ENDOCRINE: APRIL 26TH: TRANSGENDER MEDICINE & ENDOCRINE TEST

April 2022

QUESTION 1

A 20-year-old transgender male (genetic female, identifies as male) is evaluated 3 months after starting intramuscular testosterone injections. He was previously diagnosed with gender dysphoria by a psychiatrist and requested masculinizing hormone therapy. At the start of therapy, laboratory results, including complete blood count, electrolytes, and lipid panel, were normal.

Which of the following is the most appropriate test to monitor for therapy-related complications?

- A) Hematocrit
- B) Prolactin
- C) Prostate-specific antigen
- D) Serum electrolytes

QUESTION 1 ANSWER

A 20-year-old transgender male (genetic female, identifies as male) is evaluated 3 months after starting intramuscular testosterone injections. He was previously diagnosed with gender dysphoria by a psychiatrist and requested masculinizing hormone therapy. At the start of therapy, laboratory results, including complete blood count, electrolytes, and lipid panel, were normal.

Which of the following is the most appropriate test to monitor for therapy-related complications?

- **A) Hematocrit (85% correct)**
- B) Prolactin
- C) Prostate-specific antigen
- D) Serum electrolytes

EXPLANATION

In transgender males taking testosterone masculinizing therapy, hematocrit or hemoglobin should be measured regularly to assess for erythrocytosis.

Erythrocytosis (hematocrit >50%) is a known risk of testosterone therapy, and current guidelines for transgender males taking testosterone recommend hematocrit or hemoglobin measurement before starting therapy, every 3 months for the first year, then annually or semiannually.

Testosterone levels should be maintained in the physiologic normal male range (320-800 ng/dL [11-28 nmol/L]) to reduce the risk for adverse events such as erythrocytosis, sleep apnea, hypertension, excessive weight gain, sodium retention, lipid changes, and cystic acne.

Testosterone therapy should be reduced or the method of delivery changed if erythrocytosis occurs.

Current practice guidelines recommend that cancer screening for transgender persons be based on the person's anatomy and risk factors. Since this patient doesn't have a prostate, measuring PSA levels is of no use. If the patient were a genetic male taking testosterone, then monitor PSA.

EXPLANATION

Hyperprolactinemia and hyperkalemia are known complications of feminizing hormone therapy (estrogen and spironolactone therapy, respectively), not testosterone.

Estrogen can increase the growth of pituitary lactotroph cells and thus prolactinomas have been reported in transgender females on long-term, high-dose estrogen.

Periodically monitor prolactin levels in transgender females.

Spironolactone competes with aldosterone for receptor sites in the distal renal tubules leading to increased sodium and water excretion while retaining potassium.

Monitor electrolytes q3 months x1 year and then annually for transgender females on spironolactone.

QUESTION 2

A 45-year-old woman is evaluated for management of obesity and type 2 diabetes mellitus diagnosed 1 year ago. During the past 6 months, she has implemented lifestyle modifications, including a low-calorie diet, weight-loss group meetings, and exercise. She has achieved a 5.0-kg (11.0-lb) weight loss. Medical history is significant for recurrent urinary tract infections. Her only medication is metformin, 850 mg twice daily.

Vital signs and physical examination findings are unremarkable. BMI is 35.

Laboratory studies show a hemoglobin A_{1c} level of 7.6%.

Which of the following medication changes would most benefit this patient?

- A) Add dapagliflozin
- B) Add glimepiride
- C) Add liraglutide
- D) Increase metformin dosage

QUESTION 2 ANSWER

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Laboratory studies show a hemoglobin A_{1c} level of 7.6%.

Which of the following medication changes would most benefit this patient?

- A) Add dapagliflozin
- B) Add glimepiride
- **C) Add liraglutide (75% correct)**
- D) Increase metformin dosage

EXPLANATION

Goal: treating a patient with DM type II and obesity.

Adding liraglutide (a glucagon-like peptide 1 receptor agonist (GLP-1 RA) would most benefit this patient with the goal of weight loss & getting her A1C to a goal of <7%.

The GLP-1 RAs increase glucose-stimulated insulin secretion, inhibit glucagon, slow gastric emptying, and increase satiety; they can lower hemoglobin A_{1c} by 1% to 1.5%. Their additional ability to promote weight loss makes them an excellent choice for this patient.

Diabetes mellitus medications associated with weight loss include glucagon-like peptide 1 receptor agonists, sodium-glucose cotransporter 2 inhibitors, α-glucosidase inhibitors, and amylin mimetics.

SGLT2 inhibitors like dapagliflozin can increase UTIs, so not appropriate.

Insulin secretagogues, including sulfonylureas, thiazolidinediones, and insulin typically cause weight gain.

Metformin is typically weight-neutral. Some studies show a modest weight loss.

QUESTION 3

A 48-year-old woman is evaluated for a 6-month history of a 9.1-kg (20.1-lb) weight gain and easy bruising. She has newly diagnosed type 2 diabetes mellitus treated with metformin.

On physical examination, vital signs are normal. BMI is 38. The patient has central obesity, supraclavicular and dorsocervical fat pads, and wide violaceous striae on her abdomen.

Laboratory studies show elevated 24-hour urine free cortisol and late-night salivary cortisol levels.

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

- A) Abdominal CT
  B) Adrenocorticotropic hormone level measurement
- C) 8-mg Dexamethasone suppression test
- D) Inferior petrosal sinus sampling

QUESTION 3 ANSWER

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Laboratory studies show elevated 24-hour urine free cortisol and late-night salivary cortisol levels.

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

- A) Abdominal CT
  B) Adrenocorticotropic hormone level measurement (53% correct)
- C) 8-mg Dexamethasone suppression test
- D) Inferior petrosal sinus sampling

EXPLANATION

The point: Diagnose the cause of Cushing syndrome.

"Cushing syndrome" is a term used to describe hypercortisolism, regardless of the cause. At least two first-line tests must be abnormal to confirm the diagnosis, such as:

- Overnight low-dose dexamethasone suppression test
- 24-hour urine free cortisol measurement (abnormal in our pt)
- Late-night salivary cortisol measurement (abnormal in our pt)

This pt has confirmed Cushing syndrome, so now:

- 1. Determine if the Cushing syndrome is ACTH independent or dependent
- 2. Localize the source of ACTH in ACTH-dependent disease or confirm the presence of adrenal mass (or masses) in ACTH-independent disease.

EXPLANATION

So the next step in our patient is to measure the patient's ACTH level to see if it is ACTH-independent or dependent!

