Endocrinology and Metabolism: Question 1
A 67-year-old obese (body mass index, 34) white man has had type 2 diabetes mellitus for the past 8 years. The disease was originally diagnosed on the basis of a routine fasting plasma glucose level of 156 mg/dL and responded well to initiation of a nutrition and exercise plan. The hemoglobin A1C value decreased from 8.8% at diagnosis to 6.9% after 6 months of nutrition therapy and a 5.5-kg (12-Ib) weight loss. After 2 years, the hemoglobin A1C increased to 8.1%; therapy with glyburide, titrated up to 10 mg/d, was started. The hemoglobin A1C value then decreased 6.6% and remained less than 7% until 1 year ago. At that time, the patient noted a 7 kg (15-Ib) weight gain and some symptoms of distal paresthesias. The hemoglobin A1C had increased to 7.7%. The patient is counseled to intensify diet and exercise to lose 7 kg (15 lb).

What is the most appropriate additional intervention at this time?
A. Add repaglinide therapy before breakfast and dinner
B. Increase the glyburide dosage to 10 mg twice daily
C. Discontinue glyburide therapy and begin metformin therapy
D. Add metformin therapy to the current glyburide regimen
E. Switch from glyburide therapy to glipizide therapy

Endocrinology and Metabolism: Question 2
A 28-year-old woman with a history of Graves disease and thyrotoxicosis treated with radioactive iodine 18 months ago is evaluated. She has been taking levothyroxine for 15 months, initially as 0.125 mg/d, but in the past 6 months the dosage has been reduced first to 0.088 mg/d and more recently to 0.050 mg/d because of an apparently reduced requirement. On physical examination, her pulse rate is 106/min; she has a questionably small goiter or thyroid gland at the upper limit of normal size, brisk deep tendon reflexes, and a 1+ tremor. Laboratory results include a serum free T4 of 2.7 ng/dL, free T3 7.4 pmol/L (normal, 1.5-6.9 pmol/L), and a serum TSH of <0.01 IU/mL. TSH receptor antibodies are positive at 179% (normal, <130%). A 24-hour radioiodine uptake is 19.5% (normal, 8% to 30%).

What is the most likely diagnosis?
A. T3 toxicosis
B. Incompletely treated Graves disease
C. Hashitoxicosis
D. Radioiodine-induced thyrotoxicosis
E. Struma ovarii with thyrotoxicosis

Endocrinology and Metabolism: Question 3
A 42-year-old woman presents for evaluation of a 2.8-cm left adrenal mass. She was seen in the emergency department 1 week ago for abdominal pain. CT scan shows only the adrenal mass. Physical examination, vital signs, and review of systems are all normal. Medical history and family history are unremarkable.

What is the first step in management of this patient?
A. Reassure the patient and suggest follow-up CT scan in 6 months
B. Arrange CT-guided needle biopsy of the mass
C. Order a plasma and urine hormone work-up
D. Consult a general surgeon to have the mass removed
E. Order ultrasonography or MRI
Endocrinology and Metabolism: Question 4
A 20-year-old woman is referred because of an elevated serum calcium level (11.3 mg/dL) obtained during a routine preoperative evaluation before minor gynecologic surgery. All other laboratory values are normal. The parathyroid hormone level was subsequently checked and is slightly elevated (67 pg/mL). The patient is healthy except for recent metrorrhagia. Her mother and maternal grandfather both had hyperparathyroidism and underwent neck surgery but remained mildly hypercalcemic. The patient underwent a bone density study, which was normal, and renal ultrasonography, which shows no evidence of nephrolithiasis. Her 24-hour urine calcium level is 63 mg. Her diet is rich in dairy products, and she has no history of digestive illness.

What is the most likely diagnosis?
A. Primary hyperparathyroidism
B. Secondary hyperparathyroidism
C. Familial benign hypocalciuric hypercalcemia
D. Multiple endocrine neoplasia type 1
E. Milk-alkali syndrome

Endocrinology and Metabolism: Question 5
A 62-year-old white postmenopausal woman is concerned that she may have osteoporosis. Her older sister was diagnosed with osteoporosis at age 60 years and has had several vertebral compression fractures. The patient has avoided dairy products most of her life. She smoked a pack of cigarettes daily for 40 years but does not drink alcoholic beverages. She takes no medications or nutritional supplements. She has never received calcium supplementation or hormone replacement therapy. She had no other medical problems and her physical examination is normal. She is 170 cm (67 in) tall and weighs 69 kg (152 lb).

Which of the following tests would show whether this patient has osteoporosis?
A. Measurement of markers of bone resorption
B. Bone biopsy of the iliac crest
C. Dual-energy X-ray absorptiometry of the spine and hip
D. Ultrasound of the heel
E. Radiographs of the spine

Endocrinology and Metabolism: Question 6
A 34-year-old woman has had fatigue, weight gain, irregular menstrual cycles, and milky discharge from both breasts for 6 months.

Physical examination reveals a small goiter, dry skin, and bilateral expressible galactorrhea. Laboratory results include a negative pregnancy test, a serum thyroid-stimulating hormone of 43 1uU/mL, and a serum prolactin level of 55 ng/mL.

What is the most appropriate next step in the management of this patient's hyperprolactinemia?
A. Remeasure serum prolactin
B. Start estrogen therapy
C. Start dopamine agonist therapy
D. Start levothyroxine therapy
E. Obtain an MRI of the pituitary gland
Endocrinology and Metabolism: Question 7
A 52-year-old man presents with erectile dysfunction of 2 years duration. He has an unchanged libido and is happily married. The patient is 172.5 cm (68 in) tall, and over the past 10 years he has slowly gained weight to his present weight of 110 kg (242 lb); body mass index is 36.9. Five years ago, he was diagnosed with type 2 diabetes mellitus.
On physical examination, he has acanthosis nigricans on his neck and normal body hair for an adult man. Each testis is 5.0 cm long. The total serum testosterone level is 230 ng/dL, serum luteinizing hormone is 4.5 mU/mL, and serum follicle-stimulating hormone is 5.5 mU/mL.
Which of the following is the most likely explanation for this man’s low level of testosterone?
A. Pituitary adenoma
B. Cushing’s syndrome
C. Hemochromatosis
D. Low level of sex hormone-binding globulin
E. Estrogen-producing adrenal tumor

Endocrinology and Metabolism: Question 8
A 26-year-old woman has experienced a 7-kg (15-lb) weight gain, mostly in her trunk, and has increased fat accumulation in her face over the past 6 months. She has also noted gradually progressive acne, hirsutism, weakness, easy bruising, and abdominal stretch marks and has developed oligomenorrhea.
On physical examination, the patient is 160 cm (63 in) tall and weighs 67 kg (147 lb). Blood pressure is 130/96mm Hg. She has central obesity, acne on her face and trunk, facial hirsutism, and violaceous striae on her lower abdomen.
What is the best test to screen for Cushing’s syndrome in this patient?
A. Morning serum cortisol level
B. Plasma adrenocorticotropic (ACTH) level
C. 1-mg overnight dexamethasone suppression test
D. 8-mg overnight dexamethasone suppression test
E. 24-hour urinary free cortisol measurement

Endocrinology and Metabolism: Question 9
The wife of one of your patients telephones one morning to report that her husband who has type 1 diabetes mellitus had a severe hypoglycemic reaction last night that required the attention of paramedics and a visit to the emergency department. She had administered intramuscular glucagon as you had trained her, and although it seemed to revive her husband at first, he became unconscious again in less than 10 minutes. Because you are trying to tighten his overall glycemic control, this circumstance may recur.
What step should be taken to prevent this circumstance in the future?
A. Do not administer intramuscular glucagon because it is not effective in type 1 diabetes
B. Check the expiration date on the glucagon
C. Give the glucagon deeper into the muscle
D. Give oral carbohydrate after intramuscular glucagon
E. Recognize the indications for administration of intravenous D50
**Endocrinology and Metabolism: Question 10**

An 18-year-old white woman presents because she has never had a period. She was born by normal spontaneous vaginal delivery after a normal full-term gestation. She has always been small for her age but does well in school, plays soccer without difficulty, and has had no intercurrent illness. She has adequate nutritional intake. Her mother, who is 53 years of age, had a normal menarche at 12 years of age, and a sister, who is 20 years old, is taller than the patient, had menarche at 13 years of age, and has regular menses. The patient’s mother has Hashimoto’s thyroiditis. Physical examination reveals a height of 145 cm (57 in) and a body weight of 45 kg (107 lb). Blood pressure is 97/70 mm Hg. She has a low-set hairline, widely spaced nipples, no significant breast tissue, and scanty axillary and pubic hair.

Which laboratory test is most likely to reveal the cause of this patient’s amenorrhea?
A. Serum prolactin  
B. Serum testosterone  
C. Karyotype analysis  
D. Serum estradiol  
E. Serum thyroid-stimulating hormone

**Endocrinology and Metabolism: Question 11**

A 27-year-old woman presents to her obstetrician during her 12th week of pregnancy for a routine physical examination. The pregnancy has been uncomplicated, other than mild nausea in the morning and fatigue. She has gained 2 kg (5 lb) and is feeling well. She does not have cold intolerance or dry skin. She has a family history of Hashimoto’s thyroiditis. Physical examination is remarkable only for a small goiter without nodules. The fetus is easily identified on ultrasonography. The serum thyroid-stimulating hormone level is 0.3 μU/mL and the total thyroxine level is 16 μg/dL.

What is the most likely interpretation of these laboratory results?
A. Normal thyroid function tests at the end of first trimester of pregnancy  
B. Mild Graves disease  
C. Hyperemesis gravidarum  
D. Surreptitious use of levothyroxine  
E. Subacute (de Quervains) thyroiditis

**Endocrinology and Metabolism: Question 12**

A 41-year-old man is evaluated for an elevated serum thyroxine level. His mother and brother also have similar findings. Physical examination reveals a pulse rate of 64/min and a normal thyroid.

Laboratory studies:
- Serum free thyroxine 15.0 pmol/L (normal, 12-31 pmol/L)  
- Serum total thyroxine 17 μg/dL  
- Serum free thyroxine index 14  
- Serum triiodothyronine 15 ng/dL  
- Serum thyroid-stimulating hormone 0.8 μU/mL

What is the most likely diagnosis?
A. Selenium deficiency  
B. Inherited deficiency of type 1 5’-monodeiodinase enzyme  
C. Early Graves’ disease  
D. Familial dysalbuminemic hyperthyroxinemia  
E. Familial thyroid-binding globulin excess
Endocrinology and Metabolism: Question 13
A 15-year-old Hispanic male is hospitalized with polyuria, thirst, and blurred vision. He is 160 cm (63 in) tall and weighs 120 kg (265 lb). Acanthosis nigricans is noted on his neck. Plasma glucose concentration is 323 mg/dL; serum ketones are negative and arterial blood gases are normal. The patient’s grandmother has type 2 diabetes mellitus. What is the most likely cause of this patient’s hyperglycemia?
A. Type 1A diabetes mellitus
B. Type 1B diabetes mellitus
C. Type 2 diabetes mellitus
D. Secondary diabetes
E. Maturity-onset diabetes of youth

Endocrinology and Metabolism: Question 14
A 65-year-old man is hospitalized with hyponatremia and hypotension. Medical history reveals that he was diagnosed with small-cell lung cancer 20 years ago and underwent chemotherapy and radiation of the thorax, along with prophylactic whole-brain irradiation consisting of 3000 cGy in 10 fractions. For 5 years before the current hospitalization, he has had persistent hyponatremia with recurrent episodes of orthostatic hypotension, requiring frequent hospitalization and treatment with isotonic saline. His only medication is sodium tablets.
On physical examination, the patient is afebrile but very pale. The pulse rate and blood pressure are 90/min and 129/70 mm Hg, respectively, while supine and 104/64 mm Hg and 100/min while sitting. The skin is finely wrinkled and dry, axillary and pubic hair are lacking, and the testes are small. Review of systems reveals cold intolerance, chronic fatigue, constipation, pallor, loss of libido, and impotence for the past 10 years. Laboratory studies:
- Hemoglobin: 10.3 g/dL
- Hematocrit: 30%
- Blood urea nitrogen: 11 mg/dL
- Serum creatinine: 1.0 mg/dL
- Serum sodium: 123 meq/L
- Serum potassium: 3.9 meq/L
- Urine sodium: 100 meq/L
- Plasma osmolality: 264 mosm/kg H2O
- Urine osmolality: 354 mosm/kg H2O
What is the best explanation for these findings?
A. Syndrome of inappropriate antidiuretic hormone secretion
B. Primary adrenal insufficiency
C. Secondary adrenal insufficiency
D. Hypopituitarism
E. Renal salt wasting

Endocrinology and Metabolism: Question 15
A 66-year-old woman presents for a second opinion. During a recent visit to her gynecologist, her total cholesterol level was 300 mg/dL. The gynecologist prescribed a statin, but she is reluctant to take a medication. She has no other risk factors, has a healthy lifestyle, and does not have coronary heart disease.
What is the appropriate recommendation for this patient?
A. Initiation of statin therapy
B. Initiation of therapy with a bile acid sequestrant
C. Measurement of fasting lipid profile
D. Initiation of therapy with ezetimibe
Endocrinology and Metabolism: Question 16
A 25-year-old woman notices the gradual cessation of menses over 6 months. She and her husband wish to start a family soon and have been using condoms for contraception. Until the present illness, she has had regular menses since menarche at 11 years of age. Her weight is stable at 61 kg (135 lb), and her height is 157 cm (62 in). She eats a balanced diet and walks 2 miles briskly three times a week. She takes no medications or illicit recreational drugs. She has not noticed hirsutism, acne, or striae. She has not had headaches or changes in her vision.
Physical examination is normal with the exception of easily expresseable milk from both breasts. Laboratory studies include a negative pregnancy test, a serum thyroid-stimulating hormone level of 2.3 μU/mL, a serum prolactin level of 126 ng/mL, and a serum follicle-stimulating hormone level of 5.6 mU/mL.
What is the most likely cause of this patient’s amenorrhea?
A. Pituitary microadenoma
B. Androgen-secreting adrenal tumor
C. Polycystic ovary syndrome
D. Hypothalamic amenorrhea
E. Primary ovarian failure

Endocrinology and Metabolism: Question 17
A 59-year-old postmenopausal white woman has the following results from a recent dual-energy X-ray absorptiometry test. She has never experienced a fracture.
Spine: T score = -2.6; Z score = -1.2
Hip: T score = -1.4; Z score = -0.9
What is the correct diagnosis using the World Health Organization (WHO) criteria for bone mass?
A. Osteopenia
B. Osteoporosis
C. Severe osteopenia
D. Established osteoporosis
E. Normal bone mass

Endocrinology and Metabolism: Question 18
A 76-year-old black woman with type 2 diabetes of 15 years duration and hypertension presents to the emergency department with hypoglycemia. She has been treated with insulin for 10 years. This is her fourth hypoglycemic episode in the past 3 months. She has also had multiple lesser episodes of hypoglycemia, and her insulin doses have been reduced approximately 30% during this time. She takes no other medications that decrease the glucose level. Her blood pressure has also worsened, necessitating addition of diuretic therapy. The patient states that she has not changed her eating or activity pattern and has adhered to her long-standing, excellent self-care regimen. On physical examination, the patient is lean, with a body weight of 41 kg (90 lb). The lungs are clear, and no dependent edema is present.
Laboratory studies:
- Hematocrit 38%
- Leukocyte count 6500/μL
- Blood urea nitrogen 19 mg/dL
- Serum creatinine 1.3 mg/dL
- Serum sodium 137 meq/L
- Serum potassium 4.1 meq/L
- Serum carbon dioxide 28 meq/L
- Plasma glucose 144 mg/dL
- Serum alanine aminotransferase 22 U/L
- Serum albumin 4.9 mg/dL
What is the most useful diagnostic test to explain the patient's recurrent episodes of hypoglycemia?
A. Serum fructosamine
B. Urine microalbumin
C. Creatinine clearance
D. Morning serum cortisol
E. Serum thyroid-stimulating hormone

Endocrinology and Metabolism: Question 19
A 52-year-old man is undergoing preoperative assessment before removal of a solitary pheochromocytoma in the right adrenal. He has elevated levels of urine and plasma catechols, and T2-weighted MRI confirms the presence of a 4-cm mass in the right adrenal. A metaiodobenzylguanidine scan shows no other focus of tumor. The patient's medical history includes hypertension, anxiety, and tremor. His most recent set of vital signs reveals a blood pressure of 140/90 mm Hg, pulse rate of 100/min and regular, and a temperature of 37°C (98.6°F). Electrocardiography reveals normal sinus rhythm and borderline left ventricular hypertrophy by voltage criteria. The patient is medically cleared for surgery.

What is the first step in preoperative medical management of this patient?
A. Administration of normal saline and α-blockade with phenoxybenzamine
B. β-blockade with metoprolol
C. Administration of ct-methylparatyrosine to deplete the tumors catechol stores before surgery
D. Repeated 24-hour urine for vanillylmandelic acid, catechols, and metanephrines

Endocrinology and Metabolism: Question 20
A 38-year-old man has had fatigue, decreased libido, and worsening headaches for 4 years. Physical examination reveals bitemporal visual field defects on confrontation. Formal visual field examination confirms bitemporal hemianopsia. The testes are small and soft. Laboratory results include a testosterone level of 165 ng/dL, a luteinizing hormone level of 5 mU/mL, and a prolactin level of 2520 ng/mL. Levels of insulin-like growth factor-I, ct-subunit, and thyroid and adrenal hormones are normal. MRI of the pituitary gland shows a 2.7-cm mass arising from the sella and elevating the optic chiasm.

What is the most appropriate treatment for this disorder?
A. Remeasure prolactin levels in 3 months
B. Start testosterone therapy
C. Start dopamine agonist therapy
D. Refer for transsphenoidal surgery
E. Refer for radiation therapy

Endocrinology and Metabolism: Question 21
A 30-year-old man presents because he and his wife have been infertile during their 3 years of marriage, and he was found to have a sperm count of 2 million/mL. He is otherwise healthy, and has a normal libido and erectile function. He is well virilized. There is no gynecomastia. The testes are each 3.5 cm long. A varicocele is apparent when the patient is standing. The serum total testosterone level is 330 ng/dL, serum luteinizing hormone level is 6.0 mU/mL, and serum follicle-stimulating hormone level is 16.5 mU/mL.
Which of the following is the most appropriate treatment for this man's infertility?
A. Demeclocycline
B. Clomiphene
C. Varicocele repair
D. In vitro fertilization
E. Testosterone

Endocrinology and Metabolism: Question 22
A 74-year-old woman with hypertension and hyperlipidemia who underwent coronary artery bypass graft 3 years ago presents for a physical examination. She feels well and has stable body weight, a good appetite, and a fairly active lifestyle. Physical examination is remarkable only for a small goiter with several palpable nodules, all smaller than 1 cm. The heart rate is 64/min. There is no tremor, and deep tendon reflexes are normal. Laboratory studies show a serum thyroid-stimulating hormone level of 0.03 μU/mL, a free thyroxine level of 1.8 ng/dL, and a total triiodothyronine level of 165 ng/dL. Thyroid scan and uptake reveal a multinodular goiter with regions of increased function and a 24-hour radioiodine uptake of 36%.
Without appropriate treatment of hyperthyroidism, for what problems is the patient at risk?
A. Ventricular tachycardia
B. Coronary artery disease
C. Thyroid cancer
D. Pernicious anemia
E. Osteoporosis and atrial fibrillation

Endocrinology and Metabolism: Question 23
A 28-year-old woman is hospitalized with a history of weight loss, polyuria, palpitations, and diaphoresis. She is experiencing heat intolerance and fatigue. On physical examination, the patient is 173 cm (68 in) tall and weighs 52 kg (115 lb); her pulse rate is 120/min. A diffusely enlarged 75-g goiter is present, over which a bruit is auscultated. The palms are flushed and there is a tremor of the outstretched hands. Laboratory studies reveal a plasma glucose level of 350 mg/dL, positive serum ketones, strongly positive antibodies to glutamic acid decarboxylase-65, and a serum thyroid-stimulating hormone level less than 0.001 μU/mL.
What is the most likely diagnosis?
A. Type 2 diabetes mellitus
B. Hashimoto's thyroiditis
C. Autoimmune polyglandular syndrome type II
D. Multiple endocrine neoplasia type 1
E. Multiple endocrine neoplasia type 2

Endocrinology and Metabolism: Question 24
Therapy with an HMG-CoA reductase inhibitor (statin) lowers serum low-density lipoprotein (LDL) cholesterol concentration by increasing the number of LDL receptors on the cell surface.
This action is mediated by which one of the following?
A. Decreased intestinal absorption of cholesterol
B. Up-regulation of cholesterol ester transfer proteins
C. Up-regulation of lipoprotein lipase activity
D. Decreased intracellular cholesteryl concentration
E. Decreased serum triglyceride concentration
Endocrinology and Metabolism:Question 25
A 27-year-old male athlete is referred for evaluation of abnormal thyroid function test results during evaluation of an asymptomatic goiter. He has occasional headaches and loss of libido. Medical and family history are unremarkable. Physical examination reveals a pulse rate of 88/min, a diffusely enlarged 30-g thyroid gland without nodules, and slightly brisk deep tendon reflexes. Laboratory testing reveals a serum free thyroxine level of 2.4 ng/dL, a serum thyroid-stimulating hormone level of 4.3 μU/mL, and a decreased serum free testosterone level. Tests for antithyroid peroxidase and antithyroglobulin antibodies are negative. What is the most appropriate next step in the evaluation of this patient?
A. Point mutation analysis of the thyroid-stimulating hormone receptor
B. Thyroid function testing of all first-degree relatives
C. Measurement of thyroid-stimulating and thyroid-blocking antibodies
D. Gadolinium-enhanced MRI of the sella turcica
E. Measurement of antithyroxine autoantibodies

Endocrinology and Metabolism:Question 26
A 63-year-old woman is brought to the emergency department because of a mild concussion. The patient states that she has no medical problems but that she has gained 4.5 kg (10 lb) in the past 5 years. Physical examination is appropriate for age. Blood pressure and pulse are normal, and no notable abnormalities are present. Laboratory evaluation reveals a normal complete blood count and chemistry panel. The serum prolactin level is within the normal range, at 10 ng/dL. MRI of the head shows a 1.5-cm mass in the sella turcica with suprasellar extension but no compression of the optic chiasm. Which of the following is the most sensitive measure of pituitary function in this patient?
A. Measurement of serum follicle-stimulating hormone and luteinizing hormone
B. Adrenocorticotropin stimulation test
C. Measurement of serum insulin-like growth factor I
D. Measurement of serum free thyroxine
E. Measurement of serum thyroid-stimulating hormone

Endocrinology and Metabolism:Question 27
A 48-year-old woman is found to have a serum calcium concentration of 10.9 mg/dL on routine screening. Previously, a dual-energy X-ray absorptiometry showed T scores at the lumbar spine and left proximal femur of -2.14 and -2.64, respectively. There is no history or evidence of renal stones, bone fracture, cognitive impairment, or fatigue. The intact serum parathyroid hormone level is 115 pg/mL (normal range, 10 to 65 pg/mL). What is the most appropriate next step in the evaluation of this patient?
A. Chest computed tomography
B. Parathyroid surgery
C. Estrogen replacement therapy
D. Bisphosphonate therapy
E. Low-calcium diet
**Endocrinology and Metabolism: Question 28**

A 27-year-old asymptomatic Hispanic American woman is evaluated for risk of diabetes mellitus. She developed gestational diabetes with her first pregnancy, which ended successfully 12 months ago. She has a strong family history of type 2 diabetes mellitus.

On physical examination, she is 165 cm (64 in) tall and weighs 90 kg (198 lb); the body mass index is 34. The random plasma glucose level is 135 mg/dL. A 75-g glucose tolerance test shows a fasting plasma glucose level of 112 mg/dL and a 2-hour value of 178 mg/dL.

What is the most appropriate next step in the management of this patient?

A. Repeat the glucose tolerance test in 1 year
B. Begin thiazolidinedione therapy
C. Begin acarbose therapy
D. Begin metformin therapy
E. Begin intensive lifestyle intervention

**Endocrinology and Metabolism: Question 29**

A 34-year-old man has had fatigue, weakness, edema, and acne for 5 months. His medical history is otherwise unremarkable.

On physical examination, the patient is 183 cm (72 in) tall and weighs 95 kg (210 lb). Blood pressure is 145/90 mm Hg. He has facial acne, central obesity, enlarged supraclavicular fat pads, and prominent violaceous abdominal striae. The 24-hour urine cortisol excretion is 287 μg. The serum cortisol level is 18 μg/dL at baseline, 17.8 μg/dL at 8:00 A.M. after taking 1 mg of dexamethasone at bedtime, and 18.9 μg/dL at 8:00 A.M. after taking 8 mg of dexamethasone at bedtime. The plasma adrenocorticotropic hormone level is 281 pg/mL.

What is the most likely site of the disorder causing Cushing's syndrome in this patient?

A. Pituitary gland
B. Hypothalamus
C. Lungs
D. Adrenal glands
E. Pancreas

**Endocrinology and Metabolism: Question 30**

A 27-year-old woman has had oligomenorrhea and hirsutism since puberty at 14 years of age. She is not currently interested in pregnancy but would like to have children in the future. Her primary concern is her progressive hirsutism.

