

Acute Kidney Injury cases

Dr Nick Selby

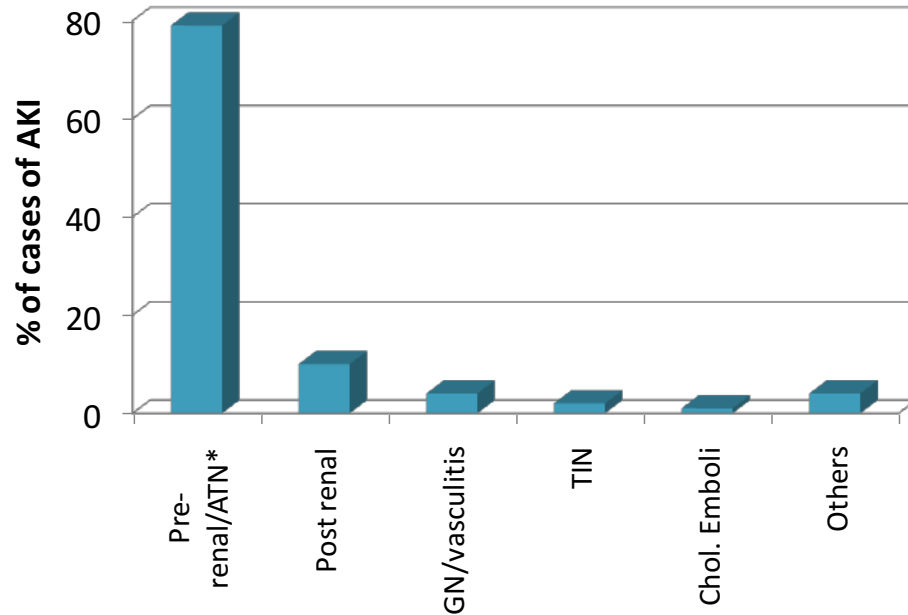
Consultant Nephrologist and Honorary Associate Professor



The University of
Nottingham

Derby Hospitals **NHS**
NHS Foundation Trust

Causes of in-hospital AKI



Pre-renal/ATN
(80% of cases)

Post-renal
obstruction
(5-10% of cases)

*ATN (ischaemic and toxic)

Liano F; Pascual J. *Kidney Int* 1996 Sep;50(3):811-8.

GD, 87M

- PMH
 - ‘Early dementia’ – recent-onset cognitive impairment & hallucinations
- DH
 - Furosemide 40mg OD, vitamin B injection every 3/12
- SH
 - Carers TDS, no ETOH, walks ½ mile 3x/week for shopping (independently mobile)

GD, 87M

- Presented to ED with confusion
 - Seen by son 20:30 previous night, left with water to drink
 - Carers attended and found drowsy/confused
- GCS 14/15 on arrival
- Then 11/15...

GD, 87M

- O/E:
 - RR 22, Kussmaul resps
 - Chest clear on auscultation, sats 98% (on air)
 - Abdomen soft, non-tender
 - BP 155 systolic
 - Diminished reflexes, no focal neurology
 - Clinically dry but peripheries well perfused
 - BM 4.8
- ECG: sinus tachycardia CXR: unremarkable
- ABG:
 - pH 7.11, HCO 8.3mmol/l, pCO2 3.1kPa, pO2 14.5kPa

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 - pH 7.11, HCO 8.3mmol/l, pCO₂ 3.1kPa, pO₂ 14.5kPa
 - BE -21.2, Lactate >20mmol/l

Anion gap

= $\text{Na}^+ - \text{Cl}^- - \text{HCO}_3^-$
(normal range 8-14)

Anion gap

$$= \text{Na}^+ - \text{Cl}^- - \text{HCO}_3^-$$

(normal range 8-14)

→ Anion gap 39

Lactate >20

Raised anion gap

G	Glycols (ethylene glycol) and toluene
O	Oxoproline (pyroglutamic acid)
L	L-lactate
D	D-lactate
M	Methanol
A	Aspirin
R	Renal failure
R	Rhabdomyolysis (rare)
K	Ketoacidosis (diabetes, starvation, alcohol)

Normal anion gap (decrease in bicarb, increase in Cl ⁻)	Raised anion gap	
GI loss of bicarb Diarrhoea, ureteric diversion	G	Glycols (ethylene glycol) and toluene
Renal loss of bicarb (RTA)	O	Oxoproline (pyroglutamic acid)
Addisons disease	L	L-lactate
	D	D-lactate
	M	Methanol
	A	Aspirin
	R	Renal failure
	R	Rhabdomyolysis (rare)
	K	Ketoacidosis (diabetes, starvation, alcohol)

Lactic acidosis

Type A

Tissue hypoperfusion

Type B

Absence of systemic hypoperfusion

- Metformin
- Chronic alcoholism
- Malignancy (mechanism not clear)
- HIV
- Mitochondrial dysfunction (including linezolid and HAART)

GD, 87M

- Bloods:
 - Na 137, K 5.5, Urea 8.8, Creatinine 193, glucose 4.4
(22/05/14 – Creatinine 90, eGFR >60)

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 - Salicylate/paracetamol normal
 - INR 1.3

GD, 87M

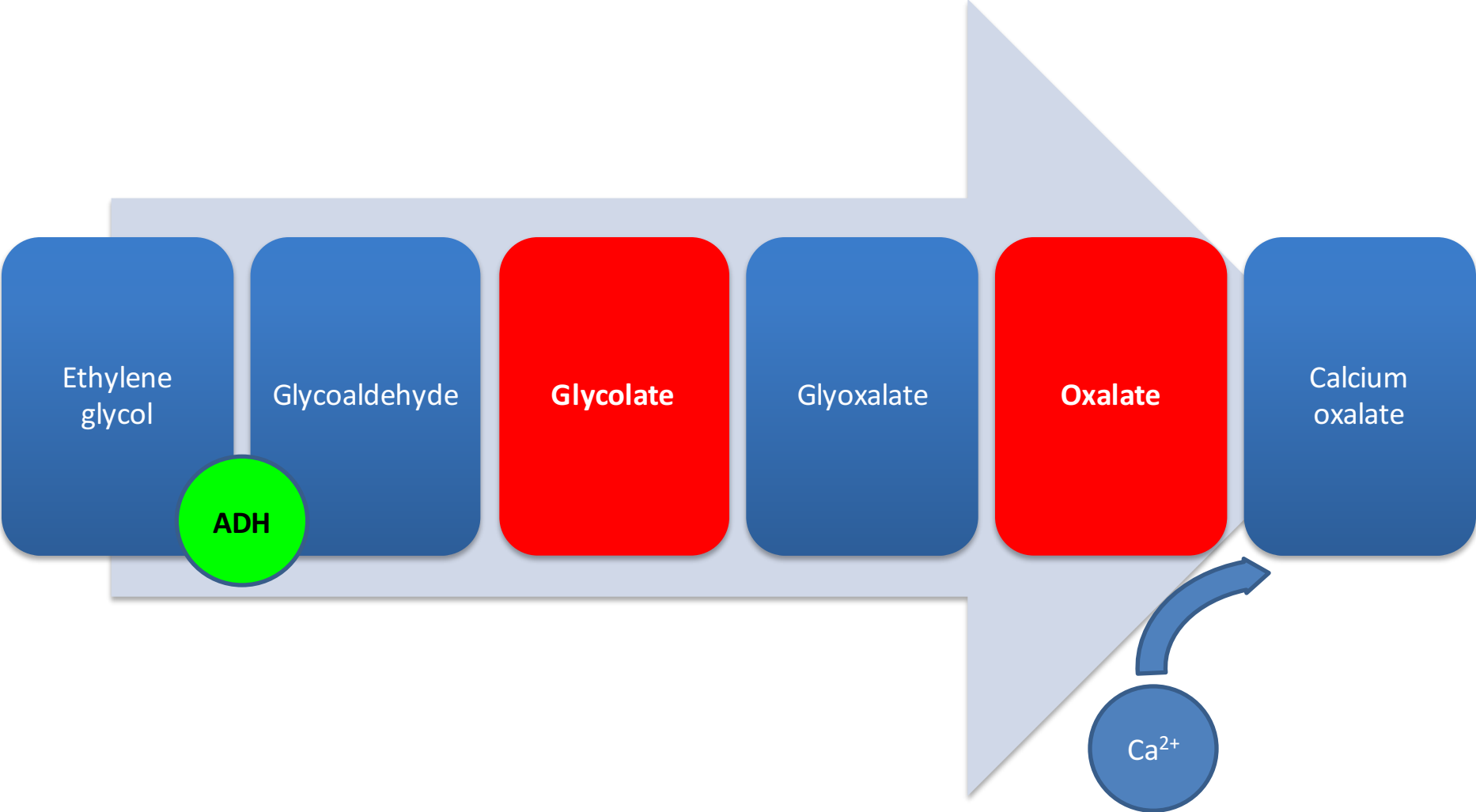
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 - INR 1.3
- Reason for raised lactate?