If ACTH-independent, ACTH will be suppressed (<5pg/mL) and then MR or CT abdomen is needed. Cortisol-secreting adrenal adenomas and (rarely) carcinomas make up 15-20% of endogenous causes of Cushing syndrome. The tumors put out cortisol and suppress pituitary ACTH production, so it is ACTH independent.

If ACTH-dependent and no pituitary tumor is seen on MRI, then 8-mg dexamethasone suppression test is used to separate out:

- Cushing disease (pituitary Cushing syndrome) from ectopic source of ACTH
- If pituitary source, then plasma cortisol at 8am will be suppressed by >50% (i.e. when it's a pituitary source of ACTH, it will response to negative feedback from high-dose Decadron). If it's an ectopic source, the ACTH level won't be suppressed.

You would only do inferior petrosal sinus sampling prior to exploratory pituitary surgery in pts with Cushing disease. This test would establish the diagnosis of Cushing disease.

QUESTION 4

A 37-year-old woman is evaluated for secondary fracture prevention 3 months after surgery for a right distal radius fracture sustained from a fall. Family history is significant for low bone mass in her mother. Her only medication is an ethinyl estradiol and norgestimate oral contraceptive. Her medical history is otherwise unremarkable.

Physical examination is normal. BMI is 22.

Which of the following is the most appropriate management?

- A) Bone mineral density measurement
- B) Calcium supplementation
- C) Fracture Risk Assessment score calculation
- D) Oral contraceptive discontinuation
- E) Therapeutic lifestyle interventions

QUESTION 4

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Physical examination is normal. BMI is 22.

Which of the following is the most appropriate management?

- A) Bone mineral density measurement
- B) Calcium supplementation
- C) Fracture Risk Assessment score calculation
- D) Oral contraceptive discontinuation
- **E) Therapeutic lifestyle interventions (22% correct)**

EXPLANATION

Goal: Evaluate low-energy fracture in a premenopausal woman.

In otherwise healthy young adults, a low-energy fracture is not an indication for bone mineral density measurement. Encourage a healthy weight, balanced nutrition, physical fitness, no smoking, and moderation of EtOH intake.

BMD testing is not indicated in young adults, with exceptions being recurrent low energy fractures or disorders known to cause metabolic bone disease, such as eating disorders, solid organ transplantation, or glucocorticoid therapy.

The role of calcium and calcium supplementation in management of postmenopausal osteoporosis is debatable, with no more than modest benefits in the absence of overt dietary deficiency or malabsorption of calcium.

In younger adults, the predictive relationship of the FRAX score to fracture risk is not clinically useful; thus, the FRAX score is not relevant to this patient's care.

QUESTION 5

A 70-year-old woman is evaluated for follow-up of osteoporosis, diagnosed 5 years ago. At that time, her left femur neck dual-energy x-ray absorptiometry (DEXA) T-score was -2.5. Treatment was initiated with denosumab. She has had no fractures. The most recent dose of denosumab was given 6 months ago.

Today, the left femur neck DEXA T-score is -1.8.

Discontinuation of denosumab is planned.

Which of the following is the most appropriate management?

- A) Alendronate
- B) Drug holiday
- C) Raloxifene
- D) Romosozumab
- E) Teriparatide

QUESTION 5 ANSWER

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- B) Drug holiday
- C) Raloxifene
- D) Romosozumab
- E) Teriparatide

EXPLANATION

Goal: Manage postmenopausal osteoporosis in a patient discontinuing denosumab (Prolia).

The effects of denosumab on bone mineral density (BMD) are transient, and initiation of antiresorptive therapy on discontinuation of denosumab is necessary to prevent loss of accrued BMD.

Optimal duration of use is unknown, but current recommendations suggest reassessing fracture risk and need for ongoing therapy after 5 to 10 years of use.

This patient's fracture risk is no longer high; thus, discontinuation of denosumab is appropriate.

Alendronate is effective to prevent bone loss during denosumab withdrawal when it is initiated 6 months after the last denosumab treatment.

EXPLANATION

Given its antiresorptive effects, raloxifene (**Option C**) could be used following denosumab withdrawal. However, it suppresses bone resorption less than bisphosphonates, and its effectiveness in this setting is unproven.

Raloxifene should be avoided in patients at risk for cardiovascular disease but may be useful in women at high risk for breast cancer because it reduces the risk for invasive breast cancer.

Although romosozumab (**Option D**) has both bone-formative and antiresorptive effects, its bone formative effect is blunted when used subsequent to antiresorptive therapy, including denosumab.

Teriparatide (**Option E**) is effective in improving BMD and reducing fracture risk by increasing bone formation. Teriparatide combined with denosumab therapy yields greater improvement in BMD than either alone. However, teriparatide accentuates the increased bone resorption and rapid loss of BMD associated with denosumab withdrawal; thus, it should not be substituted for denosumab.

QUESTION 6

A 60-year-old woman is evaluated during a follow-up visit for hypertension, coronary artery disease, obesity, and dyslipidemia. She reports a 5-kg (11.0-lb) weight gain in the past year. Her fasting blood glucose was 110 mg/dL (6.1 mmol/L) and hemoglobin A_{1c} level was 6.1% 6 months ago. Current medications are hydrochlorothiazide, lisinopril, carvedilol, low-dose aspirin, and atorvastatin.

On physical examination, blood pressure is 135/84 mm Hg. BMI is 28. The remainder of the examination is normal.

Fasting glucose is 114 mg/dL (6.3 mmol/L).

Which of the following is the most appropriate management for this patient with prediabetes?

A) Glipizide

B) Intensive lifestyle modifications

C) Metformin

D) Sitagliptin

QUESTION 6 ANSWER

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On physical examination, blood pressure is 135/84 mm Hg. BMI is 28. The remainder of the examination is normal.

Fasting glucose is 114 mg/dL (6.3 mmol/L).

Which of the following is the most appropriate management for this patient with prediabetes?