Physical examination reveals a height of 162.5 cm (64 in) and a body weight of 79 kg (173 lb), modest hirsutism of the face and nipples, no galactorrhea, and mild acanthosis nigricans of the nape of the neck. Laboratory results are normal.

Which of the following options is not appropriate for the management of this patient's disorder?

A. Clomiphene citrate
B. Metformin
C. Lifestyle changes to lose weight
D. Oral contraceptive pills
E. Spironolactone
**Endocrinology and Metabolism:Question 31**

A 69-year-old woman is referred to you after she experienced a fracture of her right hip. She stated that she had lost two inches in height over the past 5 years, and radiographs of her spine demonstrated multiple thoracic compression fractures. Dual-energy x-ray absorptiometry demonstrated a T score of -4.5 and a Z score of -2.5. A work-up for secondary causes of osteoporosis was unrevealing. In considering the therapeutic options for this woman, you wish to use a medication to treat this patient's osteoporosis that will stimulate osteoblastic bone formation. Which of the following agents approved for the treatment and prevention of osteoporosis is anabolic for bone?

A. Teriparatide  
B. Bisphosphonates  
C. Estrogens  
D. Raloxifene  
E. Calcitonin

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**Endocrinology and Metabolism:Question 32**

A 43-year-old alcoholic man with type 1 diabetes mellitus for 21 years is admitted from the emergency department for vomiting and diabetic ketoacidosis apparently caused by missing 2 days of insulin treatment. His initial metabolic values included a pH of 7.02, a blood carbon dioxide level of 8 meq/L, a serum potassium level of 5.6 meq/L, large ketones, and a plasma glucose level of 412 mg/dL. After several hours of treatment with intravenous fluids, insulin, and potassium, the glucose level decreases to 130 mg/dL. Intravenous therapy is changed to a subcutaneous twice-daily intermediate-acting insulin plus a sliding-scale short-acting insulin regimen. Eight hours later, the patient is again vomiting. His metabolic values are a pH of 7.09, large ketones, a blood carbon dioxide level of 12 meq/L, a serum potassium level of 5.2 meq/L, and a serum glucose level of 175 mg/dL.

Which of the following is not a reason for the persistent acidosis?

A. Alcohol withdrawal syndrome  
B. Volume expansion acidosis  
C. Premature discontinuation of intravenous insulin administration  
D. Failure to administer sodium bicarbonate  
E. Lack of absorption of subcutaneous insulin

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**Endocrinology and Metabolism:Question 33**

A 37-year-old man presents for a routine physical examination. He has been healthy, has no family history of hypertension, takes no medications, and denies illicit drug use. Blood pressure is 165/100 mm Hg, and pulse rate is 95/min. Therapy with hydrochlorothiazide, 25 mg/d, is started. Over the next 6 months, an angiotensin-converting enzyme inhibitor and a long-acting calcium channel blocker are added, but his blood pressure does not change substantially, although the patient says that he is compliant with therapy. He tells you that in the past few months, he has begun to have short-lived episodes of palpitations, sweating, headache, and tremor that resolve spontaneously.

What is the most appropriate next step in the evaluation of this patient?

A. MRI of the abdomen and pelvis  
B. Metaiodobenzylguanidine scan  
C. Initiation of clonidine therapy  
D. 24-Hour urine sample for measurement of vanillylmandelic acid, catecholamines, and metanephrines after an episode  
E. Exploratory laparotomy
**Endocrinology and Metabolism: Question 34**

A 52-year-old woman has had headaches and progressive loss of vision for the past 5 years. She is otherwise healthy and takes no medications. She underwent menopause at 43 years of age and has not been taking estrogen therapy. Physical examination is normal except for bitemporal hemianopsia that is confirmed on formal visual field examination. Laboratory studies show a serum prolactin level of 118 ng/mL; normal levels of insulin-like growth factor-i and ct-subunit; and low levels of serum free thyroxine, thyroid-stimulating hormone, luteinizing hormone, and follicle-stimulating hormone. Adrenal function is normal. Bone density examination shows osteoporosis of the hip and spine. MRI of the head shows a 2.4-cm mass that arises from the sella and elevates the optic chiasm.

What is the most appropriate next step in the management of this patient's disorder?

A. Repeat prolactin measurement and MRI in 3 months
B. Start estrogen therapy
C. Start dopamine agonist therapy
D. Refer for transsphenoidal surgery
E. Refer for transfrontal surgery

**Endocrinology and Metabolism: Question 35**

An 18-year-old male student presents with delayed puberty. He had a normal childhood growth rate, and was of average height until age 13 years when most of his peers grew taller than he. He does not shave, but he is otherwise healthy. There is no family history of hypogonadism or anosmia. He looks younger than his stated age and has relatively long arms and legs. There are wisps of pubic hair at the base of his penis. There is no gynecomastia. The testes are each 1.5 cm long. The serum testosterone level is 45 ng/dL and serum luteinizing hormone level is 1.0 mU/mL.

Which of the following is the most likely explanation for this man's hypogonadism?

A. Craniopharyngioma
B. Klinefelter's syndrome
C. Gonadotropin-releasing hormone receptor mutation
D. 17-hydroxylase deficiency
E. 21-hydroxylase deficiency

**Endocrinology and Metabolism: Question 36**

A 37-year-old asymptomatic woman presents for a routine physical examination. Physical examination reveals a 2-cm right-sided thyroid nodule that is firm, nontender and moves with swallowing. The rest of the physical examination is unremarkable, including normal reflexes and absence of tremor. The serum thyroid-stimulating hormone level is 1.8 μU/mL. She is referred for fine-needle aspiration biopsy of the thyroid nodule.

Which of the following is true regarding interpreting the cytologic results of thyroid fine-needle aspiration biopsy?

A. Follicular carcinoma can be accurately diagnosed.
B. Most fine-needle aspiration biopsy specimens reveal malignant cells.
C. Follicular adenoma can be accurately diagnosed.
D. Papillary carcinoma can be accurately diagnosed.
E. Cystic nodules are more likely than solid nodules to provide diagnostic material.
**Endocrinology and Metabolism:Question 37**
A 27-year-old woman undergoes screening 1-hour glucose tolerance testing with a 50-g oral glucose load at 24 weeks of her first pregnancy. The 1-hour plasma glucose value is 142 mg/dL. She has a family history of diabetes in her mother and maternal aunts. What is the next step in management?
A. Dietary counseling for gestational diabetes mellitus 
B. Diagnostic 3-hour oral glucose tolerance test with a 100-g glucose load 
C. Measurement of hemoglobin A1C 
D. Measurement of plasma glucose 2 hours after a meal 
E. Reassurance of the patient that she does not have gestational diabetes mellitus

**Endocrinology and Metabolism:Question 38**
Which of the following lipoprotein abnormalities confers a definite risk for coronary heart disease?
A. Increased low-density lipoprotein (LDL) cholesterol 
B. Increased total cholesterol 
C. Increased high-density lipoprotein (HDL) cholesterol 
D. Increased chylomicron triglyceride 
E. Decreased lipoprotein(a)

**Endocrinology and Metabolism:Question 39**
A 67-year-old man with refractory atrial fibrillation is prescribed amiodarone. Thyroid function tests, including antithyroid peroxidase antibodies, were negative before therapy was started. After 6 months, the patient has the following laboratory results:

Laboratory studies:
- Serum free thyroxine: 2.6 ng/dL
- Serum total thyroxine: 13.2 μg/dL
- Serum free triiodothyronine: 116 ng/dL
- Serum thyroid-stimulating hormone: 3.6 μU/mL

The patient has no signs or symptoms of thyrotoxicosis, and thyroid examination is normal. What is the most likely explanation for these findings?
A. Amiodarone-induced thyrotoxicosis 
B. Thyroid-stimulating hormone-producing pituitary tumor 
C. Normal results on thyroid function tests during amiodarone therapy 
D. Euthyroid sick syndrome 
E. Falsely high readings on serum total and free thyroxine assays because of amiodarone therapy

**Endocrinology and Metabolism:Question 40**
A 64-year-old man with a history of myocardial infarction presents to the emergency department with the sudden onset of a severe retro-orbital headache that is associated with dizziness and nausea without vomiting. Physical examination shows a resting blood pressure of 125/85 mm Hg that decreases to 100/60 mm Hg on standing; the pulse rate increases from 76/min to 96/min. The skin is pale and finely wrinkled, and axillary and pubic hair are sparse. Visual field testing by confrontation suggests a bitemporal hemianopsia. The patient mentions increased fatigue and cold intolerance and decreased libido over the past several years, but he attributed this to normal aging.
During evaluation of the decreased libido by a urologist 1 week ago, the serum testosterone level was 92 ng/dL and the serum thyroid-stimulating hormone level was 0.3 μU/mL. MRI in the emergency department shows a 1.8-cm sellar mass with suprasellar extension and compression of the optic chiasm as well as invasion of the cavernous sinuses bilaterally. After administration of contrast, the MRI shows evidence of a large area of hemorrhage within the mass.

What is the most appropriate initial therapy?
A. Emergency neurosurgical decompression of the sella
B. Intravenous hydrocortisone, 100 mg, then 100 mg every 6 to 8 hours
C. Oral hydrocortisone, 20 mg in the morning and 10 mg in the evening daily
D. Fludrocortisone, 0.1 mg/d
E. Levothyroxine, 100 μg intravenously, then 100 μg orally daily

**Endocrinology and Metabolism: Question 41**

A 41-year-old woman presents to the emergency department after a witnessed seizure. She underwent thyroidectomy 2 days ago to treat a 2.3-cm papillary carcinoma. Lymph nodes in the central compartment lacked evidence of metastasis. The patient was discharged the morning after surgery and felt well. She was given triiodothyronine, 25 μg twice daily, at discharge in preparation for anticipated radioiodine therapy in several weeks. On arrival at home, she noticed tremulousness and bothersome paresthesias. She attributed these symptoms to anxiety. Later, however, her right wrist froze in a flexed position when opening a jar and had to be pried off with the left hand. Soon thereafter, on the evening of admission, she collapsed while at home and had generalized convulsions. She has no history of seizure disorder.

What is the most likely cause of this patient’s seizure?
A. Thyroid storm from excessive thyroid hormone replacement
B. Cerebral metastasis from thyroid carcinoma
C. Acute hypocalcemia from surgical hypoparathyroidism
D. Inadequate thyroid replacement
E. Idiosyncratic reaction to inhalation anesthesia

**Endocrinology and Metabolism: Question 42**

A 58-year-old black man has had hypertension for 5 years. He has maintained a blood pressure of 135/85 mm Hg with use of hydrochlorothiazide, 25 mg/d. Laboratory assessment reveals a serum sodium of 141 meq/L, serum potassium of 4.1 meq/L, and fasting plasma glucose of 132 mg/dL.

These values are confirmed on remeasurement several days later.

What is most appropriate management of this patient’s hypertension?
A. Continue the current therapy, with a target blood pressure less than 140/90 mm Hg
B. Discontinue hydrochlorothiazide therapy and begin ramipril therapy
C. Add amlodipine to hydrochlorothiazide therapy
D. Add ramipril to hydrochlorothiazide therapy
E. Increase the hydrochlorothiazide dosage to 50 mg/d
**Endocrinology and Metabolism: Question 43**

A 63-year-old woman recently developed diabetes and hypertension. She has gained 4.4 kg (10 lb) in the past year. She was previously healthy and had four successful pregnancies by 35 years of age. On physical examination, the patient is 155 cm (61 in) tall and weighs 70 kg (154 lb). Blood pressure is 140/90 mm Hg. She has mild hair growth on her upper lip, moderate acanthosis nigricans in the folds of her neck, prominent supraclavicular fat pads, and mild central obesity. The 24-hour urine cortisol excretion is 411 μg. The 8:00 AM serum cortisol level is 26 μg/dL after taking 1 mg of dexamethasone at bedtime and 8.2 μg/dL after taking 8 mg of dexamethasone at bedtime. The plasma adrenocorticotropic hormone level is 50 pg/mL.

What test should be ordered next?

A. CT scan of the adrenal glands
B. MRI of the pituitary gland
C. CT scan of the lungs
D. Bilateral inferior petrosal sinus sampling for adrenocorticotropic hormone
E. Octreotide scan

**Endocrinology and Metabolism: Question 44**

A 49-year-old postmenopausal white woman has the following dual-energy X-ray absorptiometry measurements:
- Spine: T score = -0.9
- Femoral neck: T score = -1.6
- Forearm: T score = -2.6

Except for a recent kidney stone, she has been in good health. Several members of her family also have had nephrolithiasis. Her physical examination is normal.

What is the most appropriate next step in the management of this patient?

A. Observation with a repeat bone density measurement in 2 to 3 years
B. Treatment with a bisphosphonate
C. Treatment with raloxifene
D. A serum biochemical profile and a 24-hour urine calcium and creatinine measurement

**Endocrinology and Metabolism: Question 45**

A 47-year-old man who has had type 1 diabetes mellitus for more than 20 years that is meticulously controlled by using an insulin pump with no known complications presents with his wife because she is concerned that he has been acting strangely. She believes that her husband is having trouble maintaining attention and has spells of irritability that are unpredictable. He also appears to be having more nightmares and restless sleep. He states that he is feeling and acting fine and that his glucose log looks excellent; he believes that his wife is under stress and is projecting her feelings onto him. He states he has not noted hypoglycemia in his routine self-monitoring of glucose and, although he is under usual stresses caused by work and family, he has not been depressed.

Physical examination and review of symptoms are normal. Laboratory values obtained the previous week are normal.

What is the best next step?

A. Refer to a psychiatrist for marriage counseling
B. Order MRI of the head
C. Rule out adrenal insufficiency
D. Increase the frequency of glucose monitoring
E. Perform electroencephalography
Endocrinology and Metabolism:Question 46
A 27-year-old woman has had amenorrhea and infertility for the past 3 years. During an evaluation 1 year ago, a prolactin level of 88 ng/mL and a 3-mm pituitary tumor on MRI were found. Therapy with bromocriptine, 10 mg/d, was started, but the patient stopped taking the drug because of vomiting and dizziness. She then received one course of clomiphene citrate but did not ovulate or become pregnant. She presents to your office for a second opinion. She has not had a spontaneous menstrual cycle in 3 years. She is otherwise healthy and currently takes no medications but is depressed because of her continuing inability to conceive. The serum thyroid-stimulating hormone level is normal and the prolactin level is 80 ng/mL. A pregnancy test is negative.
What is the most appropriate next step in the management of this patient’s disorder?
A. Start therapy with bromocriptine, 1.25 mg/d
B. Administer another course of clomiphene citrate
C. Refer for gonadotropin therapy
D. Refer for transsphenoidal surgery
E. Counsel for depression

Endocrinology and Metabolism:Question 47
A 57-year-old man with established coronary heart disease is being treated with atorvastatin, 40 mg/d. His current lipid profile is as follows:
- Total cholesterol 202 mg/dL
- Low-density lipoprotein (LDL) cholesterol 98 mg/dL
- High-density lipoprotein (HDL) cholesterol 41 mg/dL
- Triglycerides 315 mg/dL
- Non-HDL cholesterol 161 mg/dL
- Very-low-density lipoprotein (VLDL) cholesterol 63 mg/dL
The next step in the management of this patient should focus on which one of the following target values?
A. Serum total cholesterol <200 mg/dL
B. Serum triglycerides <200 mg/dL
C. Serum HDL cholesterol >45 mg/dL
D. Serum non-HDL cholesterol <130 mg/dL
E. High-sensitivity C-reactive protein <0.5 mg/L

Endocrinology and Metabolism:Question 48
A 32-year-old man presents with enlargement and tenderness of the breasts for 6 months. For about 3 years he has been treated with a β-adrenergic antagonist for hypertension; his blood pressure is 128/82 mm Hg. On physical examination, he has bilateral breast enlargement, but no other detectable abnormalities. Laboratory studies:
- Serum testosterone 600 ng/dL
- Serum estradiol 88 pg/mL
- Serum luteinizing hormone 2.6 mU/mL
- Serum follicle-stimulating hormone 1.7 mU/mL
- Serum human chorionic gonadotropin 23,500 ng/mL
What is the most appropriate diagnostic test in this patient?
A. Breast ultrasound
B. MRI of the pituitary gland
C. Ultrasonography of the testes
D. Peripheral blood karyotype
E. Serum prolactin measurement
**Endocrinology and Metabolism: Question 49**

A 45-year-old man presents with fatigue, constipation, and a 2-kg (5-lb) weight gain. The patient has Hashimoto’s thyroiditis and is compliant with taking levothyroxine, 0.25 mg/d. Six months ago, the serum thyroid-stimulating hormone (TSH) level was 1.9 μU/mL and the serum free thyroxine level was 1.3 ng/dL. The serum TSH is now 12.0 μU/mL, and the serum free thyroxine level is 0.8 ng/dL. What is the most likely explanation for the change in thyroid hormone levels?

A. He has been taking sertraline for depression starting 3 months ago.
B. He has begun taking an over-the-counter vitamin B complex supplement and high-dose vitamin C tablets.
C. The pharmacy inadvertently dispensed 0.025-mg tablets to him 3 months earlier.
D. His weight gain has led to a decreased volume of distribution.
E. He has developed adrenal insufficiency.

**Endocrinology and Metabolism: Question 50**

A 44-year-old man presents to the emergency department with polyuria and polydipsia. He has a 2-year history of progressive ataxia, weakness, blurred vision, and slurred speech. MRI has shown lobular areas of enhancement in the pons and middle cerebral peduncles, and a bone scan has shown multiple areas of abnormal uptake. A presumptive brain tumor was diagnosed, and the patient is receiving high-dose dexamethasone (4 mg orally every 6 hours). Over the past 2 weeks, he has noted increased urination with nearly constant thirst; his physician ascribed these symptoms to corticosteroid-induced diabetes mellitus.

Physical examination reveals orthostatic hypotension, cerebellar ataxia, and diffuse muscle weakness but no focal neurologic deficits. Admission laboratory results included a serum sodium of 155 meq/L, plasma glucose of 180 mg/dL, and urine osmolality of 117 mosm/kg H2O. What is the most likely diagnosis?

A. Corticosteroid-induced diabetes mellitus
B. Central diabetes insipidus
C. Nephrogenic diabetes insipidus
D. Primary polydipsia
E. Diabetes insipidus, type undetermined

**Endocrinology and Metabolism: Question 51**

A 78-year-old woman presents for evaluation of weakness. Her medical history includes depression since the death of her husband 3 years ago, for which she takes sertraline; hyperlipidemia, for which she takes simvastatin; and Graves disease, for which she was treated with radioactive iodine 21 years ago and now takes levothyroxine replacement. Over the past year, she has noticed difficulty arising from the seated position and climbing stairs. She has diffuse discomfort in the legs and arms, which she attributes to her statin therapy. Her depression has failed to improve substantially, and she rarely leaves the house. She has anorexia and has lost 7 kg (15 lb) in the past year.

Physical examination reveals an asthenic, elderly woman with normal vital signs; a nonpalpable thyroid; mild hand tremor; marked proximal muscle weakness, especially in the thighs; and mild, diffuse tenderness overlying the long bones of the legs and arms. The rest of the examination is unremarkable. Laboratory studies:

- Hemoglobin: 12.3 g/dL
- Leukocyte count: 5200/μL
- Serum calcium: 8.9 mg/dL
- Serum phosphate: 2.2 mg/dL
- Serum thyroid-stimulating hormone: 0.54 μU/mL
- Serum creatine kinase: 59 U/L
What is the most likely combination of metabolic findings in this patient?
A. Low, parathyroid hormone, normal 25-hydroxyvitamin D3, high 1,25-dihydroxyvitamin D3
B. High parathyroid hormone, low 25-hydroxyvitamin D3, normal 1,25-dihydroxyvitamin D3
C. Low parathyroid hormone, low 25-hydroxyvitamin D3, low 1,25-dihydroxyvitamin D3
D. High parathyroid hormone, high 25-hydroxyvitamin D3, high 1,25-dihydroxyvitamin D3
E. Low parathyroid hormone, low 25-hydroxyvitamin D3, normal 1,25-dihydroxyvitamin D3

**Endocrinology and Metabolism: Question 52**
A 24-year-old woman in the 16th week of her second pregnancy presents for prenatal evaluation. She is 162.5cm (64 in) tall and weighs 56kg (123 lb). Her pre-pregnancy weight was 55kg (120 lb)(body mass index 21.5). She has no history of diabetes mellitus in first-degree relatives and no personal history of diabetes or impaired glucose tolerance. Her son, who is 2 years of age, was a full-term uncomplicated vaginal delivery and had a birth weight of 3 kg (7 lb).
What should you advise the patient regarding screening for gestational diabetes mellitus?
A. 1-Hour plasma glucose testing after a 50-g oral glucose load as soon as possible
B. 1-Hour plasma glucose testing after a 100-g oral glucose load at 26 weeks of pregnancy
C. Measurement of hemoglobin A1C
D. No screening
E. Measurement of fructosamine

**Endocrinology and Metabolism: Question 53**
An 18-year-old ballerina presents because she has been amenorrheic for the last 6 months. Her menses have waned gradually over the past 2 years. Her menarche occurred at 12 years of age, when her height was 155cm (61 in) and body weight was 51 kg (112 lb). Currently, her height is 157cm (62 in) and body weight is 44 kg (97 lb). She had regular menses until 16 years of age. At that time, she was accepted into a prestigious dancing company and increased her dancing and practice time considerably; she also became more preoccupied with maintaining her weight within “an acceptable range for the company.” She denies nausea, vomiting, and laxative or diuretic use. She denies use of illicit or recreational drugs. She states that she eats “enough.”
Which of the following is most likely to be revealed on evaluation?
A. Low sex hormone-binding globulin level
B. Low estradiol, luteinizing hormone, and follicle-stimulating hormone levels
C. Low thyroid-stimulating hormone level
D. Low estradiol level and X chromosome karyotype
E. High ferritin level
Endocrinology and Metabolism: Question 54
A 31-year-old man is referred for management of multidrug-resistant hypertension. His hypertension was diagnosed 2 years ago, and treatment with multiple blood pressure medications, both alone and in combination, has been ineffective. His current medical regimen includes oral hydrochlorothiazide, 25 mg/d; oral amlodipine, 10 mg/d; and atenolol, 100 mg/d.
Blood pressure is 160/100 mm Hg, pulse rate is 80/min and regular, and respiration rate is 18/mm. There is an S4 gallop and trace pretibial edema. The patient has been consistently hypokalemic in the past, with a serum potassium level of 2.5 to 3.4 meq/L even with potassium supplementation.
Laboratory studies:
- Serum creatinine: 1.1 mg/dL
- Blood urea nitrogen: 12 mg/dL
- Serum sodium: 136 meq/L
- Serum potassium: 2.8 meq/L
- Serum chloride: 108 meq/L
- Serum bicarbonate: 30 meq/L
Electrocardiography shows left ventricular hypertrophy by voltage criteria.
What is the most likely diagnosis?
A. Volume and potassium depletion secondary to chronic overdiuresis
B. Pheochromocytoma
C. Primary aldosteronism
D. Severe essential hypertension
E. Bartters syndrome

Endocrinology and Metabolism: Question 55
A 37-year-old woman presents with polydipsia, polyphagia, a 4.5-kg (10-lb) weight loss over the past 6 months, and poor wound healing. She gives a medical history of delivering a 4.8-kg (10.5-lb) baby with subsequent respiratory distress syndrome. The random plasma glucose level is 375 mg/dL, and the hemoglobin A1C is 10.3%.
She is 160 cm (63 in) tall and weighs 61 kg (135 lb).
What is the most appropriate initial therapy?
A. Medical nutrition
B. Metformin
C. Glimepiride
D. Basal insulin

Endocrinology and Metabolism: Question 56
A 22-year-old woman presents to the emergency department with severe dizziness, weakness, nausea, and vomiting of 1 week’s duration. She has noted fatigue and moderate weight loss over the preceding 2 months. She has a history of hypothyroidism and takes levothyroxine, 100 μg/d.
On physical examination, the patient is 168 cm (66 in) tall and weighs 53 kg (116 lb). Blood pressure is 90/60 mm Hg supine and 80/50 mm Hg standing, and pulse rate is 84/min supine and 96/mm standing. The skin is well tanned, and there is markedly increased pigmentation of the gums and palmar creases.
Laboratory studies:
- Hematocrit: 40%
- Serum creatinine: 1.2 mg/dL
- Blood urea nitrogen: 39 mg/dL
- Serum sodium: 124 meq/L
- Serum potassium: 6.8 meq/L
- Plasma glucose: 61 mg/dL
What is the most likely underlying cause of this patient’s condition?
A. Pituitary apoplexy
B. Acute adrenal hemorrhage
C. Fulminant meningococcemia
D. Autoimmune adrenalitis
E. Tuberculosis

**Endocrinology and Metabolism: Question 57**

A 62-year-old postmenopausal white woman has been treated with a combination of an estrogen and a progestin for 5 years to prevent osteoporotic fracture. Her mother died after sustaining an atraumatic hip fracture. Because of the results of the Women’s Health Initiative trial, she had decided to stop taking estrogens. She takes calcium and vitamin D and does weight-bearing exercise five times a week. The results of dual-energy X-ray absorptiometry are as follows:
Spine: T score = -2.8  
Femoral Neck: T score = -2.1
She wants to do everything she can to prevent a fracture.

