

Nephrology: Acute Kidney Injury Treatment and Prevention

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Lecture Modules

- Classification
- Treatment
- Prevention
- Renal Replacement Therapy
- Drug Toxicities

Classification

Question: 43 yo female is started on amoxicillin for sinusitis. Three days later, she presents for dysphoria and fatigue. Vital signs stable (VSS) and exam is unrevealing.

Labs show:

CBC normal; BMP with BUN 46/Cr 2.7

UA shows 3-5 WBCs with 80% eosinophils

What is the most likely diagnosis?

- A. Pyelonephritis
- B. Allergic interstitial nephritis
- C. Interstitial cystitis
- D. Drug fever

Answer Explanation

Correct answer is B

- This patient has a new exposure to a penicillin (PCN) class antibiotic and presents with AKI and eosinophiluria. This is the classic presentation of Allergic Interstitial Nephritis. Pyelonephritis would present with fever and an elevated WBC. Interstitial cystitis does not usually cause AKI. Fever is usually present in drug fever

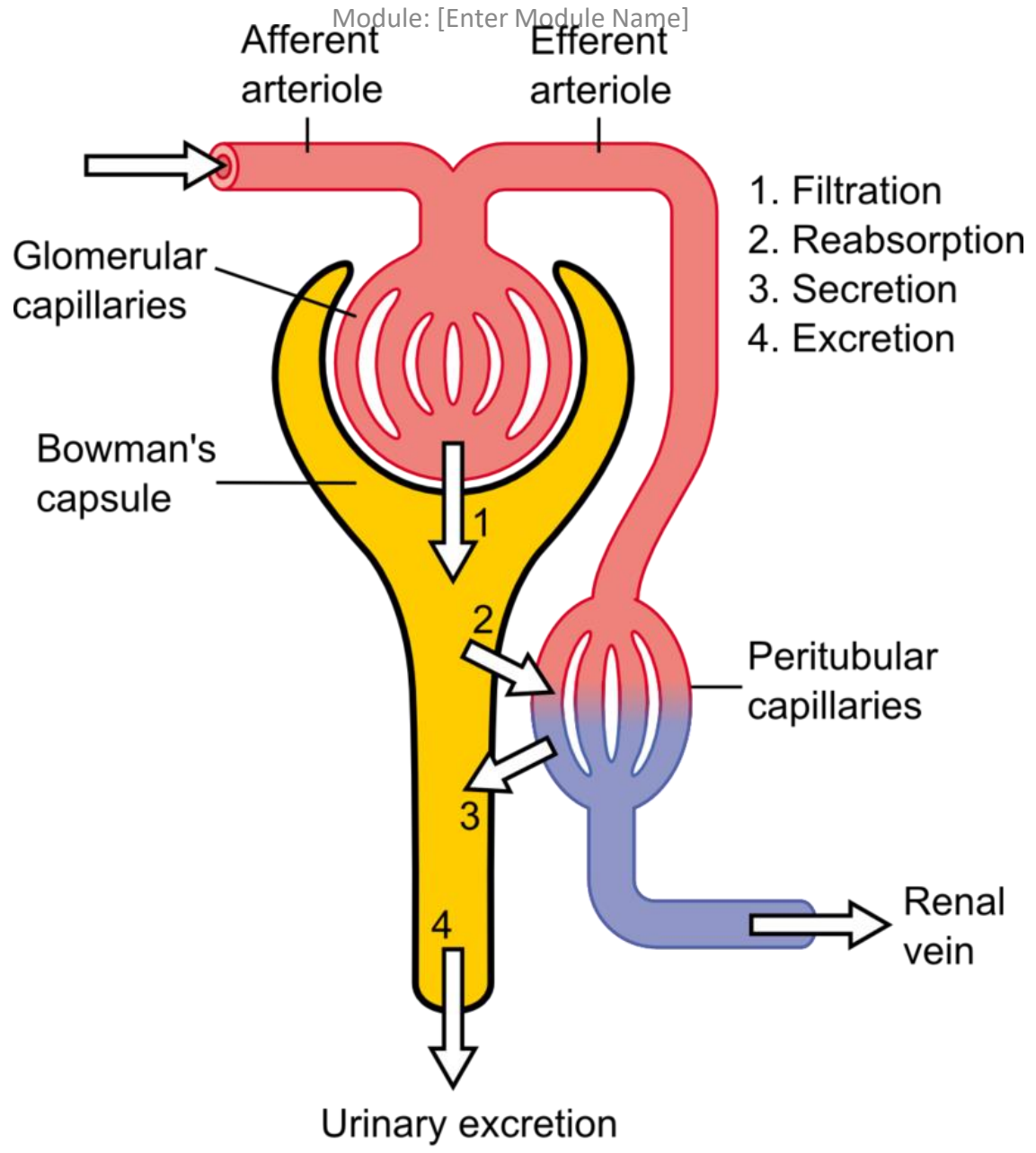
AKI – Classification

- Prerenal
- Intrarenal
 - Vascular
 - Glomerular
 - Tubular
 - Interstitial
- Postrenal



Prerenal

- This is the most common cause of AKI
 - 60%-70%
- Intravascular volume depletion
 - Fever, vomiting, diarrhea
 - Diuretics
 - Concept of effective arterial blood volume
 - More blood on venous side than arterial side (heart failure, cirrhosis)
- NSAIDs and ACEIs decrease glomerular perfusion pressure
 - NSAIDs block prostacyclin (PGI₂) and increase thromboxane (TXA₂)
→ vasoconstriction
 - ACEIs block production of angiotensin II causing vasodilation of the efferent arteriole
- Renal artery stenosis, atherosclerosis, and thrombi can decrease perfusion



$$\text{Excretion} = \text{Filtration} - \text{Reabsorption} + \text{Secretion}$$

