



Brigham and Women's Hospital

Founding Member, Mass General Brigham

TAKE HOME MESSAGES AND ADDITIONAL PEARLS IN NEPHROLOGY

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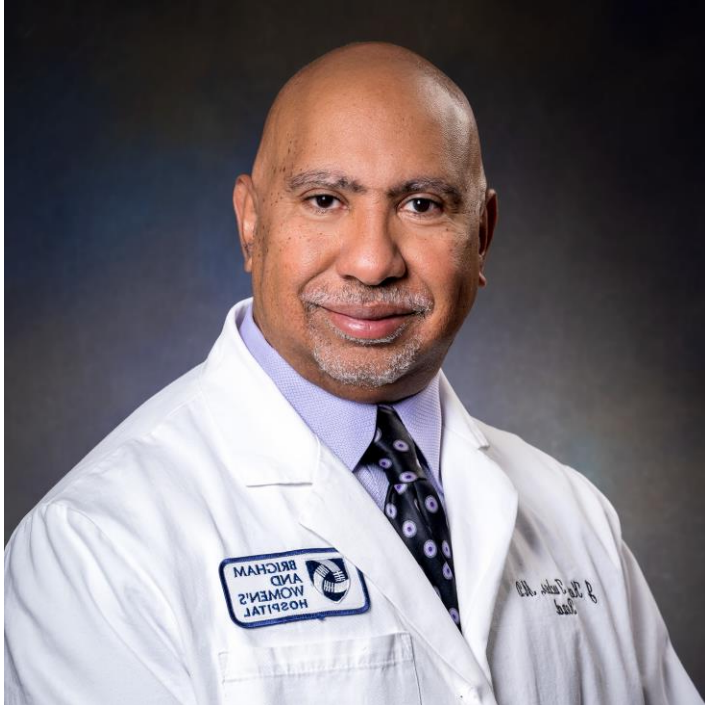
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Clinical focus: Hemodialysis and Peritoneal Dialysis

Disclosures

- None

Learning Objectives

- Understand common kidney disease related problems that arise in general internal medicine
- Apply physiologic principles to manage hyperkalemia
- Discuss strategies to treat anemia of chronic kidney disease
- Utilize conservative treatment strategies for advanced chronic kidney disease
- Review common scenarios of acute kidney injury

Case 1

An 80-year-old man who has been generally healthy and physically active—goes skiing every winter—presents to his primary care physician with complaints of feeling generally unwell with fatigue and nausea without vomiting. He denies any fevers, chills, cough, chest pain or dyspnea.

Past Medical History

- Hypertension
- BPH
- Hypercholesterolemia

Case 1-Medications

- Chlorthalidone 25 mg daily
- Atorvastatin 80 mg daily
- Tamsulosin 0.4 mg daily

Case 1-Physical Examination

- BP 131/78 mm Hg
- HR 82, regular
- T 98.2 degrees F
- No scleral icterus
- Chest clear
- RRR, normal heart sounds
- Abdomen soft and nontender
- Trace to 1+ pitting lower extremity edema

Case 1: Office management

No specific cause of the patient's symptoms were identified based upon the history and physical examination. The PCP asks the patient to go to the lab for blood tests, and she will follow-up with the patient depending upon the findings. The patient goes to the lab and then home.

About 4 hours later, the PCP receives an electronic alert related to "critical lab values."

Case 1: Critical Labs

- K^+ 7.2 mEq/L
- CO_2 16 mmol/L
- BUN 145 mg/dL
- Creatinine 11.3 mg/dL (3 months prior 0.91 mg/dL)
- Hemoglobin 9.1 g/dL (3 months prior 13.8 g/dL)

