Endocrinology and Metabolic Disease

Questions

190. A 50-year-old obese female is taking oral hypoglycemic agents. While being treated for an upper respiratory infection, she develops lethargy and is brought to the emergency room. Neurological examination is nonfocal; she does not have neck rigidity. Laboratory results are as follows:

Na: 134 mEq/L
K: 4.0 mEq/L
HCO_3: 25 mEq/L
Glucose: 900 mg/dL
BUN: 84 mg/dL
Creatinine: 3.0 mg/dL
HgA1c: 6.8%
BP: 120/80 lying down, 105/65 sitting

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

a. Diabetic ketoacidosis
b. Hyperosmolar coma
c. Inappropriate ADH
d. Noncompliance with medication
e. Bacterial meningitis

191. A 24-year-old white male presents with a persistent headache for the past few months. The headache has been gradually worsening and not responding to over-the-counter medicines. He reports trouble with his peripheral vision which he noticed while driving. He takes no medications. He denies illicit drug use but has smoked one pack of cigarettes per day since the age of 18. Past history is significant for an episode of kidney stones last year. He tells you no treatment was needed as he passed the stones, and he was told to increase his fluid intake.

Family history is positive for diabetes in his mother and a brother (age 20) who has had kidney stones from too much calcium and a "low sugar problem." His father died of some type of tumor at age 40. Physical examination reveals a deficit in temporal fields of vision and a few subcutaneous lipomas. Laboratory results are as follows:

Calcium: 11.8 mg/dL (normal 8.5-10.5)
Cr: 1.1 mg/dL
Bun: 17 mg/dL
Glucose: 70 mg/dL
Prolactin: 220 μg/L (normal 0-20)
Intact parathormone: 90 pg/mL (normal 8-51)

You suspect a pituitary tumor and order an MRI which reveals a 0.7 cm pituitary mass. Based on this patient's presentation, which of the following is the most probable diagnosis?

a. Tension headache
b. Multiple endocrine neoplasia Type 1 (MEN 1)
c. Primary hyperparathyroidism
d. Multiple endocrine neoplasia Type 2A (MEN 2A)
e. Prolactinoma

192. A 50-year-old female is 5 ft 7 in tall and weighs 185 lb. There is a family history of diabetes mellitus. Fasting blood glucose (FBG) is 160 mg/dL and 155 mg/dL on two occasions. HgA1c is 7.8%. You educate the patient on medical nutrition therapy. She returns for reevaluation in 8 weeks. She states she has followed diet and exercise recommendations but her FBG remains between 130 and 140 and HgA1C is 7.3%. She is asymptomatic, and physical examination shows no abnormalities. Which of the following is the treatment of choice?

a. Thiazolidinediones
b. Encourage compliance with medical nutrition therapy
c. Insulin
d. Metformin
e. Observation with repeat HgA1C in 6 weeks.

193. A 30-year-old female complains of palpitations, fatigue, and insomnia. On physical examination, her extremities are warm and she is tachycardic. There is diffuse thyroid gland enlargement and proptosis. There is thickening of the skin in the pretibial area. Mild clubbing of digits is present. Which of the following laboratory values would you expect in this patient?

Modified with permission, from Fauci A et al. *Harrison's Principles of Internal Medicine,* 17th ed. New York, NY: McGraw-Hill, 2008.

a. Increased free thyroxine (free T_4), increased TSH
b. Increased free thyroxine, decreased TSH
c. Increased free thyroxine, normal TSH
d. Normal free thyroxine, elevated triiodothyronine (T_3), normal TSH
e. Normal free thyroxine, decreased TSH

194. A 65-year-old black female presents for an annual examination. Physical examination is unremarkable for her age. In completing the appropriate screening tests you order a dual x-ray absorptiometry (DXA) to evaluate whether the patient has osteoporosis. DXA results reveal a T-score of −3.0 at the total hip and −2.7 at the spine, consistent with a diagnosis of osteoporosis. Since her Z-score is −2.0, you proceed with an initial evaluation of secondary osteoporosis. Laboratory evaluation reveals:

Calcium: 9.7 mg/dL
Cr: 1.0 mg/dL
Bun: 19 mg/d
Glucose: 98 mg/dL
25,OH vitamin D: 12 ng/mL (optimal > 25)
WBC: 7700/μL
Hg: 12 g/dL
HCT: 38 g/dL
PLT: 255,000/μL

Based on the above information, additional laboratory would most likely reveal which of the following?

a. Elevated iPTH (intact parathormone), low ionized calcium, normal alkaline phosphatase
b. Normal iPTH, normal ionized calcium, elevated alkaline phosphatase
c. Elevated iPTH, normal ionized calcium, elevated alkaline phosphatase
d. Normal iPTH, low ionized calcium, elevated alkaline phosphatase
e. Elevated iPTH, low ionized calcium, normal alkaline phosphatase

195. You recently evaluated a 28-year-old woman who presented with complaints of shakiness and heat intolerance. The patient plans to have children and is currently using no contraception. On examination you noted tachycardia with an HR of 102, a fine tremor, a diffuse goiter, and proptosis. You now have the laboratory results and note a TSH < 0.001, elevated total T_4 of 17.8, and increased T_3 uptake. Radionuclide uptake by the thyroid gland is elevated. You tell her that she has Graves disease. What is the best treatment plan for this patient?

a. Propylthiouracil
b. Radioactive iodine
c. Propranolol
d. Thyroid surgery
e. Oral corticosteroids

196. A 50-year-old female is evaluated for hypertension. Her blood pressure is 130/98. She complains of polyuria and mild muscle weakness. She is on no blood pressure medication. On physical examination, the PMI is displaced to the sixth intercostal space. There is no sign of congestive heart failure and no edema. Laboratory values are as follows:

Na^+: 147 mEq/dL
K^+: 2.3 mEq/dL
Cl^-: 112 mEq/dL
HCO_3: 27 mEq/dL

The patient denies the use of diuretics or over-the-counter agents to decrease fluid retention or promote weight loss. She does not eat licorice. Which of the following tests is most useful in establishing a diagnosis?

a. 24-hour urine for cortisol
b. Urinary metanephrine
c. Plasma renin activity
d. Renal angiogram
e. Ratio of serum aldosterone to plasma renin activity

197. A 36-year-old female complains of inability to lose weight despite low-calorie diet and daily exercise. She has also noticed that she is cold intolerant. She is wearing a jacket even though it is summer. She also reports constipation and hair loss. These symptoms have been worsening over the past 2 to 3 months. An elevated TSH and low total and free T_4 confirm your suspicion of hypothyroidism. You suspect the etiology of this patient's hypothyroidism to be autoimmune thyroiditis. What is the best test to confirm the diagnosis of autoimmune thyroiditis?

a. Thyroid peroxidase antibody (TPOAb)
b. Antinuclear antibody
c. 24-hour radioactive iodine uptake
d. Thyroid ultrasound
e. Thyroid aspiration

198. A 58-year-old male is referred to your office after evaluation in the emergency room for abdominal pain. The patient was diagnosed with gastritis but a CT scan with contrast performed during the workup of his pain revealed a 2-cm adrenal mass. The patient has no history of malignancy and denies erectile dysfunction. Physical examination reveals a BP of 122/78 with no gynecomastia or evidence of Cushing syndrome. His serum potassium is normal. What is the next step in determining whether this patient's adrenal mass should be resected?

a. Plasma aldosterone/renin ratio.
b. Estradiol level.
c. Plasma metanephrines and dexamethasone-suppressed cortisol level.
d. Testosterone level.
e. Repeat CT scan in 6 months.