Intrarenal

- Vascular
 - Atherosclerosis, continued state of poor renal blood flow
 - Microvascular and macrovascular disease
- Glomerular
 - Glomerulonephritis, consider nephrology consult
- Tubular
 - ATN from prolonged ischemia or toxins
- Interstitial
 - Acute interstitial nephritis

Acute Interstitial Nephritis (AIN)

- Often a result of an allergic reaction to a drug
- Fever and rash are common symptoms
- Serum and urine eosinophil counts may be elevated
- Autoimmune diseases, infections, and infiltrative disease can also cause AIN
- Remove potential drug causes and consider steroids

Postrenal

- Benign prostatic hypertrophy
- Catheters
- Tumors
- Strictures
- Crystal nephropathy (stones)
- These causes are frequently readily reversible. As such, it is imperative to rapidly exclude them
- Recovery of renal function is inversely proportional to the duration of obstruction
- Consider renal ultrasonography – no contrast dye used

Causes of AKI

Laboratory test	Prerenal	Intrarenal
BUN to creatinine ratio	>20:1	10 to 20:1
Urine specific gravity	>1.020	1.010 to 1.020
Urine osmolality, mOsm per kg	>500	300 to 500
FENa, percent	<1	>1-2
Urine sodium, mEq per L	<10	>20
Urine sediment	Hyaline casts	Granular casts

Fractional Excretion of Sodium

The FENa

- This calculation can be assist in distinguishing AKI from ATN
- If the kidney is still functioning in a prerenal state, it is trying to absorb all free water and sodium. This will leave a concentrated urine and the amount of urine sodium will be low
- If the kidney is losing function, it will “leak” sodium into the urine

Fractional Excretion of Sodium

The FENa

$$\frac{\text{Urine sodium/plasma sodium}}{\text{Urine creatinine/plasma creatinine}} \times 100$$

- A FENa <1% suggests preserved kidney function
- A FENa >2% suggests kidney failure