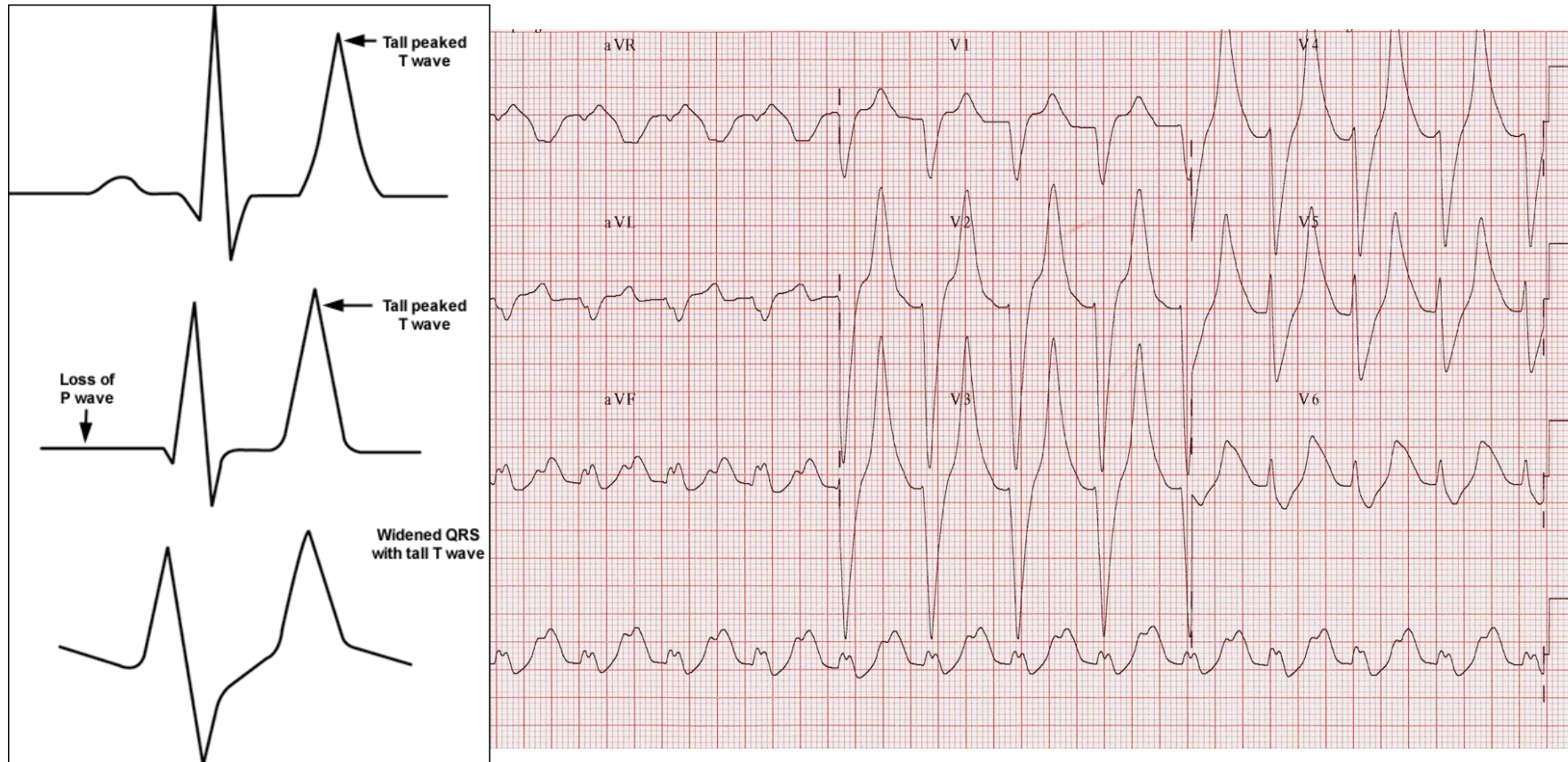
Case 1: Next steps

The PCP calls the patient and asks him to go the Emergency Department of the hospital with which she is affiliated for immediate treatment of hyperkalemia.

She enters an “expect note” in the electronic record advising that the patient will need immediate treatment for hyperkalemia.