199. On routine physical examination, a 28-year-old woman is found to have a thyroid nodule. She denies pain, hoarseness, hemoptysis, or local symptoms. Serum TSH is normal. Which of the following is the best next step in evaluation?

a. Thyroid ultrasonography
b. Thyroid scan
c. Surgical resection
d. Fine needle aspiration of thyroid
e. No further evaluation

200. A 55-year-old type-2 diabetic patient has lost weight and has had good control of his blood glucose on oral metformin, with HgA1c of 6.4%. He has a history of mild hypertension and hyperlipidemia. Which of the following statements is correct regarding routine testing for diabetic patients?

a. Dilated eye examination twice yearly
b. 24-hour urine protein annually
c. Home fasting blood glucose measurement at least once per week
d. Urine microalbumin annually
e. Referral to neurologist for peripheral neuropathy evaluation

201. As part of a review of systems, a 55-year-old male describes an inability to achieve erection. The patient has mild diabetes and is on an ACE inhibitor for hypertension. Which of the following is the most appropriate first step in evaluation?

a. Penile Doppler ultrasound
b. Serum gonadotropin level
c. Information about libido and morning erections
d. Therapeutic trial of sildenafil
e. Nocturnal penile tumescence testing

202. A 90-year-old male complains of hip and back pain. He has also developed headaches, hearing loss, and tinnitus. On physical examination the skull appears enlarged, with prominent superficial veins. There is marked kyphosis, and the bones of the leg appear deformed. Serum alkaline phosphatase is elevated. Calcium and phosphorus levels are normal. Skull x-ray shows sharply demarcated lucencies in the frontal, parietal, and occipital bones. X-rays of the hip show thickening of the pelvic brim. Which of the following is the most likely diagnosis?

a. Multiple myeloma
b. Paget disease
c. Vitamin D intoxication
d. Metastatic bone disease
e. Osteitis fibrosa cystica

203. A 58-year-old postmenopausal female presents to your office on suggestion from a urologist. She has passed 3 kidney stones within the past 3 years. She is taking no medications. Her basic laboratory work shows the following:

Na: 139 mEq/L
K: 4.2 mEq/L
HCO_3: 25 mEq/L
Cl: 101 mEq/L
BUN: 19 mg/dL
Creatinine: 1.1 mg/dL
Ca: 11.2 mg/dL

A repeat calcium level is 11.4 mg/dL; PO_4 is 2.3 mmol/L (normal above 2.5). Which of the following tests will confirm the most likely diagnosis?

a. Serum ionized calcium
b. Thyroid function profile
c. Intact parathormone (iPTH) level
d. Liver function tests
e. 24-hour urine calcium

204. A patient comes to your office for a new-patient visit. He has moved recently to your city due to a job promotion. His last annual examination was 1 month prior to his move. He received a letter from his primary physician stating that laboratory workup had revealed an elevated alkaline phosphatase and that he needed to have this evaluated by a physician in his new location. On questioning, his only complaint is pain below the knee that has not improved with over-the-counter medications. The pain increases with standing. He denies trauma to the area. On examination you note slight warmth just below the knee, no deformity or effusion of the knee joint, and full ROM of the knee without pain. You order an x-ray, which shows cortical thickening of the superior fibula and sclerotic changes. Laboratory evaluation shows an elevated alkaline phosphatase of 297 mg/dL with an otherwise normal metabolic panel. Which of the following is the treatment of choice for this patient?

a. Observation
b. Nonsteroidal anti-inflammatory
c. A bisphosphonate
d. Melphalan and prednisone
e. Ursodeoxycholic acid (UDCA)

205. Your patient is a 48-year-old Hispanic male with a 4-year history of diabetes mellitus type 2. He is currently utilizing NPH insulin/Regular insulin 40/20 units prior to breakfast and 20/10 units prior to supper. His supper time has become variable due to a new job and ranges from 5 to 8 PM. In reviewing his glucose diary you note some very low readings (40-60 mg/dL) during the past few weeks at 3 AM. When he awakens to urinate, he feels sweaty or jittery so has been checking a fingerstick blood glucose. Morning glucose levels following these episodes are always higher (200-250) than his average fasting glucose level (120-150). Which change in his insulin regimen is most likely to resolve this patient's early AM hypoglycemic episodes?

a. Increase morning NPH and decrease evening NPH.
b. Decrease morning NPH and decrease evening regular insulin.
c. Change regimen to glargine at bedtime and continue morning and evening regular insulin.
d. Discontinue both NPH and regular insulin; implement sliding scale regular insulin with meals.
e. Change regimen to glargine at bedtime with lispro prior to each meal.

206. A 40-year-old alcoholic male is being treated for tuberculosis, but he has not been compliant with his medications. He complains of increasing weakness, fatigue, weight loss, and nausea over the preceding three weeks. He appears thin, and his blood pressure is 80/50 mm Hg. There is increased pigmentation over the elbows and in the palmar creases. Cardiac examination is normal. Which of the following is the best next step in evaluation?

a. CBC with iron and iron-binding capacity
b. Erythrocyte sedimentation rate
c. Early morning serum cortisol and cosyntropin stimulation
d. Blood cultures
e. Esophagogastroduodenoscopy (EGD)

207. A 53-year-old woman suffers from long-standing obesity complicated by DJD of the knees, making it difficult for her to exercise. Recently her fasting blood glucose values have been 148 mg/dL and 155 mg/dL; you tell her that she has developed type 2 diabetes. She wonders if diet will allow her to avoid medications. In addition, her daughter also suffers from obesity and has impaired fasting glucose, and the patient wonders about the management of her prediabetes. Which of the following is a correct statement based on the American Diabetes Association 2008 guidelines regarding *nutrition recommendations and interventions for diabetes*?

a. Low-carbohydrate diets such as "South Beach" and "Atkins" should be avoided.
b. Outcomes studies show that medical nutrition therapy (MNT) can produce a 1 to 2 point decrease in hemoglobin A1c in type 2 diabetics.
c. Prediabetic patients should be instructed to lose weight and exercise but a referral to a medical nutritionist is not necessary until full-blown diabetes is diagnosed.
d. Very low-calorie diets (< 800 cal/day) produce weight loss that is usually maintained after the diabetic patient returns to a self-selected diet.
e. Bariatric surgery may be considered for patients with type 2 diabetes and a BMI of > 30 kg/m^2.

208. A 45-year-old G2P2 female presents for annual examination. She reports regular menstrual cycles lasting 3 to 5 days. She exercises 5 times per week and reports no difficulty sleeping. Her weight is stable 140 lbs and she is 5 ft 8 in tall. Physical examination is unremarkable. Laboratory studies are normal with the exception of a TSH value of 6.6 mU/L (normal 0.4-4.0 mU/L). Which of the following represents the best option for management of this patient's elevated TSH?

a. Repeat TSH in 3 months and reassess for signs of hypothyroidism.
b. Begin low dose levothyroxine (25-50 μg/d).
c. Recommend dietary iodide supplementation.
d. Order thyroid uptake scan.
e. Measure thyroid peroxidase antibodies (TPOAb).

209. A family brings their 82-year-old grandmother to the emergency room stating that they cannot care for her anymore. They tell you, "She has just been getting sicker and sicker." Now she stays in bed and won't eat because of stomach pain. She has diarrhea most of the time and can barely make it to the bathroom because of her weakness. Her symptoms have been worsening over the past year, but she has refused to see a doctor. The patient denies symptoms of depression. Blood pressure is 90/54 with the patient supine; it drops to 76/40 when she stands. Heart and lungs are normal. Skin examination reveals a bronze coloring to the elbows and palmar creases. What laboratory abnormality would you expect to find in this patient?

a. Low serum Ca^+
b. Low serum K^+
c. Low serum Na^+
d. Normal serum K^+
e. Microcytic anemia

210. A 60-year-old woman comes to the emergency room in a coma. The patient's temperature is 32.2°C (90°F). She is bradycardic. Her thyroid gland is enlarged. There is diffuse hyporeflexia. BP is 100/60. Which of the following is the best next step in management?

a. Await results of T_4 and TSH.
b. Obtain T_4 and TSH; begin intravenous thyroid hormone and glucocorticoid.
c. Begin rapid rewarming.
d. Obtain CT scan of the head.
e. Begin intravenous fluid resuscitation.

211. A 19-year-old man with insulin-dependent diabetes mellitus is taking 30 units of NPH insulin each morning and 15 units at night. Because of persistent morning glycosuria with some ketonuria, the evening dose is increased to 20 units. This worsens the morning glycosuria, and now moderate ketones are noted in urine. The patient complains of sweats and headaches at night. Which of the following is the most appropriate next step in management?

a. Measure blood glucose levels at bedtime.
b. Increase the evening dose of NPH insulin further.
c. Add regular insulin to NPH at a ratio of 2/3 NPH to 1/3 regular.
d. Obtain blood sugar levels between 2:00 and 5:00 AM
e. Add lispro via a calculated scale to each meal; continue NPH.

