Section 6: Endocrinology

CHAPTER 38: DIABETES MELLITUS

Q.1. A 61-year-old woman is seen in cardiology clinic for evaluation of a new-onset cardiomyopathy. She has had diabetes since 1986 and has been managed with glipizide 5 mg twice daily and metformin 1000 mg twice daily. At her initial visit, she was noted to have fasting triglycerides of 565 mg/dL, HbA_{1c} of 8.8, and creatinine of 2.8. Her heart failure was stable, and she had returned to her normal level of functioning. What should be done with her therapy?

A. Continue glipizide and metformin and add an injection of insulin at bedtime

B. Discontinue metformin and substitute pioglitazone

C. Discontinue metformin and substitute rosiglitazone

D. Discontinue metformin and add an injection of insulin at bedtime

E. B or D

Answer: E. This case illustrates the importance of considering underlying comorbidities in selecting therapy. The patient's renal insufficiency necessitates discontinuation of the metformin. Given her HbA_{1c}, however, she clearly needs to substitute another agent. Because her heart failure is stable and her triglycerides are so high, pioglitazone is a good choice. Pioglitazone lowers triglycerides and raises HDL, whereas rosiglitazone raises LDL and HDL. Discontinuing metformin and adding insulin at bedtime would also be a correct option.

Q.2. A 60-year-old man with a 15-year history of diabetes complicated by nephropathy visits your office. He was initially managed on oral agents but has now been taking insulin for many years. His current regimen is NPH 54 units in the morning and 42 units in the evening and insulin lispro 10 units in the morning, 8 units before lunch, and 6 units before dinner. His HbA_{1c} is 10.1%, and his creatinine is 2.4 mg/dL. What should be your next step?

A. Increase the dose of NPH insulin

B. Add metformin

C. Add pioglitazone

D. Add a sulfonylurea

E. Increase the dose of insulin lispro

Answer: C. This case illustrates the benefit of adding an insulin sensitizer to a patient's insulin regimen when he or she is on a very high dose of insulin. Increasing the insulin dose, either NPH or lispro, might further contribute to weight gain. Metformin would be another option except that this particular patient has nephropathy with a creatinine that precludes its use. Adding a sulfonylurea in

this patient on high doses of insulin with little beta-cell reserve would not be beneficial.

Q.3. A 36-year-old female with a nine-month history of diabetes diagnosed after presenting with several months of polyuria, polydipsia, fatigue, and a 15- to 20-pound weight loss, comes to your office for follow-up. She has been treated unsuccessfully with glipizide XL 10 mg twice daily, nateglinide 60 mg three times daily, and metformin 500 mg three times daily, but continues to have blood sugars in the mid-100s to mid-200s despite compliance with therapy. She has a family history of diabetes in maternal aunt who was obese. The patient also has borderline hypercholesterolemia and Hashimoto's thyroiditis. Most of her adult life, her weight was under 100 pounds, and her current weight is 125 pounds. She is approximately 5'7" tall. She has no diabetic complications. Her HbA_{1c} is 6.6, although fingerstick readings in the month prior to presentation were in the 200s to 300s. What would be the next best option for her management?

A. Discontinue nateglinide and add pioglitazone or rosiglitazone

B. Add an injection of insulin at bedtime

C. Order antithyroid peroxidase antibodies

D. Continue current therapy

Answer: B. This case illustrates reconsidering the diagnosis of diabetes in individuals aged 30 to 50 years who do not fit the typical prototype of type 2 diabetes. This woman's thin frame, lack of response to oral agents despite compliance, and history of Hashimoto's thyroiditis suggest that she may have type 1 instead of type 2 diabetes. Continuing her current therapy or changing her to other oral medications would not provide the best control for her. Antithyroid peroxidase antibodies for Hashimoto's thyroiditis would not be helpful in her diabetic management. One could order antiglutamic acid decarboxylase (GAD) and anti-islet cell antibodies, which may be positive in type 1 diabetes.

