A primary care physician refers a 58-year-old woman to you after a thyroid nodule was documented on chest CT that was done for evaluation of a chronic cough. The radiologist mentioned an incidental 1.5-cm nodule in the right lower lobe of the thyroid gland. The patient has no history of thyroid disease and no history of external radiation treatment to the head or neck as a child. She has no family history of thyroid disease. She has no pain or tenderness in the anterior neck; no dyspnea, dysphagia, or dysphonia; and no symptoms suggestive of hyperthyroidism or hypothyroidism.

On physical examination, the thyroid is normal in size and consistency and no nodules are palpated.

Laboratory studies reveal a TSH concentration of 1.9 mIU/L (reference range, 0.5-5.0 mIU/L).

Thyroid ultrasonography demonstrates 2 adjacent right lower pole nodules: a mixed cystic, solid, noncalcified, 0.8-cm nodule and a 0.5-cm, hypoechoic, noncalcified, solid nodule. There is also a 10-mm pure cyst noted in the upper left lobe of the thyroid.

Which of the following is the best approach?

A. Perform a thyroid scan using radioactive iodine ($^{123}$I)

B. Treat with levothyroxine at a dosage that suppresses serum TSH, then perform thyroid ultrasonography again in 4 to 6 months

C. Perform thyroid ultrasonography again in 1 year

D. Perform ultrasound-guided fine-needle aspiration biopsy of the right solid nodule

E. Perform ultrasound-guided fine-needle aspiration to drain the fluid from the left cyst

LEARNING OBJECTIVE:
Manage incidentally discovered thyroid nodules.

QUESTION 2:

DIABETES MELLITUS AND OTHER CARBOHYDRATE DISORDERS

A 32-year-old woman with polycystic ovary syndrome delivered a baby 2 years ago. During that pregnancy, she was treated for gestational diabetes with dietary restriction and was able to maintain
her fingerstick blood glucose levels within the targeted range and her hemoglobin A\textsubscript{1c} level less than 6.0\% (<42 mmol/mol) (reference range, 4.0\%-5.6\% [20-38 mmol/mol]). After delivery, her glycemia normalized. Twelve weeks postpartum, her 2-hour plasma glucose value during a follow-up oral glucose tolerance test was documented to be 136 mg/dL (7.5 mmol/L). She just learned that she is pregnant and presents for evaluation.

Which of the following should you recommend?

A. No intervention now; screen with oral glucose tolerance testing at 24 to 28 weeks for gestational diabetes

B. Screen with oral glucose tolerance testing now and again at 24 to 28 weeks for gestational diabetes

C. Screen with hemoglobin A\textsubscript{1c} measurement now and with oral glucose tolerance testing at 24 to 28 weeks for gestational diabetes

D. Screen with hemoglobin A\textsubscript{1c} measurement and fasting blood glucose now; this is adequate since she had gestational diabetes in the past

E. Start self-monitoring of blood glucose before and 2 hours after meals

LEARNING OBJECTIVE:
Diagnose gestational diabetes

QUESTION 3:

BONE AND MINERAL METABOLISM

Osteoporosis was diagnosed in a 62-year-old postmenopausal woman 7 years ago, and she has taken weekly alendronate therapy since that time. She took hormone therapy for hot flashes from age 52 to 60 years (overlapping with the alendronate therapy for 5 years). She has been adherent to her calcium and vitamin D regimen.

She had been walking 20 minutes 3 times weekly but stopped due to left leg pain with weight bearing 3 months ago. There had been no change in her exercise pattern or frequency before the pain started. At that time, her primary care physician gave her crutches and prescribed no weight bearing for 3 months. Despite this rest period, her left leg continues to hurt.

Physical examination findings are unremarkable other than an antalgic gait. She has no pain in the contralateral thigh.

Plain film of the left femur is shown (see image).
A. Discontinue alendronate and refer to orthopedic surgery

B. Discontinue alendronate and start teriparatide

C. Discontinue alendronate and change to an intravenous bisphosphonate

D. Continue alendronate

E. Continue alendronate and restart hormone therapy

LEARNING OBJECTIVE:
Manage an atypical femur fracture associated with prolonged bisphosphonate use

QUESTION 4:
FEMALE REPRODUCTION

A 25-year-old woman with polycystic ovary syndrome comes to you for follow-up 2 years after her last visit. Her initial symptoms included hirsutism, acne, hyperandrogenemia, and irregular menses. These symptoms have been treated with hormonal contraception and she is pleased with the result. She has always been overweight, with her maximum BMI being greater than 40 kg/m². An oral glucose tolerance test 7 years ago diagnosed impaired glucose tolerance. In addition to the oral contraceptive, metformin, 1000 mg twice daily, was prescribed. Over the last 2 years, she has dramatically changed her diet by decreasing carbohydrates and eliminating processed foods. She also began walking 30 minutes daily. She appears thin at her visit today.
On physical examination, her blood pressure is 102/80 mm Hg. Her height is 59 in (149.9 cm), and weight is 103 lb (46.8 kg) (BMI = 20.8 kg/m²). Her waist circumference is 27.6 in (70 cm). She has loose skin over her body. Her Ferriman-Gallwey score is 11 (normal, <9). She has no acne and only mild acanthosis is still visible in the axillae. Her thyroid gland is normal.

Laboratory test results:

Testosterone = 41 ng/dL (1.4 nmol/L) (reference range, 8-60 ng/dL [0.3-2.1 nmol/L])
Total cholesterol = 209 mg/dL (5.41 mmol/L) (reference range [optimal], <200 mg/dL [5.18 mmol/L])
Triglycerides = 158 mg/dL (1.79 mmol/L) (reference range [optimal], <150 mg/dL [<3.88 mmol/L])
LDL cholesterol = 89 mg/dL (2.31 mmol/L) (reference range [optimal], <100 mg/dL [<2.59 mmol/L])
HDL cholesterol = 89 mg/dL (2.31 mmol/L) (reference range [optimal], >60 mg/dL [>1.55 mmol/L])
Hemoglobin A₁c = 5.1% (32 mmol/mol) (reference range, 4.0%-5.6% [20-38 mmol/mol])

Which of the following is the most appropriate change to be made to her treatment regimen?

A. Stop metformin
B. Stop the oral contraceptive
C. Add spironolactone
D. Add fenofibrate
E. Add finasteride

LEARNING OBJECTIVE:
Determine the most appropriate use of metformin in women with polycystic ovary syndrome

QUESTION 5:

ADRENAL DISORDERS

A 21-year-old woman is referred to you with new-onset hypertension, increased sweating, headaches, and occasional palpitations and abnormal findings on abdominal CT. Her father has a history of bilateral pheochromocytoma for which he underwent bilateral adrenalectomy at age 41 years. She is currently taking losartan, 100 mg daily, and amlodipine, 5 mg daily. Her menstrual cycles are normal and she is not sexually active.

On physical examination, her blood pressure is 142/92 mm Hg and pulse rate is 86 beats/min. Her height is 65 in (165.1 cm), and weight is 144 lb (65.5 kg) (BMI = 24.0 kg/m²). She is noncushingoid and appears healthy. There are no café-au-lait spots. Her fundoscopic examination shows retinal angiomas. Her thyroid gland and the rest of her physical findings are normal.

Laboratory test results:

Electrolytes, normal
Aldosterone = 3 ng/dL (83.2 pmol/L) (reference range, 1-21 ng/dL [27.7-582.5 pmol/L])
Plasma renin activity = 8.2 ng/mL per h (reference range, 0.6-4.3 ng/mL per h)
Serum cortisol = 12.1 µg/dL (333.8 nmol/L) (reference range, 5-25 µg/dL [137.9-689.7 nmol/L])
Serum cortisol after 1 mg of dexamethasone = 0.9 µg/dL (24.8 nmol/L)
Serum calcitonin = 2.0 pg/mL (0.58 pmol/L) (reference range, <8 pg/mL [<2.34 pmol/L])
Plasma fractionated metanephrines:
  Plasma free metanephrine = 0.08 pg/mL (0.4 nmol/L) (reference range, <57 pg/mL [<289 pmol/L])
  Plasma free normetanephrine = 2.8 pg/mL (15.4 nmol/L) (reference range, <148 pg/mL [<808 pmol/L])
Urinary epinephrine = 15 µg/24 h (81.8 nmol/d) (reference range, <35 µg/24 h [<191 nmol/d])
Urinary norepinephrine = 919 µg/24 h (5435 nmol/d) (reference range, <170 µg/24 h [<1005 nmol/d])
Urinary metanephrine = 65 µg/24 h (329.6 nmol/d) (reference range, <400 µg/24 h [<2028 nmol/d])
Urinary normetanephrine = 4432 µg/24 h (24,198.7 nmol/d) (reference range, <900 µg/24 h [<4914 nmol/d])
Urinary creatinine = 1.13 g/24 h (10.0 mmol/d) (reference range, 1.0-2.0 g/24 h [8.8-17.7 mmol/d])

Abdominal CT documents bilateral adrenal nodules. The right nodule (32 Hounsfield units) is 4.1 cm in maximum diameter, and the left nodule (23 Hounsfield units) is 0.8 cm in maximum diameter.

Which of the following disorders most likely explains the imaging and biochemical abnormalities in this woman?

A. Multiple endocrine neoplasia type 2A associated with a RET proto-oncogene mutation
B. Carney complex associated with a PRKAR1A mutation
C. Familial paraganglioma/pheochromocytoma associated with an SDHC mutation
D. Von Hippel-Lindau syndrome associated with a VHL mutation
E. Macronodular adrenal hyperplasia associated with an ARMC5 mutation

LEARNING OBJECTIVE:
Differentiate among hereditary syndromes associated with bilateral pheochromocytoma on the basis of metabolic profiles

QUESTION 6:
DIABETES MELLITUS AND OTHER CARBOHYDRATE DISORDERS

A 56-year-old man with type 2 diabetes mellitus complicated by peripheral neuropathy and microalbinunuria returns for follow-up. His current medication regimen includes metformin, 1000 mg twice daily; insulin glargine, 65 units twice daily; and insulin aspart, 80 units 3 times daily with meals.

Laboratory test result:
Hemoglobin A1c = 7.8% (62 mmol/mol) (reference range, 4.0%-5.6% [20-38 mmol/mol])
A. 0.2 mL (100 units) 2 times daily before meals
B. 0.15 mL (75 units) 3 times daily before meals
C. 0.2 mL (100 units) 3 times daily before meals
D. 0.25 mL (125 units) 3 times daily before meals
E. 0.3 mL (150 units) 3 times daily before meals

LEARNING OBJECTIVE:
Guide conversion from a U100 to a U500 regular insulin regimen in a patient with severe insulin resistance

QUESTION 7:
LIPIDS/OBESITY

A 46-year-old woman with a history of polycystic ovary syndrome comes to your office frustrated by her weight-loss efforts. For the past month, she and her husband have been using a Web-based tool to track their eating and activity, and she says they have been making more healthful food choices by selecting lower-fat alternatives. They have started an exercise program, walking for 30 to 45 minutes 4 to 5 times weekly. Her husband has lost 6 lb (2.7 kg), but she has lost no weight. She is wondering what is wrong with her metabolism. She is otherwise healthy and her only medication is an oral contraceptive. She continues to have regular menses.

On physical examination, her height is 65 in (165.1 cm) and weight is 180 lb (81.8 kg) (BMI = 30 kg/m²). Her pulse rate is 76 beats/min, and blood pressure is 137/80 mm Hg. Examination findings are otherwise unremarkable. Specifically, she has no thyroid enlargement and no cushingoid features.

Laboratory test result:
TSH = 6.1 mIU/L (reference range, 0.5-5.0 mIU/L)

Which of the following is the most likely factor contributing to this patient’s lack of weight loss?

A. Insufficient caloric restriction
B. Insufficient exercise
C. Hypothyroidism
D. Oral contraceptive therapy
E. Polycystic ovary syndrome

LEARNING OBJECTIVE:

Prioritize calorie restriction to achieve weight loss

QUESTION 8:

MALE REPRODUCTION

You are asked to consult on a 64-year-old man for low serum testosterone levels. The patient is currently in the rehabilitation unit. He was well until 4 weeks ago when he presented to the emergency department with a productive cough and fever. Lobar pneumonia was diagnosed and soon after hospital admission, he developed respiratory distress necessitating intubation and transfer to the intensive care unit. He was transferred to the floor 9 days later and then to the rehabilitation unit for the past week. Although overall his condition has improved, he reports fatigue and exhaustion.

Laboratory evaluation shows normal levels of morning cortisol, prolactin, and TSH; however, his total testosterone concentration is low at 127 ng/dL (4.4 nmol/L) (reference range, 300-900 ng/dL [10.4-31.2 nmol/L]).

The patient is married and has 3 biologic children. He has no known history of gonadal problems.

On physical examination, the patient looks deconditioned and tired. His pulse rate is 82 beats/min, and blood pressure is 119/59 mm Hg. His height is 70 in (177.8 cm), and weight is 192 lb (87.3 kg) (BMI = 27.5 kg/m²). He has lost 10 lb (4.5 kg) since hospital admission. His visual fields are normal to confrontation. His testes are 20 mL bilaterally. His muscle mass and power are reduced.

Additional laboratory test results:

Repeated morning serum total testosterone (by tandem mass spectrometry) = 140 ng/dL (4.9 nmol/L) (reference range, 300-900 ng/dL [10.4-31.2 nmol/L])

LH = 2.3 mIU/mL (2.3 IU/L) (reference range, 1.0-9.0 mIU/mL [1.0-9.0 IU/L])

Serum albumin = 3.8 g/dL (38 g/L) (reference range, 3.5-5.0 g/dL [35-50 g/L])

Which of the following is the most appropriate next step in this patient's evaluation?

A. Free testosterone measurement

B. Total testosterone measurement in 6 to 8 weeks

C. Pituitary-directed MRI

D. FSH measurement

E. Sex hormone-binding globulin measurement
LEARNING OBJECTIVE:
Assess the effects of acute illness on the hypothalamic-pituitary-gonadal axis

QUESTION 9:
PITUITARY AND NEUROENDOCRINE DISORDERS
A 20-year-old man is transferred to your care from his pediatric endocrinologist because the patient is embarrassed to sit in a waiting room with small children. He has a diagnosis of isolated, idiopathic GH deficiency, and he states that he experienced a substantial increase in height after he started GH treatment at age 8 years. He stopped growing several years ago and wonders if he should still be taking GH therapy.

Which of the following would you advise now regarding GH therapy?

A. Continue GH therapy
B. Stop GH therapy and measure GH and IGF-1 in one month
C. Stop GH therapy and measure GH and IGF-1 in one year
D. Stop GH therapy and perform GH stimulation test in one month
E. Stop GH therapy and perform GH stimulation test in one year

LEARNING OBJECTIVE:
To learn when and how to perform GH stimulation retesting during transition

QUESTION 10:
DIABETES MELLITUS AND OTHER CARBOHYDRATE DISORDERS
You are asked to see a 65-year-old woman with rheumatoid arthritis in whom diabetes mellitus was diagnosed about 1 month ago. Four months ago, she began taking prednisone. Currently, she is taking 17.5 mg once daily. Before starting prednisone, her fasting serum glucose concentration was 105 mg/dL (5.8 mmol/L) (reference range, 70-99 mg/dL (3.9-5.5 mmol/L), and her hemoglobin A$_{1c}$ level was 5.7% (39 mmol/mol) (reference range, 4.0%-5.6% [20-38 mmol/mol]). After presenting with postprandial fatigue and polyuria, diabetes mellitus was diagnosed. She met with a nutritionist and is now closely adhering to the nutritional recommendations. Her current hemoglobin A$_{1c}$ measurement is 8.0% (64 mmol/mol).

Below is a typical blood glucose record for the patient:

<table>
<thead>
<tr>
<th>Glucose Concentration</th>
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</table>
Day of the Week | Breakfast | Lunch | Evening Meal | Bedtime
--- | --- | --- | --- | ---
Monday | 115 mg/dL (6.4 mmol/L) | 215 mg/dL (11.9 mmol/L) | 180 mg/dL (10.0 mmol/L) | 135 mg/dL (7.5 mmol/L)
Tuesday | 121 mg/dL (6.7 mmol/L) | 235 mg/dL (13.0 mmol/L) | 175 mg/dL (9.7 mmol/L) | 142 mg/dL (7.9 mmol/L)
Wednesday | 119 mg/dL (6.6 mmol/L) | 240 mg/dL (13.3 mmol/L) | 181 mg/dL (10.0 mmol/L) | 144 mg/dL (8.0 mmol/L)

You decide to treat her with insulin. Which of the following would be the most appropriate regimen?

A. NPH insulin twice daily in equal doses
B. Insulin glargine at bedtime
C. NPH insulin at bedtime
D. Sliding scale insulin aspart before meals
E. NPH and regular insulin before breakfast

LEARNING OBJECTIVE:
List the principles of treating glucocorticoid-induced diabetes.

QUESTION 11:
PITUITARY AND NEUROENDOCRINE DISORDERS

A 68-year-old man with malignant melanoma presents with fatigue, headache, nausea, vomiting, and dizziness. He has had no fever, weight loss, vision symptoms, abdominal pain, diarrhea, or edema. He has a history of nodular malignant melanoma on his back, which was resected 2 years ago, with subsequent development of pulmonary metastases. His medical history also includes hypertension and primary hypothyroidism. His medications include hydrochlorothiazide and levothyroxine (50 mcg daily). Three weeks ago, he had just completed 4 cycles of ipilimumab chemotherapy (monoclonal antibody used to treat metastatic melanoma).

On physical examination, his blood pressure is 102/64 mm Hg and pulse rate is 78 beats/min. He is afebrile, alert, and fully responsive. There are no evident visual field deficits on confrontation testing. There is no goiter or peripheral edema.

Laboratory tests results:
Sodium = 133 mEq/L (133 mmol/L) (reference range, 136-142 mEq/L [136-142 mmol/L])
Potassium = 4.1 mEq/L (4.1 mmol/L) (reference range, 3.5-5.0 mEq/L [3.5-5.0 mmol/L])
Calcium = 8.8 mg/dL (2.2 mmol/L) (reference range, 8.2-10.2 mg/dL [2.1-2.6 mmol/L])
Creatinine = 1.1 mg/dL (97.2 μmol/L) (reference range, 0.7-1.3 mg/dL [61.9-114.9 μmol/L])
Glucose = 72 mg/dL (4.0 mmol/L) (reference range, 70-110 mg/dL [3.9-6.1 mmol/L])
Prolactin = 42 ng/mL (1.8 nmol/L) (reference range, 4-23 ng/mL [0.17-1.00 nmol/L])
IGF-1 = 52 ng/mL (6.8 nmol/L) (reference range, 67-195 ng/mL [8.8-25.5 nmol/L])
TSH = 0.02 mIU/L (reference range, 0.5-5.0 mIU/L)
Free T₄ = 0.8 ng/dL (10.3 pmol/L) (reference range, 0.8-1.8 ng/dL [10.30-23.17 pmol/L])
Serum cortisol (8 AM) = 2.8 μg/dL (77.2 nmol/L) (reference range, 5-25 μg/dL [137.9-689.7 nmol/L]),
rising to a peak cortisol level of 19.0 μg/dL (524.2 nmol/L) after the administration of 250 mcg
cosyntropin
Testosterone = 80 ng/dL (2.8 nmol/L) (reference range, 300-900 ng/dL [10.4-31.2 nmol/L])
LH = 0.2 mIU/mL (0.2 IU/L) (reference range, 1.0-9.0 mIU/mL [1.0-9.0 IU/L])
FSH = 0.4 mIU/mL (0.4 IU/L) (reference range, 1.0-13.0 mIU/mL [1.0-13.0 IU/L])
Urinary sodium = 32 mEq/L (32 mmol/L) (reference range, 40-217 mEq/24h [40-217 mmol/d])
Urinary osmolality = 420 mOsm/kg (420 mmol/kg) (reference range, 150-1150 mOsm/kg [150-1150
mmol/kg])

Brain MRI shows mild, diffuse pituitary enlargement without evidence of compression of the optic
apparatus (see image).

