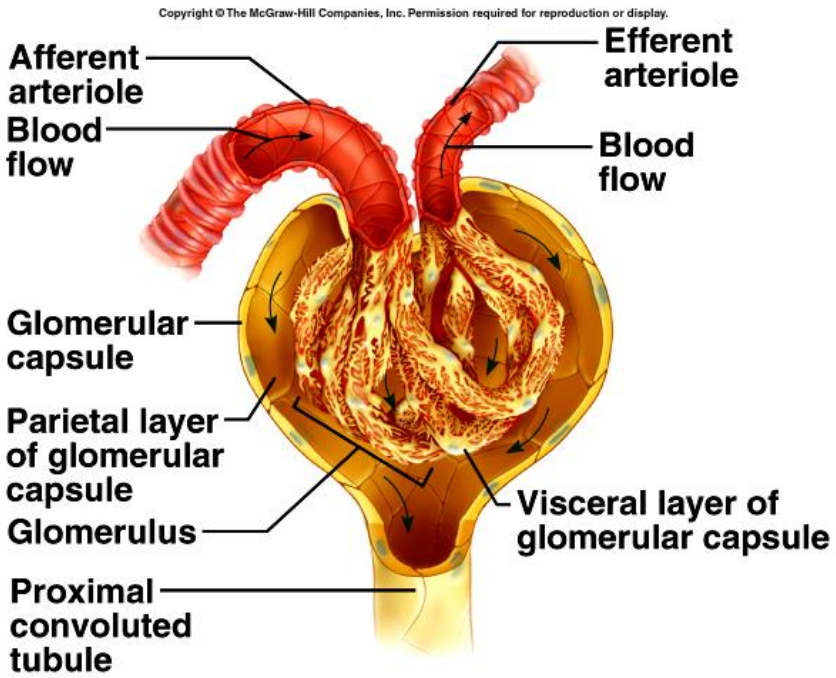
- 11 adult specific
- 6 paediatric specific
- 35 adult/paediatric

AKI not ARF: a spectrum of severity

Stage	RIFLE/pRIFLE criteria	AKIN criteria	KDIGO criteria	Urine output[d]
Risk or stage 1	eGFR decrease by ≥ 25% or 50 - 99% Cr rise from baseline within 7 days[g] (1.50-1.99 × baseline)	Rise of ≥ 26 µmol/L[e] within 48h or 50 - 99% Cr rise from baseline within 7 days[g] (1.50-1.99 × baseline)	Rise of ≥ 26 µmol/L[e] within 48h or 50 - 99% Cr rise from baseline within 7 days[g] (1.50-1.99 × baseline)	< 0.5 ml/kg/h for more than 6h (8h for pRIFLE)[f]
Injury or stage 2	eGFR decrease by ≥ 50% or 100 - 199% Cr rise from baseline within 7 days[g] (2.00-2.99 × baseline)	100 - 199% Cr rise from baseline within 7 days[g] (2.00-2.99 × baseline)	100 - 199% Cr rise from baseline within 7 days[g] (2.00-2.99 × baseline)	< 0.5 ml/kg/h for more than 12h (16h for pRIFLE)[f]
Failure or stage 3	eGFR decrease by ≥ 75% or ≥ 200% Cr rise from baseline within 7 days[g] (≥ 3.00 × baseline)	≥ 200% Cr rise from baseline within 7 days[g] (≥ 3.00 × baseline)	≥ 200% Cr rise from baseline within 7 days[g] (≥ 3.00 × baseline)	< 0.3 ml/kg/h for 24h or anuria for 12h
	or Cr rise to ≥ 354 µmol/L[h] with acute rise of ≥ 44 µmol/L	or Cr rise to ≥ 354 µmol/L[h] with acute rise of ≥ 44 µmol/L	or Cr rise to ≥ 354 µmol/L[h] with acute rise of: ≥ 26 µmol/L within 48 h or ≥ 50% rise within 7 days	
	or (pRIFLE only) eGFR <35 ml/min/1.73m^2	or any requirement for renal replacement therapy	or any requirement for renal replacement therapy	

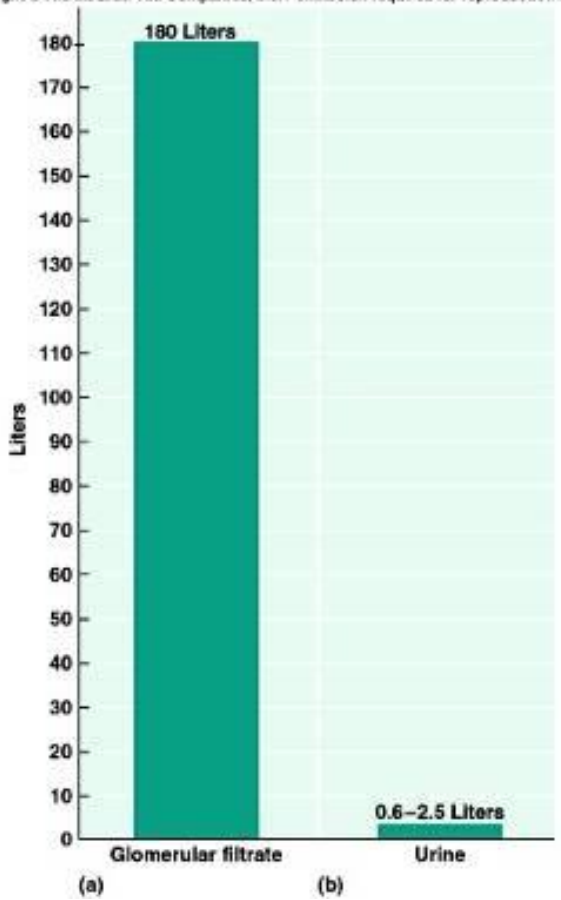
Control of Filtration Rate

- Reduced GFR
  - afferent arteriolar constriction
  - AII
  - Sympathetic nerve
  - Endothelin
- Increase GFR
  - vasodilating prostaglandins
- Autoregulation



Amounts of Glomerular Filtrate and Urine

average amounts over a 24 hour period

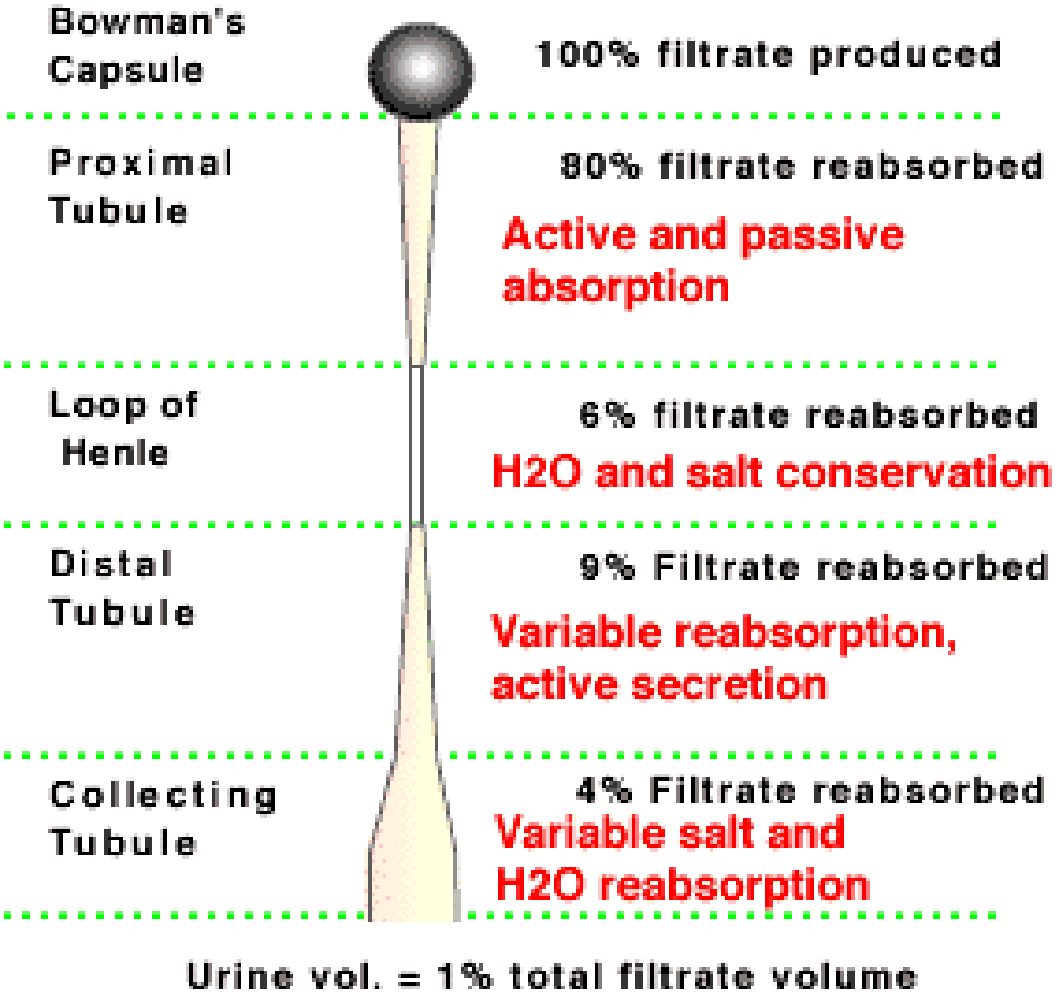


125 mls / min / 1.73 m^2

180 litres / day

= normal GFR

Summary of nephron function



requires a healthy tubule!