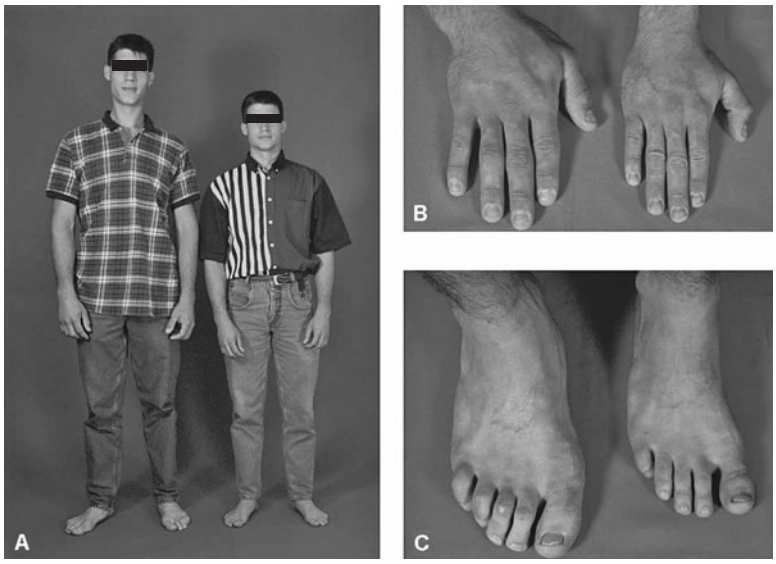
212. A 25-year-old woman is admitted for hypertensive crisis. The patient's urine drug screen is negative. In the hospital, blood pressure is labile and responds poorly to antihypertensive therapy. The patient complains of palpitations and apprehension. Her past medical history shows that she developed hypertension during an operation for appendicitis at age 23.

Hct: 49% (37-48)
WBC: 11 10^3 mm (4.3-10.8)
Plasma glucose: 160 mg/dL (75-115)
Plasma calcium: 11 mg/dL (9-10.5)

Which of the following is the most likely diagnosis?

a. Anxiety attack
b. Renal artery stenosis
c. Essential hypertension
d. Type 1 diabetes mellitus
e. Pheochromocytoma

213. The young man pictured below on the left complains of persistent headache. He has noticed gradual increase in his ring size and his shoe size over the years. He has a peculiar deep, hollow-sounding voice. Which of the following is his most likely visual field defect?



Reproduced, with permission, from Fauci A et al. *Harrison's Principles of Internal Medicine,* 17th ed. New York, NY: McGraw-Hill, 2008.

a. Bitemporal hemianopsia
b. Unilateral blindness
c. Left homonymous hemianopsia
d. Right homonymous hemianopsia
e. Diplopia

214. A patient with small cell carcinoma of the lung develops increasing fatigue but is otherwise alert and oriented. Serum electrolytes show a serum sodium of 118 mg/L. There is no evidence of edema, orthostatic hypotension, or dehydration. Urine is concentrated with an osmolality of 550 mmol/L. Serum BUN, creatinine, and glucose are within normal range. Which of the following is the next appropriate step?

a. Normal saline infusion
b. Diuresis
c. Fluid restriction
d. Demeclocycline
e. Hypertonic saline infusion

215. The 40-year-old woman shown below complains of weakness, amenorrhea, and easy bruisability. She has hypertension and diabetes mellitus. She denies use of any medications other than hydrochlorothiazide and metformin. What is the most likely explanation for her clinical findings?

Reproduced, with permission, from Fauci A et al. *Harrison's Principles of Internal Medicine,* 17th ed. New York, NY: McGraw-Hill, 2008.

a. Pituitary tumor
b. Adrenal tumor
c. Ectopic ACTH production
d. Hypothalamic tumor
e. Partner abuse (domestic violence)

216. A 24-year-old male presents with gynecomastia and infertility. On examination, he has small, firm testes and eunuchoid features. He has scant axillary and pubic hair. Which of the following is correct?

a. The patient has Turner syndrome.
b. The patient will have a normal testosterone level.
c. His most likely karyotype is 47 XXY.
d. The patient will have normal sperm count.
e. The patient is likely to have low levels of gonadotropins.

217. A 52-year-old man complains of impotence. On physical examination, he has an elevated jugular venous pressure, S_3 gallop, and hepatomegaly. He also appears tanned, with pigmentation along joint folds. His left knee is swollen and tender. The plasma glucose is 250 mg/dL, and liver enzymes are elevated. Which of the following studies will help establish the diagnosis?

a. Detection of nocturnal penile tumescence
b. Determination of iron saturation
c. Determination of serum copper
d. Detection of hepatitis B surface antigen
e. Echocardiography

218. A 30-year-old man is evaluated for a thyroid nodule. The patient reports that his father died from thyroid cancer and that a brother had a history of recurrent renal stones. Blood calcitonin concentration is 2000 pg/mL (normal is less than 100); serum calcium and phosphate levels are normal. The patient is referred to a thyroid surgeon. Which of the following studies should also be obtained?

a. Obtain a liver scan.
b. Measure parathormone level.
c. Measure urinary catecholamines.
d. Administer suppressive doses of thyroxine and measure levels of thyroid-stimulating hormone.
e. Treat the patient with radioactive iodine.

219. A 32-year-old woman has a 3-year history of oligomenorrhea that has progressed to amenorrhea during the past year. She has observed loss of breast fullness, reduced hip measurements, acne, increased body hair, and deepening of her voice. Physical examination reveals frontal balding, clitoral hypertrophy, and a male escutcheon. Urinary free cortisol and dehydroepiandrosterone sulfate (DHEAS) are normal. Her plasma testosterone level is 6 ng/mL (normal is 0.2 to 0.8). Which of the following is the most likely diagnosis?

a. Cushing syndrome
b. Arrhenoblastoma
c. Polycystic ovary syndrome
d. Granulosa-theca cell tumor
e. Ovarian teratoma

220. A 54-year-old man who has had a Billroth II procedure for peptic ulcer disease now presents with abdominal pain and is found to have recurrent ulcer disease. The physician is considering this patient's illness to be secondary either to retained antrum or to gastrinoma. Which of the following tests would best differentiate the two conditions?

a. Random gastrin level
b. Determination of 24-hour acid production
c. Serum calcium level
d. Secretin infusion
e. Insulin-induced hypoglycemia

221. A 55-year-old woman with a history of severe depression and radical mastectomy for carcinoma of the breast 1 year previously develops polyuria, nocturia, and excessive thirst. Laboratory values are as follows:

Serum electrolytes: Na^+ 149 mEq/L; K^+ 3.6 mEq/L
Serum calcium: 9.5 mg/dL
Blood glucose: 110 mg/dL
Blood urea nitrogen: 30 mg/dL
Urine osmolality: 150 mOsm/kg

Which of the following is the most likely diagnosis?

a. Psychogenic polydipsia
b. Renal glycosuria
c. Hypercalciuria
d. Diabetes insipidus
e. Inappropriate antidiuretic hormone syndrome

222. A 30-year-old nursing student presents with confusion, sweating, hunger, and fatigue. Blood sugar is 40 mg/dL. The patient has no history of diabetes mellitus, although her sister is an insulin-dependent diabetic. The patient has had several similar episodes over the past year, all occurring just prior to reporting for work in the early morning. At the time of hypoglycemia, the patient is found to have a high insulin level and a low C peptide level. Which of the following is the most likely diagnosis?

a. Reactive hypoglycemia
b. Pheochromocytoma
c. Factitious hypoglycemia
d. Insulinoma
e. Sulfonylurea use

223. A 50-year-old female presents with complaints of more than 10 severe hot flashes per day. Her last menstrual period was 13 months ago. She denies fatigue, constipation, or weight gain. Current medical issues include osteopenia diagnosed by central DXA. Family history is positive for hypertension in her father and osteoporosis in her mother. The patient uses no medications other than calcium and vitamin D supplements.