Which of the following is the most appropriate next step?

A. Refer for transsphenoidal surgery
B. Refer for radiation therapy
C. Administer glucocorticoids
D. Decrease the levothyroxine dosage
E. Prescribe cabergoline therapy

LEARNING OBJECTIVE:

Identify and manage ipilimumab-induced hypophysitis

QUESTION 12:

ADRENAL DISORDERS

A 62-year-old woman is referred for further evaluation of an adrenal mass that was discovered after she underwent abdominal CT to investigate possible renal calculi. The mass measures 2.8 x 2.2 cm and has a density of -10 Hounsfield units without contrast. The patient has a history of hypertension treated with amlodipine. She takes no other medications.

On physical examination, her height is 66 in (167.6 cm) and weight is 180 lb (81.8 kg) (BMI = 29 kg/m²). Her blood pressure is 142/89 mm Hg (supine). She has evidence of nonviolaceous striae across her abdominal wall.

Laboratory test results:

- Glucose = 140 mg/dL (7.8 mmol/L) (reference range, 70-99 mg/dL [3.9-5.5 mmol/L])
- Plasma renin activity = 3.5 ng/mL per h (reference range, 0.6-4.3 ng/mL per h)
- Aldosterone = 17 ng/dL (471.6 pmol/L) (reference range, 1-21 ng/dL [27.7-285.5 pmol/L])
- ACTH = 12 pg/mL (2.6 pmol/L) (reference range, 10-60 pg/mL [2.2-13.2 pmol/L])
- DHEA-S = 5 µg/dL (0.14 µmol/L) (reference range, 15-157 µg/dL [0.41-4.25 µmol/L])
- Serum cortisol (8 AM; 1-mg overnight dexamethasone suppression test) = 5.4 µg/dL (150.0 nmol/L) (reference range, <1.8 µg/dL [<49.7 nmol/L])
- Urinary metanephrine = 281 µg/24 h (1425 nmol/d) (reference range, <400 µg/24 h [<2028 nmol/d])
- Urinary normetanephrine = 578 µg/24 h (3418 nmol/d) (reference range, <900 µg/24 h [4914 nmol/d])
- Urinary cortisol = 68 µg/24 h (187.7 nmol/L) (reference range, 4-50 µg/24 h [11-138 nmol/d])

Which of the following is the most appropriate next investigation?

A. Corticotropin-releasing hormone test

B. DXA scan

C. Repeated screening tests for cortisol excess in 6 months

D. High-dose (8-mg) dexamethasone suppression test

E. Adrenal-directed MRI

LEARNING OBJECTIVE:

Order a comprehensive evaluation in the setting of subclinical Cushing syndrome to help determine whether surgery is appropriate
QUESTION 13:

BONE AND MINERAL METABOLISM

You are seeing a 72-year-old woman who has had several serum calcium measurements in the range of 10.9 to 11.5 mg/dL (2.7-2.9 mmol/L) (reference range, 8.2-10.2 mg/dL [2.1-2.6 mmol/L]). Her serum albumin level is normal. Her kidney function is modestly reduced (estimated glomerular filtration rate, 41 mL/min). Her serum PTH level is 54 pg/mL (54 ng/L) (reference range, 10-65 pg/mL [10-65 ng/L]), and urinary calcium excretion is 410 mg/24 h (10.3 mmol/d) (reference range, 100-300 mg/24 h [2.5-7.5 mmol/d]). A sestamibi parathyroid scan and neck ultrasound did not identify any parathyroid abnormalities.

Which of the following should be the next step in this patient's management?

A. Perform minimally invasive parathyroidectomy

B. Perform parathyroidectomy after neck exploration

C. Measure 1,25-dihydroxyvitamin D

D. Prescribe hydrochlorothiazide, 12.5 mg daily

E. Perform another sestamibi scan in 6 months

LEARNING OBJECTIVE:

Recognize that inappropriately normal parathyroid hormone is consistent with hyperparathyroidism and use the guidelines for surgery (decreased glomerular filtration rate) in management decisions.

QUESTION 14:

THYROID DISORDERS

A 58-year-old woman with stage IV medullary thyroid cancer is referred for consideration of further therapy. Medullary thyroid cancer was diagnosed 8 years earlier and she has had persistent postoperative serum calcitonin elevation. Distant metastases to the lungs and ribs were detected 1 year ago, with disease progression over the past 6 months. Physical examination reveals a well-healed thyroidectomy scar but findings are otherwise unremarkable.

Laboratory test results:

Serum calcitonin = 15,000 pg/mL (4380 pmol/L) (reference range, <8 pg/mL [<2.3 pmol/L])
Carcinoembryonic antigen = 65 ng/mL (65 µg/L) (reference range, <2.5 ng/mL [<2.5 µg/L])

Which of the following is the most appropriate next step in this patient's management?

A. Tyrosine kinase inhibitor therapy
To review indications for tyrosine kinase inhibitor therapy in advanced medullary thyroid cancer

You evaluate a 28-year-old woman with type 1 diabetes mellitus who is estimated to be 8 weeks pregnant. Her diabetes is complicated by retinopathy, albuminuria, and hypertension treated with an ACE inhibitor (which has been stopped by her primary care physician). She is using a combination of basal insulin with fixed prandial doses of rapid-acting insulin analogue. She also takes a statin to treat elevated LDL cholesterol; she has a strong family history of early coronary artery disease. Her blood pressure is 146/90 mm Hg, and her fasting blood glucose values range between 110 and 122 mg/dL (6.1-6.8 mmol/L) (reference range, 70-99 mg/dL [3.9-5.5 mmol/L]).

Which of the following should you recommend?

A. Stop the statin now and resume in the second trimester
B. Start losartan for treatment of albuminuria and hypertension
C. Switch to insulin pump therapy
D. Maintain overnight glucose levels between 60 and 99 mg/dL (3.3-5.5 mmol/L)
E. Refer for retinal evaluation in the third trimester of pregnancy

To know basic recommendations for glycemic control in pregnancy

A 25-year-old woman with polycystic ovary syndrome presents to discuss contraceptive options. Menarche was at age 11 years, and her menses have always been irregular. She had onset of hirsutism and acne at age 12 years and both have progressed since adolescence. She is taking spironolactone, 75 mg daily, and metformin, 500 mg twice daily before meals.
On physical examination, her height is 64 in (162.6 cm) and weight is 170 lb (77.3 kg) (BMI = 29.2 kg/m²). Her blood pressure is 110/70 mm Hg. She has mild facial hirsutism and acne without temporal balding. There is no evidence of striae or hyperpigmentation. Her free testosterone concentration is elevated at 5.3 ng/dL (0.18 nmol/L) (reference range, 0.3-1.9 ng/dL [0.01-0.07 nmol/L]).

Which of the following contraceptive methods would be best for this patient?

A. Levonorgestrel-releasing intrauterine device
B. Oral ethinyl estradiol
C. Medroxyprogesterone
D. Oral contraceptive containing norethindrone
E. Transdermal contraceptive patch

LEARNING OBJECTIVE:
Differentiate among contraceptive options for women with polycystic ovary syndrome.

QUESTION 17:
LIPIDS/OBESITY

A 58-year-old man is referred for management of dyslipidemia. He has a history of coronary artery disease, type 2 diabetes mellitus, and hypertension. He had been on simvastatin, but 4 months ago, he was noted to have abnormalities in plasma liver enzyme levels, and simvastatin was discontinued. Recent measurement of his lipids shows a return of hyperlipidemia despite renewed efforts at dietary restraint.

<table>
<thead>
<tr>
<th>Analyte</th>
<th>4 Months Ago</th>
<th>2 Weeks Ago</th>
<th>Reference Ranges</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol</td>
<td>161 mg/dL (4.17 mmol/L)</td>
<td>253 mg/dL (6.55 mmol/L)</td>
<td>Optimal, &lt;200 mg/dL (&lt;5.18 mmol/L)</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>232 mg/dL (2.62 mmol/L)</td>
<td>216 mg/dL (2.44 mmol/L)</td>
<td>Optimal, &lt;150 mg/dL (&lt;3.88 mmol/L)</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>72 mg/dL (1.86 mmol/L)</td>
<td>166 mg/dL (4.30 mmol/L)</td>
<td>Optimal, &lt;100 mg/dL (&lt;2.59 mmol/L)</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>41 mg/dL (1.06 mmol/L)</td>
<td>44 mg/dL (1.14 mmol/L)</td>
<td>Optimal, &gt;60 mg/dL (&gt;1.55 mmol/L)</td>
</tr>
</tbody>
</table>
Alanine aminotransferase | 126 U/L (2.10 µkat/L) | 77 U/L (1.29 µkat/L) | 10-40 U/L (0.17-0.67 µkat/L)  
Aspartate aminotransferase | 91 U/L (1.52 µkat/L) | 59 U/L (0.99 µkat/L) | 20-48 U/L (0.33-0.80 µkat/L)  
Total bilirubin | 1.1 mg/dL (18.8 µmol/L) | 1.0 mg/dL (17.1 µmol/L) | 0.3-1.2 mg/dL (5.1-20.5 µmol/L)  
Alkaline phosphatase | 84 U/L (1.4 µkat/L) | 88 U/L (1.5 µkat/L) | 50-120 U/L (0.84-2.00 µkat/L)  
Hemoglobin A₁c | 7.1% (54 mmol/mol) | 6.9% (52 mmol/mol) | 4.0%-5.6% (20-38 mmol/mol)  

He does not smoke cigarettes and drinks fewer than 5 alcohol-containing beverages per week. Current medications include metformin, lisinopril, hydrochlorothiazide, and aspirin. There is no history of hepatitis and results of serologic tests for hepatitis viruses are negative. Abdominal ultrasonography shows a hyperechoic pattern of the liver parenchyma, no dilation of the hepatic ducts, and no masses.

On physical examination, he is moderately obese with a BMI of 33.2 kg/m² (height is 69 in [175.3 cm], and weight is 225 lb [102.3 kg]). Blood pressure is 128/79 mm Hg. There is no jaundice, hepatomegaly, or edema.

Which of the following is the best next step in this patient's care?

A. Re-start simvastatin  
B. Prescribe fenofibrate  
C. Refer for liver biopsy  
D. Prescribe niacin  
E. Prescribe ezetimibe

LEARNING OBJECTIVE:  
Assess the risks and benefits of HMG-CoA reductase inhibitors and their use in preventing cardiovascular disease.

QUESTION 18:
DIABETES MELLITUS AND OTHER CARBOHYDRATE DISORDERS

A 25-year-old male graduate student with a 14-year history of type 1 diabetes mellitus inquires about continuous glucose monitoring to assist with diabetes management. He is treated with multiple daily insulin injections. He is very busy with class work, a part-time job, and extracurricular activities and has had difficulty monitoring his blood glucose as instructed. He worries that he has been experiencing fairly frequent hypoglycemic episodes and does not always have warning symptoms. He is hoping that a continuous glucose sensor will facilitate his monitoring and improve his control. His current hemoglobin A1c value is 8.9% (74 mmol/mol) (reference range, 4.0%-5.6% [20-38 mmol/mol]).

In counseling this patient, you should tell him that continuous glucose sensor systems:

A. Effectively lower hemoglobin A1c if worn more than 50% of the time
B. Are useful only in combination with insulin pump therapy
C. Measure interstitial glucose concentrations, which lag behind capillary glucose concentrations by about 30 minutes
D. Can replace fingerstick blood glucose monitoring
E. Automatically suggest insulin dose adjustments

LEARNING OBJECTIVE:

To understand that a valuable tool for assisting in glycemic management will be beneficial only if the patient uses it frequently

QUESTION 19:

PITUITARY AND NEUROENDOCRINE DISORDERS

An 18-year-old man is referred for tall stature, headaches, and sweating. His height is 82 in (208.3 cm), and weight is 273 lb (124.1 kg), both of which are at greater than the 97th percentile. On physical examination, he has enlarged hands and feet and a prognathic mandible. There are no changes in skin pigmentation and no long-bone deformities. A maternal uncle and maternal aunt both had pituitary adenomas of uncertain type. There is no known family history of calcium disorders or kidney stones.

Laboratory test results:

Random GH = 90 ng/mL (90 µg/L) (reference range, 0.01-0.97 [0.01-0.97 µg/L]) (GH does not suppress adequately during an oral glucose tolerance test)
Serum IGF-1 = 1233 ng/mL (161.5 nmol/L) (reference range, 170-640 ng/mL [22.3-83.8 nmol/L])
Prolactin = 26 ng/dL (1.1 nmol/L) (reference range, 4-23 ng/mL [0.17-1.00 nmol/L])
Thyroid axis, normal
Adrenal axis, normal
Serum calcium, normal
The patient has a bitemporal visual field defect. MRI of the brain shows a large pituitary adenoma (4.3 x 3.2 x 2.8 cm) with suprasellar extension, impingement on the optic chiasm, and invasion of the right cavernous sinus.

A germline mutation in which of the following genes is most likely to be responsible for the findings in this patient?

A. GNAS (GNAS complex locus)

B. AIP (aryl hydrocarbon receptor interacting protein)

C. PTTG1 (pituitary tumor-transforming 1)

D. TBX19 (T-box 19 transcription factor)

E. MEN1 (menin)

LEARNING OBJECTIVE:
To know the gene mutations causing familial pituitary adenoma syndromes

QUESTION 20:

BONE AND MINERAL METABOLISM

A 61-year-old woman who is asymptomatic and in apparent good health was documented to have a serum calcium level of 10.8 mg/dL (2.7 mmol/L) (reference range, 8.2-10.2 mg/dL [2.1-2.6 mmol/L]) at her recent annual examination.

Additional laboratory test results:

PTH = 89 pg/mL (89 ng/L) (reference range, 10-65 pg/mL [10-65 ng/L])
25-Hydroxyvitamin D = 15 ng/mL (37.4 nmol/L) (reference range [optimal], 25-80 ng/mL [62.4-199.7 nmol/L])
1,25-Dihydroxyvitamin D = 82 pg/mL (213.2 pmol/L) (reference range, 16-65 pg/mL [41.6-169.0 pmol/L])
Urinary calcium excretion = 275 mg/24 h (6.9 mmol/d) (reference range, 100-300 mg/24 h [2.5-7.5 mmol/d])

Which of the following is the most likely diagnosis?

A. The correct diagnosis cannot be made until her vitamin D deficiency has been corrected

B. Sarcoidosis

C. Primary hyperparathyroidism

D. Secondary hyperparathyroidism
E. Tertiary hyperparathyroidism

LEARNING OBJECTIVE:
Diagnose primary hyperparathyroidism in the setting of low 25-hydroxyvitamin D.

QUESTION 21:

LIPIDS/OBESITY

A 55-year-old woman with a history of type 2 diabetes mellitus, hypertension, atrial fibrillation, and severe psoriasis asks your opinion regarding the over-the-counter weight-loss medication orlistat.

On physical examination, her height is 65 in (165.1 cm) and weight is 187 lb (85 kg) (BMI = 31.1 kg/m$^2$). Her blood pressure today is 148/95 mm Hg.

She is currently taking cyclosporine for psoriasis, warfarin for atrial fibrillation, lisinopril for hypertension, and metformin for diabetes.

As you counsel this patient, you should tell her that over-the-counter orlistat:

A. Is contraindicated because of her uncontrolled hypertension

B. Could reduce the blood level of warfarin, resulting in a decreased INR (International Normalized Ratio)

C. Could reduce the blood level of cyclosporine, resulting in a psoriasis flare

D. Is not indicated in persons with a BMI less than 33 kg/m$^2$

E. Is medically indicated and will most likely produce a 5% weight loss

LEARNING OBJECTIVE:
To list potential drug interactions of orlistat

QUESTION 22:

MALE REPRODUCTION

A 35-year-old man is referred to you because he and his wife have failed to conceive after 12 months of frequent unprotected intercourse. The patient has never fathered any children. His wife, age 28 years, has a 2-year-old child from a previous relationship. She has normal menses. The man is healthy and takes no medications.

On physical examination, he is a well-virilized man with no gynecomastia, and genitourinary examination documents a normal penis and 15-mL testes bilaterally (no masses, tenderness, or induration).
Laboratory test results:

Total testosterone = 600 ng/dL (20.8 nmol/L) (reference range, 300-900 ng/dL [10.4-31.2 nmol/L])
FSH = 16.0 mIU/mL (16.0 IU/L) (reference range, 1.0-13.0 mIU/mL [1.0-13.0 IU/L])
LH = 3.1 mIU/mL (3.1 IU/L) (reference range, 1.0-9.0 mIU/mL [1.0-9.0 IU/L])
Seminal fluid analysis = 2.8 mL; pH, 7.4; normal fructose; no sperm
Karyotype analysis = 46,XY (no visible Yq anomalies)

Which of the following is the best next test in the assessment of his infertility?

A. Antisperm antibody assessment

B. Serum inhibin B measurement

C. Testicular ultrasonography

D. Serum estradiol measurement

E. Testicular biopsy

LEARNING OBJECTIVE:

To understand the role of testicular biopsy in the evaluation of male infertility

QUESTION 23:

BONE AND MINERAL METABOLISM

A healthy 62-year-old man presents with pain in his upper left leg that he has noted for 1 year, although it has been worse in the past 4 months. His symptoms are not affected by weight bearing, are worse at night, and are only minimally improved by nonsteroidal anti-inflammatory therapy. He takes no other medications and has no history of skeletal or rheumatologic problems or abnormalities of calcium metabolism.

Physical examination findings are normal except for some warmth over the proximal region of the left thigh. He does not have impaired range of motion of his left hip.

Laboratory test results:

Serum calcium = 9.5 mg/dL (2.4 mmol/L) (reference range, 8.2-10.2 mg/dL [2.1-2.6 mmol/L])
Serum phosphorus = 4.2 mg/dL (1.4 mmol/L) (reference range, 2.3-4.7 mg/dL [0.7-1.5 mmol/L])
Serum albumin = 4.0 g/dL (40 g/L) (reference range, 3.5-5.0 g/dL [35-50 g/L])
Serum alkaline phosphatase = 285 U/L (4.8 µkat/L) (reference range, 50-120 U/L [0.84-2.00 µkat/L])
Serum creatinine = 1.1 mg/dL (97.2 µmol/L) (reference range, 0.7-1.3 mg/dL [61.9-114.9 µmol/L])
Prostate-specific antigen = 1.0 ng/mL (1.0 µg/L) (reference range, <5.3 ng/mL [<5.3 µg/L])

X-rays of the left hip reveal a heterogeneous pattern of marked trabecular thickening and focal areas of bone lysis in the left femur. The cortices are intact, and no prominent lytic lesions are seen. The femur is not bowed, and the hip joint space is normal. Bone scan reveals increased uptake in the proximal one-third of the left femur. No other areas of increased uptake are seen.
Which of the following will provide the most benefit?