Pathophysiology

- kidneys account for 0.5% body weight

- renal blood flow 20-25% of cardiac output

- high oxygen consumption but high blood flow

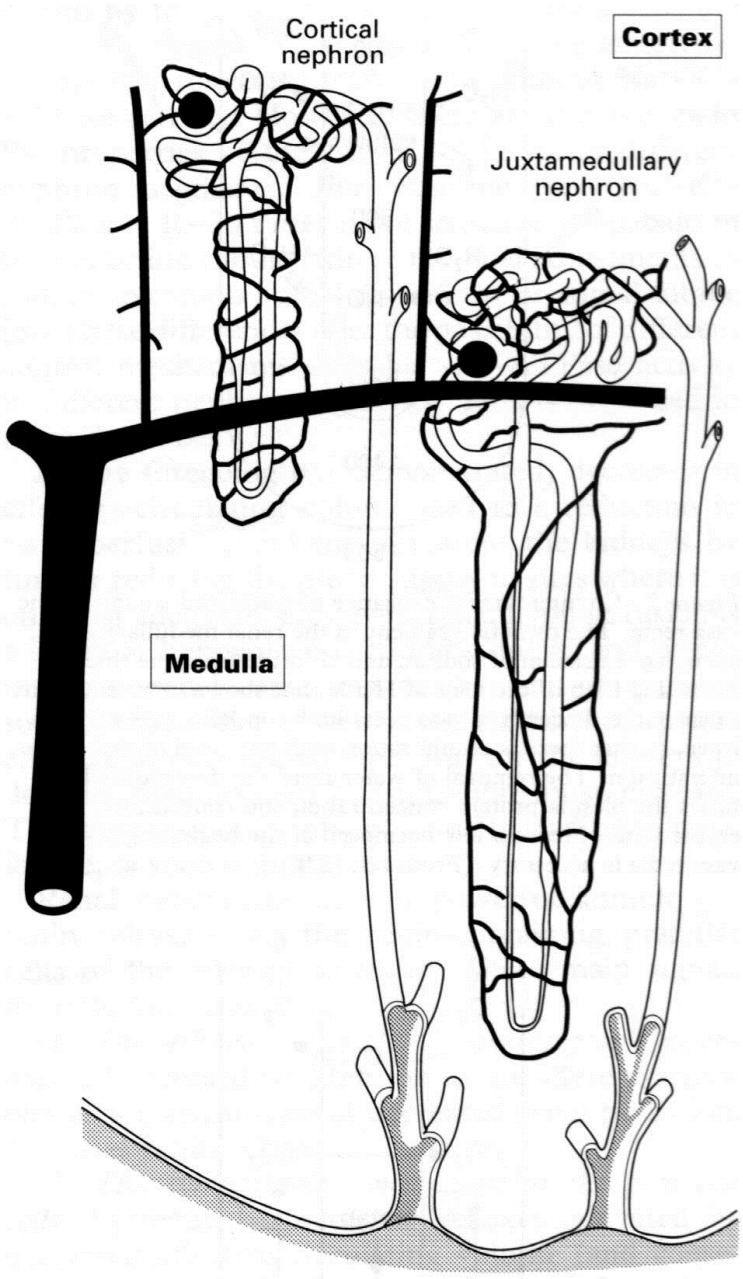
$pO_{2art} = 95$

$pO_{2vein} = 70$

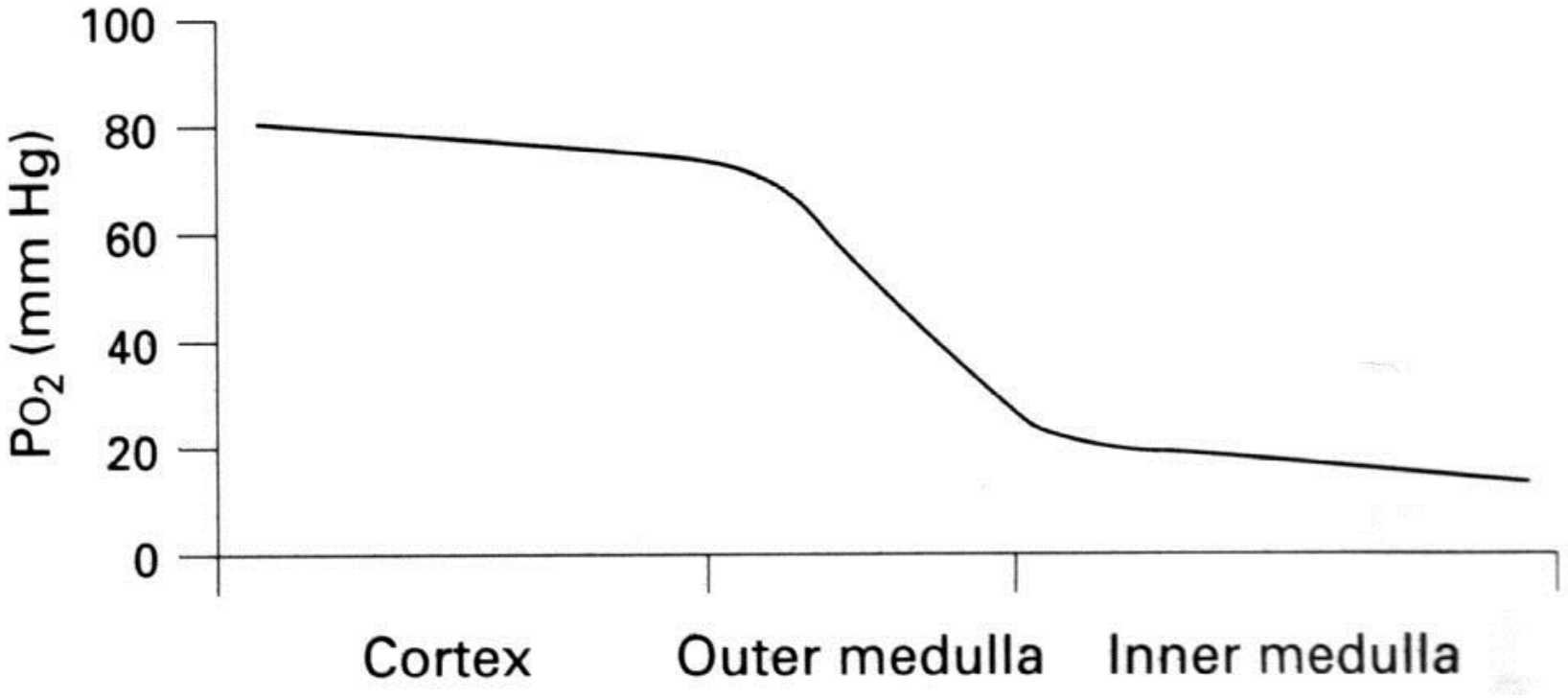
Why do the kidneys readily incur ischaemic damage in the face of an excellent blood supply?

Oxygen delivery

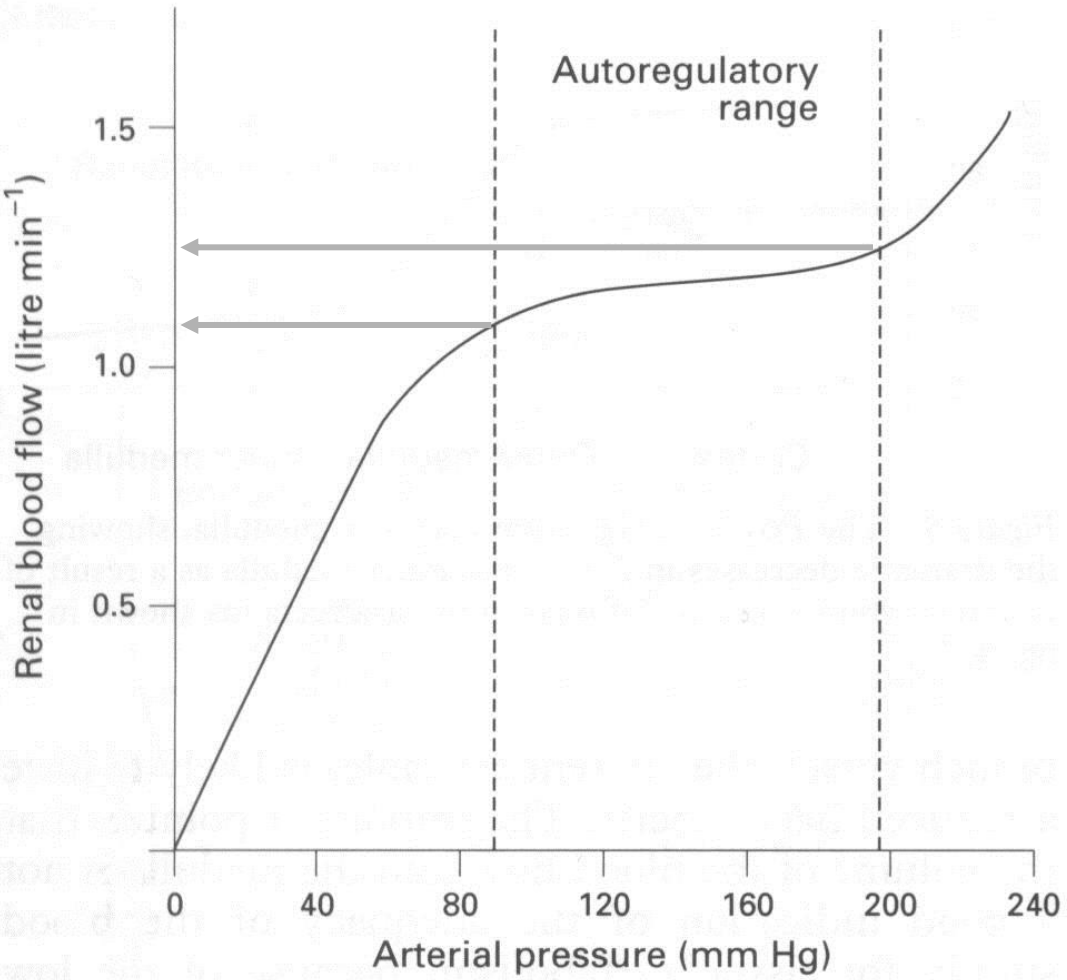
- plasma skimming ensures low haematocrit (10%) in vasa recta
- O_2 undergoes countercurrent exchange
- consequence is low O_2 delivery to medulla



Oxygen delivery - pO_2 from cortex to medulla



Renal autoregulation



Acute renal *success*..

severe hypovolaemia/
toxic insult

→ ATN

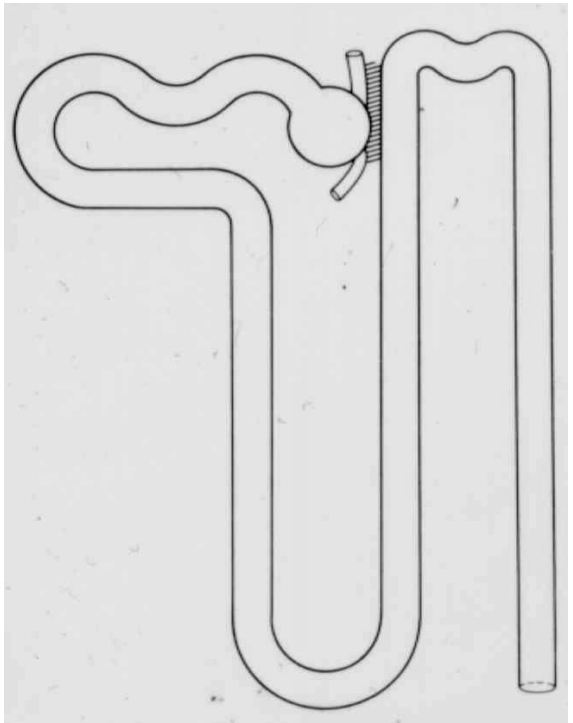
→ tubulo-glomerular feedback

→ arteriolar vasoconstriction

→ ↓GFR

→ RECOVERY

up to 6 weeks



Acute renal *success*..