Physical examination reveals weight 145 lbs, height 5ft 6 in, BMI 24, BP 126/64, HR 68. Otherwise the examination is normal.
Screening laboratory studies:
Fasting glucose: 98
Cholesterol: 200 mg/dL
LDL: 100 mg/dL
Triglycerides: 150 mg/dL
HDL: 50 mg/dL
TSH: 1.0 mU/L

The patient requests hormone therapy to decrease hot flashes. Which of the following statements is true regarding hormone replacement therapy?

a. Progesterone therapy alone can alleviate hot flashes.
b. Hormone therapy does not affect bone density.
c. Her symptoms do not warrant systemic HT.
d. Oral estrogen therapy does not affect lipid levels.
e. The risk of breast cancer is directly related to duration of estrogen use.

Questions 224 to 226

Select the most likely disease process for the clinical syndromes described. Each lettered option may be used once, more than once, or not at all.

a. Acromegaly
b. Essential hypertension
c. Empty sella syndrome
d. Cushing disease
e. TSH-secreting adenoma
f. Diabetes insipidus
g. Chronic oral glucocorticoid use
h. Prolactin-secreting adenoma

224. A 30-year-old woman has prominent cervical and dorsal fat pads, purple abdominal striae, unexplained hypokalemia, and diabetes mellitus.

225. A nonpregnant woman has headaches, bitemporal hemianopsia, irregular menses, and galactorrhea.

226. An obese hypertensive woman has chronic headaches, normal visual fields, and normal pituitary function.

Questions 227 to 229

Match each symptom or sign with the appropriate disease. Each lettered option may be used once, more than once, or not at all.

a. Subacute thyroiditis
b. Graves disease
c. Factitious hyperthyroidism
d. Struma ovarii
e. Multinodular goiter
f. Thyroid nodule
g. Iodide deficiency
h. TSH-secreting pituitary adenoma

227. 20-year-old female presents with tachycardia, tremor, and heat intolerance. On physical examination, no thyromegaly is noted, but she does have RLQ fullness on pelvic examination. TSH is < 0.01, and radionuclide scan reveals low uptake in the thyroid gland.

228. A male nursing assistant presents with weakness and tremor. Examination shows no ophthalmopathy or pretibial myxedema. No thyroid tissue is palpable. T_4 is elevated; radioactive iodine uptake is reduced.

229. A 20-year-old presents after recent upper respiratory infection. She complains of neck pain and heat intolerance. The thyroid is tender. Erythrocyte sedimentation rate is elevated; free thyroxine value is modestly elevated.

Endocrinology and Metabolic Disease

Answers

190. The answer is b. *(Fauci, p 2285.)* This obese patient on oral hypoglycemics has developed hyperglycemia and lethargy during an upper respiratory infection. Hyperosmolar nonketotic states typically occur in type 2 diabetes and can be fatal. When hyperglycemia and dehydration cause severe hypertonicity, lethargy or coma occurs. Serum osmolarity is calculated by the formula:

$$\frac{\text{Plasma glucose}}{18} + 2(Na^+ + K^+) + \frac{\text{blood urea nitrogen}}{2.8}$$

This patient's serum osmolality is as follows:

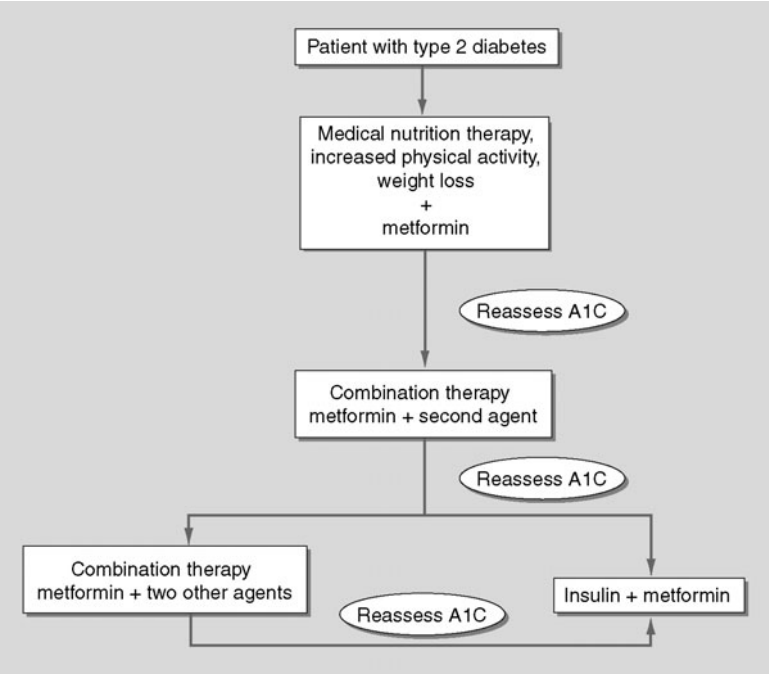
$$\frac{900}{18} + 2(134 + 4) + \frac{84}{2.8} = 50 + 276 + 30 = 356$$

Thus the serum osmolarity is greater than 350 mOsm/L. Although the serum sodium is usually the main determinant of osmolarity, extreme hyperglycemia contributes significantly to this patient's hypertonicity. Osmotically active particles in the extracellular fluid space pull water out of the intracellular space. This causes cellular dehydration in the brain and consequently the patient's CNS changes. The serum bicarbonate is too high to be consistent with diabetic ketoacidosis. The hyponatremia is minimal and is related to hyperglycemia. SIADH could not be diagnosed in this clinical setting. Patients with SIADH have an inappropriate production of ADH, leading to water retention and consequent hypotonicity. The patient's diabetes likely went out of control owing to infection.. There is no evidence of noncompliance since the patient's most recent HgA1C is 6.8% (goal < 6.5-7.0%). There is no clinical evidence for meningitis.

191. The answer is b. *(Fauci, p. 2357-2361.)* This young man presents with two obvious serum abnormalities—hypercalcemia and hyperprolactinemia most likely secondary to the pituitary tumor. This, along with his positive

family history of a younger sibling with high calcium and low blood sugar and a father who died from an unknown tumor, indicates this family has one of the multiple endocrine neoplasia syndromes. MEN I is associated with parathyroid hyperplasia/adenoma, islet cell hyperplasia/adenoma/carcinoma, pituitary hyperplasia/adenoma, pheochromocytoma, carcinoid and subcutaneous lipomas. Although MEN 2A is associated with parathyroid hyperplasia/adenoma, there is no pituitary abnormality with the MEN 2 syndromes (either MEN 2A or MEN 2B). It would not be prudent to treat the patient's issues as two separate abnormalities (primary hyperparathyroidism and prolactinoma). Tension headache is unlikely in the face of a pituitary tumor and visual field deficit.

192. The answer is d. *(Fauci, pp 2301-2302.)* The classification of diabetes mellitus has changed to emphasize the process that leads to hyperglycemia.



Reproduced, with permission, from Fauci A et al. *Harrison's Principles of Internal Medicine,* 17th ed. New York, NY: McGraw-Hill, 2008.

Type 2 DM is a group of heterogeneous disorders characterized by insulin resistance, impaired secretion of insulin, and increased glucose production. In this type 2 patient, the first intervention, medical nutrition therapy, failed to achieve the goal HgA1c of < 7.0%. *Medical nutrition therapy* (MNT) is a term now used to describe the best possible coordination of calorie intake, weight loss, and exercise. It emphasizes modification of risk factors for hypertension and hyperlipidemia, not just weight loss and calorie restriction. Blood glucose control should be evaluated after 4 to 6 weeks and additional therapy should be added; therefore, continued observation is not the best option. Metformin is considered first-line therapy in that it promotes mild weight loss, has known efficacy and side effect profile, and is available as a generic with very low cost. Thiazolidinediones ("glitazones"), sulfonylureas, and insulin are considered second line or add-on therapy for most patients with type 2 DM.

193. The answer is b. *(Fauci, pp 2233-2235.)* This patient has clinical symptoms consistent with thyrotoxicosis, and her examination is consistent with Graves disease. Most patients with thyrotoxicosis have increases in total and free concentrations of T_3 and T_4 (some may have isolated T_3 elevation). Thyrotoxicosis results in suppression of pituitary TSH secretion, so low TSH levels can confirm the diagnosis. Normal TSH with elevated T_4 usually indicates thyroid hormone resistance syndrome (or very rarely a TSH secreting pituitary tumor). Elevated free T_4 with an elevated TSH would indicate a TSH producing pituitary tumor, which might cause a diffuse goiter but would not cause proptosis or pretibial myxedema (characteristics of Graves disease).