A) Glipizide

B) Intensive lifestyle modifications (80% correct)

C) Metformin

D) Sitagliptin

EXPLANATION

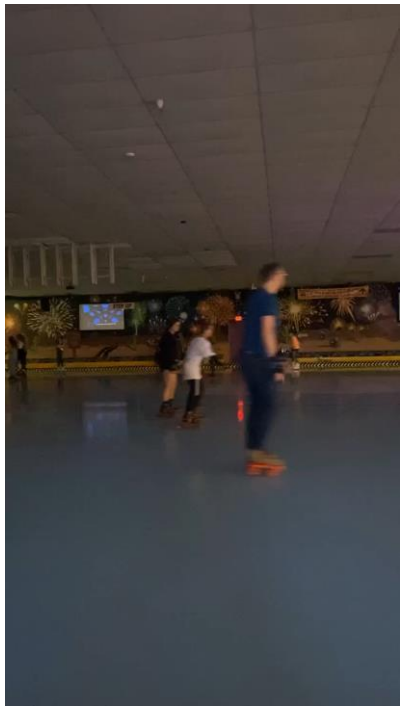
The development of type 2 diabetes mellitus in individuals at high risk can be delayed or prevented with modifications to lifestyle (diet, exercise), pharmacologic intervention, or metabolic surgery.

Lifestyle modifications can reduce the incidence of type 2 diabetes mellitus in persons with prediabetes by 58% and is the initial recommended therapy.

So what does intensive lifestyle modifications mean for your patients?

- The American Diabetes Association recommends a program for intensive lifestyle behavioral changes that includes at least a 7% weight loss over 6 months and at least 150 minutes per week of moderate-intensity exercise (ex: brisk walking, water aerobics, riding a bike, dancing, double tennis, pushing a lawn mower (not a thing here….), hiking, rollerblading.

Metformin may be considered for prevention of type 2 diabetes in patients with prediabetes unresponsive to lifestyle modifications, particularly in patients with BMI greater than 35, age younger than 60 years, or a history of gestational diabetes. If this patient fails to lose weight, metformin would be a reasonable addition.



QUESTION 7

A 70-year-old woman is evaluated for incidentally discovered hypercalcemia. She has no symptoms or other medical conditions and takes no medications.

On physical examination, vital signs are normal. A height loss of 5 cm (2.0 inches) has occurred since age 65 years. Thoracic kyphosis is noted.

Kidney-urinary-bladder radiograph is negative for kidney stones. Dual-energy x-ray absorptiometry scan shows femur neck T-score of -1.9, lumbar spine T-score -1.8, and distal one-third radius T-score of -1.7.

Which of the following is the most appropriate management?

A) Order parathyroid sestamibi scan

B) Order thoracic and lumbar spine radiography

C) Repeat serum calcium and creatinine measurement in 6 months

D) Start alendronate

Laboratory studies:	
Calcium	10.8 mg/dL (2.7 mmol/L)
Creatinine	0.8 mg/dL (70.7 µmol/L)
Phosphorus	2.5 mg/dL (0.81 mmol/L)
Parathyroid hormone	77 pg/mL (77 ng/L)
25-Hydroxyvitamin D	30 ng/mL (75.0 nmol/L)
24-Hour urine calcium	260 mg/24 h

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Which of the following is the most appropriate management?

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EXPLANATION

Goal: Manage asymptomatic primary hyperparathyroidism.

This patient has hypercalcemia, hypophosphatemia, and an inappropriately elevated serum parathyroid hormone level, establishing the diagnosis of primary hyperparathyroidism.

For asymptomatic patients with primary hyperparathyroidism, additional evaluation is necessary to determine if parathyroidectomy is indicated: assessment of kidney function, bone mineral density (BMD) measurement, and in some patients, assessment for nephrolithiasis or nephrocalcinosis.

In addition to evidence of bone disease, indications for parathyroidectomy in patients with primary hyperparathyroidism include age younger than 50 years; serum calcium 1 mg/dL (0.3 mmol/L) or greater above upper limit of normal; creatinine clearance less than 60 mL/min; 24-hour urine calcium greater than 400 mg/dL (100 mmol/L); or nephrolithiasis or increased risk for kidney stones.

This patient's evaluation is almost complete. We just need to look for vertebral fractures – especially given her height loss!

EXPLANATION

A parathyroid sestamibi scan (**Option A**) or neck ultrasonography may be appropriate for preoperative adenoma localization if surgery is indicated. Localization studies, however, do not influence the choice between surgical and medical management of primary hyperparathyroidism.

Patients without indications for parathyroidectomy require periodic reassessment that includes repeat serum calcium and creatinine measurement (**Option C**) every 6 to 12 months and BMD measurement of the lumbar spine, hip, and distal radius every 2 years.

Although alendronate (**Option D**) suppresses bone resorption and improves BMD at the lumbar spine in patients with primary hyperparathyroidism, it has not been shown to reduce fracture risk, serum calcium levels, or urine calcium levels in these patients.

QUESTION 8

A 45-year-old woman is evaluated for an incidentally found pituitary tumor. She was recently seen in the emergency department following a motor vehicle accident, where head CT demonstrated an 8-mm pituitary tumor without compression of the optic chiasm. She has otherwise been well with normal menstrual periods and no symptoms suggesting an endocrine disorder. She takes no medications.

Vital signs and the remainder of the physical examination are normal.

Laboratory evaluation reveals normal levels of 8 AM serum cortisol, thyroid-stimulating hormone, and free thyroxine .

Which of the following is the most appropriate additional test?

A) Follicle-stimulating hormone and luteinizing hormone

B) 24-hour urine cortisol

C) Prolactin and insulin-like growth factor-1

D) Urine and serum osmolality

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Which of the following is the most appropriate additional test?

A) Follicle-stimulating hormone and luteinizing hormone

B) 24-hour urine cortisol

C) Prolactin and insulin-like growth factor-1 (71% correct)

D) Urine and serum osmolality

EXPLANATION

Goal: Evaluate an incidentally noted pituitary lesion.

A pituitary lesion discovered incidentally on imaging is termed a “pituitary incidentaloma.”

Pituitary hypersecretion should be ruled out by measurement of prolactin and insulin-like growth factor 1.

Evaluation for Cushing disease is unnecessary in patients without signs or symptoms of cortisol excess. Pituitary tumors can also cause hypopituitarism.

Screening for hypopituitarism is recommended in all patients with pituitary tumors, regardless of symptoms, with measurement of follicle-stimulating hormone (FSH), luteinizing hormone (LH), cortisol, thyroid-stimulating hormone, free thyroxine, and total testosterone in men.

A history of normal menses essentially rules out hypogonadotropic hypogonadism and the need to measure FSH and LH.

QUESTION 9

A 67-year-old man is evaluated for a 4-week history of headache and fatigue. He has metastatic melanoma and receives nivolumab every 2 weeks. The patient has otherwise been well and has no additional symptoms. He takes no other medications.

On physical examination, vital signs are normal. Confrontational visual field testing is normal. No focal neurologic findings are present.

