MAYO CLINIC

Nephrology and Hypertension

Board Review Cases

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Learning Goals

- To review pertinent Nephrology and Hypertension topics
- To provide an update on recent seminal studies

NO DISCLOSURES

Case #1

A 67-year-old man is seen for increase in serum creatinine level and abnormal urinalysis found during evaluation of monoclonal gammopathy of undetermined significance (MGUS). His evaluation revealed a M–protein spike of 1.5 g/dL, <10% clonal plasma cells on bone marrow biopsy, and no evidence of anemia, hypercalcemia or lytic bone lesions skeletal survey. Immunofixation revealed IgG as the monoclonal type. He has no constitutional symptoms, no other medical problems, and takes no medication.

On physical examination, vital signs are normal. Trace lower extremity edema is noted. The reminder of the examination is unremarkable.

Case #1

Laboratory studies:

Albumin	3.6 g/dL (36 g/L)
Creatinine	1.6 mg/dL (141.4 µmol/L)
Urinalysis	pH 5.5; 2+ blood; 3+ protein; 5-8 erythrocytes/hpf
Urine albumin-creatinine ratio	400 mg/g

Case #1

Which of the following is the most appropriate next diagnosed test?

A. ANCA testing

B. β_2 microglobulin levels

C. Kidney biopsy

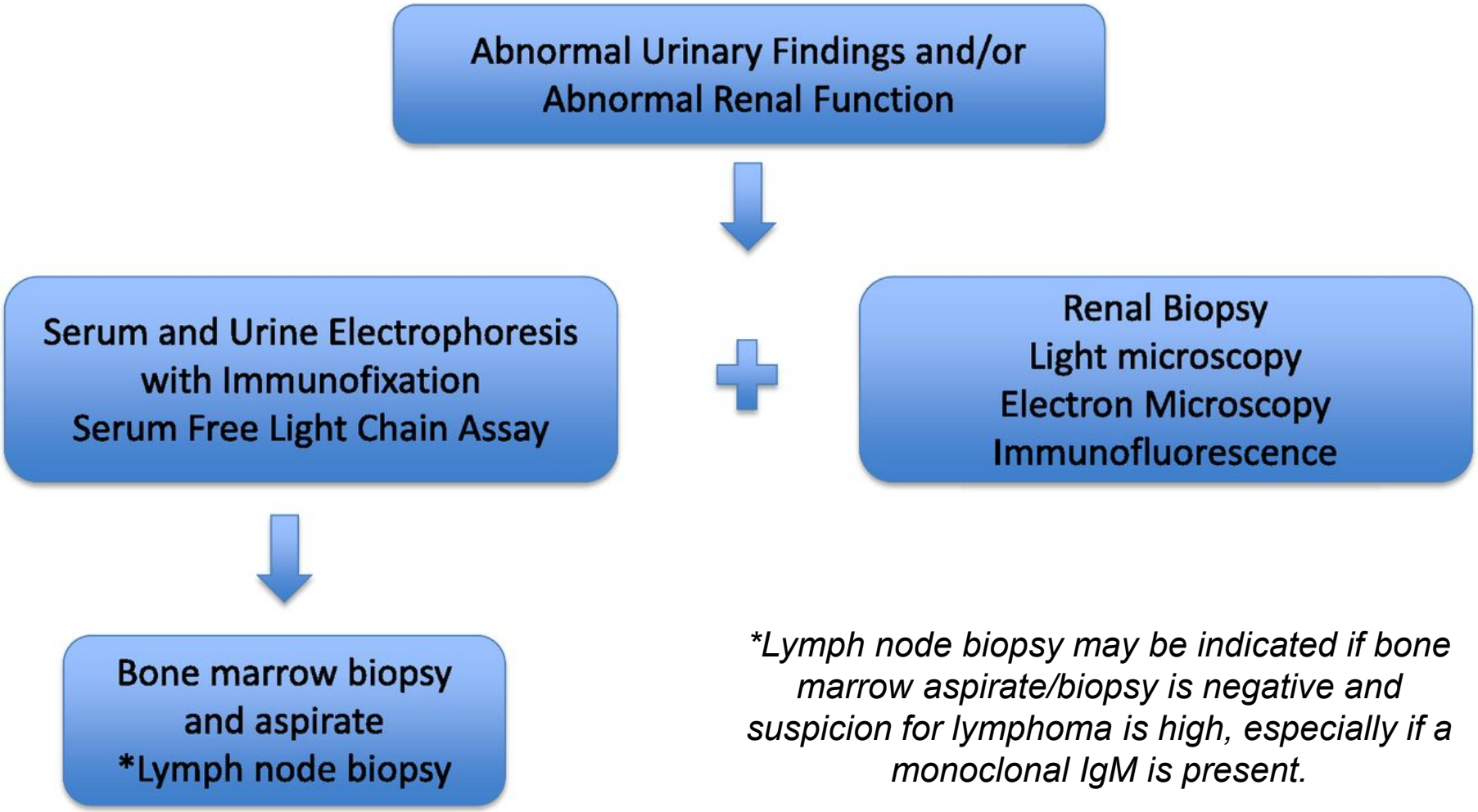
D. Serum free light chain

Case #1 Answer

- Monoclonal gammopathy of renal significance (MGRS) is diagnosed in patients who otherwise meet the criteria for MGUS but have an abnormal urine analysis and renal insufficiency; a kidney biopsy confirms the diagnosis
- The diagnosis of MGRS renal disease can be challenging, because the spectrum of renal manifestations is very wide, and the detection of the pathogenic immunoglobulin can be difficult

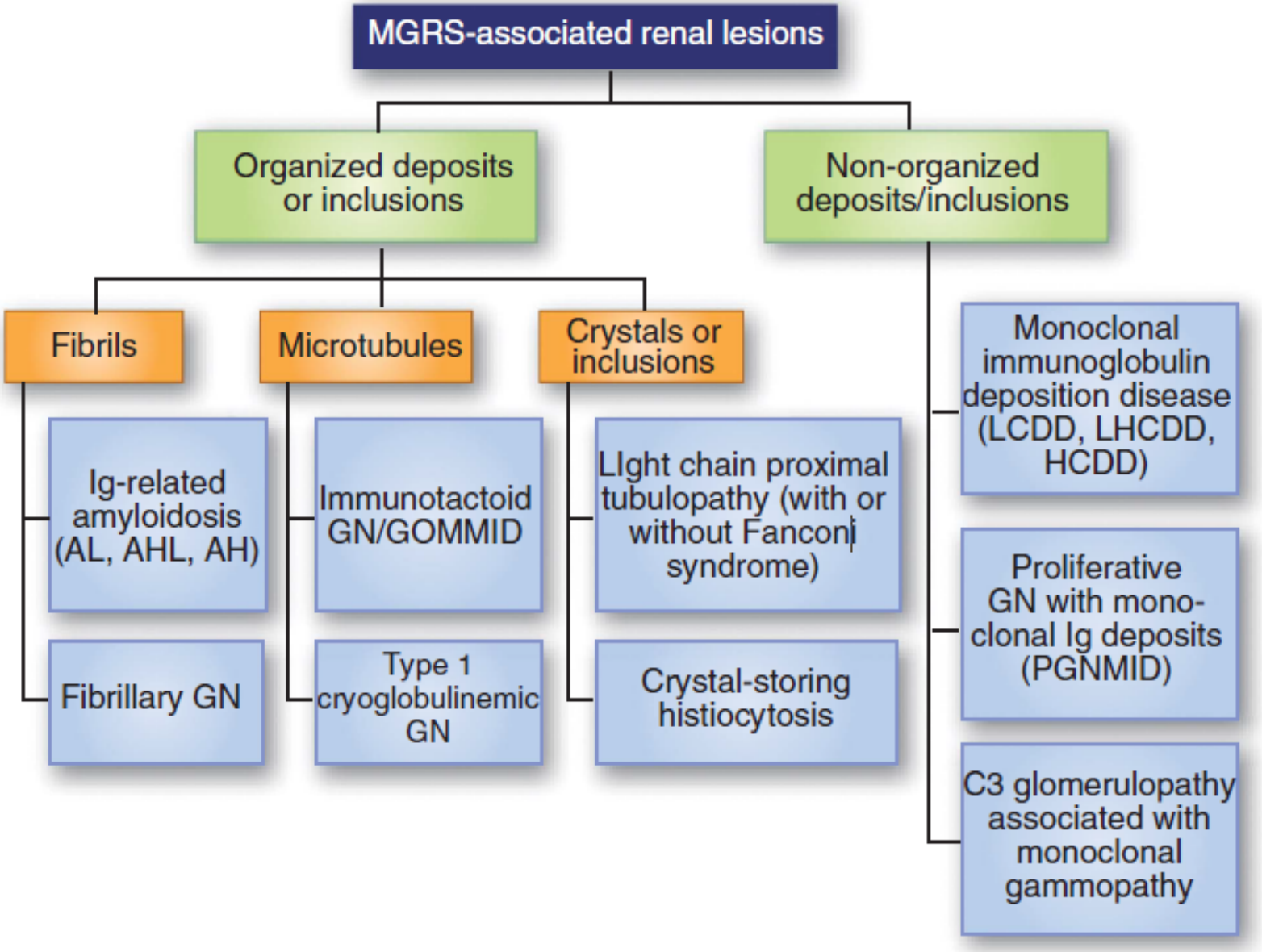
Rosner, MH et al: CJASN 2016

Diagnostic evaluation of paraprotein–related kidney disease



**Lymph node biopsy may be indicated if bone marrow aspirate/biopsy is negative and suspicion for lymphoma is high, especially if a monoclonal IgM is present.*

Rosner, MH et al: CJASN 2016



Bridoux, F et al: KI,2015

Case #2

A 38-year-old man is evaluated after passing his second kidney stone. History is significant for chronic pancreatitis secondary to a past history of alcohol abuse. Has 3-4 loose bowel movements each day. He reports no fever, flank pain, or dysuria. There is no family history of kidney disease, hyperparathyroidism, or nephrolithiasis. Current medications are pancreatic enzymes and multivitamins. Physical examination reveals a thin man. Vital signs and the remainder of examination are unremarkable.

Case #2

Laboratory studies:

Calcium	8.5 mg/dL (2.1 mmo/L)
Creatinine	0.7 mg/dL(61.9 µmol/L)
Electrolytes:	
Sodium	137 mEq/L(137mmol/L)
Potassium	3.5 mEq/L(3.5mmol/L)
Chloride	104 mEq/L(104mmol/L)
Bicarbonate	21mEq/L(21mmol/L)
Urinalysis	Specific gravity; pH 5.0; negative dipstick; positive for calcium oxalate crystals

Case #2

In addition to increasing fluid intake, which of the following is the most appropriate management?

A. Add allopurinol

B. Add potassium citrate

C. Add vitamin-C

D. Decrease calcium take

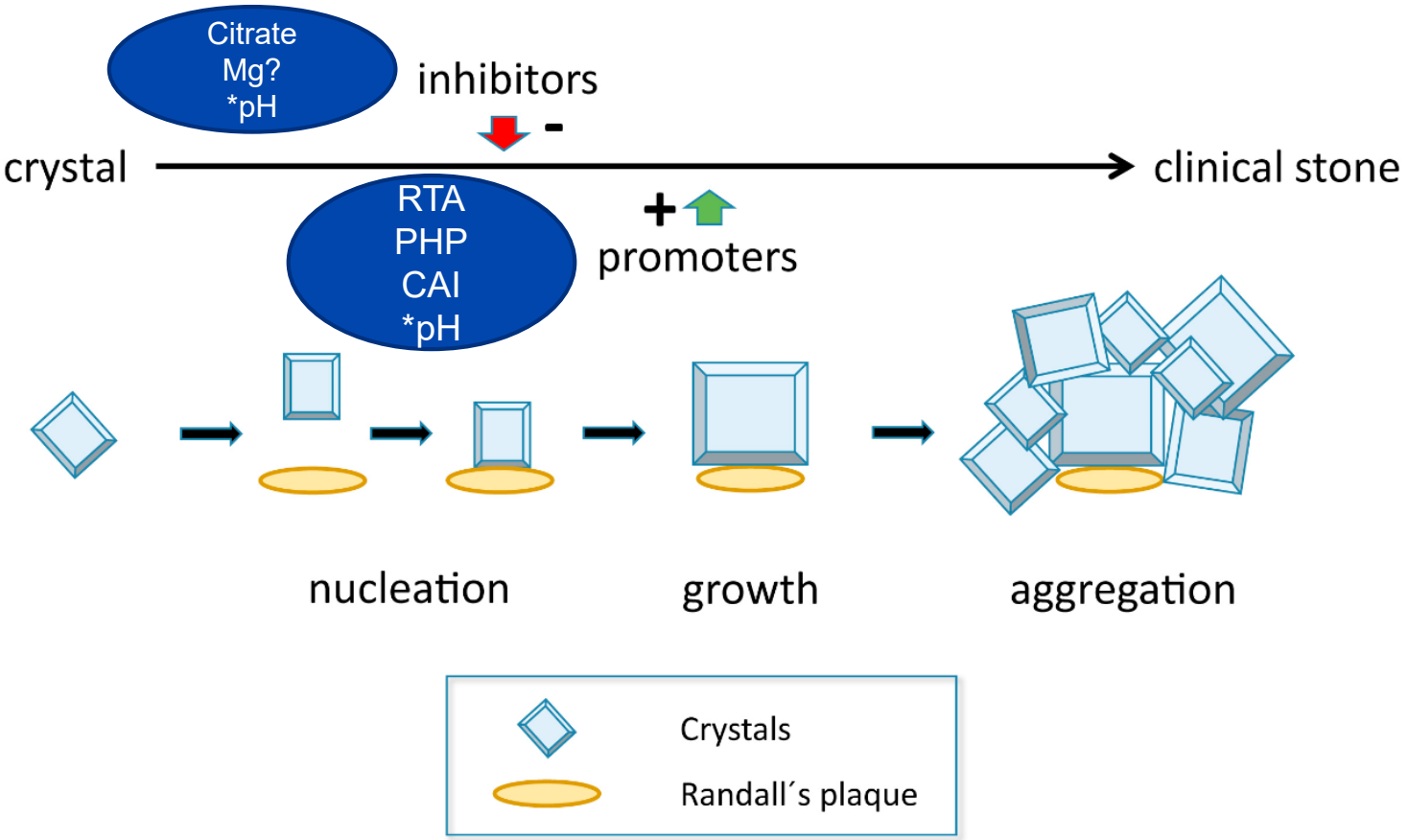
E. Increase protein intake

Case #2 Answer

- Potassium citrate can be used to help prevent calcium oxalate stones in patients with chronic diarrhea and malabsorption
- In the setting of diarrhea and metabolic acidosis, urine citrate, an inhibitor of crystallization, is often reduced and the calcium and oxalate concentration in the urine is increased due to dehydration
- In fat malabsorption calcium binds to fat as opposed to oxalate, living oxalate free to be absorbed and be excreted in the urine