Which of the following medications have been shown to decrease the risk for nonvertebral fractures in such patients?
A. Bisphosphonates and teriparatide
B. Bisphosphonates and raloxifene
C. Bisphosphonates and calcitonin
D. Raloxifene and teriparatide
E. Raloxifene and calcitonin

**Endocrinology and Metabolism: Question 58**

A 58-year-old man is being evaluated for primary hyperparathyroidism after several episodes of ureteral colic due to calcium oxalate stones. The medical history is notable for severe chronic obstructive pulmonary disease due to long-term smoking. The serum calcium level is 11.3 to 11.8 mg/dL, intact parathyroid hormone level is 168 pg/mL, and 24-hour urinary calcium output is 416 mg.
A sestamibi parathyroid scan is obtained before referral to a parathyroid surgeon. On the delayed images, an intense focus of radioisotope activity is seen in the right lower neck, which is compatible with a right inferior parathyroid adenoma.

What is the most appropriate surgery?
A. Minimally invasive parathyroidectomy with intraoperative parathyroid hormone measurement
B. Conventional parathyroidectomy with resection of the right lower parathyroid and inspection of the other three glands
C. Subtotal parathyroidectomy, leaving one-half gland in situ
D. Subtotal parathyroidectomy, transplanting one-half gland in the forearm
E. Arteriectomy followed by catheter embolization of the adenoma

**Endocrinology and Metabolism: Question 59**

A 58-year-old man presents with a 4-year history of type 2 diabetes found by incidental blood glucose testing. He is 183 cm (72 in) tall and weighs 95 kg (210 lb). He takes metformin, 1000 mg/d, and glyburide, 10 mg/d, but he continues to have home blood glucose values greater than 200 mg/dL. The hemoglobin A1C is 9.6%.
He has no microvascular or macrovascular complications.
What is the most appropriate next step in the management of this patient?
A. Begin a low-carbohydrate diet
B. Increase the glyburide dosage
C. Increase the metformin dosage
D. Begin pioglitazone therapy
E. Begin basal insulin therapy
Endocrinology and Metabolism: Question 60
A 56-year-old man has had headaches, decreasing vision, joint and muscle aches, and low libido for 10 years. Physical examination shows acromegalic features and bitemporal visual field defects. MRI shows a 3-cm pituitary mass elevating the optic chiasm. Laboratory tests show an elevated insulin-like growth factor-I level, a low testosterone level, normal prolactin level, and normal thyroid and adrenal function. He is referred to a neurosurgeon, who performs transsphenoidal debulking of the tumor.

Three months after surgery, the patient feels much better and his vision has improved. His insulin-like growth factor-I level is now mildly elevated, and MRI shows no residual tumor. The testosterone level is still low, and testosterone replacement therapy is started. Thyroid and adrenal function are still normal.

What is the most appropriate next step in this patient’s management?
A. Monitor with repeated insulin-like growth factor-I measurement and MRI in 6 months
B. Refer back to the neurosurgeon for repeat transsphenoidal surgery
C. Start bromocriptine therapy
D. Refer for radiation therapy
E. Start octreotide therapy

Endocrinology and Metabolism: Question 61
A 73-year-old woman presents with a fasting plasma glucose level of 325 mg/dL and no ketones on routine examination. She is asymptomatic and has no evidence of microvascular or macrovascular disease. She is 157 cm (62 in) tall and weighs 50 kg (110 lb). She takes no medications and has no family history of diabetes.

Measurement of which of the following would differentiate the cause of this patient's diabetes?
A. Anti-glutamic acid decarboxylase antibodies
B. Fasting C-peptide
C. Plasma insulin
D. Plasma cortisol

Endocrinology and Metabolism: Question 62
Which of the following agents is appropriate for the therapy of a patient with a serum triglyceride level of >1000 mg/dL?
A. Niacin
B. A statin
C. A bile acid sequestrant
D. Ezetemibe

Endocrinology and Metabolism: Question 63
A 23-year-old man with a delusional psychiatric illness, a history of chronic dyspepsia, and multiple overdoses in the past decade presents with polyuria and polydipsia. Medications include olanzapine and clonazepam.

Laboratory studies:
- Serum creatinine: 2.3 mg/dL
- Serum bicarbonate: 32 meq/L
- Serum phosphate: 5.8 mg/dL
- Serum calcium: 12.2 mg/dL
- Intact parathyroid hormone: <.5 pg/mL (normal, 10–65 pg/mL)
- Serum 25-hydroxyvitamin D3: 23.2 ng/mL (normal, 9–52 ng/mL)
- Serum 1,25-dihydroxyvitamin D3: 31.7 pg/mL (normal, 15–60 pg/mL)
Which of the following ingestions is likely to be the cause of this patient's hypercalcemia?
A. Dairy products
B. Calcium carbonate
C. Vitamin D
D. Lithium
E. Famotidine

Endocrinology and Metabolism: Question 64
A 34-year-old woman has mild fatigue. She does not have constipation, cold intolerance, menorrhagia, or dry skin. There is no family history of coronary artery disease.
Physical examination, including thyroid examination, is normal. Laboratory tests reveal a serum thyroid-stimulating hormone concentration of 6.0 μIU/mL and a free thyroxine level of 1.7 ng/dL. Complete blood count, renal and hepatic function, and lipid profile are normal.
What is the most appropriate next step in the management of this patient?
A. Initiate therapy with levothyroxine and repeat laboratory tests in 6 weeks
B. Measure thyroid-stimulating hormone, free thyroxine, and antithyroid peroxidase antibodies in weeks
C. Perform physical examination and thyroid-stimulating hormone measurement in 1 year
D. Start therapy with an antidepressant
E. Measure thyroid-stimulating hormone and free thyroxine in 5 years

Endocrinology and Metabolism: Question 65
A 32-year-old man presents with a 3-month history of progressive fatigue, weakness, dizziness when standing, poor appetite, frequent nausea, and a 14-kg (30-lb) weight loss. His medical history is significant only for hypothyroidism, which was diagnosed 6 months ago and is treated with levothyroxine, 150 μg/d.
On physical examination, the patient is 193 cm (76 in) tall and weighs 69 kg (151 lb). Blood pressure is 100/70 mm Hg while he is supine and 90/66 mm Hg while he is sitting upright. The skin is slightly tanned, and there is increased pigment in the palmar creases.
Laboratory studies:
- Hematocrit: 38.4%
- Serum creatinine: 1.1 mg/dL
- Blood urea nitrogen: 36 mg/dL
- Serum sodium: 132 meq/L
- Serum potassium: 5.0 meq/L
- Plasma glucose: 64 mg/dL
Which of the following tests is the most appropriate next step?
A. CT scan of the adrenal glands
B. Short cosyntropin stimulation test
C. Corticotropin-releasing factor stimulation test
D. Insulin tolerance test
E. Metyrapone test
Endocrinology and Metabolism: Question 66
A 45-year-old woman presents for an annual physical examination. Her medical history is significant only for mild arthritis and type 2 diabetes that is well controlled with metformin, 500 mg twice daily. She has no history of hypertension and does not smoke. She has no personal or family history of heart disease. She exercises daily and follows a low-fat diet. Laboratory evaluation reveals a serum total cholesterol of 220 mg/dL, HDL cholesterol of 42 mg/dL, and triglycerides of 185 mg/dL. The calculated LDL cholesterol is 141 mg/dL.
What is the next step in management?
A. Continue current diet and exercise program
B. Start low-carbohydrate diet
C. Start therapy with an HMG-CoA reductase inhibitor (a statin)
D. Start therapy with nicotinic acid
E. Start therapy with a bile acid sequestrant

Endocrinology and Metabolism: Question 67
A 52-year-old man has had type 2 diabetes for 9 years. He takes metformin, 500 mg twice daily, and a sulfonylurea. He has had no known complications of therapy. However, his hemoglobin A1C have been greater than 7.5% at the past two visits. The metformin dose was increased at the last visit, and the patient has begun an exercise program, running for 30 minutes every morning. He has restricted intake of refined carbohydrates and saturated fats but still has not lost a substantial amount of weight. At this visit, the urinary microalbumin-to-creatinine ratio is greater than 30.
What is the most appropriate next step in management?
A. Counsel the patient on restricting dietary protein
B. Begin therapy with aspirin, 81 mg/d
C. Begin therapy with an angiotensin-converting enzyme inhibitor or an angiotensin receptor blocker
D. Repeat the microalbumin test
E. Measure 24-hour urinary protein

Endocrinology and Metabolism: Question 68
A 32-year-old man presents for follow-up evaluation after he was found to have a fasting plasma glucose level of 132 mg/dL as part of a recent preemployment physical examination. He is concerned that he will be labeled as having diabetes. His mother has a history of type 2 diabetes and his father has a history of hypertension. He is active and works out at the gym for 45 minutes three times weekly. He has never been overweight. He does not have polyuria, polyphagia, or polydipsia, and his vision has been fine. His only complaint is mild fatigue.
The patient is 173 cm (68 in) tall and weighs 70 kg (155 lb) (body mass index, 23.5). Blood pressure and other findings on physical examination are normal.
What is the next step in management?
A. Measure hemoglobin A1C
B. Obtain a random blood glucose measurement
C. Measure fructosamine
D. Repeat plasma glucose concentration after an 8-hour fast
E. Reassure the patient that he does not have diabetes
Endocrinology and Metabolism: Question 69
A 67-year-old man presents for evaluation after sustaining a hip fracture during a fall. His bone density measurement shows bone loss out of proportion to his age. He has a 10-year history of excessive alcohol consumption and Pagets disease in the spine. What is the most appropriate treatment for this patient’s osteoporosis?
A. Raloxifene  
B. Alendronate  
C. Nasal calcitonin  
D. Teriparatide  
E. Testosterone

Endocrinology and Metabolism: Question 70
A 34-year-old woman presents with fatigue and constipation. She has a documented history of hypothyroidism that has been well managed with levothyroxine, 0.125 mg/d, for 5 years. She complies with her medication regimen and takes no other prescription medications. Six months ago, the serum thyroid-stimulating hormone and free thyroxine concentrations were 1.2 μU/mL and 1.8 ng/dL, respectively. Physical examination reveals dry, cool skin. The relaxation phases of the deep tendon reflexes are delayed. Laboratory studies show a thyroid-stimulating hormone of 11.3 μU/mL and a free thyroxine level of 0.85 ng/dL. Concomitant use of which of the following agents would explain the clinical change?
A. Acetaminophen  
B. Aspirin  
C. St. John's wort  
D. Calcium carbonate  
E. Famotidine

Endocrinology and Metabolism: Question 71
A 65-year-old man is referred for an elevated blood pressure. He has a blood pressure of 165/95 mm Hg; he is 170 cm (67 in) tall and weighs 86.5 kg (190 lb), with a waist circumference of 106.5 cm (42 in). Fasting lipid profile yields the following results: serum total cholesterol 284 mg/dL; triglycerides 300 mg/dL; HDL cholesterol 34 mg/dL; and LDL cholesterol 190 mg/dL. He smokes a pack of cigarettes per day, consumes a typical American diet with frequent consumption of fast food, and has a sedentary lifestyle. He has no symptoms of coronary heart disease, and his electrocardiogram is normal. The patient's calculated Framingham risk is >30% for coronary heart disease within the next 10 years. What is the most appropriate management for this patient?
A. Begin a therapeutic lifestyle change diet and exercise program with a follow-up appointment in 6 months  
B. Begin therapy with a statin with the goal of lowering his LDL cholesterol to 130 mg/dL  
C. Begin therapy with a statin with the goal of lowering his LDL cholesterol to <100 mg/dL and his non-HDL cholesterol to <130 mg/dL.  
D. Begin therapy a bile acid sequestrant  
E. Begin therapy with an insulin sensitizer
Endocrinology and Metabolism: Question 72
A 25-year-old previously healthy woman presents with severe polyuria and polydipsia over the past month. Because of near-constant thirst, she drinks 5 to 7 L of water daily in addition to other fluids. She has noted increased tiredness but attributes this to having to awaken four to five times nightly to urinate. She states that cold fluids in particular help to satisfy her thirst. Medical history is significant for the birth of her first child approximately 9 months ago and persistent amenorrhea since that time, even though she breast-fed for only 3 months. Physical examination is unremarkable except for small amounts of expressible galactorrhea bilaterally. Initial laboratory testing reveals a serum sodium level of 140 meq/L, fasting plasma glucose level of 90 mg/dL, and urine osmolality of 95 mosm/kg H2O. MRI of the head shows normal brain parenchyma. The pituitary gland is enhanced homogeneously without focal abnormalities after gadolinium administration. The posterior pituitary bright spot is absent and the pituitary stalk is thickened to 5 to 6 mm.
Which of the following would most likely identify the cause of this patient’s polyuria and polydipsia?
A. Measurement of plasma arginine vasopressin
B. Administration of 1-deamino-8-D-arginine vasopressin
C. Water deprivation test
D. Measurement of serum prolactin
E. Biopsy of the pituitary stalk

Endocrinology and Metabolism: Question 73
A 53-year-old woman presents because of frequent, increasingly severe hot flushes, daytime fatigue, loss of concentration, absent menses for the past 18 months, and dyspareunia. She is 160 cm (64 in) tall and weighs 67 kg (146 lb). She does not smoke and exercises regularly. She has had regular negative mammograms. Her mother and maternal grandmother had osteoporosis and compression fractures. She has no family history of breast, diabetes, or cardiovascular disease. The fasting plasma glucose level is 93 mg/dL, total cholesterol level is 210 mg/dL, and high-density lipoprotein cholesterol level is 57 mg/dL.
Which of the following is not indicated for management of this patient’s menopausal symptoms?
A. Raloxifene
B. Low-dose, short-term combination estrogen/progesterone therapy
C. Vaginal lubrication
D. Calcium and vitamin D

Endocrinology and Metabolism: Question 74
A 42-year-old asthmatic woman has received up to 60 mg of prednisone a day continuously for the past 2 years to control her respiratory symptoms. She is referred to you with the following dual-energy X-ray absorptiometry results:
Spine: T score = -4.5
Femoral neck: T score = -3.1
What is the most appropriate medication for the treatment of this woman’s osteoporosis and for decreasing her risk for fracture?
A. A bisphosphonate
B. Raloxifene
C. Teriparatide
D. Calcitonin
E. Fluoride
**Endocrinology and Metabolism: Question 75**

A 32-year-old woman was involved in an automobile accident and briefly lost consciousness. MRI showed no traumatic damage to the brain, but a 4-mm hypointense area in the pituitary gland was noted. She is referred to you for further evaluation of the lesion after recovery from the accident. The patient reports normal menstrual cycles, no symptoms of Cushing's syndrome or acromegaly, and no symptoms of hypothyroidism or hypoadrenalism. Physical examination is normal. The serum prolactin level and thyroid function tests are normal.

What is the most appropriate next step in this patient’s management?

A. Repeat MRI in 6 months  
B. Refer for transsphenoidal surgery to remove the tumor  
C. Refer for biopsy of the lesion  
D. Obtain formal visual field examination  
E. Start dopamine agonist therapy

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**Endocrinology and Metabolism: Question 76**

A 22-year-old woman who has had type 1 diabetes mellitus for the past 5 years presents to your office. She has been feeling well and has not experienced weight loss, polyuria, or polydipsia. A recent dilated funduscopic examination performed by her ophthalmologist did not reveal proliferative retinopathy but did show early background retinopathy. She takes a split-mix regimen of NPH and regular insulin for glycemic control. She senses hypoglycemia with palpitations, tremor, and diaphoresis and states that she has not had a hypoglycemic reaction in years.

On physical examination, the blood pressure is 110/70 mm Hg. The extremities have normal position and vibratory sensation. Pedal pulses are normal, and no skin ulcerations are noted. Laboratory studies reveal a hemoglobin A1C level of 8.2%, serum creatinine concentration of 0.8 mg/dL, and no urine microalbumin.

What is the next step in management?

A. Add an insulin sensitizer to her insulin regimen  
B. Optimize the insulin regimen to achieve a hemoglobin A1C level less than 8.0%  
C. Optimize the insulin regimen to achieve a hemoglobin A1C level less than 7.0%  
D. Optimize the insulin regimen to achieve a fasting glucose level less than 150 mg/dL  
E. Optimize the insulin regimen to achieve a postprandial glucose level less than 200 mg/dL

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**Endocrinology and Metabolism: Question 77**

A 60-year-old man consults with you to evaluate his treatment for hypogonadism. Ten years ago after several years of decreased libido and erectile dysfunction, he was found to have testosterone deficiency. At that time, the serum testosterone level was 120 ng/dL, and the prolactin level was 76 ng/mL. MRI of the pituitary gland was normal. He is treated with bromocriptine, 2.5 mg/d, with alleviation of his symptoms and improvement of sexual function. Five years ago, however, erectile dysfunction returned although his libido was intact. His physician prescribed testosterone. Although he was initially treated with injections of testosterone enanthate, two years ago he changed to testosterone gel at a dose of 10 g/d. This was associated with a good response.

Physical examination reveals bilateral gynecomastia and a slight decrease in the size of the testes to 4.0 cm in length bilaterally. The serum testosterone level is 750 ng/dL. Complete blood count shows a hemoglobin of 17.1 g/dL, hematocrit of 55%, leukocyte count of 6500/μL, and platelet count of 230,000/μL. MRI of the pituitary gland is normal.
Which of the following is the most appropriate management of this patient?
A. Change treatment from bromocriptine to cabergoline
B. Measure erythropoietin in blood
C. Measure serum iron and transferrin
D. Refer the patient for bone marrow biopsy
E. Reduce the dosage of testosterone

**Endocrinology and Metabolism: Question 78**

A 58-year-old man with a history of type 2 diabetes mellitus presents for diabetes management. His current medications include metformin, 1000 mg twice daily; ramipril, 5 mg/d; hydrochlorothiazide, 50 mg/d; and atorvastatin, 20 mg/d. The blood glucose level according to home blood glucose monitoring is less than 150 mg/dL, and the patient feels well. On physical examination, the blood pressure is 124/72 mm Hg. Mild peripheral neuropathy is present.

Hemoglobin A1C 6.5%
Plasma glucose 225 mg/dL
Serum sodium 140 meq/L
Serum potassium 4.8 meq/L
Serum bicarbonate 26 meq/L
Serum chloride 103 meq/L
Serum total cholesterol 200 mg/dL
Serum high-density lipoprotein cholesterol 43 mg/dL
Serum triglycerides 290 mg/dL

The calculated serum low-density lipoprotein cholesterol level is 99 mg/dL.

What is the most appropriate management of this patient's underlying disease?
A. Repeat lipid measurements and obtain a direct low-density lipoprotein cholesterol measurement
B. Increase the atorvastatin dosage to 40 mg/d
C. Add glyburide, 5 mg/d
D. Decrease the ramipril dosage to 2.5 mg/d
E. Discontinue hydrochlorothiazide therapy

**Endocrinology and Metabolism: Question 79**

Which of the following is not a high-risk marker for cardiovascular disease?
A. Blood pressure greater than 135/85 mm Hg
B. Low-density lipoprotein cholesterol level greater than 130 mg/dL
C. Fasting glucose level greater than 126 mg/dL
D. Urinary microalbumin-to-creatinine ratio greater than 30
E. High-sensitivity C-reactive protein level less than 0.25 mg/dL

**Endocrinology and Metabolism: Question 80**

A 45-year-old man with a history of coronary heart disease is evaluated for a lipid disorder. He has been taking simvastatin, 40 mg/d, for the past year with no significant side effects; however, his coronary heart disease has continued to progress. He exercises regularly and is following the therapeutic lifestyle change diet.

A lipid profile demonstrates the following results: serum total cholesterol 200 mg/dL; triglycerides 150 mg/dL; HDL cholesterol 41 mg/dL; and LDL cholesterol 125 mg/dL. Thyroid function and liver function are normal.

What is the most appropriate therapy for this patient?
A. Increase the dosage of simvastatin to 80 mg/d
B. No further lipid-lowering therapy
C. Add a bile acid sequestrant or ezetimide
D. Add gemfibrozil, 150 mg twice daily
**Endocrinology and Metabolism: Question 81**

A 27-year-old woman is referred for treatment of mild Graves disease with mild ophthalmopathy. Laboratory test results from her referring physician include a serum thyroid-stimulating hormone level of 0.003 μU/mL, free thyroxine level of 2.5 ng/dL, and total triiodothyronine level of 300 ng/dL. She has just missed a menstrual cycle. Physical examination shows mild proptosis, a 60-g diffuse non-nodular thyroid goiter (normal, 15 g), heart rate of 100/min at rest, and a mild fine resting tremor. Before thyroid scanning and uptake is performed, she is given atenolol, 50 mg/d, and her serum 3-human chorionic gonadotropin level indicates pregnancy.

What is the most appropriate initial therapy for this patient?

A. Continue the β-blocker and start methimazole, 60 mg/d
B. Continue the β-blocker and start propylthiouracil, 50 mg every 8 hours
C. Provide no therapy because results are consistent with normal pregnancy
D. Administer iodine-131 after the first trimester
E. Administer β-blocker only

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**Endocrinology and Metabolism: Question 82**

A 68-year-old man is referred to you for evaluation of radiographic findings in the pelvis. He presented to the emergency department 1 week ago with abdominal pain, and a radiograph of the kidneys, ureters, and bladder showed sclerotic changes in the left hemipelvis that are typical for Paget’s disease of bone; the abdominal pain resolved.

The patient has no family history of Paget’s disease and no bone pain. On physical examination, he has a full range of motion in both hips and no angioid streaks are observed on funduscopic examination. A recent measurement of serum acid phosphatase concentration was normal.

Which of the following would be most appropriate for this patient?

A. Measurement of serum alkaline phosphatase and a bone scan
B. Radiographs of his skull and long bones and measurement of a bone-specific alkaline phosphatase and urinary hydroxyproline
C. Bone biopsy of the left iliac crest
D. Treatment with no further work-up
E. No treatment and no further work-up

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**Endocrinology and Metabolism: Question 83**

Which of the following statements is true of continuous subcutaneous insulin infusion?

A. It decreases the requirements for home glucose monitoring
B. It increases the risk for hypoglycemia
C. It is associated with an increased variation in insulin absorption
D. It offers programmable insulin delivery to match physiologic needs
E. It decreases options for dosing insulin
Endocrinology and Metabolism: Question 84

A previously healthy 28-year-old man is brought unconscious to the emergency department. The blood glucose level is found to be 28 mg/dL. After being resuscitated with intravenous glucose, he reports several near-syncopal episodes over the past 6 weeks, each of which was followed by a headache. He also reports a 4.5-kg (10-Ib) weight gain. He has no medical history of such events. He denies excessive alcohol intake. His brother-in-law has type 2 diabetes and has begun insulin therapy after oral antihyperglycemic therapy failed.

Laboratory studies:

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Normal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum insulin</td>
<td>42 mU/L</td>
<td></td>
</tr>
<tr>
<td>Serum C-peptide</td>
<td>7.2 ng/mL</td>
<td>0.9 to 4.0 ng/mL</td>
</tr>
<tr>
<td>Serum proinsulin</td>
<td>74 pmol/L</td>
<td>2.0 to 2.6 pmol/L</td>
</tr>
<tr>
<td>Serum cortisol</td>
<td>30 μg/dL</td>
<td></td>
</tr>
</tbody>
</table>

What diagnostic study is most likely to identify the cause of this patient's hypoglycemia?
A. Measurement of serum insulin and proinsulin during a 72-hour fast
B. Measurement of insulin antibodies
C. Urine screening for sulfonylureas
D. Measurement of serum metformin
E. Computed tomography of the abdomen

Endocrinology and Metabolism: Question 85

You are called to consult on an 82-year-old man who is in the intensive care unit with multiple system failure and hypocalcemia. He was admitted 2 months ago with multilobar pneumococcal pneumonia and respiratory failure. His course has been complicated by difficulty in weaning from the ventilator, non-Q-wave myocardial infarction, prolonged ileus, line sepsis, and sacral decubiti. The serum calcium level has gradually decreased from 9.2 mg/dL on admission to 7.6 mg/dL on the day before the consultation.

What is the first piece of information that is needed?
A. Serum phosphate concentration
B. Serum calcium concentration
C. Serum parathyroid hormone concentration
D. Date of last blood transfusion
E. Serum albumin concentration

Endocrinology and Metabolism: Question 86

A 50-year-old man reports that he had a brief dizzy spell associated with some numbness of his extremities. He recovered completely from this episode and currently has no symptoms. MRI of the head shows a 2.1-cm mass that arises from the sella and abuts the optic chiasm. Physical examination is normal. Laboratory tests show normal levels of prolactin, insulin-like growth factor-1, and thyroid and adrenal hormones. His testosterone level is slightly low. Formal visual field examination shows small areas of bitemporal hemianopsia, of which the patient was unaware.

What is the most appropriate next step in this patient's management?
A. Repeat MRI in 6 months
B. Repeat visual field examination in 3 months
C. Refer for transsphenoidal surgery
D. Start dopamine agonist therapy
E. Start testosterone therapy
**Endocrinology and Metabolism: Question 87**

A 58-year-old woman presents with pain in her left femur, which is relieved with ibuprofen. Physical examination shows no evidence of bowing, but there is warmth over the femur. The total serum alkaline phosphatase activity is elevated, and a bone scan shows uptake of the radionuclide in the left tibia and the skull. Radiographs of the femur and skull show the typical osteoblastic changes of Paget’s disease.