On laboratory evaluation, adrenocorticotropin hormone and 8 AM serum cortisol levels are low.

Chest radiograph is normal.

Which of the following is the most likely diagnosis?

A) Hypophysitis

B) Metastatic melanoma

C) Pituitary apoplexy

D) Sarcoidsosi

QUESTION 9 ANSWER

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On laboratory evaluation, adrenocorticotropin hormone and 8 AM serum cortisol levels are low.

Chest radiograph is normal.

Which of the following is the most likely diagnosis?

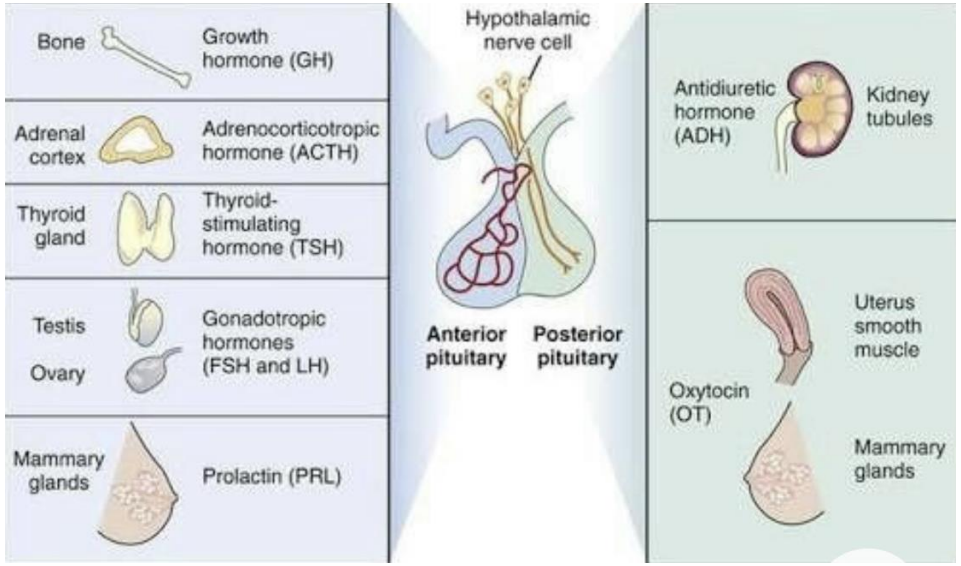
A) Hypophysitis (69% correct)

B) Metastatic melanoma

C) Pituitary apoplexy

D) Sarcoidsosi

EXPLANATION



Immune checkpoint inhibitors, including anti-programmed cell death protein-1 and anti-cytotoxic T-lymphocyte-associated protein-4 antibodies, can cause hypophysitis in 0.5% to 17% of patients and often presents with headache and fatigue.

Treatment of immune check point-related hypophysitis includes replacement of the hormone deficiencies in addition to high-dose glucocorticoids.

Evaluation usually reveals adrenocorticotropic hormone, luteinizing hormone, and thyroid-stimulating hormone deficiency, as well as low levels of growth hormone, adrenocorticotropic hormone deficiency is the most immediate concern because cortisol deficiency can be life-threatening. Diabetes insipidus is uncommon.

Treatment includes replacement of the hormone deficiencies and high-dose glucocorticoids in severe cases to treat the inflammatory process, although hormone deficiencies often persist. It is important to replace cortisol before initiation of thyroid hormone to avoid precipitating an adrenal crisis.

Metastasis to the pituitary gland is rare. It is more likely to occur in breast and lung cancers and you would see: anterior pituitary hormone deficiency can occur in pituitary metastasis, diabetes insipidus is most often the initial presentation.

Rapid expansion of a pituitary tumor caused by pituitary apoplexy (**Option C**), defined as sudden hemorrhage or infarction of a pituitary adenoma, typically causes sudden severe headache and compression of the optic chiasm (bitemporal hemianopsia)

QUESTION 10

A 62-year-old woman is evaluated for management of type 2 diabetes mellitus. Her medical history is significant for hypertension. Medications are metformin, empagliflozin, atorvastatin, and hydrochlorothiazide.

On physical examination, blood pressure is 130/80 mm Hg. The remainder of the physical examination is normal.

Laboratory studies show a hemoglobin A_{1c} level of 7.0%, estimated glomerular filtration rate of 50 mL/min/1.73 m^2, and a urine albumin-to-creatinine ratio of 98 mg/g.

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

A) Start lisinopril

B) Start verapamil

C) Stop empagliflozin

D) Stop metformin

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

A) Start lisinopril (93% correct)

B) Start verapamil

C) Stop empagliflozin

D) Stop metformin

EXPLANATION

The American Diabetes Association (ADA) recommends an ACE inhibitor or an angiotensin receptor blocker (ARB) as first-line therapy to slow progression of diabetic kidney disease and to prevent cardiovascular disease in nonpregnant women with type 2 diabetes mellitus and a modestly elevated urine albumin-to-creatinine ratio (UACR) (30-299 mg/g).

The ADA also strongly recommends this approach for patients with UACR 300 mg/g or greater or an estimated glomerular filtration rate (eGFR) less than 60 mL/min/1.73 m^2.

Diltiazem and verapamil (**Option B**), non-dihydropyridine calcium channel blockers, have a significant antiproteinuric effect and may be a reasonable therapeutic option for patients with diabetic kidney disease and persistent proteinuria despite maximum doses of ACE inhibitors or ARBs or don't tolerate ACE-I/ARBs.

For patients with type 2 diabetes and chronic kidney disease (CKD), the ADA recommends that physicians consider a sodium-glucose cotransporter 2 inhibitor (such as empagliflozin) or glucagon-like peptide 1 receptor agonist (such as liraglutide) to reduce risk for CKD progression and cardiovascular disease as part of the antihyperglycemic regimen.

Metformin is contraindicated at eGFR less than 30 mL/min/1.73 m^2, and clinicians should assess benefits and risks of continuing therapy if the eGFR is less than 45 mL/min/1.73 m^2 during therapy.

QUESTION 11

A 75-year-old woman is evaluated in follow-up for abnormal thyroid function test results. The test was obtained to evaluate unexplained weight gain over the previous 6 months. She reports no additional symptoms such as fatigue, cold intolerance, or constipation. She has no other medical concerns.

On physical examination, pulse rate is 82/min. BMI is 26. The thyroid is normal size and without nodules.