A. Risedronate, 35 mg weekly for 6 months
B. Salmon calcitonin, 100 units daily by subcutaneous injection, indefinitely
C. Alendronate, 40 mg daily for 6 months
D. Salmon calcitonin nasal spray, 100 units daily for 1 year
E. Alendronate, 70 mg weekly for 6 months

**LEARNING OBJECTIVE:**
Determine the appropriate treatment of Paget disease of bone.

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**QUESTION 24:**

**DIABETES MELLITUS AND OTHER CARBOHYDRATE DISORDERS**

A 58-year-old man with a 28-year history of type 1 diabetes mellitus has been on insulin pump therapy for 11 years. He has been experiencing recurrent, severe, unpredictable hypoglycemia over the past year. His diabetes is complicated by proliferative retinopathy, microalbuminuria with a stable creatinine concentration of 1.1 mg/dL (97.2 µmol/L) for the past 3 years, and peripheral sensory neuropathy with a history of an ulcer on his left first metatarsal. He is now seeking evaluation for possible pancreas transplant with the hope of avoiding future severe hypoglycemia.

Which of the following is the most important consideration in deciding whether to recommend pancreas transplant in this patient?

A. Better organ survival with pancreas transplant alone than with pancreas transplant plus simultaneous kidney transplant
B. Better patient survival after pancreas transplant alone
C. The effect of calcineurin-based immunosuppression on insulin action
D. His frequency and severity of hypoglycemia and comorbidities
E. The potential effect of immunosuppressive therapy on renal function

**LEARNING OBJECTIVE:**
To know the most important indications for pancreas transplantation

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**QUESTION 25:**
A 26-year-old man is referred by his internist for suspected diabetes insipidus. He reports a constant sense of thirst, and he believes he drinks more fluids and urinates more often than other people.

Laboratory test results:

- Fasting plasma glucose = 89 mg/dL (4.9 mmol/L) (reference range, 70-99 mg/dL [3.9-5.5 mmol/L])
- Total urine volume = 7.5 L/24 h with urine osmolality of 70 mOsm/kg (70 mmol/kg) (reference range, 150-1150 mOsm/kg [150-1150 mmol/kg])

A fluid deprivation test over 4 hours results in a 6.5-lb (3-kg) decrease in body weight, a rise in serum sodium from 140 to 153 mEq/L (140 to 153 mmol/L), and a rise in serum osmolality from 283 to 312 mOsm/kg (283 to 312 mmol/kg). The osmolality of urine collections over this period increases from 70 to 95 mOsm/kg (70 to 90 mmol/kg). At the end of the 4-hour period, a subcutaneous injection of DDAVP (2 mcg) is administered, and 1 hour and 2 hours after the injection, his urine osmolality rises to 300 and 420 mOsm/kg (300 and 420 mmol/kg), respectively.

On the basis of these results, which of the following treatments would be most effective for this patient?

A. Amiloride  
B. Thiazide diuretic  
C. Indomethacin  
D. Referral for psychiatric evaluation  
E. DDAVP (desmopressin)

Learning Objective:
To understand how to interpret the dehydration test when diagnosing diabetes insipidus

Question 26:

Female Reproduction

A 24-year-old woman who runs competitive track presents with low body weight and amenorrhea. She had normal menarche at age 11 years and regular menses in adolescence. However, during college she lost weight and her menses stopped 8 months ago. Her weight over the past 3 years has been stable. She is otherwise well and has no notable medical history. She has no headaches, altered vision, or breast tenderness or discharge.

On physical examination, her height is 65 in (165.1 cm) and weight is 115 lb (52.3 kg) (BMI = 19.1 kg/m²). Examination findings are normal.

Of the following, which are the most common laboratory test abnormalities you would expect in
A. High FSH, high LH, low estradiol, and normal prolactin

B. High FSH, low LH, normal estradiol, and high prolactin

C. Low FSH, low LH, low estradiol, and normal prolactin

D. Low FSH, low LH, low estradiol, and high prolactin

E. Low FSH, high LH, low estradiol, and high prolactin

LEARNING OBJECTIVE:

To review the laboratory patterns in reproductive hormones in hypothalamic amenorrhea and other reproductive disorders.

QUESTION 27:

BONE AND MINERAL METABOLISM

A 68-year-old woman has been taking alendronate, 70 mg weekly, for the past 2 years. She says that she has taken it correctly except for missing a few doses and that she has not had any adverse effects. She had a repeated bone density test at the same center as her initial study. The report indicates a significant loss of bone mineral density in the spine and gains of bone mineral density in the femoral neck and total hip. The DXA images and numeric results are shown (see images and table).
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<tr>
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A. She is not taking her alendronate correctly
B. She is not responding to alendronate
C. She has some underlying cause of secondary osteoporosis
D. Her spine bone mineral density was measured incorrectly
E. Her hip bone mineral density was measured incorrectly

LEARNING OBJECTIVE:
Carefully review DXA images and identify common technical errors.

QUESTION 28:

THYROID DISORDERS

An 84-year-old man is referred for an elevated serum TSH value. The patient has been in good health, with no history of thyroid dysfunction. On physical examination, his pulse rate is 72 beats/min and he has no goiter.

Serum TSH = 6.2 mIU/L (reference range, 0.5-5.0 mIU/L)
Free T4 = 1.1 ng/dL (14.2 pmol/L) (reference range, 0.8-1.8 ng/dL [10.30-23.17 pmol/L])
TPO antibodies, negative

These findings are stable on repeated testing.

Which of the following statements is correct regarding this patient?

A. TSH in this range is associated with increased cardiovascular mortality
B. His TSH value is normal for octogenarians
C. Elderly patients require higher weight-based dosages of levothyroxine
D. He has apathetic hypothyroidism
E. Treatment with levothyroxine will improve his quality of life
LEARNING OBJECTIVE:
To understand age-specific normal ranges for serum thyrotropin

QUESTION 29:
DIABETES MELLITUS AND OTHER CARBOHYDRATE DISORDERS
A 26-year-old nondiabetic woman whose husband has type 1 diabetes mellitus is contemplating pregnancy and is inquiring about the risk of type 1 diabetes developing in her child.

Which of the following characterizes the risk of type 1 diabetes developing in her offspring?

A. 0.1%
B. 0.4%
C. 6.0%
D. 20.0%
E. 30.0%

LEARNING OBJECTIVE:
To understand the risk of type 1 DM development in the offspring of a parent with type 1 DM

QUESTION 30:
THYROID DISORDERS
A 72-year-old woman with a history of Hashimoto thyroiditis that is treated with levothyroxine therapy is found to have a parasellar meningioma requiring surgical resection and radiation therapy. She notes fatigue and constipation, as well as occasional palpitations. Her pulse rate is 88 beats/min, and she has a small, firm goiter.

Laboratory test results:

TSH = 1.4 mIU/L (reference range, 0.5-5.0 mIU/L)
Free T<sub>4</sub> = 0.9 ng/dL (11.6 pmol/L) (reference range, 0.8-1.8 ng/dL [10.30-23.17 pmol/L])
FSH = 4.5 mIU/mL (4.5 IU/L) (reference range, >30 mIU/mL [>30 IU/L])
LH = 5.2 mIU/mL (5.2 IU/L) (reference range, >30 mIU/mL [>30 IU/L])
Plasma cortisol (8 AM) = 14 μg/dL (386.2 nmol/L) (reference range, 5-25 μg/dL [137.9-689.7 nmol/L])
IGF-1 = 65.1 ng/mL (8.53 nmol/L) (reference range, 67-195 ng/mL [8.8-25.5 nmol/L])
Prolactin = 6.5 ng/mL (0.28 nmol/L) (reference range, 4-30 ng/mL [0.17-1.30 nmol/L])

Electrocardiogram shows occasional premature ventricular contractions.
Which of the following is the most appropriate next step in this patient’s management?

A. Continue the current levothyroxine dosage

B. Decrease levothyroxine, with a TSH target of 2.0 to 3.0 mIU/L

C. Decrease levothyroxine, with a TSH target of 3.5 to 5.0 mIU/L

D. Increase levothyroxine, with a free T₄ target of 1.2 to 1.5 ng/dL (15.4 to 19.3 pmol/L)

E. Increase levothyroxine, with a free T₄ target of 1.6 to 1.9 ng/dL (20.6 to 24.5 pmol/L)

LEARNING OBJECTIVE:

Use free T4 values rather than TSH for therapeutic targets in the management of central hypothyroidism.

QUESTION 31:

MALE REPRODUCTION

A 29-year-old man is referred for evaluation of gynecomastia. He describes normal libido and erections, but he has had painless breast enlargement since puberty. In the past 2 to 3 years, the gynecomastia has become more noticeable. On review of systems, he shaves once weekly and has relatively sparse body hair. His medical history is remarkable for primary hypothyroidism due to Hashimoto thyroiditis and a history of mumps at age 13 years.

On physical examination, his height is 72 in (182.9 cm) and weight is 170 lb (77.3 kg) (BMI = 23.1 kg/m²). He has sparse facial hair, normal axillary hair, Tanner stage 4 pubic hair, 4-cm bilateral gynecomastia, and no galactorrhea. Genitourinary examination shows a normal phallus with no hypospadias and 2-mL testes that are very firm.

Laboratory test results:

- Total testosterone = 225 ng/dL (7.8 nmol/L) (reference range, 300-900 ng/dL [10.4-31.2 nmol/L])
- FSH = 48.0 mIU/mL (48.0 IU/L) (reference range, 1.0-13.0 mIU/mL [1.0-13.0 IU/L])
- LH = 27.0 mIU/mL (27.0 IU/L) (reference range, 1.0-9.0 mIU/mL [1.0-9.0 IU/L])

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

A. Partial androgen insensitivity

B. Gonadotropin-producing adenoma

C. Klinefelter syndrome

D. Autoimmune polyglandular deficiency syndrome
E. Primary hypogonadism due to mumps orchitis

LEARNING OBJECTIVE:
To recognize the clinical and biochemical manifestations of Klinefelter syndrome

QUESTION 32:
DIABETES MELLITUS AND OTHER CARBOHYDRATE DISORDERS

A 20-year-old man with type 1 diabetes mellitus describes a several-month history of diarrhea, unintentional weight loss, poor glycemic control, and a rash. On physical examination, he has no abdominal tenderness, a normal 10-g monofilament test, and a rash (see image).

Which of the following is the best initial diagnostic test to evaluate his concerns?

A. IgA tissue transglutaminase antibody measurement
B. Gastric emptying study
C. TPO antibody measurement
D. Colonoscopy
E. Skin biopsy

LEARNING OBJECTIVE:
To know the characteristic skin rash and other signs and symptoms associated with celiac disease

QUESTION 33:
BONE AND MINERAL METABOLISM

A 50-year-old woman is referred for evaluation of metabolic bone disease. She has a 4-year history
of progressive bone pain and recurrent fractures, including 2 pelvic fractures with falls, a right distal radius fracture, multiple rib fractures, compression fractures of 6 different vertebral bodies resulting in a marked kyphosis, and 3 separate metatarsal fractures. She has developed myalgias and muscle weakness. She walks short distances with great discomfort. Recently, she was found to have a fracture of the medial aspect of the left proximal femur. Each fracture has healed, but she has marked residual pain that is increasing with subsequent events.

She takes no medications. She has no family history of metabolic bone disease (no fractures or disorders of calcium metabolism), and, aside from the last 4 years, she has no notable medical history in earlier adulthood or childhood. She has 3 healthy children.

On physical examination, there is tenderness over both thighs, but examination findings are otherwise normal.

Laboratory test results:

Calcium = 9.5 mg/dL (2.4 mmol/L) (reference range, 8.2-10.2 mg/dL [2.1-2.6 mmol/L])
Albumin = 3.9 g/dL (39 g/L) (reference range, 3.5-5.0 g/dL [35-50 g/L])
Creatinine = 0.8 mg/dL (70.7 µmol/L) (reference range, 0.6-1.1 mg/dL [53.0-97.2 µmol/L])
Phosphorus = 1.2 mg/dL (0.4 mmol/L) (reference range, 2.3-4.7 mg/dL [0.7-1.5 mmol/L])
Alkaline phosphatase = 305 U/L (5.1 µkat/L) (reference range, 50-120 U/L [0.84-2.00 µkat/L])
Intact PTH = 52 pg/mL (52 ng/L) (reference range, 10-65 pg/mL [10-65 ng/L])
25-Hydroxyvitamin D = 35 ng/mL (87.4 nmol/L) (reference range [optimal], 25-80 ng/mL [62.4-199.7 nmol/L])
1,25-Dihydroxyvitamin D = 10 pg/mL (26 pmol/L) (reference range, 16-65 pg/mL [41.6-169.0 pmol/L])

Her tubular reabsorption of phosphate is 54% (normal, >85%). A transiliac bone biopsy is done after double tetracycline labeling. Evaluation of the nondecalcified specimen reveals excess osteoid and diminished tetracycline uptake.

Which of the following is the most likely diagnosis?

A. Calcium malabsorption
B. Tumor-induced osteomalacia
C. Autosomal dominant hypophosphatemic rickets
D. X-linked hypophosphatemic rickets
E. Mutation in the gene encoding the vitamin D receptor

LEARNING OBJECTIVE:
Diagnose tumor-induced osteomalacia on the basis of clinical and biochemical findings.

QUESTION 34:
THYROID DISORDERS

An 83-year-old man with refractory atrial fibrillation is prescribed amiodarone. Three months later, he reports increasing palpitations and diaphoresis. On physical examination, his pulse rate is 90 beats/min and regular, his thyroid gland is of normal size and is nontender, and he has a fine tremor.

Which of the following would be the most specific indicator of thyrotoxicosis in this patient?

A. Elevated total T₄ level
B. Elevated free T₄ level
C. Suppressed serum TSH level
D. Low radioactive iodine uptake
E. Clinical signs and symptoms

LEARNING OBJECTIVE:

Identify the pattern of thyroid function test results in patients with amiodarone-induced thyrotoxicosis.

QUESTION 35:

ADRENAL DISORDERS

A 43-year-old woman is admitted to the hospital with polyphagia, a 40-lb (18.2-kg) weight gain, and a 2-month history of generalized edema, weakness, fatigue, dyspnea, and facial hirsutism. She also has a 6-month history of type 2 diabetes mellitus treated with a sulfonylurea.

On physical examination, her blood pressure is 150/96 mm Hg. Her height is 64 in (162.6 cm), and weight is 190 lb (86.4 kg) (BMI = 32.6 kg/m²). She has moon facies, truncal obesity, and lanugo-type hair on the face. She has trace pretibial edema. She has no striae, acne, or skin atrophy.

Laboratory test results:

8-AM plasma ACTH, undetectable
8-AM serum cortisol = 32.6 µg/dL (899.4 nmol/L) (reference range, 5-25 µg/dL [137.9-689.7 nmol/L])
4-PM serum cortisol = 30.2 µg/dL (833.2 nmol/L) (reference range, 2-14 µg/dL [55.2-386.2 nmol/L])
Urinary free cortisol = 399 µg/24 h (1101 nmol/d) (reference range, 4-50 µg/24 h [11-138 nmol/d])

CT of the abdomen is shown (see image).
A 17-year-old woman is referred to you for primary amenorrhea. The patient had some breast development starting in the sixth grade, but her final breast size is small. She grew slowly throughout her teen years and is now 1 inch shorter than her predicted adult height. She has no galactorrhea, cold intolerance, dizziness, or hot flashes.

On physical examination, her height is 64 in (162.6 cm), and weight is 127 lb (57.6 kg) (BMI = 21.8 kg/m²). Her thyroid gland is normal on examination. Both breast and pubic hair development is Tanner stage 4.

Laboratory test results:

Which of the following would be the most effective treatment for this patient?

A. Laparoscopic left adrenalectomy
B. Mitotane
C. Radiation therapy
D. Ketoconazole
E. Open laparotomy and left adrenalectomy

LEARNING OBJECTIVE:
Diagnose probable adrenocortical carcinoma on the basis of clinical presentation and imaging phenotype on CT.
Prolactin = 31.7 ng/mL (1.4 nmol/L) (reference range, 4-30 ng/mL [0.17-1.30 nmol/L])
LH = 0.6 mIU/mL (reference range [prepubertal], <1.0 mIU/mL [<1.0 IU/L])
FSH = 4.4 mIU/mL (4.4 IU/L) (reference range [prepubertal], <3.0 mIU/mL [<3.0 IU/L])
Estradiol = <20 pg/mL (<73.4 pmol/L) (reference range [prepubertal], <20 pg/mL [<73.4 pmol/L])

Which of the following should you do next in this patient's evaluation?

A. Order pelvic ultrasonography
B. Measure total testosterone
C. Measure prolactin in a diluted serum sample
D. Order pituitary MRI
E. Order karyotype analysis

LEARNING OBJECTIVE:
Prioritize the workup of primary amenorrhea.

QUESTION 37:
DIABETES MELLITUS AND OTHER CARBOHYDRATE DISORDERS

A 39-year-old man is referred to you by a colleague in the psychiatry department for evaluation of "metabolic syndrome." The patient has gained 26 lb (11.8 kg) over the past year and has developed hypertension and dyslipidemia. His medical history is notable for schizophrenia/schizoaffective disorder requiring treatment with olanzapine and trazodone, which he has taken for the past 15 months. He also takes hydrochlorothiazide and a calcium channel blocker for hypertension.

On physical examination, he has a flat affect, but is coherent and answers questions appropriately. His blood pressure is 128/68 mm Hg. His height is 70 in (177.8 cm), and weight is 238 lb (108.2 kg) (BMI = 34.1 kg/m²). His waist circumference is 41.3 in (105 cm). His skin has normal mobility and thickness, he has central obesity, and his abdomen has pale striae. Muscle bulk and strength are normal.

Laboratory test results (sample drawn while fasting):

TSH = 1.1 mU/L (reference range, 0.5-5.0 mIU/L)
Glucose = 119 mg/dL (6.6 mmol/L) (reference range, 70-99 mg/dL [3.9-5.5 mmol/L])
Total cholesterol = 224 mg/dL (5.80 mmol/L) (reference range [optimal], <200 mg/dL [<5.18 mmol/L])
Triglycerides = 427 mg/dL (4.83 mmol/L) (reference range [optimal], <150 mg/dL [<3.88 mmol/L])
LDL cholesterol = 92 mg/dL (2.38 mmol/L) (reference range [optimal], <100 mg/dL [<2.59 mmol/L])
HDL cholesterol = 38 mg/dL (0.98 mmol/L) (reference range [optimal], >60 mg/dL [>1.55 mmol/L])

Which of the following is the best next step in this patient's care?
A. Perform an overnight dexamethasone suppression test

B. Discuss alternative antipsychotic regimens with the patient's psychiatrist

C. Initiate treatment with gemfibrozil

D. Initiate treatment with an HMG-CoA reductase inhibitor

E. Initiate treatment with metformin

**LEARNING OBJECTIVE:**

Recognize and manage the metabolic complications of atypical antipsychotic medications.

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**QUESTION 38:**

**BONE AND MINERAL METABOLISM**

A 55-year-old man comes to you for evaluation of recurrent kidney stones. Twelve years ago he passed a stone of uncertain composition. Two months ago, he passed a stone that was made of calcium oxalate.

His medical history is notable for sarcoidosis initially diagnosed 20 years ago when he presented with bilateral hilar adenopathy and interstitial lung disease. His pulmonary function and findings from chest x-rays have been stable, and the hilar adenopathy has resolved.

He smoked 1 pack of cigarettes daily for 20 years, but has not smoked in the last 20 years. He does not take vitamin D or calcium supplements and eats few dairy products. He has had no fractures.

His physical examination findings are unremarkable.