Which treatment option is most appropriate for this patient?
A. Nasal calcitonin  
B. A bisphosphonate  
C. Gallium nitrate  
D. Plicamycin  
E. No treatment

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**Endocrinology and Metabolism: Question 88**

A 35-year-old woman is evaluated for elevated cholesterol. Her weight is normal, and she does vigorous aerobic exercise for 1 hour five times weekly, during which she has no symptoms of coronary heart disease. She underwent a tubal ligation following the birth of her second child. There is a strong family history of coronary heart disease. On physical examination, she has cutaneous infiltrates above both eyes and large lumps on both Achilles tendons.

Laboratory studies:
- Plasma glucose: 85 mg/dL
- Serum thyroid-stimulating hormone: 1.5 μU/mL
- Serum total cholesterol: 450 mg/dL
- Serum triglycerides: 100 mg/dL
- Serum high-density lipoprotein cholesterol: 55 mg/dL
- Serum low-density lipoprotein cholesterol: 375 mg/dL

What is the most appropriate next step in the management of this patient’s condition?
A. Measure C-reactive protein, lipoprotein(a), and homocysteine.  
B. Prescribe a step 1 diet.  
C. Begin therapy with a statin.  
D. Repeat lipid profile in 6 months.  
E. Suspect laboratory error and repeat lipid profile.

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**Endocrinology and Metabolism: Question 89**

A 74-year-old man is admitted to the intensive care unit with chronic obstructive pulmonary disease and sepsis. He is intubated and not verbally responsive. He has no known endocrinopathy.

Physical examination reveals a blood pressure of 88/50 mm Hg, pulse rate of 64/min, and a temperature of 36°C (96.8°F). There are signs of right lower lobe consolidation. Thyroid function tests show a serum thyroid-stimulating hormone level of 0.4 μU/mL, free thyroxine level of 1.2 ng/dL, and total triiodothyronine level of 50 ng/dL.

What is the most probable explanation for the thyroid function test results in this patient?
A. Primary hyperthyroidism  
B. Secondary hyperthyroidism  
C. Primary hypothyroidism  
D. Secondary hypothyroidism  
E. Euthyroid sick syndrome
**Endocrinology and Metabolism: Question 90**
A 63-year-old woman with osteoporosis is referred because of hyperparathyroidism. She has a history of celiac sprue, for which she complies in part with a gluten-free diet. Previous dual-energy X-ray absorptiometry revealed T scores in the osteopenic range. The radiology report included a recommendation that secondary causes of bone loss be excluded. The serum calcium level is normal at 9.0 mg/dL, and the intact parathyroid hormone level is 73 pg/mL. For the past several years, she has supplemented her diet with 1200 mg of calcium citrate daily, including 400 IU of vitamin D.

What is the best test to further assess the patient’s calcium metabolism?
A. Repeated parathyroid hormone
B. Vitamin D metabolites
C. Tissue transglutaminase
D. Urine calcium
E. Calcitonin level

**Endocrinology and Metabolism: Question 91**
A 58-year-old man with polyostotic Paget’s disease returns to your office for follow-up 3 months after beginning therapy with alendronate.

Which of the following is the most appropriate study to assess the disease activity of this patient’s Paget’s disease?
A. Total serum alkaline phosphatase
B. Bone biopsy
C. Radiographs of the affected bone
D. Bone-specific alkaline phosphatase
E. Urinary hydroxyproline or pyridinoline crosslinks

**Endocrinology and Metabolism: Question 92**
A 34-year-old woman has a history of thyroid cancer treated with thyroidectomy and iodine-131. The disease is in complete remission, as confirmed by two whole-body iodine-131 scans and appropriate thyroid-stimulating hormone-stimulated thyroglobulin levels. She has taken levothyroxine, 0.2 mg/d, for the past 3 years, and her serum thyroid-stimulating hormone levels have been consistently near 0.1 μU/mL. She is now 7 weeks pregnant and presents for counseling on maintenance of mid TSH suppression during pregnancy to limit potential recurrence of thyroid cancer.

What change in the levothyroxine therapy would be required to maintain thyroid-stimulating hormone suppression during pregnancy?
A. No change
B. An increase in dose
C. A decrease in dose
D. Levothyroxine should be discontinued and triiodothyronine started
E. Levothyroxine should be discontinued during pregnancy
A 68-year-old man is brought to the emergency department for progressive lethargy. He has known lung cancer and has recently completed a course of radiation therapy for disease confined to the left lung and mediastinum. A bone scan obtained 1 month ago was normal. Medical history includes hypertension, for which he takes atenolol, hydrochlorothiazide, and amlodipine. Over the past 2 to 3 weeks, the family has noted increasing forgetfulness. During the past 48 hours, the patient’s level of consciousness has declined substantially.

On arrival, the patient is somnolent but intermittently arousable. Blood pressure is 102/68 mm Hg, and pulse rate is 104/min. He appears volume depleted, with poor skin turgor and dry mucous membranes. The examination is remarkable for dullness to percussion and decreased breath sounds overlying the left lung field.

Laboratory studies:
- Blood urea nitrogen: 63 mg/dL
- Serum sodium: 149 meq/L
- Serum creatinine: 2.1 mg/dL
- Serum calcium: 15.4 mg/dL
- Serum phosphate: 3.8 mg/dL

What is the least appropriate initial measure in this patient’s care?
A. Change hydrochlorothiazide to furosemide to increase urinary calcium excretion
B. Measure parathyroid hormone receptor protein
C. Measure parathyroid hormone
D. Administer intravenous saline
E. Administer intravenous zolendronate
ANSWERS
Endocrinology and Metabolism:Question 1
The correct answer is D

Educational Objectives
Understand the natural history of β-cell dysfunction in type 2 diabetes and the rationale for combination therapy.

Critique
The goals of therapy for type 2 diabetes include an ideal hemoglobin A1C level less than 6.5% to 7%. A change in the therapeutic regimen is therefore indicated. The United Kingdom Prospective Diabetes Study demonstrated the progressive nature of type 2 diabetes and secondary failure of both medical nutrition therapy and monotherapy with sulfonylureas. Furthermore, sulfonylurea therapy is frequently associated with weight gain, which worsens insulin resistance. Finally, the maximal effective dosing of sulfonylureas is less than the maximally approved dose. Glycemic control rarely improves with sulfonylurea dosing beyond approximately 50% of the approved maximum amount. Multiple studies have demonstrated the advantage of adding synergistic therapies rather than substituting therapies. The addition of metformin to sulfonylurea is considerably more advantageous than replacing the sulfonylurea in the case of secondary sulfonylurea failure. The pathophysiology of type 2 diabetes suggests a benefit to the combination of an insulin secretagogue, such as glyburide, with an insulin sensitizer, such as metformin. Although the addition of pioglitazone, another insulin sensitizer, has been shown to be effective in decreasing the hemoglobin A1C level, it is associated with further weight gain. Addition of metformin to therapy with an insulin secretagogue appears to be more weight neutral and would thus have relative advantage in a patient with progressive weight gain.

Endocrinology and Metabolism:Question 2
The correct answer is B

Educational Objectives
Recognize persistent or incompletely treated active Graves disease.

Critique
This patient has persistent Graves disease with thyrotoxicosis related to either persistence or recurrence of high titers of TSH receptor antibodies stimulating her thyroid remnants. After radioiodine therapy, there commonly occurs a form of radiation thyroiditis with associated thyroid hypofunction leading to the premature diagnosis of permanent postradioiodine hypothyroidism. Levothyroxine therapy is initiated, but the residual thyroid tissue not fully ablated by the treatment will begin to synthesize and release T4 and T3. This does not occur in the absence of TSH-receptor antibodies. The T4 being released from the thyroid gland complements that being taken as presumed replacement dosage, resulting in a total or combined supraphysiologic amount. Thus, the need for the progressively reduction in her dosage of exogenous thyroxine. This condition is not pure T3 toxicosis because the free T4 is also elevated. Hashitoxicosis is a rare presentation of hyperthyroidism in patients with Hashimoto’s thyroiditis. The latter is marked by high titers of antithyroid peroxidase and anti-thyroglobulin antibodies, but not anti-TSH receptor antibodies. Without evidence of these antibodies and in view of her history of Graves disease, there is no reason to consider a diagnosis of Hashimoto’s disease. Radioiodine-induced thyrotoxicosis occurs within days or weeks of treatment and would not occur spontaneously a year and a half later. Struma ovarii refers to ectopic thyroid tissue in an ovarian teratoma and can rarely cause thyrotoxicosis.
In such cases, the source of the thyroid hyperfunction is in the pelvis and there is no radioiodine uptake in the neck because TSH is suppressed. Although the uptake was within a normal reference range in this patient at 19.5%, this degree of uptake is clearly abnormal for a patient with an undetectably low TSH. Without TSH there is little to no stimulation of iodine uptake. Rather, in this case, it is the persistent autonomous Graves disease tissue that accounts for the uptake of radioiodine, secondary to stimulation by the TSH-receptor antibodies.

**Endocrinology and Metabolism: Question 3**
The correct answer is C

**Educational Objectives**
Evaluate a patient with an adrenal incidentaloma.

**Critique**
This patient presents with an adrenal incidentaloma. The first step in management is an evaluation of serum and urine hormone levels to determine whether the mass is functional or nonfunctional. If it is nonfunctional, follow-up CT and repeat hormone testing at 6 to 12 months are indicated to ensure the mass is not enlarging or beginning to produce hormones. At 2.8 cm, the mass has a low malignant or functional potential, and therefore there is no immediate indication for removal of the mass, biopsy, or further imaging.

**Endocrinology and Metabolism: Question 4**
The correct answer is C

**Educational Objectives**
Distinguish familial benign hypocalciuric hypercalcemia from mild primary hyperparathyroidism.

**Critique**
Mild primary hyperparathyroidism is frequently asymptomatic, and affected patients may not have osteopenia or renal tract stones. However, a low urine calcium level in an asymptomatic patient with mild hypercalcemia should raise suspicion of familial benign hypocalciuric hypercalcemia. This autosomal dominant condition results from a partial inactivating mutation of the calcium-sensing receptor, resulting in a decreased set-point for parathyroid hormone release by the parathyroids and increased renal tubular reabsorption of calcium. A history of “failed” parathyroid surgery in relatives is sometimes present. Surgical therapy is neither necessary nor effective because the condition is not associated with any of the sequelae of primary hyperparathyroidism. Primary hyperparathyroidism is possible but is usually associated with hypercalciuria (>4 mg/kg of body weight). A more precise method to assess urine calcium excretion is to calculate the calcium-to-creatinine clearance ratio from a spot urine sample, which is typically less than 0.01 in familial benign hypocalciuric hypercalcemia and greater than 0.02 in primary hyperparathyroidism. Examination of the calcium-sensing receptor gene by a research laboratory confirms the diagnosis of familial benign hypocalciuric hypercalcemia. Consultation with a specialist in mineral metabolism is helpful. Secondary hyperparathyroidism should be considered whenever the parathyroid hormone concentration is high, but the serum calcium is usually low or low-normal in this condition, usually in association with chronic renal insufficiency. Multiple endocrine neoplasia syndromes are familial conditions associated with primary hyperparathyroidism, but patients are also usually hypercalciuric and other endocrine features are usually encountered.
Endocrinology and Metabolism: Question 5
The correct answer is C
Educational Objectives
Identify the correct test to diagnose osteoporosis in a postmenopausal woman.

Critique
This woman has several risk factors for osteoporosis: she is a postmenopausal white woman and has not received hormone replacement therapy. She smokes, consumes an inadequate amount of dietary calcium, and has a significant family history of osteoporosis. Given this patient's risk factors, it is necessary to determine if she has osteoporosis. The diagnosis of osteoporosis is made by dual-energy X-ray absorptiometry. This technique is considered the gold standard because it has been extensively validated against fracture outcomes, requires relatively short scanning times and can measure bone loss in all areas of the skeleton with a high degree of accuracy and reproducibility.

No other laboratory tests or other radiographic examinations can reliably identify individuals with osteoporosis. Measurement of markers of bone resorption such as urinary hydroxyproline or serum collagen cross-links may be useful in assessing future fracture risk or in identifying persons at risk for rapid bone loss, but these markers cannot be used to diagnose osteoporosis. Bone biopsy should be reserved for the work-up of rare or puzzling causes of osteoporosis. Measurement of bone mass with quantitative ultrasound should be used for risk assessment. The results from this test cannot be used with the World Health Organization criteria for the diagnosis of osteoporosis. Standard radiographs are not sensitive indicators of bone loss since they do not consistently demonstrate significant demineralization until 30% to 40% of the bone mineral has been lost.

Endocrinology and Metabolism: Question 6
The correct answer is D
Educational Objectives
Recognize and manage hyperprolactinemia due to primary hypothyroidism.

Critique
There are many secondary causes of hyperprolactinemia that are not associated with pituitary tumor. One of the most common secondary causes of hyperprolactinemia is primary hypothyroidism. Up to 30% of women with primary hypothyroidism have a mildly elevated prolactin level. The reason for this elevation in primary hypothyroidism is thought to be increased stimulation of the pituitary gland by thyrotropin-releasing hormone, the hypothalamic hormone that stimulates thyroid-stimulating hormone and prolactin secretion from the pituitary gland. As in other secondary causes of hyperprolactinemia, serum prolactin levels in primary hypothyroidism are less than 200 ng/mL.

Treatment of primary hypothyroidism with levothyroxine to normalize serum TSH levels will also normalize prolactin levels, and irregular menses and galactorrhea should resolve. No other treatment directed specifically at the prolactin level or the hypogonadism (for example, estrogen or dopamine agonists) is usually required. MRI is unnecessary unless the elevated prolactin levels do not resolve with levothyroxine therapy.
Endocrinology and Metabolism: Question 7
The correct answer is D

Educational Objectives
Interpret the level of total testosterone in an obese man with type 2 diabetes.

Critique
The level of testosterone in the blood is dependent on the level of the high-affinity transport protein, sex hormone binding globulin (SHBG), as well as the production rate of testosterone. Obese and insulin-resistant men generally have a reduced level of total testosterone. This is primarily due to a low level of SHBG. Insulin is known to suppress SHBG mRNA expression in liver cells, and lowering the level of insulin with weight loss or diazoxide increases SHBG. In markedly obese men, the production of testosterone is also thought to decrease. Men with testosterone deficiency often complain of a reduced libido as well as erectile dysfunction. The clinical finding of acanthosis nigricans suggests insulin resistance. The findings in this patient strongly suggest that the low level of SHBG is the explanation for the low serum testosterone and likely make the other options—pituitary adenoma, Cushings syndrome, hemochromatosis, and an estrogen-producing adrenal tumor—unlikely.

Endocrinology and Metabolism: Question 8
The correct answer is E

Educational Objectives
Identify the appropriate screening test in patients in whom Cushings syndrome is suspected.

Critique
The 24-hour urinary free cortisol measurement is the best screening test for Cushings syndrome. The 1-mg overnight dexamethasone suppression test may also be used to screen for this condition, but has a lower degree of accuracy. Serum cortisol and plasma ACTH levels are unreliable because of their marked fluctuations throughout the day. The 8-mg overnight dexamethasone suppression is not a screening test but is useful for determining the cause of Cushings syndrome after the condition has been diagnosed.

Endocrinology and Metabolism: Question 9
The correct answer is D

Educational Objectives
Recognize that glucagon injection for treatment of hypoglycemia must be followed by carbohydrate intake, especially in patients with type 1 diabetes.

Critique
Intramuscular glucagon has an effective half-life of only several minutes. Unless carbohydrate is ingested (or another method is used to increase the glucose level in a sustained manner) hypoglycemia is likely to recur. Intramuscular glucagon is less effective in type 1 than in type 2 diabetes, but it is effective nonetheless. The current glucagon injection kit has no expiration date because the active ingredient is in a powdered form before reconstitution with the provided diluent. Depth of injection into the muscle has not been shown to significantly affect the action of glucagon.
Endocrinology and Metabolism: Question 10
The correct answer is C

Educational Objectives
Evaluate primary amenorrhea.

Critique
This patient presents with primary amenorrhea, short stature, failure of development of secondary sexual characteristics, and somatic abnormalities suggestive of Turner’s syndrome (gonadal agenesis). This condition is most often caused by an X0 genotype, which is readily diagnosed by standard karyotype analysis.

Patients with androgen resistance syndrome may also present with primary amenorrhea and have male level testosterone values and an XY karyotype, but they have adequate breast development, normal stature, and no somatic abnormalities.

Patients with hyperprolactinemia may present with primary or secondary amenorrhea, and they have normal stature and no somatic abnormalities. Patients with primary hypothyroidism may present with amenorrhea or precocious puberty, with or without growth retardation but without somatic abnormalities. Low serum estradiol is a nonspecific finding in all cases of amenorrhea with reduced pituitary or ovarian function.

Endocrinology and Metabolism: Question 11
The correct answer is A

Educational Objectives
Recognize changes in thyroid values that occur in pregnancy.

Critique
Results of thyroid function tests and thyroid gland volume normally change in pregnancy. These alterations are mediated by the high circulating levels of human chorionic gonadotropin that occur in the first trimester of pregnancy. Human chorionic gonadotropin is a weak agonist of the thyroid-stimulating hormone receptor and can cause mild elevations in the thyroxine level, subsequent mild decreases in the thyroid-stimulating hormone level, and the development of a small goiter. Serum thyroid-stimulating hormone levels can be as low as 0.1 μU/mL in normal pregnancy and typically normalize in early second trimester. Mildly elevated levels of total thyroxine are expected in pregnancy because of the effects of estrogen on production of thyroid-binding globulin. Free thyroxine levels are, however, typically normal or slightly increased in late first trimester.

Like other autoimmune diseases, Graves’ disease usually remits during pregnancy. The diagnosis is made by the presence of Graves’ orbitopathy or dermopathy, a larger goiter with a bruit, more severe hyperthyroidism, or an undetectable thyroid-stimulating hormone level during the second trimester. It may also be useful to measure circulating thyroid-stimulating immunoglobulins.

Hyperemesis gravidarum is associated with hyperthyroidism, and the cause appears related to markedly elevated circulating concentrations of human chorionic gonadotropin. Patients typically lose weight because of severe vomiting. Subacute thyroiditis is usually a painful process that may cause transient thyrotoxicosis. Surreptitious use of levothyroxine could cause laboratory test results similar to those in this patient but would suppress the thyroid gland; thus, a goiter would not be expected.
Endocrinology and Metabolism: Question 12
The correct answer is D
Educational Objectives
Recognize thyroid function test patterns caused by binding protein abnormalities.
Critique
Patients with familial dysalbuminemic hyperthyroxinemia are frequently overlooked because of widespread measurement of thyroid-stimulating hormone, alone or in conjunction with serum free thyroxine (T4). Familial dysalbuminemic hyperthyroxinemia results from mutations within the albumin gene that increase the affinity of albumin for T4 but generally not triiodothyronine (T3). As a result, reliance on an elevated total T4 level or an elevated free thyroxine index (which is the product of a normal T3 resin uptake and an elevated T4 level) may be misleading. Defects in 5-monodeiodination (conversion of T4 to T3) due to selenium deficiency (a necessary element for this enzyme) or an inherited deficiency do not fit with the normal serum T3 level in this patient. He does not have early Graves disease because the thyroid-stimulating hormone level is normal. He does not have familial thyroid-binding globulin excess, since the T3 level is normal rather than elevated.

Endocrinology and Metabolism: Question 13
The correct answer is C
Educational Objectives
Recognize the clinical presentation of type 2 diabetes mellitus in a young person.
Critique
Although type 1 diabetes remains the most common form of diabetes in children and teens, the marked increase in obesity in recent years has increased the prevalence of type 2 diabetes in this age group. In addition, there is increasing recognition of autoimmune diabetes in older individuals, so-called latent autoimmune diabetes of adulthood (LADA). As a result, age at diagnosis is no longer a decisive criterion for the specific type of diabetes. This obese teenager already has several clinical features of insulin resistance and early-onset type 2 diabetes mellitus is the most likely diagnosis. The lack of serum ketones and acidemia argues against absolute insulin deficiency, as would be seen in either type 1A (positive autoimmune markers) or type 1B (absent autoimmune markers) diabetes. Secondary diabetes refers to hyperglycemia resulting from a defined underlying clinical entity, such as pancreatitis or Cushing's syndrome, yet there is no definitive evidence described for any such phenomenon. Maturity onset diabetes of youth (MODY) is a form of secondary diabetes, being associated with recognized genetic mutations, most of which are known to affect 13-cell function. The hyperglycemia in MODY patients is typically mild, but may be severe. Certainly, the presentation may be similar to that observed in this patient. However, a family history in at least three generations is required to make this diagnosis, suggesting an autosomal dominant mode of inheritance.

Endocrinology and Metabolism: Question 14
The correct answer is D
Educational Objectives
Recognize the presenting symptoms and signs of hypopituitarism.
Critique
This case illustrates the importance of defining the underlying cause of hyponatremia before assuming that all such cases represent the syndrome of inappropriate antidiuretic hormone secretion. Hyponatremia is also a well-known manifestation of primary adrenal insufficiency. Among 264 reported cases of primary adrenal insufficiency, 88% demonstrated hyponatremia.
Less frequently, hyponatremia develops in patients with secondary adrenal insufficiency. Although hyponatremia may develop in primary or secondary adrenal insufficiency, the mechanisms of hyponatremia differ in each case. Patients with Addisons disease have solute-depletion hyponatremia and present clinically with vascular collapse. They are hypotensive and dehydrated because of volume contraction. In contrast, patients with secondary adrenal insufficiency have dilutional hyponatremia; they do not present with hyperkalemia, because aldosterone levels are normal. However, they can have hypotension because of the permissive effects of corticosteroids on sympathetically mediated vasoconstriction. Secondary adrenal insufficiency causes hypogonadism because adrenocorticotropin hormone is absent rather than increased, as in primary adrenal insufficiency. In this case, hypovolemia as manifested by orthostatic hypotension rules out the syndrome of inappropriate antidiuretic hormone secretion. Primary adrenal insufficiency is unlikely because hyperpigmentation and hyperkalemia are not present. The patients urine sodium concentration is 100 meq/L. A high urine sodium level is often thought to represent renal salt wasting in a patient with hypotension and hyponatremia. However, in this case, the high urine sodium level could instead reflect an appropriate natriuretic response by the kidney to mild volume expansion from free water retention caused by corticosteroid deficiency. Patients with secondary adrenal insufficiency develop hyponatremia because of an inability to excrete free water, which is most often caused by inappropriately high arginine vasopressin levels and possible direct renal effects. These findings therefore can be attributable to secondary corticosteroid deficiency with free water retention or to renal salt wasting. The presence of hypopigmentation more strongly favors secondary corticosteroid deficiency. Although secondary adrenal insufficiency can account for the hyponatremia, hypotension, and hypopigmentation in this case, it cannot explain the hypothyroidism (cold intolerance, chronic fatigue, dry skin, and constipation) and hypogonadism (loss of libido; impotence; fine, wrinkled skin; absence of axillary and pubic hair; and testicular atrophy). The overall presentation is therefore best explained by complete panhypopituitarism as a result of the prophylactic whole-brain irradiation. Deficiencies of all anterior pituitary hormones are documented after radiotherapy in which the hypothalamus and pituitary are included in the treatment field. This effect has been best demonstrated in patients receiving radiation therapy for pituitary tumors, nasopharyngeal carcinoma, or primary brain tumors.

**Endocrinology and Metabolism: Question 15**

**The correct answer is C**

**Educational Objectives**

Understand the use of lipid measurement for the management of patients with lipoprotein abnormalities.

**Critique**

The value of the total cholesterol measurement is principally for the purpose of screening persons for cardiac risk. When the concentration is elevated, a full lipid profile should always be measured before initiating pharmacologic therapy. Therapy should never be based solely on a total cholesterol measurement. The total cholesterol measurement does not represent the cholesterol content of a single lipoprotein moiety, but it is the sum of the cholesterol content in all of the circulating lipoprotein fractions: very-low-density lipoprotein (VLDL), low-density lipoprotein (LDL), and high-density lipoprotein (HDL) cholesterol. In this case, the patient had an HDL cholesterol of 140 mg/dL. Her triglycerides were 150 mg/dL and her calculated LDL cholesterol was 130 mg/dL. She does not require drug therapy. Total cholesterol can also be increased by an elevation of the VLDL cholesterol, which is clinically recognized by an increase in triglycerides.
The therapy for elevated triglycerides may be significantly different than the therapy for elevated LDL cholesterol. Finally, a low HDL cholesterol will lower the total cholesterol, potentially masking elevations in LDL cholesterol or triglycerides. Therefore, whenever possible, HDL cholesterol should also be measured to screen for cardiovascular risk.