Laboratory studies show a thyroid-stimulating hormone level of 9 µU/mL (9 mU/L) and a free thyroxine level of 1.0 ng/dL (12.9 pmol/L).

Which of the following is the most appropriate management?

A) Initiate levothyroxine

B) Measure triiodothyronine level

C) Repeat thyroid function studies in 6 to 8 weeks

D) No additional management

QUESTION 11 ANSWER

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On physical examination, pulse rate is 82/min. BMI is 26. The thyroid is normal size and without nodules.

Laboratory studies show a thyroid-stimulating hormone level of 9 µU/mL (9 mU/L) and a free thyroxine level of 1.0 ng/dL (12.9 pmol/L).

Which of the following is the most appropriate management?

A) Initiate levothyroxine

B) Measure triiodothyronine level

C) Repeat thyroid function studies in 6 to 8 weeks (49% correct)

D) No additional management

EXPLANATION

This patient has subclinical hypothyroidism. Subclinical hypothyroidism is typically asymptomatic and diagnosed by a serum thyroid-stimulating hormone (TSH) level above the upper limit of the reference range and a normal free thyroxine (T_4) level. It affects 5% to 10% of the general population.

The rate of progression from subclinical to overt hypothyroidism is 2% to 4% per year, whereas normal thyroid function will spontaneously return in one third of patients.

The normal range for TSH increases with age; a TSH level of up to 10 µU/mL (10 mU/L) is within the normal range for persons 80 years and older.

Initiating levothyroxine (**Option A**) for subclinical hypothyroidism with TSH less than 20 µU/mL (20 mU/L) should be considered in younger patients, those attempting to become pregnant, or if severe symptoms are present.

No evidence supports that treatment of subclinical hypothyroidism improves quality of life, cognitive function, blood pressure, or weight.

Measuring the triiodothyronine level (**Option B**) in the setting of hypothyroidism is not necessary or recommended; normal levels are maintained unless hypothyroidism is severe. TSH will become elevated in hypothyroidism first, followed by abnormalities in the T_4 level.

QUESTION 12

A 73-year-old woman is seen during a routine evaluation. She has been taking amiodarone for atrial fibrillation for 1 year with good control until a recurrence 1 week ago. Thyroid function tests were normal before starting amiodarone. She has no history of iodinated contrast use. She is otherwise well and takes no additional medications.

On physical examination, pulse rate is 110/min and irregular; remaining vital signs are normal. Other than an irregular tachycardia, the thyroid and remainder of the examination are normal.

Laboratory studies show a thyroid-stimulating hormone level of less than 0.01 µU/mL (0.01 mU/L) and free thyroxine level of 3.5 ng/dL (45.0 pmol/L).

ECG shows atrial fibrillation.

Which of the following is the most appropriate diagnostic test?

A) Serum thyroglobulin measurement

B) Thyroid peroxidase antibody titer

C) Thyroid scintigraphy with radioactive iodine uptake

D) Thyroid ultrasonography with Doppler studies

QUESTION 12 ANSWER

A 73-year-old woman is seen during a routine evaluation. She has been taking amiodarone for atrial fibrillation for 1 year with good control until a recurrence 1 week ago. Thyroid function tests were normal before starting amiodarone. She has no history of iodinated contrast use. She is otherwise well and takes no additional medications.

On physical examination, pulse rate is 110/min and irregular; remaining vital signs are normal. Other than an irregular tachycardia, the thyroid and remainder of the examination are normal.

Laboratory studies show a thyroid-stimulating hormone level of less than 0.01 µU/mL (0.01 mU/L) and free thyroxine level of 3.5 ng/dL (45.0 pmol/L).

ECG shows atrial fibrillation.

Which of the following is the most appropriate diagnostic test?

A) Serum thyroglobulin measurement

B) Thyroid peroxidase antibody titer

C) Thyroid scintigraphy with radioactive iodine uptake

D) Thyroid ultrasonography with Doppler studies (12% correct)

EXPLANATION

This patient has developed thyrotoxicosis while taking amiodarone, which occurs in 5% of people taking amiodarone.

Type 1 amiodarone-induced thyrotoxicosis (AIT) (hyperthyroidism) occurs in patients with Graves disease or thyroid nodules, which is usually treated with methimazole.

Type 2 AIT (destructive thyroiditis) is more common and occurs in patients without underlying thyroid disease. Type 2 AIT is usually self-limiting but sometimes requires treatment with glucocorticoids.

Thyroid ultrasonography with Doppler studies can help distinguish type 1 amiodarone-induced thyrotoxicosis (increased vascularity) from type 2 (decreased vascularity).

Serum thyroglobulin measurement (**Option A**) is useful in distinguishing endogenous thyrotoxicosis from exogenous thyrotoxicosis, with the former leading to increased or normal levels and the latter leading to low levels. This test would be useful for patients who may be surreptitiously taking thyroid hormone.

Thyroid peroxidase (TPO) antibodies are present in most patients with Hashimoto thyroiditis that is a cause of hypothyroidism; however, this patient has hyperthyroidism. Additionally, in evaluation of hypothyroidism, assessment of the TPO antibody titer (**Option B**) is unnecessary unless the diagnosis is unclear.

The evaluation of AIT with thyroid scintigraphy is difficult and unreliable, however, because the high iodine load from amiodarone impairs thyroid uptake of iodine.

QUESTION 13

A 67-year-old man is evaluated in the hospital for hyperglycemia 3 days after admission for a COPD exacerbation. Appropriate treatment was initiated with antibiotics, bronchodilators, supplemental oxygen, and systemic glucocorticoids. The patient's oral intake remains good. Since the initiation of systemic glucocorticoids, fasting blood glucose levels have been consistently greater than 180 mg/dL (10.0 mmol/L) and postprandial levels occasionally greater than 250 mg/dL (13.9 mmol/L).

On admission, hemoglobin A_{1c} was 5.3%.

Which of the following is the most appropriate management of this patient's hyperglycemia?

- A) Basal and correctional insulin
- B) Basal, prandial, and correctional insulin
- C) Correctional insulin
- D) Metformin

QUESTION 13 ANSWER

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On admission, hemoglobin A_{1c} was 5.3%.

Which of the following is the most appropriate management of this patient's hyperglycemia?

- A) Basal and correctional insulin
- **B) Basal, prandial, and correctional insulin (39% correct)**
- C) Correctional insulin
- D) Metformin

EXPLANATION

Basal, prandial, and correctional insulin is the recommended treatment for hyperglycemia in non-critically ill hospitalized patients who have good oral intake.