Initial management of ethylene glycol poisoning

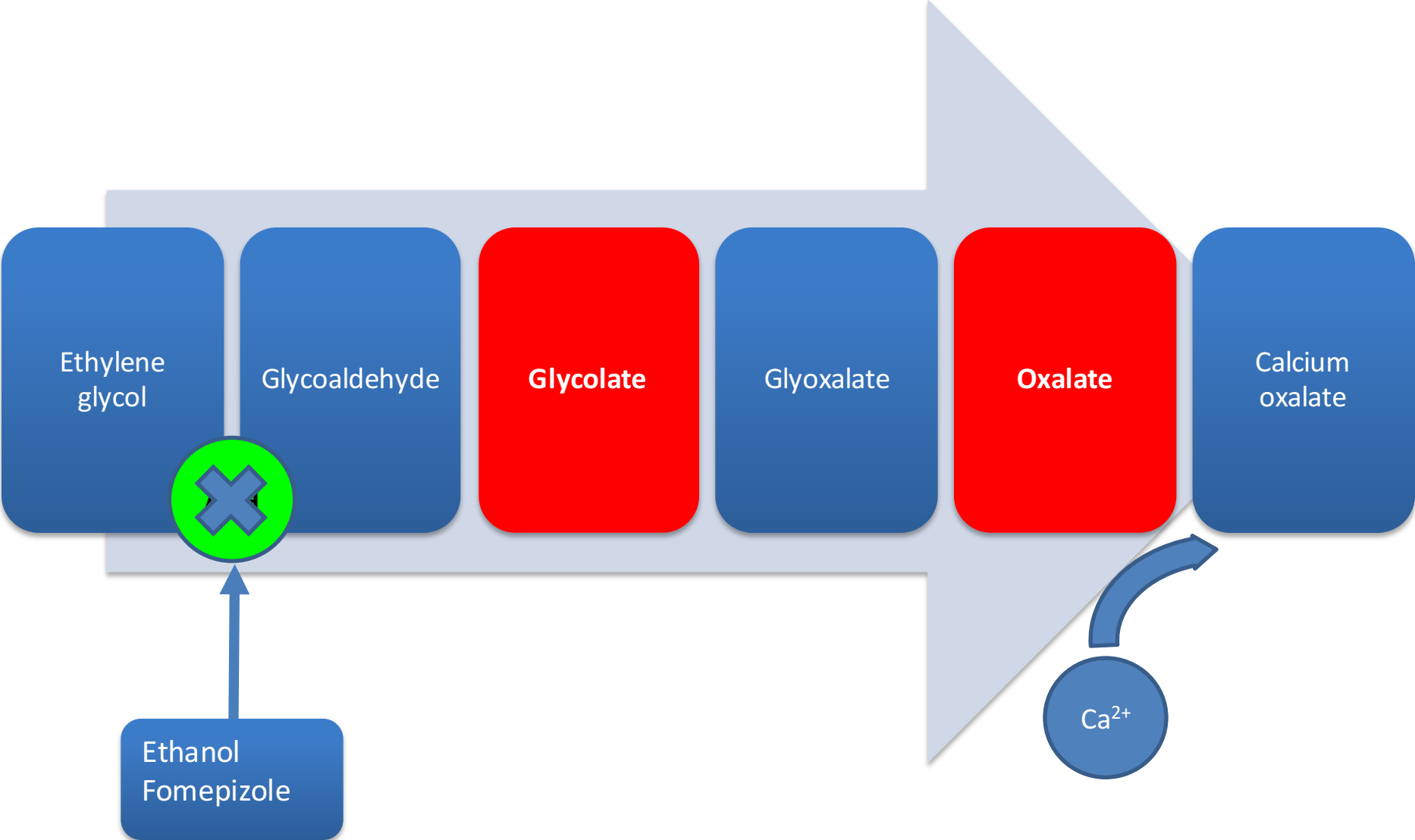
Initial management of ethylene glycol poisoning

1. Don't wait for drug level before commencing Rx
2. Correct acidosis with IV sodium bicarb (Jacobsen Med Toxicol 1986)
3. ADH inhibition
4. Consider dialysis
5. Give co-factors

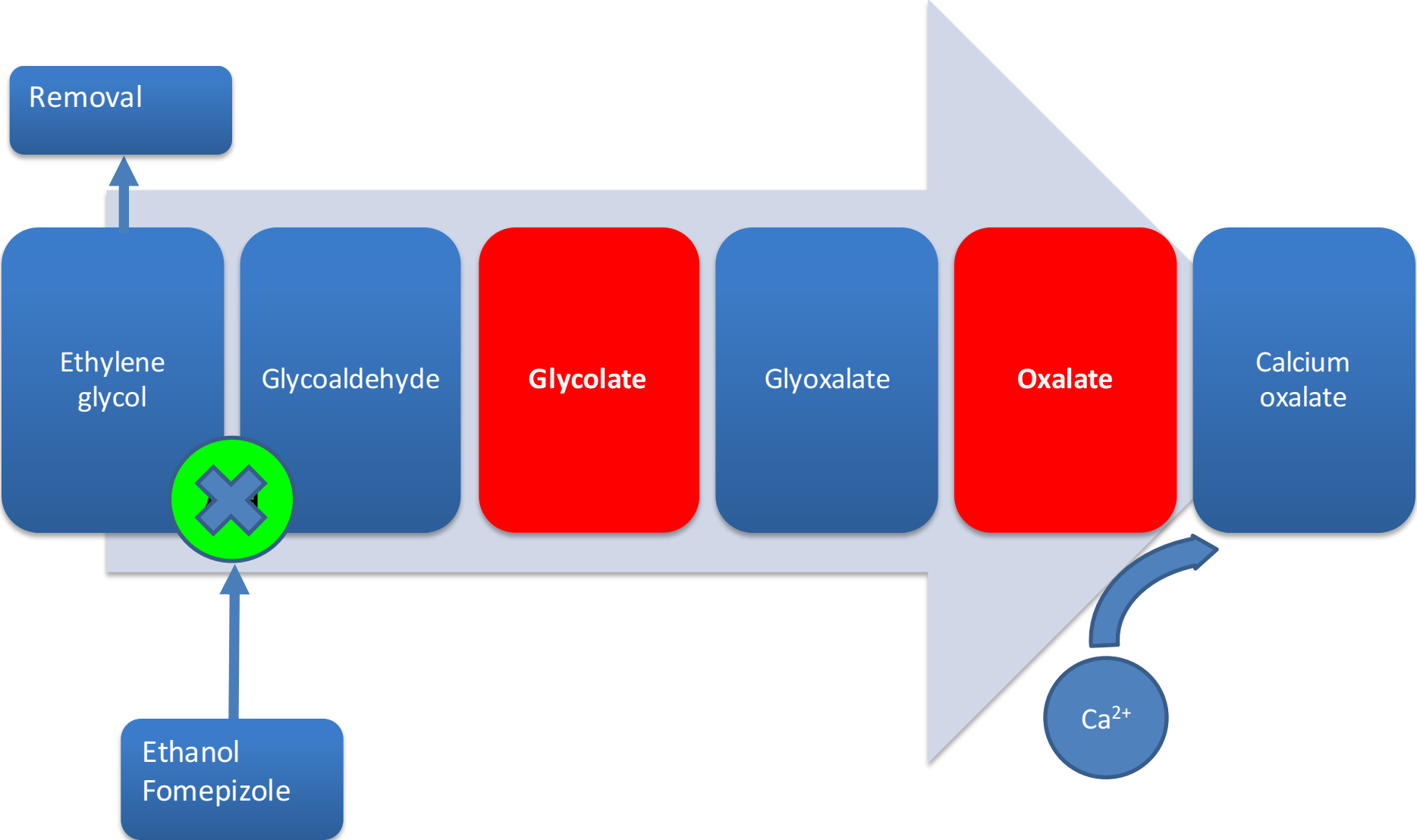
Metabolism of ethylene glycol



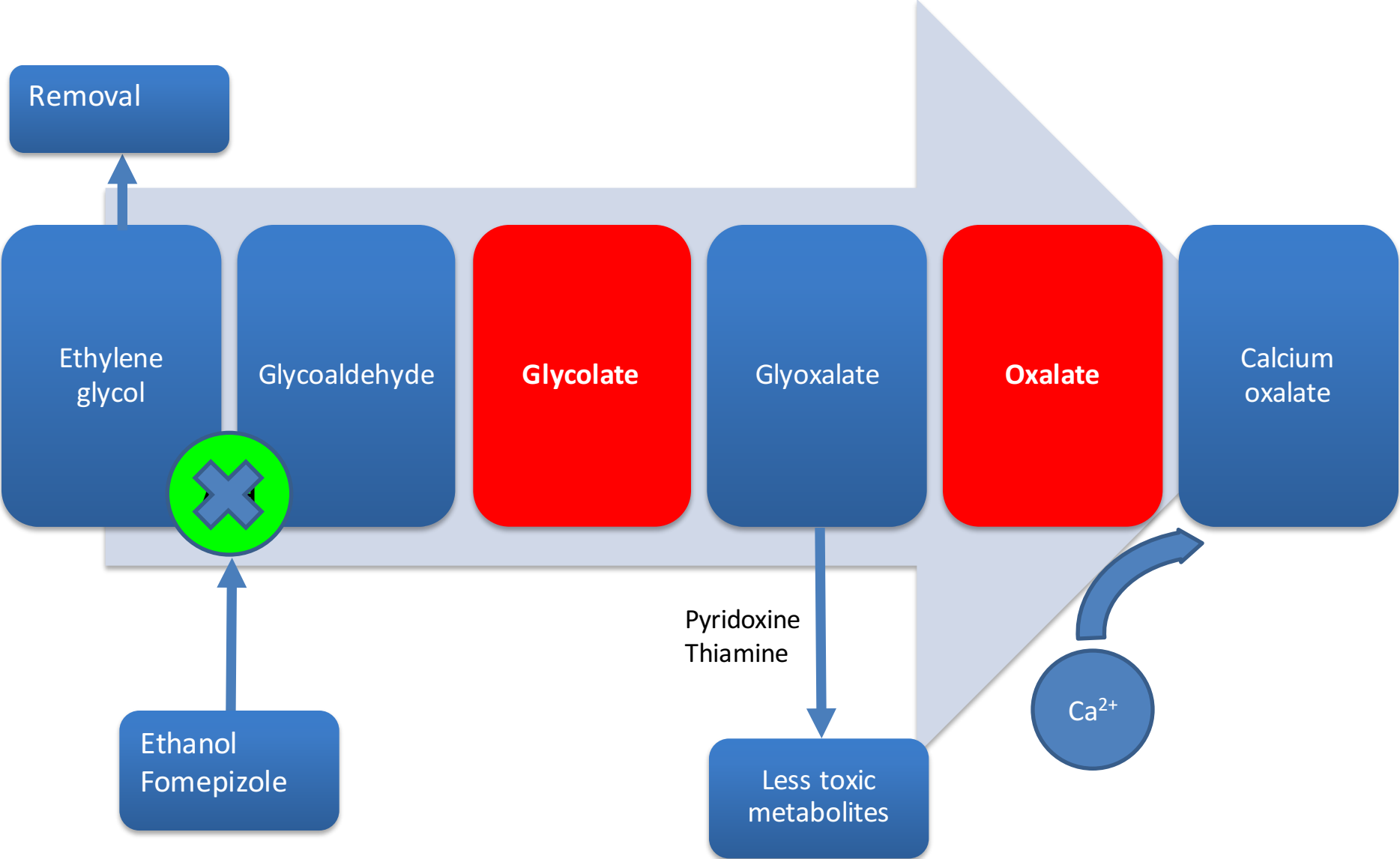
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Metabolism of ethylene glycol



Metabolism of ethylene glycol



GD, 87M

- Fomepizole commenced (15mg/kg loading dose)
- Immediate transfer for HD via femoral line
- Dose: 1mg/kg/hr during dialysis & change to 10mg/kg every 12hrs off dialysis
- *If no fomepizole: give Ethanol*
 - IV – difficult to dose, aim 1/3 of ethylene glycol levels or >100mg/dl*
 - NG or oral as last resort*

Day 2

- BP 85/39, HR 76
- Further fluid resuscitation

- 12:30pm
- On ivi. BP 96/52 on HD, AF to SVT rate 150, given Mg^{2+} and 1L saline
- BP drops to 60 systolic, SVT/flutter. 50J DCCU performed – SR. Further 100J as reverted, responded. Subsequently loaded with amiodarone.
- Rpt VBG: pH 7.23, Lac 10.5, HCO 14. CVC R IJV inserted.
- BP 130/80, HR 80. Put back on HD, no fluid off, low bicarb.