Endocrinology and Metabolism:Question 16
The correct answer is A
Educational Objectives
Recognize the clinical manifestations and implications of hyperprolactinemia.
Critique
In all cases of secondary amenorrhea, pregnancy must first be excluded. In this patient, the elevated serum prolactin level in the absence of primary hypothyroidism or drug ingestion is probably caused by a pituitary microadenoma, which may be visible on MRI of the pituitary. MRI should be performed even though not all microadenomas are large enough to be visible, nor would lactotroph hyperplasia be seen radiologically. Nonfunctional microadenomas may occur, but the prolactin level here is clearly abnormal and in a range frequently seen with small microprolactinomas. Most important, MRI may rule out a non-prolactin-secreting tumor causing stalk compression. The latter tumors do not respond to medication and may require surgery, whereas prolactinomas respond well to dopamine agonist therapy, with suppression of prolactin production, restoration of normal ovulation, and, often, shrinkage of the tumor. After MRI, the best course is a trial of a dopamine agonist.
Even if a tumor cannot be seen, reduction of prolactin and restoration of ovulation to induce fertility should be tried first. Hysterography should be done to evaluate fallopian tube patency only if pregnancy does not ensue and male factor infertility is excluded.
The patient does not present with clinical signs of hirsutism or virilization; therefore, a serum androgen measurement will probably not be helpful. An adrenal tumor would likely have caused significant and relatively rapidly progressive signs. Polycystic ovary disease generally presents with oligomenorrhea that began in puberty and is often associated with hirsutism. Even though the polycystic ovary syndrome may be associated with hyperprolactinemia, the latter condition is not improved with insulin-sensitizing therapy with metformin. Hyperprolactinemia is a significant cause of osteoporosis, but restoration of normal ovarian function (and subsequent pregnancy) will help to reverse this condition. Bisphosphonates are contraindicated when pregnancy is considered or ongoing because of their effect on fetal bone development and their long half-life.

Endocrinology and Metabolism:Question 17
The correct answer is B
Educational Objectives
Select the most appropriate diagnosis using the World Health Organization (WHO) criteria for bone mass.
Critique
The World Health Organization (WHO) criteria define osteoporosis as a bone mass 2.5 standard deviations or more below that of a “young normal” adult (a T-score at or below -2.5). This definition applies to T-scores from any skeletal site. With a T-score at the spine of -2.6, this woman meets the definition for osteoporosis. Osteopenia or low bone mass is a bone mineral density between 1 and 2.5 standard deviations below that of a “young normal” adult (a T-score between -1 and -2.5).
Since osteoporosis is present in the spine, this diagnosis takes precedence over the low bone mass (osteopenia) present in the hip of this woman. The WHO criteria have no classification of severe osteopenia. Established osteoporosis is defined as a bone density in the osteoporotic range with one or more fragility fractures. This patient did not have a bone fracture. Normal bone mass is a bone mineral density within 1 standard deviation of a “young normal” adult (a T-score of -1.0 or greater). It must be remembered that although the WHO definitions are used to establish the prevalence of osteoporosis, they should not be used as the sole determinant for treatment decisions.

Endocrinology and Metabolism: Question 18
The correct answer is C

Educational Objectives
Recognize that new-onset hypoglycemia may be a sign of previously unsuspected renal insufficiency.

Critique
The most likely explanation for the marked decrease in insulin requirement is renal insufficiency due to diabetes and hypertension, which is especially common in black persons. The seemingly normal serum creatinine underestimates renal insufficiency in diabetic patients, elderly persons, lean persons, and women. A creatinine concentration of 1.3 mg/dL may equal a creatinine clearance of less than 30 mL/min in this patient. The increase in blood pressure is both caused by and worsens renal failure. There is decreased alanine substrate for gluconeogenesis in patients with renal insufficiency. Circulating insulin action is significantly prolonged in renal insufficiency.

Fructosamine (glycosylated albumin) is a short-term measure of average blood glucose and would be expected to show recent low glucose values, for which ample evidence already exists in this patient. It is not used to test for hypoglycemia. Microalbumin does not indicate anything about renal clearance and may be negative in renal insufficiency that is caused primarily by hypertension. Deficiencies of cortisol and thyroxine can diminish the activities of enzymes involved in gluconeogenesis but these deficiencies alone rarely cause hypoglycemia.

Endocrinology and Metabolism: Question 19
The correct answer is A

Educational Objectives
Manage a patient before surgery for pheochromocytoma.

Critique
Perioperative management of a patient undergoing surgery for a pheochromocytoma is a complicated and stepwise process. Because these patients are volume depleted and vasoconstricted secondary to catechol excess, the first step in management is administration of fluids together with α-blockade, typically with phenoxybenzamine. After the patient is euvoletic, a β-blocker is added to control hypertension and reflex tachycardia. α-Methylparatyrosine can be used as a second-line agent to deplete catechol stores of the pheochromocytoma, but this should be done only after the above steps are taken. Repeated measurement of urine vanillylmandelic acid, catechols, or metanephrines is of no value in this patient.
Endocrinology and Metabolism: Question 20
The correct answer is C

Educational Objectives
Recognize and manage a large prolactin-secreting pituitary tumor.

Critique
This patient has a large prolactin-secreting pituitary tumor. With the occasional exception of chronic renal failure combined with medication use, no other cause of hyperprolactinemia leads to a prolactin elevation of this magnitude. The hyperprolactinemia is the probable cause of his hypogonadism, because prolactin directly suppresses gonadotropin-releasing hormone levels. Luteinizing hormone and testosterone levels are low because gonadotropin-releasing hormone normally stimulates secretion of luteinizing hormone and follicle-stimulating hormone. Another possible cause of hypogonadism is mass effect of the tumor on the normal pituitary and hypothalamus. The mass of the tumor causes headaches and compresses the optic chiasm, resulting in bitemporal hemianopsia. In this patient, the tumor is not producing any other hormone or causing deficiencies in any other hormone, as shown by the normal levels of insulin-like growth factor-i, ct-subunit, and thyroid and adrenal hormones. Therefore, this can be treated as a pure prolactin-secreting tumor.

The best initial treatment for prolactin-secreting macroadenomas is medical therapy with a dopamine agonist, such as bromocriptine or cabergoline. Dopamine agonist therapy leads to decreases in prolactin levels, tumor shrinkage, and improvement in visual fields and pituitary function in most patients with macroprolactinomas. It also avoids the possible complications of surgery or radiation therapy, which include further vision loss and hypopituitarism. In addition, many patients with macroprolactinomas are not cured by surgery and will still require dopamine agonist therapy. Monitoring alone is inappropriate because the tumor is already causing headaches, compromising vision, and causing hypogonadism. Testosterone therapy will not treat the tumor and may instead increase prolactin levels and cause tumor growth in patients with macroprolactinomas. Transsphenoidal surgery or radiation therapy is reserved for the rare patient who does not tolerate or respond to dopamine agonist therapy.

Endocrinology and Metabolism: Question 21
The correct answer is D

Educational Objectives
Select the most appropriate treatment for an infertile man with seminiferous tubular failure.

Critique
Approximately 5% of adult men are infertile or subfertile. In most cases the men are otherwise healthy as in this case, and the explanation for their infertility cannot be readily established. When the testes are small and the level of serum FSH is elevated seminiferous tubular damage is generally quite substantial. The level of FSH increases because inhibin-B production by Sertoli cells is reduced. Varicocele is a dilatation of the veins of the pampiniform plexus of the scrotum. Although it is a relatively common finding among infertile men (25%), controlled studies have shown that repair of the varicocele does not reverse hypospermatogenesis. At one time, genital tract infections and gonadotropin deficiency were thought to play a role in male infertility, but therapies directed at these causes (demeclocycline, clomiphene, and testosterone) are also ineffective. In vitro fertilization, especially with intracytoplasmic sperm injection, has revolutionized the treatment options for men with impaired sperm production.
Endocrinology and Metabolism: Question 22
The correct answer is E

Educational Objectives
Recognize potential complications of mild hyperthyroidism in an elderly patient.

Critique
Patients with mild hyperthyroidism (subclinical hyperthyroidism), defined as normal levels of thyroxine and free thyroxine but suppressed thyroid-stimulating hormone, are at risk for atrial fibrillation, particularly if the thyroid-stimulating hormone level is less than 0.1 1iU/mL. This is true even for patients with normal serum levels of thyroxine. Increased bone loss has also been demonstrated in postmenopausal women with mild hyperthyroidism, but not in other patient groups. These findings support the need to achieve euthyroid laboratory results in patients with mild hyperthyroidism.

Patients with mild hyperthyroidism are not at increased risk for ventricular tachycardia, coronary artery disease, thyroid cancer, or pernicious anemia.

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Endocrinology and Metabolism: Question 23
The correct answer is C

Educational Objectives
Recognize the clinical presentation of autoimmune polyglandular syndrome type II.

Critique
This patient has autoimmune polyglandular syndrome type II, or Schmidts syndrome. The dominant disorders are autoimmune thyroid disease (Graves disease or hypothyroidism), type 1A diabetes mellitus, and Addison’s disease. Because these disorders usually occur in a continuum, this patient must be observed carefully for the possible onset of adrenal insufficiency over time. Other conditions associated with autoimmune polyglandular syndrome type II include celiac disease, hypogonadism, vitiligo, alopecia, pernicious anemia, and myasthenia gravis.

Autoimmune polyglandular syndrome type II is strongly influenced by HLA alleles, and patients with type 1A diabetes mellitus have the high-risk alleles DR3 and DR4. Autoimmune polyglandular syndrome type II is more common than type I. Type 2 diabetes tends to develop in obese persons (who constitute >80% of patients with type 2 diabetes) when resistance to insulin action can no longer be compensated by insulin secretion. Additionally, type 2 diabetes is more common in older, physically inactive persons. Diabetic ketoacidosis rarely occurs in patients with type 2 diabetes since they do not have absolute insulin deficiency. They maintain enough insulin secretion to prevent ketoacidosis. Hashimoto’s thyroiditis, an autoimmune disorder, is the most common cause of hypothyroidism. This form of thyroiditis is also referred to as chronic lymphocytic thyroiditis and autoimmune thyroiditis. Although it occurs in all age groups, it is most common in middle aged persons and is much more common in women than in men. MEN type 1 consists of two or more of the major combinations of pituitary, pancreatic islet, and parathyroid tumors. The genetic abnormality has been mapped to 11q13. MEN type 2 consists of the major combination of medullary thyroid carcinoma, adrenomedullary, and parathyroid tumors. There are two variants of MEN type 2. In MEN 2A, affected patients have a normal physical appearance, whereas those with MEN-2B have an unusual phenotype including eye and oral (mucosal, tongue) and labial ganglioneuromas, a marfanoid habitus, and prominent corneal nerves. Parathyroid disease is rare in MEN 2B. In MEN 2A there is a mutation in the RET protooncogene on chromosome 10. In MEN 2B there is one missense mutation within the catalytic core of the RET tyrosine kinase domain.
Endocrinology and Metabolism: Question 24

The correct answer is D

Educational Objectives
Understand LDL metabolism.

Critique
The number of LDL receptors is the principal regulator of LDL clearance, which is the major determinant of the LDL cholesterol concentration in the blood. When the concentration of intracellular cholesterol is decreased, LDL receptor synthesis is upregulated resulting in increased numbers of LDL receptors and increased clearance of LDL from the blood. When the intracellular cholesterol concentration is increased, the synthesis of LDL receptors is down-regulated with a decrease in LDL clearance. The serum cholesterol concentration is, therefore, determined by the LDL receptor number rather than influencing it. Cholesteryl ester transfer protein mediates the transfer of cholesterol among the various circulating lipoprotein particles and has no direct effect on LDL receptors. Lipoprotein lipase is responsible for the removal of triglycerides from chylomicrons and VLDL which facilitates their clearance, but does not affect LDL receptor number.

Endocrinology and Metabolism: Question 25

The correct answer is D

Educational Objectives
Identify the cause of discordant or inappropriate thyroid-stimulating hormone secretion.

Critique
This patient has an inappropriately high-normal serum thyroid-stimulating hormone (TSH) level despite an elevated free thyroxine level. He is clinically mildly thyrotoxic and has a pulse rate of 88/min (which is high for an athlete) and brisk deep tendon reflexes. The primary distinction to be made is between a TSH-producing pituitary adenoma and thyroid hormone resistance with variable tissue responsiveness to thyroid hormone. A TSH-producing pituitary tumor is less common than other hyperfunctional tumors of the pituitary but is the best fit for this patient's findings. Approximately 70% of patients with TSH-producing pituitary tumors have macroadenomas (those larger than 10 mm in diameter) that can be seen in the sella turcica on MRI of the pituitary. Another clue to the central etiology in this patient is the loss of libido and low serum free testosterone level, most likely because of concomitant loss of luteinizing hormone secretion due to mass effect from the pituitary macroadenoma.

Activating mutations of the TSH receptor have been found in autonomously functioning (‘hot) thyroid nodules and rare families with congenital thyrotoxicosis, but serum TSH levels should be suppressed in these cases rather than inappropriately elevated. The negative family history argues against thyroid hormone resistance, which is inherited in an autosomal dominant pattern. Therefore, screening first-degree relatives is not indicated at this stage. Fluctuating thyroid function may be seen in patients with Graves disease and those with variable levels of thyroid-stimulating and thyroid-blocking immunoglobulins, but this does not lead to inappropriately elevated TSH levels concurrently with an elevated free thyroxine level. Antithyroxine and antithyrothryonine antibodies may cause spuriously elevated thyroid hormone levels but do not cause clinical thyrotoxicosis.
Endocrinology and Metabolism: Question 26
The correct answer is A

Educational Objectives
Evaluate pituitary function in a postmenopausal woman with a sellar mass lesion.

Critique
Endocrine deficits with hypopituitarism differ in the pattern of progression depending on the cause of the hypopituitarism. When hypopituitarism is produced by pressure on the anterior pituitary or by pituitary irradiation, pituitary hormone loss has an orderly and generally predictable progression, starting with growth hormone (GH) and followed by prolactin, follicle-stimulating hormone/luteinizing hormone (LH), thyroid-stimulating hormone, and adrenocorticotropic hormone (ACTH). GH is the most sensitive measure of early pituitary dysfunction, whereas ACTH loss is the least sensitive measure of early hypopituitarism. In this case, hypopituitarism results from pressure caused by the mass lesion in the sella turcica. Random GH levels are difficult to interpret because of the episodic secretion of this hormone, and because the normal range for insulin-like growth factor is wide, a level may be within the normal range but still relatively low for a given person. In view of lack of symptoms or signs of hypothyroidism or adrenal insufficiency, measurement of free thyronine or ACTH stimulation testing would probably be nondiagnostic.

In evaluating pituitary function, stimulation testing is generally more sensitive and specific than basal hormone levels, but it is time-consuming and relatively expensive. However, postmenopausal women are unique in that FSH and LH levels should be chronically elevated because of an absence of negative feedback on secretion that is normally exerted by circulating estrogen levels; in effect, this represents an in vivo stimulation test. Consequently, normal FSH and LH levels in a postmenopausal woman indicate pituitary dysfunction. Therefore, gonadotropin-releasing hormone stimulation testing is not necessary to evaluate the adequacy of pituitary FSH and LH reserve in postmenopausal women. Measurement of basal FSH and LH is the simplest and most sensitive measure of pituitary function with mass lesions of the sella turcica in these patients.

Endocrinology and Metabolism: Question 27
The correct answer is B

Educational Objectives
Recognize the indications for parathyroidectomy in a patient with asymptomatic, mild primary hyperparathyroidism.

Critique
This patient has mild hypercalcemia and osteoporosis of the hip. The most common cause of this presentation is primary hyperparathyroidism, which is confirmed in this patient on the basis of an elevated serum parathyroid hormone concentration. According to the National Institutes of Health’s recommendations for treatment of otherwise asymptomatic patients with primary hyperparathyroidism, this patient’s bone loss is itself an indication for surgery. She should be referred to an experienced parathyroid surgeon for resection of what is likely to be a single parathyroid adenoma. The calcium metabolism should normalize postoperatively, and bone density is likely to improve. Chest CT is unlikely to provide useful information because the elevated parathyroid hormone concentration makes hypercalcemia of malignancy essentially impossible. Estrogen replacement therapy or a bisphosphonate will reduce bone turnover and may stabilize bone density, but in patients with a recognized secondary cause of bone loss, correction of the underlying abnormality is more logical. However, if surgery were considered too risky or if declined by the patient, medical antiresorptive therapy may have a short-term salutary effect on the skeleton in older women with hyperparathyroidism.
Recent studies, however, have also demonstrated a significant increase in the risk of breast cancer and cardiovascular disease in women treated with postmenopausal estrogen/progestin regimens. A low-calcium diet will probably do little to correct hypercalcemia, may increase the parathyroid hormone concentration further, and may increase the risk of further bone loss.

**Endocrinology and Metabolism: Question 28**
**The correct answer is E**

**Educational Objectives**
Recognize prediabetes as a treatable risk factor for type 2 diabetes.

**Critique**
The patient has four identified risk factors for the development of diabetes: strong family history, membership in a high-risk ethnic group, obesity, and a history of gestational diabetes mellitus. The random glucose level is suspicious but nondiagnostic of an abnormality of carbohydrate tolerance. The fasting glucose level is consistent with impaired fasting glucose, and the 2-hour value is consistent with impaired glucose tolerance. These characteristics are now called 'prediabetes, a state of great risk for type 2 diabetes. Prospective, randomized controlled trials have demonstrated an annual incidence of diabetes of 11% among persons with these characteristics.

Multiple interventions are effective in delaying or preventing the development of diabetes. The Finnish Diabetes Prevention Study and the Diabetes Prevention Program demonstrated a 58% reduction in the cumulative incidence of diabetes in patients with impaired glucose tolerance after initiation of an intensive lifestyle intervention. The goals of the intervention were to increase exercise to at least 150 minutes weekly and achieve and maintain a 7% weight loss by reducing caloric intake. The magnitude and consistency of the effects of lifestyle intervention make it the optimal initial therapeutic approach.

Thiazolidinedione therapy with troglitazone was shown to prevent diabetes in Hispanic American women with a history of gestational diabetes mellitus. However, the study was ended prematurely, and troglitazone was withdrawn from the market because of hepatotoxicity. Ongoing trials with the remaining thiazolidinediones (rosiglitazone and pioglitazone) aim to show that these agents also prevent diabetes, but no conclusions can be yet drawn.

Acarbose therapy was shown to delay the onset of diabetes in a similar population with impaired glucose tolerance. The effect was smaller (25% reduction) than that seen with lifestyle intervention in the Diabetes Prevention Study or the Diabetes Prevention Program. The rate of diabetes development in the intervention group after discontinuation of acarbose therapy matched that of the placebo group. Early reports suggest, however, that acarbose also reduced the incidence of cardiovascular disease in this high-risk group.

In the Diabetes Prevention Program, metformin therapy reduced development of diabetes, but not to the same extent as lifestyle intervention (31% vs. 58%, respectively). By the end of the study, 20% of patients randomized to metformin therapy were taking less than 80% of the prescribed dose because of contraindications or unacceptable side effects. In addition, metformin is not approved for this indication by the U.S. Food and Drug Administration.
Endocrinology and Metabolism: Question 29
The correct answer is C
Educational Objectives
Identify the most common site of the disorders responsible for Cushings syndrome.
Critique
In approximately 80% of patients, endogenous Cushings syndrome is caused by an adrenocorticotropic hormone (ACTH)-secreting pituitary tumor. In approximately 10% of patients, the cause is ectopic ACTH secretion from a tumor elsewhere in the body, most commonly the lungs. Approximately 10% of patients have a cortisol-secreting adrenal tumor.
In patients with ACTH-secreting pituitary tumors, the plasma ACTH level is usually normal or only slightly elevated and the serum cortisol is greatly suppressed in response to the 8-mg dexamethasone test. In patients with cortisol-producing adrenal adenomas, the plasma ACTH level is very low. This patient has a very elevated plasma ACTH level, and his serum cortisol level does not become suppressed in response to 8 mg of dexamethasone. These findings are characteristic of the ectopic ACTH syndrome, and the most common tumors that cause this syndrome are located in the lungs (for example, small-cell carcinoma or bronchial carcinoids).

Endocrinology and Metabolism: Question 30
The correct answer is A
Educational Objectives
Manage polycystic ovary disease.
Critique
Polycystic ovary disease is a chronic disorder that generally first manifests at puberty with oligomenorrhea and variable degrees of hirsutism and acne. Its signal skin lesion, acanthosis nigricans, is present to a variable degree and reflects insulin resistance and elevated levels of insulin-like growth factor-1. Management depends on the age of the patient and her desires. Reduction of androgens and blockade of androgen receptors with estrogen/progesterone and spironolactone, respectively, often achieve excellent cosmetic results. Insulin resistance may be reduced by the use of metformin, which decreases androgen levels to a variable degree and often restores ovulation. For this reason, metformin use should be accompanied by contraception in patients who do not wish to conceive. Clomiphene citrate and other agents to induce ovulation, with or without the use of metformin, are reserved for women who are actively seeking pregnancy and require ovulation induction. Although this patient is at risk for diabetes and the other components of the insulin resistance/metabolic syndrome, her fasting plasma glucose level is normal. She does not yet have diabetes. Counseling about weight loss and exercise are most appropriate to prevent future progression.

Endocrinology and Metabolism: Question 31
The correct answer is A
Educational Objectives
Recognize the mechanism of action of approved medications for the treatment and/or prevention of osteoporosis.
Critique
Multiple therapeutic options are available for osteoporosis. Both antiresorptive and anabolic agents have been shown to increase bone mass and reduce the risk of fracture. Given the severity of this woman’s osteoporosis and her increased fracture risk, treatment with an anabolic agent is a reasonable option.
Once-daily administration of teriparatide, recombinant human parathyroid hormone (1-34), stimulates new bone formation on bone surfaces by preferential stimulation of osteoblastic activity over osteoclastic activity. Teriparatide improves both bone mass and strength. Bisphosphonates, estrogens, raloxifene, and calcitonin inhibit osteoclastic bone resorption, thus permitting a favorable balance in bone remodeling, improved bone mass and reduced fracture risk.

**Endocrinology and Metabolism: Question 32**

The correct answer is E

**Educational Objectives**

Understand that failure to clear acidosis in the treatment of diabetic ketoacidosis may have several causes.

**Critique**

Glucose is only one of the variables that need to be followed in diabetic ketoacidosis. It typically takes a longer time for ketones to clear than for glucose values to normalize. Because hyperglycemia almost invariably resolves before ketosis is controlled, glucose (usually in the form of 5% dextrose) should be added to the intravenous fluids when the plasma glucose concentration reaches 250 to 300 mg/dL. This step prevents an excessive decline in plasma osmolality, that could lead to cerebral edema and avoids hypoglycemia. Insulin infusion should continue until significant correction of ketonemia has been achieved (as evidenced by the closure of the anion gap). A common mistake is discontinuing the insulin infusion prematurely before adequate clearance of ketoacids from the serum, or without provision for conversion to a longer-acting form of insulin, placing the patient at risk for rebound acidosis.

Hyperchloremic acidosis is the rule in the recovery period from diabetic ketoacidosis. Ketoacid anions are metabolized with regeneration of bicarbonate, and therefore the prior loss of ketoacid anions in the urine hinders regeneration of bicarbonate, leading to hyperchloremic acidosis. Additionally, during development of ketoacidosis, sodium is lost in excess of chloride as the sodium salt of ketoacids. Replacement solutions have equal parts sodium and chloride. Because chloride losses are smaller than sodium losses, relative hyperchloremia occurs with therapy.

The use of bicarbonate in the treatment of diabetic ketoacidosis has been controversial. Severe acidemia has been associated with impaired myocardial contractility and vascular refractoriness to adrenergic action. Several studies have failed to show any objective benefit of alkali therapy. Bicarbonate therapy has been implicated in worsening hypokalemia, causing paradoxical central nervous system acidosis and delaying ketone body clearance. The available data suggest that bicarbonate therapy should not be given in diabetic ketacidosis unless the pH is <6.9 or other indications (severe hyperkalemia, shock) are present.

There is no syndrome of lack of absorption of subcutaneous insulin, even in dehydration with peripheral vasoconstriction. This condition is now known to be a syndrome of noncompliance with insulin therapy.
Endocrinology and Metabolism: Question 33
The correct answer is D

Educational Objectives
Evaluate a patient for pheochromocytoma.

Critique
Diagnosis of a pheochromocytoma depends on the finding of excessive catecholamine levels in urine or plasma. A hormonal diagnosis must be established before any other testing is performed. The most common clinically accepted work-up includes collection of a 24-hour urine sample to measure vanillylmandelic acid, catecholamines, and metanephrines. Plasma free metanephrines can also be measured, but reliable laboratories that perform this analysis are not widely available. After a biochemical diagnosis is established, the tumor is best localized with noninvasive imaging, such as MRI or CT scan. Metaiodobenzylguanidine scanning is reserved for localization of extra-adrenal tumors or metastases. Clonidine suppression was previously used to diagnose pheochromocytoma, but it lacks adequate sensitivity or specificity.

Endocrinology and Metabolism: Question 34
The correct answer is D

Educational Objectives
Recognize and manage a large nonfunctioning pituitary tumor with secondary hyperprolactinemia.