194. The answer is c. *(Fauci, pp 2375-2376.)* This patient has vitamin D deficiency, a common cause of secondary osteoporosis, as diagnosed by the suboptimal serum 25,OH vitamin D level. Vitamin D deficiency at less than 15 ng/mL can lead to low bone density. Vitamin D deficiency leads to impaired intestinal absorption of calcium and lower serum calcium levels. The low serum calcium causes elevated iPTH. In order to maintain serum calcium homeostasis, calcium is sacrificed from the skeleton leading to low bone density. With increasing bone turnover alkaline phosphatase levels can be increased. With significant vitamin D deficiency the following pattern is characteristic: elevated iPTH, normal ionized calcium, and elevated alkaline phosphatase. The patient with uncomplicated postmenopausal osteoporosis (ie, primary osteoporosis) has normal iPTH, ionized calcium, and alkaline phosphatase levels.

195. The answer is a. *(Fauci, p 2236.)* Antithyroid drugs are the treatment of choice in a patient with Graves disease who may become pregnant. Iodine 131

has been used successfully in Graves disease and is a reasonable option if the patient is willing to practice secure contraception for at least 6 months.. However, it often causes permanent hypothyroidism and may worsen ophthalmopathy in some patients. The treatment of choice is the oral agent propylthiouracil. Propylthiouracil is chosen in cases such as this owing to low transplacental transfer. Methimazole is preferred in men and non–childbearing women because it can be given once daily. Propranolol relieves the adrenergic symptoms resulting from Graves disease but will not treat the underlying disease. Subtotal thyroidectomy is reserved for thyrotoxic pregnant women who have had severe side effects to medication. Surgical complications include hypoparathyroidism and recurrent laryngeal nerve injury. Corticosteroids are used in thyroid storm but not in the stable patient with Graves disease.

196. The answer is e. *(Fauci, p 2260.)* The patient has diastolic hypertension with unprovoked hypokalemia. She is not taking diuretics. There is no edema on physical examination. Inappropriate aldosterone overproduction is a prime consideration in hypertension with hypokalemia. Hypersecretion of aldosterone increases distal tubular exchange of sodium for potassium with progressive depletion of body potassium. The hypertension is caused by increased sodium absorption. Interestingly, peripheral edema does not occur despite the sodium retention.

Elevated aldosterone level and low plasma renin activity suggest the diagnosis of primary hyperaldosteronism. The plasma aldosterone to renin ratio is a useful screening test. A high ratio of > 30 strongly suggests aldosterone oversecretion. Lack of suppression of aldosterone (ie, autonomous overproduction), however, is necessary to definitively diagnose primary hyperaldosteronism. High aldosterone levels that are not suppressed by a 2 L saline load prove the diagnosis. CT scan of the adrenal glands is then ordered to distinguish an aldosterone producing tumor from bilateral adrenal hyperplasia. Renin levels alone lack specificity. Suppressed renin activity occurs in about 25% of hypertensive patients with essential hypertension. Twenty-four-hour urine for free cortisol would be used in the workup of a patient with Cushing syndrome. Urinary metanephrine is a screening test for pheochromocytoma. Renal angiography is a test for renal artery stenosis.

197. The answer is a. *(Fauci, pp 2230-2232.)* Once hypothyroidism is diagnosed (clinical features, a low free T_4 and elevated TSH), the etiology can be confirmed by measuring the presence of autoantibody—particularly thyroid peroxidase (TPOAb), which is present in 90% to 95% of patients

with autoimmune hypothyroidism. Ultrasound can be used to decide if a thyroid nodule is solid or cystic but will not help determine the pathogenesis of hypothyroidism. The thyroid uptake scan is useful in the diagnosis of hyperthyroidism, not in hypothyroidism.. Antinuclear antibodies are normal in immune-mediated endocrine disorders. Biopsy by fine needle aspirate is used to evaluate thyroid nodules, not autoimmume thyroiditis.

198. The answer is c. *(Fauci, pp 2257-2259.)* This patient has what is commonly referred to as an adrenal incidentaloma. If the mass is > 1 cm the first step is to determine whether it is a functioning or nonfunctioning tumor via measurement of serum metanephrines (pheochromocytoma) and dexamethasone suppressed cortisol (Cushing syndrome) levels. As the patient has no history of malignancy, a CT-guided fine-needle aspiration is not required. The patient has normal BP and potassium; therefore, plasma aldosterone/plasma renin level to evaluate primary hyperaldosteronism is not required. There are no signs of feminization or erectile dysfunction, so sex-steroid measurement is not indicated. Unenhanced CT would be required after appropriate serum workup to determine true size and characteristics (Hounsfield units). Malignant indicators include large size (>4-6 cm), irregular margins, soft tissue calcifications, tumor inhomogeneity, or high unenhanced CT attenuation values >10 HU. CT scans should be performed in 6 months and again in 1 year to ensure stability of the adrenal mass, but only after a functioning tumor has been excluded.

199. The answer is d. *(Fauci, p 2247.)* Palpable thyroid nodules are common, occurring in about 5% of all adults. Thyroid fine needle biopsy now plays a central role in the differential diagnosis of thyroid nodules. If the TSH is normal, as it is in this patient, then fine needle aspirate biopsy is indicated and will distinguish cysts from benign lesions or neoplasms. In about 14% of such cases, biopsy will be suspicious or diagnostic for malignancy and surgery will be necessary. Thyroid scan can show a "hot" nodule, which is almost always benign, but the TSH is suppressed in most autonomously overactive nodules. Thyroid sonography by itself cannot rule out malignancy in palpable nodules. Thyroid cancer can present even in a young, asymptomatic patient like this; so option e would not be appropriate.

200. The answer is d. *(Fauci, p 2302.)* Guidelines for ongoing medical care in diabetic patients recommend that the following screenings or interventions be performed annually: dilated eye examination, lipid profile, and medical

nutrition therapy and education. Annual screening for diabetic nephropathy begins with dipstick assessment of urine protein and, if negative, testing of a single voided specimen for albumin/creatinine ratio. Twenty-four-hour urine testing is not recommended. A foot examination should be performed yearly by the physician and daily by the patient. Peripheral neuropathy is first suggested by distal loss of sensation on clinical exam. HgA1c testing should be performed 2 to 4 times a year depending on patient's diabetes control (if patient HgA1c at goal, twice yearly is adequate). Blood pressure should be measured quarterly. Home glucose measurements are usually performed once daily in well-controlled type 2 diabetics.

201. The answer is c. *(Fauci, pp 297-298.)* The first step in the evaluation of erectile dysfunction is a complete and detailed history, including onset, libido, interpersonal relationship issues, and ability to attain spontaneous erection unrelated to sexual intercourse. Most men will obtain erection during REM sleep and will wake with at least a partial if not full erection. Loss of all erectile function including spontaneous morning erections suggests vascular, neuropathic, or other organic cause for the disease. Erectile dysfunction will often occur in the wake of an extramarital relationship; therefore, evaluation of interpersonal relationship issues is crucial. Diabetes may cause impotence because of its effect on penile blood supply or parasympathetic nervous system function. Serum testosterone and prolactin should be measured after psychogenic ED is ruled out. If testosterone level is low, serum gonadotropins should be measured. Specialized imaging/testing (eg, penile Doppler, nocturnal penile tumescence testing) can be performed at the discretion of the clinician, but cost and invasiveness limit its use. Physicians should not institute sildenafil or other phosphodiesterase inhibitors without considering the potential etiology of the impotence, as important diseases (pituitary tumor, peripheral arterial disease, diabetes) can be missed.

202. The answer is b. *(Fauci, p 1764, pp 2409-2410.)* This patient has widespread Paget disease of bone. Excessive resorption of bone is followed by replacement with dense, trabecular, disorganized bone. Hearing loss and tinnitus result from direct involvement of the ossicles of the inner ear. Neither myeloma, metastatic bone disease, nor osteitis fibrosa cystica would result in bony changes such as skull enlargement or long bone deformity. Serum alkaline phosphatase levels indicate increased bone turnover and are always elevated in Paget disease. The alkaline phosphatase level is normal in purely tic processes such as multiple myeloma. Hypervitaminosis D causes

hypercalcemia owing to excess intestinal absorption of calcium and would not cause these bony changes.