The use of correctional insulin in hospitalized patients as the only means to control hyperglycemia is strongly discouraged by the American Diabetes Association.

The American Diabetes Association (ADA) recommends initiation of insulin therapy for treatment for persistent hyperglycemia starting at a threshold of 180 mg/dL (10.0 mmol/L).

After insulin therapy is started, a target glucose range of 140 to 180 mg/dL (7.8-10.0 mmol/L) is recommended for most critically ill and non-critically ill patients.

A randomized controlled trial has shown that basal-prandial insulin treatment improved glycemic control and reduced hospital complications compared with use of only correctional insulin ("sliding scale insulin") regimens in general surgery patients with type 2 diabetes mellitus.

The ADA notes that basal insulin, or a basal plus correction regimen (**Option A**), is the preferred treatment for non-critically ill hospitalized patients with poor oral intake or those with oral intake restriction.

Research on the safety of oral hypoglycemic drugs in the hospital setting is ongoing, and conclusive findings have not yet been established. Harm is also a concern, particularly in patients who may experience changes in volume status, exposure to contrast agents, and unpredictable meals because of testing or clinical status changes. Initiating metformin (**Option D**) is not the best choice for this patient. Side note: Med/Peds folks: at PCH, Endocrine regularly continues Metformin and/or starts it on the inpatient side.

QUESTION 14

An 18-year-old man is evaluated for hypercalcemia that developed 30 days after hospitalization for a spinal cord injury at cervical vertebra 6.

On physical examination, vital signs are normal. Quadriplegia and muscle atrophy in the arms, trunk, and legs is noted.

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

A) Bone alkaline phosphatase measurement

B) 24-h urine calcium measurement

C) 1,25-hydroxyvitamin D measurement

D) Skeletal survey radiography

E) Thyroid-stimulating hormone measurement

Laboratory studies:

Calcium	11.3 mg/dL (2.8 mmol/L)
Creatinine	0.8 mg/dL (70.7 µmol/L)
Phosphorus	4 mg/dL (1.29 mmol/L)
Parathyroid hormone	<10 pg/mL (<10 ng/L)

QUESTION 14 ANSWER

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On physical examination, vital signs are normal. Quadriplegia and muscle atrophy in the arms, trunk, and legs is noted.

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

A) Bone alkaline phosphatase measurement (41% correct)

B) 24-h urine calcium measurement

C) 1,25-hydroxyvitamin D measurement

D) Skeletal survey radiography

E) Thyroid-stimulating hormone measurement

Laboratory studies:

Calcium	11.3 mg/dL (2.8 mmol/L)
Creatinine	0.8 mg/dL (70.7 µmol/L)
Phosphorus	4 mg/dL (1.29 mmol/L)
Parathyroid hormone	<10 pg/mL (<10 ng/L)

EXPLANATION

Goal: Diagnose hypercalcemia caused by immobilization.

Acute and prolonged immobilization in young adults may lead to excessive bone resorption relative to formation and hypercalcemia caused by rapid efflux of calcium from the skeleton.

The diagnosis of hypercalcemia due to immobilization can be supported by elevated serum bone alkaline phosphatase and confirmed by durable remission of hypercalcemia with antiresorptive therapy.

The differential diagnosis of parathyroid hormone (PTH)-independent hypercalcemia is broad and can be narrowed by first determining the mechanism of hypercalcemia: impaired renal excretion, increased intestinal absorption, or excessive bone resorption.

EXPLANATION

In a young patient whose normal rate of bone turnover is high, acute and prolonged immobilization may lead to excessive bone resorption relative to formation and hypercalcemia caused by rapid efflux of calcium from the skeleton.

Most patients with hypercalcemia also have hypercalciuria. However, three hypercalcemic conditions are associated with hypocalciuria: milk alkali syndrome, thiazide diuretic use, and familial hypocalciuric hypercalcemia.

Because immobilization is a more likely cause of hypercalcemia in this patient, measurement of 24-hour urine calcium excretion (**Option B**) is unnecessary.

Unregulated conversion of 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D may occur in granulomatous tissue associated with fungal infection, tuberculosis, sarcoidosis, and lymphoma, leading to increased intestinal absorption of calcium. These conditions are associated with hypercalcemia and an inappropriately normal or frankly elevated 1,25-dihydroxyvitamin D level and suppressed PTH. However, hypercalcemia would be expected to be present on admission

QUESTION 15

A 59-year-old man is evaluated for headaches, pallor, and panic attacks for the past year. His long-term hypertension has also become harder to control. Medications are chlorthalidone, lisinopril, metoprolol, and diltiazem.

On physical examination, blood pressure is 164/98 mm Hg. The remainder of the examination is normal.

Which of the following is the most appropriate diagnostic test?

A) Adrenal CT

B) Adrenal venous catecholamine sampling

C) Iodine 123-metaiodobenzylguanidine scan

D) Plasma free metanephrine measurement

QUESTION 15 ANSWER

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EXPLANATION

Goal: Diagnose pheochromocytoma.

In context of a high index of suspicion for pheochromocytoma, plasma free metanephrine is an appropriate screening test, whereas urine fractionated metanephrine and catecholamines may be a better option for cases with low suspicion.

Imaging for pheochromocytoma should be performed only after documentation of elevated catecholamine levels.

Common indications to initiate testing for pheochromocytoma include adrenergic-type spells (headache, sweating, tachycardia) with or without hypertension, resistant hypertension, onset of hypertension at a young age, and idiopathic cardiomyopathy.

Other indications include familial syndromes that predispose to pheochromocytoma (e.g., multiple endocrine neoplasia type 2), or a family history of pheochromocytoma.

EXPLANATION

Initial tests for pheochromocytoma include measurement of plasma free metanephrine collected with the patient in a supine position or 24-hour urine fractionated metanephrine and catecholamine levels.

Levels more than four times the upper limit of normal, in absence of acute stress or illness, are consistent with a catecholamine-secreting tumor.

The plasma free metanephrine test is highly sensitive (96%-100%). The specificity is 85% to 89%. Urine fractionated metanephrine and catecholamines have higher specificity (98%) and high sensitivity (up to 97%).

The search for a tumor should begin when a biochemical diagnosis of pheochromocytoma/paraganglioma is supported by laboratory results, to avoid misdiagnosing an incidental nonfunctioning adrenal mass as a pheochromocytoma. If biochemical testing supports the diagnosis of pheochromocytoma, an adrenal CT scan (**Option A**) or MRI of the abdomen should be performed. Imaging is not an initial diagnostic test.