Critique
This patient has a large, clinically nonfunctioning pituitary tumor. All of her pituitary hormone levels are normal or low, except for a mildly elevated prolactin level. Elevated prolactin levels can indicate a prolactin-secreting tumor, but in that case, the degree of prolactin elevation should correlate with the size of the tumor. A prolactin level of 118 ng/mL would indicate a small prolactinoma, not a 2.4-cm prolactin macroadenoma. The prolactin elevation is probably due to interruption of dopamine input to the pituitary gland. Dopamine is the normal prolactin inhibitory hormone secreted by the hypothalamus. Any mass or infiltrative process that interrupts normal hypothalamic-pituitary connections can lead to elevations in prolactin levels up to approximately 200 ng/mL. In this patient, the prolactin is coming from normal pituitary lactotrophs, not from the tumor. Therapy with bromocriptine or another dopamine agonist would decrease prolactin levels but would not stop tumor growth or improve vision. The patient requires referral to a neurosurgeon experienced in transsphenoidal pituitary surgery. The tumor can probably be debulked, although not cured. Patients with pituitary macroadenomas rarely require transfrontal surgery (which has increased morbidity rates) because transsphenoidal surgery usually provides adequate tumor debulking. Debunking the tumor will probably improve the patient's headaches and vision problems. Patients with central hypothyroidism should receive preoperative thyroxine. The thyroid and adrenal axes should be reevaluated after surgery. Lifelong thyroid hormone therapy is usually required, although pituitary function sometimes improves after surgery. Hypoadrenalism may develop after surgery, depending on characteristics of the tumor and experience of the surgeon. Of note, this patient has gonadotropin deficiency due to the tumor, as evidenced by her luteinizing hormone and follicle-stimulating hormone levels, which should be elevated in a postmenopausal woman. The tumor may have caused her early menopause yet went undetected, since these tumors often grow slowly and exist for many years before diagnosis. Estrogen therapy can be used to treat low bone density, but this decision is separate from the decision to treat the tumor. Monitoring without treatment is not an option in a patient with headache and vision loss.
Endocrinology and Metabolism: Question 35
The correct answer is C

Educational Objectives
Recognize the clinical presentation of men with congenital hypogonadotropic hypogonadism.

Critique
Delayed puberty occurs with gonadotropin deficiency, testicular failure, and chronic illness, as well as in constitutional delay of puberty, a condition associated with short stature and delayed but otherwise normal pubertal development. Although the latter is the most common cause of delayed puberty, this diagnosis is very unlikely at age 18 years, because this man's age is many standard deviations beyond the usual age for pubertal onset. The low level of serum LH excludes testicular failure, and the patient is otherwise healthy. The lack of headaches, symptoms of diabetes insipidus, or visual complaints makes a suprasellar tumor such as craniopharyngioma unlikely. 17-Hydroxylase deficiency and 21-hydroxylase deficiency are two forms of congenital adrenal hyperplasia. In the former, a defect in testosterone biosynthesis causes ambiguous genitalia, whereas in the latter, the production of androgens by the adrenal gland is increased causing precocious puberty. Neither condition produces the clinical picture in this patient. Congenital hypogonadotropic hypogonadism may occur with GnRH deficiency or with mutations of the GnRH receptor. In the former group, midline defects such as anosmia, cleft palate, or horseshoe kidney may occur, and the condition is known as Kallmann's syndrome. In the absence of these clinical findings, GnRH receptor mutation is a possible diagnosis. In most patients the etiology remains unknown.

Endocrinology and Metabolism: Question 36
The correct answer is D

Educational Objectives
Recognize the limitations of fine-needle aspiration biopsy of thyroid nodules.

Critique
Fine-needle aspiration biopsy is the most important test in evaluation of a patient with a thyroid nodule. This method has become routine in many centers, but it has limitations, even when done by the most experienced cytologists. Inadequate samples occur in approximately 10% to 15% of cases and are more common for cystic nodules, which contain few cells. Repeated aspiration or aspiration under ultrasonography guidance, in which the needle can be directed toward the wall of the cyst, can increase the likelihood of obtaining a diagnostic sample. When adequate samples are obtained, approximately 85% of nodules are benign adenomatoid, cellular, or cystic. A certain proportion can be characterized as papillary cancers on the basis of the presence of typical nuclear features found in those cancers. However, fine-needle aspiration biopsy cannot distinguish between malignant and benign follicular neoplasms because these entities are cytologically identical. Histologic identification of vascular, lymphatic, or capsular invasion is required to diagnose follicular carcinoma. Thus, in many cases, patients with papillary carcinoma or follicular neoplasm on fine-needle aspiration biopsy are referred for thyroid surgery.
Endocrinology and Metabolism: Question 37
The correct answer is B
Educational Objectives
Diagnose gestational diabetes mellitus.

Critique
Gestational diabetes mellitus is defined as any degree of glucose intolerance with onset or first recognition during pregnancy. The definition is applicable regardless of whether insulin or dietary intervention is used as therapy and whether the condition persists after pregnancy. A fasting plasma glucose level of 126 mg/dL or greater or a casual plasma glucose level of 200 mg/dL or greater meets the threshold for the diagnosis of diabetes and should be confirmed on a subsequent day. Initial screening involves measurement of plasma glucose 1 hour after a 50-g oral glucose load. If the 1-hour value is 140 mg/dL or greater, a 3-hour diagnostic oral glucose tolerance test with a 100-g glucose load should be performed. Gestational diabetes mellitus is diagnosed when any two of the following four values are met or exceeded: fasting glucose level, 95 mg/dL; 1-hour level, 180 mg/dL; 2-hour level, 155 mg/dL; 3-hour level, 140 mg/dL. The test should be done in the morning after an overnight fast of 8 to 14 hours and after at least 3 days of unrestricted diet (150 g or less carbohydrate per day) and unlimited physical activity. The patient should remain seated and not smoke throughout the test.

Once gestational diabetes mellitus has been diagnosed, a consistent carbohydrate diet should be instituted. A 1-hour plasma glucose measurement after a meal has not been standardized for diagnosis of gestational diabetes mellitus. The hemoglobin A1C value is not used to diagnose gestational diabetes mellitus but is used to assess glycemic control once diabetes has been diagnosed. Measurement of hemoglobin A1C is insensitive, especially in mild gestational diabetes mellitus.

Endocrinology and Metabolism: Question 38
The correct answer is A
Educational Objectives
Recognize atherogenic lipoprotein abnormalities.

Critique
Increased LDL cholesterol is the lipoprotein abnormality that confers the greatest and most consistent risk for coronary heart disease. An increased total cholesterol does not allow the prediction of risk because multiple lipoprotein abnormalities may contribute to an elevated total cholesterol, including an increased HDL cholesterol. An increased HDL cholesterol lowers the risk for coronary heart disease. Although an elevated chylomicron triglyceride level may contribute to the development of pancreatitis, it is not predictive of coronary heart disease.

Endocrinology and Metabolism: Question 39
The correct answer is C
Educational Objectives
Recognize the effect of amiodarone therapy on thyroid physiology and results of thyroid function testing.

Critique
Apart from drug-induced hyperthyroidism (5% of treated patients) or hypothyroidism (7%), amiodarone has dramatic effects on thyroid function tests in clinically euthyroid patients. A large iodine load (74 mg of total iodine, 7.4 mg of free iodine per 200 mg tablet) is delivered with each dose. Amiodarone inhibits peripheral and central (intraptituditary) conversion of T4 to T3 through its action on D1 and D2 monodeiodinase enzymes, respectively. Amiodarone also has T3-antagonistic effects at the nuclear level.
The common pattern shown in this euthyroid patient is primarily the effect of the latter two actions of amiodarone. Amiodarone-induced thyrotoxicosis is associated with a suppressed TSH level and clinical manifestations of thyrotoxicosis, neither of which is present in this patient. A pituitary tumor is unlikely in this patient and would be associated with clinical thyrotoxicosis. This patient’s thyroid function pattern is unlikely to be due to euthyroid sick syndrome because he is not acutely ill and the pattern is atypical. Amiodarone does not cause spurious laboratory results for total or free T4.

Endocrinology and Metabolism: Question 40

The correct answer is B

Educational Objectives

Prioritize appropriate therapies for hypopituitarism.

Critique

This patient presents with classic pituitary apoplexy, as manifested by the acute onset of severe headaches and symptoms of acute hypopituitarism in association with findings of a new hemorrhage within a sellar mass on magnetic resonance imaging. The laboratory results obtained 3 days earlier are consistent with partial hypopituitarism: deficiencies of growth hormone (low levels of growth hormone and insulin-like growth factor-I), follicle-stimulating hormone and luteinizing hormone (symptoms of hypogonadism with inappropriately low levels of follicle-stimulating hormone and luteinizing hormone despite a low testosterone level), and thyroid-stimulating hormone (symptoms of hypothyroidism with a low free thyronine level and no elevation in the thyroid-stimulating hormone level) but normal adrenocorticotropic hormone function. (Any cortisol level ≥ 18 μg/dL, whether random or after an adrenocorticotropic hormone stimulation test, is considered to demonstrate an adequate hypothalamic-pituitary-adrenal axis). However, an acute hemorrhage into a preexisting pituitary adenoma can quickly destroy any remaining pituitary function, rendering a patient with partial hypopituitarism or intact pituitary function completely panhypopituitary within hours. In this patient, dizziness, orthostatic hypotension, and nausea all strongly suggest acute hypocortisolism because none of his other hormonal deficits are associated with these effects. Consequently, full stress doses of corticosteroids are the most appropriate initial therapy, because adrenocorticotropic hormone deficiency is the only pituitary deficit that is acutely life threatening. Although the patient will probably require therapy only with maintenance doses of hydrocortisone at some point, the initial therapy of a hypotensive patient with presumed hypocortisolism must always entail higher doses of this hormone, and administration must be parenteral in case the patient’s nausea leads to vomiting. Similarly, the patient will probably require replacement therapy with both levothyroxine and testosterone, but neither of these agents is critical in the acute setting; administration of levothyroxine is contraindicated in a patient with potential hypocortisolism until cortisol replacement has begun (particularly in a patient with known coronary artery disease).

Whether all patients with pituitary apoplexy require acute neurosurgical decompression is controversial. This patient has signs and symptoms of chronic pituitary dysfunction, suggesting that the mass has been present for several years before the acute hemorrhage. Therefore, whether the bitemporal hemianopsia is an acute visual compromise as a result of the hemorrhage or has been present for some time as a result of progressive growth of the pituitary macroadenoma is unknown. Indications for resection of sellar mass lesions include hypersecretory pituitary adenoma (except in the case of prolactin-secreting adenomas that can be treated with dopamine agonists), the presence of mass symptoms (visual or neurologic) that cannot be treated with dopamine agonists or other means, significant interference
with normal pituitary function that cannot be treated with dopamine agonists or other means, or a nonsecretory macroadenoma in a young or middle-aged person that is expected to enlarge slowly over time and eventually cause symptoms. In this patient, it is not known whether the mass can be successfully treated with dopamine agonist therapy until a serum prolactin level is obtained. Although some physicians would choose surgical decompression because of the size of the mass and the presence of visual field defects, others would observe the patient carefully and only perform acute decompression to treat signs of progression of visual defects while awaiting the prolactin level. However, no patient with apoplexy should undergo neurosurgery without administration of stress-dose corticosteroid therapy; therefore, neurosurgery is not the most appropriate initial therapy.

Endocrinology and Metabolism: Question 41
The correct answer is C

Educational Objectives
Recognize the complications of acute hypocalcemia.

Critique
Hypoparathyroidism resulting in acute hypocalcemia can occur after thyroid surgery, because of direct injury to the parathyroid glands or indirect injury from disruption of their vascular supply. The risk of hypoparathyroidism correlates with the extent of the dissection - it is seen almost exclusively in bilateral procedures - and the experience and skill of the surgeon. Acute hypocalcemia decreases the threshold for nerve depolarization, leading to paresthesias, tetany, and, in severe cases, seizures. Thyroid storm does not occur with what appears to be a reasonable temporary dosing regimen of triiodothyronine. Cerebral metastases from a localized papillary thyroid carcinoma are unlikely. Hypothyroidism cannot occur this quickly after thyroid resection, particularly in a patient taking replacement therapy. A late idiosyncratic reaction to general anesthesia is also unlikely.

Endocrinology and Metabolism: Question 42
The correct answer is D

Educational Objectives
Manage hypertension in a patient with diabetes mellitus.

Critique
The confirmed fasting glucose level greater than 126 mg/dL establishes the diagnosis of diabetes. As such, the goals of antihypertensive therapy become more stringent. Although some disagreement remains about the optimal target blood pressure, 140/90 mm Hg is no longer acceptable. Improved cardiovascular outcomes in patients with diabetes have been demonstrated after reduction of diastolic pressures to less than 80 mm Hg. Thiazide diuretics are effective first-line therapy, with documented reduction in cardiovascular events; however, patients with diabetes experience greater renal protection at any blood pressure with use of an angiotensin-converting enzyme (ACE) inhibitor or an angiotensin receptor blocker. Because this patient has unacceptably high blood pressure, additional therapy is warranted. Increasing the hydrochlorothiazide dosage provides little additional decrease in blood pressure and increases the potential for electrolyte imbalance. Substituting an ACE inhibitor for hydrochlorothiazide is unlikely to achieve the desired blood pressure and will not offer the cardioprotection provided by the thiazide therapy. Although they are very effective in lowering blood pressure, calcium channel blockers (particularly dihydropyridines, such as amlodipine) are not renoprotective and may increase the risk for cardiovascular disease in patients with diabetes.
Endocrinology and Metabolism: Question 43
The correct answer is B
Educational Objectives
Order and interpret tests designed to locate the site of Cushing’s syndrome.
Critique
MRI of the pituitary gland should be done next. The normal plasma adrenocorticotropic hormone (ACTH) level indicates that Cushing’s syndrome in this patient is ACTH dependent. This finding narrows the possibilities down to an ACTH-producing pituitary tumor and an ectopic ACTH-producing tumor. Plasma ACTH levels tend to be much higher in the latter condition. Suppression of the serum cortisol level after oral administration of 8 mg of dexamethasone at bedtime is characteristic of an ACTH-producing pituitary tumor. Therefore, the next test in this patient should be an imaging procedure to find the suspected pituitary tumor. If no pituitary tumor is identified, bilateral inferior petrosal sinus sampling for ACTH levels or CT scan of the lungs is the next test to perform.

Endocrinology and Metabolism: Question 44
The correct answer is D
Educational Objectives
Understand that certain medical conditions may cause osteoporosis.
Critique
There are several features that suggest the possibility of a secondary cause for this woman’s osteoporosis. The pattern of bone loss demonstrates preservation of bone mass in trabecular bone (spine) and preferential bone loss at a cortical site (forearm). This pattern is different from that observed in postmenopausal osteoporosis, where the bone loss is greater in the spine and relatively preserved in the forearm. The personal and strong family history of nephrolithiasis suggests the possibility of a secondary cause of osteoporosis such as primary hyperparathyroidism or hypercalciuria. Therefore, further work-up with a measurement of the serum calcium and urine calcium excretion is warranted. Observation alone would not lead to the correct diagnosis and treatment. Treatment with either a bisphosphonate or raloxifene for osteoporosis would be premature since parathyroidectomy results in significant increases in bone mass (at both the lumbar spine and the femoral neck) in patients with primary hyperparathyroidism. Bisphosphonates have also been shown to increase bone mass in patients with primary hyperparathyroidism. Treatment with hydrochlorothiazide would decrease her elevated urine calcium excretion and improve her bone density if she had idiopathic hypercalciuria.

Endocrinology and Metabolism: Question 45
The correct answer is D
Educational Objectives
Recognize the subtle presentation of hypoglycemia unawareness and its treatment.
Critique
Hypoglycemia unawareness is a common problem in patients with tightly controlled diabetes who are using insulin. It occurs as part of the blunting of adrenergic and related responses to hypoglycemia. The hypoglycemic reaction can be subtle and seem like a behavioral problem. Commonly, the patient denies or rationalizes the problem, and it is those around him who bring it to attention. Hypoglycemic unawareness is often not detected on routine glucose monitoring because the monitoring is usually not done during a period of hypoglycemia. Increasing the frequency of glucose monitoring, especially during the periods of behavioral change, can help to diagnose hypoglycemic unawareness. Decreasing the insulin doses
should alter the behavior pattern if hypoglycemia is the cause, after which it will be easier to perform diagnostic self-glucose monitoring and a more critical self-assessment.

There is no evidence that the couple in this case requires psychiatric intervention, whether joint or individual, since the patient is ‘denying’ a condition of which he is not aware. Supportive psychotherapy may be helpful if the patient refuses to address the hypoglycemic pattern because of irrational concerns about loosening control. Primary adrenal insufficiency is a related autoimmune disease (Addison disease) that can lead to hypoglycemia, but it is relatively rare. In addition, the patient with Addisons disease typically has dark pigmentation of all skin, including palms and gums, and hyponatremia, hyperkalemia, and an elevated blood urea nitrogen level.

**Endocrinology and Metabolism: Question 46**

The correct answer is **A**

**Educational Objectives**

Manage infertility caused by prolactin microadenomas.

**Critique**

The patient has a prolactin-secreting microadenoma, as indicated by the mild hyperprolactinemia and small tumor on MRI. She has no obvious causes of secondary hyperprolactinemia, including primary hypothyroidism or medication use, and she requires no further work-up for hyperprolactinemia. She does not require repeated MRI because her prolactin levels have been stable over 1 year and small prolactinomas do not usually grow.

The most common symptoms of a small prolactinoma are oligomenorrhea and infertility. Many patients have galactorrhea, but the absence of galactorrhea does not exclude the diagnosis. The hypogonadism is due to direct suppression of gonadotropin-releasing hormone by the elevated prolactin levels. Gonadotropin-releasing hormone is the normal hypothalamic-stimulating hormone for secretion of luteinizing hormone and follicle-stimulating hormone. Normalization of prolactin levels in patients with small prolactinomas almost always leads to normalization of gonadal function and fertility.

To restore fertility, the best treatment option for this patient is dopamine agonist therapy. Transsphenoidal surgery may cure the tumor but carries the risk of further pituitary damage. In addition, rates of recurrence are high after surgery for prolactin-secreting microadenomas. Dopamine agonist therapy has been shown to be safe and effective in inducing ovulation in women with prolactinomas. Clomiphene citrate is unlikely to be effective in the face of continued hyperprolactinemia.

Exogenous gonadotropin therapy may work but exposes the patient to excess risks compared with dopamine agonist therapy.

Of the dopamine agonists, bromocriptine has been most extensively studied during pregnancy. Because bromocriptine use appears to be safe during early pregnancy, it is the dopamine agonist of choice in a woman who desires pregnancy. Cabergoline is also highly effective in restoring fertility in such women, but less information is available on its safety in early pregnancy. In this patient, the previous initial bromocriptine dosage was too high. Almost any patient started on 10 mg of bromocriptine per day will develop symptoms. Thus, patients should be started on a low dose (1.25 to 2.5 mg/d, at night and with food). The patient should be counseled that nausea or dizziness may develop but will resolve within 1 to 2 weeks. Prolactin levels can be checked after 1 month of low-dose therapy; in many cases, prolactin levels will have normalized, and no further dose adjustments are needed. If the prolactin level is still elevated after 1 month of treatment at 2.5 mg/d, the bromocriptine dose can be gradually titrated upward by 1.25 to 2.5 mg per month. Most patients with prolactinomas of this size require daily doses of 2.5 to 7.5 mg, not
10 mg. This patient would probably respond well to low-dose bromocriptine therapy and experience no serious or lasting side effects. Patients should also be counseled that they can become pregnant soon after starting bromocriptine, since resumption of ovulation can occur within the first month. It is often prudent to have the patient use a barrier method of birth control until menstrual cycles are reestablished, so that pregnancy can be diagnosed soon after conception.

**Endocrinology and Metabolism: Question 47**
The correct answer is D

**Educational Objectives**
Recognize management target goals for a patient with coronary heart disease.

**Critique**
Evidence from a number of intervention trials of lipid management to prevent coronary heart disease have established that the control of LDL cholesterol is the most important goal of therapy. In patients with established coronary heart disease or risk equivalents, lowering LDL cholesterol to <100 mg/dL results in better outcomes than when the LDL cholesterol level is >100 mg/dL. After the primary LDL goal is achieved as in the patient in this case, the recommended secondary goal in patients with triglyceride levels >200 mg/dL is to lower the non-HDL cholesterol level to <130 mg/dL. Non-HDL cholesterol represents all atherogenic apo B-100-containing lipoproteins and indicates the additional role that these lipoproteins play in the pathophysiology of atherosclerosis. Sufficient evidence was not available to the National Cholesterol Education Programs Adult Treatment Panel III panel to set therapeutic goals for HDL cholesterol or triglycerides, and therefore, the surrogate of non-HDL cholesterol was used.

**Endocrinology and Metabolism: Question 48**
The correct answer is C

**Educational Objectives**
Recognize that germ cell tumors of the testes produce hOG, and lead to breast enlargement in young men.

**Critique**
Transient gynecomastia is common during puberty, and breast enlargement often occurs in older men. But when painful breast enlargement occurs in young adult men, hormonal stimulation is suspected. Breast enlargement occurs with androgen deficiency or with estrogen excess. In this case the level of hCG is increased markedly. hCG activates the aromatase gene and allows for increased conversion of substrate testosterone to estradiol and of androstenedione to estrone. hOG is usually absent in the plasma in men, and high levels suggest the diagnosis of choriocarcinoma, an aggressive germ cell tumor. These tumors are located either in the testes or in the retroperitoneal space of the abdomen or chest. Although sometimes palpable, tumors of the testis may be too small to be detected by physical examination. Ultrasonography is a reliable and valuable tool in the diagnosis of testicular tumors. Tumors in the chest or abdomen are often evident by CT scanning.
Endocrinology and Metabolism: Question 49
The correct answer is A
Educational Objectives
Recognize determinants of worsening hypothyroidism in patients taking levothyroxine replacement therapy.

Critique
This patient’s disease was previously well controlled on a stable dose of levothyroxine. He currently has a low-normal free thyroxine (T4) level and an elevated thyroid-stimulating hormone (TSH) level. Other than noncompliance with therapy, causes of worsening control include the addition of medications that interfere with absorption (calcium, iron, lipid resins, aluminum hydroxides, or sucralfate) or medications that increase the metabolic clearance of levothyroxine (phenytoin, phenobarbital, and probably sertraline). Vitamin B complexes and vitamin C are not known to interfere with absorption of levothyroxine. Pharmacy error or an unannounced change in levothyroxine brand is a possible cause of decreased control of hypothyroidism, but a 10-fold reduction in dose would lead to more profound hypothyroidism than is present in this patient. An increased rather than decreased volume of distribution due to weight gain may increase the requirement for thyroid hormone. Adrenal insufficiency is a known cause of an isolated elevation in the thyroid-stimulating hormone because of absence of the suppressive effect of corticosteroids on thyrotrophs, but the free thyroxine level should not drop by this mechanism.

Endocrinology and Metabolism: Question 50
The correct answer is E
Educational Objectives
Diagnose diabetes insipidus in a patient who presents with hyperosmolality.

Critique
This patient is clearly hyperosmolar, since twice the serum sodium level is 310 mosm/kg H2O. The appropriate renal response to hyperosmolality is to maximally concentrate the urine (generally to greater than 800 mosm/kg H2O). This response is not seen in this patient. Thus, he has either diabetes insipidus or a solute diuresis. A solute diuresis is most often caused by hyperglycemia. This patient does have a plasma glucose level of 180 mg/dL; however, this degree of elevation is unlikely to cause significant solute diuresis because the renal threshold for glucose reabsorption in most persons is 200 to 225 mg/dL. Furthermore, solute diuresis is usually characterized by isotonicity of the urine, whereas this patient has a markedly hypotonic urine. Consequently, diabetes mellitus is unlikely. Hyperosmolar patients without glucosuria who have submaximally concentrated urine have diabetes insipidus by definition. Patients with primary polydipsia also manifest polyuria and polydipsia but do not become hyperosmolar. However, whether this patient has central or nephrogenic diabetes insipidus cannot be determined from the data supplied. Distinguishing between central and nephrogenic diabetes insipidus in a patient who is already hyperosmolar can be done by measuring plasma arginine vasopressin (AVP); patients with central diabetes insipidus have an inappropriately low level, whereas patients with nephrogenic diabetes insipidus have a normal to elevated level) or by evaluating the response to administered AVP (5 U subcutaneously) or, preferably, the selective AVP V2 receptor agonist desmopressin (1-deamino-8-D-arginine vasopressin, 1 to 2 μg subcutaneously or intravenously). A significant increase in urine osmolality (greater than 50%) within 1 to 2 hours after injection indicates insufficient endogenous AVP secretion, and, therefore, central diabetes insipidus, whereas a lack of response indicates renal resistance to the effects of AVP and, therefore, nephrogenic diabetes
insipidus. Until one of these tests is done, the patient has diabetes insipidus of undetermined etiology.

**Endocrinology and Metabolism: Question 51**
**The correct answer is B**

**Educational Objectives**
Recognize the clinical presentation and laboratory findings of nutritional osteomalacia.

**Critique**
Nutritional osteomalacia (vitamin D deficiency) is likely in this elderly woman with depression, poor diet, and lack of exposure to sunshine. Muscle weakness and bone pain are common. In this setting, the plasma concentration of 25-hydroxyvitamin D3 will be low because it is representative of total body vitamin D stores. The parathyroid hormone level will be elevated because of the ensuing secondary hyperparathyroidism, as the parathyroid glands try to maintain normal serum ionized calcium levels in the face of decreased supply from the gastrointestinal tract. 1,25-Dihydroxyvitamin D levels are regulated by parathyroid hormone (by increasing 1α-hydroxylation of 25-hydroxy) and are likely to be within the normal range in this patient.