Q.4. A 57-year-old male with type 2 diabetes was readmitted for possible wound infection two months after his bypass surgery. He was discharged with tube feeds around the clock and on 55 units of lantus at bedtime. Upon readmission, his diet has advanced to mechanical soft and is administered three times a day. He is ordered sliding scale regular insulin (SSI) only without basal insulin. His creatinine on admission is 1.7. His blood glucose readings over a 48- hour period were as follows:

	Breakfast	**Lunch**	**Dinner**	**Bedtime**	**Breakfast**	**Lunch**	**Dinner**	**Bedtime**	**0300**
Glucose	270	245	86	253	—	—	594	477	35
SSI	12	9	0	12	0	0	24	24	0

At the last reading, when the patient's glucose was 35, he was administered 1 amp of

D50. What is the most likely etiology of his hypoglycemia?

A. Insulin stacking due to overlapping effects of regular insulin administered in large doses without basal insulin administration

B. Continued effects of lantus insulin previously administered when patient was on tube feedings

C. Renal insufficiency

D. A and C

Answer: D. This case illustrates the danger of using sliding scale insulin alone without the administration of basal and prandial insulin. Because of the half life of regular insulin, the tail end of the dose given at dinnertime for the blood glucose of 594 overlaps with the peak of the dose given at bedtime for the blood glucose of 477, resulting in hypoglycemia at 3 a.m. In addition, insulin is cleared by the kidneys and, in the setting of renal insufficiency, its action is prolonged. This also increases the risk of hypoglycemia.

Q.5. The patient presented in the previous case weighs 175 pounds and has type 2 diabetes. What is the approximate total daily insulin dose that he requires?

A. 40 units/day

B. 80 units/day

C. 20 units/day

D. 150 units/day

Answer: B. In calculating his daily insulin dose, he weighs 175 pounds, which is equivalent to 78 kg (1 kilogram = 2.25 pounds). As a type 2 diabetic, he requires 1.0 units/kg/day. Therefore, his calculated daily insulin need is approximately 80 units/day. 50% of this should be administered as basal insulin in the form of 40 units of insulin glargine (Lantus) qhs or 20 units of NPH qam and qhs. The remaining 50% should be administered as prandial insulin in the form of 12 to 14 units of insulin aspart (or lispro) four times daily or 20 units of regular before breakfast and dinner.

Q.6. A 55-year-old male with recently diagnosed type 2 diabetes presents for further management following a recent myocardial infarction that required stent placement. His HbA_{1c} is 8.8%, and his lipid profile shows triglycerides of 255, HDL cholesterol of 40, and LDL cholesterol of 124. His blood pressure is 122/70 on lisinopril 5 mg a day, and he has no evidence of proteinuria. He is already taking atorvastatin 80 mg a day. In addition to starting him on glucose-lowering therapy, you would

A. Add gemfibrozil to treat his triglycerides

B. Add ezetimibe or a bile acid-binding resin to help lowering his LDL cholesterol further

C. Switch to another statin

D. Continue his current therapy without changes

E. Increase atorvastatin to 160 mg a day

Answer: B. The primary target of lipid-lowering therapy for individuals with diabetes is the LDL cholesterol, with a goal of being a level well below 100 mg/dL. This often requires combination therapy with a statin and a bile-acid binding resin or a cholesterol absorption inhibitor. His triglycerides are most likely elevated due to poor glycemic control. Glycemic control should always be optimized prior to starting fibrate therapy for high triglycerides, as glycemic improvement alone often leads to a decrease of the triglyceride levels into the normal range.

Q.7. A 14-year-old Hispanic adolescent presents to an STD clinic complaining of increased frequency of urination. She is not reporting any dysuria or vaginal discharge. On examination she is 5'5" and weighs 85 kg. Her abdominal examination is negative for CVA or suprapubic tenderness. Her examination is otherwise significant for hyperpigmented velvety patches behind her neck and in the axilla. Her blood glucose is 215. Urinalysis is remarkable for 2+ glucose. Her diagnosis is most likely

A. Type 1 diabetes

B. Type 2 diabetes

C. MODY

D. Cushing's syndrome

E. Urinary tract infection

Answer: B. This adolescent is obese and has acanthosis nigricans, a sign strongly associated with insulin resistance. Type 2 diabetes now accounts for one third of newly diagnosed diabetes in the second decade of life. The diagnosis of MODY should be suspected in lean adults with new-onset diabetes.