If the CT is negative, reconsidering the diagnosis is the first step; however, if suspicion of a catecholamine-secreting tumor is high, the next step is an iodine 123-metaiodobenzylguanidine scan (**Option C**).

QUESTION 16

A 55-year-old man is evaluated for primary aldosteronism. He has resistant hypertension despite therapy with three drugs at adequate dosages, including a diuretic. He has no other medical concerns. Medications are hydrochlorothiazide, amlodipine, and losartan.

On physical examination, blood pressure is 152/98 mm Hg and pulse rate is 72/min. The remainder of the vital signs and physical examination are unremarkable.

Serum electrolytes are normal.

Which of the following is the most appropriate test?

A) Adrenal CT

B) Aldosterone measurement after oral sodium loading

C) 24-hour urine potassium measurement

D) Plasma renin activity measurement

QUESTION 16 ANSWER

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On physical examination, blood pressure is 152/98 mm Hg and pulse rate is 72/min. The remainder of the vital signs and physical examination are unremarkable.

Serum electrolytes are normal.

Which of the following is the most appropriate test?

A) Adrenal CT

B) Aldosterone measurement after oral sodium loading

C) 24-hour urine potassium measurement

D) Plasma renin activity measurement (58% correct)

EXPLANATION

Goal: Diagnose primary aldosteronism in a patient taking an angiotensin receptor blocker.

Screening for primary hyperaldosteronism in patients with hypertension is recommended if any of the following are present: resistant hypertension, hypokalemia (spontaneous or substantial, if diuretic induced), incidentally discovered adrenal mass, family history of early-onset hypertension, or stroke at younger than 40 years.

In patients with suspected primary hyperaldosteronism taking an ACE inhibitor or an angiotensin receptor blocker, an elevated serum renin level excludes hyperaldosteronism.

In patients taking an ACE inhibitor or an angiotensin receptor blocker, PRA should be elevated; therefore, a simple initial test in these patients is a PRA measurement. If PRA is suppressed, the likelihood of primary aldosteronism is high and then PAC/PRA should be calculated; if PRA is elevated, hyperaldosteronism is ruled out.

The most reliable case-detection test is calculation of plasma aldosterone concentration (PAC)/PRA by measuring PAC and PRA (or direct renin concentration) in a midmorning seated sample.

After the diagnosis of primary aldosteronism has been established, the localization study of choice is a dedicated adrenal CT (**Option A**).

QUESTION 17

A 56-year-old man is evaluated during a wellness visit. He has an 18-year history of type 2 diabetes mellitus. He is in good health. His vaccinations are current for influenza and COVID-19, and he received the 23-valent pneumococcal polysaccharide vaccine 3 years ago and tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine 6 years ago. He also received the measles, mumps, rubella vaccine as a child. Medications are atorvastatin and metformin.

Which of the following is the most appropriate vaccination to recommend at this time?

A) Hepatitis B

B) Quadrivalent meningococcal conjugate

C) Tetanus and diphtheria toxoids

D) 13-Valent pneumococcal conjugant

QUESTION 17 ANSWER

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Which of the following is the most appropriate vaccination to recommend at this time?

A) Hepatitis B (40% correct)

B) Quadrivalent meningococcal conjugate

C) Tetanus and diphtheria toxoids

D) 13-Valent pneumococcal conjugant

EXPLANATION

Patients with diabetes mellitus should receive the 23-valent pneumococcal polysaccharide vaccine and annual influenza vaccinations.

Patients with diabetes mellitus aged 18 through 59 years should receive the hepatitis B vaccine; vaccination in patients with diabetes aged 60 years and older is at the clinician's discretion.

The ACIP recommends annual influenza vaccination and a 23-valent pneumococcal polysaccharide vaccine (PPSV23). At age 65 years, a second dose of PPSV23 can be administered if 5 years have passed since the first dose.

ACIP recommends routine vaccination with a quadrivalent meningococcal conjugate vaccine (MenACWY) vaccine (**Option B**) for children age 11 or 12 years, with a booster dose at age 16 years. MenACWY meningococcal vaccine is recommended for some adults, including those with complement deficiency, those with functional or anatomic asplenia, HIV, and travelers and residents in countries in which the disease is common.

EXPLANATION

The MenB meningococcal vaccine is also recommended for patients with complement deficiency and asplenia. Diabetes is not an indication for meningococcal vaccination.

Adults aged 19 years and older should receive a tetanus and diphtheria toxoids (Td) vaccine (**Option C**) or the tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) booster every 10 years. In adults who did not receive the Tdap during adolescence, at least one of the 10-year booster doses should be with Tdap vaccine. This patient received the Tdap 6 years ago and does not require revaccination at this point.

QUESTION 18

A 57-year-old woman is evaluated for enlargement of her hands and feet. Medical history is significant for hypertension. Her only medication is amlodipine.

On physical examination, vital signs are normal. BMI is 24. The patient has a wide nose and enlargement of hands and feet. Prognathism is noted.

Which of the following is the most appropriate diagnostic test?

A) Insulin-like growth factor-1 measurement

B) Oral glucose tolerance test

C) Pituitary MRI

D) Random growth hormone measurement

QUESTION 18 ANSWER

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On physical examination, vital signs are normal. BMI is 24. The patient has a wide nose and enlargement of hands and feet. Prognathism is noted.

Which of the following is the most appropriate diagnostic test?

A) Insulin-like growth factor-1 measurement (78% correct)

B) Oral glucose tolerance test

C) Pituitary MRI

D) Random growth hormone measurement

EXPLANATION

Goal: Diagnose acromegaly.

An insulin-like growth factor-1 level is the best screening biomarker for the diagnosis of acromegaly.

In patients with an elevated insulin-like growth factor-1 level, the diagnosis of acromegaly can be confirmed with an oral glucose tolerance test.

Acromegaly is caused by excess growth hormone (GH) secretion from a pituitary tumor in 95% of patients.

If a patient's IGF-1 level is elevated, then an oral glucose tolerance test (**Option B**) can confirm the diagnosis of acromegaly. This test is performed by administering 75 g of oral glucose and measuring GH levels every 30 minutes for 120 minutes. GH less than 0.2 ng/mL (0.2 µg/L) is a normal response, whereas a GH nadir of 1.0 ng/mL (1.0 µg/L) or greater is diagnostic of acromegaly.

Because the diagnosis of an endocrine disorder is always made on the basis of laboratory evaluation before imaging, a pituitary MRI (**Option C**) should not be obtained in this patient before measuring her IGF-1.