Hyperkalemia

ECG Changes of hyperkalemia



<http://www.aafp.org/afp/2006/0115/p283.html>

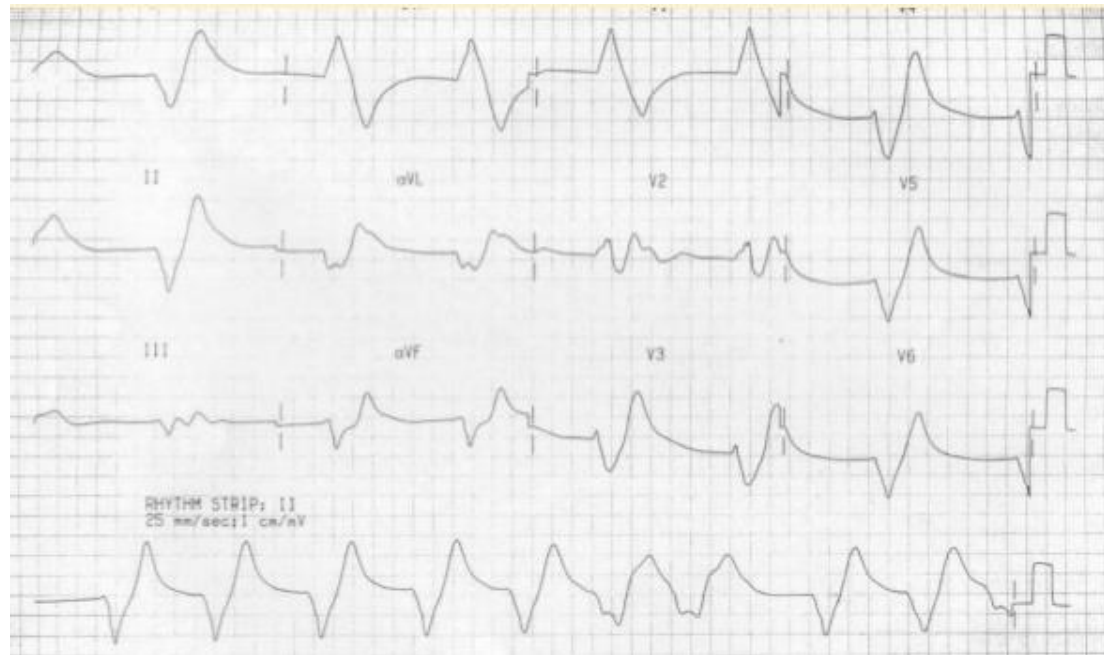
Peaked T waves

P wave wide and flat

Prolonged QRS interval with bizarre QRS morphology, high-grade AV block with slow junctional and ventricular escape rhythms, conduction block (bundle branch blocks, fascicular blocks)

(Development of a sine wave appearance (a pre-terminal rhythm))

Pre-terminal rhythm with very high K⁺



K = 9.9 mEq/L

SOURCE: <https://www.slideshare.net/ravirajmenon/hyperkalemia-56833946>

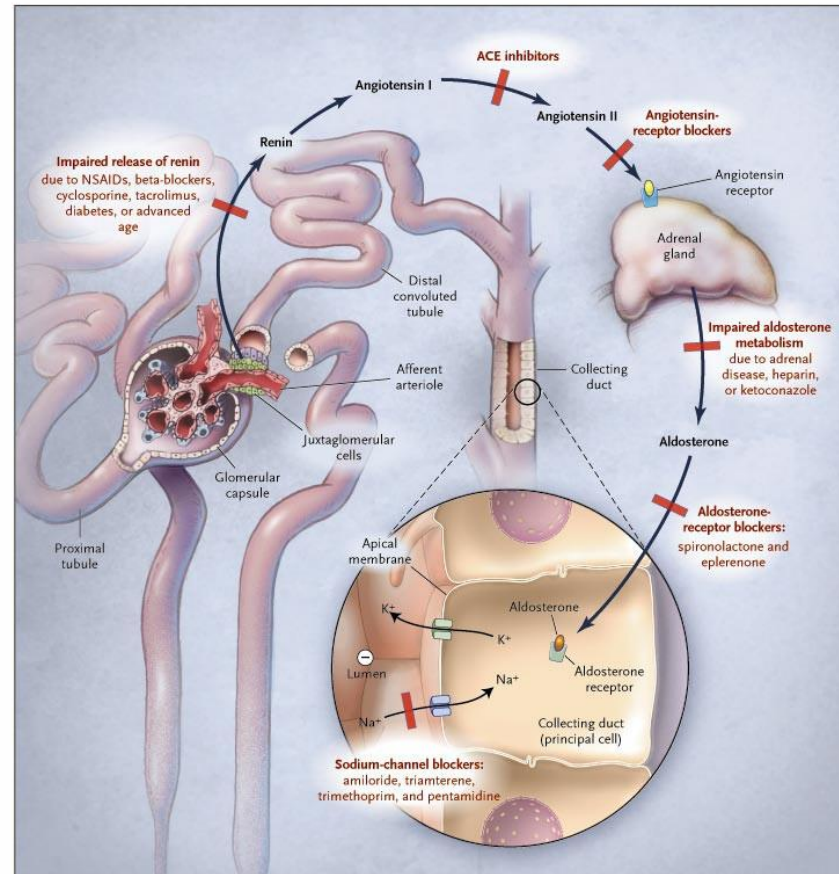
Causes of hyperkalemia

- Increased K⁺ intake
 - K⁺ supplements
 - Diet
 - Transfusions
- Decreased renal excretion
 - CKD, especially type IV RTA
 - Medications
 - NSAIDs
 - Amiloride
 - Trimethoprim
 - Triamterene

Causes of hyperkalemia

- Intra to extracellular shift
 - Insulinopenia
 - Hyperosmolarity
 - Medications (β blockers)
 - Metabolic acidemia
- Artifactual
 - In vitro hemolysis
 - Leukocytosis
 - Thrombocytosis

Regulation of Potassium Excretion in the Kidney

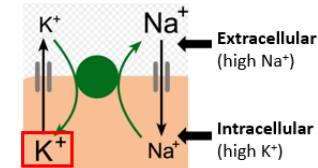


HyperK⁺ therapies harness normal physiology!

