nephSAP Volume 19, Number 1, May 2020

Article 1: Evaluation

Question 1

Correct Answer: (C) Recommend that she purchase a validated home BP monitor and provide her with guidance on appropriate measurement technique

Learning Objective: Describe the indications for and distinctions between different methods of BP measurement, including clinic BP measurement, ambulatory BP monitoring, and self-monitoring of BP at home

Answer Explanation: The correct answer is C: Recommend that she purchase a validated home BP monitor and provide her with guidance on appropriate measurement technique. This patient presumably does not have a known history of hypertension, and in-office corroboration of her BP measurements is not immediately available. As a result of its greater prognostic utility, out-of-office BP monitoring is widely recommended for use in the diagnosis of hypertension and would be an appropriate option to help determine if she does have a diagnosis of hypertension. It is quite possible that this patient has white coat hypertension or that her BP was incorrectly measured (e.g., using a nonvalidated wrist BP monitor or while lying supine in a dental chair), and she requires additional, correctly performed BP measurements using a validated device with correct technique to confirm the diagnosis of hypertension.

With regard to answers A and D, there is no evidence to support the initiation of antihypertensive treatment in individuals without a confirmed diagnosis of hypertension, which requires correctly performed office BP readings from at least two separate visits, ambulatory BP monitoring, or correctly performed self-monitoring of BP at home. For answer B, kiosk-based measurements are unreliable because of several barriers to accurate measurement using this method, including ambient noise, lack of sufficient rest time, and lack of published validation studies for most of these devices.

References

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Question 2

Correct Answer: (D) Recommend 24-hour ambulatory BP monitoring to confirm the presence of masked uncontrolled hypertension

Learning Objective: Identify which patients should be evaluated for masked hypertension, white coat hypertension, and nocturnal hypertension and the prognostic importance of these BP patterns

Answer Explanation: The correct answer is D: Recommend 24-hour ambulatory BP monitoring to confirm the presence of masked uncontrolled hypertension. This patient has evidence of masked uncontrolled hypertension (elevated BP out of the office with normal BP in the office). Out-of-office BP monitoring is particularly useful for evaluating individuals with potential discrepancies between BP readings performed out of the office and BP readings performed in the clinic. Owing to its distinctively strong association with adverse cardiovascular outcomes, ABPM is considered to be the reference standard for BP measurement.

Answers A and B are not correct, because masked uncontrolled hypertension is associated with an increased risk of adverse cardiovascular outcomes that is comparable in magnitude to that of sustained hypertension, and the possibility of this diagnosis should not be ignored or dismissed. Individual validation of his home BP monitor and education on appropriate technique can typically minimize measurement error from self-monitoring of BP. Because it has not been determined if this patient's home device is validated or if the patient is performing self-measurements correctly, answer C would be the next best step following confirmatory 24-hour ambulatory BP monitoring. Current guidelines recommend using out-of-office BP monitoring, when performed correctly, to guide therapy in individuals with masked and masked uncontrolled hypertension.

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Question 3

Correct Answer: (A) Recommend that he undergo 24-hour ambulatory BP monitoring

Learning Objective: Explain the importance of using validated BP monitors in and out of the office

Answer Explanation: The correct answer is A: Recommend that he undergo 24-hour ambulatory BP monitoring. This patient has evidence of severe labile hypertension based on the use of a home cuffless BP monitor. Out-of-office BP monitoring is extremely helpful for the evaluation of labile hypertension. Owing to uncertainty regarding the accuracy of the device and patient measurement technique, ambulatory BP monitoring is the ideal way to corroborate this patient's reported readings.

With regard to answers B and C, this patient's device is most likely not validated and should not be used to guide therapy. Validated cuffless devices are not yet available, although several are undergoing evaluation for possible clinical use. At this point in time, cuffless devices require extremely frequent recalibration with a reference BP device or are otherwise not studied across broad populations of patients, making them inadequately reliable for clinical use. Of note, most countries do not have stringent requirements for device validation prior to permitting devices to be marketed to the public, and less than 15% of commercially available BP measurement devices have a published validation study. For answer D, as noted in Question 1, kiosk-based measurements are unreliable owing to several barriers to accurate measurement using this method, including ambient noise, lack of sufficient rest time, and lack of published validation studies for most of these devices.