GD, 87M

- 16:25
- Rpt level = 60
- VBG: pH 7.29, Lac 5.1, HCO 18.7, BE -7.3
- Further dialysis:
- Post VBG – pH 7.34, Lac 1.2, HCO 24.2, BE 0.1

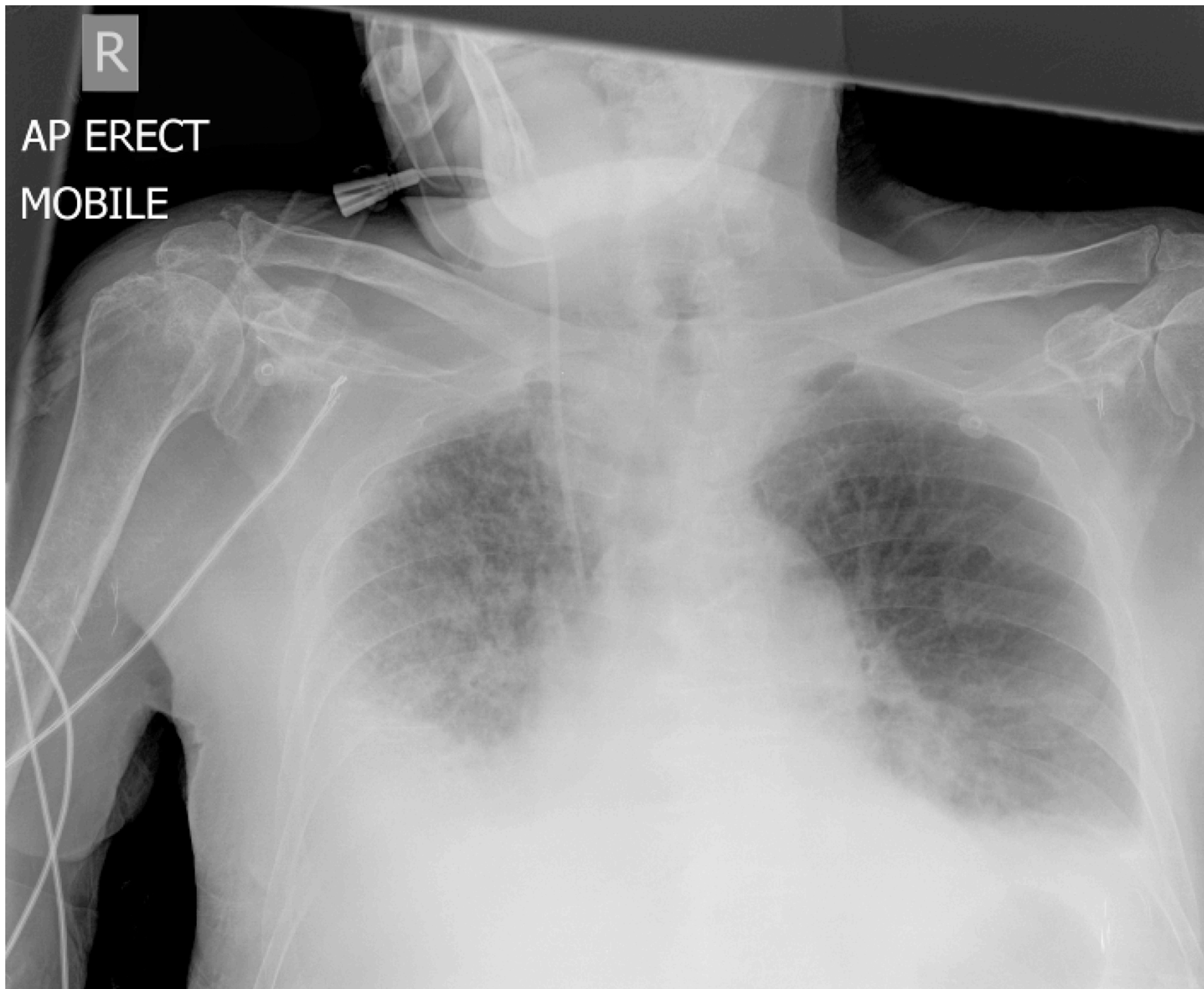
GD, 87M

Day 3

- Fluctuating GCS continued, fomepizole stopped
- Remained oligoanuric
- Acute desaturation to 65%, to 91% on 15L
- ABG: pH 7.35, pO₂ 4.5, Lac 1.7, HCO 22.0, BE -2.9
- CXR: fluid/infection, started on taz & furosemide (had 200mg iv)

R

AP ERECT
MOBILE



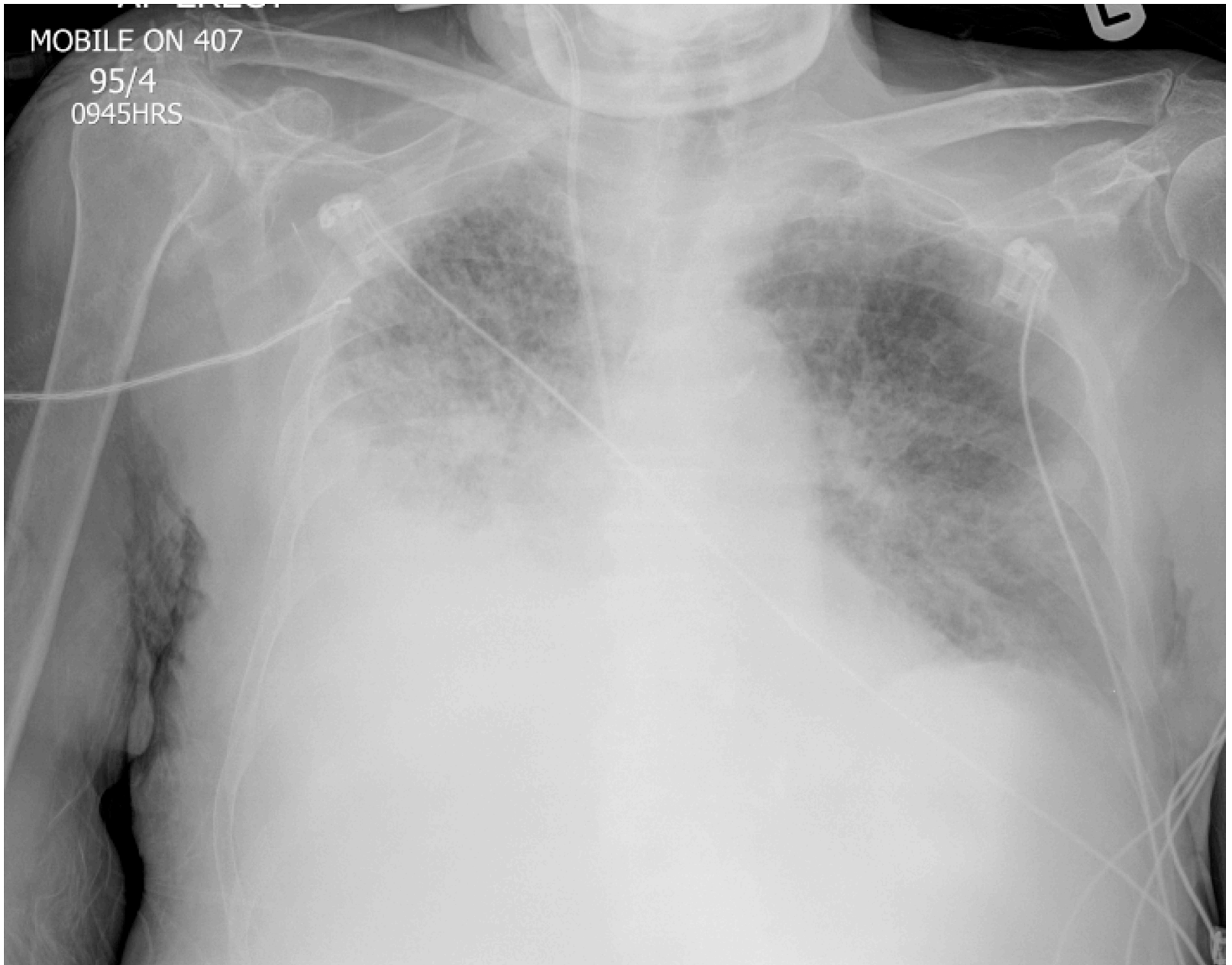
GD, 87M

- Seen overnight – new acidosis pH 7.26, pCO₂ 6.8, pO₂ 7.6, lac 0.9, started on CPAP
- Significant respiratory distress next day...