Q.8. A 20-year-old type I diabetic presents to the emergency department with ear pain and a swollen, red, scaley external ear. He has had ear pain for the past week but now has developed nausea and vomiting and dizziness. He is started on antipseudomonal antibiotics, insulin infusion, and intravenous saline. Laboratory data show rising serum ketones after six hours of therapy:

	Presentation	**Six Hours after Initiation of Therapy**
Blood glucose	460	330
Anion gap	24	18
Serum ketone titer	1:8	1:32

Appropriate management at this time is

A. Increase the rate of insulin infusion

B. Continue current therapy

C. Begin bicarbonate infusion for increasing acidosis

D. Initiate antifungal therapy

E. Discontinue insulin infusion an start subcutaneous insulin injections

Answer: B. This patient has DKA caused by malignant external otitis. He is being treated appropriately with continuous intravenous insulin, hydration with normal saline, and antipseudomonal antibiotics. During the treatment of DKA, beta-hydroxybutyrate which is not measured in standard serum ketone assays is converted to acetone which is measured. Thus, plasma ketones appear to worsen during therapy and are not useful in following the treatment of DKA. The anion gap is a more useful measure. Because the anion gap is still elevated, however, it is too early to switch to subcutaneous insulin injections.

Q.9. A 36-year-old woman with type 2 diabetes presents reporting that she has missed her most recent menstrual cycle. Urine human chorionic gonadotropin testing in the office confirms that she is pregnant. Her diabetes has been treated with glyburide 10 mg once a day. Her most recent hemoglobin A_{1c} has been 8.2. At this point, she should

A. Continue with her current regimen

B. Increase the dosage of her sulfonylurea

C. Add metformin to her regimen

D. Discontinue glyburide and start insulin

E. Switch glyburide to metformin

Answer: D. Insulin is the drug of choice for control of blood sugar during pregnancy. The patient should be educated about the importance of as near normal blood glucose levels as possible during the pregnancy. She should also be referred to a maternal-fetal medicine specialist and/or an endocrinologist for management.

Q.10. A 42-year-old woman presents with concerns regarding diabetes. She reports that her father and mother and two siblings have diabetes. She denies any polyuria or polydipsia, blurry vision, or recent weight change. On examination, she has a BMI of 28 and a blood pressure of 128/80. Which of the following regarding testing for diabetes is *false*?

A. Fasting plasma glucose of greater than or equal to 126 mg/dL is diagnostic

B. Two-hour post glucose challenge of greater than or equal to 200 mg/dL is diagnostic

C. Random plasma glucose of greater than or equal to 200 mg/dL is diagnostic

D. A positive test should be repeated

Answer: C. Random plasma glucose of greater than or equal to 200 mg/dL *with symptoms* is diagnostic. In the absence of symptoms, this criterion is not diagnostic. The other criteria are correct. A positive test should be confirmed via repeat testing.

Q.10. All of the following are important concerns in choosing a sulfonylurea in a patient except

A. Risk of hypoglycemia

B. Hepatic and renal function

C. Potential for causing cardiovascular disease

D. Risk of weight gain

Answer: C. Important considerations for choosing therapy with a sulfonylurea include risk of hypoglycemia, especially in elderly patients and those with renal and hepatic insufficiency. Weight gain may occur as they act as insulin secretagogues. Despite initial concern that sulfonylureas may increase cardiac risk, the large UKPDS trial has not shown any increase in cardiovascular events.

Q.11. Which of the following statements regarding metformin therapy is *not* correct?

A. It should not be used above age 80

B. Lactic acidosis is a rare complication

C. It can be used with significant renal insufficiency if creatinine levels are monitored closely

D. It reduces insulin resistance

Answer: C. Metformin decreases hepatic glucose production and reduces peripheral insulin resistance. The most severe adverse event is the development of lactic acidosis. The risk of this complication is increased by renal insufficiency. Therefore it is contraindicated in men with a creatinine above 1.5 or women with a creatinine above 1.4 or in elderly patients above age 80.