QUESTION 19

A 46-year-old man is evaluated for a thyroid nodule discovered 2 years ago. Thyroid ultrasonography performed at that time showed a 2-cm left upper pole isoechoic solid nodule without microcalcification or irregular margin. The sonographic pattern was characterized as low suspicion for malignancy. Fine-needle aspiration biopsy showed benign cytology.

On physical examination, vital signs are normal. A 2-cm left upper pole thyroid nodule is firm and mobile. No lymphadenopathy is evident.

Laboratory studies show a thyroid-stimulating hormone level of 2.0 µU/mL (2.0 mU/L).

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

A) Fine-needle aspiration biopsy

B) Levothyroxine initiation

C) Thyroid scintigraphy with radioactive iodine uptake

D) Thyroid ultrasonography

E) No further evaluation

QUESTION 19 ANSWER

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On physical examination, vital signs are normal. A 2-cm left upper pole thyroid nodule is firm and mobile. No lymphadenopathy is evident.

Laboratory studies show a thyroid-stimulating hormone level of 2.0 µU/mL (2.0 mU/L).

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

A) Fine-needle aspiration biopsy

B) Levothyroxine initiation

C) Thyroid scintigraphy with radioactive iodine uptake

D) Thyroid ultrasonography (29% correct)

E) No further evaluation

EXPLANATION

Goal: Manage a benign thyroid nodule.

The most appropriate next step is thyroid ultrasonography (**Option D**). This patient has a persistent 2-cm thyroid nodule previously evaluated by thyroid ultrasonography and fine-needle aspiration biopsy (FNAB).

Thyroid nodule evaluation begins with a thyroid-stimulating hormone (TSH) measurement; if it is normal or elevated, ultrasonography and FNAB are performed.

Repeat ultrasonography should be performed in 6 to 12 months for all high-suspicion thyroid nodules, 12 to 24 months for intermediate- and low-suspicion nodules, and 24 months or longer for very low-suspicion nodules.

Repeat fine-needle aspiration biopsy is indicated for all high-suspicion thyroid nodules, nodules with concerning new sonographic findings, and intermediate or low-suspicion nodules that increase significantly in size.

EXPLANATION

Based on past use to reduce TSH levels, levothyroxine initiation (**Option B**) may theoretically prevent thyroid nodule growth. However, studies have not shown the efficacy of this treatment, and the risk for thyrotoxicosis and adverse effects is increased.

Thyroid scintigraphy with radioactive iodine uptake (**Option C**) is useful in evaluating thyroid nodules associated with a suppressed TSH, indicating a possibly autonomously functioning and likely benign thyroid nodule. In this patient, the TSH is normal and thyroid scintigraphy with radioactive iodine uptake would not be warranted.

No further evaluation (**Option E**) of the thyroid nodule is inappropriate. Proceeding with a repeat ultrasonography in 6 to 24 months after the initial ultrasound is recommended by the American Thyroid Association to avoid the possibility of a false-negative test for malignancy with the first ultrasound and to detect interim changes in nodule morphology that may result in a change in treatment.

QUESTION 20

A 43-year-old man has developed changes in skin color and is evaluated for weight loss, nausea, and weakness.

Skin findings are shown.

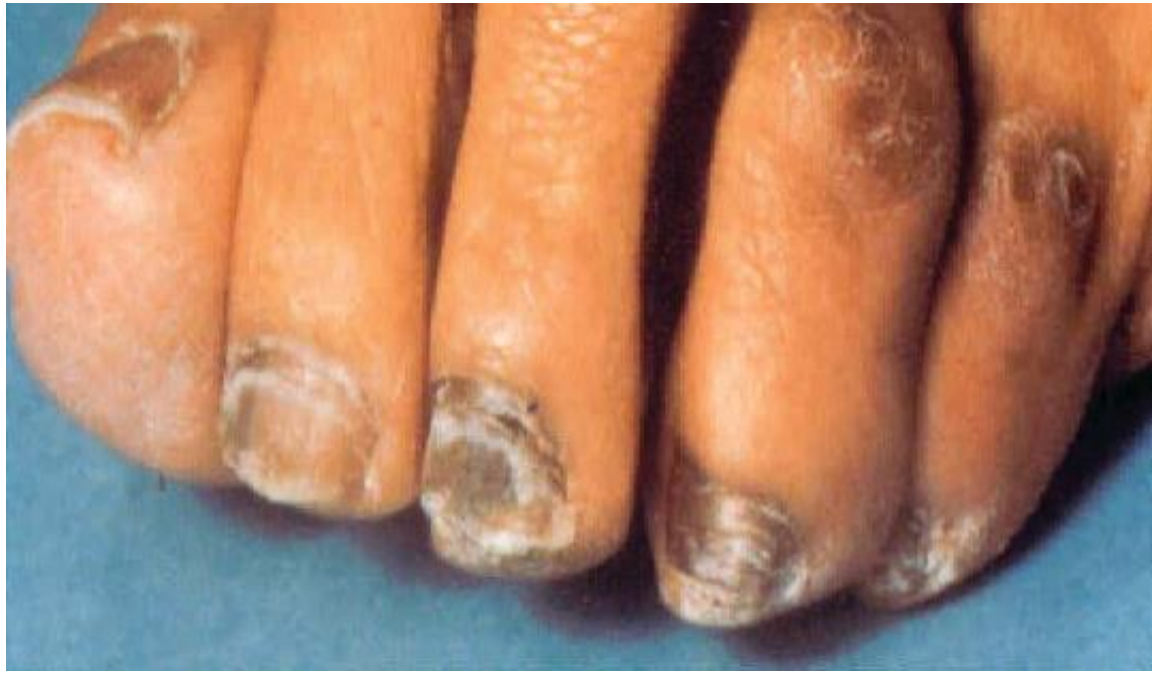
Which of the following is the most likely diagnosis?

A) Acanthosis nigricans

B) Diffuse melanosis cutis

C) Primary adrenal insufficiency

D) Secondary adrenal insufficiency



EXPLANATION

Answer: Primary adrenal insufficiency (72% correct)

Goal: Diagnose primary adrenal insufficiency.

Only patients with primary adrenal insufficiency have excessive adrenocorticotropic hormone, melanocyte-stimulating hormone, and pro-opiomelanocortin secretion, which results in darkly pigmented skin.

An example of diffuse pigmentation owing to primary adrenal insufficiency in a different patient is shown.