**Endocrinology and Metabolism: Question 52**
**The correct answer is D**

**Educational Objectives**
Recognize that patients at low risk do not need screening for gestational diabetes mellitus.

**Critique**
About 7% of pregnancies (about 200,000 cases annually) are complicated by gestational diabetes. Risk for gestational diabetes mellitus should be assessed at the first prenatal visit. High-risk patients (those with marked obesity, personal history of gestational diabetes mellitus, glycosuria, or a family history of diabetes) should undergo glucose testing as soon as possible, and if results are negative, be retested at 24 to 28 weeks of gestation. A 1-hour plasma glucose value after a 50-g oral glucose load is used for screening. Average-risk patients should be tested at 24 to 28 weeks of pregnancy. Patients at low risk require no glucose testing and are characterized by age younger than 25 years, normal weight before pregnancy, member of an ethnic group with a low prevalence of gestational diabetes mellitus, no known diabetes in first-degree relatives, no history of abnormal glucose tolerance, and no history of poor obstetric outcome.

Hemoglobin A1C and fructosamine are used to monitor glycemic control once the diagnosis of diabetes has been established. Hemoglobin A1C assesses glycemic control over 120 days, whereas fructosamine (glycosylated albumin) assesses glycemic control over 3 weeks.
**Endocrinology and Metabolism: Question 53**

**The correct answer is B**

**Educational Objectives**
Recognize the physiologic findings in amenorrhea due to nutritional deprivation.

**Critique**
A low sex hormone-binding globulin occurs in the polycystic ovary syndrome, which this patient does not have. Other than weight loss, no evidence suggests that she has become hyperthyroid. An elevated androstenedione level of ovarian or adrenal origin would not be expected, nor would high levels of any estrogenic metabolite including estradiol. Since the patient has had regular menses in the past, XO gonadal dysgenesis is not likely. Although hemochromatosis may occasionally present with pituitary involvement, nothing in the case suggests this condition, and if anything, the ferritin level is probably low from nutritional deprivation.

**Endocrinology and Metabolism: Question 54**

**The correct answer is C**

**Educational Objectives**
Recognize primary aldosteronism

**Critique**
Primary aldosteronism is the most likely disorder in this patient for two reasons: the lack of control of hypertension despite multidrug therapy and the longstanding and clinically significant hypokalemia despite potassium supplementation. History and physical examination reveal no other obvious secondary cause for the hypertension. Pheochromocytoma is in the differential diagnosis but is less likely because of the mild edema and hypokalemia, two signs not usually seen with pheochromocytoma. Severe essential hypertension is less likely given the patient’s age and lack of family history.

**Endocrinology and Metabolism: Question 55**

**The correct answer is D**

**Educational Objectives**
Identify the initial therapy for diabetes to meet the immediate clinical requirements.

**Critique**
The patient presents with acutely symptomatic diabetes in the setting of a suspected history of gestational diabetes. This condition is usually the harbinger of type 2 diabetes rather than type 1 diabetes. Nonetheless, the patient only weighs 20% more than her ideal body weight and has marked symptoms. Medical nutrition therapy is intrinsic to the management of all cases of diabetes, but it is unlikely to relieve her symptoms and control her blood glucose level immediately, as she has already had a 7% weight loss over the previous 6 months. Metformin or glimepiride are appropriate initial oral antidiabetic agents in patients with subclinical onset of disease. Metformin requires slow titration from the initial dosage of 500 mg/d to an effective dosage, to minimize gastrointestinal side effects. This slow titration precludes its use in the treatment of symptomatic disease. Glimepiride works more acutely and does not require titration for efficacy. In general, however, sulfonylureas reduce the hemoglobin A1C level by only 2%, which would leave this patient with an value still greater than 8% and lacking adequate control. Fixed mixtures of a sulfonylurea and metformin have recently been brought to market, emphasizing the dual defects inherent in type 2 diabetes. In theory, they should increase adherence because of the reduced complexity of administration compared with use of multiple individual agents. The need to titrate metformin to avoid gastrointestinal side effects limits the concentration of the metformin in these fixed combination tablets, and titration of the dose to as many as four pills daily is needed for maximal efficacy. The
use of generic preparations could achieve the same dosing levels with only three pills daily at considerably less cost. The American Diabetes Association recommends use of insulin as the initial therapy in type 2 diabetes when patients present with acute symptoms, pregnancy, or hyperglycemic emergencies. Insulin therapy is the quickest means of alleviating symptoms and stabilizing weight loss. Reduction of glucose toxicity and lipotoxicity improves both 3-cell response and peripheral insulin sensitivity and may allow later discontinuation of insulin therapy and maintenance of control with oral antidiabetic agents.

**Endocrinology and Metabolism: Question 56**
The correct answer is D
**Educational Objectives**
Recognize the most likely cause of adrenal insufficiency.
**Critique**
This patient presents with an acute adrenal crisis with dehydration, hyponatremia, and hyperkalemia, all of which strongly suggest primary adrenal insufficiency. Central adrenal insufficiency due to pituitary apoplexy can present with an acute crisis, but headaches and visual field abnormalities are usually prominent features and hyperkalemia does not generally occur. Primary adrenal insufficiency can result from all of the other causes shown as options, but autoimmune adrenalitis (Addison's disease) is the most common of these in the United States. The presence of hypothyroidism in this patient makes autoimmune adrenalitis even more likely, since these two disorders occur together in patients with autoimmune polyglandular syndromes.

**Endocrinology and Metabolism: Question 57**
The correct answer is A
**Educational Objectives**
Identify the approved medications for the treatment of osteoporosis that prevent nonvertebral fractures.
**Critique**
At present, only the bisphosphonates (alendronate and risedronate) and recombinant human parathyroid hormone 1-34 (teriparatide) have been shown to decrease nonvertebral fractures. Teriparatide should be used for the treatment of postmenopausal women who are at high risk for fracture. This includes women with a history of osteoporotic fracture, those who have multiple risk factors for fracture, or those who have failed to respond to or are intolerant of other medications for osteoporosis. Calcitonin and raloxifene, while decreasing vertebral fractures, have not been shown to decrease nonvertebral fractures in postmenopausal women.

**Endocrinology and Metabolism: Question 58**
The correct answer is A
**Educational Objectives**
Select the most appropriate surgical procedure for a patient with primary hyperparathyroidism.
**Critique**
This patient has a clearly defined parathyroid adenoma on a sestamibi scan. He is a suboptimal candidate for general anesthesia because of his intrinsic lung disease. Minimally invasive parathyroidectomy, using a unilateral incision under local anesthesia, is an ideal option in this patient. Serial measurement of parathyroid hormone intraoperatively will help the surgeon to quickly document cure of the hyperparathyroidism on resection of the abnormal gland. If this occurs, further neck exploration is not necessary. If minimally invasive surgery were not available, the
alternative approach is conventional single parathyroidectomy, which could also be performed with the assistance of intraoperative parathyroid hormone measurement. If parathyroid hormone could not be measured intraoperatively, the surgeon would have to inspect the other three parathyroids for normal appearance, because double adenomas are present in up to 10% of patients. Subtotal parathyroidectomy is typically reserved for patients with parathyroid hyperplasia, as may be seen in multiple endocrine neoplasia syndromes or in tertiary hyperparathyroidism. Catheter embolization is not a primary approach to the treatment of hyperparathyroidism. Although the procedure was used in the past, development of less invasive approaches has made it less desirable.

Endocrinology and Metabolism: Question 59
The correct answer is E

Educational Objectives
Recognize the indications for insulin therapy in the management of type 2 diabetes.

Critique
The patients glucose control remains unacceptable (hemoglobin A1c level >6.5% to 7%) despite use of maximally effective doses of sulfonylurea and metformin. Although the dosages of both drugs could be increased, no improved efficacy would be seen. The patients body weight is approximately 20% greater than the ideal value, and he would benefit from a weight loss program. Medical nutrition therapy is appropriate and may improve glycemic control. Use of a low-carbohydrate diet remains controversial. If a low-carbohydrate diet is begun, calories should be preferentially derived from monounsaturated fats, with less than 10% of total calories from saturated fat sources. Monounsaturated fat is calorie-dense compared with carbohydrate, and an equivalent volume of food may contain considerably more calories than does a higher carbohydrate meal. No data support the long-term use or benefit of a low-carbohydrate diet in the treatment of type 2 diabetes. Data supporting use of triple oral antidiabetic therapy are limited. Troglitazone was approved in combination with sulfonylureas and metformin shortly before its removal from the market, on the basis of one uncontrolled trial and one controlled clinical trial. The addition of a glitazone to existing oral antidiabetic therapy decreased the hemoglobin A1C level by 0.9% to 1.3%. The addition of a bedtime dose of basal insulin to oral agent therapy reduced the hemoglobin A1C level from a baseline value of 8.6% to 6.9%. Either NPH or insulin glargine achieved glycemic control, but glargine did so with a significant reduction in the risk of hypoglycemia.

Endocrinology and Metabolism: Question 60
The correct answer is E

Educational Objectives
Recognize and manage acromegaly.

Critique
This patient has a growth hormone-secreting pituitary macroadenoma that was compromising his vision and causing his other symptoms. It interfered with his gonadal function but not his thyroid or adrenal function. Growth hormone-secreting tumors often also secrete prolactin, but not in this case. The patient underwent the appropriate evaluation and initial treatment. After surgery, his pituitary function was not damaged, but his insulin-like growth factor-I level is still high. Therefore, he still has active acromegaly, despite the lack of gross residual tumor on MRI. Active acromegaly causes severe long-term cardiovascular and musculoskeletal morbidity, and patients have increased mortality rates. Therefore, treatment is required even if no residual tumor is seen on MRI. Monitoring this patient is not acceptable. Referral back to the neurosurgeon is not necessary because there is no
The best treatment option for this patient is the long-acting somatostatin analogue octreotide. Somatostatin suppresses normal and neoplastic growth hormone secretion and decreased growth hormone and insulin-like growth factor-i levels in acromegaly. Because it causes tumor shrinkage in some but not all patients with acromegaly, it is not usually used as sole therapy. However, in this patient debulking was successful. In the past, octreotide had to be given as multiple daily subcutaneous injections; the development of depot forms has simplified administration. This patient should start therapy with depot octreotide and be followed with insulin-like growth factor-i measurement and MRIs; if octreotide therapy successfully normalizes the insulin-like growth factor-i levels and the tumor has not regrown, further therapy may not be needed. In addition, pegvisomant, a growth hormone receptor antagonist, has recently become available to treat acromegaly.

Endocrinology and Metabolism:Question 61
The correct answer is A

Educational Objectives
Differentiate type 1 and type 2 diabetes mellitus.

Critique
Although the patients age, asymptomatic state, and absence of ketones seem to point toward type 2 diabetes, the low body mass index of 20.3 and lack of family history are unusual. No drug history or physical stigmata suggest Cushing’s syndrome as a secondary cause of diabetes. This patient has an atypical presentation of type 1 diabetes (latent autoimmune diabetes of aging) or type 2 diabetes. Plasma insulin and fasting and stimulated C-peptide levels are measures of endogenous insulin production. At the onset of diabetes, none of these substances are clear delineators of the natural history of β-cell destruction. Type 1 diabetes is an autoimmune destruction of β cells that is characterized by the presence of anti-islet cell antibodies and antibodies against glutamic acid decarboxylase. In approximately 15% of older persons with new-onset diabetes, the presence of anti-glutamic acid decarboxylase antibodies indicates a slowly evolving autoimmune form of diabetes. Its natural history is progressive β-cell failure over a prolonged period; insulin therapy is ultimately required for glycemic control. Early insulin therapy is recommended for these patients. Residual insulin secretory capacity, as measured by insulin or C-peptide levels, fails to delineate the cause of β-cell failure. Residual C-peptide secretion can occur for many years in well-controlled type 1 diabetes and may be suppressed because of glucotoxicity and lipotoxicity in type 2 diabetes. Thus, measures of β-cell autoimmunity are more valuable than insulin secretory capacity in differentiating type 1 from type 2 diabetes.
Endocrinology and Metabolism: Question 62
The correct answer is A
Educational Objectives
Understand appropriate pharmacological therapy of very high triglyceride levels.
Critique
Triglyceride levels >1000 mg/dL confer a significant risk for the development of pancreatitis and should be treated promptly and effectively. Effective drug therapy for very high triglycerides is provided by niacin, the fibric acid derivatives, or omega-3 fatty acids in the form of fish oil. Niacin therapy should be begun promptly in addition to immediate lifestyle changes to lower triglycerides. Secondary causes of increased triglycerides should also be ruled-out. Although each of the statins has the capacity to lower triglyceride levels, their potency is limited and should not be used as primary therapy to treat very high triglycerides. The bile acid sequestrants are contraindicated as primary therapy in patients with hypertriglyceridemia, as these agents may result in a significant further elevation of triglyceride levels. Ezetemibe has limited potency to reduce triglycerides.

Endocrinology and Metabolism: Question 63
The correct answer is B
Educational Objectives
Recognize the risk factors for and laboratory signs of the milk-alkali syndrome.
Critique
The patient has non-parathyroid-mediated hypercalcemia. His psychiatric illness places him at risk for various ingestions. The constellation of hypercalcemia, metabolic alkalosis, and renal failure strongly suggests the milk-alkali syndrome. In this syndrome, patients have consumed large quantities of both calcium and alkali (such as in calcium carbonate, which is widely available in over-the-counter forms), a combination that significantly decreases renal excretion of calcium and bicarbonate. Parathyroid hormone levels are suppressed, which attenuates urinary phosphate clearance. The resulting hypercalcemia, particularly in conjunction with hyperphosphatemia, increases the risk of nephrocalcinosis and, as a result, renal failure. The decreased glomerular filtration rate may further increase serum calcium and phosphate levels. High calcium diets from dairy products alone should not lead to hypercalcemia in someone with otherwise normal parathyroid status. Vitamin D intoxication could explain both the hypercalcemia and hyperphosphatemia, as well as the renal failure (from nephrocalcinosis). However, hypervitaminosis D is ruled out by the normal 25-hydroxyvitamin D3 level, the best marker of overall vitamin D supply. Lithium therapy or toxicity is also associated with hypercalcemia, although this prescription drug is not easily available to patients. In addition, in lithium-induced hypercalcemia, parathyroid hormone levels are usually normal to high, because lithium decreases the set-point for parathyroid hormone release through effects at the calcium-sensing receptor. Famotidine, a histamine-2 receptor blocker, is not associated with hypercalcemia.

Endocrinology and Metabolism: Question 64
The correct answer is B
Educational Objectives
Evaluate and manage patients with mild thyroid failure.
Critique
Mild thyroid failure is defined as a high normal or elevated serum thyroid-stimulating hormone concentration with a normal free thyroxine level. Data suggest that elderly women with mild thyroid failure may be at increased risk of atherosclerosis and that treatment of mild thyroid failure may reduce low-density lipoprotein cholesterol
levels, particularly when thyroid-stimulating hormone concentrations are greater than 12 μU/mL. However, for younger female and male patients, prospective data demonstrating that levothyroxine improves symptoms or benefits atherosclerotic variables or events are limited. In contrast, treatment of more significant biochemical hypothyroidism appears to be beneficial in all age groups. The presence of antithyroid peroxidase antibodies, a marker of thyroid autoimmunity, predicts the likelihood that a particular patient will progress from mild to overt hypothyroidism over time.

Autoimmune thyroiditis is the most likely diagnosis. Because this patient is young and her thyroid-stimulating hormone level is in the high normal range, the most appropriate action is to repeat the laboratory tests in 6 weeks and measure antithyroid peroxidase antibodies. If the thyroid-stimulating hormone level is elevated and antibodies are present, therapy should be initiated.

**Endocrinology and Metabolism: Question 65**
The correct answer is B

**Educational Objectives**
Recognize the most appropriate test to diagnose adrenal insufficiency.

**Critique**
This patient has all the features of primary adrenal insufficiency: fatigue, weakness, dizziness, skin hyperpigmentation, hyponatremia, and hyperkalemia. The short cosyntropin stimulation test is the best test to identify primary adrenal insufficiency. Results of this test will also be abnormal in patients with chronic central adrenal insufficiency, since the adrenal glands atrophy in the absence of the trophic effect of ACTH. However, patients with acute central adrenal insufficiency (<3 weeks) often have a normal response to this test, because the adrenal glands do not atrophy this quickly. The corticotropin-releasing factor test, insulin tolerance test, and metyrapone tests are more cumbersome and expensive than the cosyntropin test, and the insulin tolerance test can also be dangerous. Although CT scan of the adrenal glands may be useful to determine whether the glands are atrophic or enlarged, the diagnosis of adrenal insufficiency should be established biochemically before this test is ordered.

**Endocrinology and Metabolism: Question 66**
The correct answer is C

**Educational Objectives**
Recognize diabetes mellitus as a cardiovascular disease risk equivalent

**Critique**
Although this patient has no other risk factors for cardiovascular disease, diabetes mellitus is a cardiovascular risk equivalent. Therefore, the target LDL cholesterol level is less than 100 mg/dL and the target triglyceride level is less than 150 mg/dL. The calculated LDL cholesterol level (total cholesterol - HDL cholesterol level - triglyceride level/5) is 141 mg/dL despite daily exercise and a low-fat diet. The best step would be to initiate therapy with a statin. The CARE trial, and the Heart Protection Study found significant improvement in cardiovascular outcomes with statin therapy in patients with diabetes. Continuing the same therapy will not significantly change cholesterol levels. Although early data show that low-carbohydrate diets may increase short-term weight loss, the long-term effects on cholesterol and cardiovascular disease are not yet known. Bile acid sequestrants are poorly tolerated—more than 20% of patients report adverse events—and they may elevate the serum triglyceride level. Nicotinic acid causes insulin resistance and may worsen hyperglycemia in patients already being treated for overt diabetes mellitus. Nicotinic acid may also cause a dose-dependent
Elevation in plasma homocysteine levels that offsets its positive effects on plasma lipids.

**Endocrinology and Metabolism: Question 67**

**The correct answer is D**

**Educational Objectives**

Recognize a false-positive urine microalbumin test.

**Critique**

Microalbuminuria is an important predictor of renal insufficiency and cardiovascular disease. Screening for microalbuminuria should be done annually from the time of diagnosis in patients with type 2 diabetes and after 5 years of disease in patients with type 1 diabetes. False-positive results can occur after exercise, such as running; during a febrile illness, urinary tract infection, or any condition that causes hematuria; and with certain medications. Microalbumin should be measured again once confounding factors are not present and be demonstrated to be positive on two occasions before the diagnosis is considered definitive. Dietary protein restriction is difficult to implement, is uncomfortable for the patient, and often requires more carbohydrate and fat than would otherwise be recommended. Accordingly, it should be reserved as the last resort in the treatment of significant proteinuria. Aspirin therapy may be appropriate for anyone with diabetes but is not specific to microalbuminuria. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers are first-line agents for treatment of microalbuminuria, but the diagnosis of pathologic microalbuminuria has not been established in this patient and use of these agents in all diabetics to prevent microalbuminuria is not a routine recommendation. Quantification of 24-hour urine protein is not required at the onset of microalbuminuria, although it can be helpful at later stages of renal disease.

**Endocrinology and Metabolism: Question 68**

**The correct answer is D**

**Educational Objectives**

Recognize the current criteria for the diagnosis of diabetes mellitus.

**Critique**

The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus has revised the criteria for the diagnosis of diabetes. Three ways to diagnose diabetes are possible: symptoms of diabetes plus a casual plasma glucose concentration of ≥200 mg/dL; 2-hour plasma glucose concentration of ≥200 mg/dL during an oral glucose tolerance test; and fasting plasma glucose of ≥126 mg/dL. Each of these methods must be confirmed on a subsequent day by any one of the other methods. "Casual" is defined as any time of the day without regard to time since last meal. The classic symptoms of diabetes include polyuria, polydipsia, and unexplained weight loss. "Fasting" is defined as no caloric intake for at least 8 hours. The 2-hour plasma glucose measurement during an oral glucose tolerance test should be obtained as described by the World Health Organization, by using a glucose load containing the equivalent of 75 g of anhydrous glucose dissolved in water. Measurement of fasting plasma glucose is the recommended test. The oral glucose tolerance test is no longer recommended for routine use in the interest of standardization, to facilitate fieldwork, and to decrease cost and demands. Hemoglobin A1C measurement is not currently recommended for diagnosis of diabetes, although some studies have shown that the frequency distributions for hemoglobin A1C have characteristics similar to those of the fasting plasma glucose level. Hemoglobin A1C is valuable for monitoring glycemic control.
Fructosamine (glycosylated albumin) is likewise used to monitor glycemic control. It provides assessment of glycemic control over 3 weeks.

**Endocrinology and Metabolism: Question 69**
The correct answer is B

**Educational Objectives**
Select the most appropriate treatment for men with osteoporosis.

**Critique**
There is controversy about appropriate diagnostic criteria for osteoporosis in men. A consensus recommendation that osteoporosis be defined by a T score of 2.5 or below has recently been published. However, evidence of significant bone loss for his age, the presence of a significant risk factor for male osteoporosis and the history of a hip fracture make treatment of this man for osteoporosis a reasonable consideration. Alendronate significantly increases spine, hip, and total body bone mineral density and decreases vertebral fractures in men and is the only bisphosphonate approved for the treatment of male osteoporosis. Raloxifene, calcitonin, and risedronate have not been shown to be effective in increasing bone mass in men. Although teriparatide has been shown to increase bone mass in the spine and hip of men and is approved for treatment of osteoporosis in men, this medication is contraindicated for use in this patient. Teriparatide should not be prescribed for patients who are at increased risk for osteosarcoma. This includes those with Paget’s disease of bone or unexplained elevations of serum alkaline phosphatase, open epiphyses, or prior radiation therapy involving the skeleton.

**Endocrinology and Metabolism: Question 70**
The correct answer is D

**Educational Objectives**
Identify substances that interfere with levothyroxine absorption.

**Critique**
Several drugs interact with levothyroxine absorption and metabolism. Many of these agents are not prescription drugs and are available as supplements. Iron, calcium, and soy protein block absorption of levothyroxine in the gastrointestinal tract. None of the other medications listed, all of which are available without a prescription, have known effects on the absorption or metabolism of levothyroxine.

**Endocrinology and Metabolism: Question 71**
The correct answer is C

**Educational Objectives**
Understand the use of coronary heart disease risk assessment to determine appropriate management of a patient with hyperlipoproteinemia.

**Critique**
This patient has multiple risk factors and has the diagnostic characteristics of the metabolic syndrome. A 10-year risk profile calculated by the Framingham Risk Assessment tool indicates that he has a risk of >30% for a hard coronary heart disease event (a definite myocardial infarction or sudden cardiac death) within the next 10 years. This patient qualifies for the category of coronary heart disease risk equivalent, and this mandates immediate effective therapy with a lipid-lowering medication. A statin is the drug of choice for this individual as it has the potential to control his LDL cholesterol to the goal level of <100 mg/dL and has an excellent chance of also diminishing his non-HDL cholesterol to the goal level of <130 mg/dL. A bile acid sequestrant is contraindicated due to the elevated level of triglycerides, and it is not likely to achieve the desired LDL cholesterol goal. Bile acid sequestrants as mono therapy may significantly increase triglycerides in individuals whose
triglyceride level is already elevated. In this patient, a significant acute risk for pancreatitis could also be introduced by the use of a bile acid sequestrant prior to the reduction of the triglyceride level by lifestyle change and/or the use of another pharmacologic agent.

**Endocrinology and Metabolism: Question 72**

The correct answer is C

**Educational Objectives**

Understand the appropriate evaluation for diabetes insipidus in a patient presenting with polyuria and polydipsia but normal urine osmolality.

**Critique**

This patient has all of the classic symptoms of diabetes insipidus: relatively sudden onset of pronounced thirst, polyuria and nocturia and a preference for cold fluids to assuage thirst. Patients with diabetes mellitus and those with primary polydipsia usually maintain a normal serum sodium level and plasma osmolality; in the former patients, water intake keeps up with urinary losses, and in the latter, renal water excretion keeps up with fluid intake. Consequently, the serum sodium level is generally of limited differential value except at the extremes: A low serum sodium level suggests primary polydipsia because patients with diabetes mellitus rarely overcompensate by drinking so much that they exceed their renal water excretion capability, and a high serum sodium level is diagnostic of diabetes mellitus because patients with primary polydipsia maintain a water-expanded state with subsequent dilution of the serum.

Diabetes mellitus must always be considered because it is a much more common cause of polyuria and polydipsia than is diabetes insipidus, but in this case, the fasting plasma glucose level is normal. Despite classic symptoms and a MRI result suggestive of central diabetes mellitus (a lack of a posterior pituitary bright spot and a thickened pituitary stalk), some hypothalamic diseases (for example, histiocytosis and sarcoidosis) can present with the same findings on MRI but with primary polydipsia rather than diabetes mellitus. Therefore, a formal water deprivation test is essential to differentiate primary polydipsia from diabetes insipidus in this case. A random plasma arginine vasopressin level in the setting of a normal serum sodium level is uninterpretable, but a similar finding under hyperosmolar conditions after a water deprivation test can differentiate diabetes mellitus (inappropriately low arginine vasopressin level) from primary polydipsia (normal arginine vasopressin level for the degree of hyperosmolality produced). Administration of 1-deamino-8-D-arginine vasopressin will differentiate central from nephrogenic diabetes mellitus but will not reliably rule out primary polydipsia, and continued fluid intake may lead to dangerous degrees of hyponatremia in patients with primary polydipsia.

