165. A 19-year-old white man is brought to your office by his parents. They are concerned that he has become more distant. He has lost 20 pounds in the last 4 months and has intermittent abdominal pain and nausea. He has also complained of increasing fatigue. He denies any past medical problems, tobacco, alcohol, or drug use. On physical exam, his heart rate is 110, respiratory rate 18, blood pressure 90/60, and oxygen saturations are 99 percent on room air. On exam he appears thin and withdrawn. His lungs are clear, and his heart is tachycardic without murmurs. His abdomen is soft without hepatosplenomegaly. He appears slightly tanned, especially in his palmar creases. You order basic labs that reveal the following: WBC 6000/μL; eosinophils 8%; hemoglobin 14 g/dL; sodium 130 mEq/dL; potassium 5.8 mEq/dL; chloride 107 mEq/dL; bicarbonate 24 mEq/L; BUN 18 mg/dL; creatinine 0.8 mg/dL; glucose 68 mg/dL. What is the most likely diagnosis?

A. Hyperthyroidism
B. Hypothyroidism
C. Primary hypoadrenalism
D. Secondary hypoadrenalism
E. Hyperaldosteronism

166. A 35-year-old white woman presents to your office with complaints of irregular menses. She started menstruating at age 15. Her periods have always been irregular, occurring every 28 to 50 days. She is currently trying to get pregnant and has been trying for more than 3 years. She is on phenobarbital for a seizure disorder. She denies any illicit drug, alcohol, or tobacco use. Vital signs are within normal limits. Her BMI is 28. Physical exam is notable for dark hair on her upper lips, arms, and abdomen. She has mild acne on her face and her upper back. Initial CBC is normal and pregnancy test is negative. TSH is 3.5 mU/L and free T4 is normal. The most likely cause of her hirsutism is:

A. Idiopathic hirsutism
B. Polycystic ovarian syndrome
C. Pituitary neoplasm
D. Phenobarbital
E. Hypothyroidism

167. A 75-year-old Hispanic man was recently seen in the ED for complaints of fatigue, weight loss of 15 pounds in 6 months, and cough. He has brought the results of basic labs taken at that time to your office and wants you to interpret the results. The patient has a past medical history significant for hypertension on a β-blocker and a smoking history of one pack per day for 40 years. Vitals are within normal limits with the exception of a respiratory rate of 24 and saturations of 90% on room air. Exam is significant for a thin man in no acute distress. Lung exam is significant for decreased breath sounds at the left lung base. The rest of his exam is essentially normal. The labs values are: Sodium 140 mEq/dL; potassium 4.6 mEq/dL; chloride 105 mEq/dL; bicarbonate 23 mEq/L; BUN 27 mg/dL; creatinine 1.1 mg/dL; glucose 80 mg/dL; calcium 12.5 mg/dL. The most likely etiology for this man's laboratory abnormality is:

A. Parathyroid adenoma
B. Sarcoidosis
C. Squamous cell lung carcinoma
D. β-blocker
E. Thyrotoxicosis

168. A 24-year-old white woman presents to your office with complaints of palpitations, shaking hands, and sweatiness. She states the symptoms started about 1 hour ago. You quickly review her chart and see that she has a medical history significant for depression and one suicide attempt 5 years ago. She denies any ingestions, drug, alcohol, or tobacco use. Her family history is significant for depression and type I diabetes in a 14-year-old sister. Her vital signs are within normal limits, but she is pale and diaphoretic. You check a glucose level and it is 30 mg/dL. As you replete her glucose stores, you order some lab tests. Which would be the most helpful in determining the etiology of her hypoglycemia?