severe hypovolaemia/
toxic insult

→ ATN

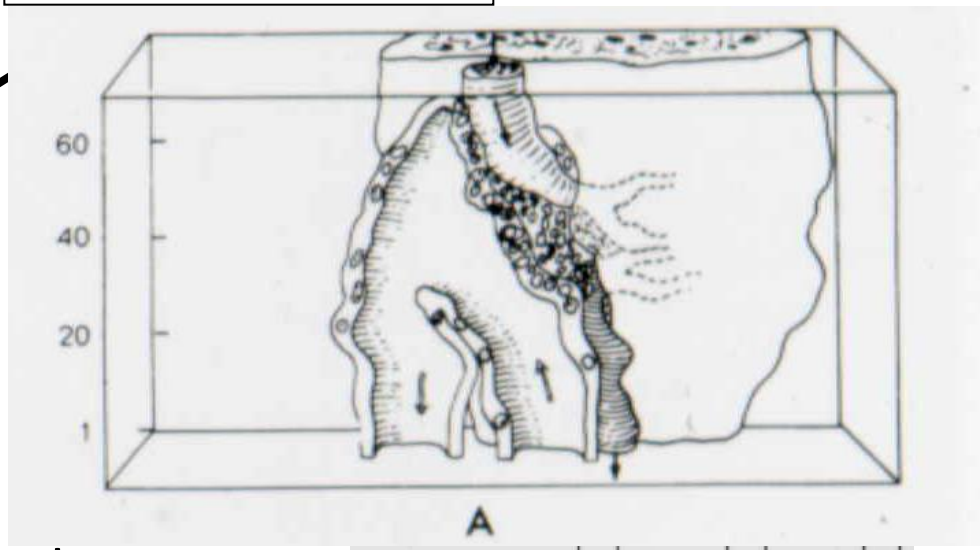
→ tubulo-glomerular feedback

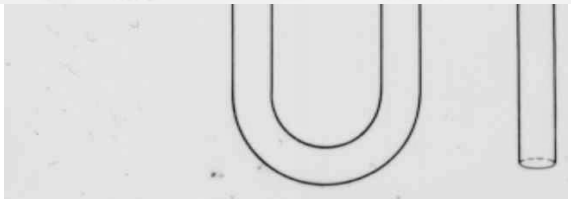
→ arteriolar vasoconstriction

→ ↓GFR

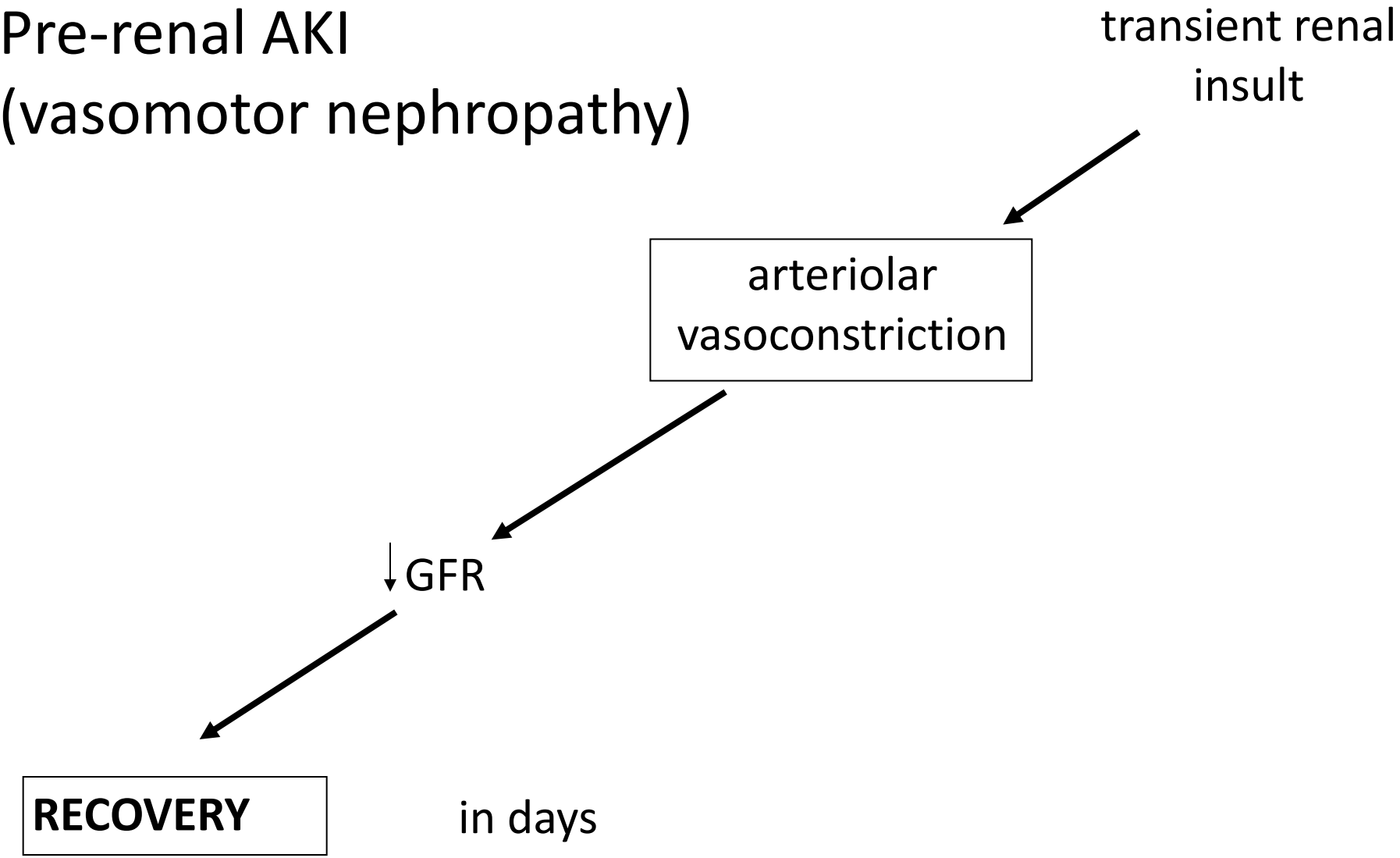
→ RECOVERY

up to 6 weeks

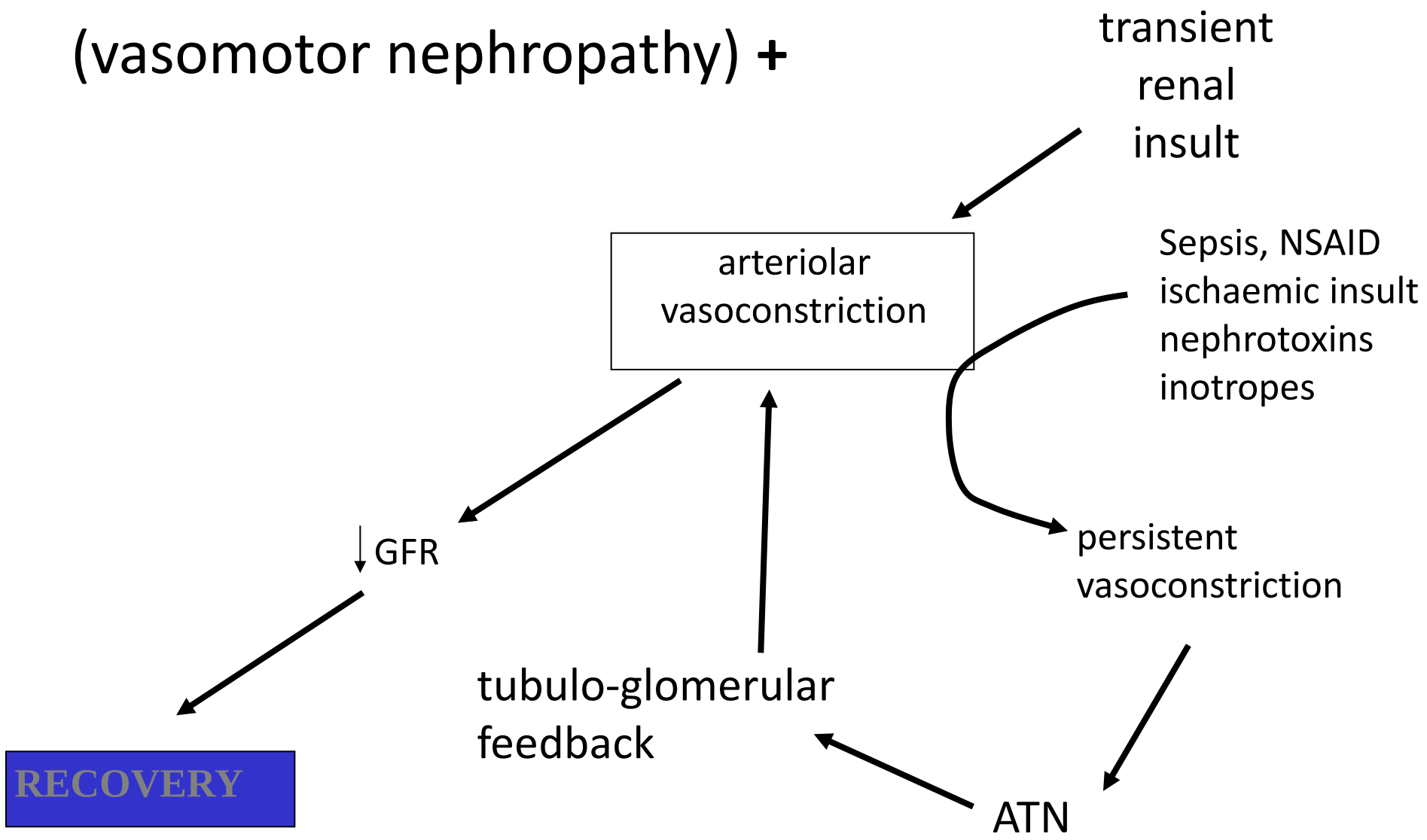




Pre-renal AKI (vasomotor nephropathy)