In the absence of a central nervous system tumor or infiltrative disease, more than 50% of cases of central 1-deamino-8-D-arginine vasopressin had been classified as idiopathic. However, over the past decade, reports have suggested that many of these cases are due to an autoimmune process called lymphocytic infundibuloneurohypophysitis, in which lymphocytic invasion of the posterior pituitary and pituitary stalk is seen pathologically. This process is similar to the lymphocytic infiltration of the anterior pituitary seen with lymphocytic hypophysitis, but in general these two disorders do not occur together. A characteristic finding of this disorder is marked thickening of the pituitary stalk on MRI, as is seen in this case. Such patients must be followed by serial MRI to ensure that stalk thickening does not represent an occult tumor, such as a germinoma or an infiltrating glioma, but in most cases the stalk thickening regresses over time. This effect is consistent with an inflammatory rather than a neoplastic process. Therefore, biopsy is not be indicated unless the lesion has grown on serial MRI rather than remaining stable or becoming smaller.
Although the presence of galactorrhea suggests hyperprolactinemia, probably from the inflammatory changes in the stalk that can impair delivery of dopamine to the anterior pituitary in this case, the presence or absence of hyperprolactinemia will not assist in the determination of the cause of polyuria and polydipsia.

Endocrinology and Metabolism: Question 73
The correct answer is A

Educational Objectives
Understand the current guidelines on management of postmenopausal women.

Critique
This woman has severe menopausal symptoms that are real and not a sign of psychopathology. Estrogen therapy, combined with progesterone if the patient has a uterus, will probably alleviate the symptoms considerably. However, the Womens Health Initiative found an increased risk of breast cancer in women taking a specific form of this combination therapy, as well as a higher risk of heart disease and thromboembolic disease. Estrogen is therefore no longer considered appropriate for long-term or lifetime use, and it is suggested that it be used for the shortest period possible to relieve symptoms. Estrogen in this and other studies significantly reduced the risk of osteoporotic fractures, but other nonhormonal medications may perform just as well. At a minimum, the patients baseline bone density should be determined and she should continue her exercise, healthy diet, and supplemental calcium and vitamin D. If she already has substantial bone loss, additional therapy can be used. The patient does not meet National Cholesterol Education Program criteria for pharmacologic therapy to decrease the cholesterol level and has a normal fasting plasma glucose level and no other risk factors for diabetes; a glucose tolerance test is therefore not necessary. Although raloxifene therapy has a salutary effect on bone mineral density and breast cancer risk, it worsens hot flushes.

Endocrinology and Metabolism: Question 74
The correct answer is A

Educational Objectives
Recognize the most appropriate treatment options for patients with corticosteroid-induced osteoporosis.

Critique
Corticosteroid-induced bone loss should be treated by modification of risk factors for osteoporosis, weight-bearing physical exercise as tolerated, calcium and vitamin D supplementation, and an oral bisphosphonate. Only bisphosphonates have been approved for the treatment of corticosteroid-induced osteoporosis. Both alendronate and risedronate produce significant increases in bone mass and decreases in fractures in such patients. To date, there have been no large randomized studies of the use of raloxifene in these patients. Teriparatide has been shown to increase bone mass in corticosteroid-treated patients, but no fracture data are available. Calcitonin increases bone mass in corticosteroid-treated patients, but it has not been shown to reduce the risk of fractures.

Endocrinology and Metabolism: Question 75
The correct answer is A

Educational Objectives
Evaluate and manage a small incidental pituitary lesion.

Critique
This patient has an incidentally discovered small pituitary lesion. It is most likely a nonfunctioning adenoma, but it may be a cyst or other benign lesion. Such lesions are common, and their evaluation is controversial. In a patient with no symptoms of
excess or deficient pituitary hormone secretion, a limited evaluation is the most cost-effective option. Measurement of serum prolactin is appropriate because prolactinomas are the most common type of pituitary tumor, and they may not cause symptoms if they are small and produce only modest amounts of prolactin. The other functioning pituitary tumors, including Cushing's syndrome, acromegaly, and thyrotropin-secreting hormone tumors, are rare and usually cause symptoms. Therefore, it is not cost effective to evaluate an asymptomatic patient with a small lesion for these tumors. Formal visual field examination is not indicated because the lesion is small and not located near the optic chiasm. Referral for pituitary surgery or biopsy is not indicated because the lesion is not causing symptoms. In addition, fewer than 5% of these small lesions enlarge over time. Thus, immediate surgery is not indicated, but the patient should undergo periodic monitoring with MRI. If the result is unchanged in 6 months, imaging can be repeated 1 year later and then at increasing intervals as the natural history of the lesion becomes apparent.

**Endocrinology and Metabolism: Question 76**

**The correct answer is C**

**Educational Objectives**

Understand the targets of glycemic control in patients with type 1 diabetes.

**Critique**

Although normalization of all aspects of metabolism is ideal in treatment of type 1 diabetes, this goal is rarely attained. The American Diabetes Association has set target preprandial glucose values of 80 to 120 mg/dL and bedtime values of 100 to 140 mg/dL. The target value for hemoglobin A1C is less than 7%. Keeping the 2-hour postprandial glycemic excursion less than 160 mg/dL is reasonable. Because many variables preclude achievement of these target values, individualization is important. One of the main obstacles to achievement of euglycemia is hypoglycemia, which can be life-threatening and debilitating.

The Diabetes Control and Complications Trial, which was performed in patients with type 1 diabetes, showed a 60% reduction in risk for diabetic retinopathy, nephropathy, and neuropathy between the intensive treatment group (which achieved a hemoglobin A1C level of 7.2%) and the standard treatment group over an average of 7 years. The benefit of intensive therapy resulted in a delay in the onset and a major slowing of the progression of these three complications. The benefits of intensive therapy were seen in all patients regardless of age, sex, or duration of diabetes. The documented methods to achieve tight control in type 1 diabetes include multiple (three or more) daily injections of insulin or treatment with an insulin pump. The major danger of tight control is hypoglycemia. Serious hypoglycemia may result in altered consciousness, coma, or convulsions that injure the patient or others. The intensive treatment group in the Diabetes Control and Complications Trial had a threefold greater risk of severe hypoglycemia than did the standard treatment group. The risk of hypoglycemia must be taken into consideration but can be reduced by frequent glucose monitoring and appropriate adjustment of the insulin dosage.

Although oral insulin sensitizers are helpful in achieving glucose target values in patients with type 2 diabetes, they are not indicated in patients with type 1 disease. Occasionally, patients with type 1 diabetes may manifest features of insulin resistance, such as obesity and high insulin requirements. In that setting, a trial of insulin sensitizers may be reasonable, although it would be an 'off-label’ use.
Endocrinology and Metabolism: Question 77
The correct answer is E
Educational Objectives
Recognize polycythemia as a side effect of testosterone treatment.

Critique
Testosterone is known to stimulate production of erythropoietin, and the hematocrit and erythrocyte indices rise significantly during testosterone replacement therapy. Polycythemia is more common during treatment with injectable testosterone esters than with patches or testosterone-containing gels because high levels of testosterone often occur in the first few days after injection. The risk of polycythemia is increased if the patient has another risk factor for polycythemia, such as chronic obstructive pulmonary disease with sleep apnea syndrome. Lowering the dosage of testosterone will generally reduce the hematocrit.

Endocrinology and Metabolism: Question 78
The correct answer is B
Educational Objectives

Critique
This patients type 2 diabetes puts him at high risk for heart disease. In the Heart Protection Study, appropriate lipid management reduced the incidence of cardiovascular disease by 24%. Although this patient has a calculated LDL cholesterol level of 99 mg/dL, which is less than the target value in the third Adult Treatment Panel guidelines, his triglycerides remain significantly elevated, which is an independent risk factor for heart disease. In patients with a high triglyceride level, treatment of non-HDL cholesterol is a secondary target in lipid management and may be a better tool for risk assessment than is the LDL cholesterol level. The goal for non-HDL cholesterol is a concentration that is 30 mg/dL higher than that of LDL cholesterol. The non-HDL cholesterol is calculated as the difference between the total cholesterol level and HDL cholesterol level and represents the cholesterol present in lipoprotein particles, including LDL, lipoprotein(a), intermediate-density lipoprotein, and very-low-density lipoprotein.
This patients non-HDL cholesterol level is 157 mg/dL, which is greater than the target value of 130 mg/dL, and should be treated regardless of the directly measured LDL. Atorvastatin is a potent HMG-CoA reductase inhibitor that decreases the LDL cholesterol level and, to a lesser extent, the triglyceride level. This patient is taking a submaximal dose of atorvastatin. Increasing the dosage will probably decrease the non-HDL cholesterol level and, therefore, the risk for cardiovascular disease.
A change in blood pressure medications is not indicated. The target blood pressure for this patient is less than 130/80 mm Hg. The patient reports no side effects of his current medication, and his electrolyte values are within normal limits. Additional oral hypoglycemic agents are not indicated. Although the patients glucose level is 225 mg/dL, this is an isolated measurement. The hemoglobin A1C level, which represents the mean blood glucose concentration over the past 6 weeks, is 6.5%, which meets the standards for glycemic control set forth by the American Diabetes Association. Adding glyburide would increase the risk of hypoglycemia.
Endocrinology and Metabolism: Question 79
The correct answer is E
Educational Objectives
Recognize cardiovascular risk markers.
Critique
Elevated blood pressure and low-density lipoprotein level have long been recognized as cardiovascular risk factors. A fasting plasma glucose level greater than 126 mg/dL defines diabetes, which is a cardiovascular risk factor. Microalbuminuria has long been recognized as a marker for development of diabetic renal disease but is now also recognized as an important marker of endothelial dysfunction and increased likelihood of developing cardiovascular disease. A C-reactive protein level less than 1.0 mg/dL is considered low risk and has not been shown to be linked to increased risk for cardiovascular disease.

Endocrinology and Metabolism: Question 80
The correct answer is C
Educational Objectives
Understand the use of combination drug therapy in lipoprotein management.
Critique
The Adult Treatment Panel III defines an optimal LDL cholesterol level as <100 mg/dL, and sets this as the goal for patients with coronary heart disease and coronary heart disease risk equivalents. In this patient with known coronary heart disease, his LDL cholesterol is inappropriately elevated at 125 mg/dL. His triglyceride levels and HDL cholesterol are not increased; therefore, the safest and most likely agent to achieve the desired LDL cholesterol goal is either a bile acid sequestrant or ezetimide. A further increase in the statin dosage is not appropriate because he is at the maximal dose and any further increase will be ineffective in achieving the LDL cholesterol goal and will be potentially unsafe. Gemfibrozil is not indicated because it does not significantly lower LDL cholesterol and confers an added risk of development of myositis that sometimes occurs with a statin/fibric acid combination. In some patients, particularly those with elevated triglycerides, gemfibrozil may actually elevate LDL cholesterol.

Endocrinology and Metabolism: Question 81
The correct answer is B
Educational Objectives
Manage hyperthyroidism in pregnancy.
Critique
This patient has mild thyrotoxicosis that probably indicates Graves disease, on the basis of the ophthalmopathy and the diffuse goiter. The laboratory test results are not consistent with normal pregnancy, as she is only about 3 weeks pregnant, the goiter is larger than expected, and ophthalmopathy is present. Because she has Graves disease, treatment with the lowest dose of antithyroid medications that can induce a euthyroid state and alleviate tachycardia is appropriate. Propylthiouracil is the preferred agent because it is less likely than methimazole to cause congenital abnormalities. Methimazole can be used if a patient cannot tolerate propylthiouracil, but at a lower dose than usual (approximately 10 mg once or twice daily). β-Blockers can be used as an adjunctive therapy to alleviate tachycardia and tremor while the patient is still hyperthyroid. They do not treat the underlying hyperthyroidism and would not be appropriate as monotherapy. Once thyroid hormone levels have normalized, β-blocker therapy can be discontinued. Most pregnant women with hyperthyroidism are successfully managed during pregnancy and deliver healthy children. Because of rare cases of placental passage of high levels of thyroid-
stimulating immunoglobulins, the fetus and newborn must be monitored for intrauterine growth retardation and perinatal hyperthyroidism, and thyroid-stimulating immunoglobulins should be measured during the 1 to 2 months of pregnancy.

**Endocrinology and Metabolism: Question 82**

**The correct answer is A**

**Educational Objectives**
Select the initial diagnostic tests for a patient with Paget’s disease of bone.

**Critique**
Radiographic evidence of bone involvement does not necessarily reflect metabolically active Paget’s disease. A radionuclide bone scan and measurement of the total serum alkaline phosphatase will determine the extent of the Paget’s disease and allow identification of active lesions. The active pagetic bone lesions are associated with an elevated serum alkaline phosphatase activity and avid uptake of the scanning agent. Burned out’ pagetic lesions are seen with normal or near-normal serum alkaline phosphatase activity and little or no uptake on bone scan. The bone scan is more sensitive than bone radiographs because the bone scan will detect many pagetic lesions not visualized on standard radiographs. Radiographs should be taken of bones affected by Paget’s disease. In most cases, markers of bone resorption (bone-specific alkaline phosphatase and urinary hydroxyproline) add little information to the total serum alkaline phosphatase activity. Bone biopsy is rarely indicated, as the characteristic radiographic and laboratory findings are diagnostic in most instances. A decision about treatment or observation should be based on the results of the bone scan and measurement of the serum alkaline phosphatase activity.

**Endocrinology and Metabolism: Question 83**

**The correct answer is D**

**Educational Objectives**
Understand the advantages of continuous subcutaneous insulin infusion.

**Critique**
Continuous subcutaneous insulin infusion delivers basal and bolus insulin doses with precision and provides a basal rate that remains steady after peak absorption of subcutaneous insulin. This method permits the patient to determine how much insulin is required before a meal and to deliver exactly that amount. Because the infusion of insulin is continuous, there is flexibility in dosing. Advantages of continuous subcutaneous insulin infusion include that only rapid-acting insulin, which has more predictable absorption than regular insulin, is used; only one region for injection is targeted, thus reducing variation in insulin absorption caused by site rotation; most of the subcutaneous insulin depot is eliminated, lowering the risk of hypoglycemia; and programmable insulin delivery matches physiologic needs. Continuous subcutaneous insulin infusion can help improve metabolic control during pregnancy. Candidates for continuous subcutaneous insulin infusion must be strongly motivated to improve glycemic control and willing to work with their physician in assuming substantial responsibility for their day-to-day care. They must also understand and demonstrate use of the insulin pump, self-monitoring of blood glucose, and use of the data thereby obtained. Ideally, continuous subcutaneous insulin infusion therapy should be prescribed, implemented, and followed by a skilled professional team familiar with the method and capable of supporting the patient.
Endocrinology and Metabolism: Question 84
The correct answer is C
Educational Objectives
Identify appropriate diagnostic tests for evaluation of hypoglycemia.
Critique
This patient has inappropriately high insulin, proinsulin, and C-peptide levels in the presence of hypoglycemia. The most important cause of hypoglycemia in the presence of high insulin and C-peptide levels is insulinoma, but factitious causes of hypoglycemia must be ruled out before surgical or medical intervention. Factitious hypoglycemia results from insulin or secretagogues, such as sulfonylurea or meglitinides. A 72-hour fast is not indicated at this time. The critical values for evaluation of hypoglycemia were already obtained by the emergency department physician and showed high insulin and C-peptide levels during an episode of hypoglycemia. Because the elevated C-peptide level rules out factitious insulin use, measurement of insulin antibodies is not likely to have clinical value. Metformin alone does not stimulate insulin secretion and is unlikely to cause recurrent hypoglycemia.

Endocrinology and Metabolism: Question 85
The correct answer is E
Educational Objectives
Recognize the decrease in total serum calcium level that accompanies hypoalbuminemia in patients with critical illness and malnutrition.
Critique
The measured serum calcium concentration combines bound and free fractions (approximately 50% each). Because calcium is bound to plasma proteins, chiefly albumin, hypoalbuminemia invariably leads to a decreased total serum calcium level, yet free or ionized calcium levels will remain normal. Therefore, before a diagnostic search is begun for the cause of hypocalcemia, it is necessary to determine whether the ionized calcium level is actually low. This can be done by direct measurement of ionized calcium. A quick determination can also be performed, by adding 0.8 mg/dL to the total serum calcium level for each 1-g/L reduction in the serum albumin level below 4.0 g/L. If, for example, the albumin were 2.5 g/L, addition of 1.2 mg/dL to the measured calcium level is appropriate, thereby “correcting” the value to 8.8 mg/dL—a value that is only low-normal. In this patient with severe illness and multiple complications affecting his nutritional status, substantial hypoalbuminemia would be expected. The serum phosphate level is elevated in patients with hypoparathyroidism but is likely to be low-normal in this patient (unless renal failure coexists). For unclear reasons, parathyroid hormone levels tend to be lower than expected in critically ill patients. Large-volume blood transfusions may decrease the serum calcium level by complexing with citrate. This matter may be more pertinent if the ionized calcium level is low.

Endocrinology and Metabolism: Question 86
The correct answer is C
Educational Objectives
Evaluate and manage a large incidental pituitary lesion.
Critique
This patient has an incidentally discovered large pituitary lesion that is probably a nonfunctioning macroadenoma. Such lesions are less common than incidentally discovered microadenomas. This lesion probably had nothing to do with the patients initial symptoms of dizziness and numbness. Patients with pituitary macroadenomas, even those that are incidentally discovered,
should be evaluated for mass effect, loss of pituitary function, and hypersecretion of pituitary hormones. In this case, the tumor is not secreting hormones but is probably causing hypogonadism. Therefore, the patient may later require testosterone therapy. However, this should not be the sole or initial therapy because the tumor is also causing visual compromise. For the same reason, monitoring without therapy is inappropriate in a healthy patient who has no contraindications to surgery. The best option is to refer this patient to an experienced neurosurgeon for transsphenoidal surgery. The tumor has already shown a tendency to grow and will continue to threaten the patients vision if not treated. Medical treatment with bromocriptine is inappropriate because it will not shrink the tumor significantly unless the tumor is secreting prolactin. After transsphenoidal surgery, the patient can be reevaluated for pituitary function. He may not be hypogonadal and thus not require testosterone. Tumor regrowth should be monitored with MRI.

**Endocrinology and Metabolism:Question 87**

The correct answer is B

**Educational Objectives**

Recognize approved therapies for Pagets disease of bone.

**Critique**

Indications for treatment of Pagets disease of bone include pain, deformity, fracture, involvement of the skull or weight-bearing bones, preparation for surgery of pagetic lesions, hypercalcemia during immobilization, serum alkaline phosphatase concentration twice the upper limit of normal, and neurologic complications. Bisphosphonates suppress or reduce osteoclastic bone resorption. Currently, there are five bisphosphonates approved for the treatment of Pagets disease. A majority of patients affected by Pagets disease can achieve a sustained remission and avoid the complications of this disease when treated with one of the bisphosphonates. Nasal calcitonin, although approved by the FDA for use in postmenopausal osteoporosis, is not approved for the treatment of Paget’s disease. Subcutaneous calcitonin, the first widely used therapy for Pagets disease, is now used primarily for patients who do not tolerate bisphosphonates. Plicamycin (formally called mithramycin) is approved for the treatment of cancer-associated hypercalcemia and was used as an early investigational agent for treatment of Paget’s disease. Several studies have also used gallium nitrate in the treatment of Pagets disease. Therapy with plicamycin and gallium nitrate is rarely indicated.

**Endocrinology and Metabolism:Question 88**

The correct answer is C

**Educational Objectives**

Recognize and treat the familial hypercholesterolemia syndrome.

**Critique**

This patient has a presumptive diagnosis of heterozygous familial hypercholesterolemia on the basis of her extremely elevated LDL cholesterol and the presence of xanthelasma and tendinous xanthomata. Xanthomata are highly indicative of a significant familial abnormality of lipoprotein metabolism and the extremely elevated LDL cholesterol in this patient confirms the diagnosis of familial hypercholesterolemia. Despite the fact that she is still relatively young and has preserved ovarian function, she is at very high risk for a coronary heart disease event within the next 10 years. Both men and women with heterozygous familial hypercholesterolemia experience their first myocardial infarction in their mid-40s, and it is often fatal. In this patient dietary manipulation will be inadequate to reduce
her risk of coronary heart disease. The most effective drug for reducing the LDL cholesterol level is a statin, but she will almost certainly require the combination of multiple hypolipidemic drugs to adequately control her extremely high level. In addition, she will require effective birth control while taking a statin. Patients who are homozygous for familial hypercholesterolemia have very high levels of LDL cholesterol and seldom survive into their teens without aggressive lipid lowering therapy. Pharmacologic therapy is often minimally effective in homozygous patients, and lipopheresis or liver transplantation may be required to control LDL cholesterol levels to lower the extremely high coronary heart disease risk.

Endocrinology and Metabolism: Question 89
The correct answer is E
Educational Objectives
Recognize laboratory test results that are consistent with nonthyroidal illness.
Critique
Nonthyroidal illness has various effects on the hypothalamic-pituitary-thyroid axis, including reduced secretion of thyroid-stimulating hormone (TSH) and altered metabolism of thyroxine (T4) to triiodothyronine (T3), with production instead of biologically inactive reverse T3. The euthyroid sick syndrome is characterized by low or low normal TSH values, free T4 levels that are usually in the low normal range (but that can occasionally be lower or higher), and low T3 levels. These laboratory abnormalities improve over time, usually with a transient increase in the TSH concentration to stimulate production and release of thyroidal T4 and T3. During this “recovery” phase, the TSH level may be mildly elevated, leading to possible confusion with primary hypothyroidism. Primary or secondary hyperthyroidism would be characterized by elevated levels of free T4 and total T3 and abnormal thyroid examination. Primary hypothyroidism is generally characterized by an elevated TSH concentration and a low free T4 level.

Endocrinology and Metabolism: Question 90
The correct answer is D
Educational Objectives
Recognize risk factors for calcium malabsorption and secondary hyperparathyroidism and understand the importance of measuring urine calcium output during such an evaluation.
Critique
Patients with celiac sprue are at risk for calcium malabsorption, particularly if they are not fully compliant with a diet that is free of gluten. The low gastrointestinal calcium supply results in stimulation of parathyroid cells and secondary hyperparathyroidism. Urinary calcium output is reduced in such patients, because of a relatively low calcium concentration in the glomerular filtrate and as a direct result of elevated circulating parathyroid hormone levels. Thus, the 24-hour urinary calcium level provides an indirect measurement of dietary calcium supply and gastrointestinal calcium absorption. In this patient, the parathyroid hormone level is already known to be elevated; repeated measurement would therefore not be helpful. Vitamin D levels are usually normal in patients with celiac sprue, because the abnormal villous architecture affects primarily the proximal small bowel, whereas fat-soluble vitamins are absorbed more distally. Measurement of serum calcitonin is helpful almost exclusively in patients suspected of having medullary thyroid carcinoma.
**Endocrinology and Metabolism: Question 91**

**Educational Objectives**
Select the most appropriate test to monitor the disease activity of patients with Paget's disease of bone.

**Critique**
In the absence of significant liver disease or pregnancy, a decrease in the total serum alkaline phosphatase activity is sufficient to indicate and determine changes in the activity of pagetic lesions of most patients. Routine use of a bone biopsy is not needed in the care of most patients with Paget's disease. However, a biopsy may be necessary to rule out osteosarcoma in a pagetic lesion. This rare complication is usually heralded by the onset of new or worsening bone pain and a rapid rise in serum alkaline phosphatase activity in an otherwise previously stable patient. Serial radiographs of affected bones or measurement of other biochemical indices of bone turnover offer no advantage compared to measurement of the cheaper standard total serum alkaline phosphatase in monitoring Paget's disease activity.

**Endocrinology and Metabolism: Question 92**

**Educational Objectives**
Recognize that thyroid hormone doses often must be increased during pregnancy.

**Critique**
Levothyroxine requirements typically increase during pregnancy because of rapid metabolism of thyroxine by the placenta, increased volume of distribution during pregnancy, and potential interference in absorption of levothyroxine by prenatal vitamin supplements. The usual increase in the levothyroxine dose is approximately 0.025 to 0.05 mg daily, depending on the initial dose. Because the amount of increase in an individual patient can vary, thyroid-stimulating hormone and free thyroxine should be monitored periodically during pregnancy.

**Endocrinology and Metabolism: Question 93**

**Educational Objectives**
Manage suspected acute hypercalcemia of malignancy.

**Critique**
This patient has acute hypercalcemia, probably of humoral origin, that is related to his lung cancer, which is most likely squamous cell in origin. To confirm this diagnosis, parathyroid hormone and parathyroid hormone receptor protein should be measured; the former values will be suppressed, and the latter will be elevated. Volume expansion with saline is the best initial therapy, followed by intravenous therapy with a bisphosphonate, such as pamidronate or zolendronate. The patients thiazide diuretic may be contributing to the hypercalcemia by further increasing renal calcium reabsorption. Therapy with furosemide may help eventually by increasing urinary calcium excretion. However, the patient appears volume depleted, and he must be rendered euvoletic before administration of loop diuretics is considered, so as not to exacerbate hypovolemia.