Q.12. Which of the statements regarding thiazolidenediones is *incorrect*?

A. They reduce peripheral insulin resistance

B. They may be rapidly titrated for effect

C. They may be initiated if ALT is less than 2.5 times the upper limit of normal

D. Liver function tests should be followed every two months for the first year of therapy

E. The drug should be discontinued if ALT is above three times the upper limit of normal during therapy

Answer: B. Thiazolidinediones act via binding of nuclear receptors to modify peripheral insulin resistance. They take six to eight weeks to effect this change and should be titrated upwards slowly at this interval. The most severe adverse event associated with this class is hepatic dysfunction that can be fulminant. Baseline ALT should be measured and the drug should not be initiated if ALT is above 2.5 times the upper limit of normal. Levels should be followed every two months and therapy should be discontinued if ALT rises to above three times the upper limit of normal.

CHAPTER 39: THYROID DISEASE

Q.1. A 26-year-old woman develops typical symptoms of hyperthyroidism and is diagnosed with Graves' disease. She has mild ophthalmopathy and a large goiter with a bruit. Which is true about possible treatment options?

A. Radioactive iodine therapy should be used, but may worsen her mild ophthalmopathy

B. Propranolol is preferable to atenolol for symptomatic relief

C. Surgery is indicated to debulk the thyroid first before pursing radioactive iodine therapy

D. Given the large size of the goiter, radioactive iodine may be inadequate and antithyroid drugs alone are the best option to achieve remission

E. Radioactive iodine should be avoided in this patient of child-bearing age due to the long-term association with infertility

Answer: A. Radioactive iodine therapy is a reasonable first-line choice of therapy, but may worsen her underlying eye disease. Beta-blocker therapy is appropriate for symptom relief. Longer acting agents (atenolol as opposed to propranolol) are preferable to avoid frequent symptom recurrence. Surgery is usually not indicated for Graves' disease unless there is evidence of tracheal compression or the patient refuses other options. Antithyroid drugs are less likely to achieve remission in patients with large goiters. Finally, radioactive iodine has not been associated with infertility or birth defects and is fine to use in women of child-bearing age.

Q.2. A 55-year-old woman is seen in your office for a routine annual physical. On examination, you find a small, firm, nontender nodule in the left thyroid lobe that is approximately 1 cm in diameter. She has no symptoms, although she does recall that her mother also had a thyroid nodule. You order a TSH, which is normal. What do you recommend?

A. You recommend watchful waiting with close observation, given her lack of symptoms, no evidence of rapid growth, and lack of cervical adenopathy

B. You recommend a fine needle biopsy to rule out malignancy

C. You recommend an ultrasound to help determine if the nodule is benign or malignant, and thus whether biopsy is recommended

D. You recommend a calcitonin level, given her family history of thyroid disease

Answer: B. This patient has an asymptomatic thyroid nodule. It is nearly impossible to discern malignancy by physical exam alone, and watchful waiting would be inappropriate. A biopsy is required to determine if the nodule if benign or malignant. An ultrasound is not helpful in this determination, unless it shows a small, simple cyst. A calcitonin level is useful in screening for medullary thyroid cancer in patients with family history of medullary cancer or MEN II (not present in her family history). It is not useful in the routine workup of thyroid nodules.

Q.3. A 65-year-old woman is brought to the emergency room for fever and change in mental status. Her family found her lying in bed, mumbling unintelligibly. On examination she is diaphoretic and clammy. She answers to her name but is otherwise incoherent. An ECG shows atrial fibrillation at a rate of 125. TSH was undetectable a week ago in her primary doctor's office.