Laboratory test results:

- 1,25-Dihydroxyvitamin D = 120 pg/mL (312 pmol/L) (reference range, 16-65 pg/mL [41.6-169.0 pmol/L])
- 25-Hydroxyvitamin D = 25 ng/mL (62.4 nmol/L) (reference range [optimal], 25-80 ng/mL [62.4-199.7 nmol/L])
- PTH = 10 pg/mL (10 ng/L) (reference range, 10-65 pg/mL [10-65 ng/L])
- TSH = 1.0 mIU/L (reference range, 0.5-5.0 mIU/L)
- Albumin = 4.0 g/dL (40 g/L) (reference range, 3.5-5.0 g/dL [35-50 g/L])
- Calcium = 10.6 mg/dL (2.7 mmol/L) (reference range, 8.2-10.2 mg/dL [2.1-2.6 mmol/L])
- Phosphorus = 4.4 mg/dL (1.4 mmol/L) (reference range, 2.3-4.7 mg/dL [0.7-1.5 mmol/L])
- Serum urea nitrogen = 20 mg/dL (7.1 mmol/L) (reference range, 8-23 mg/dL [2.9-8.2 mmol/L])
- Urinary calcium = 520 mg/24 h (13 mmol/d) (reference range, 100-300 mg/24 h [2.5-7.5 mmol/d])
- Urinary creatinine = 1.1 g/24 h (9.7 mmol/d) (reference range, 1.0-2.0 g/24 h [8.8-17.7 mmol/d])

In addition to increasing his fluid intake, initiation of which of the following should you recommend?
A glucocorticoid
B. A thiazide
C. Nasal calcitonin
D. A low-oxalate diet
E. Potassium citrate supplementation

LEARNING OBJECTIVE:
Diagnose and treat granulomatous hypercalcemia and hypercalciuria.

QUESTION 39:
LIPIDS/OBESITY

A 32-year-old woman had a peak lifetime BMI of 69 kg/m². Nine weeks ago, she had a laparoscopic gastric bypass procedure. After being discharged from the hospital she did well for several weeks. However, for the last 3 weeks, she has experienced frequent episodes of vomiting. Over the last week, she has been vomiting almost everything that she eats. Over the last 2 days, her family says that she has become increasingly confused and unsteady on her feet and has complained of double vision. In the emergency department, she is found to be confused, dysarthric, and unsteady on her feet. On neurologic examination, she has a right third nerve palsy, nystagmus, and decreased sensation over her lower extremities.

A deficiency of which of the following is most likely?

A. Zinc
B. Vitamin D
C. Thiamine
D. Folate
E. Vitamin B₁₂

LEARNING OBJECTIVE:
To be able to identify specific vitamin deficiencies that develop following bariatric surgery

QUESTION 40:
BONE AND MINERAL METABOLISM

A 63-year-old man who has had diabetes mellitus for 10 years is admitted to the hospital with a
history of severe itching of his legs for 1 and a half months and painful ulcers on his right leg that have been present for 2 weeks. His diabetes is complicated by peripheral neuropathy, gastroparesis, and chronic renal insufficiency. Serum creatinine has been steadily increasing for the past 1 and a half years. He is awaiting the initiation of hemodialysis.

Over the past week, his leg pain has worsened and has been associated with redness and swelling of his lower extremities, fever, chills, and rigors.

On physical examination, he appears quite ill. Blood pressure is 140/75 mm Hg, pulse rate is 112 beats/min, respiratory rate is 14 breaths/min, and temperature is 100.1°F (37.8°C). The oral mucosa is pink and dry. Findings from cardiopulmonary examination are normal. There are multiple dark-colored, shallow ulcers on the anterior and lateral aspects of the distal third of the right leg (see image). The bases of the lesions are firm to leathery in consistency, and you observe surrounding erythema of the adjacent skin. Pedal pulses are barely palpable bilaterally; there is good capillary refill. Sensation to touch (monofilament) is reduced on the dorsal surface of both feet.

Serum laboratory test results:

- Sodium = 130 mEq/L (130 mmol/L) (reference range, 136-142 mEq/L [136-142 mmol/L])
- Potassium = 4.9 mEq/L (4.9 mmol/L) (reference range, 3.5-5.0 mEq/L [3.5-5.0 mmol/L])
- Chloride = 90 mEq/L (90 mmol/L) (reference range, 96-106 mEq/L [96-106 mmol/L])
- Bicarbonate = 18 mEq/L (18 mmol/L) (reference range, 21-28 mEq/L [21-28 mmol/L])
- Serum urea nitrogen = 97 mg/dL (34.6 mmol/L) (reference range, 8-23 mg/dL [2.9-8.2 mmol/L])
- Creatinine = 8.2 mg/dL (724.9 µmol/L) (reference range, 0.7-1.3 mg/dL [61.9-114.9 µmol/L])
- Calcium = 8.3 mg/dL (2.1 mmol/L) (reference range, 8.2-10.2 mg/dL [2.1-2.6 mmol/L])
- Albumin = 2.9 g/dL (29 g/L) (reference range, 3.5-5.0 g/dL [35-50 g/L])
- Phosphorus = 8.5 mg/dL (2.7 mmol/L) (reference range, 2.3-4.7 mg/dL [0.7-1.5 mmol/L])
- PTH (intact) = 1130 pg/mL (1130 ng/L) (reference range, 10-65 pg/mL [10-65 ng/L])
- 1,25-Dihydroxyvitamin D = <10 pg/mL (<26 pmol/L) (reference range, 16-65 pg/mL [41.6-169.0 pmol/L])

Which of the following assessments is most likely to confirm the presumptive diagnosis?

A. Bone scan
B. Parathyroid sestamibi scan
C. Parathyroid ultrasonography
D. Skin biopsy
E. Plain x-ray of the lower extremities
LEARNING OBJECTIVE:
Confirm the suspected diagnosis of calciphylaxis in the setting of renal failure.

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QUESTION 41:

PITUITARY AND NEUROENDOCRINE DISORDERS

A 68-year-old woman with hypertension (controlled on metoprolol) is referred to you for a thyroid nodule. She does not have dysphagia, dyspnea, or hoarseness.

Her blood pressure is 135/88 mm Hg, and her pulse rate is 68 beats/min. She has frontal bossing, deep nasolabial folds, increased dental spacing, and a prognathic jaw. There is a 1.5-cm, soft, nontender nodule palpable in the left thyroid lobe. There is no cervical lymphadenopathy. Her hands and feet appear enlarged and doughy.

Laboratory test results:

- TSH = 0.7 mIU/L (reference range, 0.5-5.0 mIU/L)
- Free T₁ = 1.3 ng/dL (16.7 pmol/L) (reference range, 0.8-1.8 ng/dL [10.30-23.17 pmol/L])
- IGF-1 = 1064 ng/mL (139.4 nmol/L) (reference range, 67-195 ng/mL [8.8-25.5 nmol/L])
- Prolactin = 16 ng/mL (0.7 nmol/L) (reference range, 4-30 ng/mL [0.17-1.30 nmol/L])
- Liver function, normal

Brain MRI shows a mass on the left side of the sella involving the left cavernous sinus (see image). There is aneurysmal dilatation of the left intracavernous carotid artery. There is no pressure on the optic apparatus.

[Image of MRI scan]

Two experienced pituitary neurosurgeons are consulted, but neither recommends surgery. Octreotide LAR therapy is begun and is titrated to a dosage of 30 mg every 4 weeks. She tolerates the medication well without notable gastrointestinal adverse effects or hyperglycemia.
dosage, her serum IGF-1 concentration decreases to 654 ng/mL (85.7 nmol/L). A follow-up brain MRI shows no change in tumor size.

Which of the following is the best management step now?

A. Switch to lanreotide depot
B. Switch to pegvisomant
C. Add cabergoline
D. Add pegvisomant
E. Add bromocriptine

LEARNING OBJECTIVE:
Recommend combination medical therapy (somatostatin analogue plus pegvisomant) in selected patients with acromegaly

QUESTION 42:
DIABETES MELLITUS AND OTHER CARBOHYDRATE DISORDERS

A 31-year-old man with a 20-year history of type 1 diabetes mellitus has been on insulin pump therapy for more than 5 years. He presents for follow-up and help with recurrent mild hypoglycemia. He reports having mild hypoglycemic episodes many afternoons, which occur at least 4 hours after lunch and are characterized by sweating and anxiety. During these episodes, self-monitored blood glucose values are between 50 and 60 mg/dL (2.8 and 3.3 mmol/L). You examine his log book and see documented hypoglycemic values between 50 and 64 mg/dL (2.8 and 3.6 mmol/L), approximately 4 times per week at 5 PM.

The patient uses insulin aspart in his pump. Current pump settings:

- **Basal rates:**
  - Midnight to 6 AM: 0.7 units/h
  - 6 AM to midnight: 1.0 units/h
- **Correction (sensitivity) factor:** 1 unit/40 mg glucose
- **Insulin-to-carbohydrate ratio:** 1 unit:15 g

His height is 71 in (180.3 cm), and weight is 187 lb (85 kg) (BMI = 26.1 kg/m²).

Which of the following is the best advice now to alleviate his hypoglycemic episodes?

A. Increase his carbohydrate intake at lunch
B. Have a carbohydrate snack at 3 or 4 PM
C. Change the prelunch carbohydrate ratio to 1:10
D. Change the prelunch carbohydrate ratio to 1:20

E. Perform a check of the basal rate from breakfast until dinner

LEARNING OBJECTIVE:
Devise a strategy to identify and correct a common problem encountered with the use of continuous subcutaneous insulin infusion.

QUESTION 43:
ADRENAL DISORDERS

You are asked to evaluate a 16-year-old adolescent for adrenal insufficiency. He has a 2-year history of attention deficit disorder, for which he is currently treated with methylphenidate. He has had a rapid onset of neurologic symptoms, including weakness in his lower extremities, gait instability, slurred speech, and confusion. On physical examination, he has hyperpigmentation in sun-exposed areas, brisk deep tendon reflexes, clonus in the left ankle, and bilateral Babinski sign. There is no family history of any endocrine disorders. Pituitary-adrenal function testing documents a morning basal plasma ACTH concentration of 144 pg/mL (31.7 pmol/L) (reference range, 10-60 pg/mL [2.2-13.2 pmol/L]) and a serum cortisol concentration of 3.7 µg/dL (102.1 nmol/L) (reference range, 5-25 µg/dL [13.7.9-689.7 nmol/L]). There is no further increase in cortisol after administration of 250 mcg of intravenous cosyntropin.

Which of the following should you recommend to identify the most likely cause of adrenal insufficiency in this patient?

A. Measure very-long-chain fatty acids

B. Measure 21-hydroxylase antibodies

C. Measure lupus anticoagulant

D. Perform CT of the adrenal glands

E. Discontinue methylphenidate and repeat pituitary-adrenal testing

LEARNING OBJECTIVE:
Include adrenoleukodystrophy in the differential diagnosis of any young male patient with primary adrenal insufficiency of unknown cause, especially in the presence of concomitant neurologic symptoms.

QUESTION 44:
BONE AND MINERAL METABOLISM

A 79-year-old woman recently began treatment with zoleedronic acid, 5 mg intravenously, for
osteooporosis documented by DXA. Several days after receiving the medication, she experienced intermittent severe cramps in her hands and legs, as well as some tightening in her throat.

Her medical history includes a total thyroidectomy for a large goiter when she was a teenager. She also has a history of rare, grand mal seizures well controlled with anticonvulsant agents. Current medications include levothyroxine and phenobarbital.

On physical examination, Chvostek and Trousseau signs are present. Electrocardiography shows that the QTc interval is prolonged to 0.51 seconds.

Laboratory test results:

Calcium = 6.5 mg/dL (1.6 mmol/L) (reference range, 8.2-10.2 mg/dL [2.1-2.6 mmol/L])
Phosphorus = 6.5 mg/dL (2.1 mmol/L) (reference range, 2.3-4.7 mg/dL [0.7-1.5 mmol/L])
Magnesium = 2.0 mg/dL (0.8 mmol/L) (reference range, 1.5-2.3 mg/dL [0.6-0.9 mmol/L])
PTH = 15 pg/mL (15 ng/L) (reference range, 10-65 pg/mL [10-65 ng/L])
Serum urea nitrogen = 6 mg/dL (2.1 mmol/L) (reference range, 8-23 mg/dL [2.9-8.2 mmol/L])
Creatinine = 0.6 mg/dL (53.0 μmol/L) (reference range, 0.6-1.1 mg/dL [53.0-97.2 μmol/L])
TSH = 8.3 mIU/L (reference range, 0.5-5.0 mIU/L)

Electrolytes, normal

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

A. Hypothyroidism
B. Vitamin D deficiency
C. Hypomagnesemia
D. Phenobarbital
E. Hypoparathyroidism

**LEARNING OBJECTIVE:**

Identify hypoparathyroidism after thyroid surgery as the cause of hypocalcemia.

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**QUESTION 45:**

**FEMALE REPRODUCTION**

A 16-year-old girl presents with primary amenorrhea. She underwent thelarche at age 10 years, but had no axillary or pubic hair development. She has had no hot flashes, acne, hirsutism, galactorrhea, or symptoms of thyroid disease, and she is not sexually active.

On physical examination, her blood pressure is 110/80 mm Hg. Her height is 69 in (175.3 cm), and weight is 147 lb (66.8 kg) (BMI = 21.7 kg/m²). On skin examination, she has no axillary or pubic hair. Her breasts are Tanner stage 4. Pelvic examination reveals a vaginal length of 1.5 cm. A mass is palpated in the right inguinal area.
Laboratory test results:

Prolactin = 8.6 ng/mL (0.37 nmol/L) (reference range, 4-30 ng/mL [0.17-1.30 nmol/L])
FSH = 3.2 mIU/mL (3.2 IU/L) (reference range [prepubertal], <3.0 mIU/mL [<3.0 IU/L])
LH = 15.0 mIU/mL (15.0 IU/L) (reference range [prepubertal], <1.0 mIU/mL [<1.0 IU/L])
Testosterone = 390 ng/dL (13.5 nmol/L) (reference range, 8-60 ng/dL [0.3-2.1 nmol/L])
Estradiol = 45 pg/mL (165.2 pmol/L) (reference range [prepubertal], <20 pg/mL [<73.4 pmol/L])
\( \beta \)-hCG = <3.0 mIU/mL (<3.0 IU/L) (reference range, <3.0 mIU/mL [<3.0 IU/L])

Which of the following is the best therapeutic option now?

A. Estradiol

B. Gonadectomy

C. Low-dosage oral contraceptive

D. Spironolactone

E. Estradiol and progesterone

LEARNING OBJECTIVE:

Recommend treatment for a woman with complete androgen insensitivity syndrome

QUESTION 46:

BONE AND MINERAL METABOLISM

A 63-year-old woman presented 5 years ago with a calcium concentration of 11.8 mg/dL (3.0 mmol/L) and a PTH concentration of 259 pg/mL (259 ng/L). A sestamibi imaging study was positive for uptake in the left neck. Parathyroidectomy was performed with an appropriate drop in intraoperative intact PTH levels and normalization of serum calcium to 9.4 mg/dL (2.4 mmol/L). Her calcium level remained normal until 4 months ago, when it was documented to be 10.6 mg/dL (2.7 mmol/L).

She reports no confusion or fatigue, constipation, kidney stones, or history of fractures. She has a history of hypertension and takes amlodipine. Her family history is unremarkable.

Physical examination findings are unremarkable.

Laboratory test results:

Albumin = 4.4 g/dL (44 g/L) (reference range, 3.5-5.0 g/dL [35-50 g/L])
Calcium = 10.7 mg/dL (2.7 mmol/L) (reference range, 8.2-10.2 mg/dL [2.1-2.6 mmol/L])
Creatinine = 0.9 mg/dL (79.6 µmol/L) (reference range, 0.6-1.1 mg/dL [53.0-97.2 µmol/L])
Phosphorus = 1.7 mg/dL (0.5 mmol/L) (reference range, 2.3-4.7 mg/dL [0.7-1.5 mmol/L])
PTH = 95 pg/mL (95 ng/L) (reference range, 10-65 pg/mL [10-65 ng/L])
25-Hydroxyvitamin D = 27 ng/mL (67.4 nmol/L) (reference range [optimal], 25-80 ng/mL [62.4-199.7 nmol/L])
24-Hour urinary measurements:

Volume = 2600 mL/24 h
Creatinine = 0.9 g/24 h (7.9 mmol/d) (reference range, 1.0-2.0 g/24 h [8.8-17.7 mmol/d])
Calcium = 294 mg/24 h (7.4 mmol/d) (reference range, 100-300 mg/24 h [2.5-7.5 mmol/d])

Bone mineral density measurement reveals low bone density (osteopenia) with the lowest T score at the femoral neck of -1.9.

Which of the following should be the next management step?

A. Initiation of bisphosphonate treatment
B. Initiation of cinacalcet treatment
C. Initiation of estrogen treatment
D. Neck exploration
E. Observation with serum calcium monitoring

LEARNING OBJECTIVE:

Use the guidelines for surgery to determine care of patients with asymptomatic primary hyperparathyroidism.

QUESTION 47:

MALE REPRODUCTION

A 62-year-old man with a 10-year history of type 2 diabetes mellitus seeks help for erectile dysfunction. He reports a normal libido. He jogs 2 miles in about 25 minutes 3 times a week and has no chest pain or claudication. Other than the erectile dysfunction, he feels well and has no other concerns. His medical history includes hypertension and dyslipidemia. Current medications are ramipril, 10 mg daily; atorvastatin, 40 mg daily; and metformin, 2000 mg daily.

On physical examination, his blood pressure is 128/72 mm Hg and heart rate is 68 beats/min. His height is 68 in (172.7 cm), and weight is 185 lb (84.1 kg) (BMI = 28.1 kg/m²). He is well virilized. Findings on cardiopulmonary and abdominal examinations are normal. He has 20-mL testes bilaterally.

Laboratory test results:

Total testosterone = 280 ng/dL (9.7 nmol/L) (reference range, 300-900 ng/dL [10.4-31.2 nmol/L])
Fasting lipid panel
  Total cholesterol = 215 mg/dL (5.57 mmol/L) (reference range [optimal], <200 mg/dL [<5.18 mmol/L])
  HDL cholesterol = 35 mg/dL (0.91 nmol/L) (reference range [optimal], >60 mg/dL (>1.55 mmol/L))
**LEARNING OBJECTIVE:**

Determine whether a patient needs formal cardiovascular assessment before starting an oral phosphodiesterase inhibitor for erectile dysfunction.

**QUESTION 48:**

**DIABETES MELLITUS AND OTHER CARBOHYDRATE DISORDERS**

A 70-year-old woman with a 10-year history of type 2 diabetes mellitus presents for her usual follow-up appointment. She has taken glyburide for 7 years, but began to require additional therapy 3 years ago. She did not tolerate metformin and had no response to rosiglitazone; thus, insulin was added to her regimen. Initially, her condition was well controlled with a combination of glyburide and bedtime NPH insulin. Over the past 18 months, glyburide was stopped, and she has required a twice-daily dose of both NPH and regular insulin, given before breakfast and dinner. Over the past 6 months, despite an increased insulin dosage, her hemoglobin A\textsubscript{1c} level has increased to 9.0% (75 mmol/mol) (reference range, 4.0%-5.6% [20-38 mmol/mol]). Nevertheless, while taking this higher insulin dosage, she has developed hypoglycemia both before lunch and during the night.

Which of the following is the best solution to her problem?

A. Move the before-dinner NPH insulin to bedtime; no other change in the insulin regimen

B. Move the before-dinner NPH insulin to bedtime; stop all regular insulin doses

C. Replace the twice-daily regular insulin with a rapid-acting insulin analogue; no change in NPH insulin

D. Replace the twice-daily regular insulin with a rapid-acting insulin analogue; reduce the morning rapid-acting analogue dosage slightly; increase the morning...
NPH insulin dose; move the before-dinner NPH insulin to bedtime

E. Replace the twice-daily NPH insulin with a single daily dose of insulin glargine; stop all regular insulin doses

LEARNING OBJECTIVE:

Improve insulin regimens when there is concomitant high hemoglobin A1c levels and recurrent hypoglycemia.