A. Insulin level
B. C-peptide level
C. Sulfonylurea level
D. Liver enzyme tests (AST and ALT)
E. Thyroid function tests

169. A 36-year-old white woman comes to your office with her husband. He states that for the last few days she has been complaining of diffuse abdominal pain and bone pain. Today he noted that she was acting a bit confused. She has a past medical history significant for hypertension for which she takes a thiazide diuretic. This has never happened before, and she denies any alcohol, drug, or tobacco use. She has not had any fevers or chills, nausea, vomiting, or diarrhea. He thinks she has been constipated lately. On exam, temperature is 98.8°F (37.1°C), heart rate 80, respiratory rate 16, blood pressure 140/80, and oxygen saturations 99% on room air. Abdominal exam is significant for mild left lower quadrant pain to deep palpation. On neurologic exam, cranial nerves II through XII are intact, and muscle strength and sensorium are intact. Deep tendon reflexes are diminished throughout. You order basic labs, which reveal the following: CBC normal; sodium 140 mEq/L; potassium 4.6 mEq/L; chloride 108 mEq/L; bicarbonate 24 mEq/L; BUN 28 mg/dL; creatinine 0.8 mg/dL; glucose 90 mg/dL; calcium 13.0 mg/dL. The next step in the treatment of this patient is:

A. Glucocorticoid
B. Furosemide
C. Bisphosphonate
D. Calcitonin
E. Normal saline bolus

170. A 55-year-old white man comes to your office for routine check-up. He currently has no complaints. He has well-controlled hypertension on a β-blocker and a history of gout controlled with NSAIDs. His exam is essentially within normal limits. You note that he has not had a cholesterol level checked in the last 5 years. The fasting lipid panel reveals: LDL 116 mg/dL; HDL 50 mg/dL; triglycerides 600 mg/dL. You decide to start him on a fibrate. The mechanism by which this medication works is:

A. Reduces secretion of very low density lipoprotein (VLDL), increases stimulation of lipoprotein lipase
B. Reduces intrahepatic cholesterol, leading to increases in LDL receptor turnover
C. Inhibits production of VLDL, reduces transfer of HDL to VLDL
D. Binds bile acids in the intestine, thus lowering the cholesterol pool
E. Impairs dietary cholesterol absorption at the intestinal brush border

P1: IML/FFX P2: IML/FFX QC: IML/FFX T1: IML
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a baseline cortisol level and then giving the patient a dose of adrenal corticotropin hormone (ACTH) to try to stimulate the adrenal glands. A cortisol level is obtained at 30, 60, and 90 minutes after the ACTH is given. The cortisol level should rise appropriately to indicate that the adrenals are able to function appropriately when stimulated. This patient does not have Addison's disease.

D. Hashimoto's thyroiditis is a clinical state of hypothyroidism. It is usually seen in women aged 20 to 60 years and may be secondary to autoimmune destruction with lymphocytic infiltration of the thyroid gland. Thyroid-stimulating hormone is usually elevated and patients present with symptoms of hypothyroidism including fatigue, depression, cold intolerance, and weight gain. Treatment is with thyroid hormone replacement.

165. **C.** This patient likely has primary adrenal insufficiency or Addison's disease. Symptoms include weakness, lethargy, and fatigue as well as nausea, vomiting, abdominal pain, headaches, and weight loss. The adrenal glands produce cortisol, mineralocorticoids, and sex hormones. Deficiency of mineralocorticoids such as aldosterone causes the hyponatremia and hyperkalemia that are the hallmark electrolyte disturbances of primary adrenal insufficiency. Patients may be somewhat hypoglycemic due to cortisol deficiency. The patient's skin pigmentation is due to overproduction of ACTH-pro-opiate melanocorticotropin (POMC) from the hypothalamus/pituitary that is an attempt to stimulate the failing glands. The precursor hormone of ACTH is ACTH-POMC. POMC is cleaved from ACTH and stimulates melanocytes to produce melanin. Lastly, eosinophilia is sometimes seen in primary adrenal insufficiency. In the United States, primary adrenal insufficiency is most often due to an autoimmune destruction of the gland.

A. Patients with hyperthyroidism also experience weight loss, anxiety, and tremulousness, but they should not have the hyperpigmentation or the electrolyte disturbances that are seen in primary adrenal insufficiency.

B. Hypothyroidism gives a clinical picture of fatigue, sluggishness, and lethargy. Patients will also complain of weight gain, constipation, and cold intolerance. They will not have skin color changes or electrolyte abnormalities.

D. Secondary hypoadrenalism is a lesion of the pituitary and presents with symptoms similar to primary hypoadrenalism, with the exception of hyperkalemia and increased pigmentation. In these patients, ACTH levels are low. Remember that aldosterone is released from the adrenal gland because of the stimulation of the renin-angiotensin system and *not* because of the stimulation of ACTH. This is why, in secondary adrenal insufficiency, the potassium is usually normal. (Glucocorticoids affect water/sodium balance, allowing patients with secondary hypoadrenalism to have some degree of hyponatremia.)