Pre-renal AKI (vasomotor nephropathy) +



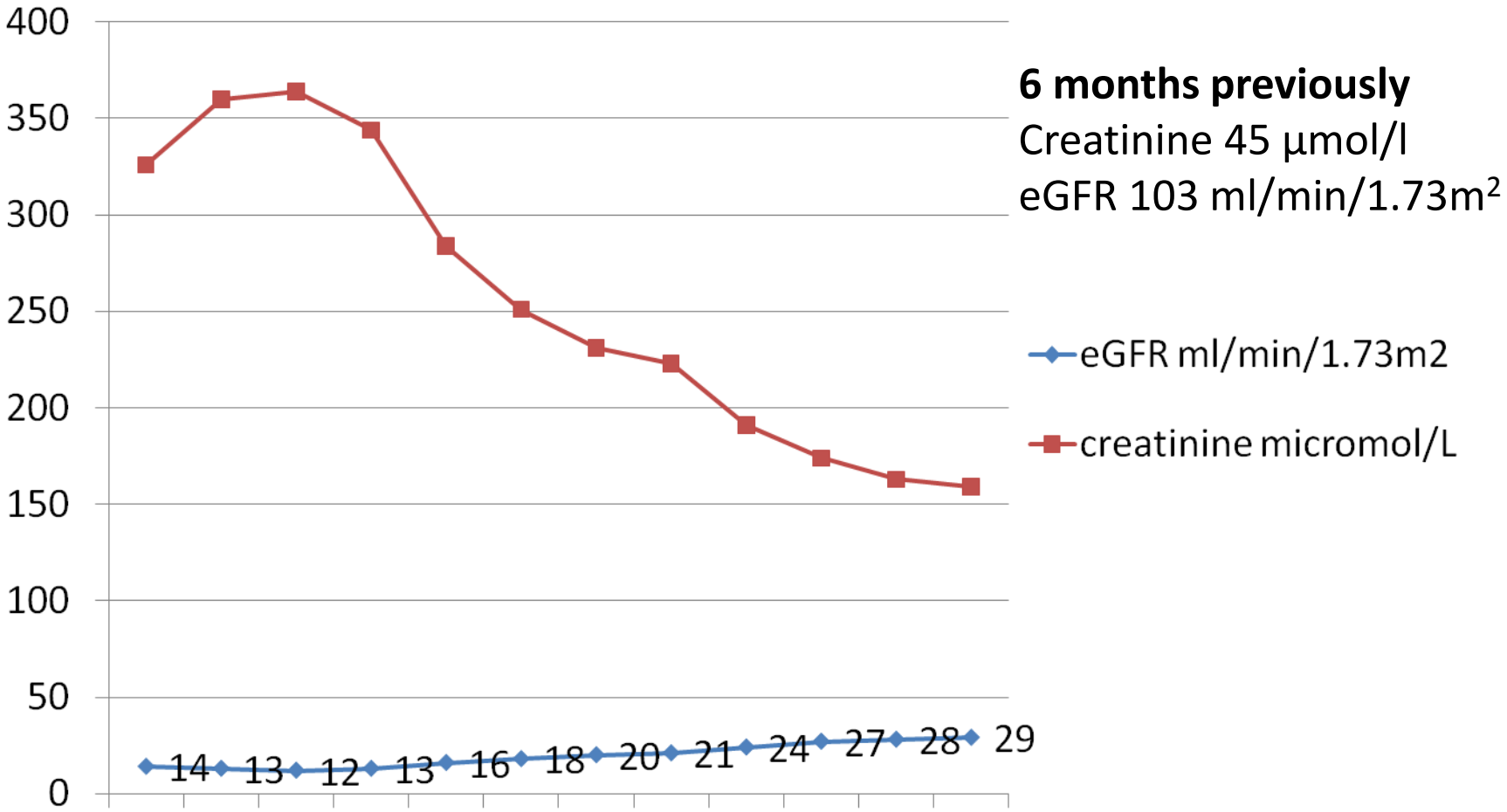
Case 15 yr old male

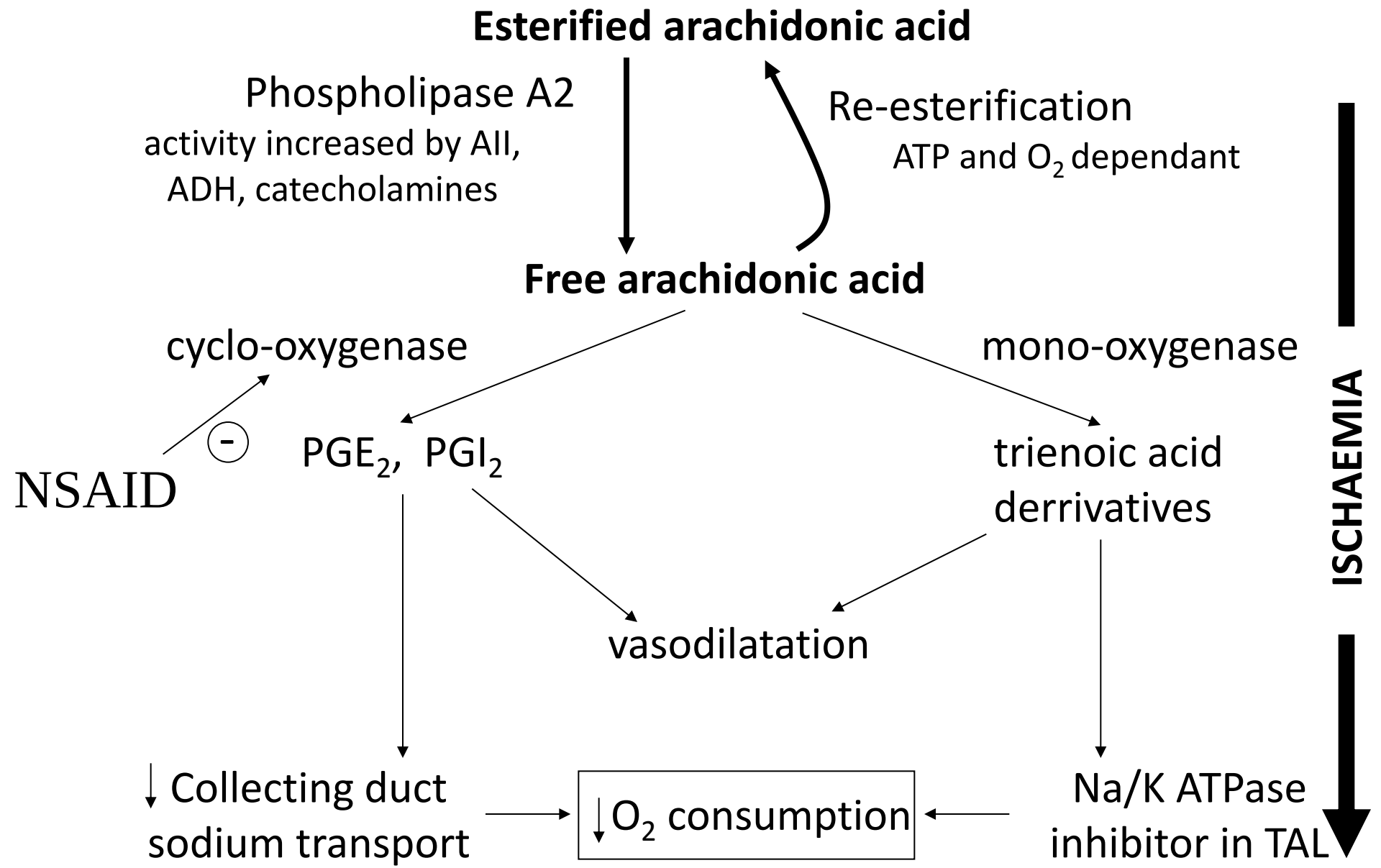
- Attends ED 3 day h/o abdominal pain & loose stools
- **PEWS = 4 (no BP measured initially)**
  - Weight 47 Kg (51.1 kg 4 weeks before)
- at triage given
  - paracetamol 700 mg
  - ibuprofen 400mg
- Urine
  - brown/red in colour, SG 1.03, bld/prot +

Progress …….

- **Examination:**
  - poor volume peripheral pulses, cool peripheries, sunken eyes, RIF pain
  - BP 100/60 PEWS = 5 orange
- **Impression:**
  - unwell, dehydrated ?appendicitis +/- perforation
- **Plan :**
  - IV access and bloods,
  - 1000ml fluid bolus, reviewed by ED consultant