Acute Tubular Necrosis

- If prerenal injury is treated with fluids and removal of toxins, the kidneys often recover
- ATN occurs when a persistent prerenal state progresses to failure of kidney function
 - Heart Failure patient started in furosemide 40 mg bid with follow up in 2-4 weeks
- ATN has 3 phases
 - Initiation after the kidney damage/insult
 - Maintenance – usually lasts 1 to 2 weeks
 - Recovery – may be accompanied by marked diuresis and slow return of kidney function
- To date, no therapy has been shown to hasten recovery from acute tubular necrosis

Some Are Trying Starbucks to Induce Diuresis...to
No Avail



Classification Key Points

- Use the BUN/Cr ratio, the urine spec. grav., and the FENa to localize the renal disorder.
 - Specifically, a BUN/Cr>20 → prerenal
- Prevent ATN with adequate hydration in a prerenal condition.
 - Once ATN occurs, supportive care is key
- With AIN, remove offending agents and consider steroids
- Consider an ultrasound (U/S) to evaluate postrenal issues

Treatment

Question: A 44 yo male, previously healthy, has had nausea and vomiting for 3 days. He is now feeling weak and lightheaded when he stands. In the ED, his vital signs are:

T 99.3, P 105, RR 18, BP 94/52, PO2 99%

Labs are notable for BUN 54, Creatinine 1.9, Hgb 16.2

UA: spec grav 1.030, ketones 2+, blood neg, protein neg

Which of the following is the best treatment plan?

- A. Contrast CT of abdomen and pelvis
- B. IV normal saline at 100 cc/hr
- C. IV dopamine to maintain blood pressure
- D. IV normal saline at 200 cc/hr

Answer Explanation

Correct answer is D

- This patient has AKI from prerenal azotemia, dehydration, intravascular volume depletion. He should be treated with IVF in either boluses and 1.5-2x maintenance IV fluid rates. A CT with contrast may exacerbate the AKI. IV dopamine can maintain BP but does not prevent AKI. IVF at 100cc/hr is maintenance; 200cc/hr is therapeutic in prerenal AKI

AKI – Treatment

- Prerenal
 - Fluids
 - Removal of toxins
 - Maintenance of electrolytes
- Intrarenal/ATN
 - Fluid balance
 - Removal of toxins
 - Maintenance of electrolytes
 - Renal replacement therapy (hemodialysis)
- Postrenal
 - Relieve obstruction – place Foley catheter
 - Consider urology consultation
(or gynecology (GYN) if uterine fibroids)

IVF Maintenance Rate Calculation: 40/20/10

- The first 10 kg's of a patient's weight receive 40 cc/hr of IVF
- The second 10 kg's receive 20 cc/hr
- For every subsequent increment of 10 kg, the patient receives 10 cc/hr

- Of note, for fluid replacement, the rate is usually 1.5-2x maintenance

IVF Rate Calculation Example #1

- 90 kg patient
 - First 10 kg → 40 cc/hr
 - Second 10 kg → 20 cc/hr
 - 70 kg remaining...for each 10 kg pt receives 10 cc/hr → 70 kg = 70cc/hr
 - Total maintenance rate for a 90 kg pt = 130 cc/hr

IVF Rate Calculation Example #2

- 115 kg patient
 - First 10 kg → 40 cc/hr
 - Second 10 kg → 20 cc/hr
 - 95 kg remaining...for each 10 kg pt receives 10 cc/hr → 95 kg = 95 cc/hr
 - Total maintenance rate for a 90 kg pt = 155 cc/hr

Treatment Key Points

- Consider a trial of IV fluids in most patients, unless volume overloaded
- Remove offending agents/drugs
- Avoid contrast dye
- Remove obstruction if present
- Monitor electrolytes closely

Prevention

Question: A 65 yo female must undergo a contrast CT procedure. Which of the following therapies is most helpful to decrease the incidence of contrast nephropathy?