References

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Question 4

Correct Answer: (C) What medications or drugs, prescription or otherwise, are you using?

Learning Objective: Identify which patients should be evaluated for secondary causes of hypertension, including renovascular disease, aldosterone excess, and catecholamine-secreting tumors

Answer Explanation: The correct answer is C: "What medications or drugs, prescription or otherwise, are you using?" A thorough drug exposure history is essential because several illicit, prescription, and over the counter medications may elevate the blood pressure.

With regard to answer A, the number of steps per day is useful when weighing overall cardiovascular risk, but not helpful in looking for mechanisms that elevate BP. For answer B, the number of meals eaten at home is useful in counseling patients on how to reduce sodium and weight, but again less helpful in looking for a mechanism that elevates BP, although indirectly it may help identify a high salt intake. Similarly, answer D, travel history, is unlikely to help with identifying a secondary cause for BP elevation.

References

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Question 5

Correct Answer: (B) A urine dipstick registering ++ protein

Learning Objective: State the appropriate screening tests in patients with suspected secondary causes of hypertension

Answer Explanation: The correct answer is B: A urine dipstick registering ++ protein. A goal in the evaluation of a new hypertensive is to identify comorbidities that increase cardiovascular risk. A urine dipstick registering significant albuminuria is an established risk factor for stroke and other major adverse cardiovascular events, and a reflection of kidney disease. Furthermore, appropriate antihypertensive agents reduce proteinuria and chronic kidney disease progression.

With regard to answers A and C, neither a low white blood cell count nor a right bundle branch block on the electrocardiogram are known to increase cardiovascular risk. Whereas answer D, elevated C-reactive protein, is associated with elevated cardiovascular risk, it is not helpful in guiding the selection of antihypertensive agents.

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Question 6

Correct Answer: (C) "Now that you have had a heart attack, your body is showing us that it is vulnerable to things like an elevated BP, and we really need to work hard to get this under control soon."

Learning Objective: State the optimal management of patients with secondary hypertension

Answer Explanation: The correct answer is C: "Now that you have had a heart attack, your body is showing us that it is vulnerable to things like an elevated BP, and we really need to work hard to get this under control soon." When treating elevated BP in the secondary

prevention mode, when a patient has already experienced target organ damage, the benefits of treatment are even more evident in that the numbers needed to treat to prevent another cardiovascular outcome are lower than numbers needed in those without prior damage. Answers A, B, and D represent perceptions about target organ damage and BP control that existed until about the 1990s. Since that time, it has become clear that after target organ damage occurs, it is even more important to manage cardiovascular risk factors.

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Question 7

Correct Answer: (D) He is at increased risk for a major adverse cardiovascular event or death.

Learning Objective: Identify which patients should be evaluated for masked hypertension, white coat hypertension, and nocturnal hypertension and the prognostic importance of these blood pressure patterns

Answer Explanation: Both elevated short- and long-term BP variability are associated with increased risk of major cardiovascular events and mortality. Patients with CKD and ESRD are particularly vulnerable to increased BP variability

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Question 8

Correct Answer: (D) Evaluate her for primary aldosteronism

Learning Objective: Identify which patients should be evaluated for secondary causes of hypertension, including renovascular disease, aldosterone excess, and catecholamine-secreting tumors

Answer Explanation: Recent studies support frequent screening for primary aldosteronism in hypertensive patients. Even if BP is controlled with medication, patients with primary aldosteronism are at higher cardiovascular risk compared with those with essential hypertension. Recent guidelines recommend screening for primary aldosteronism in all patients with hypertension and hypokalemia, even if diuretic induced.

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Article 2: Management

Question 9

Correct Answer: (B) Intensive BP control was associated with reduced risk of mild cognitive impairment at 5 years follow-up

Learning Objective: Describe the effect of lower BP targets on the risk of cognitive impairment and dementia

Answer Explanation: According to the SPRINT MIND study, intensive BP control to target systolic BP <120 mmHg as compared with <140 mmHg was associated with a significant decrease in the risk of cognitive impairment at 5 years follow up (B). The risk of dementia was also decreased, but this effect did not reach statistical significance.