AKI progression over 2 weeks following admission

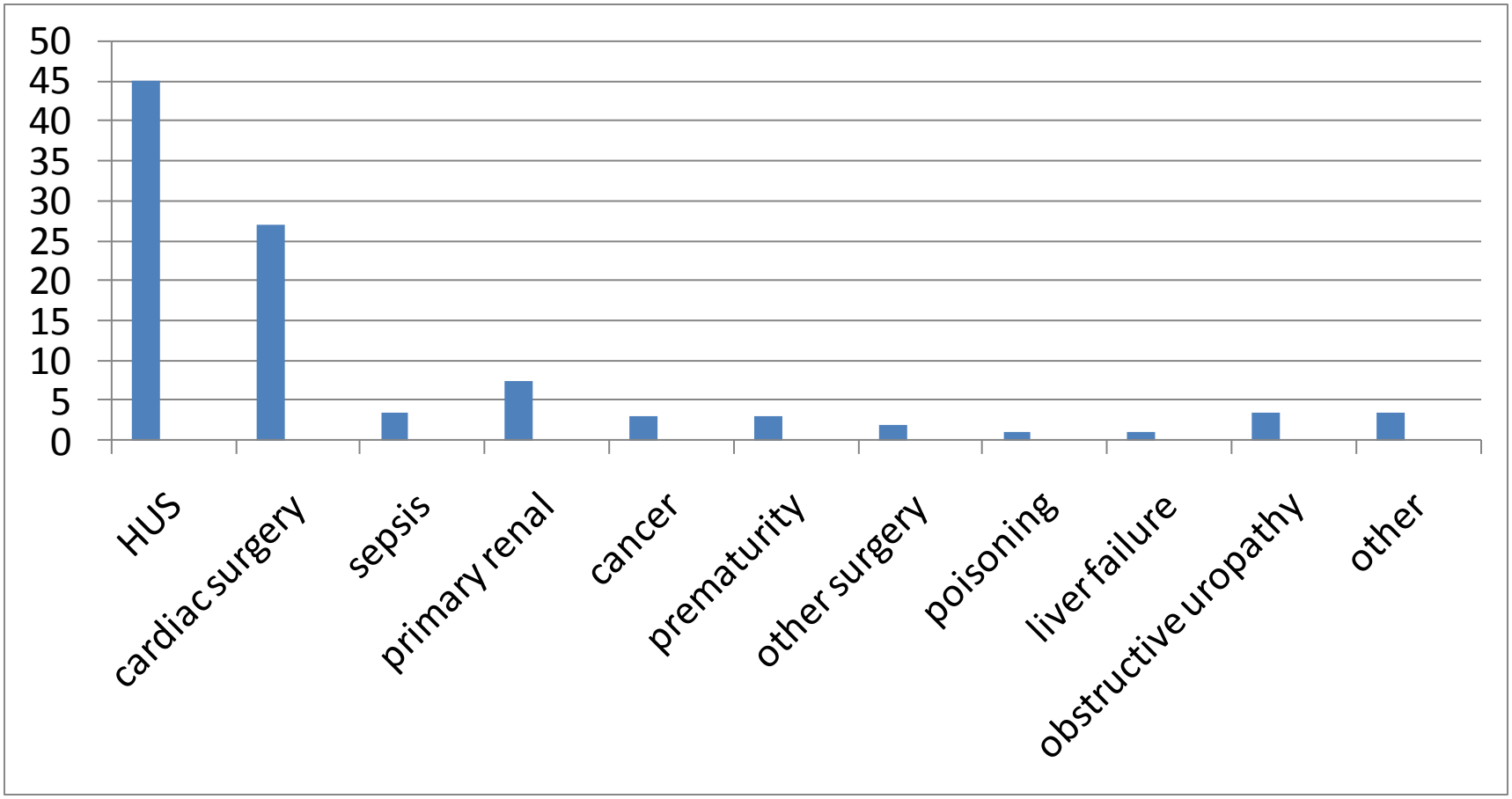



Esterified arachidonic acid
Phospholipase A2
activity increased by AII,
ADH, catecholamines
Re-esterification
ATP and O_2 dependant
Free arachidonic acid
cyclo-oxygenase
mono-oxygenase
NSAID
PGE2, PGI2
trienoic acid
derrivatives
vasodilatation
↓ Collecting duct
sodium transport
↓O_2 consumption
Na/K ATPase
inhibitor in TAL
ISCHAEMIA

Is it AKI or CKD?

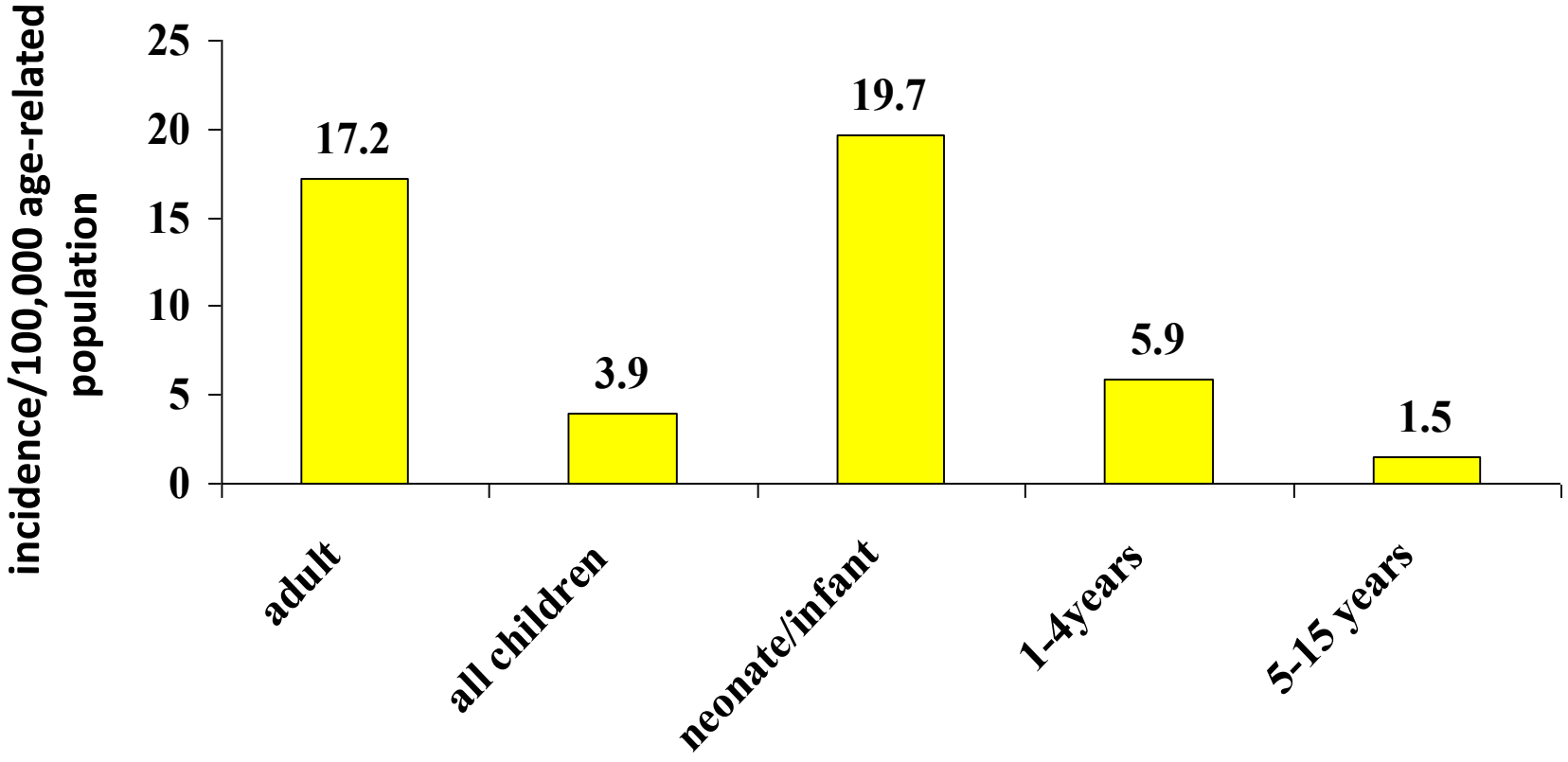
- Best discriminant renal USS
  - CKD: small kidneys, scarred kidneys, cysts, calculi
  - AKI: big, bright kidneys
  - Dilated urinary tract: CKD or AKI
- Blood results
  - anaemia: CKD, unless HUS
  - high phosphate: CKD
  - high PTH: CKD

All causes of AKI 3 (%)



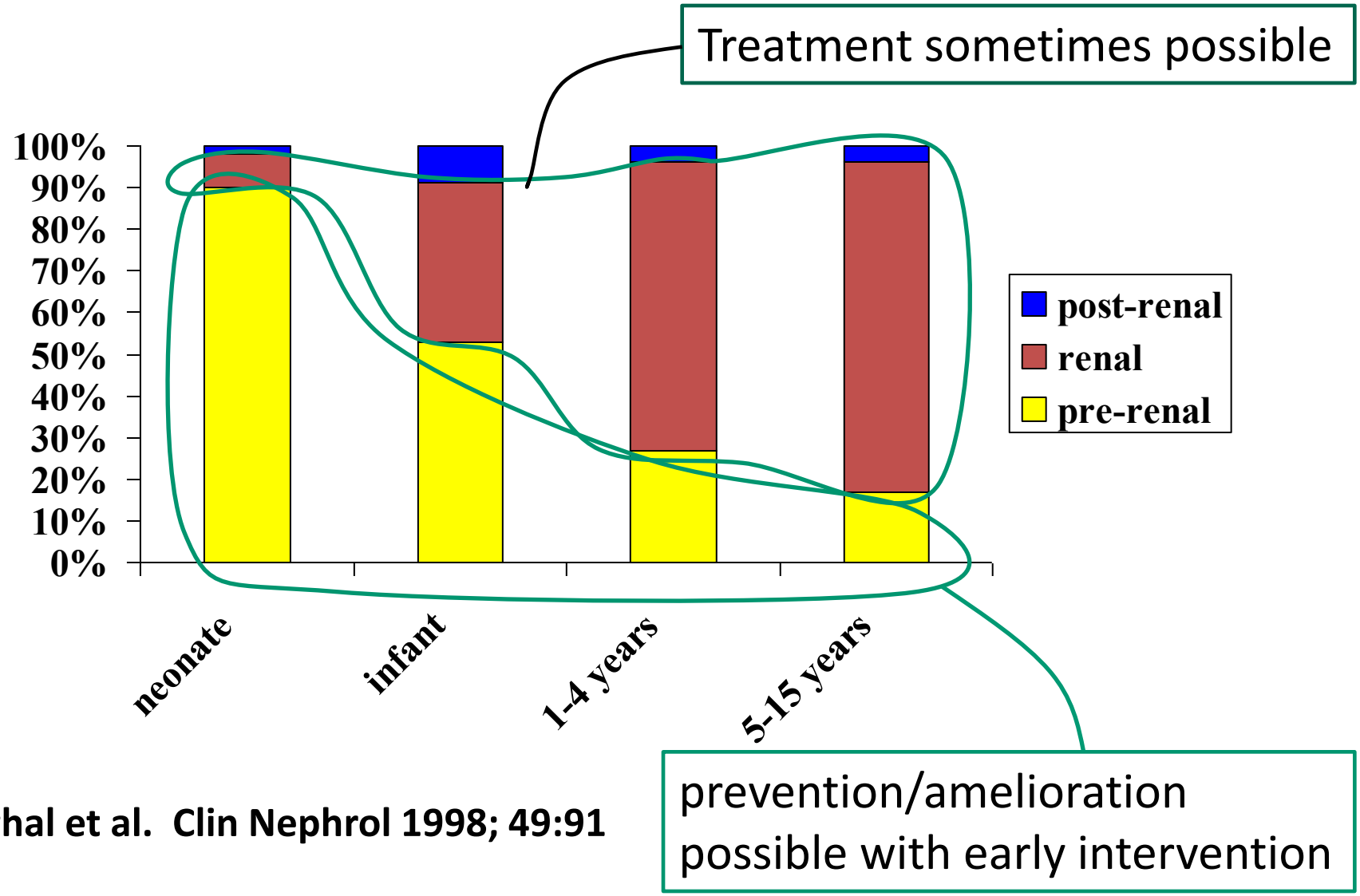
Moghal et al. Clin Nephrol 1998; 49:91

Effect of age on incidence of AKI 3



Moghal et al. Clin Nephrol 1998; 49:91

Aetiology of AKI 3 in children by age



Moghal et al. Clin Nephrol 1998; 49:91

NICE guidance

1. Assessing risk of AKI

- CKD, heart failure, liver disease
- Previous AKI
- Oliguria (<0.5 ml/kg/hr)
- Neuro/developmental delay
- Hypovolaemia, hypotension
- Nephrotoxic drugs
- Urological obstruction
- Sepsis
- Deteriorating PEWS
- Severe diarrhoea/bloody diarrhoea
- Symptoms/signs of nephritis
- Haematological malignancy

Measure PCr and compare with baseline in acutely ill children

2. Detecting AKI

- Measure serum creatinine regularly in those with or at risk of AKI

3. Identify cause

- Identify cause of AKI and record in notes
- If no cause/risk of obstruction, undertake renal USS in less than 24 hours