203. The answer is c. *(Fauci pp 2380)* Hypercalcemia must first be confirmed since misleading laboratory values can be caused by hemoconcentration of the serum sample. Ninety percent of hypercalcemia is attributed either to hyperparathyroidism or to malignancy. Almost all patients with malignancy-associated hypercalcemia have previously diagnosed cancer or symptoms (weight loss, anorexia, cough, hemoptysis) to suggest this diagnosis. In this otherwise healthy patient, confirmed hypercalcemia should lead to measurement of intact parathyroid hormone (iPTH). Other causes of hypercalcemia include familial hypocalciuric hypercalcemia, Vitamin D intoxication, sarcoidosis and other granulomatous diseases, hyperthyroidism, prolonged immobilization, and milk-alkali syndrome. Thyroid studies and liver enzymes (to evaluate for granulomatous hepatitis) might be ordered if the iPTH level is suppressed. Urine calcium excretion is assessed before parathyroidectomy to rule out familial hypocalciuric hypercalcemia, which can otherwise mimic hyperparathyroidism. Urine calcium determination, however, would not be the first test obtained in the assessment of hypercalcemia. Osteoporosis should be considered in this postmenopausal woman with hyperparathyroidism and appropriate screening for osteoporosis performed with central dual x-ray absorptiometry (DXA).

204. The answer is c. *(Fauci, pp 2410-2411.)* The radiographs and elevated alkaline phosphatase suggest Paget disease of the bone. Most patients with Paget disease do not require treatment, as they are asymptomatic. Bone pain, hearing loss, bony deformity, congestive heart failure, hypercalcemia, and repeated fractures are all indications for specific therapy beyond just symptomatic treatment for pain. Bisphosphonates bind to hydroxyapatite crystals to decrease bone turnover; they are now recommended as the treatment of choice for symptomatic Paget disease. Newer bisphosphonates such as alendronate and risedronate have replaced editronate because they are more potent and do not produce mineralization defects. The recommended dose in Paget disease is higher than the bisphosphonate dose used to treat osteoporosis. Subcutaneous injectable calcitonin is still used in patients who cannot tolerate the GI side effects of bisphosphonates. Melphalan and prednisone can be used to treat multiple myeloma, but myeloma causes osteolytic (rather than sclerotic) changes and does not cause elevation of the serum alkaline phosphatase. Ursodeoxycholic acid (UDCA) is utilized in the

treatment of primary biliary cirrhosis (which can also present with elevated alkaline phosphatase) but has no effect on bone mineralization.

205. The answer is e. *(Fauci, pp 2297-2298.)* To recognize the best insulin regimen, you must first understand the pharmacokinetics of different insulin preparation—namely the peak time of onset of action and effective duration. The following describes the insulin preparations from shortest to longest duration. Lispro has a peak onset of 0.5 to 1.5 hours and effective duration of 3 to 4 hours. Regular insulin has a peak onset of 2 to 3 hours and effective duration of 4 to 6 hours. NPH has a peak onset of 6 to 10 hours and effective duration of 10 to 16 hours. Glargine provides basal insulin with an effective duration of 24 hours and no peak effect. This patient is experiencing early morning hypoglycemia resulting from his erratic supper time; in addition his fasting blood glucose levels (120 to 150 mg/dL) are not adequately controlled. The most appropriate insulin regimen for this patient is a long-acting insulin such as glargine at bedtime along with a short-acting insulin such as lispro before each meal. This will allow better regulation of basal glucose levels while providing coverage at mealtime and will address the issue of variable mealtimes. Twice daily regimens with NPH and regular insulin have fallen out of favor as they rarely provide sufficient coverage for either basal or meal-associated glucose production. Although premeal regular insulin is cheaper, lispro more closely matches the meal-associated glucose surge and provides better overall control. .

206. The answer is c. *(Fauci, pp 2263-2264.)* This patient's symptoms of weakness, fatigue, and weight loss in combination with hypotension and extensor hyperpigmentation are all consistent with Addison disease (adrenal insufficiency). Tuberculosis can involve the adrenal glands and result in adrenal insufficiency. Measurement of serum cortisol baseline and then stimulation with ACTH will confirm the clinical suspicion. The ACTH stimulation test is used to determine the adrenal reserve capacity for steroid production. Cortisol response is measured 60 minutes after cosyntropin is given intramuscularly or intravenously; a value of 18 μg/dL or above effectively excludes adrenal insufficiency. Hemochromatosis can cause hyperpigmentation but not the weight loss and hypotension. Bacteremia would not cause the gradually increasing symptoms or the hyperpigmentation. In some patients with weight loss and nausea, an EGD may be warranted; however, the clinical features of adrenal insufficiency in conjunction with poorly treated tuberculosis would first direct attention toward adrenal status.

207. The answer is b. *(ADA, pp S61-S78)* The 2008 ADA *Guidelines for Nutrition Recommendations and Diabetes* is a position statement based on evidence-based information. Medical nutrition therapy has been shown to reduce the HgA1c in type 2 diabetics by 1 to 2 points. The guidelines state that both low carbohydrate AND low-fat diets can produce beneficial weight loss in diabetes. However, if a low-carbohydrate diet is utilized, renal function, lipid profile and protein intake should be monitored (especially in patients with nephropathy). This is because low carbohydrate diets are high in animal protein. Referral to a medical nutritionist is recommended for both prediabetics and diabetics. Although very low-calorie diets (< 800 calories) produce beneficial weight loss, weight gain is usually occurs after self-selecting diet resumes. Bariatric surgery is an option for diabetic patients with a BMI of >35 kg/m^2 NOT 30 kg/m^2.

208. The answer is a. *(Fauci, p 2233)* In this patient with a TSH below 10 mU/L and no symptoms of hypothyroidism, the diagnosis is subclinical hypothyroidism. Recommendations include checking a free thyroxine level (it should be normal in subclinical hypothyroidism) and repeating the TSH in 3 months to monitor for progression toward overt hypothyroidism. The patient should be informed about the symptoms of hypothyroidism. Thyroxine therapy is not currently recommended for asymptomatic patients in whom the TSH level is below 10 mU/L.

Although an abnormal TPOAb increases the risk of progression to overt hypothyroidism, it does not affect your present management. Thyroid uptake scan may be useful in the diagnosis of hyperthyroidism, but not in possible hypothyroidism. Iodide deficiency is not seen in the United States because of dietary iodide supplementation.

209. The answer is c. *(Fauci, pp 2263-2264.)* This patient's presentation suggests adrenal insufficiency (Addison disease). Hyponatremia is caused by loss of sodium in the urine (aldosterone deficiency) and free-water retention. Sodium loss causes volume depletion and orthostatic hypotension. Hyperkalemia is caused by aldosterone deficiency, impaired glomerular filtration, and acidosis. Ten to twenty percent of patients with adrenal insufficiency will have mild hypercalcemia; hypocalcemia is not expected. Complete blood count can reveal a normocytic anemia, relative lymphocytosis, and a moderate eosinophilia. Microcytic anemia would suggest an iron disorder or thalassemia. The hyperpigmentation results from the release of pro-opiomelanocortin which has melanocyte stimulating activity.

Hyperpigmentation is not seen if pituitary dysfunction is causing the adrenal insufficiency (ie, in secondary hypoadrenalism).

210. The answer is b. *(Fauci, pp 2233.)* The clinical picture strongly suggests myxedema coma. Unprovoked hypothermia is a particularly important sign. Myxedema coma constitutes a medical emergency; treatment should be started immediately. Should laboratory results fail to support the diagnosis, treatment can be stopped. An intravenous bolus of levothyroxine is given (500 mcg loading dose), followed by daily intravenous doses (50 to 100 mcg). Impaired adrenal reserve may accompany myxedema coma; so parenteral hydrocortisone is given concomitantly. Intravenous fluids are also needed but are less important than thyroxine and glucocorticoids; rewarming should be accompanied slowly, so as not to precipitate cardiac arrhythmias. If alveolar ventilation is compromised, then intubation may also be necessary. Hyponatremia and an elevated PCO_2 are laboratory markers of severe myxedema. CT of the head would not be the first choice, since a structural brain lesion would not explain the hypothermia, diffuse goiter, or hyporeflexia seen in this case.