PRESERVE looked at the effect of two different BP targets, intensive (systolic BP <125 mmHg) vs standard (systolic BP 130–140 mmHg) on cerebral perfusion, as assessed by magnetic resonance imaging in patients with imaging-confirmed lacunar stroke. This small study showed no effect of tighter BP target on cerebral perfusion, or rates of adverse events including falls (C and D).

A subset of patients enrolled in SPRINT MIND underwent baseline and follow-up magnetic resonance imaging of the brain 4 years after randomization. In follow-up magnetic resonance imaging, those in the tighter control group showed less progression of white matter ischemic lesions but also had a decrease in overall brain volume (A).

References

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Question 10

Correct Answer: (C) Treatment with thiazide diuretics has been associated with better BP control and reductions in cardiovascular outcomes, as compared with other first-line agents for management of hypertension.

Learning Objective: Explain the most effective initial agents for treatment of hypertension based on recent studies

Answer Explanation: LEGEND-HTN used a big data approach to analyze administrative claims and electronic health record databases to identify patients initiating antihypertensive medications, and assess clinical outcomes. This study found that as compared with angiotensin-converting enzyme (ACE) inhibitors, dihydropyridine calcium channel blockers, and angiotensin receptor blockers, thiazide diuretics were associated with better BP control and reduced rates of cardiovascular events including hospitalization for heart failure, stroke and myocardial infarction (C).

This study also found inferior outcomes in patients treated with nondihydropyridine calcium channel blockers (A) as a first-line agent. Chlorthalidone and hydrochlorthiazide had similar effects on rates of myocardial infarction, heart failure, and stroke, but treatment with chlorthalidone was associated with higher rates of hyponatremia, hypokalemia, and acute kidney injury (B).

Wei et al. performed a meta-analysis of 46 clinical trials of treatment of hypertension. In contrast to LEGEND-HTN, this particular analysis showed that ACE inhibitors, dihydropyridine calcium channel blockers, and thiazide diuretics were similarly effective in reducing overall cardiovascular events. It also found that ACE inhibitors were most effective in reducing risk of myocardial infarction (D).

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Question 11

Correct Answer: (A) As compared with monotherapy, initiation of combination antihypertensive therapy is associated with reduced mortality at 3-year follow-up.

Learning Objective: Summarize the outcomes of combination drug therapy compared with a stepped care approach

Answer Explanation: In an observational study of 100,982 patients started on a single agent and 24,653 patients started on a two-drug fixed combination, the combination group had a 20% lower risk of mortality at 3 years follow up (A). Only 36% of those started on a single agent were on combination therapy by 3 years, despite higher rates of hospitalization for cardiovascular events and higher mortality, suggesting poorer control (D).

In a study of black African patients with uncontrolled hypertension, combination therapy with perindopril/amlodipine or hydrochlorthiazide/amlodipine led to better BP control than combination therapy with perindopril/hydrochlorthiazide at 6-month follow-up (B). It has been suggested that the shorter duration of action of hydrochlorthiazide may be a factor in this study, and it is unclear if the combination of ACEi with chlorthalidone (longer acting) would have been more effective.

The TRIUMPH study of triple BP control therapy (telmisartan, amlodipine, and chlorthalidone) versus usual care enrolled 700 patients in Sri Lanka. Triple therapy was associated with improved BP control, without increased rates of adverse events. A recommendation to use triple therapy has been included in the recent European Society of Hypertension guideline (C).

References

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Question 12

Correct Answer: (B) Intensive BP control in SPRINT was associated with a small but persistent decline in GFR compared with standard BP control

Learning Objective: Describe the effect of lower blood pressure targets on the risk of progression to ESRD or acute kidney injury

Answer Explanation: Beddhu et al. in 2017 evaluated changes in eGFR and risk for acute kidney injury for SPRINT participants without kidney disease at enrollment and reported a 3.5-fold higher hazard of developing incident CKD (defined as at least 30% reduction to eGFR <60 mL/min per 1.73 m^2) with intensive treatment. However, no patient in either treatment arm developed ESRD (A) and many recovered completely or partially. There was an initial decline in eGFR in the intensive treatment arm in the first 6 months, which plateaued after 30 months but remained at 4 mL/min per 1.73 m^2 lower than in the standard treatment arm (B).