MOBILE ON 407

95/4

0945HRS

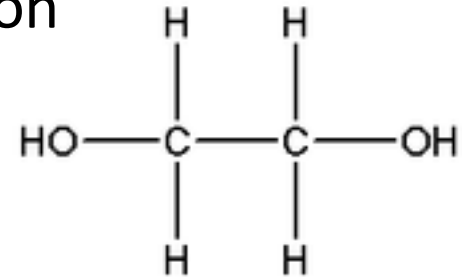


GD, 87M

- Further HD but no response
- Kept comfortable on ward with family input

Ethylene glycol

- (1,2-Ethanediol)
- Molecular weight 62.07 (cf. methanol 32.04, ethanol 46.7)
- 0.5-0.8L/kg distribution
- 80% hepatic, 20% renal excretion
- Half-life 3 to 8 hours



- Found in:
 - Car antifreeze, brake fluid, de-icer
- Rapidly absorbed from gut
- Inhalation/skin absorption not so concerning

Ethylene glycol poisoning

- No data on UK episodes but 5300 cases reported to American Association of Poison Control Centres in US in 2012
- $>0.1\text{g/kg}$ pure ethylene glycol = medical assessment
- $>0.15\text{g/kg}$ (0.13ml/kg) = likely antidote required
- Fatal dose: 90ml pure ethylene glycol
- 75kg male = 9.75ml
- GD potentially drank 150ml
- Serious toxicity reported from as little as 8g

Ethylene glycol poisoning

- Initial high osmolar gap >20 mOsm/L
 - Low molecular weight serum substance
 - Higher than ketoacidosis or lactic acidosis (<20)
- Followed by falling osmolar gap & rising anion gap
 - Glycolic acid metabolite produced
- Important factors
 - Dose ingested & time to antidote

Ethylene glycol poisoning

- **Stage 1 (30 mins – 12 hrs) = neurological**
 - *Apparent intoxication (but no ethanol breath)*
 - *N&V, coma and convulsions (often focal)*
 - *CNS effects: nystagmus, ataxia, ophthalmoplegia, papilloedema, hypotonia, hyporeflexia, myoclonic jerks, tetanic contractions, CN palsies (II, V, VII, VIII, IX, X, XII)*
- **Stage 2 (12-24 hrs) = cardiopulmonary**
 - *Tachypnoea, sinus tachycardia, hypertension*
 - *Arrhythmias*
 - *Pulmonary oedema and CCF develop*

Ethylene glycol poisoning

- ***Stage 3 (24-72 hrs) = renal dysfunction***
 - *Flank pain, renal angle tenderness, ATN, hypocalcaemia*
 - *Calcium oxalate monohydrate crystalluria, hyperkalaemia and hypomagnesaemia develop*
 - *Severe metabolic acidosis, hyperkalaemia, seizures and coma carry poorest prognosis*

Treatment – HD

- Indications:
 - Metabolic acidosis
 - Renal impairment
 - Ethylene glycol level >50
- HD versus CVVH

Treatment – Monitoring

- To continue fomepizole until level <50 mg/L
AND acidosis/toxicity signs resolved
- OR ethylene glycol level undetectable

EG poisoning clues

- If similar presentation to alcohol but no smell
- Severe metabolic acidosis with raised anion gap
- Abnormally high lactate with lab discrepancy
- Abnormally high osmolar gap

Case

5/7/12

PC

2008

— ABNORMAL BLOODS

HPC

— SAW GP TODAY WHO CHECKED SOME

ROUTINE BLOODS — AKI + PATIENT SENT IN.

FEELS WELL

NO RECENT ILLNESSES

NO DYSURIA / HAEMATURIA

E+D ✓

PMHx

— INVESTIGATED FOR WEIGHT LOSS 6/12 AND — NAD

↑LIPIDS

↑B/P

	Feb 2008	Mar 2010	Oct 2010	Nov 2011	4/7/12
Creatinine	82	87	97	93	246

Case

DATE & TIME

CONTINUATION NOTES

PRINT NAME DESIGNATION & BLEEP NO. ALONGSIDE SIGNATURE

5/7/12

PC

ABNORMAL BLOODS

2005

HPC

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E+D ✓

PMHx

INVESTIGATED FOR WEIGHT LOSS 6/12 AND - NAD

↑LIPIDS

↑BP

DHx

AMLODIPINE 5mg

SIMVASTATIN 40mg

NKDA

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INVESTIGATED FOR WEIGHT LOSS 6/12 AND - NKDA

↑LIPIDS

↑BP

Siemens Diagnostics
Clinitek Status

Patient Name:

Case 1

Multistix 10 SG

Test date Not Entered

Time 10:00AM

Operator

Test Number 0001

Color Not Entered

Clarity Not Entered

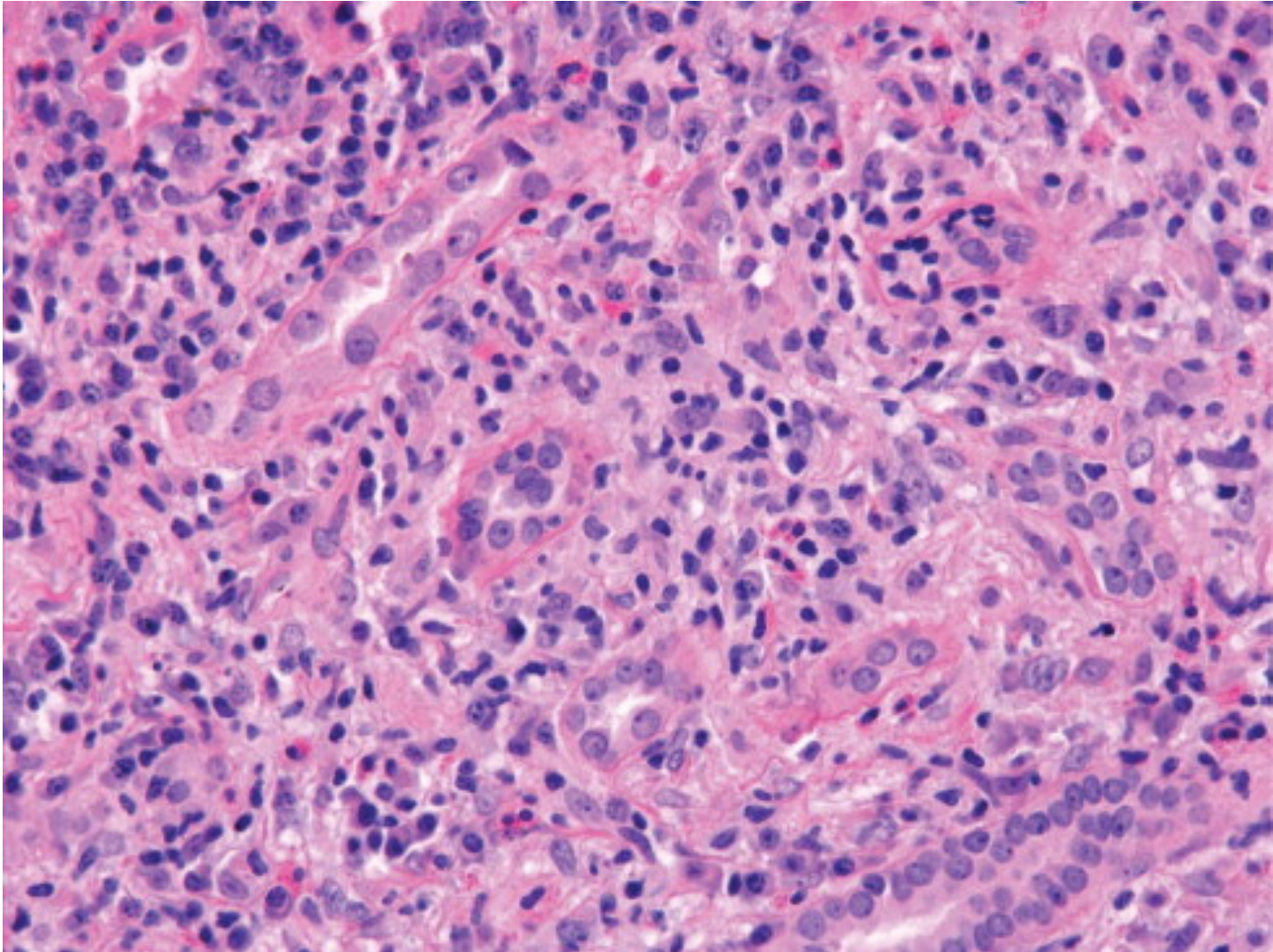
- GLU Negative
- BIL Negative
- KET Negative
- BLO Negative
- PROT 30mg/dL
- URO 0.2 E.U./dL
- NIT Negative
- LEU Negative

	Feb 2008	Mar 2010	Oct 2010	Nov 2011	4/7/12
Creatinine	82	87	97	93	246

Subsequent investigations

- Examination: normal
- U/S – normal appearance of kidneys with no evidence of hydronephrosis
- Myeloma screen –ve
- ANA and ANCA –ve