E. Hyperaldosteronism usually manifests itself as hypertension and hypokalemia. This patient is hypotensive and hyperkalemic, more suggestive of someone with relative hypoaldosteronism, effects of which can be seen with primary adrenal insufficiency.

166. **B.** Polycystic ovarian syndrome is a constellation of oligo-ovulation, hyperandrogenism, and ovarian cysts. Hirsutism is secondary to increased levels of androgens.

A. Idiopathic hirsutism is associated with regular ovulatory cycles and no other medical problems. It may be related to ethnicity, and some people from Mediterranean populations are especially hairy. The most important question to ask a woman who presents with complaints of hirsutism is whether her menses are regular or not. If she says that her menses are extremely regular, then there is no further work-up to do. Patients may be referred to dermatologists or cosmetologists for hair removal.

C. Pituitary neoplasms, such as prolactinomas, can cause irregular periods but usually cause other symptoms such as headache, visual changes (depending on tumor size), and galactorrhea. Prolactinomas are not associated with hirsutism.

D. Medications can cause hirsutism, but phenobarbital is not one of these medications. Phenytoin, glucocorticoids, and pencillamine are known to cause increased hair growth.

E. Hypothyroidism can cause irregular periods and changes in hair growth (more coarse), but this patient has normal TSH and thyroxine levels.

167. **C.** This patient's hypercalcemia is likely secondary to malignancy, especially given his history of weight loss, smoking, and physical exam findings. Malignancy can cause hypercalcemia by many different paraneoplastic syndromes. Solid tumors such as squamous cell carcinoma and renal cell carcinoma often secrete parathyroid hormone-related peptide (PTH-rP) that stimulates the release of calcium from bone into the circulation. Breast cancer and melanoma cause hypercalcemia because of the direct invasion of bone. Lymphomas often cause an increase in calcium secondary to an increase in the amount of 1,25 hydroxyvitamin D.

A. Primary hyperparathyroidism causes elevated calcium by secretion of PTH. Parathyroid adenomas account for 80% of these cases, and parathyroid hyperplasia accounts for 15% to 20% of primary hyperparathyroidism. The diagnosis is often made by incidental laboratory findings of mildly elevated calcium levels. When work-up is done to evaluate the cause of the hypercalcemia, the intact PTH is found to be elevated inappropriately for the calcium level. (Normally, hypercalcemia should suppress intact PTH.)

B. Vitamin D excess can cause hypercalcemia. Vitamin D levels may become elevated, resulting in hypercalcemia, secondary to granulomatous disease such as sarcoidosis, coccidioidomycosis, histoplasmosis, and tuberculosis.

D. Various medications can cause hypercalcemia. β-blockers are not common contributors. Thiazides, lithium, vitamin A, and calcium-containing antacids are known to cause hypercalcemia.

E. Hyperthyroidism can cause hypercalcemia secondary to increased bone turnover. Immobilization and Paget's disease also cause hypercalcemia by the same mechanism. This patient's history and physical exam do not suggest elevated thyroid hormone levels.

168. **B.** A C-peptide level would help determine the difference between endogenous and exogenous insulin administration. If this patient had surreptitiously injected insulin, her C-peptide level should be low. C-peptide is a portion of the proinsulin produced endogenously.

A. An elevated insulin level would be suggest either an endogenous source of insulin such as an insulinoma or exogenous insulin levels. It cannot distinguish between the two.

C. A sulfonylurea level would help determine if the patient had ingested sulfonylurea. This patient has no contact with anyone taking oral hypoglycemics, so this is unlikely.

D. Elevated liver enzymes can suggest a toxic (e.g., acetaminophen overdose), shock, or viral insult to the liver that cause hypoglycemia. This patient denies any Tylenol use and has no history of chronic alcohol use, which could also cause hypoglycemia.