4. Managing AKI

discuss with a paediatric nephrologist when:

- Possible diagnosis requiring specialist investigation/management eg vasculitis
- AKI with no clear cause
- When there is inadequate response to treatment
- Complications associated with AKI
- Stage 3 AKI (AKIN, pRIFLE,KDIGO)
- In a patient with a renal transplant
- In a patient with CKD 4 or 5

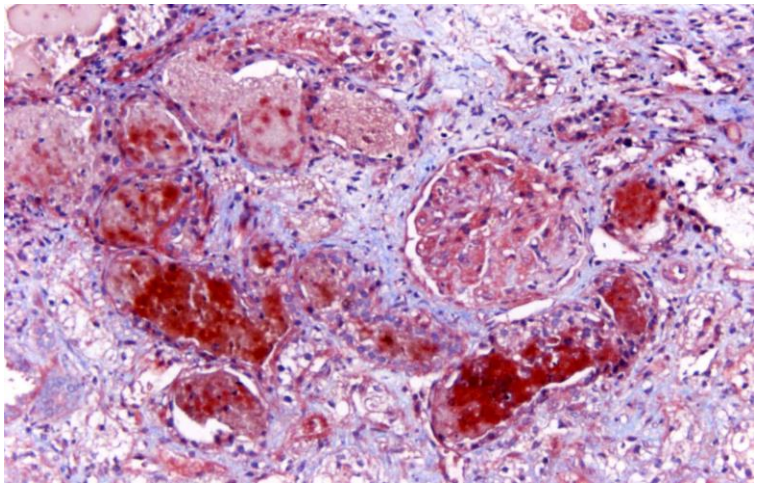
What also worries me…. (see NICE recommendation 45)

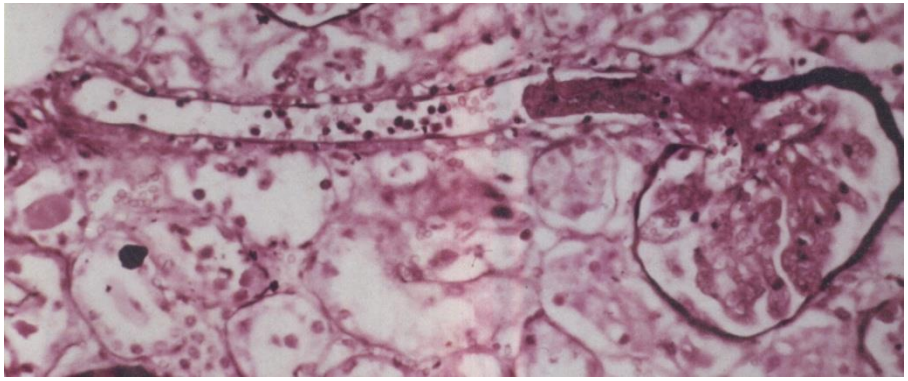
- Any stage of AKI +
  - hypertension
  - nephritic/nephrotic
  - other system involvement (esp lungs, skin, brain)

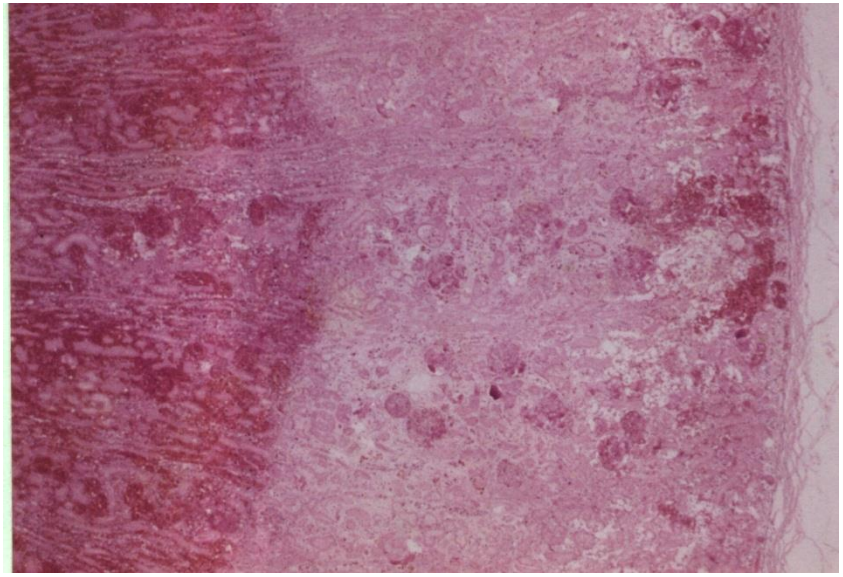
Prevention/amelioration of AKI

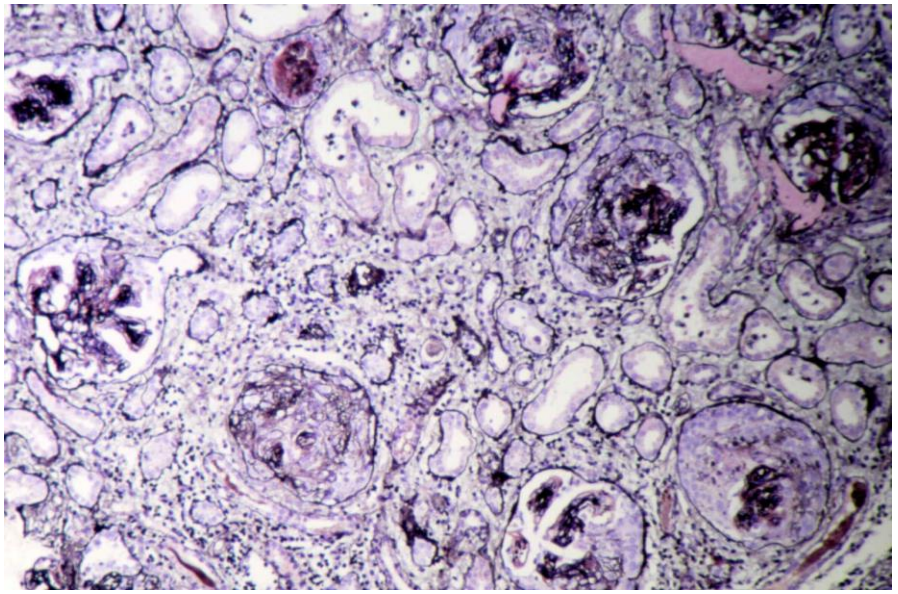
- Careful physiological monitoring of at risk patients
  - use PEWS to identify deterioration early
  - measure and record urine output
- Maintain/normalize
  - blood pressure, $SaO_{2,}$ glucose, lactate
- Accurate fluid balance, attention to nutrition
- Treat sepsis promptly and effectively
- Avoid NSAID, ACEi, ARB
- Avoid/minimise nephrotoxic drugs, inotropes

It’s not possible when…..









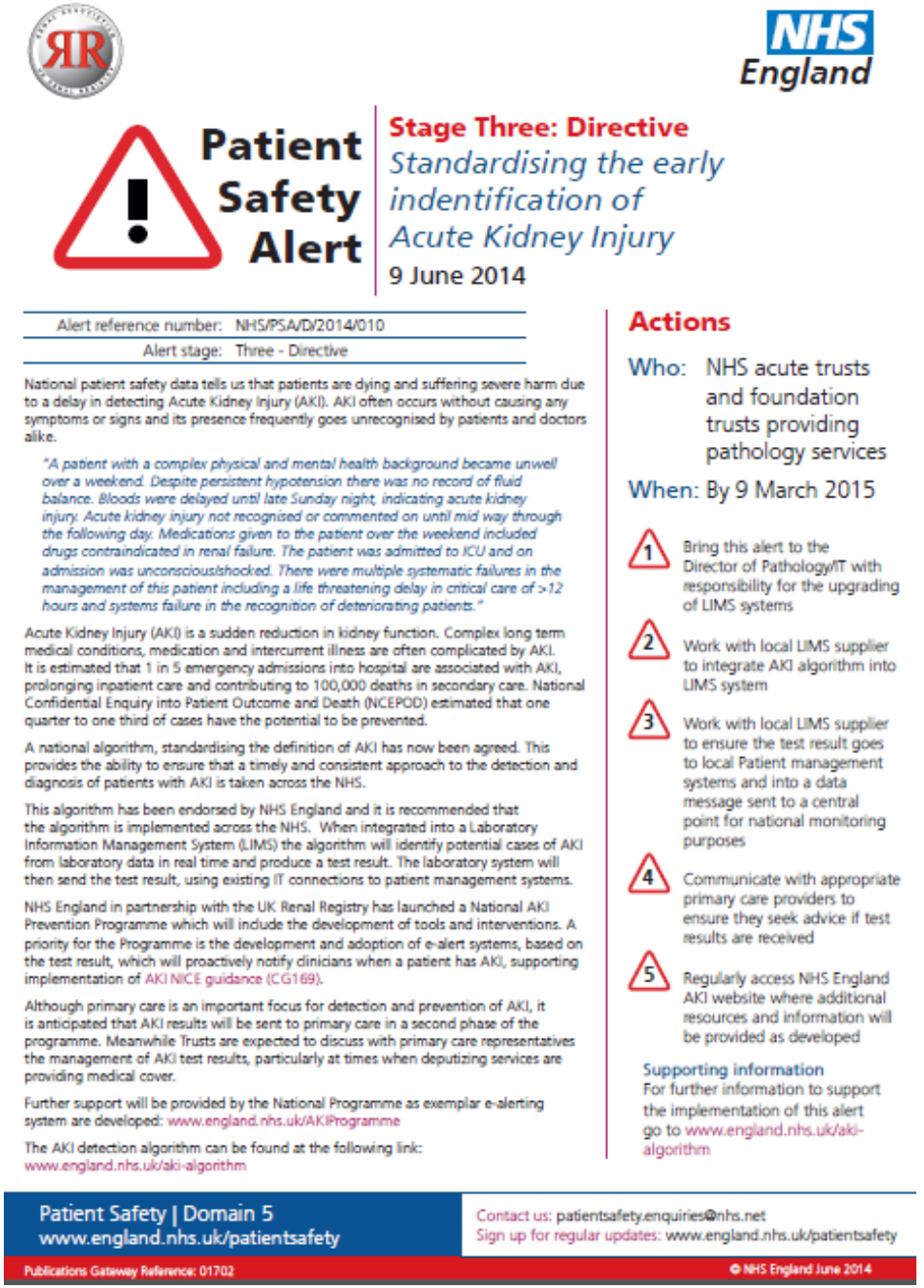
NHS England Patient Safety Steering Group

AKI National Programme Board

- **Risk**
  - Advisory Group
- **Education**
- **Detection**
  - Algorithm Sub-Group
  - Software **Implementation Sub-Group**
  - Best Practice in E-alert Group
  - Expert Reference Group
- **Intervention**
- **Implementation**
- **Measurement**

Hydration Sub-Group

Detection workstream



NHS England

Patient Safety Alert

Stage Three: Directive

Standardising the early indentification of Acute Kidney Injury

9 June 2014

Alert reference number: NHS/PSA/D/2014/010

Alert stage: Three - Directive

National patient safety data tells us that patients are dying and suffering severe harm due to a delay in detecting Acute Kidney Injury (AKI). AKI often occurs without causing any symptoms or signs and its presence frequently goes unrecognised by patients and doctors alike.