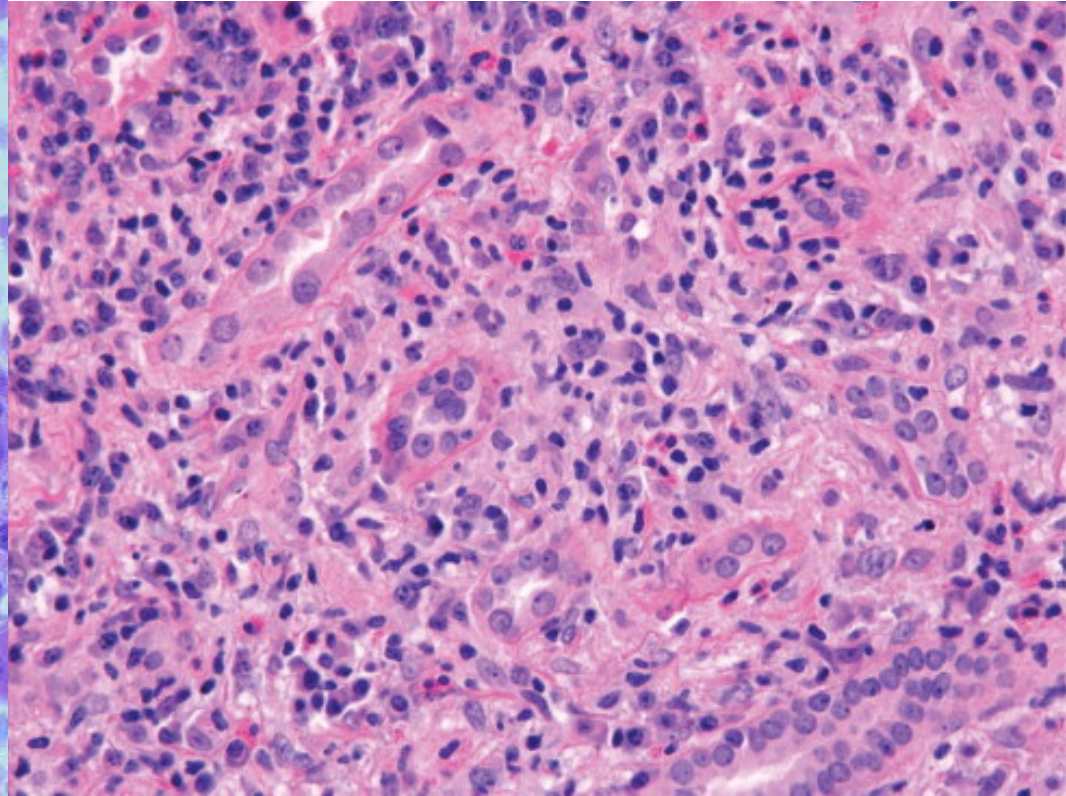
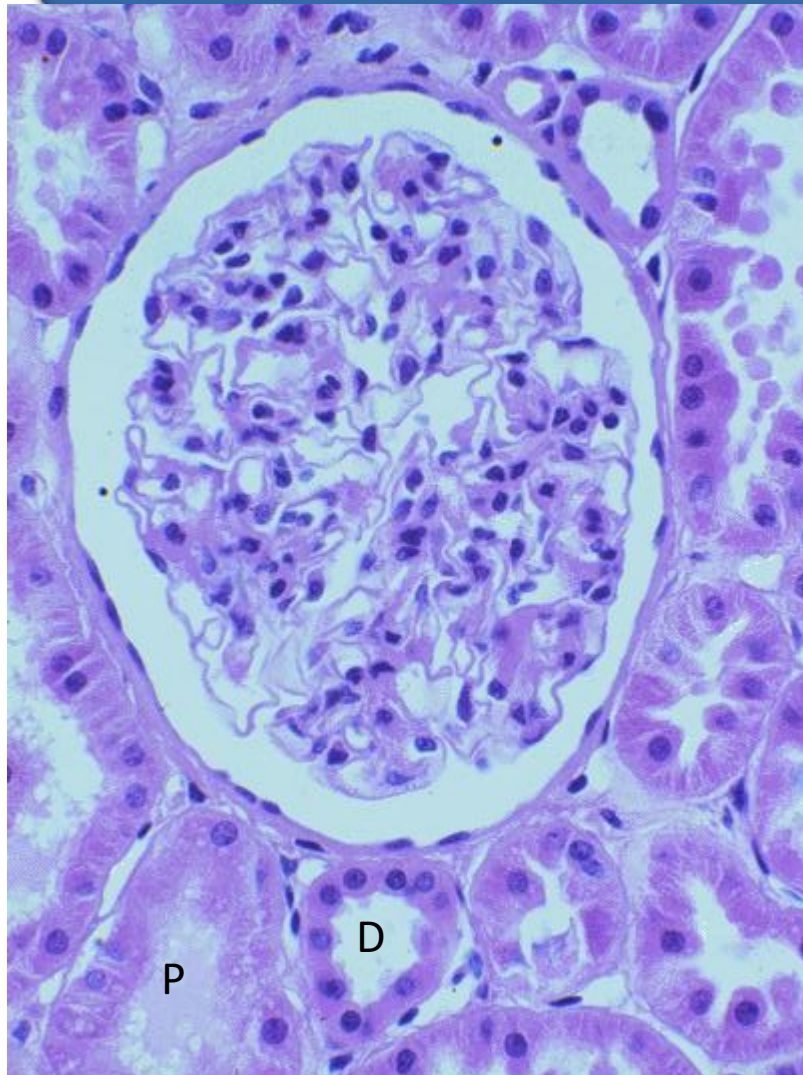
Renal biopsy: interstitial nephritis



Drug induced TIN

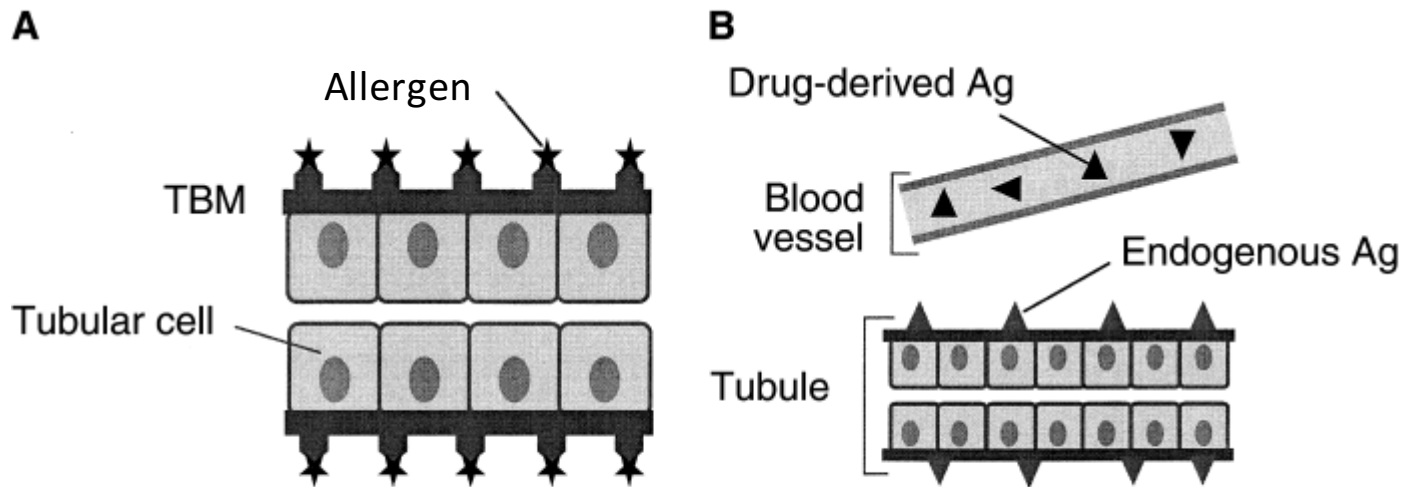
- Eosinophilia, rash – often occurs without these
- Urine dip:
 - 1+ WBC, blood, protein
 - Can be NAD
- Antibiotics, PPI, NSAIDs, diuretics, allopurinol but lots more
- Sometimes – only clue is lack of other causes of AKI plus temporal relationship with drug

Drug induced TIN



There is lack of other causes of AKI
plus temporal relationship with drug

Mechanisms whereby a drug (or one of its metabolites) can induce acute interstitial nephritis



- (A) The drug can bind to a normal component of the tubular basement membrane (TBM) and act as an allergen.
- (B) The drug can mimic an antigen normally present within the TBM or the interstitium and induce an immune response that will also be directed against this antigen.

Management of TIN

- Stop drug!
 - And make sure no re-exposure
- Steroids?
 - Lack of evidence
 - If severe
 - Without early improvement
 - Starting late associated with worse response

Drugs and AKI

- Very common and important cause/contributor to AKI
- Variety of mechanisms:
 - Pre-renal
 - *Diuretics, ACE inhibitors, NSAIDs*
 - Direct tubular toxicity
 - *Aminoglycosides, contrast media*
 - ‘Allergic’ – tubulo-interstitial nephritis
 - *Antibiotics, NSAIDs, PPIs, + many more*

(Can also cause GN but rarer)

Case

- 43 male, referred from Burton CCU with AKI, shortness of breath and weight loss
- Unwell for 2-3 weeks with increasing SOB
- Ankle oedema
- Cough with dark brown sputum
- Weight loss
- PMH
 - Asthma
 - Nasal polyps
- DH
 - Symbicort

Examination

- BP 110/70
- HR 110
- Ankle oedema
- Gallop rhythm
- Expiratory wheeze



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- Urine dip
 - Blood 4+
 - Prot 3+

- Blood tests from Burton:
 - Creatinine 178
(was 91 two weeks ago)
 - Trop T 4915



Aug-12 06:50

D Dimers.

D Dimers 445 **↑↑** [0-230 ug/

Aug-12 19:15

Full Blood Count.

Specimen Comment



White Cells	10.32		[4.5-11.0 1
Red Cells	3.72	↓	[4.5-6.5 10
Haemoglobin	11.7	↓	[13.5-18.0
Haematocrit	0.333	↓	[0.42-0.52]
Mean Cell Volume	89.5		[80-100 fL]
Mean Cell Haemoglobin	31.5		[27-32 pg]
Mean Cell Haemoglobin Concentration	35.1	↑	[30-35 g/d
Platelets	538	↑	[150-450 1
Neutrophils AB	7.71	↑	[2.5-7.5 10
Lymphocytes AB	1.43	↓	[1.5-3.5 10
Eosinophils AB	0.43	↑	[0.04-0.4 1
Monocytes AB	0.72		[0.2-0.8 10
Basophils AB	0.03		[0.01-0.1 1

ID:H01071051

19-AUG-2012 14:24:57

SDAH NHS TRUST

28-MAY-1969 (43 yr)
Caucasian

Vent. rate	114	BPM
PR interval	162	ms
QRS duration	106	ms
QT/QTc	338/465	ms
P-R-T axes	61 111 146	

Loc:15

Med:

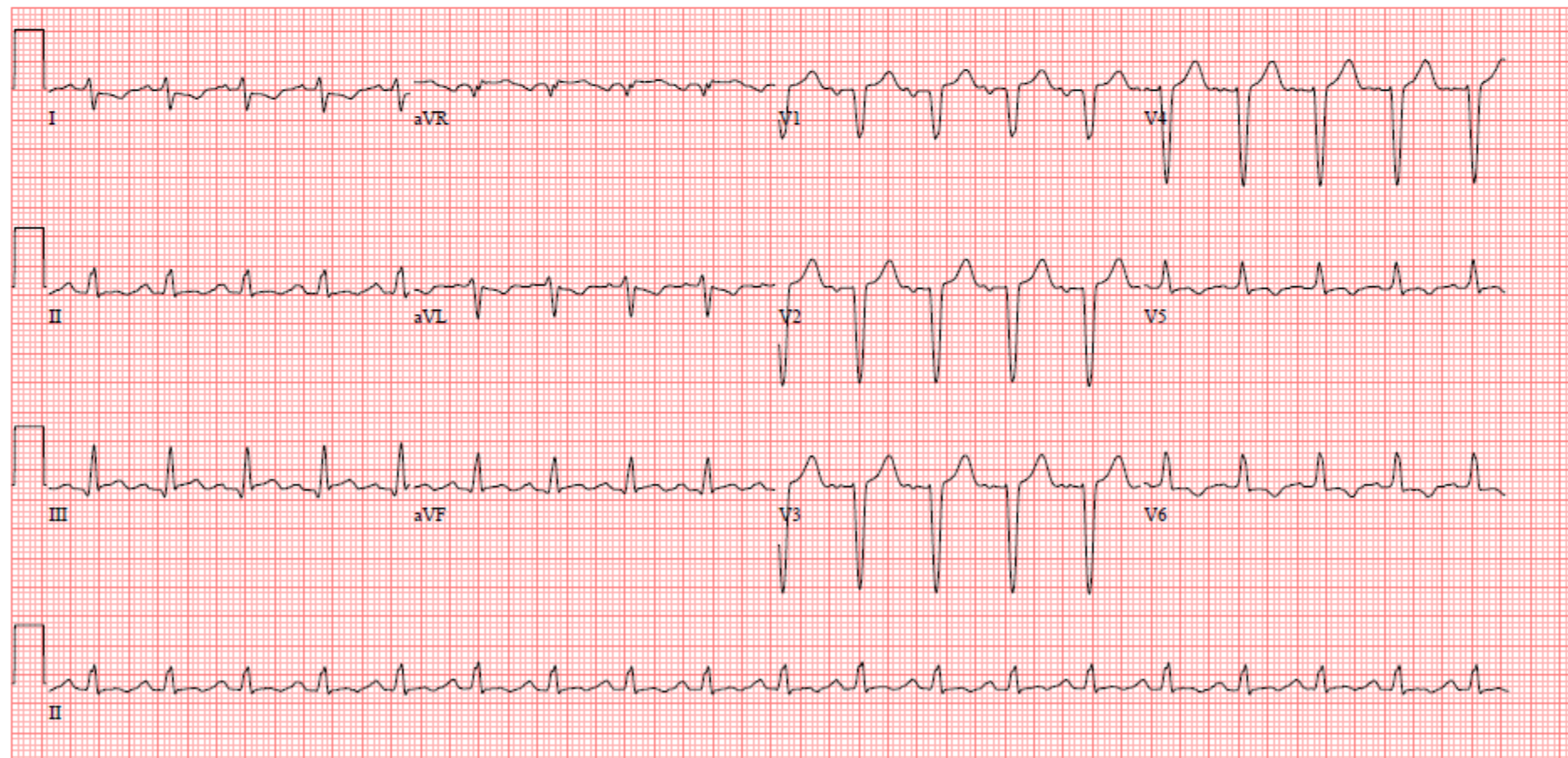
NURSE NAME:PAUL REED

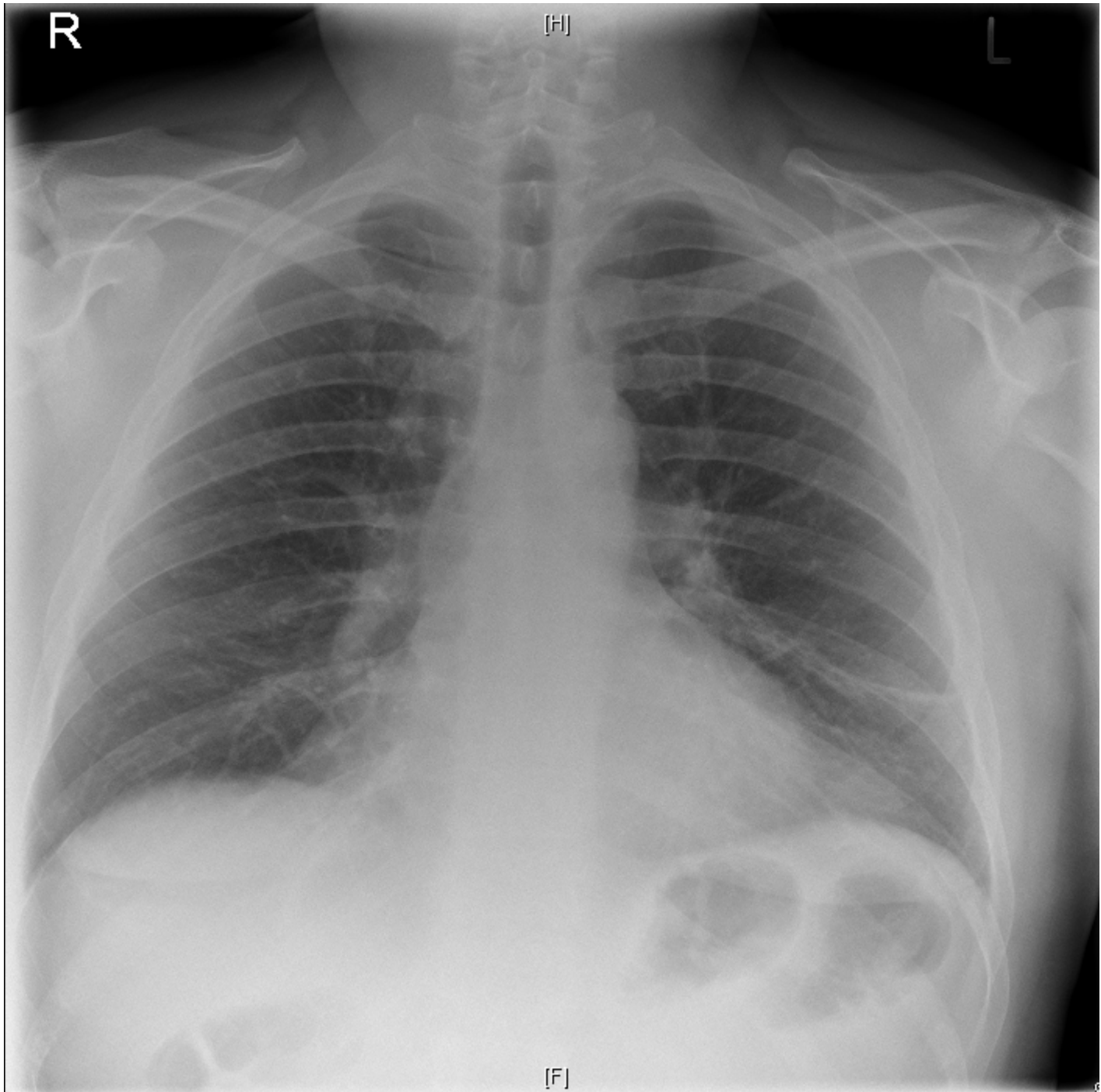
WARD:407

Referred by:

CONSULTANT:FLUCK

Confirmed By: REPORT PROVISIONAL





Summary and differential?

Summary and differential?

- AKI
 - Active urine dip
- Systemic symptoms
 - Cardiac involvement
 - Haemoptysis?
- Nail fold infarct
 - Small vessel inflammation
 - » Vessel lumen: Embolic, DIC, TTP, CAPS
 - » Vessel wall: primary vasculitis (incl. infection related and cryo)
- Abnormal bloods including eosinophilia

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Primary
vasculitis:
Churg-Strauss
Syndrome

ANCA +ve

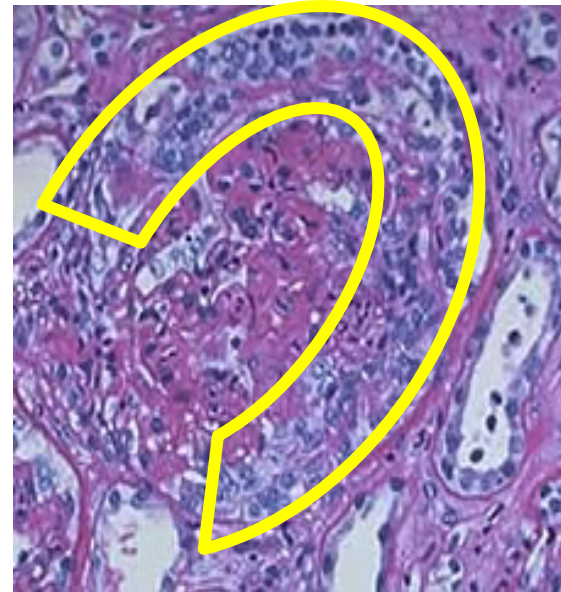
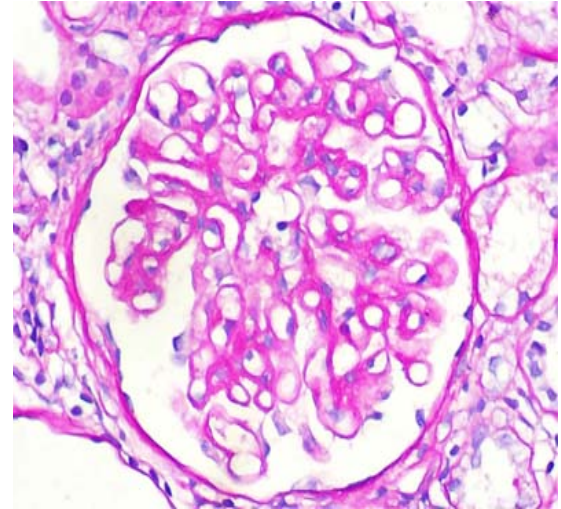
AKI and eosinophilia

- Acute TIN
- Cholesterol emboli
- Churg-Strauss syndrome

- DRESS syndrome
- Lymphoma
- Hypereosinophilic syndrome
- Schistosomiasis

Subsequent progress

- Echo – severely impaired LV function with LV thrombus
- High dose steroids and cyclophosphamide
- Anticoagulated
- Good renal and cardiac recovery over following 6/12



'Inflammatory' renal disease

ACTIVE URINE

More than 2+ of blood and protein

VASCULITIC RASH

SYSTEMIC SYMPTOMS

Often present for months – myalgias, arthralgias, malaise

EPISTAXIS, SINUSITIS, HAEMOPTYSIS

Low platelets

**ALWAYS DIP THE
URINE**

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*Urine dip is **not** to look
for infection, it's to help
with diagnosis*

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*Urine dip is **not** to look for infection, it's to help with diagnosis*

NAD

Pre-renal
Post-renal
Myeloma
Drug-induced TIN
(Renovascular)

Blood and protein

Still can be ATN,
but raises the
possibility of
inflammatory renal
disease
e.g. vasculitis

Proteinuria (PCR>3)

(=Protein loss >3g per day)

**Definitely
glomerular**

Case

- 62yr male
 - Admitted to MAU
 - General decline over 2 months
 - Loss of appetite, weight loss,
- PMH
 - Hypertension
 - Meds
 - Bendrofluazide
 - Antacids

O/E

- Clinically dry
- BP 118/67
- HS normal
- Chest clear
- Abdo soft
- No abnormal neurological findings