For the subgroup of patients who developed incident CKD during SPRINT, Zhang et al. measured nine urinary biomarkers of kidney damage at baseline and 1 year after enrollment in 162 case patients (128 in the intensive and 34 in the standard group) and 162 matched controls and reported that those who developed incident CKD in the intensive treatment arm had decreases rather than increases in biomarkers of kidney damage, supporting a benign hemodynamic process rather than intrinsic and permanent injury (C).

From the primary SPRINT study, intensive treatment did not prevent renal outcomes in patients with or without CKD (D).

References

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Question 13

Correct Answer: (C) He should be instructed on lifestyle modification with the decision on medication dependent on assessment of 10-year CVD event risk

Learning Objective: Describe the effect of lower BP targets on the risk of progression to ESRD or acute kidney injury

Answer Explanation: The 2017 ACC/AHA guideline recommends initiation of lifestyle modification for all patients with elevated BP or hypertension (A). However, he does have some CVD risk factors, primarily his age, sex, and smoking history. For those at high risk for CVD events because of a prior history of CV disease or events, diabetes, or CKD, medication should also be started at BP of 130/80 mmHg or higher (B). As this man has not had a CVD event, diabetes mellitus, or CKD, the decision to treat with medication would be based on his predicted 10-year CVD risk (C). Using the Atherosclerotic Cardiovascular Disease risk calculator, his 10-year risk is 19%, above the threshold of 10%, and he should be started on medication, so (A) is incorrect. As his BP is within 10/5 mmHg of his goal BP, it is reasonable to start with one agent (D).

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Question 14

Correct Answer: (D) Spironolactone is the most appropriate next agent

Learning Objective: Discuss additional drug choices after the first three agents for patients with resistant hypertension

Answer Explanation: This patient has resistant hypertension, defined as BP above goal despite three or more agents at full or appropriate doses including a diuretic. In addition to an ACE inhibitor or angiotensin receptor blocker, a calcium channel blocker and an appropriate dosed diuretic, the strongest data for selection of a fourth agent comes from the PATHWAY study in which a mineralocorticoid receptor antagonist spironolactone was far superior to the other choices of a β-blocker (C), or placebo (D).

Thiazide-type diuretics, such as chlorthalidone, are effective antihypertensives in CKD and can be used to an eGFR down to 30 mL/min and should be continued in this patient (answer A is incorrect). Combination treatment with ACE inhibitors and angiotensin receptor blockade is contraindicated and associated with worse long-term renal outcomes (answer B is incorrect). This patient already has a relative bradycardia with a heart rate of 55 beats/min, and may not tolerate β-blockade which would also be less effective (answer C is incorrect).

References

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Question 15

Correct Answer: (D) Smartphone apps that provide reminder alerts, adherence reports, and peer support may improve medication adherence

Learning Objective: Summarize recent studies on the role of nonadherence and implementation strategies to address it

Answer Explanation: Nonadherence or suboptimal adherence to antihypertensive medications is a major reason for inadequate BP control, and only about 50% of patients adhere to antihypertensive medication (answer A is incorrect).

In a randomized trial, electronic health record (EHR)-based medication management tools with education promoted greater understanding of medications and dosing but did not appear to improve medication adherence (B).

In a randomized trial, systolic BP control was similar between patients who used a smart phone app that provided reminder alerts, adherence reports, and peer support and patients who did not use the app, but adherence based on self-assessment increased modestly among app users, particularly among those with the lowest adherence at baseline (answer D is correct). However, the effect was limited, and such interventions were not shown to appreciably affect BP (answer C is incorrect).

References

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Article 3: Epidemiology

Question 16

Correct Answer: (D) Number of deaths and disability related to hypertension continued to rise while age-standardized rates declined between years 2007 and 2017.

Learning Objective: Discuss the burden of hypertension based on current epidemiology

Answer Explanation: Globally, the absolute number of deaths and disability resulting from hypertension and hypertension-related complications continue to rise. However, when corrected for an aging population, rates of deaths and disability due to hypertension and hypertension-related complications have declined.