- A. Preprocedure IV fluids
- B. Furosemide (Lasix)
- C. Prednisone
- D. Lisinopril
- E. N-acetylcysteine (Mucomyst)

Answer Explanation

Correct answer is A

- Using IV fluids before and during a procedure has the strongest weight of evidence. There is no evidence that steroids prevent AKI. ACEIs and diuretics may induce AKI rather than prevent AKI. While acetylcysteine may have had some initial support for prevention, the current evidence is neutral, but not harmful

Practice Recommendation

Dopamine should not be used to prevent acute renal failure

Source: Bellomo R, Chapman M, Finfer S, et al. Low-dose dopamine in patients with early renal dysfunction: a placebo-controlled randomised trial. Australian and New Zealand Intensive Care Society (ANZICS) Clinical Trials Group. Lancet 2000;356:2139-43. Kellum JA, Decker MJ. Use of dopamine in acute renal failure: a meta-analysis. Crit Care Med 2001; 29:1526-31. Denton MD, Chertow GM, Brady HR. "Renal-dose" dopamine for the treatment of acute renal failure: scientific rationale, experimental studies and clinical trials. Kidney Int 1996;50:4-14.

Practice Recommendation

Diuretics should not be used to treat oliguria in patients with acute renal failure

Source: Cantarovich F, Rangoonwala B, Lorenz H, et al, High-dose furosemide for established ARF: a prospective, randomized, double-blind, placebo-controlled, multicenter trial. *Am J Kidney Dis* 2004;44: 402-9. Mehta RL, Pascual MT, Soroko S, et al, PICARD Study Group. Diuretics, mortality, and nonrecovery of renal function in acute renal failure. *JAMA* 2002;288:2547-53.

AKI – Prevention Strategies

- Maintain renal perfusion
 - Adequate oral hydration
 - Can elderly or bedbound respond to their thirst?
 - Take care when prescribing diuretics
 - Consider close follow up when initiating in at-risk patients
- Avoid nephrotoxins when possible
 - Outpatient meds to include NSAIDs, ACEIs, metformin

Prevention Key Points

- Avoid nephrotoxins when possible (NSAIDs)
- IV hydration preprocedure
- Mucomyst has minimal evidence of support
- Dopamine does not prevent AKI
 - It does, however, do a good job with low BP
- Diuretics are not effective in preventing AKI
 - Attempting to convert oliguric to nonoliguric AKI is not efficacious

Renal Replacement Therapy

Question: A 65 yo male with chronic CKD presents with altered mental status and an ABG with:

pH 7.2/pO₂ 75/pCO₂ 30/HCO₃ 25

BMP shows BUN/Cr = 89/6.5, and K⁺ = 7.1.

The best initial therapy at this point is:

- A. Bicarbonate drip
- B. Normal saline at 150cc/hr
- C. Renal replacement therapy (HD)
- D. Intubation and mechanical ventilation

Answer Explanation

Correct answer is C

- This patient has altered mental status, significant acidosis, and hyperkalemia. These are indications for renal replacement therapy. A bicarb drip does not rapidly correct AKI. Normal saline is not efficacious for this degree of acidosis. Intubation is not initially necessary in a patient that is still ventilating