QUESTION 49:

LIPIDS/OBESITY

A 13-year-old boy is referred to you for evaluation of severe obesity, short stature, mild mental retardation, delayed sexual maturation, and behavioral problems. At birth, he had hypotonia and poor feeding and failed to gain weight normally. Between the ages of 4 and 6 years, he continued to have hypotonia and short stature and began gaining weight rapidly. Between the ages of 6 and 13 years, he had dramatic weight gain due to ravenous hunger. He did poorly in school and was placed in special education. There is no family history of severe obesity. On physical examination, his height is 53 in (134.6 cm) and weight is 280 lb (127.3 kg) (BMI = 70.1 kg/m²). He appears prepubertal on examination. Testes are not palpable.

Although a number of issues must be addressed, replacing or supplementing which of the following hormones is most likely to improve his body composition and overall health?

A. Thyroid hormone
B. Leptin
C. Growth hormone
D. Testosterone
E. Hydrocortisone

LEARNING OBJECTIVE:

To understand the benefits of providing growth hormone supplementation to children with Prader-Willi syndrome

QUESTION 50:

FEMALE REPRODUCTION

A 51-year-old healthy woman presents with recent onset of severe hot flashes and insomnia. She had normal menarche and had regular menses until her late 40s. At age 50 years, an evaluation for irregular menses identified leiomyomata requiring total abdominal hysterectomy and oophorectomy.
The operation was performed 4 months ago. Since her surgery, she has had intractable hot flashes, trouble sleeping, cognitive issues, and urinary frequency.

Her grandmother had breast cancer at age 78 years, her father has hypertension and hyperlipidemia, and her mother has osteoporosis. The patient runs 3 times a week and adheres to a healthful diet and lifestyle. She does not drink alcohol and has no history of angina or claudication.

On physical examination, her height is 66 in (167.6 cm) and weight is 124 lb (56.4 kg) (BMI = 20 kg/m²). Blood pressure is 110/60 mm Hg. The rest of her physical examination findings are normal.

Results of laboratory studies are normal, including a lipid panel:

- Total Cholesterol = 138 mg/dL (3.57 mmol/L) (reference range [optimal], <200 mg/dL [5.18 mmol/L])
- HDL cholesterol = 61 mg/dL (1.58 mmol/L) (reference range [optimal], >60 mg/dL [>1.55 mmol/L])
- LDL cholesterol = 59 mg/dL (1.53 mmol/L) (reference range [optimal], <100 mg/dL [<2.59 mmol/L])
- Triglycerides = 88 mg/dL (0.99 mmol/L) (reference range [optimal], <150 mg/dL [<3.88 mmol/L])

On the basis of this patient's history and physical examination, for which of the following complications would she be at increased risk after initiation of estradiol therapy?

A. Myocardial infarction
B. Breast cancer
C. Stroke
D. Pancreatitis
E. Colon cancer

LEARNING OBJECTIVE:
Discuss the pros and cons of physiologic HT at the menopause

QUESTION 51:
DIABETES MELLITUS AND OTHER CARBOHYDRATE DISORDERS

A 48-year-old, morbidly obese woman with an 8-year history of type 2 diabetes mellitus comes to you seeking a second opinion. She states that her diabetes has never been well controlled; however, she admits that she has never been completely adherent to the diet and exercise plan that her physician prescribed. She has been taking a sulfonylurea and metformin for the past 5 years, and she mentions that her hemoglobin A₁c level has always been close to 8.0% (64 mmol/mol) (reference range, 4.0%-5.6% [20-38 mmol/mol]).

Her medical history is notable for longstanding hypertension and hyperlipidemia. She has had stable renal function for the past 3 years with a serum creatinine level of 1.4 mg/dL (123.8 μmol/L) (reference range, 0.6-1.1 mg/dL [53.0-97.2 μmol/L]) and a creatinine clearance of 75 mL/min (reference range, 90-140 mL/min). Findings from her physical examination are most notable for
obesity (BMI = 40 kg/m²), but she has no obvious physical signs of diabetic retinopathy or neuropathy.

In discussing whether a dipeptidyl-peptidase 4 inhibitor is a potential therapeutic option, which of the following should you tell this patient?

A. She can expect to experience severe nausea and/or vomiting

B. Patients who use these medications lose, on average, 10 lb (4.5 kg), whether or not they experience any gastrointestinal adverse effects

C. She will be able to use these medications even though her renal function is not entirely normal

D. She would be unlikely to experience any significant improvement in glycemic control

E. There is no risk of hypoglycemia if she adds this medication to her present regimen

LEARNING OBJECTIVE:
Prescribe dipeptidyl-peptidase 4 inhibitors in the treatment of type 2 diabetes mellitus.

QUESTION 52:
BONE AND MINERAL METABOLISM

You are asked to see a 73-year-old postmenopausal woman for osteoporosis with previous vertebral compression fractures. Assessment of bone mineral density reveals a T score of -2.6 at the hip. She has a history of diabetes mellitus. Chronic kidney disease has been diagnosed, and she will need hemodialysis in the future. She also has a history of anemia, hyperlipidemia, and hypothyroidism treated with levothyroxine.

Laboratory tests results:

Creatinine = 2.8 mg/dL (247.5 µmol/L) (reference range, 0.6-1.1 mg/dL [53.0-97.2 µmol/L])
(glomerular filtration rate = 20.4 mL/min)
Calcium = 8.6 mg/dL (2.2 mmol/L) (reference range, 8.2-10.2 mg/dL [2.1-2.6 mmol/L])
Albumin = 3.6 g/dL (36 g/L) (reference range, 3.5-5.0 g/dL [35-50 g/L])
Phosphorus = 4.0 mg/dL (1.3 mmol/L) (reference range, 2.3-4.7 mg/dL [0.7-1.5 mmol/L])
Alkaline phosphatase = 172 U/L (2.9 µkat/L) (reference range, 50-120 U/L [0.84-2.00 µkat/L])
PTH = 648 pg/mL (648 ng/L) (reference range, 10-65 pg/mL [10-65 ng/L])
25-Hydroxyvitamin D = 7 ng/mL (17.5 nmol/L) (reference range [optimal], 25-80 ng/mL [62.4-199.7 nmol/L])
1,25-Dihydroxyvitamin D = 7 pg/mL (18.2 pmol/L) (reference range, 16-65 pg/mL [41.6-169.0 pmol/L])
TSH = 1.1 mIU/L (reference range, 0.5-5.0 mIU/L)

Which of the following medications should you prescribe?
A. Alendronate
B. Cinacalcet
C. Calcitriol
D. Raloxifene
E. Ergocalciferol

LEARNING OBJECTIVE:
Plan the treatment of osteoporosis in a patient with chronic kidney disease.

QUESTION 53:

PITUITARY AND NEUROENDOCRINE DISORDERS
A 31-year-old woman with a history of prolactinoma is now in her 37th week of pregnancy. Two years ago, a 14-mm prolactinoma was identified. Her initial prolactin level was 320 ng/mL (13.9 nmol/L) (reference range, 4-30 ng/mL [0.17-1.30 nmol/L]), and there was suprasellar extension on MRI, chiasmal compression, and a small visual field defect. With cabergoline, 0.5 mg twice weekly, her prolactin normalized, her galactorrhea and amenorrhea resolved, her visual field normalized, and her tumor decreased in size to 5 mm. She stopped cabergoline when she learned she was pregnant. She now reports increasing headaches that are quite severe. Goldmann visual field testing is normal.

Which of the following is the best next step in her management?

A. Measure serum prolactin
B. Deliver the baby
C. Proceed with transsphenoidal surgical tumor removal
D. Perform a pituitary-directed MRI
E. Perform a pituitary-directed CT

LEARNING OBJECTIVE:
Manage prolactinoma during pregnancy.

QUESTION 54:

DIABETES MELLITUS AND OTHER CARBOHYDRATE DISORDERS
A 31-year-old woman presents for routine follow-up of type 1 diabetes mellitus of 18 years duration.
She has maintained good control of her glucose with hemoglobin A1c values less than 7.2% (<55 mmol/mol) for the last 10 years. She has mild, nonproliferative retinopathy, but no other chronic complications. For the last 1 to 2 years, she has reported some loss of hypoglycemic recognition and has experienced at least 1 severe hypoglycemic episode requiring assistance after a day of high physical activity.

Medications include insulin glargine, 15 units in the morning, and insulin lispro, 1 unit per 18 g of carbohydrate and 1 unit per 50 mg/dL (2.8 mmol/L) correction with a premeal blood glucose target of 120 mg/dL (6.7 mmol/L).

Her blood pressure is 116/71 mm Hg, and pulse rate is 68 beats/min. Her height is 64 in (162.6 cm), and weight is 126 lb (57.3 kg) (BMI = 21.6 kg/m²). Physical examination findings are normal other than scattered microaneurysms on an undilated funduscopic examination.

Laboratory test results:

- Creatinine = 0.7 mg/dL (61.9 µmol/L) (reference range, 0.6-1.1 mg/dL [53.0-97.2 µmol/L])
- Potassium = 4.1 mEq/L (4.1 mmol/L) (reference range, 3.5-5.0 mEq/L [3.5-5.0 mmol/L])
- Sodium = 138 mEq/L (138 mmol/L) (reference range, 136-142 mEq/L [136-142 mmol/L])
- LDL cholesterol = 73 mg/dL (1.89 mmol/L) (reference range [optimal], <100 mg/dL [<2.59 mmol/L])
- Hemoglobin A1c = 6.6% (49 mmol/mol) (reference range, 4.0%-5.6% [20-38 mmol/mol])
- Albumin to creatinine ratio = 11 µg/mg creatinine

The following are the most recent blood glucose readings from her meter download and are similar to the glucose values that were downloaded from the last month.

<table>
<thead>
<tr>
<th>Day of Week</th>
<th>Breakfast</th>
<th>Lunch</th>
<th>Dinner</th>
<th>Bedtime</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wednesday</td>
<td>60 mg/dL (3.3 mmol/L)</td>
<td>254 mg/dL (14.1 mmol/L)</td>
<td>133 mg/dL (7.4 mmol/L)</td>
<td>102 mg/dL (5.7 mmol/L)</td>
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<tr>
<td>Thursday</td>
<td>317 mg/dL (17.6 mmol/L)</td>
<td>211 mg/dL (11.7 mmol/L)</td>
<td>175 mg/dL (9.7 mmol/L)</td>
<td>121 mg/dL (6.7 mmol/L)</td>
</tr>
<tr>
<td>Friday</td>
<td>276 mg/dL (15.3 mmol/L)</td>
<td>202 mg/dL (11.2 mmol/L)</td>
<td>113 mg/dL (6.3 mmol/L)</td>
<td>95 mg/dL (5.3 mmol/L)</td>
</tr>
<tr>
<td>Saturday</td>
<td>83 mg/dL (4.6 mmol/L)</td>
<td>132 mg/dL (7.3 mmol/L)</td>
<td>87 mg/dL (4.8 mmol/L)</td>
<td>170 mg/dL (9.4 mmol/L)</td>
</tr>
<tr>
<td>Sunday</td>
<td>62 mg/dL (3.4 mmol/L)</td>
<td>262 mg/dL (14.5 mmol/L)</td>
<td>142 mg/dL (7.9 mmol/L)</td>
<td>123 mg/dL (6.8 mmol/L)</td>
</tr>
</tbody>
</table>
Which of the following actions is most appropriate now?

A. Perform a continuous glucose monitoring study

B. Change the carbohydrate counting ratio to 1:12 g carbohydrate at breakfast

C. Increase the insulin glargine dosage to 17 units

D. Recommend no intervention because her blood glucose is well controlled

E. Change the insulin glargine timing from morning to evening without alteration of meal dosing

LEARNING OBJECTIVE:
Describe the utility of continuous glucose monitoring in confirming nocturnal hypoglycemia.

QUESTION 55:
ADRENAL DISORDERS

A 63-year-old man presents with a 3-month history of diarrhea and facial flushing. One year ago, he underwent surgery to remove a rectal mass that was confirmed to be a carcinoid tumor by histopathologic evaluation. Abdominal CT performed immediately after his operation was reportedly normal.

On physical examination, he has facial plethora. His blood pressure is 128/78 mm Hg.

His concentration of urinary 5-hydroxyindoleacetic acid is 125 mg/24 h (654 µmol/d) (reference range, 2-9 mg/24 h [10.5-47.1 µmol/d]). Abdominal MRI (see image) shows multiple hypodense liver lesions (largest measuring 6 cm), enlarged para-aortic lymph nodes, and peritoneal nodules. All findings are consistent with metastatic carcinoid. No octreotide-avid lesion is identified on ¹¹¹In-octreotide scan.

Which of the following is the most appropriate next step in managing this patient's symptoms?
A. Octreotide therapy
B. Liver transplant
C. Sunitinib therapy
D. Radiofrequency ablation of liver metastases
E. Interferon-α therapy

LEARNING OBJECTIVE:
Recommend a trial of somatostatin analogue therapy for symptomatic relief in the setting of metastatic carcinoid syndrome, even if the disease is not octreotide avid.

QUESTION 56:

LIPIDS/OBESITY

You are referred a 48-year-old man with a 12-year history of coronary artery disease and multiple hospitalizations for coronary artery stent placements. The patient's family has a strong history of heart disease: his father and 2 paternal uncles died before age 50 years. The patient takes atorvastatin, 80 mg daily.

Laboratory test results (on his current statin):

- Total cholesterol = 210 mg/dL (5.44 mmol/L) (reference range [optimal], <200 mg/dL [<5.18 mmol/L])
- LDL cholesterol = 150 mg/dL (3.89 mmol/L) (reference range [optimal], <100 mg/dL [<2.59 mmol/L])
- HDL cholesterol = 40 mg/dL (1.04 mmol/L) (reference range [optimal], >60 mg/dL [>1.55 mmol/L])
- Triglycerides = 100 mg/dL (1.13 mmol/L) (reference range [optimal], <150 mg/dL [<3.88 mmol/L])

Which of the following are you most likely to find on physical examination?

A. Lipemia retinalis
B. Achilles xanthomas
C. Eruptive xanthomas
D. Palmar xanthomas
E. Arthropathy

LEARNING OBJECTIVE:
Identify physical findings of hyperlipidemias.
A 42-year-old woman is referred to you for assistance in the management of hypercalcemia. Six months ago, screening laboratory testing revealed a calcium concentration of 11.1 mg/dL (2.78 mmol/L) and a normal creatinine concentration of 0.7 mg/dL (61.9 µmol/L). Six weeks ago, the patient returned for further laboratory tests when she had a positive home pregnancy test:

- Calcium = 10.8 mg/dL (2.7 mmol/L) (reference range, 8.2-10.2 mg/dL [2.1-2.6 mmol/L])
- Albumin = 4.0 g/dL (40 g/L) (reference range, 3.5-5.0 g/dL [35-50 g/L])
- Alkaline phosphatase = 42 U/L (0.70 µkat/L) (reference range, 50-120 U/L [0.84-2.00 µkat/L])
- PTH = 95.7 pg/mL (95.7 ng/L) (reference range, 10-65 pg/mL [10-65 ng/L])
- 25-Hydroxyvitamin D = 28 ng/mL (69.89 nmol/L) (reference range [optimal], 25-80 ng/mL [62.4-199.7 nmol/L])
- 1,25-Dihydroxyvitamin D = 84 pg/mL (218.4 pmol/L) (reference range, 16-65 pg/mL [41.6-169.0 pmol/L])
- Urinary calcium = 281 mg/24 h (7.02 mmol/d) (reference range, 100-300 mg/24 h [2.5-7.5 mmol/d])

She is now 10 weeks pregnant. Physical examination findings are normal, including those from head and neck exam. You learn that her mother had hyperparathyroidism diagnosed at age 60 years. You discuss with the patient her condition and its implications for the current pregnancy. She is reluctant to do anything regarding her hypercalcemia out of concern for the fetus.

The pregnancy progresses normally and the patient's calcium concentration remains between 10.7 mg/dL and 11.3 mg/dL (2.7-2.8 mmol/L). The baby is delivered vaginally at 40 weeks' gestation.

Which of the following represents the most likely immediate postpartum complication for the baby?

A. Hypercalcemia
B. Hypocalcemia
C. Fracture
D. Nephrocalcinosis
E. Renal malformation

LEARNING OBJECTIVE:
Counsel patients on the risk of maternal primary hyperparathyroidism to the developing fetus and newborn and review the physiology of calcium homeostasis in pregnancy.

QUESTION 58:
PITUITARY AND NEUROENDOCRINE DISORDERS
A 42-year-old man is referred to you for further evaluation of possible Cushing syndrome. The patient has been generally healthy, and he fathered 2 children (4 and 8 years ago). However, over the past 2 years, he has gained about 25 lb (11.3 kg), mostly around his abdomen, despite dieting and exercising. He visited his primary care physician last month. The physician noted that he had new-onset hypertension and was concerned about his physical changes. He sent off laboratory tests and ordered a pituitary MRI; when these results returned, he referred the patient to you.

On physical examination, the patient's blood pressure is 140/92 mm Hg. He has a small dorsocervical fat pad, acne, a ruddy complexion, a protuberant abdomen, and proximal muscle weakness in his lower extremities.

Laboratory test results:

- Plasma ACTH = 86 pg/mL (18.9 pmol/L) (reference range, 10-60 pg/mL [2.2-13.2 pmol/L])
- Serum cortisol (8 AM) = 18 µg/dL (496.6 nmol/L) (reference range, 5-25 µg/dL [137.9-689.7 nmol/L])
- Serum cortisol (8 AM) after 8 mg of dexamethasone the night before = 10 µg/dL (reference range, >50% reduction in cortisol)
- Urinary free cortisol = 360 µg/24 h (993.6 nmol/d) (reference range, 4-50 µg/24 h [11-138 nmol/d])
- Potassium = 2.8 mEq/L (2.8 mmol/L) (reference range, 3.5-5.0 mEq/L [3.5-5.0 mmol/L])

MRI of the pituitary demonstrates a 4-mm lesion on the right side of the pituitary that is hypoenhancing after gadolinium contrast administration.

Which of the following should be performed next?

A. Bilateral adrenal venous sampling
B. Inferior petrosal sinus sampling
C. Corticotropin-releasing hormone stimulation test after dexamethasone suppression
D. Midnight salivary free cortisol measurements
E. No further testing is needed; proceed to transsphenoidal resection of the pituitary lesion

LEARNING OBJECTIVE:
Select the appropriate tests for the differential diagnosis of Cushing syndrome.

QUESTION 59:
DIABETES MELLITUS AND OTHER CARBOHYDRATE DISORDERS

You are asked to see a 19-year-old college student with newly recognized diabetes mellitus that was identified through the use of a home glucose meter belonging to her father who has type 1 diabetes mellitus.

On physical examination, her height is 65 in (165.1 cm) and weight is 158 lb (71.8 kg) (BMI = 26.3 kg/m²). Her blood pressure is 106/67 mm Hg, and pulse rate is 62 beats/min. All findings from your
examination are normal, and, specifically, there are no skin or thyroid abnormalities.

Islet-cell antibodies, insulin autoantibodies, and glutamic acid decarboxylase antibodies are absent.

**Which of the following tests, if available to you, could be useful in confirming type 1 diabetes in this patient?**

A. Zinc transporter (ZnT8) antibody testing

B. Genetic testing for maturity onset diabetes of the young (DNA sequencing of $HNF4A$ and $HNF1A$)

C. HLA genotyping

D. Transcription factor 7-like 2 ($TCF7L2$) genetic testing

E. Intravenous glucose tolerance testing

**LEARNING OBJECTIVE:**

Incorporate autoantibody testing in the diagnosis of type 1 diabetes mellitus.