> *"A patient with a complex physical and mental health background became unwell over a weekend. Despite persistent hypotension there was no record of fluid balance. Bloods were delayed until late Sunday night, indicating acute kidney injury. Acute kidney injury not recognised or commented on until mid way through the following day. Medications given to the patient over the weekend included drugs contraindicated in renal failure. The patient was admitted to ICU and on admission was unconscious/shocked. There were multiple systematic failures in the management of this patient including a life threatening delay in critical care of >12 hours and systems failure in the recognition of deteriorating patients."*

Acute Kidney Injury (AKI) is a sudden reduction in kidney function. Complex long term medical conditions, medication and intercurrent illness are often complicated by AKI. It is estimated that 1 in 5 emergency admissions into hospital are associated with AKI, prolonging inpatient care and contributing to 100,000 deaths in secondary care. National Confidential Enquiry into Patient Outcome and Death (NCEPOD) estimated that one quarter to one third of cases have the potential to be prevented.

A national algorithm, standardising the definition of AKI has now been agreed. This provides the ability to ensure that a timely and consistent approach to the detection and diagnosis of patients with AKI is taken across the NHS.

This algorithm has been endorsed by NHS England and it is recommended that the algorithm is implemented across the NHS. When integrated into a Laboratory Information Management System (LIMS) the algorithm will identify potential cases of AKI from laboratory data in real time and produce a test result. The laboratory system will then send the test result, using existing IT connections to patient management systems.

NHS England in partnership with the UK Renal Registry has launched a National AKI Prevention Programme which will include the development of tools and interventions. A priority for the Programme is the development and adoption of e-alert systems, based on the test result, which will proactively notify clinicians when a patient has AKI, supporting implementation of AKI NICE guidance (CG169).

Although primary care is an important focus for detection and prevention of AKI, it is anticipated that AKI results will be sent to primary care in a second phase of the programme. Meanwhile Trusts are expected to discuss with primary care representatives the management of AKI test results, particularly at times when deputizing services are providing medical cover.

Further support will be provided by the National Programme as exemplar e-alerting system are developed: www.england.nhs.uk/AKIProgramme

The AKI detection algorithm can be found at the following link: www.england.nhs.uk/aki-algorithm

Actions

Who: NHS acute trusts and foundation trusts providing pathology services

When: By 9 March 2015

1. Bring this alert to the Director of Pathology/IT with responsibility for the upgrading of LIMS systems
2. Work with local LIMS supplier to integrate AKI algorithm into LIMS system
3. Work with local LIMS supplier to ensure the test result goes to local Patient management systems and into a data message sent to a central point for national monitoring purposes
4. Communicate with appropriate primary care providers to ensure they seek advice if test results are received
5. Regularly access NHS England AKI website where additional resources and information will be provided as developed

Supporting information

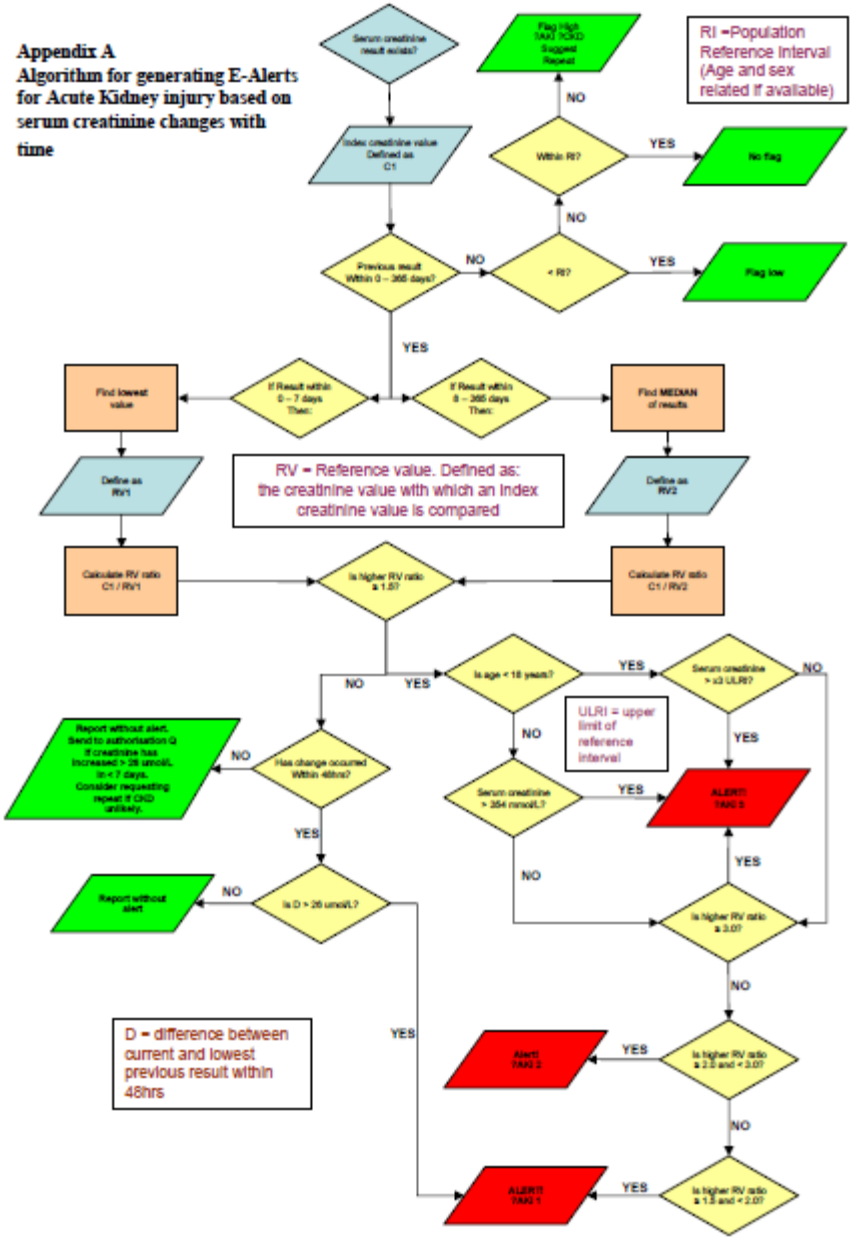
For further information to support the implementation of this alert go to www.england.nhs.uk/aki-algorithm

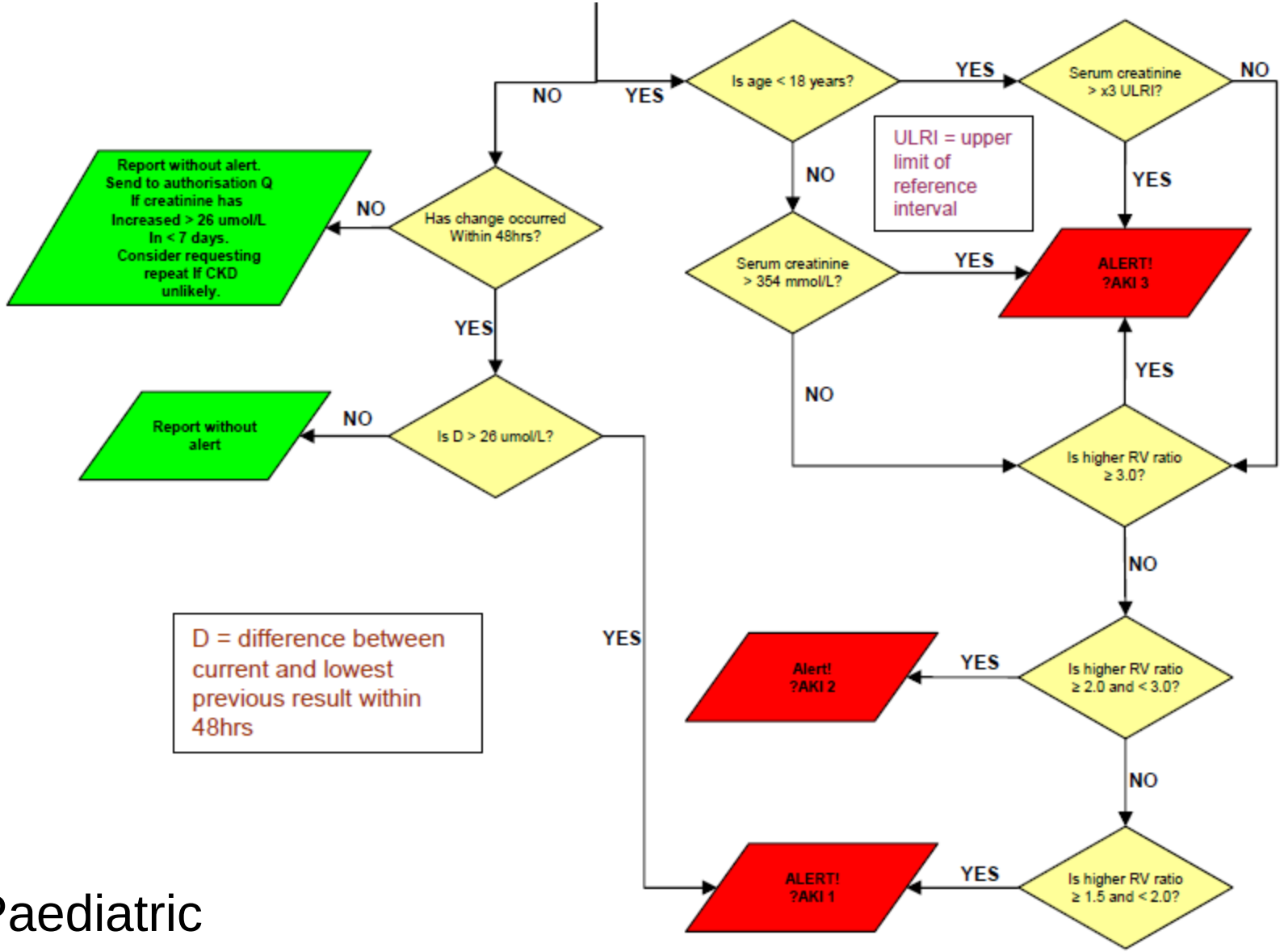
Patient Safety | Domain 5
www.england.nhs.uk/patientsafety