Indications for Renal Replacement Therapy/Hemodialysis

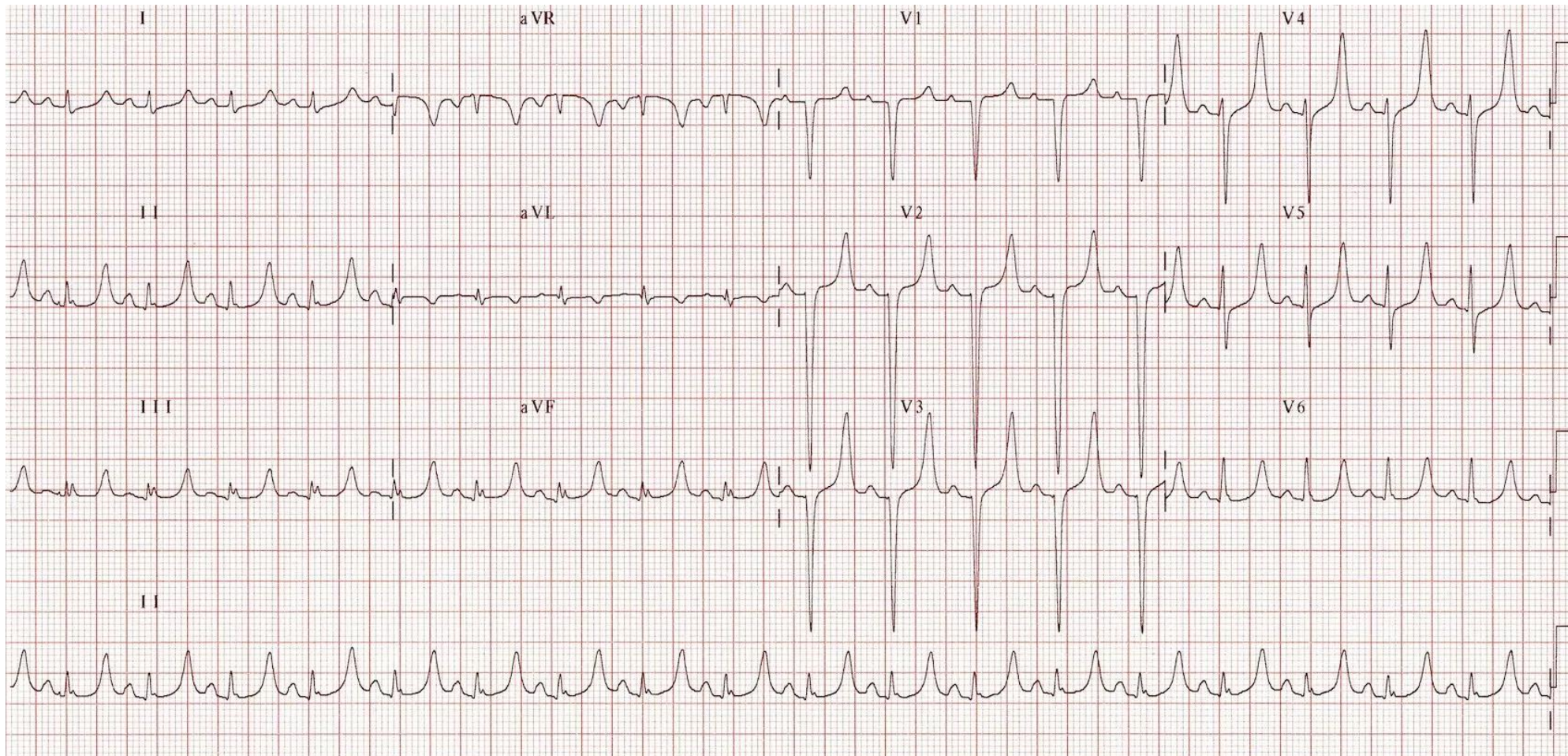
- Acidosis unresponsive to medical therapy
- Acute, severe, refractory electrolyte changes (e.g., hyperkalemia)
- Encephalopathy
- Significant azotemia (blood urea nitrogen level >100 mg per dL [36 mmol per L])
- Uremic pericarditis
- Volume overload