IV insulin +/- dextrose
Albuterol (β-agonist)



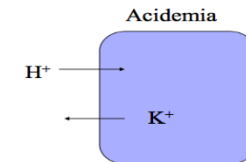
Increased activity of the Na⁺-K⁺ ATPase
(more K⁺ into the cell)



Bicarbonate infusion



H⁺-K⁺ exchange moves
more K⁺ **into** the cell



K⁺ excretion



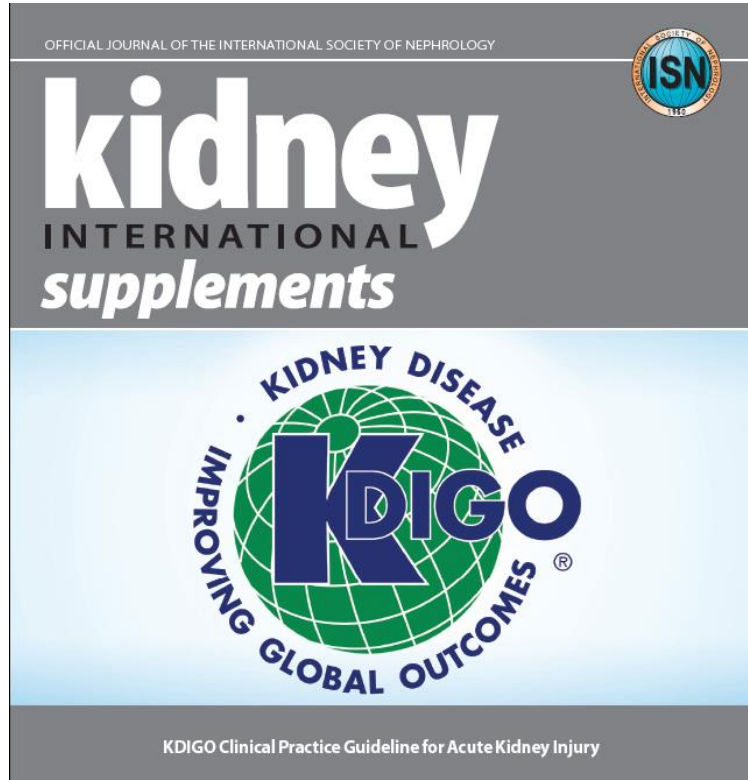
Sodium polystyrene sulfonate
Patiromer
Sodium zirconium cyclosilicate
Loop diuretics

Sodium polystyrene complications

- Ischemic colitis and colonic necrosis
 - Greater risk with enema form
 - Often fatal
 - Greater risk with sorbitol but can occur without sorbitol
 - Post-transplant and post-operative patients at greater risk
- Volume overload
- Reduction in serum calcium
- Iatrogenic hypokalemia

Acute Kidney Injury

Current Consensus Definition of AKI



Kidney Int, 2012

Slide Courtesy of Dr. David Leaf

“KDIGO” Definition of AKI

Any of the following:

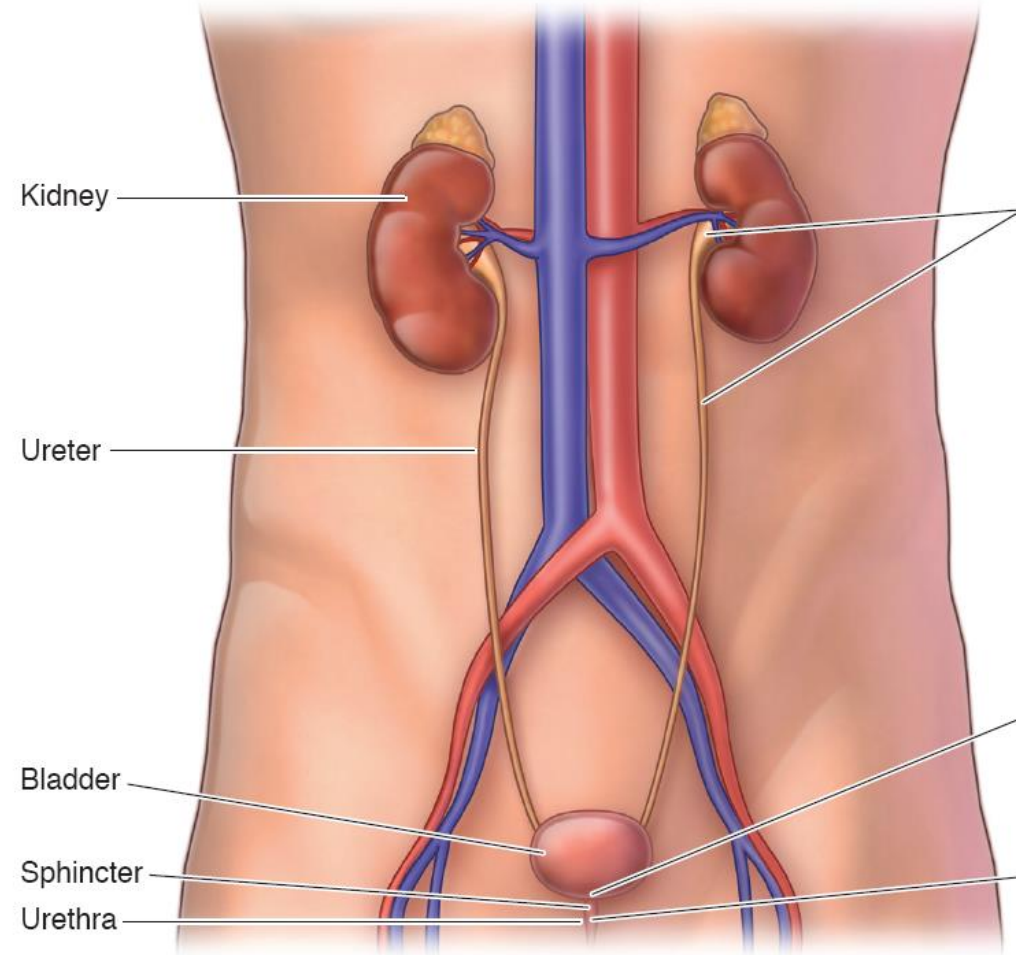
- $\uparrow \text{SCr} \geq 0.3 \text{ mg/dL}$ in 48h or $\geq 50\%$ in 7d
- Oliguria ($\text{UOP} < 0.5 \text{ ml/kg/h} \times 6\text{h}$)
- Dialysis

Approach to the patient with AKI

Pre-Renal

Intrinsic Renal

Post-Renal



Waikar & Bonventre, AKI chapter in Harrison's Principles of Internal Medicine, 18th ed.

Workup of patient's kidney disease

- Creatinine was normal 3 months prior
- Demographic clue: 80-year-old man
- History of BPH
- Diagnostic test: Renal Ultrasound
 - Bilateral hydronephrosis

Hydronephrosis

Grades of hydronephrosis



Hydronephrosis



normal



mild



moderate



severe

Case 1 Follow-Up

After confirmation of bilateral hydronephrosis, a Foley catheter was placed with immediate drainage of a liter of urine and continued brisk urine output. The potassium had fallen within one hour by 1 mEq/L, and over the ensuing eight hours completely normalized.

The patient had no EKG changes of hyperkalemia so never received any adjunctive therapies.

Case 2

A 62-year-old woman with a 10-year history of CKD from diabetes has slowly worsening renal function. She sees you in the office and says that she is feeling well, working full time and exercising.