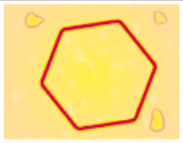
Pfau, A et al: AJKD, 2016

Mechanisms of Stone Formation



Modified from Pfau, A et al: AJKD, 2016

Kidney Stone type

Stone type	Morphology of Associated Crystals (Urine Microscopy)	Urinary Risk Factor	Clinical Settings
Calcium oxalate monohydrate	Dumbbell 	Hypercalciuria	Hyperparathyroidism, immobilization, vitamin D excess, sarcoidosis, Cushing syndrome, high sodium intake, genetic disorders (eg, Dent disease), idiopathic, etc
		Hyperoxaluria	• Increased oxalate absorption (eg, bowel pathologies) • Primary hyperoxaluria • Excess vitamin C intake
Calcium oxalate dihydrate	Envelope (X) 	As outlined for calcium oxalate monohydrate	As outlined for calcium oxalate monohydrate
Calcium phosphate	Flat shaped or wedge-shaped prisms; prisms often in rosettes 	• Hypercalciuria • Hypocitraturia • Urine pH > 7	• As outlined for calcium oxalate monohydrate • Distal renal tubular acidosis • Drugs with carbonic anhydrase inhibitory function (eg, topiramate, acetazolamide)
Struvite	Coffin-lid 	High levels of ammonium and bicarbonate	Urinary tract infections with urease-splitting microorganisms
Uric acid	Rhomboid/ football-shaped; multiple forms possible; often yellow/brown 	• Urine pH < 5.5 • Hyperuricosuria	Patients with metabolic syndrome, insulin resistance, type-2 diabetes
Cystine	Hexagonal 	Cystinuria	Genetic disorder

Pfau, A et al: AJKD, 2016

Case #3

A 48-year-old woman is evaluated in the emergency department for a 1-day history of hearing voices. History is significant for bipolar disorder. Medications are lithium carbonate and quetiapine. On physical examination, the patient is disheveled and looks chronically ill. She is alert oriented, but appears anxious. Blood pressure is 138/78 mmHg, and pulse rate is 80/min without orthostatic changes. There is no edema. The reminder of examination is normal.

Case #3

Laboratory studies:

BUN	6 mg/dL (2.1 mmo/L)
Creatinine	0.9 mg/dL(79.6 µmol/L)
Electrolytes:	
Sodium	126 mEq/L(126mmol/L)
Potassium	3.5 mEq/L(3.5mmol/L)
Chloride	94 mEq/L(94mmol/L)
Bicarbonate	26 mEq/L(26mmol/L)
Glucose	156 mg/dL(8.7mmol/L)
urine sodium	12 mEq/L(12mmol/L)
urine osmolality	96 mOsm/Kg H_2O

Case #3

Which of the following is the most likely cause of this patient's hyponatremia?

A. Hyperglycemia

B. Nephrogenic diabetes insipidus

C. Polydipsia

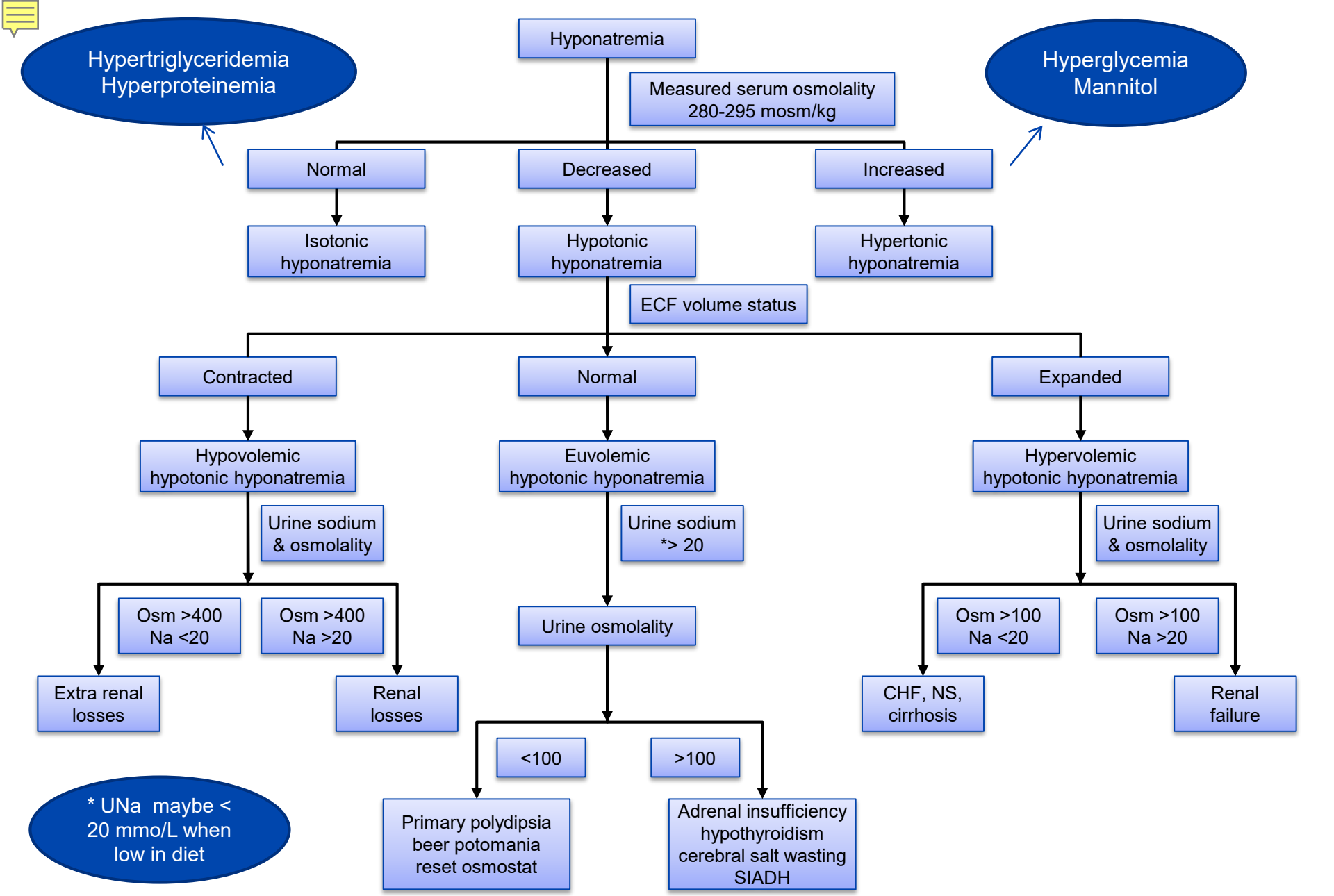
D. Syndrome of inappropriate antidiuretic hormone secretion

E. Volume depletion

Case #3 Answer

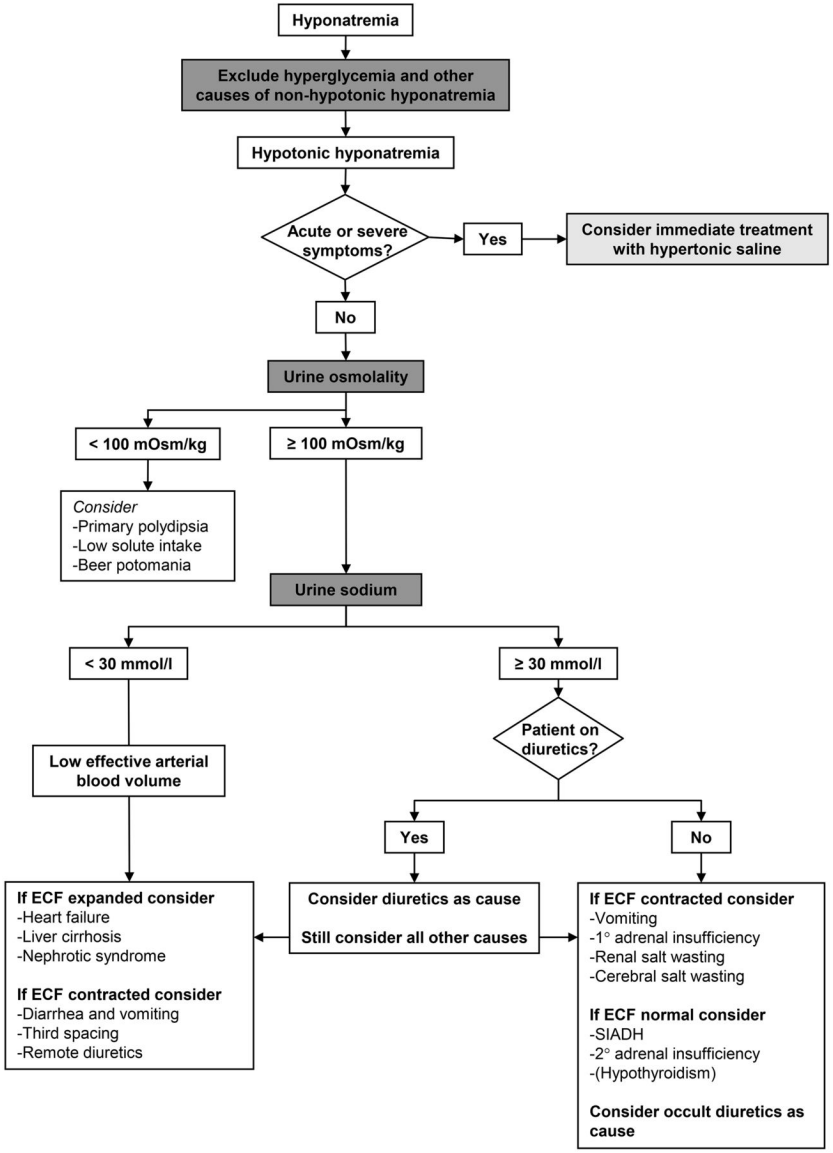
- Isovolemic hypotonic hyponatremia associated with urine osmolality < 100 Osm/Kg H_2O indicates excessive water intake, as seen with psychogenic polydipsia or poor solute intake
- Isovolemic hypotonic hyponatremia secondary either to impaired dilution of urine or to water intake that exceeds the kidney's ability to excrete diluted urine

Hoorn EJ & Zietse R: JASN, 2017



Modified from Reddy and Mooradian: Int J Clin Pract, 2009

Diagnostic algorithm for hyponatremia.



Case #4

A 75-year-old woman is hospitalized for a 1-week history of dizziness, nausea, vomiting, increased urination, and decreased appetite. History is significant for hypertension treated with hydrochlorothiazide. She also takes calcium carbonate for bone health.

On physical examination, blood pressure is 150/85 mmHg supine and 122/70 mmHg standing, pulse rate 78/min supine in 100/min standing, and respiration rate is 18/min. There is no neck vein distention. Cardiac, pulmonary and abdominal examination is unremarkable there is no lower extremity edema.

Case #4

Laboratory studies:

Hematocrit	30%
Leukocyte count	3000/µL(3.0 x10^9/L)
Platelet count	82,000/µL(82x10^9/L)
Calcium	12.8mg/dL (3.2 mmo/L)
Creatinine	3.7 mg/dL(327.1 µmol/L)
Electrolytes:	
Sodium	132 mEq/L(132mmol/L)
Potassium	4.9 mEq/L(4.9mmol/L)
Chloride	115 mEq/L(115mmol/L)
Bicarbonate	17 mEq/L(17mmol/L)

Case #4

Laboratory studies:

Phosphorus	6.2 mg/dL(2 mmol/L)
urine sodium	15 mg/L(15 mmol/L)
Urinalysis	Specific gravity 1.018; trace protein, few erythrocytes/hpf, occasional leukocytes/hpf, few granular casts, numerous hyaline casts

Case #4

Which of the following is the most likely cause of this patient's and acute kidney injury?