E. Hypothyroidism may rarely cause hypoglycemia, but this patient has no evidence of hypothyroidism on physical exam.

169. **E.** This patient has hypercalcemia manifesting as mental status changes and abdominal and bone pain. A possible etiology is her thiazide diuretic use, but regardless of the etiology, patients with hypercalcemia have undergone an osmotic diuresis due to the high calcium's effect on the kidneys and are significantly volume depleted. A normal saline bolus, even upwards of 4 to 6 liters, is required to lower her serum calcium levels before any other intervention, such as Lasix. Giving fluids is the first step in treating a patient with symptomatic hypercalcemia.

A. Glucocorticoids are useful in treating hypercalcemia that is related to high levels of vitamin D, such as the hypercalcemia found in sarcoidosis and certain lymphomas. The calcium level improves within days, and mechanism of action is unknown.

B. Furosemide, along with normal saline, is also one of the first steps in treating symptomatic hypercalcemia. It is only started after a patient is intravascularly repleted. Like normal saline, it promotes natriuresis and therefore increases calcium excretion.

C. Bisphosphonates inhibit osteoclast function. Osteoclasts resorb bone, which releases calcium into the circulation; therefore, bisphosphonates inhibit the release of calcium. They are very useful in treating the hypercalcemia of malignancy. Onset of action is 1 to 2 days, and duration of therapy is up to 2 weeks.

D. Calcitonin simulates the endogenous hormone that is produced by the parathyroid glands and that aids in putting serum calcium into bone. Onset is within hours, and duration of effect is 2 to 3 days. Unfortunately, a major side effect is tachyphylaxis.

170. **A.** Fibrates decrease secretion of VLDL and increase stimulation of lipoprotein lipase, which in turn leads to increased clearance of triglycerides. Fibrates are used primarily to reduce elevated triglycerides, but also may increase serum HDL.

B. Statins are inhibitors of hydroxy-methylglutaryl-coenzyme A (HMG-CoA) reductase, which is the rate-limiting step in cholesterol synthesis. Inhibition of this reductase leads to increased LDL receptor turnover, thus leading to decreases in serum LDL. Statins are the most effective medication for reducing LDL levels. Side effects include hepatitis and myopathy and are more common in patients who are on both statins and fibrates. Therefore, it is very important to educate patients about the side effects.

C. Niacin inhibits production of VLDL and, in turn, LDL. It also reduces transfer of HDL to VLDL, thereby increasing serum HDL levels. Niacin is used in patients to lower LDL, increase HDL, and decrease triglycerides. Side effects include flushing, pruritus, and insulin resistance.

D. Bile acid sequestrants such as cholestyramine inhibit bile acid reabsorption, which leads to a decreased pool of cholesterol. This in turn increases the number of LDL receptors, which lowers serum LDL levels. These medications primarily work to lower LDL levels. Side effects include abdominal distension and change in bowel habits.

E. Cholesterol absorption inhibitors are a relatively new class of medications that inhibit the absorption of cholesterol at the intestinal brush border without affecting the absorption of fat-soluble vitamins. This treatment is currently thought to be adjunctive therapy to statins in lowering serum LDL levels. Side effects include hepatitis, so liver function tests should be followed.

171. **E.** Vitamin D deficiency can be caused by decreased intake, inadequate production in the skin, or renal failure. In renal failure there is decreased hydroxylation of calcidiol to calcitriol, the end product of vitamin D. The function of vitamin D is to increase absorption of calcium and phosphate at the level of the intestine. Deficiency causes reduced absorption of both calcium and phosphate, which leads to increased production of PTH (secondary hyperparathyroidism) as an attempt to improve serum calcium levels, which then lowers serum phosphate levels.

172. **B.** Hypercalcemia of malignancy can be secondary to production of a PTH-related protein or local osteoclastic activity at the level of bone. Calcium levels are elevated and phosphate levels can vary depending on the etiology of the elevated calcium. Endogenous PTH levels will be low in response to feedback inhibition from the elevated serum calcium.

173. **C.** Hypoparathyroidism can be isolated, secondary to surgery, or due to decreased magnesium levels. PTH is responsible for increasing serum calcium from bone, increasing serum calcium resorption at the level of the kidney, and decreasing serum phosphate levels by excretion by the kidney. Thus, in hypoparathyroidism, calcium levels should be low and phosphate levels should be elevated.