Urine dip	
Blood	NEG
Alb	NEG
WBC	1+
Nitrites	NEG

Initial workup

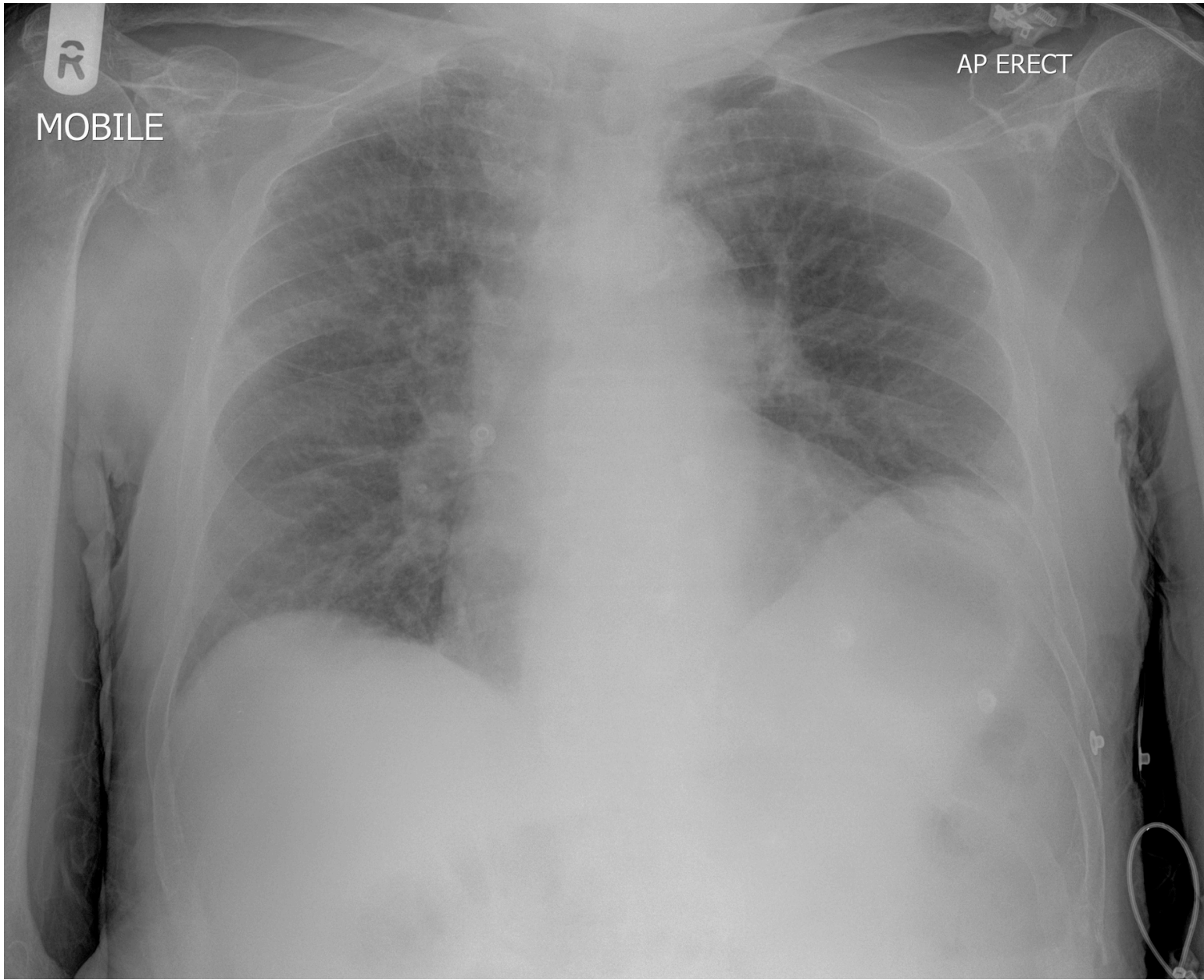
Hb	11.1
WBC	11.2
Plt	268
MCV	89

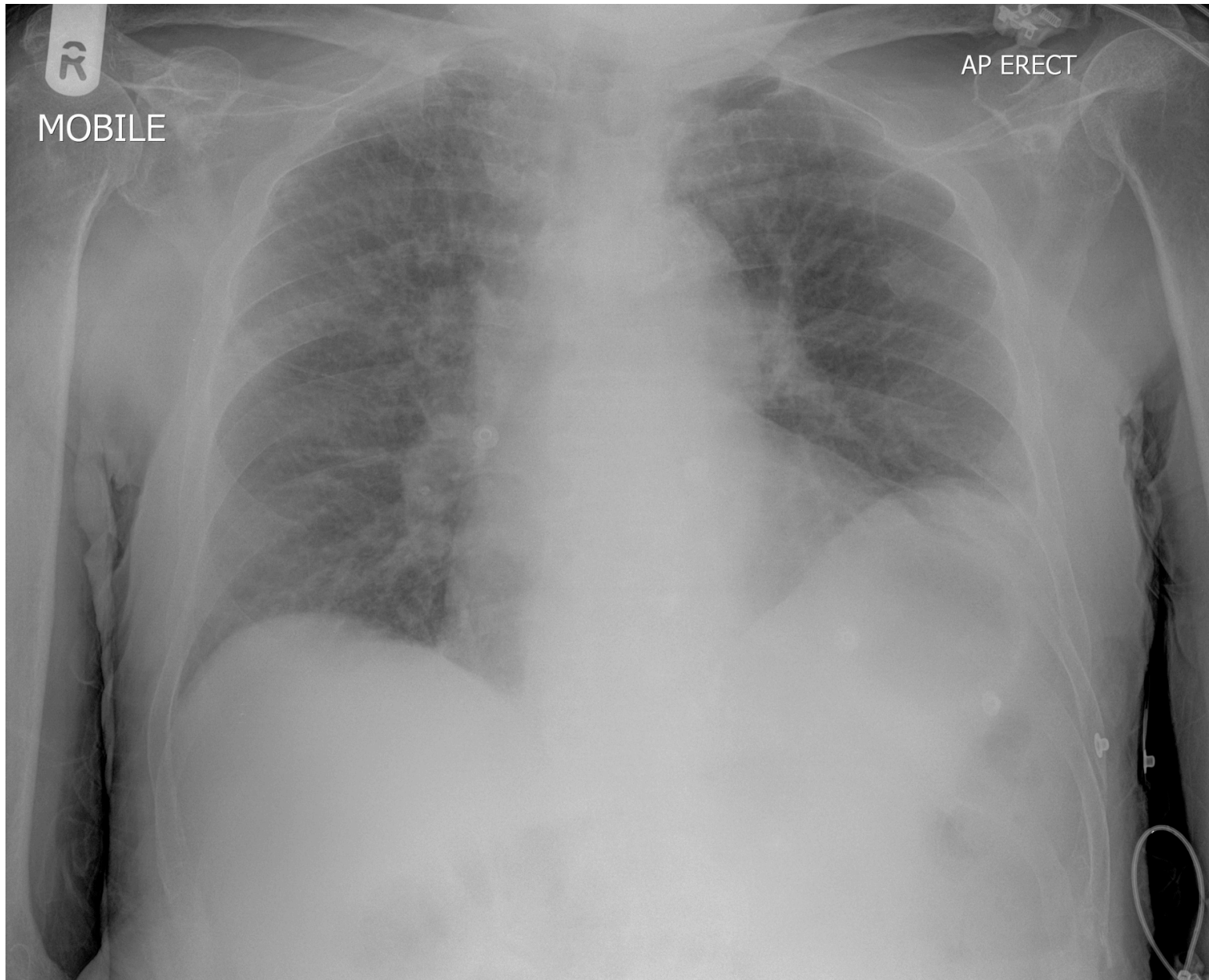
Na	145
K	3.9
Urea	39
Creatinine	426 (previously 89)
Corrected Ca ²⁺	3.45
P04	1.9
Bil	5
AIP	180
ALT	55
Alb	32

R

AP ERECT

MOBILE





→ Summary and differential diagnosis?

AKI and hypercalcaemia

- Hypercalcaemia itself can cause reduced GFR
 - 90% of hypercalcaemia is malignancy or primary hyperpara
 - Medications
- Specific conditions that involve the kidney and cause increased Ca^{2+}
 - Myeloma
 - Sarcoidosis
 - Lymphoma
 - TB

Initial Management

Initial Management

- Correct volume depletion
 - Normal saline
- Reduce plasma calcium levels
 - Bisphosphonates
 - Frusemide
 - Calcitonin
 - Steroids
 - Dialysis
 - Cinacalcet
- Stop relevant medications
 - Thiazide, antacids
- Initiate investigations

Further investigations?

- PTH
- Myeloma screen
- Imaging

Further investigations?

- PTH → 2pg/ml
- Myeloma screen → negative
- Imaging

Progress

- Calcium improved over 3-4 days with rehydration alone, 2.72mmol/l on day 4
- Creatinine also improved but stuck at around ~200

- Multiple enlarged lymph nodes
- Enlarged spleen
- Suspicious of lymphoma



- Haematology, surgical, radiology review
- Lymph node excision biopsy:

- Haematology, surgical, radiology review
- Lymph node excision biopsy:
 - Non-caseating granulomata consistent with sarcoid, no evidence of lymphoma

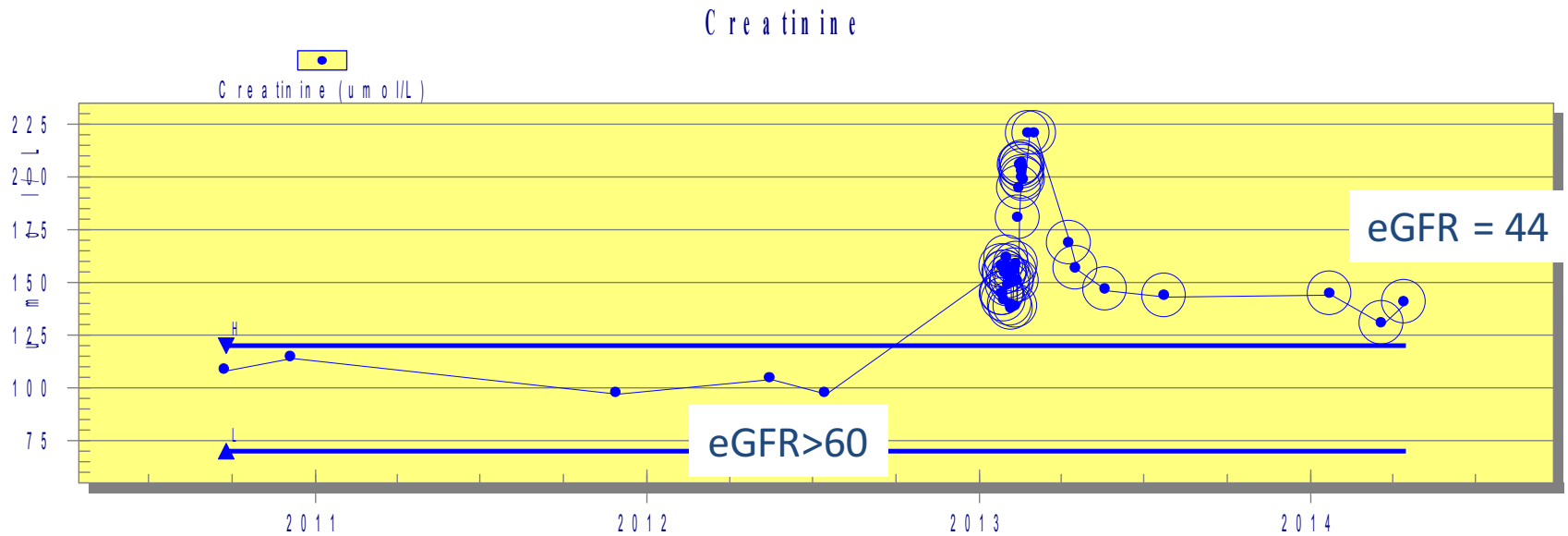
- Haematology, surgical, radiology review
 - Lymph node excision biopsy:
 - Non-caseating granulomata consistent with sarcoid, no evidence of lymphoma
- Prednisolone 50mg od, tapering course
- Resolution of renal impairment over 8 weeks