Reference

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Question 17

Correct Answer: (A) Patients with BP of ≥130/80 mmHg before the age of 40 years are at increased risk of cardiovascular disease

Learning Objective: Discuss the impact of the 2017 ACC/AHA Blood Pressure Guideline

Answer Explanation: Risk of hospitalization and death due to cardiovascular disease is higher in both male and female individuals with a BP of ≥130/80 mmHg before the age of 40 years

Reference

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Question 18

Correct Answer: (D) Recommendation for antihypertensive medication will increase by only <2% of the adult US population

Learning Objective: Discuss the impact of the 2017 ACC/AHA Blood Pressure Guideline

Answer Explanation: Hypertension prevalence increased from 31.9% (72.2 million adults) to 45.6% (10.3.3 million adults), corresponding to an increase of 13.7% (31.1 million adults). Hypertension prevalence more than doubled (increased from 10.5% to 24%) in adults in the age group of 20 to 44 years. In adults aged 65 to 74 years, prevalence increased from 63.6% to 75.6%, and in adults aged ≥75 years, prevalence increased from 75.1% to 82.3%. Antihypertensive medication was advised for 36.2% of US adults compared with 34.3% of adults, corresponding to 1.9% (4.2 million) additional adults recommended for antihypertensive medication.

Reference

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Question 19

Correct Answer: (A) Antihypertensives may be less effective in the presence of periodontitis

Learning Objective: Discuss updated information on risk factors for hypertension and hypertension control

Answer Explanation: Patients with periodontal disease who are on antihypertensive medication generally have higher systolic BP and higher odds of unsuccessful antihypertensive treatment compared with patients who are on antihypertensive medication but do not have periodontal disease; suggesting that antihypertensive treatment may be less effective in the presence of periodontitis. Also, treatment of periodontitis is associated with lower BP.

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Question 20

Correct Answer: (B) Low BP in patients her age is linked to dementia if patients have a history of high BP

Learning Objective: Discuss updated information on dementia as a complication of hypertension

Answer Explanation: Recent evidence suggests that sustained hypertension in midlife to late life and a pattern of midlife hypertension and late-life hypotension, compared with midlife and late-life normal BP, were associated with increased risk for subsequent dementia. Evidence was inconclusive for patients with late-life hypotension but normal BP in midlife.

Reference

1. Walker KA, Sharrett AR, Wu A, Schneider ALC, Albert M, Lutsey PL, et al. Association of midlife to late-life blood pressure patterns with incident dementia. *JAMA* 322:535–545, 2019.

Question 21

Correct Answer: (D) Assure him that long working hours are associated with both masked hypertension and sustained hypertension

Learning Objective: Discuss updated information on risk factors for hypertension and hypertension control

Answer Explanation: In a recent study of white-collar workers, compared with working <35 hours per week, working >48 hours was associated with increased risk of masked hypertension as well as sustained hypertension.

Reference

1. Trudel X, Brisson C, Gilbert-Ouimet M, Trudel X, Brisson C, Gilbert-Ouimet M, et al. Long working hours and the prevalence of masked and sustained hypertension. *Hypertension* 75:532–538, 2020.

Question 22

Correct Answer: (B) Hypertension generally correlates with the prevalence of obesity and physical inactivity

Learning Objective: Discuss updated information on risk factors for hypertension and hypertension control

Answer Explanation: Socioeconomic status, assessed by income, education, and/or occupation, is a major determinant of hypertension. However, although individuals with low socioeconomic status generally exhibit a high prevalence of hypertension, the same association is not observed across all world economic regions. In a recent study, whereas the prevalence of hypertension was higher in individuals of lower socioeconomic class in high-income countries, the prevalence of hypertension was higher in individuals of higher socioeconomic class in low-income countries.

This was attributed to the lower prevalence of obesity and physical inactivity among individuals of higher socioeconomic status in high-income countries, and the higher prevalence of obesity and physical inactivity among individuals of higher socioeconomic status in low-income countries. The same study showed that the risk of major cardiovascular events was greater among those with low levels of education in all types of country studied and was attributable to inadequate access to primary and secondary prevention, and access to medical care among people with the lowest levels of education in low-income countries.

BP control is lowest among individuals of lower socioeconomic class, particularly in low-income countries.