Past Medical History

- Hypertension
- Diabetes mellitus type 2
- Hypercholesterolemia
- CVA

Case 2-Physical Examination

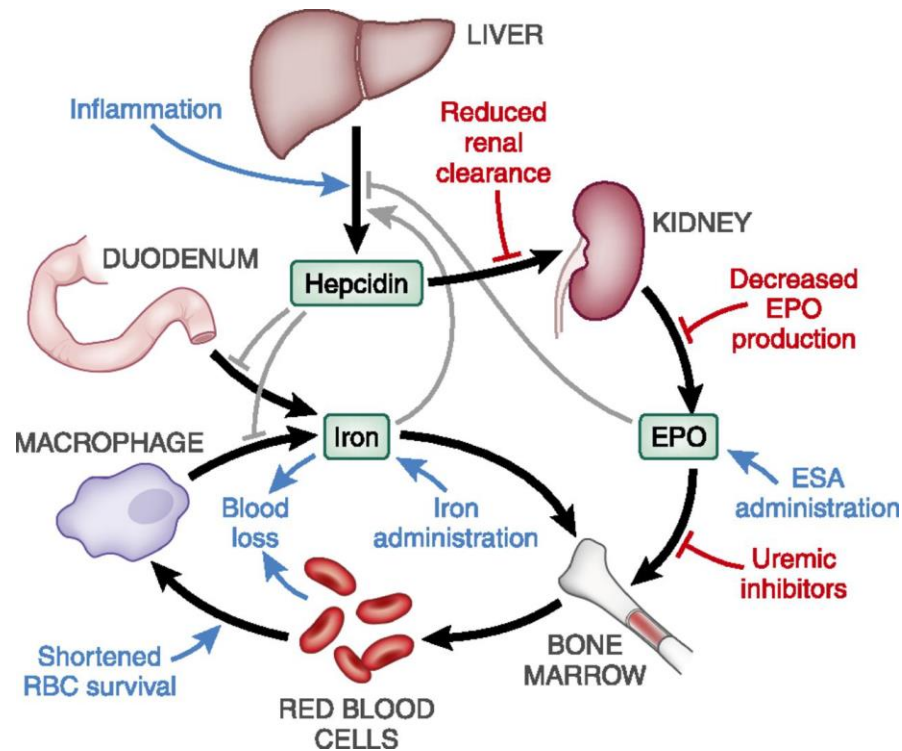
- BP 122/69 mm Hg
- HR 76, regular
- T 98.6 degrees F
- No scleral icterus
- Chest clear
- RRR, normal heart sounds
- Abdomen soft and nontender
- No lower extremity edema

Case 2: Labs

- BUN 48 mg/dL
- Creatinine 4.2 mg/dL
- eGFR 18 mL/min/1.73m²
- Hemoglobin 9.1 g/dL
- T-sat 30%
- Ferritin 282 ug/L

Anemia

Anemia in CKD patients



- Causes include
 - Iron deficiency (reduced absorption, poor intake)
 - Blood loss (frequent blood draws, GI bleeding)
 - Relative erythropoietin deficiency

Where are We Now?

Despite EPO therapy costing billions of dollars each year, anemia is sub-optimally treated in CKD patients