A. Hydrochlorothiazide therapy

B. Milk alkali syndrome

C. Multiple myeloma

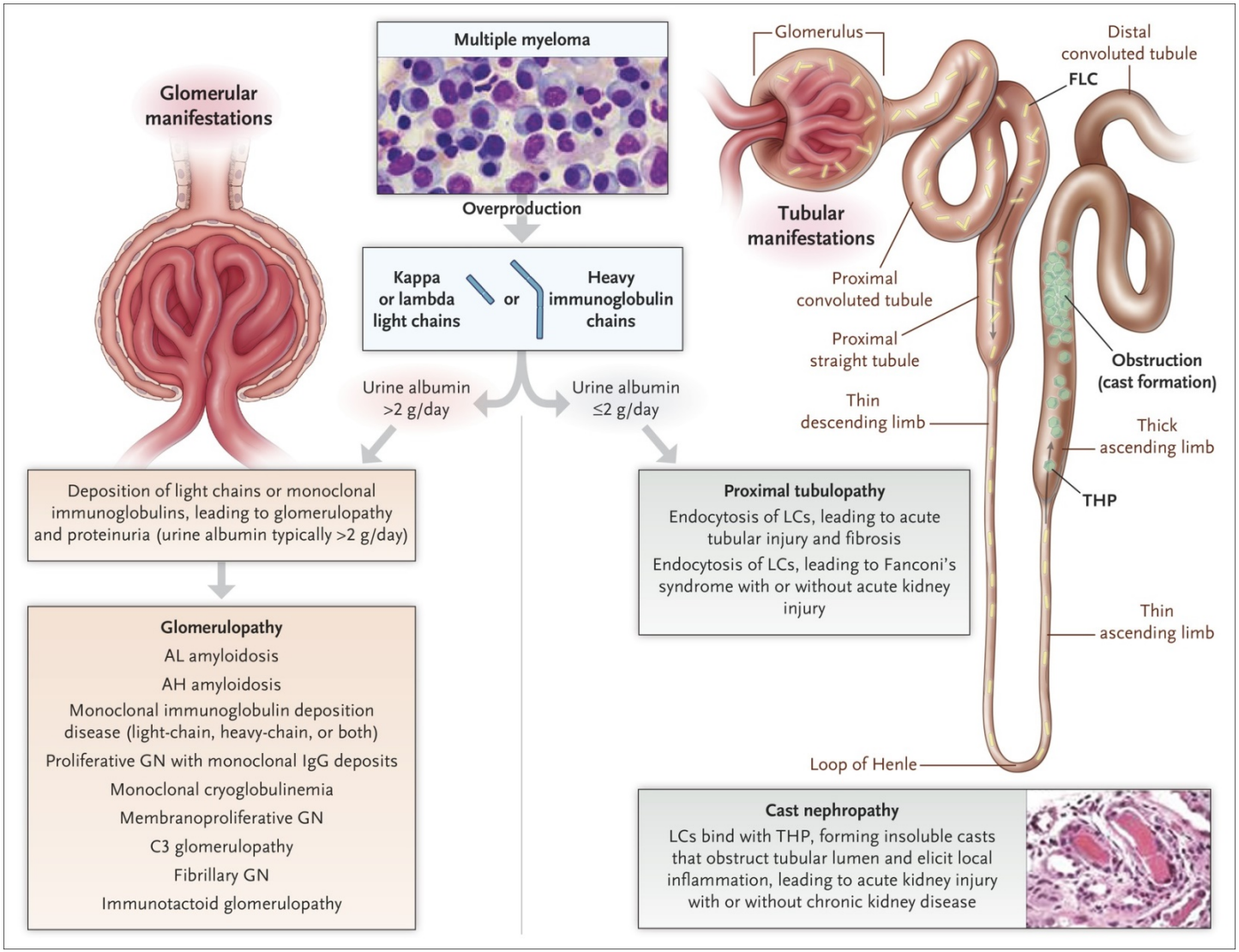
D. Primary hyperparathyroidism

Case #4 Answer

- A diagnosis of multiple myeloma is suggested by the constellation of anemia, hypercalcemia, normal anion gap metabolic acidosis, and acute kidney injury

Rosner, MH & Perazella, MA: NEJM, 2017

Diagnostic Approach to Patients Presenting with Acute Kidney Injury and Suspected Myeloma



Rosner, MH & Perazella, MA: NEJM, 2017

Case #5

A 25-year-old woman is evaluated in the emergency department after suicide attempt. History is significant for major depression. She takes no medication.

On physical examination temperature is normal, blood pressure is 142/92 mmHg, pulse rate 110/min, and his respiration rate 22/min. The patient is obtunded. The remainder of the exam is normal.

Case #5

Laboratory studies:

Blood urea nitrogen	28 mg/dL(10 mmol/L)
Creatinine	2.2 mg/dL(194.5 µmol/L)
Electrolytes:	
Sodium	136 mEq/L(136mmol/L)
Potassium	4.0 mEq/L(4.0mmol/L)
Chloride	100mEq/L(100mmol/L)
Bicarbonate	12 mEq/L(12mmol/L)
Ethanol	Undetected
Glucose	90 mg/dL(5mmol/L)
Osmolality	314 mOsm/Kg H_2O
Arterial blood gases	
pH	7.25
PCO_2	28 mmHg (3.7 κPa)

Case #5

Which of the following is the most appropriate management?

A. Activated charcoal gastric decontamination

B. Intravenous Ethanol

C. Intravenous hydration, fomepizole and hemodialysis

D. Intravenous sodium bicarbonate

Case #5 Answer

- Management of ethylene glycol toxicity in the context of organ-specific toxicity, severe acidemia, or with very large ingestions, includes aggressive fluid resuscitation, fomepizole and hemodialysis
- Typical findings of ethylene glycol toxicity include CNS depression, an increased anion gap metabolic acidosis and an increase in osmolal gap
- Osmolal gap is considered elevated when the measured osmolality excedes the calculate osmolality by > 10 mOsm/Kg H_2O
- Serum osmolality (mOsm/kg of H2O)

= 2Na (mEq/L) + SUN(mg/dL) /2.8 + glucose (mg/dL) /18

Kruse, JA: Crit Care Clin, 2012

Disorders Linked to High-Anion-Gap Metabolic Acidosis and an Increase in Serum Osmolal Gap

- Methanol intoxication
- Ethylene glycol intoxication
- Diethylene glycol intoxication
- Propylene glycol intoxication
- Isopropanol intoxication
- Lactic acidosis
- Alcoholic or diabetic ketoacidosis
- Acute kidney injury
- Salicylate intoxication

	High Anion Gap
G	Glycols
O	Oxoproline
L	L-Lactate
D	D-Lactate
M	Methanol
A	Aspirin
R	Renal failure
K	Ketoacidosis
S	Sodium Thiosulfate

Kraut, JA & Xing, SX: AJKD, 2011

Disorders Linked to High-Anion-Gap Metabolic Acidosis and an Increase in Serum Osmolal Gap

- Increased serum osmolal gap with or without high-anion-gap metabolic acidosis can be an important clue to toxic alcohol intoxications
- The presence and magnitude of serum osmolal gap depends on several factors, including molecular weight of the offending alcohol, baseline serum osmolal gap, and state of metabolism of the parent alcohol
- Patients with toxic alcohol intoxications can present with an increase in serum osmolality alone, increased serum osmolality and high-anion-gap acidosis, or increased-anion-gap acidosis alone
- Rare cases in which both serum osmolality and anion gap are within reference ranges also might occur

Kraut, JA & Xing, SX: AJKD, 2011

Disorders Linked to High-Anion-Gap Metabolic Acidosis and an Increase in Serum Osmolal Gap

- Kidney failure, lactic acidosis, and diabetic ketoacidosis also can cause high-anion-gap metabolic acidosis associated with a large serum osmolal gap
- Given the potential severity of all these disorders, they should be excluded in all individuals presenting with serum osmolal gap, serum osmolal gap and high-anion-gap metabolic acidosis, or high-anion-gap metabolic acidosis alone

Kraut, JA & Xing, SX: AJKD, 2011

Case #6

A 68-year-old woman is evaluated during follow-up visit for 3-week history of nephrotic syndrome. She otherwise has been well and reports no additional symptoms. She has a 50-pack-year history of cigarette smoking with ongoing tobacco use. On physical examination, vital signs are normal. Pitting edema to the ankles is present. The reminder of the examination is unremarkable.

Case #6

Laboratory studies:

Albumin	2.9 g/dL(29g/L)
C3	Normal
C4	Normal
Creatinine	Normal
Rapid plasma reagin	Normal
Antinuclear antibodies	Normal
Hepatitis B antibodies	Normal
Hepatitis C antibodies	Normal
24 hrs urine protein excretion	10000 mg/24hs

Case #6

Kidney ultrasound shows normal-appearing kidneys with no evidence of thrombus in the renal veins. Lower extremity Doppler ultrasounds showed no evidence of deep venous thrombosis. The kidney biopsy shows membranous glomerulopathy with negative staining for phospholipase A2 receptor (PLA2R) on immunofluorescence.

Case #6

Which of the following is the most appropriate management?

A. Age- and sex-appropriate cancer screening

B. Immunosuppression therapy

C. Prophylactic anticoagulation

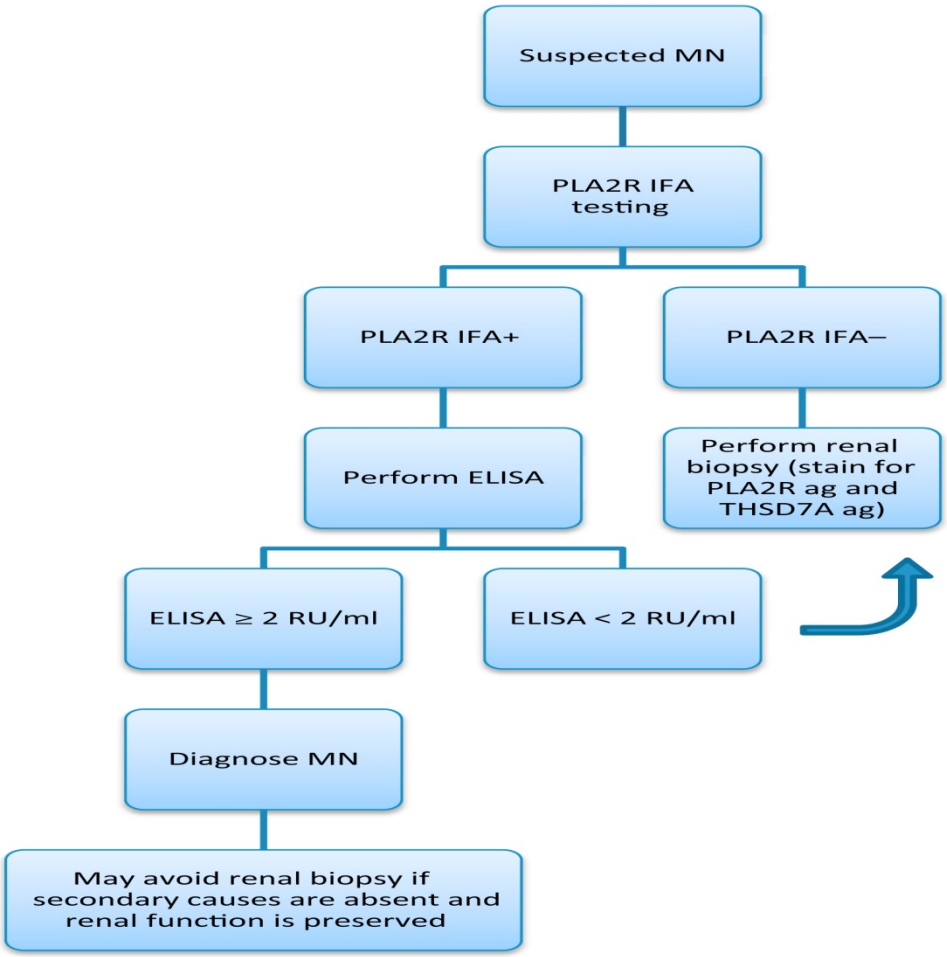
D. Serologic testing for anti-PLA2R antibodies

Case #6 Answer

- The association between membranous nephropathy (MN) and cancer has been well documented
- Approximately 75% of the cases of MN are idiopathic (+PLA2R) , whereas the remainder are associated with infections, malignancies, autoimmune diseases and drug toxicity
- Initial step in the management of newly diagnosed MN is to evaluate for secondary forms of the disease, which account for approximately 25% of the case

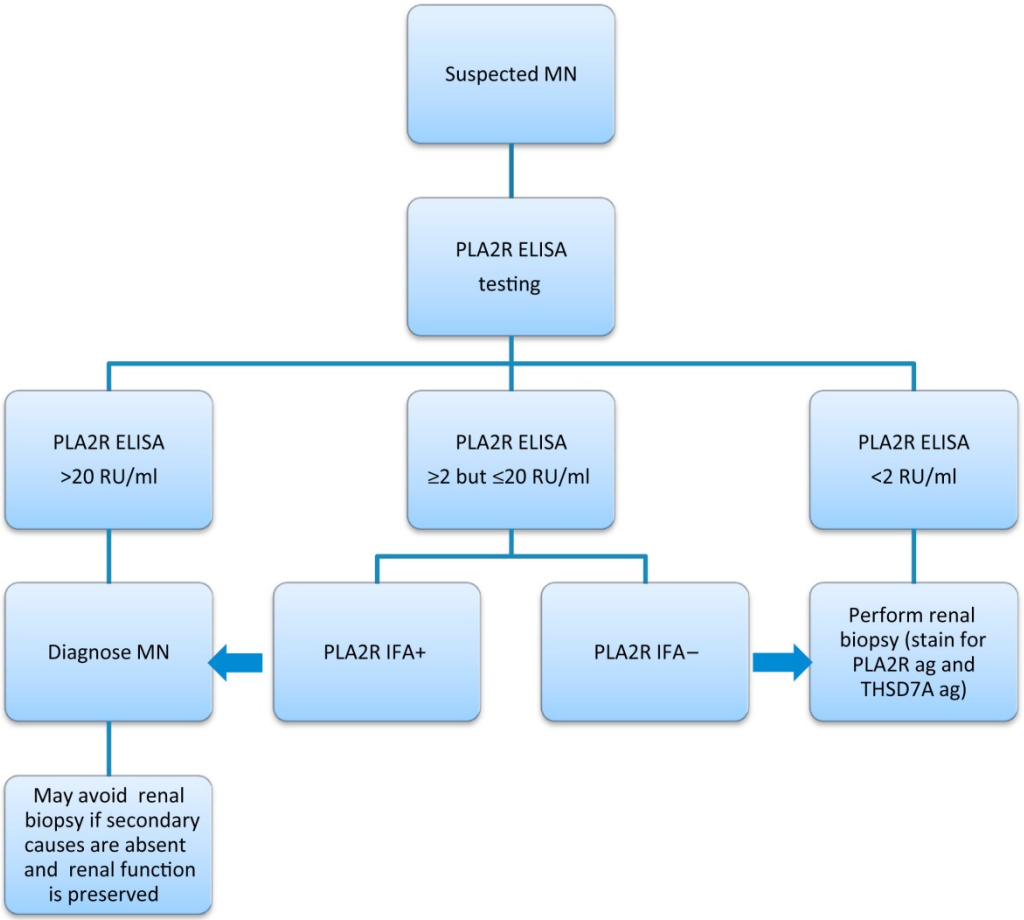
Leeaphorn, N et al: Am J Nephrol, 2014

Algorithm for centers preferentially performing immunofluorescence assays (IFAs)
Only for patients with normal renal function and absence of secondary causes of MN



Bobart,SA et al: KI, 2019

Algorithm for centers preferentially performing enzyme-linked immunosorbent assays (ELISAs) Only for patients with normal renal function and absence of secondary causes of MN



Increased rate of malignancy in THSD7A-associated MN

Bobart,SA et al: KI, 2019

Case #7

A 52-year-old woman was hospitalized 3 days ago for laparoscopic resection of sigmoid colon secondary to recurrent diverticulitis. Diet has been advanced to a full diet. She has a 20 year history of hypertension, stage 3 chronic kidney disease, and migraine headaches. Medications are amlodipine, Heparin, Topiramate and as needed intravenous morphine.