Hyperkalemia

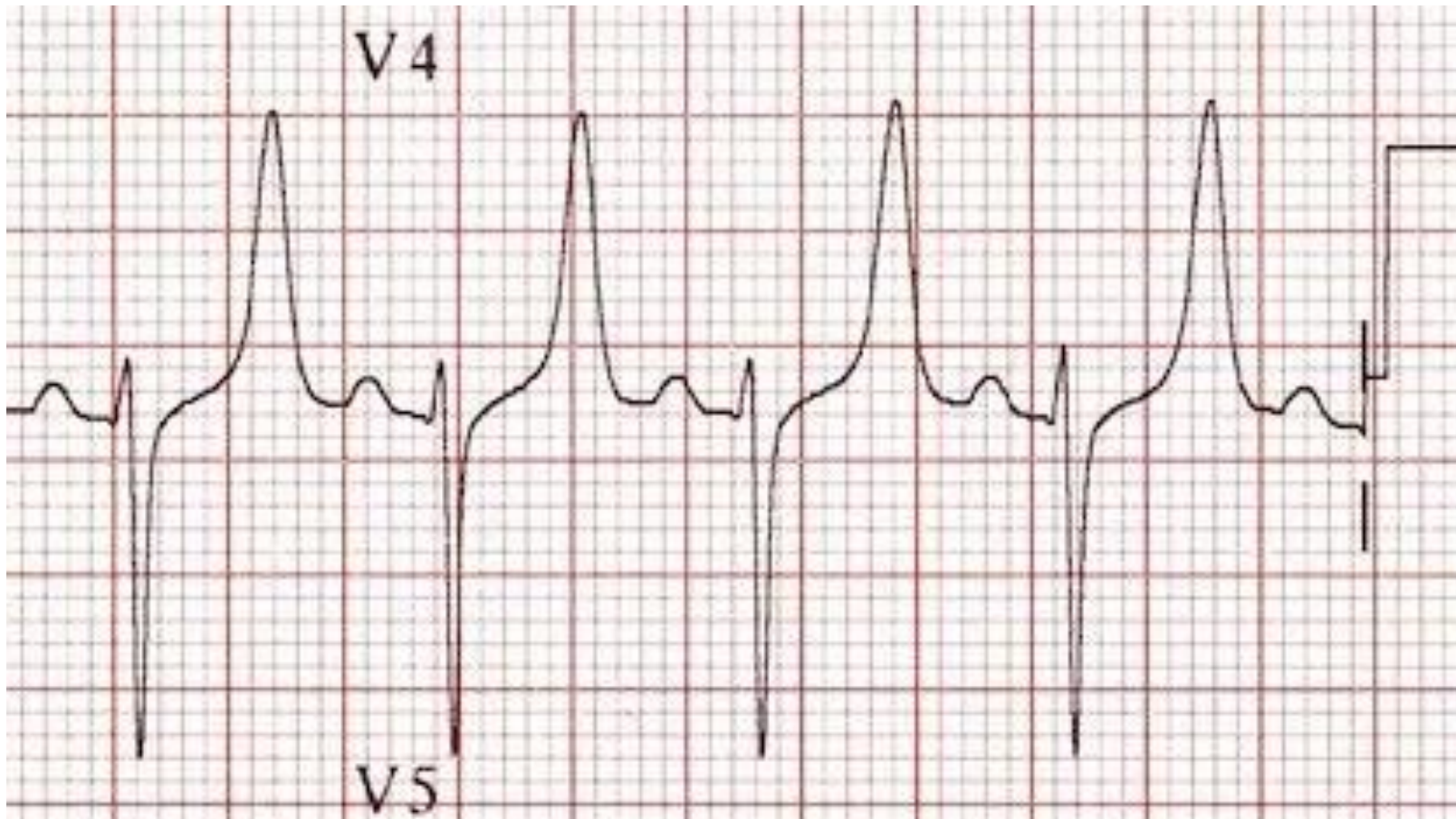
- Repeat the test to cure the acute Lab-oma
 - Secondary to hemolysis from the tourniquet
- Mild elevation of the potassium can be treated with GI resin binders
 - Sodium polystyrene sulfonate (Kayexalate)

Hyperkalemia – Severe

- Check for peaked T waves on the EKG
- If you don't want to sit on the T wave, it's peaked!