Contact us: patientsafety.enquiries@nhs.net
Sign up for regular updates: www.england.nhs.uk/patientsafety

Publications Gateway Reference: 01702

Appendix A
Algorithm for generating E-Alerts for Acute Kidney injury based on serum creatinine changes with time

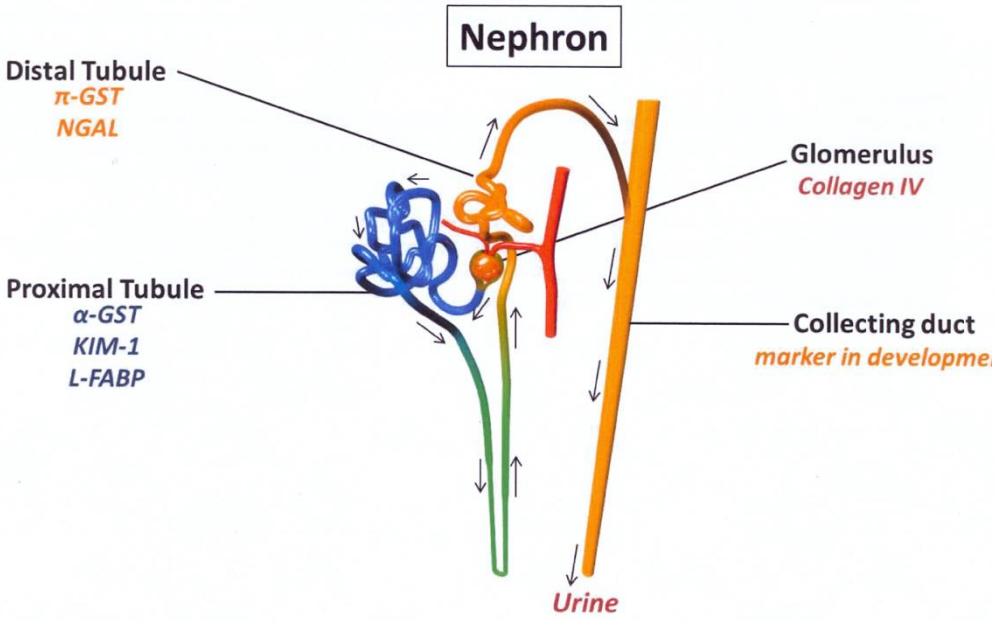


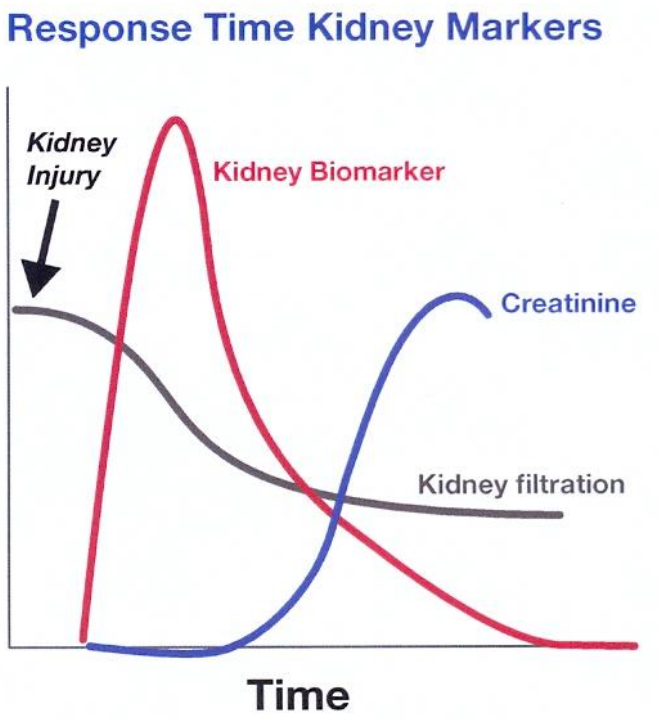


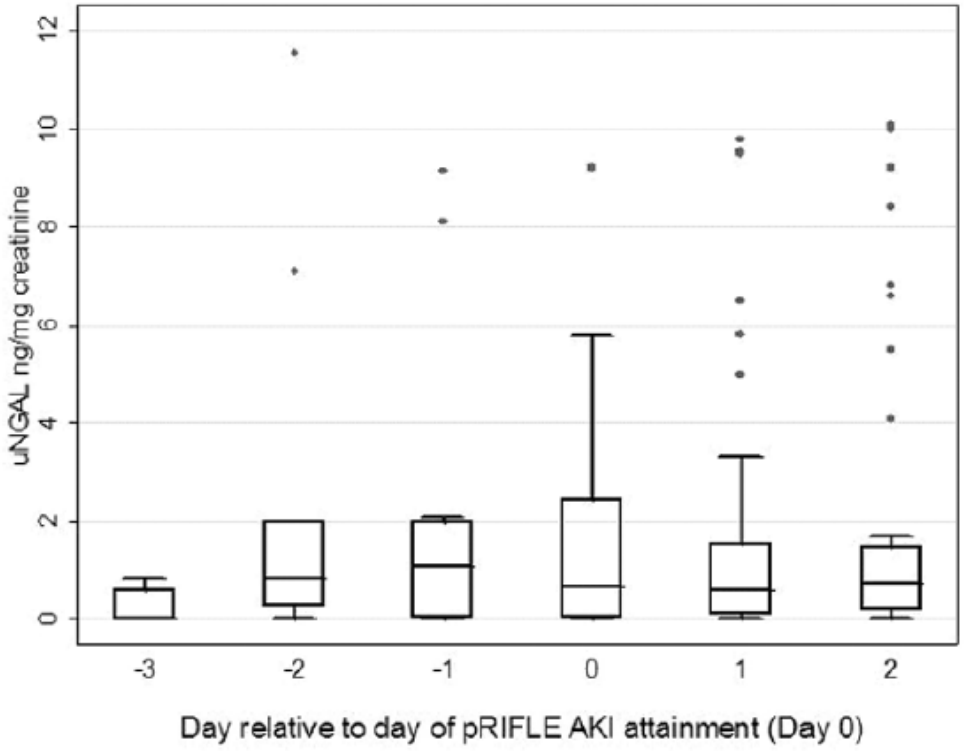
Paediatric guidelines to be developed

Emerging strategies in AKI

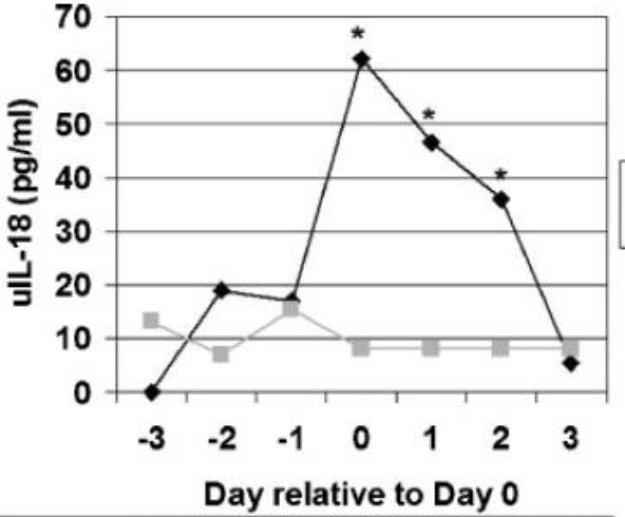
- clinical scoring to identify patients at risk, compare therapies
  - RIFLE/pRIFLE/AKIN/KDIGO
- biomarkers
  - NGAL, IL-18, KIM-1
  - will differ in
    - disease specificity (eg sepsis)
    - time course (early v. late)
    - prognostic value (acute or long term)


Nephron
Distal Tubule
π-GST
NGAL
Glomerulus
Collagen IV
Proximal Tubule
α-GST
KIM-1
L-FABP
Collecting duct
marker in developme
Urine


Response Time Kidney Markers
Kidney Injury
Kidney Biomarker
Creatinine
Kidney filtration
Time



Zappitelli et al Critical Care 2007; 11: R84



Day	-3	-2	-1	0	1	2	3
AKI patients (n)	5	9	13	20	47	45	49
Controls (n)	18	34	52	65	63	65	65

Washburn et al. NDT 2008; 23:566

Conclusions – AKI

- AKI is often part of MODS
- AKI may be prevented/ameliorated if recognised early and appropriate steps taken
- Early AKI can be successfully managed conservatively if recognised early
- ‘uraemia’ or plasma creatinine alone is seldom an indication for RRT – fluid balance, acidosis or electrolyte imbalance more important

Questions/comments

Urine output in AKI

- Urine output is more sensitive to changes in renal function than biochemical markers.
- It is not specific except when severely decreased or absent. Severe AKI can exist despite normal urine output (high output AKI)
- Changes in urine output often occur before biochemical changes are apparent.

Diuretic Effects in ARF

- Diuretics have been commonly used to enhance urine output, and convert oliguric to non-oliguric ARF
- Despite the frequent use of diuretics there is no evidence that this intervention shortens the duration of ARF, reduces the need for dialysis or improves outcomes in patients with ARF.
- Loop diuretics might even be deleterious for the kidney because they disturb the protective corticomedullary redistribution of blood flow

Indications for RRT

- fluid overload with oliguria
- electrolyte imbalance (K^+)
- acidosis
- control of urea, creatinine = ‘uraemia’
- removal of ‘toxins’
  - metabolic eg ammonia
  - drugs, myoglobin, cytokines

Emerging strategies in AKI

- **Tubular obstruction**
- rasburicase (synthetic urate oxidase)
- synthetic RDG peptides (anti-integrin therapy)

- **Tubular cell regeneration/protection**
- IGF-1
- erythropoeitin
- stem cell transfusion

- **Blood flow**
- vasodilating prostaglandins (PGE2, PGI)
- synthetic ANP (anaritide)
- anti-endothelin
- ROS/peroxynitrile scavengers
- iNOS inhibitor
- theophylline (may block adenosine receptor)
- fenoldopam (DA-1 receptor agonist)

Pediatr Nephrol (2006) 21: 891–895
DOI 10.1007/s00467-006-0173-8

EDITORIAL COMMENTARY

Stuart L. Goldstein

Pediatric acute kidney injury: it's time for real progress

Pediatr Nephrol (2008) 23:2147–2149
DOI 10.1007/s00467-008-1014-8

EDITORIAL

Acute kidney injury in children: the dawn of a new era

Robert H. Mak