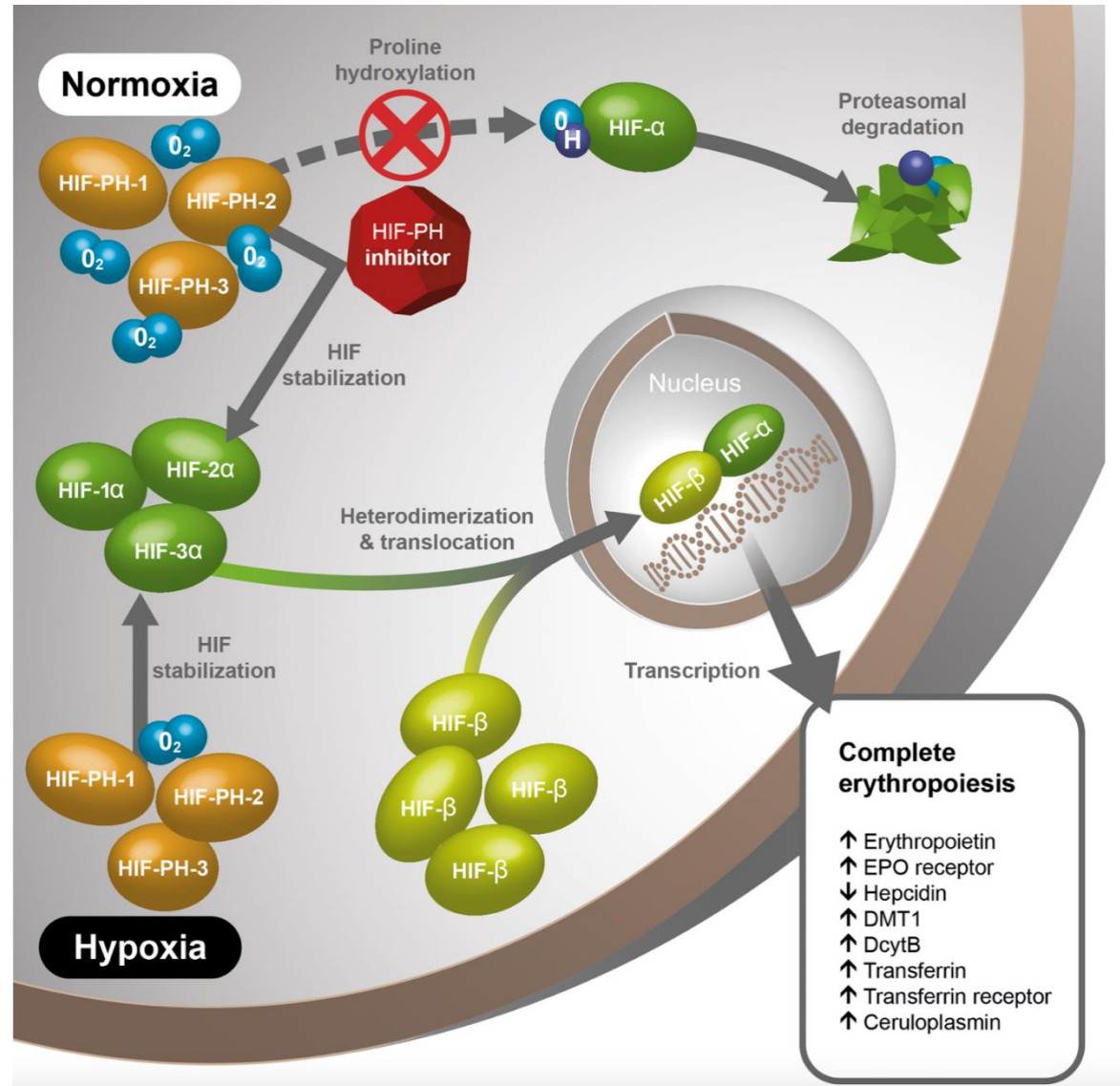
- Normalization of Hb associated with increased mortality and CVD risk
- No consistent and meaningful improvement in quality of life
- Patients treated to subnormal Hb target of 10-11 g/dL in US and 10-12 g/dL in Europe
- Patients require SC/IV injection, increased visits to health care provider
- Higher health systems costs

Anemia Treatment in Dialysis and Non-Dialysis Patients

- Don't need treatment if patient asymptomatic with Hb >10 g/dL (usually start treatment Hb <10 g/dL)
- Make sure patient is iron replete
 - TSAT >20%, Ferritin >100
- Target range: Hb 10-11 g/dL
- Use an ESA (2 ESA's in US – EPO or Darbepoietin)
- Newer ESA's – prolyl hydroxylase inhibitors (PHIs) not approved in US currently (for non-dialysis patients)
- Be cautious with ESA treatment in patients with a history of stroke and/or cancer

Innovation: New drugs to treat anemia of chronic kidney disease

- HIF prolyl hydroxylase inhibitors
 - Stabilize the HIF complex
 - Stimulate endogenous EPO production
 - Orally administered



Why look for alternatives to erythropoietin?

- Cost
- Intravenous or subcutaneous route of administration
- Adverse cardiovascular events
 - CHOIR study: erythropoietin: more CHF in high-hemoglobin group
 - TREAT study: diabetic subjects; more strokes in high hemoglobin group