A. Supportive care, including β-blockers for cardiac rate control and cooling blankets for hyperthermia, should be administered

B. Aggressive temperature control with aspirin is imperative

C. Methimazole is the preferred antithyroid agent, as it inhibits peripheral conversion of T4 to T3

D. Given the severity of her illness, potassium iodide is recommended

E. Both A and D are correct

Answer: E. This patient is suffering from acute thyroid storm, as evidenced by her delirium, fever, and atrial fibrillation. This is a medical emergency. Supportive care, antithyroid medications, and potassium iodide are all recommended. Aspirin should be avoided, as it binds to thyroid-binding globulin, displaces T4, and causes free T4 to rise. Propylthiouracil is the preferred antithyroid agent, as it inhibits the peripheral conversion of T4 to T3.

Q.4. A 23-year-old woman presents with a two-month history of nervousness, heat intolerance, and a 10-pound weight loss. Her physical examination reveals a pulse of 85 beats per minute and a slightly enlarged nontender thyroid. There is no proptosis. Thyroid function tests are as follows: Free T4 2.5 ng/dL (0.8–1.8), T3 200 ng/dL (70–180), TSH <0.05 mU/L (0.5–5). What would be the next most appropriate step?

A. Start an antithyroid drug at a low dose (e.g., PTU 50 mg tid or methimazole 10 mg daily)

B. Refer for radioiodine therapy

C. Order a 24-hour radioiodine uptake

D. Neasure antithyroid antibodies

E. Check thyroid stimulating antibodies (TSAb)

Answer: C. It is unclear whether this patient has mild Graves' disease or silent thyroiditis. The 24-hour radioiodine uptake would establish the diagnosis. It is inappropriate to begin antithyroid drug therapy until the diagnosis is clear. Measuring antithyroid antibodies would not be of use because they can be positive in silent thyroiditis, as well as in Graves' disease. Because her disease is mild, TSAb would likely be normal even if Graves' disease were present.

Q.5. A 54-year-old man notes a lump in his neck while shaving. He has no prior history of thyroid disease, no family history of thyroid disease, and has no compressive symptoms, such as dysphagia, hoarseness, shortness of breath, or neck pain. His physical examination reveals a 2.5 × 2.5 cm rubbery left thyroid nodule. There is no cervical lymphadenopathy. The remainder of the exam is normal. Thyroid function tests are as follows: Free T4 1.3 ng/dL, TSH 1.0 m U/L. A thyroid sonogram shows a mildly hypoechoic nodule in the left lobe measuring 2.5 cm. There is another nodule on the right side measuring 0.6 cm. FNA of the dominant nodule is reported as an "adenomatoid nodule." What should be done next?

A. Refer the patient for surgery

B. Start thyroxine suppression therapy at a dose of 1 µg per pound of body weight

C. Start thyroxine therapy at a dose of 50 µg daily

D. Advise the patient to return for follow-up ultrasound in three months

E. Advise the patient to return in one year for follow-up ultrasound

Answer E. The patient has a benign thyroid nodule. Thyroid hormone therapy either to suppress TSH or in smaller doses is not effective and not recommended. A follow-up in three months is too soon for any change to have occurred.

Q.6. A 25-year-old woman has been taking thyroxine replacement therapy for hypothyroidism for 10 years. Thyroid function tests have generally been normal. She is seen for a routine follow-up exam and aside from mild fatigue, she reports feeling well. Her physical examination is normal, and her thyroid is not palpable. Thyroid function tests are as follows: Free T4 1.0 ng/dL, TSH 25 m U/L. Which of the following is *not* an explanation for these results?

A. Iron therapy

B. Calcium supplementation

C. Over-the-counter cimetidine

D. Oral contraceptives

Answer: C. Iron supplements, calcium, and oral contraceptives can increase thyroxine requirements. Iron and calcium block thyroxine absorption. Oral contraceptives increase thyroid-binding globulin levels which, in turn, transiently decrease free T4, which results in an increased thyroid hormone output in normal individuals. H_2-blockers and proton pump inhibitors have no effect on thyroxine absorption.

Q.7. A 40-year-old woman presents with a two-week history of a fever, malaise, and anterior neck pain. Her physical examination is remarkable for a pulse of 100 beats per minute, and an exquisitely tender thyroid that is firm, irregular, and three-fold enlarged. There is a mild tremor. Thyroid function tests are as follows: Free T4 2.0 ng/dL, TSH less than 0.05 m U/L. The erythrocyte sedimentation rate is 100 mm/hour. Which of the following statements is true about this patient's condition?