---

**QUESTION 60:**

**BONE AND MINERAL METABOLISM**

You are asked to evaluate a 57-year-old woman after she sustained 2 vertebral compression fractures. Two months ago, she was stepping off a curb and fell. She experienced immediate, sharp pain in her mid and lower back. Radiographs revealed T11 and L3 compression fractures. She was treated with bed rest and analgesics without improvement. She underwent vertebroplasty 3 weeks after the initial event and her pain improved immediately.

Menopause occurred at age 52 years. She does not smoke cigarettes and has never been on glucocorticoid therapy. Her mother sustained a hip fracture at age 84 years. The patient takes 500 mg of elemental calcium and 1000 IU of vitamin D$_3$ daily. There is no history of nephrolithiasis.

Physical examination findings are normal, aside from modest discomfort with palpation over the 2 involved vertebral bodies. There is no evidence of thyroid disease or hypercortisolism. Results from a thorough laboratory investigation for causes of bone loss (including a chemistry panel, serum and urine protein electrophoresis, thyroid function tests, and vitamin D levels) are normal.

You order a DXA scan with vertebral morphometric analysis, and the results are shown:
Spine morphometry.

On the basis of these findings, you discuss the importance of treating her osteoporosis and
commence therapy with alendronate, 70 mg weekly.

Which of the following adverse events is most likely within the coming year?

A. Additional vertebral fracture
B. Femoral neck fracture
C. Subtrochanteric femoral fracture
D. Osteonecrosis of the jaw
E. Nephrolithiasis

LEARNING OBJECTIVE:
Assess risk of future adverse events in a patient after fragility fracture and subsequent treatment

QUESTION 61:

LIPIDS/OBESITY

A 28-year-old man presents to the emergency department with crushing chest pain and is found to have a myocardial infarction. He does not smoke cigarettes, and until this event he was healthy and taking no medications. He is adopted, so no family history is available.

On physical examination, he appears well. His height is 72 in (182.9 cm), and weight is 210 lb (95.5 kg) (BMI = 28.5 kg/m²). After a careful physical examination, the only abnormalities you identify are thickening of his Achilles tendons bilaterally and xanthelasmas.

Fasting laboratory test results:

- Total cholesterol = 405 mg/dL (10.49 mmol/L) (reference range [optimal], <200 mg/dL [<5.18 mmol/L])
- HDL cholesterol = 52 mg/dL (1.35 mmol/L) (reference range [optimal], >60 mg/dL [>1.55 mmol/L])
- LDL cholesterol = 336 mg/dL (8.70 mmol/L) (reference range [optimal], <100 mg/dL [<2.59 mmol/L])
- Triglycerides = 85 mg/dL (0.96 mmol/L) (reference range [optimal], <150 mg/dL [<3.88 mmol/L])

A mutation in the gene encoding which of the following is the most likely cause of his dyslipidemia?

A. LDL receptor
B. Lipoprotein lipase
C. Apolipoprotein E
D. Apolipoprotein CII
E. Lipoprotein (a)

LEARNING OBJECTIVE:
Differentiate among the genetic syndromes that cause elevated LDL cholesterol

QUESTION 62:

DIABETES MELLITUS AND OTHER CARBOHYDRATE DISORDERS

An 18-year-old man presents to the endocrinology clinic with symptoms of polyuria and polydipsia, as well as home glucose monitoring results documenting hyperglycemia. Eight years ago, his mother started monitoring his blood glucose levels using an over-the-counter blood glucose monitor. For the last several years, fasting blood glucose values were above 100 mg/dL (>5.6 mmol/L), and postprandial blood glucose values were below 140 mg/dL (<7.8 mmol/L). Screening for type 1 diabetes mellitus (C-peptide and islet-cell antibodies) was negative when performed at an initial visit at age 10 years. Results from initial glucose tolerance testing were also normal. Subsequently, the patient developed mild hyperglycemia that was treated with very low-dosage basal insulin. He has continued this treatment and now presents for his appointment wanting to know whether to continue the insulin and what to expect regarding his long-term glycemic control.

In asking about his family history, you learn that his maternal aunt, 2 maternal uncles, and maternal grandmother have type 2 diabetes.

On physical examination, his height is 69.5 in (176.5 cm) and weight is 110 lb (50 kg) (BMI = 16 kg/m²). His pulse rate is 76 beats/min, and blood pressure is 106/74 mm Hg. His thyroid gland is normal without nodularity, and his skin does not have hyperpigmentation or acanthosis nigricans. He has no symptoms of peripheral neuropathy, vision changes, or other diabetes-associated complications. The rest of the examination findings are normal.

Which of the following assessments would best categorize his type of diabetes?

A. Test for islet-cell antibodies and insulin autoantibodies

B. Order genetic testing for mutations in the glucokinase gene (GCK)

C. Perform a 75-g oral glucose tolerance test

D. Measure glutamic acid decarboxylase antibodies

E. Measure zinc transporter (ZnT8) autoantibodies

LEARNING OBJECTIVE:
Suspect maturity-onset diabetes of the young in a patient with an atypical clinical course.

QUESTION 63:
MALE REPRODUCTION

A 72-year-old man in whom secondary hypogonadism was recently diagnosed presents to the endocrine clinic for initiation of testosterone therapy. His medical history includes hypertension, mild benign prostatic hypertrophy, and coronary artery disease (for which he underwent angioplasty 7 years ago). He has no symptoms from his medical conditions, with no complaints of hesitancy, change in urinary stream, angina, or claudication. His hypertension is controlled with hydrochlorothiazide, 50 mg daily.

On physical examination, his height is 70 in (177.8 cm) and weight is 190 lb (86.4 kg) (BMI = 27.3 kg/m²). Blood pressure is 130/82 mm Hg. Findings on cardiovascular and pulmonary examinations are normal. He has a mildly enlarged prostate without any nodules.

Laboratory test results:

- Total testosterone = 189 ng/dL (6.6 nmol/L) (reference range, 300-900 ng/dL [10.4-31.2 nmol/L])
- Prostate-specific antigen = 2.1 ng/mL (2.1 µg/L) (reference range, <6.5 ng/mL [<6.5 µg/L])
- Complete blood cell count, normal

Which of the following adverse effects is this patient most likely to experience if testosterone replacement therapy is initiated?

A. Acute urinary retention
B. Prostate-specific antigen elevation above 4 ng/mL (>4 µg/L)
C. Myocardial infarction
D. Erythrocytosis
E. Stroke

LEARNING OBJECTIVE:

Anticipate the most likely adverse effect of testosterone therapy in older men.

QUESTION 64:

ADRENAL DISORDERS

You are called from the emergency department for advice about a 28-year-old man with a right-sided, firm testicular lump and abnormal abdominal CT findings (see image). The patient is intoxicated, and he has been having abdominal pain and vomiting. The patient says he has adrenal insufficiency and has a wallet card confirming this. The patient's abdominal CT scan reveals bilateral 16-cm heterogeneous adrenal masses (~ 20 Hounsfield units).
After you recommend intravenous hydrocortisone, you explain to the emergency department physician that this man most likely has which of the following?

A. Adrenomyeloneuropathy

B. Congenital adrenal hyperplasia

C. Autoimmune polyglandular syndrome type 2

D. Bilateral adrenal hemorrhage

E. Metastatic testicular carcinoma

**LEARNING OBJECTIVE:**

To appreciate that adrenal enlargement—particularly adrenal myelolipoma—may complicate the course of patients with poorly controlled congenital adrenal hyperplasia

**QUESTION 65:**

**LIPIDS/OBESITY**

You are asked to see a 32-year-old woman in her 29th week of pregnancy regarding a lipemic blood sample. She presented the day before with vaginal bleeding and uterine contractions and was admitted for observation, but these problems have now abated.

She has been in general good health and takes no medications. Her pregnancy has been unremarkable except for weight gain greater than recommended (33 lb [15 kg]). The patient has no history of hyperlipidemia, hypertension, or diabetes (including during a previous pregnancy when she had a formal evaluation for gestational diabetes). She reports a healthy childhood with no abnormalities of growth and development. She has no history of recurrent gastrointestinal symptoms, abdominal pain, or pancreatitis. She is unsure whether there is a history of hyperlipidemia in her family members.

On physical examination, her height is 66 in (167.6 cm) and weight is 200 lb (90.9 kg) (BMI = 32.3
kg/m²). Blood pressure is 96/57 mm Hg. She has several clusters of eruptive xanthomata across her back and on the dorsal aspects of her arms. Her abdomen is gravid but not tender.

Laboratory test results (sample drawn while fasting):

Total cholesterol = 324 mg/dL (8.39 mmol/L) (reference range [optimal], <200 mg/dL [<5.18 mmol/L])
Triglycerides = 2677 mg/dL (30.25 mmol/L) (reference range [optimal], <150 mg/dL [<3.88 mmol/L])
HDL cholesterol = 42 mg/dL (1.09 mmol/L) (reference range [optimal], >60 mg/dL [>1.55 mmol/L])
Glucose = 76 mg/dL (4.2 mmol/L) (reference range, 70-99 mg/dL [3.9-5.5 mmol/L])
TSH = 1.2 mIU/L (reference range, 0.5-5.0 mIU/L)

Her blood glucose concentration 60 minutes after a 50-g oral glucose drink was 121 mg/dL (6.7 mmol/L) at 27 weeks' gestation.

Which of the following is the best next step in management?

A. Prescribe gemfibrozil
B. **Recommend a fat-restricted diet**
C. Provide total parenteral nutrition with minimum fat
D. Prescribe simvastatin
E. Perform plasma apheresis

**LEARNING OBJECTIVE:**
Select the appropriate strategy to manage severe hypertriglyceridemia during pregnancy.

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**QUESTION 66:**

**DIABETES MELLITUS AND OTHER CARBOHYDRATE DISORDERS**

A 32-year-old woman with type 1 diabetes is in her second trimester of pregnancy and presents to the ophthalmologist for a dilated eye examination. She has no known history of diabetic retinopathy or any other diabetes-associated complications. The upper image shows a picture of her dilated fundus from an examination several years ago, and the lower image shows a picture from her current examination.

**Upper image**
The images shown depict which of the following:

<table>
<thead>
<tr>
<th>Answer</th>
<th>Upper Image</th>
<th>Lower Image</th>
</tr>
</thead>
<tbody>
<tr>
<td>A.</td>
<td>Normal retina</td>
<td>Microaneurysms</td>
</tr>
<tr>
<td>B.</td>
<td>Normal retina</td>
<td>Nonproliferative diabetic retinopathy with retinal hemorrhages and hard exudates</td>
</tr>
<tr>
<td>C.</td>
<td>Nonproliferative diabetic retinopathy</td>
<td>Proliferative diabetic retinopathy</td>
</tr>
</tbody>
</table>
**Learning Objective:**
Characterize diabetic retinopathy and explain the effects of pregnancy on retinopathy progression

**Question 67:**

**Lipids/Obesity**

A 48-year-old woman with cardiovascular disease and a 10-year history of type 2 diabetes mellitus is referred by her internist for more intensive lipid-lowering therapy. While on her current regimen of atorvastatin, 80 mg daily, she has recently required a stent for a new right coronary artery occlusion. On metformin and once-daily, long-acting insulin, her hemoglobin A$_1c$ level is less than 7.0% (<53 mmol/mol) (reference range, 4.0%-5.6% [20-38 mmol/mol]). During the past 3 years, the patient has gained 30 lb (13.6 kg).

Laboratory test results:

- Total cholesterol = 160 mg/dL (4.14 mmol/L) (reference range [optimal], <200 mg/dL [<5.18 mmol/L])
- Triglycerides = 300 mg/dL (3.39 mmol/L) (reference range [optimal], <150 mg/dL [<3.88 mmol/L])
- HDL cholesterol = 35 mg/dL (0.91 mmol/L) (reference range [optimal], >60 mg/dL [>1.55 mmol/L])
- LDL cholesterol = 65 mg/dL (1.68 mmol/L) (reference range [optimal], <100 mg/dL [<2.59 mmol/L])
- Non-HDL cholesterol = 125 mg/dL (3.24 mmol/L) (reference range [optimal], <130 mg/dL [<3.37 mmol/L])

In addition to encouraging exercise and weight loss, you recommend fenofibrate as an approach to reduce her non-HDL cholesterol.

*Which of the following might be an additional benefit of fenofibrate treatment in this patient with type 2 diabetes?*

A. Decreased hemoglobin A$_1c$ level
B. Decreased proteinuria
C. Decreased blood pressure
D. Decreased retinopathy
E. Increased insulin sensitivity

LEARNING OBJECTIVE:
Use combined lipid-lowering therapies in patients with cardiovascular disease.

QUESTION 68:
DIABETES MELLITUS AND OTHER CARBOHYDRATE DISORDERS

A 48-year-old woman with type 2 diabetes mellitus presents for a follow-up visit. Her glycemic control has recently worsened and a change in therapy is needed. Her diabetes is currently treated with glimepiride, 8 mg daily, in conjunction with metformin, 1000 mg twice daily. A review of her blood glucose values reveals the following profile:

- Fasting blood glucose = 140-170 mg/dL (7.8-9.4 mmol/L) (reference range, 70-99 mg/dL [3.9-5.5 mmol/L])
- 2-Hour postmeal blood glucose = 180-220 mg/dL (10.0-12.2 mmol/L)

She has no symptomatic or documented hypoglycemia. She expresses concern over the weight gain that she has experienced while on sulfonylurea therapy and does not want to consider therapies that might exacerbate this further. She has not been adherent to recommended lifestyle modifications.

On physical examination, she is an obese woman without any cushingoid features. Her height is 65.5 in (166.4 cm), and weight is 190 lb (86.4 kg) (BMI = 31.1 kg/m²).

Laboratory test results:
- Hemoglobin A₁C = 7.6% (60 mmol/mol) (reference range, 4.0%-5.6% [20-38 mmol/mol])
- Sodium = 138 mEq/L (138 mmol/L) (reference range, 136-142 mEq/L [136-142 mmol/L])
- Potassium = 4.5 mEq/L (4.5 mmol/L) (reference range, 3.5-5.0 mEq/L [3.5-5.0 mmol/L])
- Creatinine = 0.8 mg/dL (70.7 μmol/L) (reference range, 0.6-1.1 mg/dL [53.0-97.2 μmol/L])
- Urinary albumin excretion = 10 mg/24 h (reference range, <25 mg/24 h)

In addition to optimizing diet and exercise therapy, and keeping in mind the patient’s concerns, which of the following would be the best therapeutic addition?

A. Basal insulin at bedtime
B. A thiazolidinedione
C. Rapid-acting insulin at mealtime
D. A sodium-glucose cotransporter 2 inhibitor
E. An amylin analogue
LEARNING OBJECTIVE:
Appropriately recommend sodium-glucose cotransporter 2 inhibitor therapy in a patient with type 2 diabetes mellitus

QUESTION 69:
THYROID DISORDERS

A 55-year-old man presented 3 months ago with a solitary 3-cm nodule in the left thyroid lobe. Findings from an aspiration biopsy show typical features of papillary thyroid cancer including nuclear inclusions. Near-total thyroidectomy is performed. A 3.5-cm papillary thyroid cancer is found, and 2 of 5 left paratracheal lymph nodes are positive for metastases. No gross or capsular invasion is noted. Some areas of the malignancy have a solid architecture, but there is no evidence of vascular invasion.

Postoperatively, he received 125 mCi of radioactive iodine with recombinant human TSH support to treat residual uptake in the thyroid bed. No distant metastases are present in the posttherapy scan. He is prescribed suppressive thyroid hormone therapy with subsequent suppression of his serum TSH concentration to 0.08 mIU/L (reference range, 0.5-5.0 mIU/L).

Six months later, his serum TSH concentration is 0.38 mIU/L and his thyroglobulin concentration is 28 ng/mL (28 µg/L) with undetectable thyroglobulin antibodies.

Which of the following steps would be most helpful now?

A. Perform MRI of the cervical area
B. Perform neck ultrasonography
C. Refer him back to the surgeon to perform a right paratracheal dissection
D. Increase the dosage of thyroid hormone therapy to titrate to a TSH concentration less than 0.1 mIU/L and recheck serum TSH and thyroglobulin in 6 weeks
E. Perform a recombinant human TSH-stimulated radioiodine whole-body scan

LEARNING OBJECTIVE:
Determine the best management for a patient with a history of thyroid cancer when an increasing thyroglobulin level is observed.

QUESTION 70:
FEMALE REPRODUCTION

A 37-year-old new mother comes to see you for alactogenesis 7 days postpartum. Two and a half years ago, she had a pregnancy that was complicated by preeclampsia and labor was subsequently
induced. The vaginal delivery was complicated by a 1300-cc hemorrhage. She did not try to breastfeed the baby because of her medical complications. She required fertility treatment with gonadotropins to become pregnant the second time. After her current delivery, she noted colostrum, but no milk has come in.

On physical examination, her blood pressure is 110/60 mm Hg. Her height is 66 in (167.6 cm), and weight is 242 lb (110 kg) (BMI = 39.1 kg/m²). Her breast examination is remarkable for lack of venous engorgement and soft breast texture without palpable glandular tissue.

Laboratory test results:

- **Prolactin** = 9 ng/mL (1.3 nmol/L) (reference range [nonlactating women], 4-30 ng/mL [0.17-1.30 nmol/L]; [lactating women], 10-200 ng/mL [0.43-8.70 nmol/L])
- **TSH** = 0.55 mIU/L (reference range, 0.5-5.0 mIU/L)
- **Free T₄** = 0.7 ng/dL (9.01 pmol/L) (reference range, 0.8-1.8 ng/dL [10.30-23.17 pmol/L])
- **Cortisol (8 AM)** = 23.1 μg/dL (637.3 nmol/L) (reference range, 5-25 μg/dL [137.9-689.7 nmol/L])

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

A. Primary hypothyroidism  
B. Secondary hypothyroidism  
C. Cushing syndrome  
D. Lymphocytic hypophysitis  
E. Sheehan syndrome

**LEARNING OBJECTIVE:**

Diagnose the cause of postpartum alactogenesis

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**QUESTION 71:**

**PITUITARY AND NEUROENDOCRINE DISORDERS**

A colleague refers a 28-year-old woman to your clinic for evaluation. A pituitary adenoma was incidentally discovered on cranial MRI performed to investigate headache. She reports no change in appearance or weight. She has a regular menstrual cycle; her last menstrual period was 1 month ago, and a pregnancy test obtained yesterday is negative. She is currently sexually active, and she and her husband would like to conceive as soon as possible.

On physical examination, she has no hirsutism, acne, and or obvious features of GH or cortisol excess. Her height is 62 in (157.5 cm), and weight is 123 lb (56 kg) (BMI = 22.5 kg/m²). Her blood pressure is 118/69 mm Hg.

Laboratory test results:
TSH = 1.8 mIU/L (reference range, 0.5-5.0 mIU/L)
Free T<sub>4</sub> = 1.1 ng/dL (14.2 pmol/L) (reference range, 0.8-1.8 ng/dL [10.30-23.17 pmol/L])
Cortisol (8 AM) = 18 μg/dL (496.6 nmol/L) (reference range, 5.0-25.0 μg/dL [137.9-689.7 nmol/L])
IGF-1 = 168 ng/mL (22.0 nmol/L) (reference range, 117-321 ng/mL [15.3-42.1 nmol/L])
Prolactin = 28 ng/mL (1.2 nmol/L) (reference range, 4-30 ng/mL [0.17-1.30 nmol/L])

MRI shows a 9-mm, low-attenuation lesion in the center and right side of the pituitary gland (see images, coronal image on the left and sagittal image on the right). It elevates the pituitary gland overlying it, abutting and minimally compressing the left side of the optic chiasm and deviating the pituitary stalk to the left. Findings on visual field assessment are normal.