Vadadustat receives approval for treatment of anemia in ESRD

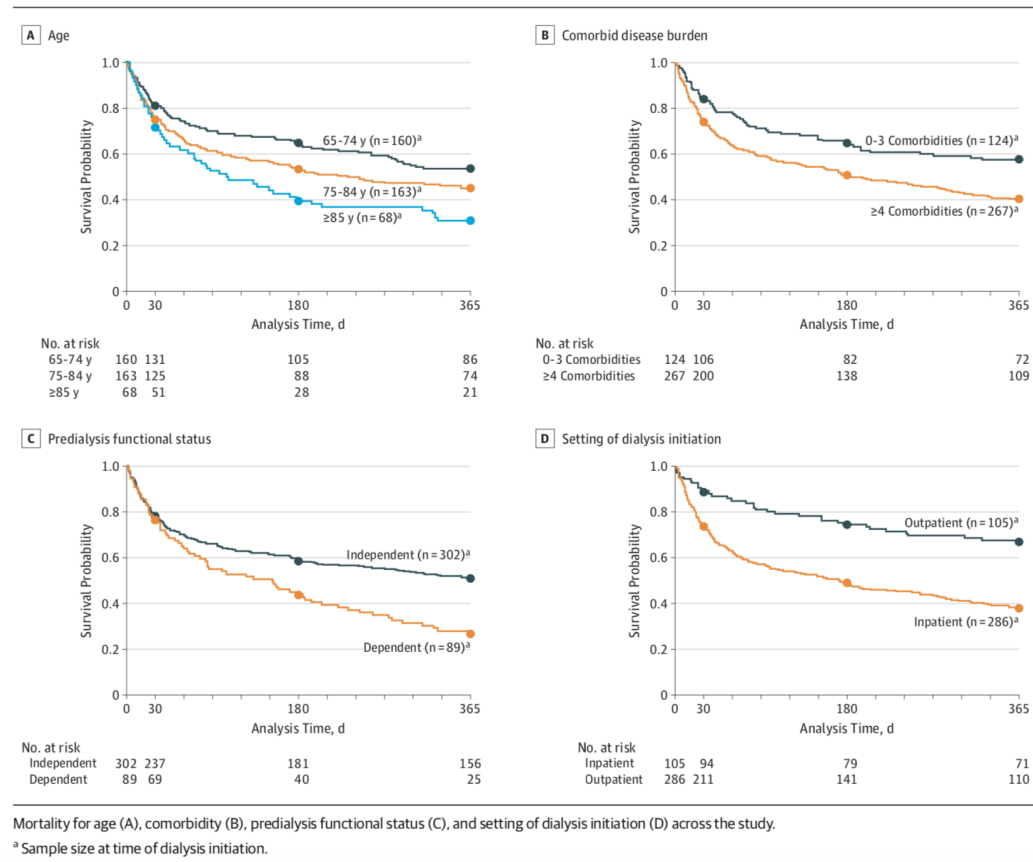
- FDA approved vadadustat for treatment of anemia in anemia of ESRD in patients *who have been receiving maintenance dialysis for at least three months*
- Currently the only HIF-PH inhibitor available in the United States

Case 3

An 81-year-old woman with advanced chronic kidney disease is admitted to hospital from a skilled nursing facility for worsening kidney function. Her creatinine has risen over the last several months to 5.0 mg/dL with an eGFR of 8 mL/min. Her potassium is 4.9 mEq/L and CO₂ is 19 mmol/L. Hemoglobin is 8.9 g/dL. Her co-morbidities include type 2 diabetes and hypertension. She has been bedbound since a CVA seven months prior. Her appetite has been stable. She has no specific symptoms of uremia.

Conservative management

High mortality among the elderly starting dialysis



Wachterman M *et al* JAMA Internal Med. 2019; 179: 987-990

Long-term Outcomes Among Patients with Advanced Kidney Disease Who Forgo Maintenance Dialysis

- Systematic review of 41 cohort studies comprising 5102 adults with advanced kidney disease who did not pursue dialysis
- Forty-one cohort studies comprising 5102 patients (range, 11-812 patients) were included in this systematic review .
- Median survival of cohorts ranged from 1 to 41 months as measured from a baseline mean estimated glomerular filtration rate ranging from 7 to 19 mL/min/1.73 m²
- Patients generally experienced 1 to 2 hospital admissions, 6 to 16 in-hospital days, 7 to 8 clinic visits, and 2 emergency department visits per person-year.

Long-term Outcomes Among Patients with Advanced Kidney Disease Who Forgo Maintenance Dialysis

- During an observation period of 8 to 24 months, mental well-being improved, and physical well-being and overall quality of life were largely stable until late in the illness course.
- Among patients who died during follow-up, 20% to 76% had enrolled in hospice, 27% to 68% died in a hospital setting and 12% to 71% died at home; 57% to 76% were hospitalized, and 4% to 47% received an invasive procedure during the final month of life.
- Many patients who do not pursue dialysis survived several years and experienced sustained quality of life until late in the illness course. Nonetheless, use of acute care services was common and intensity of end-of-life care highly variable across cohorts.

Conservative management

- Conservative (non-dialysis) therapy may be appropriate in some patients
 - No increase in survival and no improvement in quality of life in frail elderly who are started on dialysis
- Engage the multidisciplinary team to manage complications
- Refer to hospice care when appropriate



References

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- Gupta N and Wish JB. Am J Kidney Dis 2017; 69: 815-826
- Babitt JL and Lin HY 2012; J Am Soc Nephrol 2012; 1631-1634
- KDIGO Clinical Practice Guideline for Acute Kidney Injury 2012; Kidney Int 2012; Volume 2, Supplement 1
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- Wong SPY *et al* *JAMA Netw Open*. 2022;5(3):e222255