On physical examination, vital signs are normal. Mild incisional tenderness is present. The remainder of the physical examination is unremarkable.

Case #7

Laboratory studies:

	On admission	Today
Creatinine	1.6mg/dL	1.9mg/dL
Electrolytes		
Sodium	140 mEq/L	138 mEq/L
Potassium	4.9 mEq/L	5.6 mEq/L
Chloride	102 mEq/L	110 mEq/L
Bicarbonate	25 mEq/L	20 mEq/L
Glucose	116 mEq/L	128 mEq/L

Urine output during the past 24 hrs is 1400 mL

Case #7

Which of the following is the most likely cause of this patient's elevated serum potassium?

A. Acute kidney injury

B. Heparin

C. Hyperglycemia

D. Metabolic acidosis

E. Topiramate

Case #7 Answer

- Hypoaldosteronism caused by heparin, inhibitors of the renin angiotensin system, type 4 RTA, or primary adrenal disease can cause hyperkalemia, specially patients with CKD or diabetes mellitus, home or in does take an ACE inhibitor or angiotensin receptor blocker
- Both unfractionated and LMW heparin use is associated with a decrease in aldosterone synthesis

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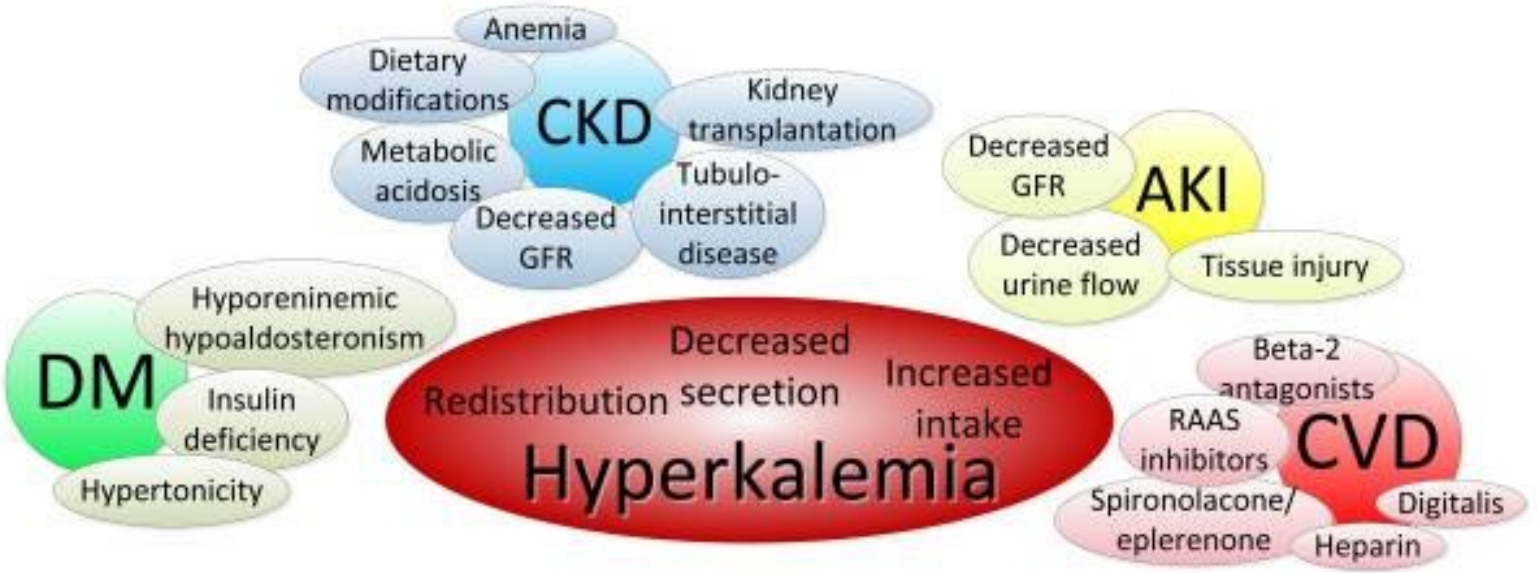
Kovesdy, CP: Rev Endocr Metab Disord, 2017

Mechanisms of action of the development of hyperkalemia in patients with chronic kidney disease and associated comorbid conditions



Kovesdy, CP: Rev Endocr Metab Disord, 2017

Case #8

A 44-year-old male evaluated during a follow-up visit for treatment of persistent elevated blood pressure. He takes no medications.

Physical examination reveals a well-developed muscular man in no apparent distress. Blood pressure is of 165/98 mmHg, pulse rate 70/min, other vital signs are normal. BMI is 26. Jugular venous pressure is normal. Cardiac examination is unremarkable.

Case #8

Laboratory studies:

Bicarbonate	27mEq/L (27mmol/L)
Creatinine	1.3 mg/dL(114.9 µmol/L)
Potassium	4.5mEq/L (4.5mmol/L)
Estimated glomerular filtration rate	> 60mL/min/1.73m^2
Urine toxicology screen	Negative

Electrocardiogram reveals normal sinus rhythm, voltage criteria for left ventricular hypertrophy are present.

Case #8

Which of the following is the most appropriate treatment?

A. Amlodipine/Benazepril combination once a daily

B. Doxazosin and metoprolol, each once daily

C. Hydralazine 3 times daily

D. Telmisartan and ramipril, each once daily

Case #8 Answer

BLOOD PRESSURE CATEGORY	SYSTOLIC mm Hg (upper number)		DIASTOLIC mm Hg (lower number)
NORMAL	LESS THAN 120	and	LESS THAN 80
ELEVATED	120 – 129	and	LESS THAN 80
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 1	130 – 139	or	80 – 89
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 2	140 OR HIGHER	or	90 OR HIGHER
HYPERTENSIVE CRISIS (consult your doctor immediately)	HIGHER THAN 180	and/or	HIGHER THAN 120

Whelton PK et al: Hypertension, 2017

Case #8 Answer

- The 2017 ACC/ AHA blood pressure (BP) guidelines recommends combination therapy with 2 first-line antihypertensive drugs of different classes (separately or as a single dose pill)for adults with stage 2 hypertension and an average BP of 20/10 mmHg above blood pressure target

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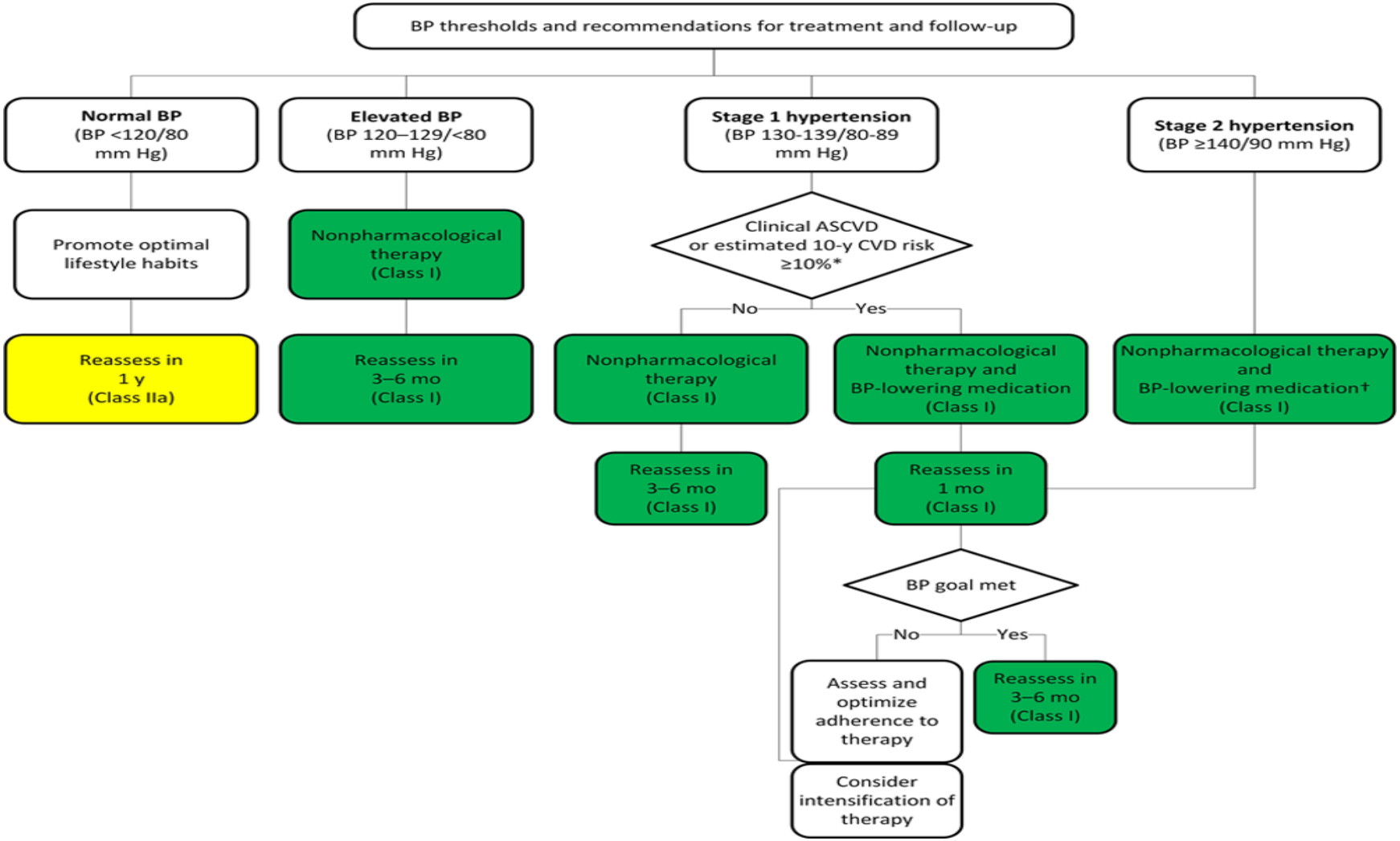
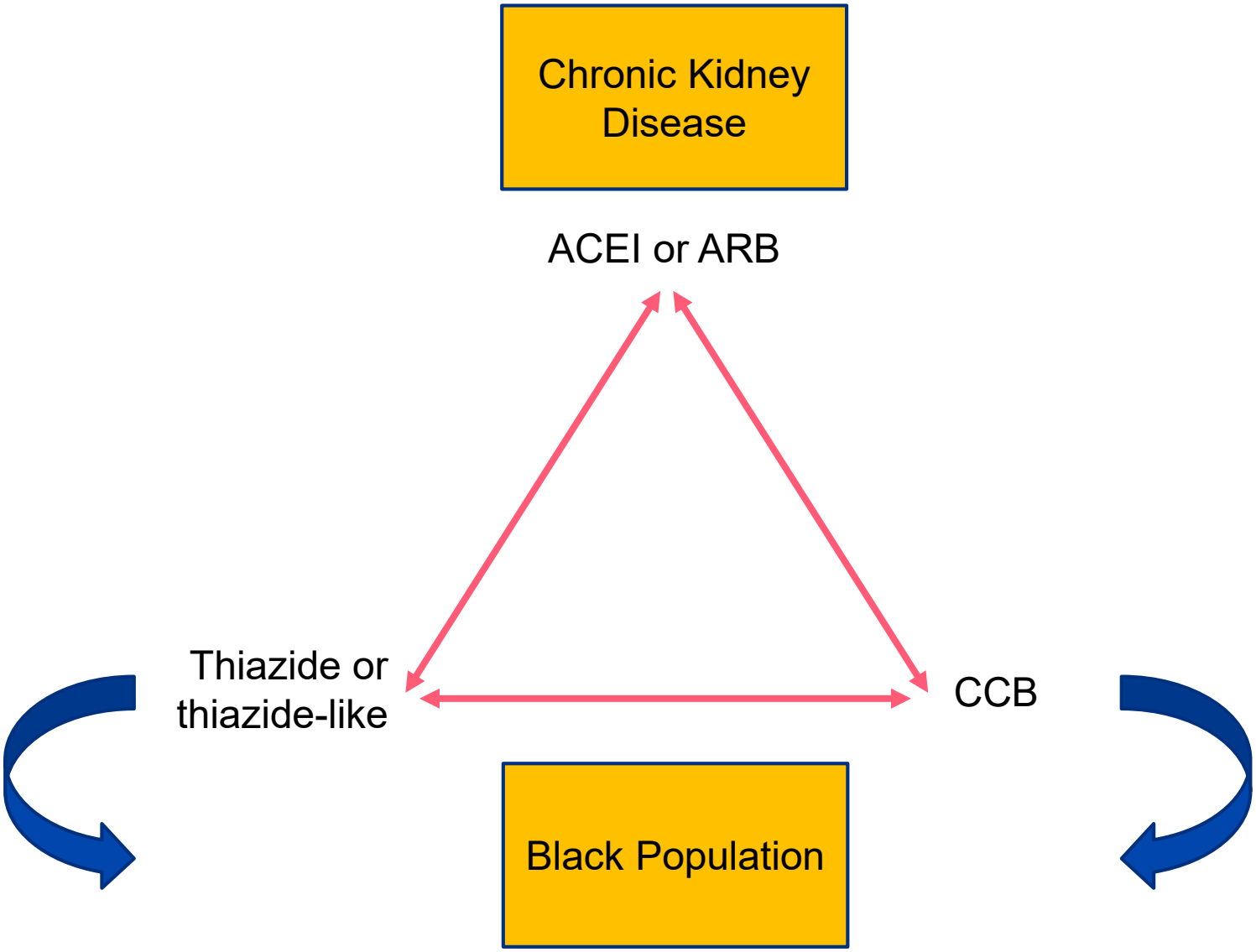
Whelton PK et al: Hypertension, 2017



2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines, Volume: 71, Issue: 6, Pages: e13-e115, DOI: (10.1161/HYP.0000000000000065)



Case #9

A 36-year-old man is evaluated in the emergency department for renal colic. He is in otherwise good health and takes no medications. Physical examination reveals left carotid vertebral angle tenderness. The reminder of the examination is normal. Noncontrast helical CT scan shows an 11 mm stone at the left ureteral pelvic junction and mild left caliectasis. Analgesics are initiated.