**Which of the following is the best management option?**

A. Refer for pituitary surgery

B. Initiate cabergoline therapy

C. Initiate octreotide therapy

D. Initiate metformin therapy

E. Perform ovarian ultrasonography

**LEARNING OBJECTIVE:**

Devise an appropriate follow-up plan of an incidentally discovered pituitary microadenoma and explain the impact of pregnancy on pituitary volume
QUESTION 72:

DIABETES MELLITUS AND OTHER CARBOHYDRATE DISORDERS

You are asked to assist in the management of a hospitalized 67-year-old man who is recovering from a myocardial infarction. The patient's medical history is notable for obesity, obstructive sleep apnea, hypertension, and prediabetes. Cardiac catheterization performed subsequent to his admission has revealed multivessel coronary artery disease. The patient's medical team has recommended that he begin statin therapy to reduce his risk of future cardiovascular events; however, the patient is aware that statin therapy may increase his risk of progression to diabetes and he therefore wishes to discuss this treatment further.

Laboratory test results:

- Hemoglobin A1c = 5.9% (41 mmol/mol) (reference range, 4.0%-5.6% [20-38 mmol/mol])
- Creatinine = 0.8 mg/dL (70.7 µmol/L) (reference range, 0.7-1.3 mg/dL [61.9-114.9 µmol/L])
- Total cholesterol = 176 mg/dL (4.56 mmol/L) (reference range [optimal], <200 mg/dL [<5.18 mmol/L])
- LDL cholesterol = 101 mg/dL (2.62 mmol/L) (reference range [optimal], <100 mg/dL [<2.59 mmol/L])
- HDL cholesterol = 41 mg/dL (1.06 mmol/L) (reference range [optimal], >60 mg/dL (>1.55 mmol/L))
- Triglycerides = 172 mg/dL (1.94 mmol/L) (reference range [optimal], <150 mg/dL [<3.88 mmol/L])

Liver function tests, within normal limits

In addition to intensive lifestyle modification, which of the following should you recommend to this patient now?

A. Low-intensity statin therapy

B. High-intensity statin therapy

C. High-intensity statin therapy plus metformin

D. Low-intensity statin therapy plus fenofibrate

E. Fenofibrate monotherapy

LEARNING OBJECTIVE:
Counsel a patient with prediabetes and coronary disease on the risks and benefits of statin therapy

QUESTION 73:

MALE REPRODUCTION

A 27-year-old man comes to the endocrine clinic for evaluation of infertility. The patient and his wife have been trying for pregnancy for the past 2 years without success. His wife has normal menstrual cycles and findings from a thorough gynecologic evaluation are normal. The couple has been timing sexual intercourse around her ovulation. He is now referred to you for evaluation of possible male-factor infertility.
The patient underwent puberty at age 13 years and started shaving at the same time as his peers. He recalls some increase in testicular size at puberty along with development of bilateral gynecomastia, which has remained stable. His sense of smell is normal. He reports normal libido and erectile function. He takes no medications.

On physical examination, he is a well-developed man without eunuchoid habitus. His blood pressure is 120/72 mm Hg. His height is 69 in (175.3 cm), and weight is 180 lb (81.8 kg) (BMI = 26.6 kg/m²). He has normal axillary and chest hair. There is bilateral, nontender gynecomastia, 6 x 4 cm on the right side and 5 x 5 cm on the left side. There is no galactorrhea, nipple retraction, or skin discoloration. His phallus and scrotum are normal. His testes are firm and 4 mL bilaterally. His muscle bulk is slightly reduced, but tone and power are normal.

Laboratory test results:

Morning total testosterone (by tandem mass spectrometry) = 349 ng/dL (12.1 nmol/L) (reference range, 300-900 ng/dL [10.4-31.2 nmol/L])
TSH = 2.1 mIU/L (reference range, 0.5-5.0 mIU/L)

Azoospermia is documented on semen analysis (2 specimens, each taken after 3 days of abstinence).

Which of the following should be the next diagnostic step in this patient's evaluation?

- A. Measurement of dihydrotestosterone
- B. Testicular ultrasonography
- C. Measurement of gonadotropins
- D. Testicular biopsy
- E. Mammography

LEARNING OBJECTIVE:
Describe the clinical presentation of a man with mosaic Klinefelter syndrome and recommend appropriate diagnostic tests.

QUESTION 74:

THYROID DISORDERS

A 37-year-old man is referred to you for treatment of hyperthyroidism. He was in good health until 2 years ago when he developed typical hyperthyroid symptoms and Graves disease was diagnosed. He was seen by an endocrinologist who treated him with radioactive iodine (¹³¹I). Records of the radioactive iodine uptake, scan, and estimate of thyroid size are not available.

Soon after the ¹³¹I treatment, the patient moved to your city and did not visit a physician until today's appointment. He is taking no medications.
Laboratory test results:

Serum free $T_4 = 1.6$ ng/dL (20.6 pmol/L) (reference range, 0.8-1.8 ng/dL [10.30-23.17 pmol/L])
Serum total $T_3 = 134$ ng/dL (2.1 nmol/L) (reference range, 70-200 ng/dL [1.08-3.08 nmol/L])
Serum TSH = 0.28 mIU/L (reference range, 0.5-5.0 mIU/L)

His history is unremarkable, except for smoking 1 and a half packs of cigarettes daily for 15 years. He acknowledges that his eyes are large but reports they have been stable in appearance for the past 2 years.

On eye examination, he has globe protrusion, upper-lid edema, and injection of the conjunctivae, primarily on the right side. Hertel measurements are 24 mm on the right and 21 mm on the left (baseline 104 mm). Extraocular muscle movements are intact, and both visual acuity and color vision are normal. His thyroid gland is minimally enlarged, firm, and without nodules. The rest of the examination findings are normal and reveal no evidence of hyperthyroidism.

In addition to referring him to a smoking cessation program, which of the following actions would you now recommend?

A. Administer another dose of $^{131}I$
B. Prescribe atenolol, 50 mg daily
C. Prescribe methimazole, 20 mg daily
D. Measure serum thyroid-stimulating immunoglobulin
E. Follow-up with serum TSH measurements at 6-month intervals

LEARNING OBJECTIVE:
Describe the course of thyroid function in patients with Graves disease treated with $^{131}I$.

QUESTION 75:

DIABETES MELLITUS AND OTHER CARBOHYDRATE DISORDERS

A 62-year-old African American man with a 10-year history of type 2 diabetes mellitus complicated by microalbuminuria and nonproliferative retinopathy returns for a follow-up appointment. He is currently on metformin and an insulin regimen that includes insulin glargine, 50 units daily, and insulin aspart, 12 units with each of his 3 daily meals. Family history is pertinent for type 2 diabetes mellitus in both parents and sickle cell trait in several family members.

At his last appointment, his hemoglobin $A_{1c}$ value was 9.6% (81 mmol/mol) (reference range, 4.0%-5.6% [20-38 mmol/mol]). However, his insulin doses were not increased at that visit because he had reported fairly frequent episodes of hypoglycemia. He describes excellent adherence to his prescribed regimen. Most of his fasting and premeal blood glucose values are between 90 and 150 mg/dL (5.0-8.3 mmol/L) (reference range, 70-99 mg/dL [3.9-5.5 mmol/L]); however, he has frequent hypoglycemia occurring 1 to 2 hours after breakfast, before his evening meal, and during the
overnight hours, sometimes followed by hyperglycemia.

Laboratory test results:

- Hemoglobin A1c = 9.1% (76 mmol/mol) (reference range, 4.0%-5.6% [20-38 mmol/mol])
- Fructosamine = 299 µmol/L (reference range, 190-270 µmol/L)
- Creatinine = 1.2 mg/dL (106.1 µmol/L) (reference range, 0.7-1.3 mg/dL [61.9-114.9 µmol/L])
- Estimated glomerular filtration rate = 78.6 mL/min per 1.73 m² (reference range, >60 mL/min per 1.73 m²)
- TSH = 2.2 mIU/L (reference range, 0.5-5.0 mIU/L)
- Serum electrolytes and liver function tests, within normal limits

Which of the following should you recommend now?

A. Measurement of fingerstick blood glucose values 2 hours after all meals
B. Measurement of fingerstick blood glucose values at 2:00 to 3:00 AM several nights per week
C. Diagnostic 72-hour glucose sensor placement
D. Repeated hemoglobin A1c testing using a boronate affinity chromatography method
E. Cosyntropin stimulation test

LEARNING OBJECTIVE:
Identify clinical conditions that may affect the reliability of hemoglobin A1c assays

QUESTION 76:

THYROID DISORDERS

You are consulted to help manage the thyroid hormone therapy of a 71-year-old man with hypothyroidism. His serum TSH concentration has become progressively elevated during hospitalization after a cerebrovascular accident. The patient has a preexisting diagnosis of hypothyroidism and had been taking levothyroxine, 88 mcg daily as an outpatient, which resulted in serum TSH concentrations of 3.2 and 4.1 mIU/L at his last 2 outpatient visits. The patient has not yet been allowed to resume oral medication or feeding because of his impaired mental status and persistent swallowing difficulties after his stroke.

Currently, he is receiving continuous tube feedings, and medications are being delivered via the nasogastric tube.

Other than altered mental status, his physical examination findings are unremarkable. His thyroid gland is normal to palpation. You review the laboratory data from his hospital stay, which include the following thyroid function tests and levothyroxine dosages.
Timing After Admission

<table>
<thead>
<tr>
<th>Measurement</th>
<th>1 Week</th>
<th>2 Weeks</th>
<th>3 Weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH</td>
<td>15.7 mIU/L</td>
<td>23.0 mIU/L</td>
<td>35.0 mIU/L</td>
</tr>
<tr>
<td>Free T&lt;sub&gt;4&lt;/sub&gt;</td>
<td>....</td>
<td>0.6 ng/dL (7.7 pmol/L)</td>
<td>0.5 ng/dL (6.4 pmol/L)</td>
</tr>
<tr>
<td>Total T&lt;sub&gt;3&lt;/sub&gt;</td>
<td>....</td>
<td>....</td>
<td>60 ng/dL (0.9 nmol/L)</td>
</tr>
<tr>
<td>Levothyroxine dosage</td>
<td>88 mcg daily</td>
<td>100 mcg daily</td>
<td>112 mcg daily</td>
</tr>
</tbody>
</table>

Reference ranges: TSH, 0.5-5.0 mIU/L; free T<sub>4</sub>, 0.8-1.8 ng/dL (10.30-23.17 pmol/L); total T<sub>3</sub>, 70-200 ng/dL (1.08-3.08 nmol/L).

Which of the following initial recommendations will you make to the team caring for the patient?

A. Switch his thyroid hormone replacement to liothyronine, 25 mcg orally twice daily

B. Add liothyronine, 5 mcg orally twice daily

C. Increase his oral levothyroxine dosage to 250 mcg daily

D. Switch his regimen to levothyroxine, 75 mcg daily given intravenously

E. Administer intravenous liothyronine, 5 mcg twice daily

**LEARNING OBJECTIVE:**

Manage levothyroxine therapy in a hospitalized patient receiving enteral feeding

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**QUESTION 77:**

**ADRENAL DISORDERS**

You have been asked to see a 17-year-old woman for newly recognized hypertension and hypokalemia. Because of primary amenorrhea, her primary care physician obtained a karyotype. The findings are 46,XX. She is of Dutch Mennonite heritage. Physical examination reveals a blood pressure of 152/98 mm Hg. There are no flank or epigastric bruits. There are no features of Cushing syndrome. However, she lacks development of secondary sexual characteristics, and secondary sex hair is minimal.

Laboratory test results:
Sodium = 146 mEq/L (146 mmol/L) (reference range, 136-142 mEq/L [136-142 mmol/L])
Potassium = 3.1 mEq/L (3.1 mmol/L) (reference range, 3.5-5.0 mEq/L [3.5-5.0 mmol/L])
DHEA-S = 14 µg/dL (0.38 µmol/L) (reference range, 44-332 µg/dL [1.19-9.00 µmol/L])
Plasma aldosterone concentration, undetectable
Plasma renin activity, undetectable

Which of the following is most likely responsible for this presentation?

A. 11β-Hydroxylase (CYP11B1) deficiency
B. Deoxycorticosterone-producing tumor
C. Primary cortisol resistance
D. 11β-Hydroxysteroid dehydrogenase type 2 deficiency
E. 17α-Hydroxylase (CYP17A1) deficiency

LEARNING OBJECTIVE:
Identify causes of hypertension and hypokalemia not associated with aldosterone excess.

QUESTION 78:
LIPIDS/OBESITY

A 57-year-old man presents to discuss lipid-lowering therapy. He has never had cardiovascular disease, does not smoke cigarettes, and does not have a family history of premature cardiovascular disease. He has hypertension controlled on only one medication.

On physical examination, his height is 66 in (167.6 cm) and weight is 150 lb (68.2 kg) (BMI = 24.2 kg/m²). His blood pressure is 122/76 mm Hg, and heart rate is 72 beats/min. Examination findings are normal.

Fasting laboratory test results:

Total cholesterol = 166 mg/dL (4.30 mmol/L) (reference range [optimal], <200 mg/dL [<5.18 mmol/L])
HDL cholesterol = 37 mg/dL (0.96 mmol/L) (reference range [optimal], >60 mg/dL [>1.55 mmol/L])
LDL cholesterol = 102 mg/dL (2.64 mmol/L) (reference range [optimal], <100 mg/dL [<2.59 mmol/L])
Triglycerides = 138 mg/dL (1.56 mmol/L) (reference range [optimal], <150 mg/dL [<3.88 mmol/L])

You enter his values into the American College of Cardiology/American Heart Association atherosclerotic cardiovascular disease risk calculator. His 10-year risk of a cardiovascular event is estimated to be 7.5% with a lifetime risk of 50%.

Which of the following factors is the strongest indicator for starting a statin in this patient?

A. LDL-cholesterol concentration above the target of 100 mg/dL (2.59 mmol/L)
B. HDL-cholesterol concentration below the target of 40 mg/dL (1.04 mmol/L)

C. Age (older than 50 years)

D. Diagnosis of hypertension

E. Estimated 10-year risk of a cardiovascular event of 7.5%

LEARNING OBJECTIVE:

Recommend lipid-lowering therapy with statins on the basis of global cardiovascular risk rather than on specific lipid targets

QUESTION 79:

BONE AND MINERAL METABOLISM

You are asked to consult regarding hypocalcemia in a previously healthy 42-year-old woman who was hospitalized because of a 1-month history of progressive bloody diarrhea, anorexia, and a 22-lb (10-kg) weight loss. For 2 days before admission, she had a fever, chills, and lightheadedness. In addition, she has experienced progressive weakness, muscle cramping, and palpitations. Ulcerative colitis was diagnosed following emergency flexible sigmoidoscopy the night of admission.

Since admission, she has received approximately 3 L of intravenous normal saline and has been started on prednisone, 80 mg daily, and mesalamine.

On physical examination, she is a thin, ill-appearing woman. Her height is 65 in (165.1 cm), and weight is 105 lb (47.7 kg) (BMI = 17.5 kg/m²). She has temporal wasting and tenting on skin examination. Abdominal examination reveals diminished bowel sounds and diffuse discomfort to palpation without rebound tenderness. Chvostek sign is positive. There is no evidence of vitiligo or hyperpigmentation.

Laboratory test results:

Calcium = 7.0 mg/dL (1.75 mmol/L) (reference range, 8.2-10.2 mg/dL [2.1-2.6 mmol/L])
Albumin = 2.9 g/dL (29 g/L) (reference range, 3.5-5.0 g/dL [35-50 g/L])
Phosphorus = 2.6 mg/dL (0.84 mmol/L) (reference range, 2.3-4.7 mg/dL [0.7-1.5 mmol/L])
Magnesium = 0.4 mg/dL (0.16 mmol/L) (reference range, 1.5-2.3 mg/dL [0.6-0.9 mmol/L])
Potassium = 3.0 mEq/L (3.0 mmol/L) (reference range, 3.5-5.0 mEq/L [3.5-5.0 mmol/L])

Electrocardiogram documents premature ventricular contractions, widening of the QRS complex, and peaking of the T waves.

Which of the following patterns of PTH and vitamin D levels would be most likely?

<table>
<thead>
<tr>
<th></th>
<th>PTH</th>
<th>1,25-Dihydroxyvitamin D</th>
</tr>
</thead>
<tbody>
<tr>
<td>A.</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>B.</td>
<td>↑</td>
<td>↑</td>
</tr>
</tbody>
</table>
A 56-year-old woman presents with recent-onset headache, nausea, and decreased stamina. She reports increased thirst and fluid intake and for the past 3 weeks, she has been getting up several times a night to urinate. She was previously healthy, takes no medication, and has never smoked cigarettes. Her menses stopped at age 50 years.

On physical examination, her blood pressure is 100/62 mm Hg and pulse rate is 80 beats/min. There are no features suggestive of GH or cortisol excess. Extraocular movements are intact and there are no visual field defects detected on confrontation testing. There is no edema.

Laboratory tests results:

- Sodium = 147 mEq/L (147 mmol/L) (reference range, 136-142 mEq/L [136-142 mmol/L])
- Potassium = 3.9 mEq/L (3.9 mmol/L) (reference range, 3.5-5.0 mEq/L [3.5-5.0 mmol/L])
- Calcium = 9.1 mg/dL (2.3 mmol/L) (reference range, 8.2-10.2 mg/dL [2.1-2.6 mmol/L])
- Glucose = 92 mg/dL (5.1 mmol/L) (reference range, 70-99 mg/dL [3.9-5.5 mmol/L])
- Creatinine = 1.1 mg/dL (97.2 µmol/L) (reference range, 0.6-1.1 mg/dL [53.0-97.2 µmol/L])
- Prolactin = 38 ng/mL (1.7 nmol/L) (reference range, 4-30 ng/mL [0.17-1.30 nmol/L])
- IGF-1 = 23 ng/mL (3.0 nmol/L) (reference range, 78-220 ng/mL [10.2-28.8 nmol/L])
- Morning cortisol = 3.0 µg/dL (82.8 nmol/L) (reference range, 5.0-25 µg/dL [137.9-689.7 nmol/L])
- TSH = 1.0 mIU/L (reference range, 0.5-5.0 mIU/L)
- Free T<sub>4</sub> = 0.6 ng/dL (7.7 pmol/L) (reference range, 0.8-1.8 ng/dL [10.30-23.17 pmol/L])
- FSH = 1.0 mIU/mL (1.0 IU/L) (reference range, >30 mIU/mL [30 IU/L])
- Urinary sodium = 24 mEq/L (24 mmol/L) (reference range, 40-217 mEq/24 h [40-217 mmol/d])
- Urinary osmolality = 120 mOsm/kg (120 mmol/kg) (reference range, 150-1150 mOsm/kg [150-1150 mmol/kg])

Brain MRI shows a sellar mass that does not exert pressure on the optic apparatus (see image). Hydrocortisone, desmopressin, and levothyroxine are administered with good effect.
Which of the following should you advise next?

A. A water deprivation test
B. Measurement of serum α-fetoprotein
C. CT of the chest, abdomen, and pelvis
D. Measurement of serum hCG
E. Iron studies (iron, total iron binding capacity, ferritin)

LEARNING OBJECTIVE:
Recognize the possibility of metastatic disease to the pituitary in a patient presenting with anterior hypopituitarism and diabetes insipidus

QUESTION 81:

DIABETES MELLITUS AND OTHER CARBOHYDRATE DISORDERS

You are asked to evaluate a hospitalized 69-year-old man with a history of type 2 diabetes mellitus, hypertension, and hyperlipidemia. He just underwent a coronary artery bypass graft procedure. Postoperative glycemic control was adequately achieved with intravenous insulin infusion.