Case

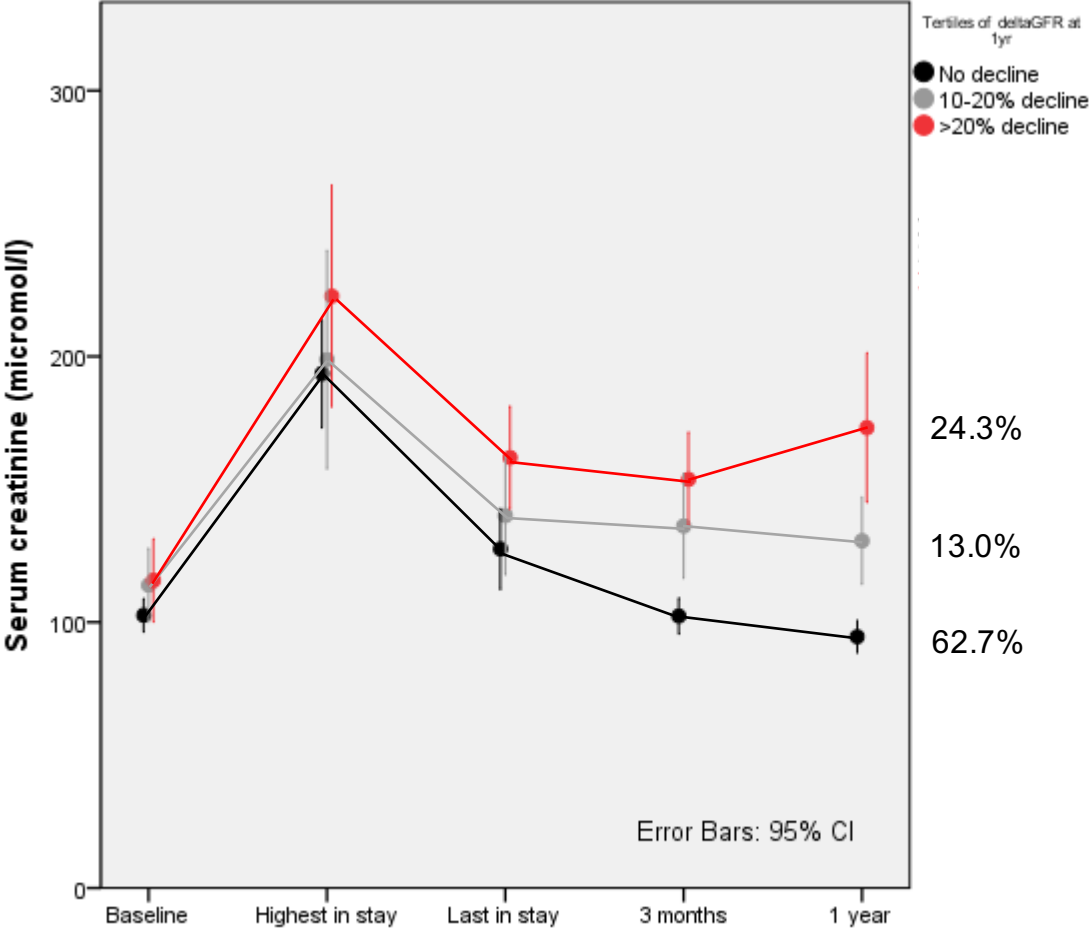
- 76yr old male
- PMH
 - CKD stage 3A
 - CCF (LVEF <35%)
 - Previous AKI episodes x2
- DH
 - Aspirin 75mg od
 - Frusemide 80mg bd
 - Ramipril 10mg od
 - Spironolactone 25mg od
 - Allopurinol 300mg od
 - Atorvastatin 40mg od
 - Omeprazole 20mg od
- Admitted with high temperature, vomiting and SOB
- BP 132/82
- Sats 93% air
- Crepitations R base
- CXR – right basal consolidation
- Creatinine 3 weeks ago 144
- Creatinine now 322

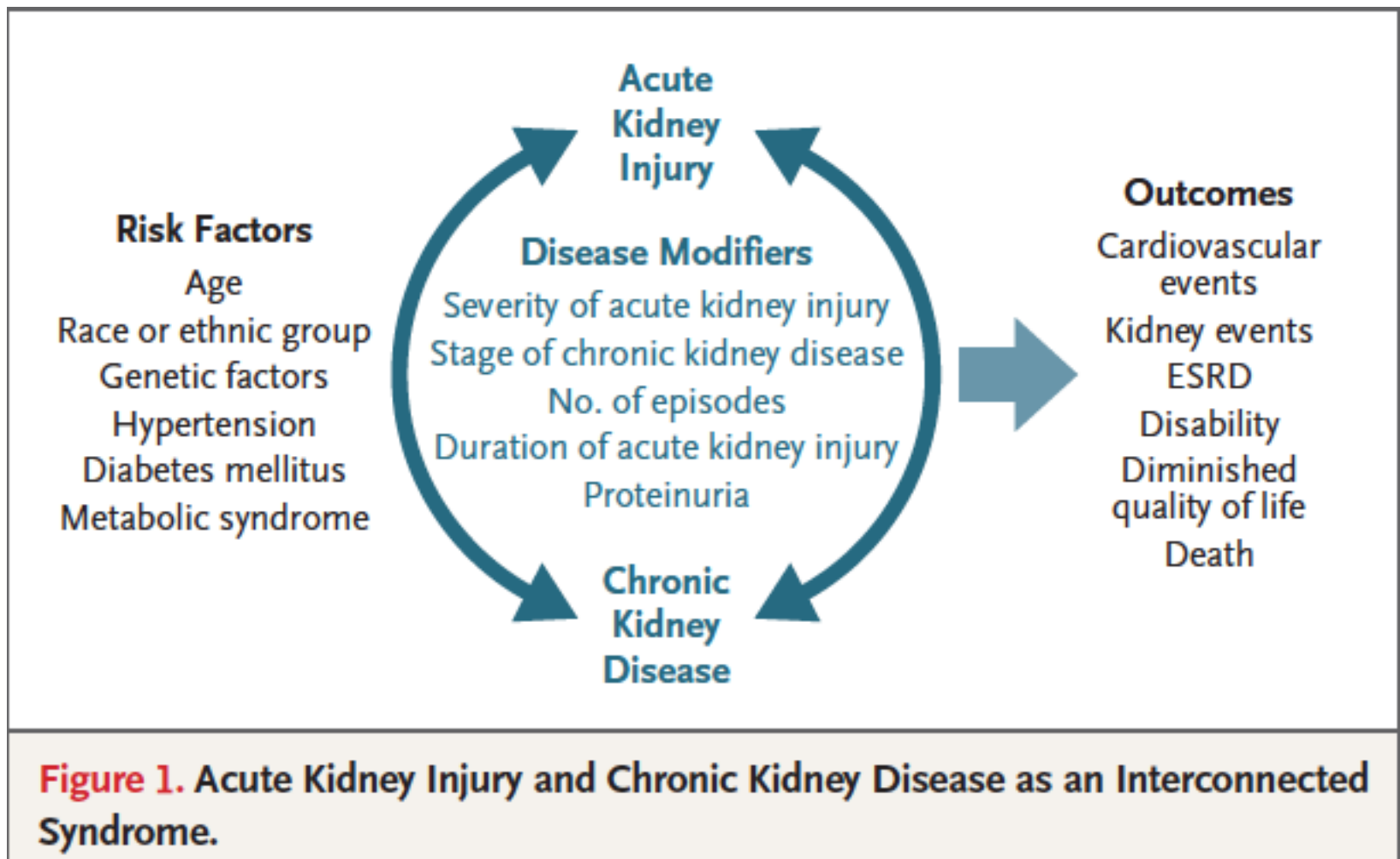
- All drugs stopped
 - IV fluids
 - IV ABs for community acquired pneumonia
- does well. Creatinine improves but settles at 201 after 5 days, K⁺ 5.2mmol/l
patient ready for discharge

Serial creatinine plot



AKI leads to CKD (in some people)





What is your post discharge plan?

- 76yr old male
- PMH
 - CKD stage 3A
 - CCF (LVEF <35%)
 - Previous AKI episodes x2
- DH
 - Aspirin 75mg od
 - Frusemide 80mg bd
 - Ramipril 10mg od
 - Spironolactone 25mg od
 - Allopurinol 300mg od
 - Atorvastatin 40mg od
 - Omeprazole 20mg od

What is your post discharge plan?

- 76yr old male
- PMH
 - CKD stage 3A
 - CCF (LVEF <35%)
 - Previous AKI episodes x2
- DH
 - Aspirin 75mg od
 - Frusemide 80mg bd
 - Ramipril 10mg od
 - Spironolactone 25mg od
 - Allopurinol 300mg od
 - Atorvastatin 40mg od
 - Omeprazole 20mg od
- Repeat U/Es – specify when?
- Restart meds – which ones and when?
- AKI avoidance advice
- Refer nephrology if non-recovery

Approach to AKI

AKI is a marker of the unwell patient



AKI is not a diagnosis



Treatment of AKI is basic medical care



Don't forget about post-AKI care

- Spot unusual features
- Dip the urine
- Rule out intrinsic dis and obstruction

- Go back and reassess
- Don't ignore the deteriorating patient