Case #9

Which of the following is the most appropriate next step in management?

A. Extracorporeal shock wave lithotripsy

B. Forced diuresis with IV normal saline

C. Nifedipine

D. Tamsulosin

Case #9 Answer

- Urologic interventions is required in all patients with evidence of infection, acute kidney injury, intractable nausea pain, and stones that fall to pass or unlikely to pass
- Only 50% of stones >6 mm in size will pass spontaneously
- Shockwave lithotripsy can be used for stones in the renal pelvis and proximal ureter, but is less effective for stones located middle/distal ureter or lower pole calix, stones more than 15 mm and hard stones (calcium oxalate monohydrate are cystine)
- Medical expulsive therapy no longer recommended

Lawler, AC et al: Curr Urol Rep, 2017
Meltzer, AC et al: JAMA, 2018

Case #10

A 68-year-old woman is hospitalized for chest pain. History is significant for stage 3 chronic kidney disease. Hypertension, coronary artery disease, and type 2 diabetes mellitus. Medications are aspirin, losartan, basal and prandial insulin, metoprolol, nitroglycerin paste and unfractionated heparin. On physical examination, blood pressure is 130/80 mmHg, other vital signs are normal. S_1 and S_2 are normal. There is no S_3, lungs crackles or edema. Laboratory studies show serum creatinine level of 1.8 mg/dL (159.1µmol/L) and an elevated serum troponin level. EKG shows a 2-mm-ST segment depression in leads I, aVL and V_4 through V_6. Cardiac catheterization is planned.

Case #10

Which one of the following is the most appropriate procedure management?

A. Administer furosemide before cardiac catheterization

B. Administer intravenous isotonic fluids before and after cardiac catheterization

C. Administer oral sodium bicarbonate before cardiac catheterization

D. Initiate hemodialysis following cardiac catheterization

Case #10 Answer

- IV isotonic fluids are the mainstay in prevent contrast-induced nephropathy(CIN) in patients with CKD administered before and after cardiac catheterization
- Furosemide before catheterization is incorrect because it can induce volume contraction and activate RAAS increasing the risk for CIN
- Hemodialysis does not improve CIN outcomes, but rather may exacerbate acute kidney injury

Fahling, M et al: Nat Rev Nephrol, 2017

Pathophysiology of Contrast-Induced Nephropathy

Vasoconstriction

Vasoconstriction

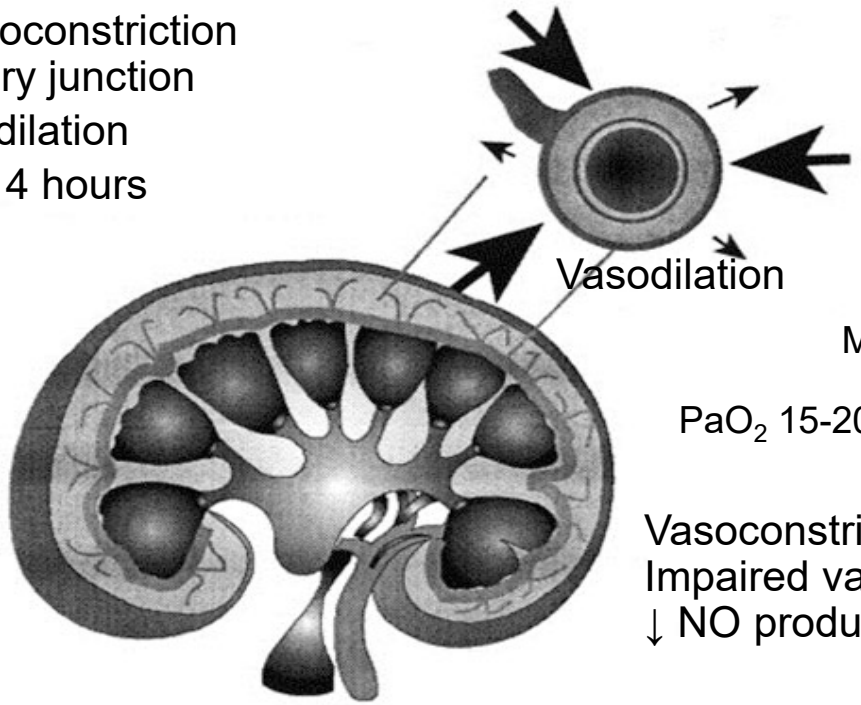
Ca^{++} influx

Endothelial release

Selective vascoconstriction corticomedullary junction

Imparied vasodilation

Duration up to 4 hours



Direct tubular toxicity

Medullary hypoxia

PaO_2 15-20 mm Hg

Vasoconstriction

Impaired vasodilation

↓ NO production

Oxidative stress

$OH^{\cdot}$ $O_2^{\cdot -}$ free radicals

Tumlin et al: AJC 98, 2006

ORIGINAL ARTICLE

Outcomes after Angiography with Sodium Bicarbonate and Acetylcysteine

S.D. Weisbord, M. Gallagher, H. Jneid, S. Garcia, A. Cass, S.-S. Thwin, T.A. Conner, G.M. Chertow, D.L. Bhatt, K. Shunk, C.R. Parikh, E.O. McFalls, M. Brophy, R. Ferguson, H. Wu, M. Androsenko, J. Myles, J. Kaufman, and P.M. Palevsky, for the PRESERVE Trial Group*

ABSTRACT

Table 3. Primary and Secondary End Points.

Outcome	Sodium Bicarbonate (N=2511)	Sodium Chloride (N=2482)	Odds Ratio (95% CI)	P Value	Acetylcysteine (N=2495)	Placebo (N=2498)	Odds Ratio (95% CI)	P Value
	no. of patients (%)				*no. of patients (%)*			
Primary end point*	110 (4.4)	116 (4.7)	0.93 (0.72–1.22)	0.62	114 (4.6)	112 (4.5)	1.02 (0.78–1.33)	0.88
Secondary end points								
Contrast-associated acute kidney injury†	239 (9.5)	206 (8.3)	1.16 (0.96–1.41)	0.13	228 (9.1)	217 (8.7)	1.06 (0.87–1.28)	0.58
Death by 90 days	60 (2.4)	68 (2.7)	0.87 (0.61–1.24)	0.43	67 (2.7)	61 (2.4)	1.10 (0.78–1.57)	0.59
Need for dialysis by 90 days	32 (1.3)	29 (1.2)	1.09 (0.65–1.81)	0.73	30 (1.2)	31 (1.2)	0.97 (0.58–1.60)	0.90
Persistent kidney impairment by 90 days	28 (1.1)	25 (1.0)	1.10 (0.64–1.91)	0.71	26 (1.0)	27 (1.1)	0.96 (0.56–1.66)	0.89
Hospitalization with acute coronary syndrome, heart failure, or stroke by 90 days	272 (10.8)	251 (10.1)	1.08 (0.90–1.29)	0.40	244 (9.8)	279 (11.2)	0.86 (0.71–1.04)	0.11
All-cause hospitalization by 90 days	1071 (42.7)	1052 (42.4)	1.01 (0.90–1.13)	0.85	1069 (42.8)	1054 (42.2)	1.03 (0.91–1.15)	0.64

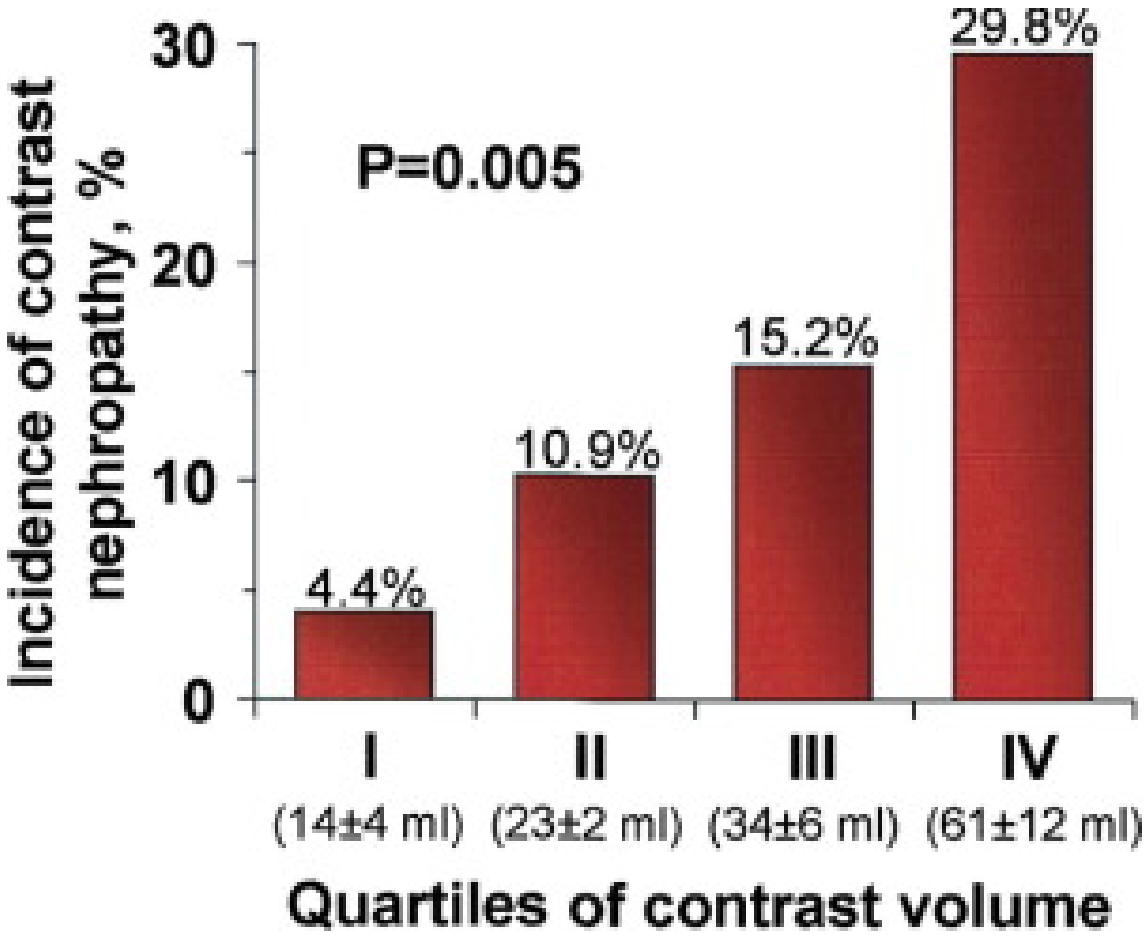
Weisbord, SD et al: NEJM , 2018

Conclusion

- Patients with high risk for renal complications who were undergoing angiography, there was no benefit of IV sodium bicarbonate over IV sodium chloride or of oral NAC over placebo for the prevention of death, RRT, or persistent decline in kidney function at 90 days or for the prevention of contrast-associated acute kidney injury

Weisbord, SD et al: NEJM , 2018

Ultra-Low Contrast Volumes Reduce Rates of CIN in Patients With CKD Undergoing Coronary Angiography



Kane, G et al: JACC 2008

Case #11

A 45-year-old woman is evaluate for recent onset of resistant hypertension. During her last visit, chlorthalidone was added to her medication regimen. She reports no symptoms, and review of systems is otherwise unremarkable. Current medications are metoprolol, amlodipine, hydralazine, and chlorthalidone. Physical examination, blood pressure is 160/96 mmHg and pulse rate 65/min, other vital signs are normal. BMI is 24. There is no proptosis. The thyroid gland is not enlarged and the reminder of the examination is unremarkable.

Case #11

Laboratory studies:

Bicarbonate	34mEq/L (34mmol/L)
Creatinine	0.8 mg/dL(70.7 µmol/L)
Potassium	2.9mEq/L (2.9mmol/L)
Urine albumin-creatinine ratio	10mg/g

Case #11

Which one of the following is the most appropriate diagnostic tests to perform next?