Hyperkalemia – Severe



Hyperkalemia – Severe Treatment

- IV insulin to push K^+ intracellularly
- IV glucose to draw K^+ and prevent hypoglycemia
- IV calcium to stabilize the cellular membranes, decrease dysrhythmias
- Remove etiologic agents
- Consider renal replacement therapy
- Consider bicarbonate if acidosis present
- Consider beta-agonists, e.g., albuterol
- Consider loop diuretics if kidneys functional

Renal Replacement Therapy (RRT)

Key Points

- Use RRT as indicated. Common uses
 - Volume overload
 - Unresponsive acidosis
 - Hyperkalemia
- Treat hyperkalemia urgently to stabilize conductive membranes and prevent dysrhythmias

Drug Toxicities

Question: Which drug has been associated with fatal lactic acidosis?

- A. Ramipril (Altace)
- B. Metformin (Glucophage)
- C. Sitagliptin (Januvia)
- D. Fomepizole (Antizol)

Answer Explanation

Correct answer is B

- None of the drugs mentioned except metformin is significantly associated with lactic acidosis. Of note, fomepizole is used to treat patients with ethylene glycol or methanol poisonings, often in combination with renal replacement therapy

Indications to Stop Metformin

- GFR < 30 mL/min – contraindication
- GFR 30-45 → not recommended to start
- GFR falls below 45 → assess risks vs benefits
- GFR falls below 30 → discontinue
- Patients scheduled for a contrast procedure and withhold for 48 hours after procedure. Verify renal function before re-instituting therapy @ 48 hours
- Patients scheduled for surgery
- Lactic acidosis - 50% mortality rate in some studies

Metformin – Cautions (for Reference)

- Heart failure: use caution in patients with congestive heart failure requiring pharmacologic management, particularly in patients with unstable or acute heart failure; risk of lactic acidosis may be increased secondary to hypoperfusion
- Hepatic impairment: avoid use in patients with impaired liver function due to potential for lactic acidosis

Selected Nephrotoxins

- Acyclovir (Zovirax)
- Aminoglycosides*
- Amphotericin B (Fungizone)
- Angiotensin-converting enzyme inhibitors*
- Cancer drugs: cisplatin (Platinol AQ), ifosfamide (Ifex)
- Cocaine
- Cyclosporine (Sandimmune)
- Foscarnet (Foscavir)
- Heavy metals
- Myeloma light chains
- Nonsteroidal anti-inflammatory drugs*
- Oxalic acid
- Pentamidine (NebuPent, Pentam 300, Pneumopent)
- Pigment: hemoglobin, myoglobin
- Radiocontrast media*
 - *Recent data suggest neutral risk*
- Uric acid

*Most common toxins

Practice Recommendation

Isotonic saline should be used for pre-hydration to decrease the incidence of acute renal failure

Source: Venkataraman R, Kellum J, Prevention of Acute Renal Failure. Chest 2007; 131: 300-308.

ACEI in AKI

- ACEIs provide protection from the progression of diabetic nephropathy
- When to start or stop with CRF?
- If starting an ACEI, the GFR may increase up to 30% and still be acceptable
- Any increase in GFR $> 30\%$ \rightarrow discharge (D/C) ACEI

When to Start or Remove ACEIs

- Consider ACEIs as initial therapy in most patients needing blood pressure control and renal protection
- If starting in patients with CKD stage 3-5 (GFR <60 ml/min), closely follow renal function and potassium, BUT do consider ACEIs
- If a patient is already on RRT (renal replacement therapy or dialysis), renal injury is no longer an issue

ACEIs vs. Angiotensin II Receptor Blockers (ARBs) in CKD

- ACEIs are first line to prevent and decrease the progression of nephropathy
- When a patient is ACEI intolerant (cough), consider an ARB

Drug Toxicities Key Points

- Do not use metformin when GFR <30
- Use one daily dosing of aminoglycosides when they're indicated
- When starting ACEIs, follow the creatinine
- Use NSAIDs only when necessary