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Question 23

Correct Answer: (B) Observational data suggest that working >48 hours weekly is associated with increased risk of hypertension compared with working <35 hours weekly

Learning Objective: Discuss updated information on risk factors for hypertension and hypertension control

Answer Explanation: The relationship between light to moderate alcohol intake and incident hypertension has been controversial. Some studies suggest light to moderate amount of alcohol intake is associated with decreased hypertension risk, but these data have been questioned because of inadequate assessment of alcohol intake and because of residual confounding due to the known association between type, quantity, and pattern of drinking with socioeconomic factors and other lifestyle behaviors.

A recent study reported an association of long working hours with the prevalence of masked and sustained hypertension. Compared with working <35 hours per week, working >?48 hours was associated with increased risk of masked hypertension (prevalence ratio = 1.42; 95% CI = 1.09–2.64) and sustained hypertension (prevalence ratio = 1.66; 95% CI = 1.15–2.50).

A recent study including data from 512,715 Chinese adults used genetic variants to classify people by alcohol intake and compared this classification with that determined by self-reporting. In this study, genetic variant-predicted alcohol intake was positively associated with systolic BP, along with high-density lipoprotein and γ-glutamyl transferase (a marker for alcohol use). This association was particularly strong among men.

References

1. Briasoulis A, Agarwal V, Messerli FH. Alcohol consumption and the risk of hypertension in men and women: A systematic review and meta-analysis. *J Clin Hypertens (Greenwich)* 14:792–798, 2012.
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Article 4: Mechanism/Pathophysiology

Question 24

Correct Answer: (A) Renal tubular α-adrenergic receptors

Learning Objective: Differentiate between the common causes of secondary hypertension and their associated mechanisms

Answer Explanation: The correct answer is A. Because the question specifically asks which is "directly contributing to the sodium retention," the most obvious answers should be renal in nature. Therefore, the cardiac and vascular responses, while likely involved in the pathogenesis of hypertension (resulting in vasoconstriction and increased cardiac output), would not directly influence renal sodium reabsorption. Answer C is inherently incorrect because α-2 receptors, not β-receptors, are considered key preganaglionic adrenergic receptor subtypes. The juxtaglomerular apparatus would be stimulated to release renin in response to β-adrenergic receptor activation, not α.

Reference

1. Lang CC, Rahman AR, Balfour DJK, Struthers AD. Effect of noradrenaline on renal sodium and water handling in euhydrated and overhydrated man. *Clin Sci (Lond)* 85:487–494, 1993.

Question 25

Correct Answer: (B) Decreased expression of the (pro)renin receptor

Learning Objective: Discuss how the renin-angiotensin-aldosterone and immune systems are implicated in BP regulation and development of hypertension

Answer Explanation: The correct answer is B, Inhibition of (pro) renin receptor results in a reduction of BP. Inhibition of (pro)renin receptor resulted in a reduction of BP, decreased prostaglandin E-2 excretion, and reduced plasma renin activity. A decreased expression of sodium-potassium-chloride cotransporter could reduce BP; however, it would likely result in an increase in plasma renin activity. Increasing the expression of the renin-angiotensin system components (either ACE or AT1) in several tissues (including the kidney) is associated with an increase in BP.

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Question 26

Correct Answer: (A) Increased sodium delivery to the collecting duct epithelial sodium channel to stimulate potassium excretion

Learning Objective: Compare and contrast the influence of high or low dietary sodium and potassium intakes on natriuresis and BP regulation

Answer Explanation: The correct answer is A, because an increase in dietary potassium will result in an overall decrease sodium reabsorption in the early nephron that stimulates increase sodium reabsorption in the distal nephron in exchange for the excess dietary potassium. Although the distal sodium reabsorption will increase, it is not sufficient and will result in an overall natriuretic and kaliuretic response. The high fruit and vegetable content of the DASH diet is associated with increased urinary flow and pH, suggesting a preserved or even elevated filtrate bicarbonate concentration and increased pH (answers B and C). An increase in sodium channels along the nephron would likely result in increased sodium reabsorption and thus not support natriuresis (answer D).