A. Kidney ultrasonography with Doppler

B. Plasma aldosterone concentration/plasma renin activity ratio

C. Plasma fractionated metanephrines

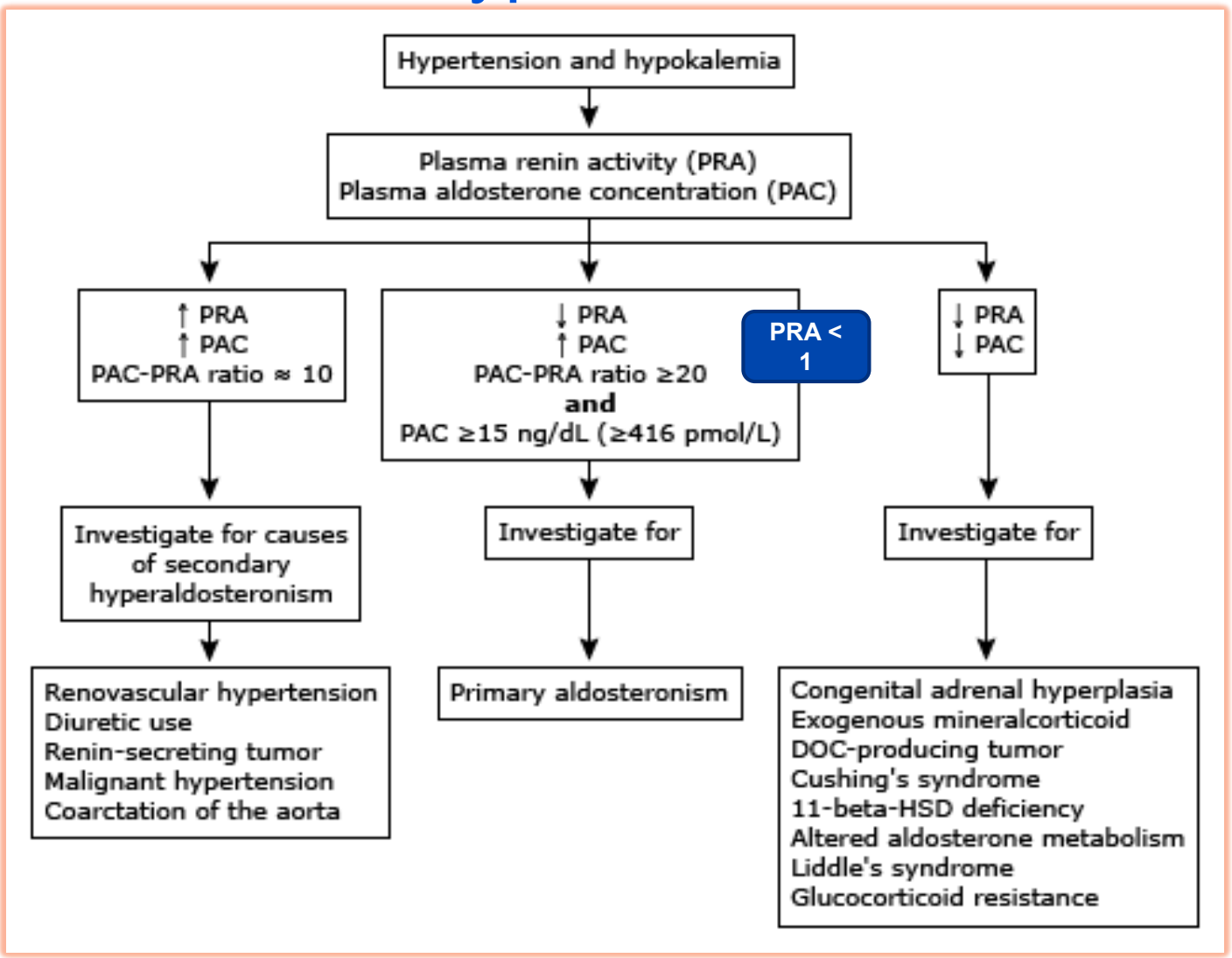
D. Polysomnography

Case #11 Answer

- Calculation of PAC / PRA ratio is used to diagnose primary hyperaldosteronism (PH)
- Triad of resistant hypertension, metabolic alkalosis and hypokalemia followed addition of thiazide diuretic, raises suspicion for primary hyperaldosteronism
- Testing for PH recommended for resistant hypertension, hypokalemia, incidentally discovered adrenal mass, family history of early onset hypertension, stroke at age of < 40 y/o

Braam, B et al: CJAN, 2017

PAC/PRA ratio in Hypertension and Hypokalemia



Modified from UpToDate

Primary Hyperaldosteronism Evaluation

- Must distinguish between (unilateral) aldosterone-producing adenoma and bilateral hyperplasia.
- Adrenal CT should be initial study for evaluation.
- However, CT findings can be misleading.
- Adrenal vein sampling should be performed.
  - Continuous cosyntropin (ACTH) infusion.
  - Measure aldosterone and cortisol levels from right adrenal vein, left adrenal vein, and IVC.
  - Cortisol-corrected aldosterone ratio

  >4:1 ⇨ adenoma, <3:1 ⇨ bilateral hyperplasia.

Case #12

A 28-year-old woman is evaluated in the emergency department for muscle cramps and weakness. She notes a weight loss of 15 kg (33 lb) over the past 3 months, baseline weight was 115 kg (254 lb). She reports no abdominal pain or diarrhea. She has a 1 year history of type 2 diabetes mellitus, for which she takes metformin. On physical examination temperature is normal blood pressure is 122/72mmHg, pulse rate is 100/min and have respiration rate 18/min. BMI is 36. Muscle strength of the lower and upper extremities is 4/5. Other than weakness neurologic examination is normal.

Case #12

Laboratory studies:

Electrolytes:	
Sodium	138 mEq/L(138mmol/L)
Potassium	2.4 mEq/L(2.4mmol/L)
Chloride	92 mEq/L(92mmol/L)
Bicarbonate	34 mEq/L(34mmol/L)
Arterial blood gases:	
pH	7.50
Pco_2	45 mm Hg (6.0 κPa)
Urine sodium	40 mEq/L(40mmol/L)
Urine potassium	60 mEq/L(60mmol/L)
Urine chloride	5 mEq/L(5mmol/L)

Case #12

Which one of the following is the most likely diagnosis?

A. Cushing syndrome

B. Gitelman syndrome

C. Primary hyperaldosteronism

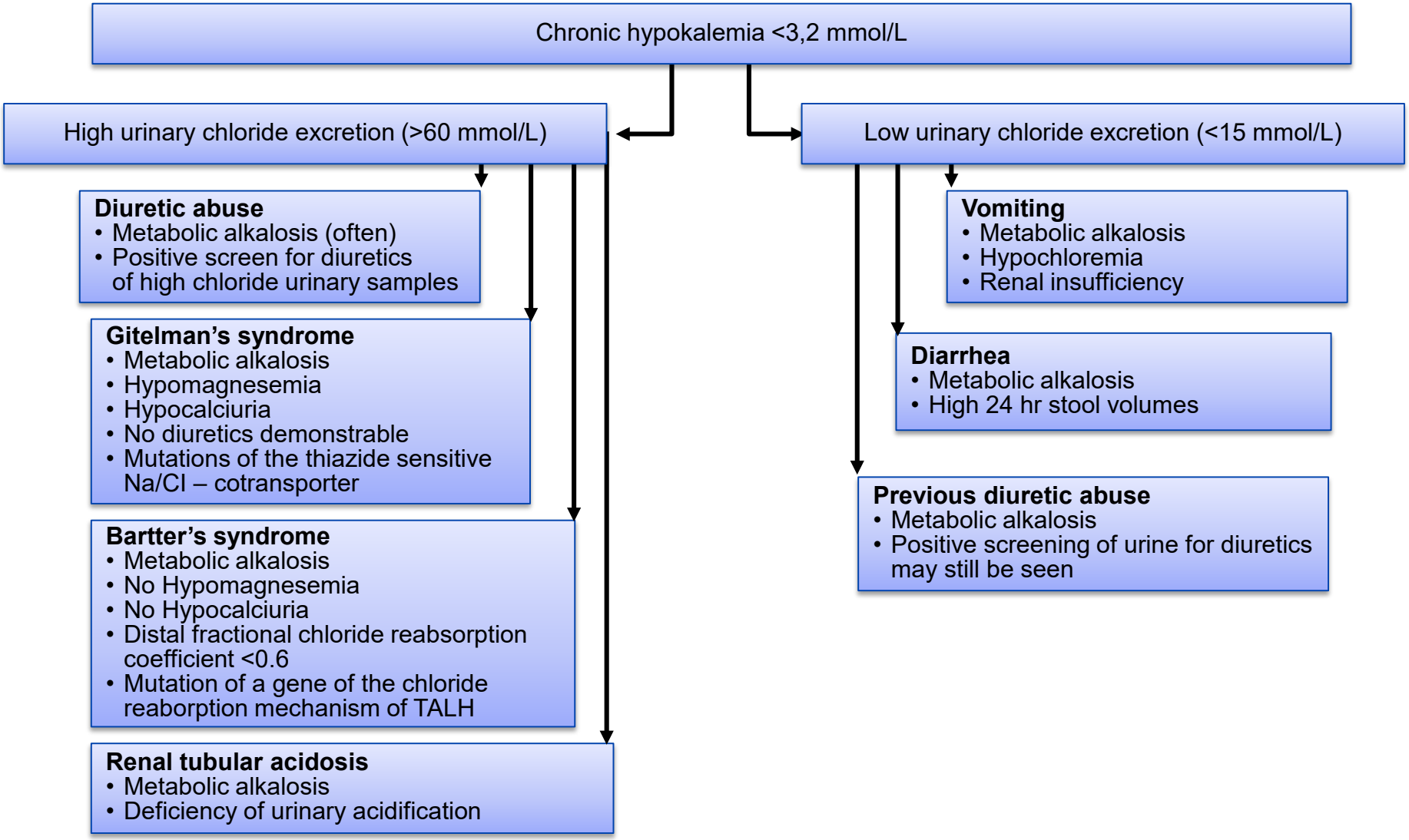
D. Surreptitious vomiting

Case #12 Answer

- Saline response metabolic alkalosis typically presents with hypovolemia and low urine chloride of < 15 mEq/L, the most common causes are vomiting, nasogastic catheter suction and diuretic use

Soifer,JT & Kim, HT: Emerg Med Clin North Am, 2014

Diagnostic Guide for Chronic Hypokalemia



Reimann & Gross; NDT, 1999

Case #13

A 64-year-old man is evaluate for a 2-month history of increasing fatigue and bilateral swelling on the submandibular region. History is significant autoimmune pancreatitis treated with prednisone 2 years ago, hypertension, and allergic rhinitis. Medications are losartan and fluticasone propionate. On physical examination, blood pressure is 148/84mmHg, and pulse rate 78/min. There is no rash. Head and neck examination reveals bilateral submandibular gland swelling. Trace edema of the ankles is present. The remainder of the examination is normal.

Case #13

Laboratory studies:

Hemoglobin	12 g/dL(120g/L)
Leukocyte count	10,000/µL($10x10^9$/L) 33% eosinophils
Platelet count	180,000/µL($180x10^9$/L)
C3	65mg/dL (650mg/L)
C4	7 mg/dL(70mg/L)
Creatinine	3.1mg/dL(274µmol/L); 6 months ago:1.8mg/dL (159.1µmol/L)

Case #13

Laboratory studies:

IgG	2600mg/dL (26g/L)
IGE	500U/mL(500kU/L)
Antinuclear antibodies	1:640
Urinalysis	Specific gravity 1010; trace protein;6-10 leukocytes/hpf

Kidney ultrasound demonstrates bilateral markedly enlarged kidneys measuring 15cm in size with hyperechoic cortex and peripheral cortical nodules.

Case #13

Which of the following is the most likely diagnosis?

A. IgG 4-related disease

B. Lupus nephritis

C. Sarcoidosis

D. Sjogren syndrome

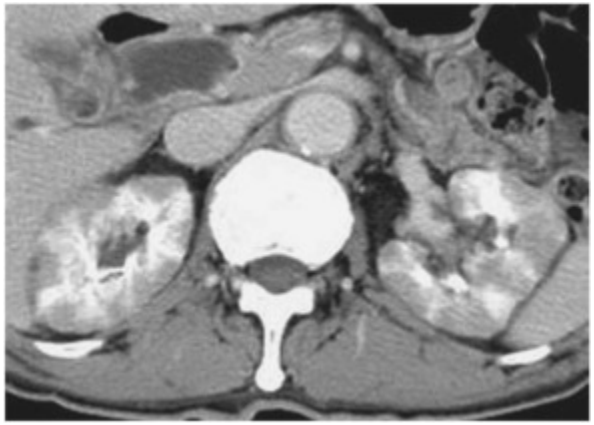
Case #13 Answer

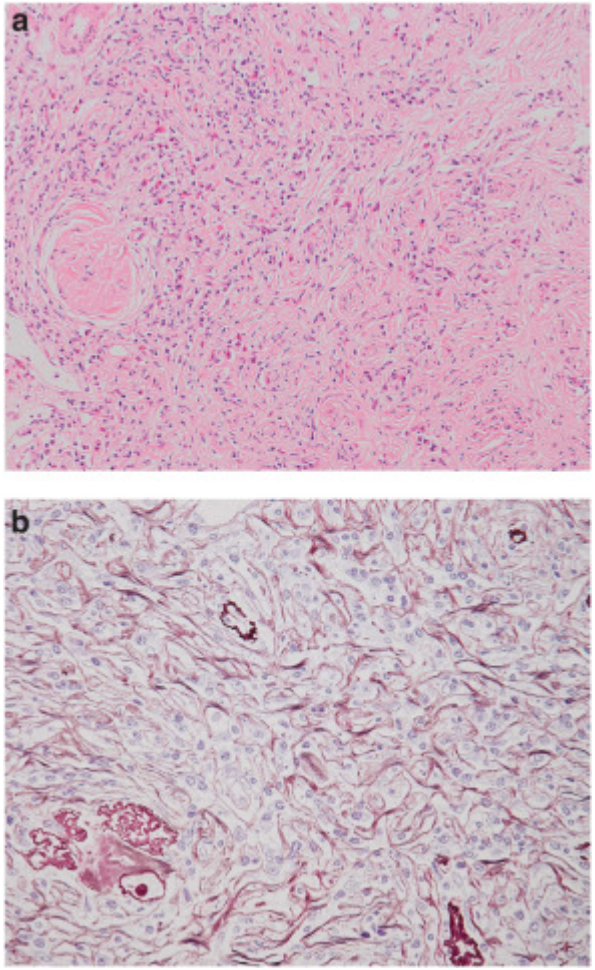
- Tubulointerstitial nephritis is the most common kidney manifestation of IgG4-related disease and typically presented with pyuria, proteinuria and elevated serum IgG and IgE levels, on kidney imaging may show enlarged kidney or renal masses. Hypocomplementemia and allergy symptoms such as asthma and allergic rhinitis may be present IgG 4-related disease.