Over the past 24 hours, intravenous insulin infusion rates ranging between 1.3 and 3.1 units per hour have resulted in fingerstick blood glucose readings between 109 and 181 mg/dL (6.1-10.0 mmol/L). During the 8-hour period overnight, his glycemic control was stable on an insulin infusion rate of 1.3 units per hour. The surgical team will discontinue the intravenous insulin infusion today and has requested that you assist with his further diabetes management.

A transition to which of the following is the best next step in this patient's care?

A. Metformin monotherapy
B. Correction doses of a subcutaneous rapid-acting insulin before intake of meals

C. Subcutaneous insulin glargine at a dosage of 25 units once daily

D. Subcutaneous insulin glargine at a dosage of 40 units once daily

E. Subcutaneous regular insulin at a dosage of 10 units every 6 hours

LEARNING OBJECTIVE:

Guide the transition of an intravenous insulin infusion regimen to a subcutaneous insulin regimen

QUESTION 82:

THYROID DISORDERS

A 63-year-old woman is referred to you after having undergone $^{18}$F- fluorodeoxyglucose positron emission tomography (FDG-PET) for surveillance of her lung cancer. She underwent a left lung lobectomy 2 years ago and she has been thought to be free of disease on the basis of her imaging studies. On this recent PET scan, no suspicious uptake was seen in the chest. However, diffuse uptake was noted within the thyroid gland. She has no history of thyroid problems. Tuberculosis was diagnosed several years ago; she was treated for 1 year with antibiotics and was subsequently told she was cured.

On physical examination, her thyroid gland is palpable, nontender, and slightly enlarged. You review the PET scan images; the FDG uptake is evident throughout both lobes of the thyroid gland (see images). The standard uptake ratio value is 8.5. You order thyroid testing and obtain the following results:

TSH = 3.9 mIU/L (reference range, 0.5-5.0 mIU/L)
Free $T_4 = 1.1$ ng/dL (14.2 pmol/L) (reference range, 0.8-1.8 ng/dL [10.30-23.17 pmol/L])
TPO antibodies = 40 IU/mL (40 IU/L) (reference range, <2.0 IU/mL [<2.0 kIU/L])

Which of the following is the most likely explanation for the uptake of FDG within this patient's thyroid gland?

A. Hashimoto thyroiditis

B. Lung cancer metastases to the thyroid gland
C. Normal physiologic uptake within the thyroid gland

D. Graves disease

E. Tuberculosis affecting the thyroid gland

LEARNING OBJECTIVE:
Develop a differential diagnosis for the incidental finding of fluorodeoxyglucose uptake within the thyroid gland

QUESTION 83:

ADRENAL DISORDERS

A 27-year-old woman seeks your advice at 6 weeks' gestation in her first pregnancy. She has a history of salt-wasting congenital adrenal hyperplasia due to 21-hydroxylase deficiency, for which she takes hydrocortisone and fludrocortisone. She is concerned that her baby may have congenital adrenal hyperplasia.

Which of the following is the best next step in this patient's management?

A. Measure serum 17-hydroxyprogesterone

B. Add dexamethasone, 0.5 mg at bedtime

C. Perform molecular genetic testing for CYP21A2 mutations in the baby's father

D. Perform amniocentesis to determine fetal sex

E. Secure fetal DNA via chorionic villus sampling for CYP21A2 mutation analysis

LEARNING OBJECTIVE:
To understand that congenital adrenal hyperplasia is an autosomal recessive disorder

QUESTION 84:

FEMALE REPRODUCTION

A 27-year-old woman presents to you for advice after unsuccessfully trying to get pregnant for 6 months. She underwent menarche at age 10 years. Her menstrual cycles are regular; she menstruated every 28 days until age 17, but now she has a menses every 33 to 35 days. She has no acne, hirsutism, hot flashes, or night sweats. She has gained weight since high school when she used to weigh 140 lb (63.6 kg). She has no history of pelvic surgery or sexually transmitted infections. Her husband has previously fathered a child.

On physical examination, her blood pressure is 120/80 mm Hg. Her height is 63 in (160 cm), and
weight is 223 lb (101.4 kg) (BMI = 39.5 kg/m²). She has no acne or hirsutism. There is no galactorrhea on breast examination. Findings on pelvic examination are normal.

Laboratory test results (day 19 of menstrual cycle):

TSH = 2.6 mIU/L (reference range, 0.5-5.0 mIU/L)
Prolactin = 8.6 ng/mL (0.4 nmol/L) (reference range, 4-30 ng/mL [0.17-1.30 nmol/L])
FSH = 8.1 mIU/mL (8.1 IU/L) (reference range [follicular], 4.0-36.0 mIU/mL [4.0-36.0 IU/L]; [luteal], 1.0-9.0 mIU/mL [1.0-9.0 IU/L])
Progesterone = 9.9 ng/mL (31.5 nmol/L) (reference range [follicular], ≤1.0 ng/mL [≤3.2 nmol/L]; [luteal], 2.0-20.0 ng/mL [6.4-63.6 nmol/L])
Hemoglobin A₁c = 4.9% (30 mmol/mol) (reference range, 4.0%-5.6% [20-38 mmol/mol])
hCG, negative

How would you advise this patient to maximize her chances of pregnancy?

A. Time intercourse between days 11 and 21 of the menstrual cycle

B. Check an ovulation kit on cycle days 10, 12, and 14 and time intercourse to the day the kit is positive

C. Measure a progesterone level 7 days before expected menses

D. Take basal body temperatures and time intercourse to the temperature rise

E. Lose weight to improve ovulation

LEARNING OBJECTIVE:

Recommend timed intercourse for couples planning pregnancy

QUESTION 85:

DIABETES MELLITUS AND OTHER CARBOHYDRATE DISORDERS

You are asked to evaluate a 52-year-old African American woman with newly diagnosed diabetes mellitus. She has recently completed a successful course of pegylated-interferon-α and ribavirin therapy for chronic hepatitis C virus infection. Approximately 1 month after this treatment was completed, she presented to the emergency department with weight loss, fatigue, polydipsia, and polyuria. Diabetic ketoacidosis was diagnosed. She was admitted to the hospital, and with appropriate management the ketoacidosis has quickly resolved. The patient is receiving an intravenous insulin infusion at a rate of 0.5 units per hour. Over the past 10 hours, her glycemic control has been excellent, and no adjustments to her insulin infusion rate have been required. The patient will begin eating solid food later this morning. Her renal function and serum electrolytes are now within normal limits.

The patient has no personal or family history of diabetes. Laboratory testing for glutamic acid decarboxylase autoantibodies was negative when performed at the start of her course of antiviral therapy. She tolerated that therapy well, had an excellent response in her viral load, and was without
evidence of hyperglycemia during treatment. The patient is afebrile and has normal physical examination findings. Her height is 66 in (167.6 cm), and weight is 160 lb (72.7 kg) (BMI = 25.8 kg/m²).

Which of the following is the best management plan?

A. Transition from intravenous insulin infusion to a scheduled subcutaneous basal-bolus insulin regimen
B. Transition from intravenous insulin infusion to twice-daily metformin therapy
C. Discontinue all antihyperglycemic therapy but continue to monitor blood glucose values
D. Begin high-dosage glucocorticoid therapy and continue the intravenous insulin infusion
E. Consult gastroenterology for resumption of pegylated-interferon-α and ribavirin therapy

LEARNING OBJECTIVE:
Manage new-onset diabetes in a patient with interferon-treated hepatitis C infection

QUESTION 86:

MALE REPRODUCTION

A 77-year-old man is referred to you for management of osteoporosis. A high-grade, locally invasive prostate cancer was diagnosed 8 months ago after a screening prostate-specific antigen level was found to be elevated. He was started on androgen deprivation therapy with a GnRH agonist 6 months ago, along with radiation therapy, and his prostate-specific antigen concentration is now undetectable. His oncologist plans to continue androgen deprivation therapy for the next 12 to 18 months. A screening DXA scan documented osteoporosis of the spine (T score, -3.1) and femoral neck (T score, -2.9).

The patient has no known history of osteoporosis or fractures, but reports that he has lost 2 in (5.1 cm) in height. His mother experienced a hip fracture at age 70 years. His other medical history is notable for gastroesophageal reflux disease. His current medications include a proton-pump inhibitor and calcium citrate plus vitamin D.

On physical examination, the patient has kyphosis. His pulse rate is 78 beats/min, and blood pressure is 132/82 mm Hg. His height is 73 in (185.4 cm), and weight is 203 lb (92.3 kg) (BMI = 26.8 kg/m²). Findings on cardiac examination are normal. His testes are 15 mL bilaterally.

Relevant laboratory test results:

25-Hydroxyvitamin D = 39 ng/mL (97.3 nmol/L) (reference range [optimal], 25-80 ng/mL [62.4-199.7 nmol/L])
Calcium = 9.7 mg/dL (2.4 mmol/L) (reference range, 8.2-10.2 mg/dL [2.1-2.6 mmol/L])
PTH = 32 pg/mL (32 ng/L) (reference range, 10-65 pg/mL [10-65 ng/L])
Which of the following medications would be the best initial choice in treating this patient’s osteoporosis?

A. Denosumab  
B. Alendronate  
C. Nasal calcitonin  
D. Raloxifene  
E. Recombinant PTH

**LEARNING OBJECTIVE:**
Select the optimal treatment for osteoporosis in men undergoing androgen deprivation therapy

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**QUESTION 87:**

**BONE AND MINERAL METABOLISM**

You are asked to see an 18-year-old woman for evaluation of bone health. She has a history of anorexia nervosa first diagnosed at age 4 years. She has required multiple inpatient admissions and has struggled with maintaining normal weight despite psychiatric intervention. Other medical problems include anemia, carotenemia, depression, and social anxiety for which she takes a selective serotonin reuptake inhibitor daily. She has not had a menstrual period in more than 2 years. She is not currently taking an oral contraceptive because she is fearful this will cause weight gain. At age 17 years she sustained a T11 compression fracture after tripping on a rug.

On physical examination, she is a malnourished woman appearing older than her stated age. She has diffuse alopecia and bilateral temporal wasting. Her height is 61 in (154.9 cm), and weight is 61 lb (27.7 kg) (BMI = 11.5 kg/m²). Her blood pressure is 97/61 mm Hg, and pulse rate is 69 beats/min. Muscle strength in her upper and lower extremities is 3/5 bilaterally.

Laboratory test results:

- LH = 0.3 mIU/mL (0.3 IU/L) (reference ranges, 1.0-18.0 mIU/mL [1.0-18.0 IU/L] [follicular]; 20.0-80.0 mIU/mL [20.0-80.0 IU/L] [midcycle]; 0.5-18.0 mIU/mL [0.5-18.0 IU/L] [luteal])
- FSH = 0.9 mIU/mL (0.9 IU/L) (reference ranges, 2.0-12.0 mIU/mL [2.0-12.0 IU/L] [follicular]; 4.0-36.0 mIU/mL [4.0-36.0 IU/L] [midcycle]; 1.0-9.0 mIU/mL [1.0-9.0 IU/L] [luteal])
- Estradiol, undetectable
- 25-Hydroxyvitamin D = 18 ng/mL (44.9 nmol/L) (reference range [optimal], 25-80 ng/mL [62.4-199.7 nmol/L])

In addition to ongoing psychiatric care, the addition of calcium supplementation, and the restoration of a normal vitamin D level, which of the following treatment recommendations is indicated to stabilize her bone density?
A. Denosumab
B. A bisphosphonate
C. Low-dosage estradiol and progesterone
D. Weight-bearing exercise program
E. Teriparatide

LEARNING OBJECTIVE:
Recommend appropriate treatment of osteoporosis in women who are severely underweight

QUESTION 88:
DIABETES MELLITUS AND OTHER CARBOHYDRATE DISORDERS

A 53-year-old man with type 2 diabetes mellitus returns for a follow-up visit with concerns about worsening peripheral neuropathy. He is currently treated with liraglutide, which he is tolerating without any concerns. He has no diabetes-associated complications other than neuropathy, which is treated with gabapentin, 200 mg 3 times daily, that he has taken regularly for the past 4 months. He has experienced modest pain control on this treatment, but notes somnolence while driving. He practices good foot care and has not had any acute foot ulcerations. However, over the last few months, he has been experiencing a "pins and needles" sensation in his lower extremities bilaterally and periodic severe pain, which occasionally restricts his walking. He also reports waking at night because of foot pain. He has no calf pain.

On physical examination, he is in mild distress because of foot pain. His height is 76 in (193 cm), and weight is 210 lb (95.5 kg) (BMI = 25.6 kg/m²). His blood pressure is 100/65 mm Hg, and pulse rate is 82 beats/min. Neurologic examination reveals loss of sensation on Semmes-Weinstein monofilament testing and loss of ankle reflexes bilaterally. The rest of his examination findings are normal.

Laboratory test results:

Hemoglobin A₁c = 5.8% (40 mmol/mol) (reference range, 4.0%-5.6% [20-38 mmol/mol])
Vitamin B₁₂ = 500 pg/mL (369 ng/L) (reference range, 180-914 pg/mL [180-914 ng/L])

Which of following is the best next therapeutic step?

A. Increase the gabapentin dosage to 600 mg 3 times daily
B. Add treatment with acetaminophen and codeine
C. Add treatment with capsaicin cream
D. Add vitamin B₁₂ replacement therapy
E. Switch gabapentin to pregabalin

LEARNING OBJECTIVE:

Manage pain in a patient with established diabetic neuropathy

QUESTION 89:

LIPIDS/OBESITY

You are seeing a 55-year-old Hispanic woman who underwent Roux-en-Y gastric bypass surgery 4 years ago. She now presents with a 3-month history of abdominal pain and diarrhea. Her preoperative weight was 259 lb (117.7 kg) (BMI = 43.6 kg/m²); after surgery, her nadir weight was 161 lb (73.2 kg) and her current weight is 190 lb (86.4 kg).

She is adherent to the prescribed dietary and vitamin supplement recommendations. Trying a gluten-free diet did not ameliorate her symptoms. She describes her abdominal pain as discomfort with bloating and gas. There is no discrete area of pain and no associated nausea or vomiting. She has 3 to 4 bowel movements daily that are often loose and malodorous, but not greasy and not difficult to flush.

On physical examination, her height is 65 in (165.1 cm) and weight is 190 lb (86.4 kg) (BMI = 31.6 kg/m²). Abdominal examination reveals hyperactive bowel sounds.

Laboratory test results:

- Complete blood cell count, normal
- Ferritin, normal
- 25-Hydroxyvitamin D = 33 ng/mL (82.4 nmol/L) (reference range [optimal], 25-80 ng/mL [62.4-199.7 nmol/L])
- Hemoglobin A1c = 5.6% (38 mmol/mol) (reference range, 4.0%-5.6% [20-38 mmol/mol])

Which test will most likely identify the cause of her symptoms?

A. Colonoscopy

B. Stool sample to test for enteric pathogens

C. 48-Hour stool fat excretion

D. Tissue transglutaminase antibody measurement

E. Carbohydrate breath test

LEARNING OBJECTIVE:

Assess for small-bowel bacterial overgrowth as a cause of abdominal symptoms and diarrhea in patients after Roux-en-Y gastric bypass
QUESTION 90:

ADRENAL DISORDERS

A 61-year-old woman with a 50 pack-year history of cigarette smoking presents with the recent onset of hypertension and peripheral edema. She appears cachectic and chronically ill. Her blood pressure is 182/104 mm Hg, and pulse rate is 94 beats/min. She has 4+ pretibial edema and severe muscle weakness.

Laboratory test results:

Sodium = 134 mEq/L (134 mmol/L) (reference range, 136-142 mEq/L [136-142 mmol/L])
Potassium = 2.0 mEq/L (2.0 mmol/L) (reference range, 3.5-5.0 mEq/L [3.5-5.0 mmol/L])
Chloride = 90 mEq/L (90 mmol/L) (reference range, 96-106 mEq/L [96-106 mmol/L])
Bicarbonate = 42 mEq/L (42 mmol/L) (reference range, 21-28 mEq/L [21-28 mmol/L])
Serum urea nitrogen = 22 ng/dL (7.9 mmol/L) (reference range, 8-23 mg/dL [2.9-8.2 mmol/L])
Creatinine = 0.7 mg/dL (61.9 µmol/L) (reference range, 0.6-1.1 mg/dL [53.0-97.2 µmol/L])
Aldosterone = <1 ng/dL (<27.7 pmol/L) (reference range, 1-21 ng/dL [27.7-582.5 pmol/L])
Plasma renin activity = <0.1 ng/mL per h (reference range, 0.6-4.3 ng/mL per h)

Spironolactone, potassium chloride, and valsartan are initiated. CT of the chest and abdomen shows bilateral adrenal enlargement, with a 2-cm left adrenal nodule (19 Hounsfield units) and a large left inferior lobe lung mass.

Which of the following is the most likely cause of the hypertension and hypokalemia in this patient?

A. Adrenocortical carcinoma with pulmonary metastases
B. Liddle syndrome
C. Surreptitious use of diuretics
D. Ectopic ACTH-secreting small cell carcinoma of the lung
E. Aldosterone-secreting adrenal adenoma

LEARNING OBJECTIVE:

To understand the clinical and biochemical presentation of the ectopic ACTH syndrome and differential diagnosis of patients with hypertension, hypokalemia, and subnormal plasma renin and aldosterone

QUESTION 91:

DIABETES MELLITUS AND OTHER CARBOHYDRATE DISORDERS

A 47-year-old man with an unremarkable medical history is referred for evaluation of symptoms suggestive of hypoglycemia. These symptoms occur at variable times and are characterized by
sweating, tremor, and tachycardia. Most commonly, symptoms occur when he wakes in the morning, but sometimes the symptoms occur 1 to 2 hours after meals. The patient has thus started waking up 3 times during the night to consume a snack, and he carries orange juice with him constantly. These symptoms have been present to some degree for about 2 years, but have worsened in the past 4 months.

Examination findings are unremarkable except for a BMI of 43 kg/m². A 72-hour fast is performed during which the patient is asymptomatic for the first 48 hours. However, symptoms of neuroglycopenia eventually develop and blood is drawn for laboratory testing. Then glucagon is administered, and glucose is measured 10, 20, and 30 minutes after administration.

Laboratory values are shown in the Table.

<table>
<thead>
<tr>
<th>Time</th>
<th>Glucose</th>
<th>Insulin</th>
<th>C-Peptide</th>
<th>Proinsulin</th>
<th>Sulfonylurea Screen</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:15 PM</td>
<td>44 mg/dL (mmol/L)</td>
<td>11 µIU/mL (76.4 pmol/L)</td>
<td>6.0 ng/mL (2.0 nmol/L)</td>
<td>176.4 pg/mL (20 pmol/L)</td>
<td>Negative</td>
</tr>
<tr>
<td>8:25 PM</td>
<td>58 mg/dL (3.2 mmol/L)</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>8:35 PM</td>
<td>70 mg/dL (3.9 mmol/L)</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>8:55 PM</td>
<td>75 mg/dL (4.2 mmol/L)</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>

Which of the following would be appropriate management now?

A. Selective arterial calcium stimulation test

B. No further testing; instead, a consultation with a dietitian to prescribe an "anti-dumping" diet

C. Abdominal CT with intravenous contrast

D. Transabdominal ultrasonography

E. Octreotide scan

LEARNING OBJECTIVE:

Recognize potential reasons for inconsistency in testing for hypoglycemic disorders and choose optimal management strategies in a patient with insulinoma presenting with both fasting and postprandial symptoms.