211. The answer is d. *(Fauci, pp 2296-2305)* Episodic hypoglycemia at night is followed by rebound hyperglycemia. This condition, called the Somogyi effect, develops in response to excessive insulin administration. An adrenergic response to hypoglycemia results in increased glycogenolysis, gluconeogenesis, and diminished glucose uptake by peripheral tissues; hence the prebreakfast blood sugars are often elevated. Checking the blood sugars at 2 and 5 AM will demonstrate the hypoglycemia and allow the proper treatment changes—less long-acting insulin at bedtime, not more—to be made. Nocturnal hypoglycemia is a common problem with intermediate-acting insulins such as NPH and lente. The nearly peakless long-acting insulins glargine and detimir infrequently lead to the Somogyi effect.

212. The answer is e. *(Fauci, pp 2269-2270.)* Hypertensive crisis in this young woman suggests a secondary cause of hypertension. In the setting of palpitations, apprehension, and hyperglycemia, pheochromocytoma should be considered. Pheochromocytomas are derived from the adrenal medulla. They are capable of producing and secreting catecholamines. Unexplained hypertension associated with surgery or trauma may also suggest the disease. Clinical symptoms are the result of catecholamine secretion. For example, the patient's hyperglycemia is a result of a catecholamine effect of insulin suppression and stimulation of hepatic glucose output. Hypercalcemia has

been attributed to ectopic secretion of parathormone-related protein. Renal artery stenosis can cause severe hypertension but would not explain the systemic symptoms or laboratory abnormalities in this case. An anxiety attack can produce palpitations, apprehension and mild to moderate elevation in blood pressure but would not produce hypercalcemia nor elevated blood pressure poorly responsive to treatment. Essential hypertension can occur in a 25-year-old but again would not account for the laboratory changes. Diabetes mellitus does not cause hypertension unless renal insufficiency has already developed; her hyperglycemia will likely resolve when the pheochromocytoma is removed. Once pheochromocytoma is suspected, a 24-hour urine specimen for metanephrines or fractionated catecholamines is the commonly used diagnostic study. After biochemical evidence of catecholamine overproduction is found, imaging studies (CT scan, radionuclide imaging) will localize the problem for curative surgery.

213. The answer is a. *(Fauci, p 2203 and p 2210.)* The patient shows excessive growth of soft tissue that has resulted in coarsening of facial features, prognathism, and frontal bossing—all characteristic of acromegaly. This growth hormone–secreting pituitary tumor will result in bitemporal hemianopsia when the tumor impinges on the optic chiasm, which lies just above the sella turcica. Growth hormone secreting tumors are the second commonest functioning pituitary tumors (second to prolactinomas). Serum IGF-1 (insulin-like growth factor-1) level will be elevated and is usually the first diagnostic test. Growth hormone secretion is pulsatile and a single GH level is often equivocal; the GH level must be suppressed (usually with glucose) to diagnose autonomous overproduction. Unilateral blindness would be caused by optic neuritis or occlusion of the ophthalmic artery, as in temporal arteritis. Homonymous hemianopsia occurs with disease posterior to the optic chiasm—in the optic radiation or the occipital lobe. A right-sided lesion would cause left homonymous hemianopsia and vice versa. Diplopia usually implies an abnormality in cranial nerve three, four, or six, or else an eye muscle imbalance (as in Graves disease or myasthenia gravis).

214. The answer is c. *(Fauci, pp 2222-2223.)* The patient described has hyponatremia, normovolemia, and concentrated urine. These features are sufficient to make a diagnosis of inappropriate antidiuretic hormone secretion. If ADH were responding normally to the patient's hypotonic state, the urine would be dilute and the excess water load would be excreted. Treatment necessitates restriction of fluid (free water) intake. Insensible and

urinary water loss results in a rise in serum Na^+ and serum osmolality and symptom improvement. If the patient has CNS symptoms such as confusion, obtundation, or seizures, hypertonic saline is cautiously administered to raise the serum sodium out of the danger zone (usually a rise of 4-8 mEq/L). Normal saline would treat volume depletion, but this patient is euvolemic. Isotonic saline would not address the free water excess. Loop diuretics lead to modest free water loss in the urine but would be less important than fluid restriction. The tetracycline derivative demeclocycline decreases renal response to ADH and can be used in cases where the hyponatremia does not respond to fluid restriction. SIADH can occur as a side effect of many drugs or from carcinoma (especially small cell carcinoma of the lung), CNS disorders (head trauma, CNS infection) or benign lung diseases (especially lung abscesses or other chronic infections).

215. The answer is a. *(Fauci, pp 2255-2256.)* The clinical findings all suggest an excess production of cortisol by the adrenal gland. Hypertension, truncal obesity, and dark abdominal striae are common physical findings; patients often have ecchymoses at points of trauma (especially legs and forearms) because of increased capillary fragility. The process responsible for hypercortisolism is most often an ACTH-producing pituitary microadenoma. An adrenal adenoma that directly produces cortisol is the next most likely option. Most ectopic ACTH-producing neoplasms (usually small cell carcinoma of the lung) progress too rapidly for the full Cushing syndrome to develop. These patients usually present with muscle weakness due to profound hypokalemia. The initial test to diagnose endogenous cortisol overproduction is either the overnight dexamethasone suppression test (in normals, the AM cortisol should suppress to less than 2 micrograms/dL after a midnight dose of 1 mg dexamethasone) or 24-hour urine collection for free cortisol. More extensive testing is then required to determine the source. Hypothalamic tumors can affect ADH production and eating behavior but do not produce cortisol or ACTH. Unexpected bruising should prompt questions about domestic violence, but partner abuse would not account for the constellation of this patient's findings.

216. The answer is c. *(Fauci, pp 2341-2342.)* The picture of infertility, gynecomastia, and tall stature (arms and legs longer than expected for truncal size) is consistent with Klinefelter syndrome and an XXY karyotype. The patient has abnormal gonadal development with hyalinized testes that result in low testosterone levels. Pituitary function in Klinefelter syndrome is normal, so gonadotropin levels are elevated in response to underproduction of

testosterone. Although Klinefelter patients may have sexual function, they do not produce sperm and are infertile. Turner syndrome refers to the 45 XO karyotype that results in abnormal sexual development in a female.

217. The answer is b. *(Fauci, pp 2430-2431.)* Iron overload should be considered among patients who present with any one or a combination of the following: hepatomegaly, weakness, hyperpigmentation, atypical arthritis, diabetes, impotence, unexplained chronic abdominal pain, or cardiomyopathy. Diagnostic suspicion should be particularly high when the family history is positive for similar clinical findings. The most frequent cause of iron overload is the common genetic disorder (idiopathic) hemochromatosis. Secondary iron storage problems can occur after multiple transfusions in a variety of anemias. The most practical screening test is the determination of serum iron, transferrin saturation, and ferritin. Transferrin saturation greater than 50% in males or 45% in females suggests increased iron stores. Substantially elevated serum ferritin levels confirm total body iron overload. Genetic screening is now used to assess which patients are at risk for severe fibrosis of the liver. Definitive diagnosis can be established by liver biopsy. Determination of serum copper is needed when Wilson disease is the probable cause of hepatic abnormalities. Wilson disease does not cause hypogonadism, heart failure, diabetes, or arthropathy. Chronic liver disease caused by hepatitis B would not account for the heart failure, hyperpigmentation, or diabetes. Nocturnal penile tumescence and echocardiogram can confirm clinical findings but will not establish the underlying diagnosis.

218. The answer is c. *(Fauci pp 2361-2362.)* For the patient described, the markedly increased calcitonin level indicates the diagnosis of medullary carcinoma of the thyroid. In view of the family history, the patient most likely has multiple endocrine neoplasia (MEN) type IIA, which includes medullary carcinoma of the thyroid gland, pheochromocytoma, and parathyroid hyperplasia. Pheochromocytoma may exist without sustained hypertension, as indicated by excessive urinary catecholamines. Before thyroid surgery is performed on this patient, a pheochromocytoma must be ruled out through urinary catecholamine determinations; the presence of such a tumor might expose him to a hypertensive crisis during surgery. The serum calcium serves as a screening test for hyperparathyroidism. At surgery, the entire thyroid gland must be removed because foci of parafollicular cell hyperplasia, a premalignant lesion, may be scattered throughout the gland. Successful removal of the medullary carcinoma can be monitored with serum

calcitonin levels. Medullary carcinoma of the thyroid rarely metastases to the liver; so a liver scan would be unnecessary if liver enzymes are normal. Thyroxine will be needed after surgery, but MEN type II is not associated with hypothyroidism. Radioactive iodine can be used to treat malignancies that arise from the follicular cells of the thyroid; parafollicular cells, however, do not take up iodine and do not respond to radioactive iodine. Hyperparathyroidism, while unlikely in this eucalcemic patient, is probably present in his brother.