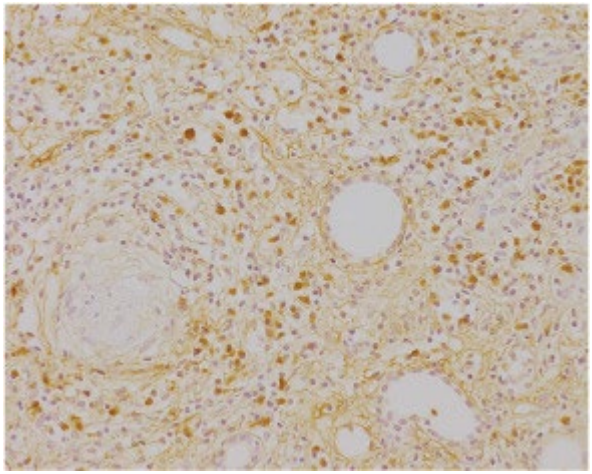
MAYO CLINIC

Zhang P & Cornell, LD: Adv Chronic Kidney Dis, 2017

IgG4-related Kidney Disease







Saeki & Kawano; KI, 2014

Major Organ Manifestation of IgG-4 Related Disease

Pancreas	Type 1 autoimmune pancreatitis
Salivary glands	Sialadenitis
Eye/orbit/lacrymal glands	Orbital inflammation/pseudotumor and dacryoadenitis
Aorta/artery/retroperitoneum periaortitis	Periaortitis/periarteritis and retroperitoneal fibrosis
Kidney	Tubulointerstitial nephritis and pyelitis
Lymph nodes	Lymphadenopathy
Lung	Lung disease (inflammatory pseudotumor, alveolar interstitial disease, and pleuritis)
Biliary system	Sclerosing cholangitis and cholecystitis
Liver	Pseudotumor and hepatopathy
Central/peripheral nervous system	Pachymeningitis and infraorbital nerve swelling
Endocrine system	Hypophysitis and thyroiditis
Others	Prostatitis, mastitis, mediastinitis, and pericarditis skin (nodules and papules)

Saeki & Kawano; KI, 2014

IgG4-related Kidney Disease

- IgG4-related disease (IgG4-RD) is a systemic disease
- Diagnosis of IgG4-RD is based on characteristic pathology: a lymphoplasmacytic infiltrate enriched with IgG4+ plasma cells, and storiform fibrosis
- Serum IgG4 levels are elevated in most patients with IgG4-RD
- IgG4-related TIN is the most common form of IgG4-related kidney disease. the condition is characterized by unique findings on contrast-enhanced CT and the hallmark pathology of IgG4-RD
- Membranous glomerulonephropathy secondary to IgG4-RD is a rare manifestation and it is not associated PLA2r AB
- Steroids are the standard therapy for IgG4-RD

Case #14

A 42-year-old woman is evaluated during a routine visit. She recently had her blood pressure measured at the workplace, two measurements were taking and both were elevated. The patient feels well and review of system is unremarkable. Family history is significant for hypertension in her father, mother and two siblings. Her father had stroke and her mother had heart failure. She takes no medications. On physical examination average of three blood pressure measures is 128/78. BMI is 30 and the reminder for examination is normal.

Case #14

Laboratory studies:

Bicarbonate	24mEq/L (24mmol/L)
Creatinine	0.9mg/dL(79.6 µmol/L)
Potassium	4mEq/L (4mmol/L)
Urine albumin-creatinine Ratio	10mg/g

EKG reveals normal sinus rhythm and positive voltage criteria for left ventricular hypertrophy.

Case #14

Which of the following is most appropriate test performed next?

A. 24-hr ambulatory blood pressure monitoring

B. Plasma aldosterone concentration/plasma renin activity ratio

C. Polysomnography

D. Thyroid-stimulating hormone measurement

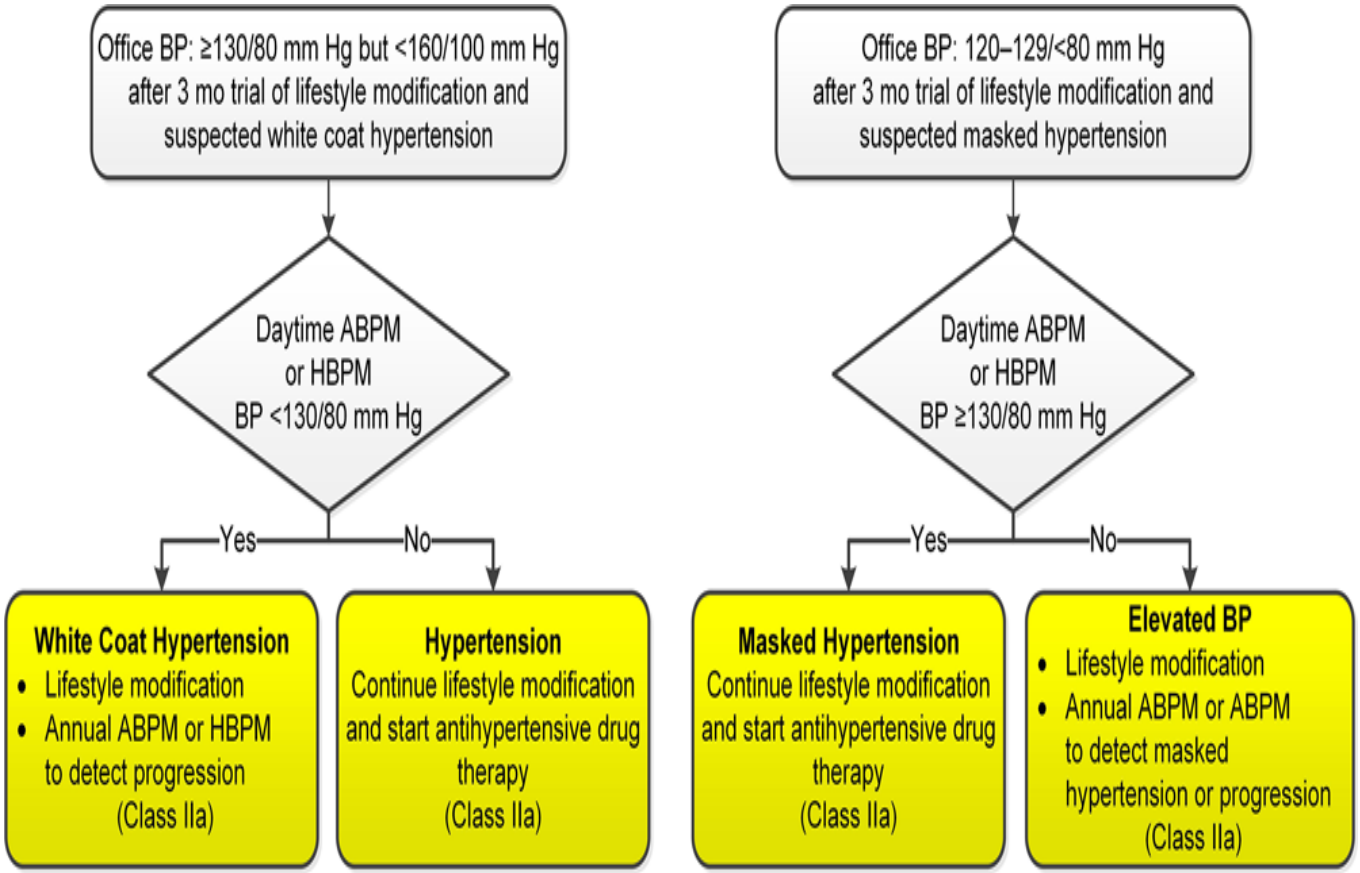
Case #14 Answer

- Suspected masked hypertension (is defined as blood pressure that is normal in the office but elevated in the ambulatory setting) should be confirmed with ABPM on home blood pressure monitoring

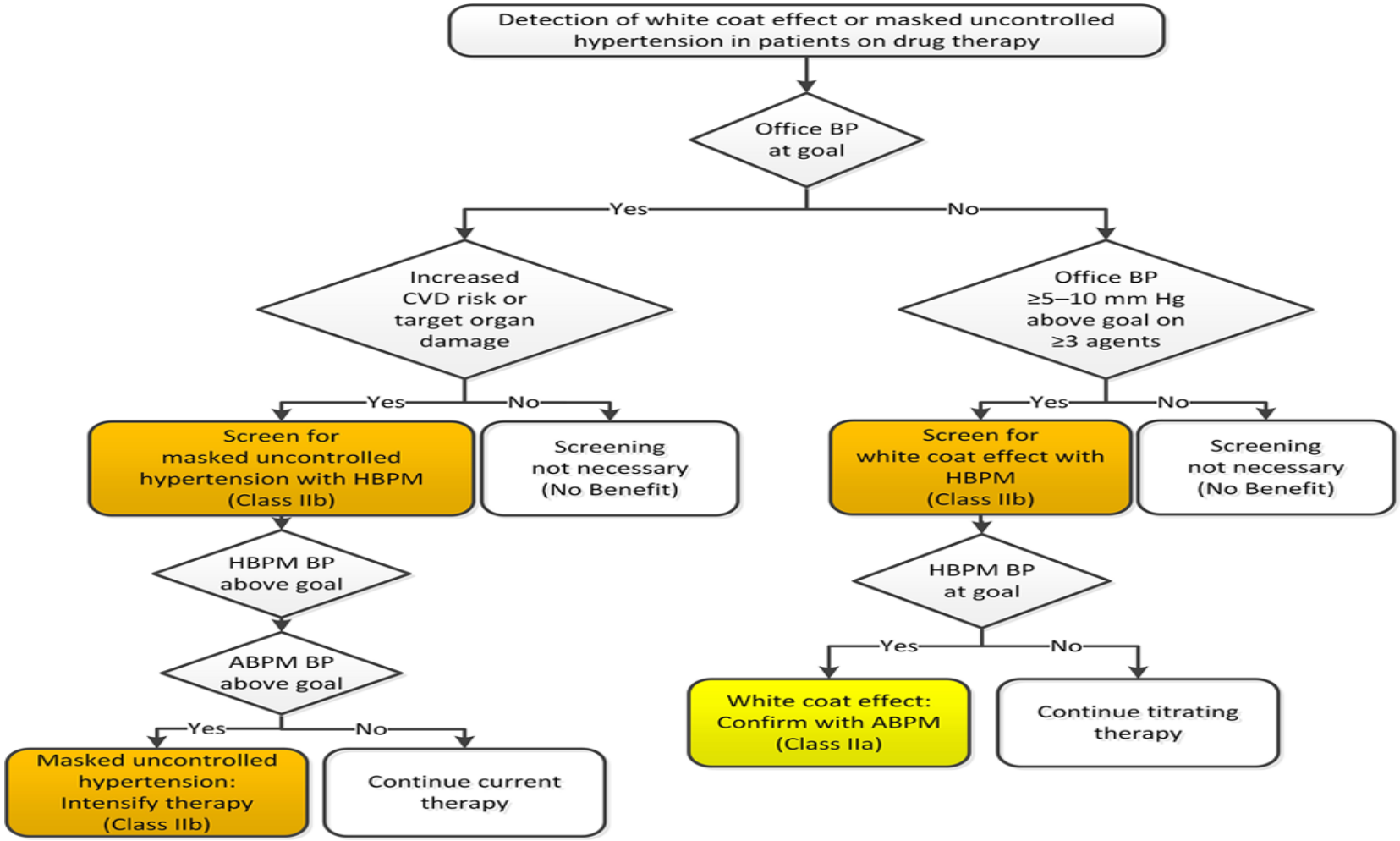
MAYO CLINIC

Whelton PK et al: Hypertension, 2017

Detection of White Coat Hypertension or Masked Hypertension in Patients not on Drug Therapy



2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines, Volume: 71, Issue: 6, Pages: 1269-1324, DOI: (10.1161/HYP.0000000000000066)



2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines, Volume: 71, Issue: 6, Pages: 1269-1324, DOI: (10.1161/HYP.0000000000000066)

Case #15

A 72-year-old woman evaluated during routine visit. History is significant for hypertension treated with amlodipine and losartan. She has no other medical problems. She remains physically active and routinely plays tennis and golf. On physical examination, blood pressure is 142/84mmHg, and pulse rate 72/min, other vital signs are normal. BMI is 24. The remainder of the examination is unremarkable.

Laboratory studies shows serum creatinine level of 0.8 mg/dL(70.7µmol/L) and serum potassium level of 4.0 mEq/L (4.0mmol/L)

Case #15

According to the target blood pressure goes recommended by the American College of physicians in the American academy of family physicians, which of the following would be most appropriate management?

A. Add chlorthalidone

B. Increase the amlodipine dose

C. Increase the losartan dose

D. Make no changes to antihypertensive medications

Case #15 Answer

- Based on evidence that the greatest absolute benefit of antihypertensive therapy is seen patients with the highest blood pressure in cardiovascular risk, the American College of Physicians in American Academy of Family Physicians recommended antihypertensive drugs be initiated patients ≥ 60 years old if BP is above 150/90 mmHg, with a goal of reducing systolic blood pressure less than < 150 mmHg. The ACC/AHH recommends a systolic blood pressure <130 mmHg in patients ≥ 65 years old.