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1. McDonough AA, Youn JH. Potassium homeostasis: The knowns, the unknowns, and the health benefits. *Physiology (Bethesda, Md)* 32(2): 100–111, 2017.
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Question 27

Correct Answer: (E) Prior destruction of EVs from this patient will reduce acetylcholine-induced vasodilation

Learning Objective: Define the mechanisms by which extracellular vesicles and myoendothelial projections modulate vascular tone and blood pressure

Answer Explanation: Answer E is the best choice. Prior destruction of EVs from hypertensive individuals restored the ability of EVs to reduce acetylcholine-induced vasodilation. As described in the section, EVs isolated from normotensive or hypertensive rats and humans were not shown to have a direct impact on vascular tone in isolated vessels. Therefore, answers B and C are incorrect. Studies by the Erbrugger laboratory found that EVs from normotensive individuals caused reduced acetylcholine-induced vasodilation, but not EVs from hypertensive individuals. Therefore, answer D is incorrect.

Reference

1. Good ME, Musante L, La Salvia S, Howell NL, Carey RM, Le TH, et al. Circulating extracellular vesicles in normotension restrain vasodilation in resistance arteries. *Hypertension* 75:218–228, 2019.

Question 28

Correct Answer: (D) Decreased activity of renal nerves

Learning Objective: Describe the mechanisms by which the nervous system is implicated in the pathogenesis of hypertension

Answer Explanation: Answer D is the best choice. Animal studies and a recent proof-of-concept clinical trial suggest that renal denervation decreases hypertension and lessens severity of OSA. In a mouse model of OSA, renal denervation reduced urinary norepinephrine excretion, systolic BP, and renal angiotensinogen and increased sodium excretion. Therefore, answer choices A, B, C and E are incorrect.

In a recent proof-of-concept randomized phase II trial that enrolled patients with resistant hypertension and OSA, renal denervation was shown to significantly reduce systolic (~20 mmHg) and diastolic (~8 mmHg) blood pressure and improve the parameters of healthy sleep. The mechanism by which renal denervation lessens the severity of OSA is not understood, but it may reflect a decrease in sodium and water retention with diminished edema of the upper airway, or a direct effect of reduced BP.

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3. Azizi M, Amar L, Lorthioir A. Resistant hypertension and obstructive sleep apnea: Is there a specific indication for endovascular renal denervation? *Hypertension* 72:281–282, 2018.

Question 29

Correct Answer: (C) Renal denervation may decrease hypertension and the severity of OSA

Learning Objective: Describe the mechanisms by which the nervous system is implicated in the pathogenesis of hypertension

Answer Explanation: Answer C is the best choice. In a recent proof-of-concept randomized phase-II trial which enrolled patients with resistant hypertension and OSA, renal denervation was shown to significantly reduce systolic (approximately 20 mmHg) and diastolic (approximately 8 mmHg) BP and improve parameters of healthy sleep. Therefore answer choices A and B are incorrect. Answer D is incorrect as evidence is unclear whether improved compliance of CPAP has a greater effect on blood pressure than renal denervation.

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7. Azizi M, Amar L, Lorthioir A. Resistant hypertension and obstructive sleep apnea: Is there a specific indication for endovascular renal denervation? *Hypertension* 72: 281–282, 2018.

Question 30

Correct Answer: (B) Hypertension correlates better with the dietary sodium/potassium ratio than with sodium intake alone

Learning Objective: Compare and contrast the influence of high or low dietary sodium and potassium intakes on natriuresis and BP regulation

Answer Explanation: Answer B is the best choice, because hypertension correlates far better with dietary sodium/potassium ratio. While patients with advanced kidney disease may not be able to tolerate a high potassium diet because of the risks of hyperkalemia, prospective studies suggest that higher potassium intake correlates with lower incidence of hypertension and slower progression of chronic kidney disease (answer A is incorrect). The DASH study showed that a low sodium, high potassium, high alkali diet lowered systolic BP more than sodium reduction alone (answer B is correct).

Recent animal studies show that increasing dietary potassium increases natriuresis by increasing sodium delivery to the collecting duct epithelial sodium channel. This results in increased sodium absorption but also, because there is greater sodium delivery than can be reabsorbed, a potassium-rich-rich diet induced natriuresis. Increased dietary potassium provokes a significant natriuretic response analogous to taking a loop or thiazide diuretic, but without the accompanying risk of hypokalemia. An important takeaway message is that handling of sodium and potassium are intrinsically linked and that potassium homeostasis has precedence over sodium homeostasis.

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