219. The answer is b. *(Fauci, p 301, p 606, p 2195.)* The symptoms of masculinization (eg, alopecia, deepening of voice, clitoral hypertrophy) in this patient are characteristic of an active androgen-producing tumor. Such extreme virilization is very rarely observed in polycystic ovary syndrome or in Cushing syndrome; moreover, the presence of normal cortisol and adrenal androgens (DHEA-S) plus markedly elevated plasma testosterone levels indicates an ovarian rather than adrenal cause of the findings. Arrhenoblastomas are the most common androgen-producing ovarian tumors. Their incidence is highest during the reproductive years. Composed of varying proportions of Leydig and Sertoli cells, they are generally benign. In contrast to arrhenoblastomas, granulosa-theca cell tumors produce feminization, not virilization. Dermoid cysts (benign teratomas) do not produce gonadotropins but cause symptoms by enlargement or ovarian torsion (pain) or rupture with contents spilling into the peritoneal cavity.

220. The answer is d. *(Fauci, p 2354, p 2359.)* The diagnosis of gastrinoma should be considered in all patients with recurrent ulcers after surgical correction for peptic ulcer disease, ulcers in the distal duodenum or jejunum, ulcer disease associated with diarrhea, or evidence suggestive of the multiple endocrine neoplasia (MEN) type I (familial association of pituitary, parathyroid, and pancreatic tumors) in ulcer patients. Because basal serum gastrin and basal acid production may both be normal or only slightly elevated in patients with gastrinomas, provocative tests may be needed for diagnosis. Both the secretin and calcium infusion tests are used; a paradoxical increase in serum gastrin concentration is seen in response to both infusions in patients with gastrinomas. In contrast, other conditions associated with hypergastrinemia, such as duodenal ulcers, retained antrum, gastric outlet obstruction, antral G cell hyperplasia, and pernicious anemia, will respond with either no change or a decrease in serum gastrin. Serum calcium level should be obtained to rule out concomitant hyperparathyroidism

but would not help in the assessment of gastrinoma per se. Insulin-induced hypoglycemia is used as a provocative test for adrenal insufficiency, not for the evaluation of acid hypersecretory states.

221. The answer is d. *(Fauci, pp 2218-2219.)* Metastatic tumors rarely cause diabetes insipidus, but of the tumors that cause it, carcinoma of the breast is by far the most common. In this patient, the diagnosis of diabetes insipidus is suggested by hypernatremia and low urine osmolality. To distinguish between central (ADH deficiency) and nephrogenic (peripheral resistance to ADH action) diabetes insipidus, vasopressin (ADH by another name) is administered. If the urine osmolality rises and the urine output falls, the diagnosis is central DI. There will be little response to vasopressin in nephrogenic DI.

Psychogenic polydipsia is an unlikely diagnosis since serum sodium is usually mildly reduced in this condition. Renal glycosuria would be expected to induce higher urine osmolality than this patient has because of the osmotic effect of glucose. While nephrocalcinosis secondary to hypercalcemia may produce polyuria, hypercalciuria does not. Finally, the findings of inappropriate antidiuretic hormone syndrome are the opposite of those observed in diabetes insipidus and thus are incompatible with the clinical picture in this patient.

222. The answer is c. *(Fauci, p 2299, p 2309.)* This clinical picture and laboratory results suggest factitious hypoglycemia caused by self-administration of insulin. The diagnosis should be suspected in healthcare workers, patients or family members with diabetes, and others who have a history of malingering. Patients present with symptoms of hypoglycemia and low plasma glucose levels. Insulin levels will be high, but C peptide will be undetectable. Endogenous hyperinsulinism, such as would be seen with an insulinoma, would result in elevated plasma insulin concentrations (> 36 pmol/L) and elevated C peptide levels (> 0.2 mmol/L). C peptide is derived from the breakdown of proinsulin, which is produced endogenously; thus C peptide will not rise in the patient who develops hypoglycemia from exogenous insulin. Reactive hypoglycemia occurs after meals and is self-limited. A rapid postprandial rise in glucose may induce a brisk insulin response that causes transient hypoglycemia hours later. It may be associated with gastric or intestinal surgery. Pheochromocytoma causes hyperglycemia due to the insulin counter-regulatory effect of catecholamines. Sulfonylurea, an insulin secretagogue, would increase natural insulin secretion resulting in elevated insulin and elevated C peptide levels.

223. The answer is e. *(Fauci, pp 2335-2336.)* Estrogen is the most effective medication for decreasing vasomotor symptoms related to menopause. Hormone therapy (HT) favorably affects the lipid panel by decreasing LDL and increasing HDL, but HT also increases triglyceride levels. HT has an antiresorptive effect on bone, thus stabilizing or increasing bone density. In the Women's Health Initiative Study, HT was shown to decrease the incidence of hip fractures. Hormone therapy should be implemented in women with moderate to severe hot flashes who lack contraindications to use (endometrial cancer, history of venous thromboembolism, breast cancer, or gallbladder disease). This patient has a low risk for cardiovascular disease and has no direct contraindications for HT. The risk of breast cancer with HT use is directly related to the length of use. Five or more years is considered long-term use and is the cut-off where most research studies and meta-analyses found increasing risk of breast cancer. Progestational agents alone do not improve vasomotor symptoms.

224 to 226. The answers are 224-d, 225-h, 226-c. *(Fauci, pp 2255, 2205-2206, 2199.)* Cushing disease produces hypercortisolism secondary to excessive secretion of pituitary ACTH. It often affects women in their childbearing years. Prominent cervical fat pads, purple striae, hirsutism, and glucose intolerance are characteristic features, as well as muscle wasting, easy bruising, amenorrhea, and psychiatric disturbances. Diabetes mellitus can result from chronic hypercortisolism. Exogenous glucocorticoid use will not produce hirsutism but will produce cervical fat pad, purple striae, muscle wasting, easy bruising and secondary diabetes mellitus. Prolactinoma, or prolactin-secreting adenoma, may cause bitemporal hemianopsia—as can all pituitary tumors. Galactorrhea (lactation not associated with pregnancy) and irregular menses or amenorrhea are the clinical clues. Serum prolactin levels are usually over 250 ng/mL, higher than usually seen in other causes of hyperprolactinemia such as medications or renal failure. Empty sella syndrome is enlargement of the sella turcica from CSF pressure compressing the pituitary gland. It is most common in obese, hypertensive women. There are no focal findings. Some patients have chronic headaches; others are asymptomatic. MRI will distinguish this syndrome from a pituitary tumor. These patients have normal pituitary function, the rim of pituitary tissue being fully functional.

227 to 229. The answers are 227-d, 228-c, 229-a. *(Fauci, pp 2233-2238.)* In a young female with hyperthyroidism, low or absent radioiodine uptake in the thyroid and a coexisting pelvic mass, you should consider struma ovarii

(ectopic thyroid tissue in a teratoma of the ovary). Whole body radionuclide scanning can demonstrate ectopic thyroid tissue. Surreptitious use of thyroid supplements (factitious hyperthyroidism) can occur in healthcare workers who have access to thyroid hormone. Classic symptoms of hyperthyroidism occur and the serum T_4 is elevated. Radioactive iodine uptake would show subnormal values, as there is no thyroid hormone production in the gland itself. The thyroid gland is not palpable. A tender thyroid gland and elevated ESR make subacute thyroiditis a likely diagnosis. Hyperthyroid symptoms are common early in the illness. The condition is self-limited (usually lasting 6-8 weeks); so antithyroid drugs are not used. Beta-blockers can alleviate symptoms until the inflammation resolves.