Kansagara, D et al: Ann Intern Med, 2017

Summary of the American College of Physicians and American Academy of Family Physicians Joint Guideline on Pharmacologic Treatment of Hypertension in Adults Aged 60 Years or Older to Higher Versus Lower Blood Pressure Targets

Disease/Condition	Hypertension
Target Audience	All clinicians
Target Patient Population	Adults aged ≥60 y with hypertension
Treatments Evaluated	Treatment to higher (<150 mm Hg) vs. lower (≤140 mm Hg) SBP targets
Outcomes Evaluated	All-cause mortality, morbidity and mortality related to stroke, cardiac events, and harms
Benefits	Incidence of stroke and cardiac events were reduced with treatment. Treating to 140 mm Hg did not have additional benefit.
Harms	Increased withdrawals due to adverse events with higher vs. lower BP targets Increased cough, hypotension, and risk for syncope with treating to lower vs. higher BP targets No difference between higher and lower BP targets for renal outcomes, cognitive outcomes, or falls and fractures
Adverse Effects	Some of the adverse effects associated with antihypertensive medications include (but are not limited to) the following: Thiazide-type diuretics: electrolyte disturbances, gastrointestinal discomfort, rashes and other allergic reactions, sexual dysfunction in men, photosensitivity reactions, and orthostatic hypotension ACEIs: cough and hyperkalemia ARBs: dizziness, cough, and hyperkalemia Calcium-channel blockers: dizziness, headache, edema, and constipation β-blockers: fatigue and sexual dysfunction
Recommendations	*Recommendation 1: ACP and AAFP recommend that clinicians initiate treatment in adults aged 60 years or older with systolic blood pressure persistently at or above 150 mm Hg to achieve a target systolic blood pressure of less than 150 mm Hg to reduce the risk for stroke, cardiac events, and possibly mortality. (Grade: strong recommendation, high-quality evidence). ACP and AAFP recommend that clinicians select the treatment goals for adults aged 60 years or older based on a periodic discussion of the benefits and harms of specific blood pressure targets with the patient.* *Recommendation 2: ACP and AAFP recommend that clinicians consider initiating or intensifying pharmacologic treatment in adults aged 60 years or older with a history of stroke or transient ischemic attack to achieve a target systolic blood pressure of less than 140 mm Hg to reduce the risk for recurrent stroke. (Grade: weak recommendation, moderate-quality evidence). ACP and AAFP recommend that clinicians select the treatment goals for adults aged 60 years or older based on a periodic discussion of the benefits and harms of specific blood pressure targets with the patient.* *Recommendation 3: ACP and AAFP recommend that clinicians consider initiating or intensifying pharmacologic treatment in some adults aged 60 years or older at high cardiovascular risk, based on individualized assessment, to achieve a target systolic blood pressure of less than 140 mm Hg. (Grade: weak recommendation, low-quality evidence). ACP and AAFP recommend that clinicians select the treatment goals for adults aged 60 years or older based on a periodic discussion of the benefits and harms of specific blood pressure targets with the patient.*
Clinical Considerations	Accurate measurement of BP is important before initiating treatment for hypertension. Some patients may have elevated BP in clinical settings, and ambulatory measurement may be appropriate. Clinicians should consider treatment with nonpharmacologic options, including weight loss, dietary changes, and an increase in physical activity, initially or concurrently with pharmacologic treatment. Many older adults may be taking various medications. Clinicians should consider treatment burden and drug interactions when deciding on treatment options. When selecting pharmacologic therapy, clinicians should prescribe generic drugs where available. Evidence for adults who are frail or those with multimorbidity is limited.

MAYO CLINIC

Qaseem, A et al: Ann Intern Med, 2017

Case # 16

A 66-year-old woman was diagnosed with metastatic melanoma and initiated therapy every 3 weeks with pembroluzimab (PD-1 inhibitor). She is seen in consultation for acute kidney injury. She has been taking for several years Lisinopril, hydrochlorothiazide, citalopram and omeprazole. She has recently been noted to develop acute renal insufficiency and mild pancreatitis associated with a rash and mild elevated amylase and lipase. Her physical exam is remarkable for blood pressure of 136/83 mmHg, and heart rate is 98/min. Examination of the skin shows maculopapular exanthema. The remainder of the examination is unremarkable.

Case # 16

Laboratory studies:

sodium 136 mEq/L, potassium 5.1 mEq/L, chloride 108 mEq/L, Bicarbonate 19 mmol/L, BUN 48 mg/dl, creatinine 2.6 mg/dl (3 weeks ago was 1.2mg/dL and 6 weeks ago 0.9mg/dL) ,

Microscopic examination of the urinary sediment shows 1-3WBC/hpf and trace proteinuria

Case #16

Which of the following is the most likely cause of the acute kidney injury?

A. Omeprazole

B. Lisinorpil

C. Pembrolizumab

D. Hydrochlorothiazide

Perazella, MA & Shiralli, AC: JASN,2018

Case #16 Answer

- The most likely cause of her acute kidney injury is related to immune check point inhibitor(CPIs) therapy. By inhibition of negative co-stimulatory signaling through cytotoxic T lymphocyte associated protein 4 (CTLA-4) or programmed cell death protein-1/programmed cell death protein-ligand 1 (PD-1/PD-L1) on T cells, CPIs restore tumor-directed T-cell responses and are able to induce long-lasting responses in a subset of patients receiving these medications. However, this boost in T-cell reactivity is also the cause of the CPI-associated side effect, namely immune-related adverse events (iRAEs)

Perazella, MA & Shiralli, AC: JASN,2018
Sprangers, B: CKJ, 2018

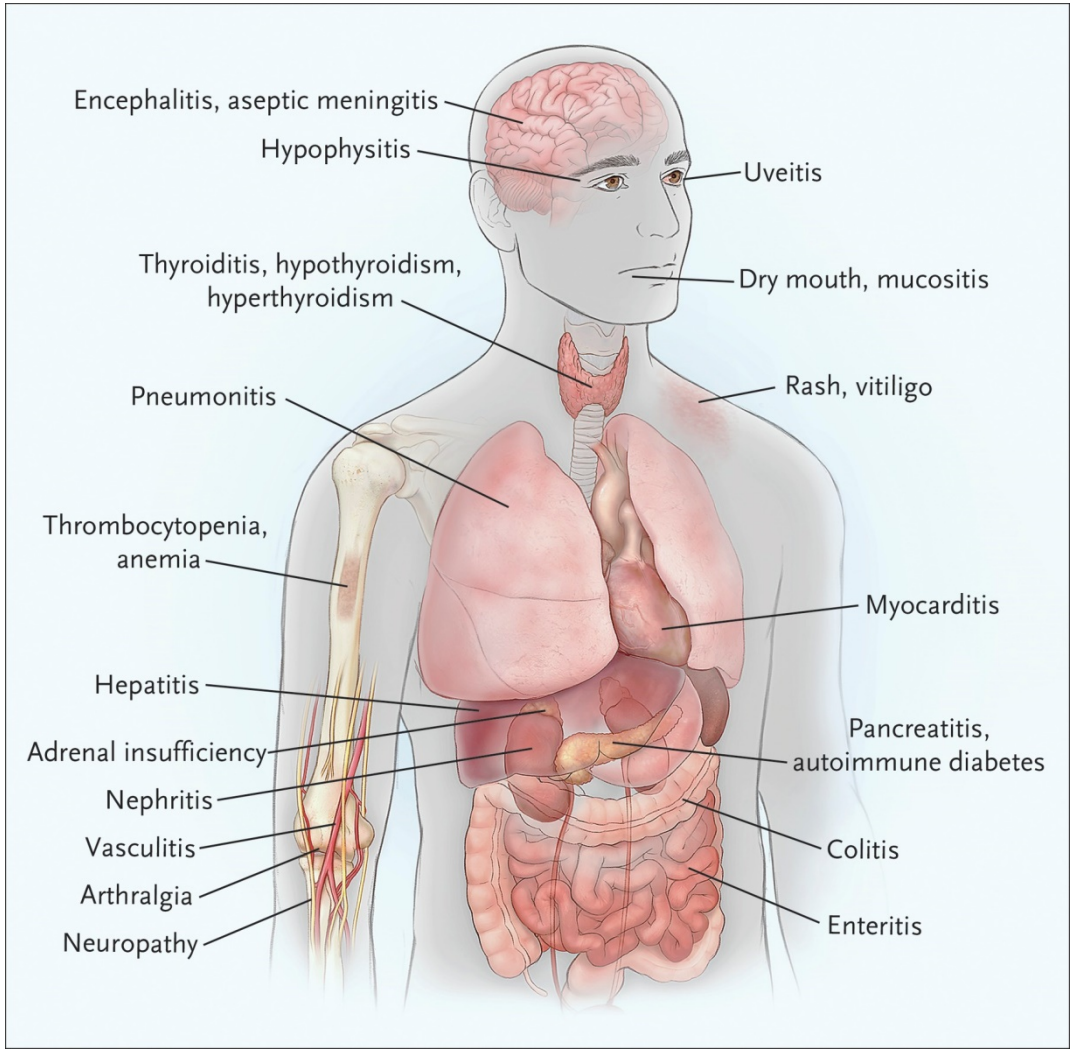
Immune Checkpoint Inhibitors Approved by FDA

Drug	Target	Indication
Ipilimumab	CTLA-4	Melanoma
Nivolumab	PD-1	Melanoma, non–small-cell lung cancer, renal-cell carcinoma, hepatocellular carcinoma, classic Hodgkin's lymphoma, squamous-cell carcinoma of the head and neck, urothelial carcinoma, colorectal cancer with high microsatellite instability or mismatch-repair deficiency
Pembrolizumab	PD-1	Melanoma, non–small-cell lung cancer, classic Hodgkin's lymphoma, squamous-cell carcinoma of the head and neck, urothelial carcinoma, gastric cancer, solid tumors with high microsatellite instability or mismatch-repair deficiency
Atezolizumab	PD-L1	Non–small-cell lung cancer, urothelial carcinoma
Avelumab	PD-L1	Merkel-cell carcinoma, urothelial carcinoma
Durvalumab	PD-L1	Urothelial carcinoma

CTLA-4 denotes cytotoxic T-lymphocyte antigen 4, PD-1 programmed cell death 1, and PD-L1 programmed cell death ligand 1.

Postow, MA et al: NEJM, 2018

Organs Affected by Immune Checkpoint Blockade



Postow, MA et al: NEJM, 2018

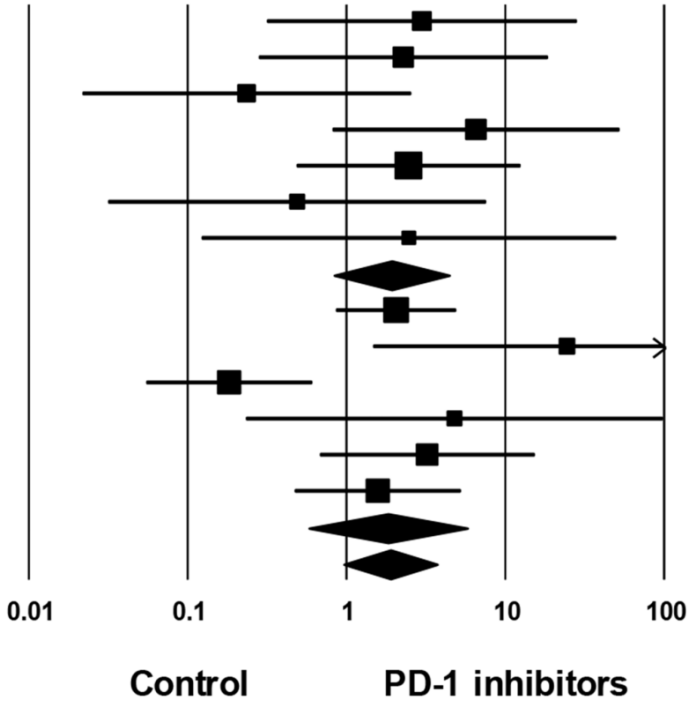
Forest plot of included studies comparing the risk of AKI in patients treated with PD-1 inhibitors versus non-PD-1 inhibitors

Risk of AKI

Study name	Subgroup	Risk ratio	Lower limit	Upper limit	P-value
Robert *et al.* (1)	Nivolumab	2.99	0.31	28.46	0.34
Weber *et al.*	Nivolumab	2.28	0.28	18.74	0.44
Ferris *et al.*	Nivolumab	0.24	0.02	2.57	0.24
Borghaei *et al.*	Nivolumab	6.54	0.81	52.78	0.08
Brahmer *et al.*	Nivolumab	2.46	0.48	12.57	0.28
Postow *et al.*	Nivolumab	0.49	0.03	7.65	0.61
Hodi *et al.*	Nivolumab	2.47	0.12	50.50	0.56
		1.89	0.82	4.35	0.13
Bellmunt *et al.*	Pembrolizumab	2.05	0.85	4.96	0.11
Herbst *et al.*	Pembrolizumab	24.47	1.46	410.77	0.03
Reck *et al.*	Pembrolizumab	0.18	0.05	0.61	0.01
Ribas *et al.*	Pembrolizumab	4.79	0.23	99.42	0.31
Robert *et al.* (2)	Pembrolizumab	3.23	0.67	15.47	0.14
Langer *et al.*	Pembrolizumab	1.58	0.47	5.31	0.46
		1.80	0.57	5.65	0.32
		1.86	0.95	3.64	0.07

Statistics for each study

Risk ratio and 95% CI



The overall pooled RR of AKI in patients treated with PD-1 inhibitors versus control was 1.86 (95% CI 0.95–3.64; I2 = 48%)

Manohar, S et al: NDT, 2018

Questions & Discussion

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Mayo Clinic Locations