A. Following the hyperthyroid phase, the patient will likely become permanently hypothyroid

B. The best treatment for this condition is broad-spectrum antibiotics

C. The radioiodine uptake will be markedly elevated

D. Antithyroid drugs should be given until thyroid function is normal

E. Nonsteroidal anti-inflammatory drugs are often helpful in alleviating pain

Answer: E. This patient has subacute thyroiditis. Following the hyperthyroid phase, most patients ultimately recover normal thyroid function. The best treatment is nonsteroidals, although prednisone may be needed in severe cases. The radioiodine uptake is low and antithyroid drugs are not indicated.

Q.8. A 52-year-old man is admitted to the CCU with an acute anterior myocardial infarction. He subsequently develops cardiogenic shock and requires aortic balloon pump. Later in his hospital course, he also develops acute renal failure treated with low-dose intravenous dopamine, as well as drug-induced hepatitis. He is clinically improving and is slowly recovering kidney function. The medical student on the team feels a goiter and thyroid function tests are obtained. These reveal a TSH of 9 m U/L (normal 0.5–4.5) and a free T4 of 0.8 ng/dL (normal 0.8–1.8 ng/dL). Which of the following is true?

A. The patient is probably hypothyroid given the low free T4 and high TSH; to aid in recovery, thyroxine should be started

B. Intravenous dopamine has probably caused a temporary increase in the TSH level; nothing further is required

C. TSH is only mildly elevated in the setting of acute illness and a normal free T4; nothing further should be done

D. A radioactive thyroid scan would be useful in determining if the patient is truly hypothyroid

E. None of the above

Answer: C. The diagnosis of thyroid disease can be quite difficult in acutely ill patients. The patient is in the recovery phase of an acute illness. It is not uncommon to see mild elevations of TSH in this situation (although usually not above 20 m U/L). Given his normal T4, the patient is probably euthyroid and does not require treatment. Dopamine (and glucocorticoids) tends to cause a decrease in TSH secretion by the pituitary, not an increase. A radioactive thyroid scan is not useful in diagnosing hypothyroidism, especially in the setting of an acutely ill patient.

Q.9. A 28-year-old woman presents to your office with a tender neck. She gave birth to her first child approximately 11 months ago. Last week, she describes having a sore throat, nasal congestion, and rhinorrhea. She self-medicated with antihistamines and initially improved. She then developed a fever and severe neck pain radiating to the left ear. On exam, you are able to palpate an enlarged thyroid that is exquisitely tender to touch. Initial labs reveal a WBC of 7000 and a TSH of less than 0.01 m U/L. The most likely diagnosis is

A. Hashimoto's thyroiditis

B. Subacute thyroiditis

C. Silent (postpartum) thyroiditis

D. Acute bacterial thyroiditis

E. Acute onset of Graves' disease

Answer: B. The constellation of neck pain, fever, and a tender thyroid in a patient with a recent viral illness is highly suggestive of subacute (de Quervain's) thyroiditis. During the acute phase, the TSH is often suppressed. Hashimoto's thyroiditis is usually seen in older women (above age 59), and the onset is typically more gradual. The TSH should also be elevated, not suppressed. In postpartum thyroiditis the onset is usually sooner than 11 months from delivery, and patients often have a firm, nontender goiter. Acute bacterial thyroiditis is a reasonable consideration, but most patients with this remain euthyroid and have a pronounced leukocytosis. Finally, acute onset of Graves' disease would be consistent with the low TSH, but patients do not usually have severe neck pain.

Q.10. A 70-year-old woman with long-standing hypothyroidism is brought to the emergency room for a witnessed seizure. She had been well until three weeks ago, when she underwent colon resection for early stage colon cancer. She initially

did well, but has experienced progressive lethargy over the last two weeks. She reports that her only medication is oxycodone for postoperative pain. While in the emergency room, she is found to have a temperature of 95.4° F and a TSH of 77 m U/L. Which of the following is true?

A. Therapy should be instituted with a loading dose of intravenous levothyroxine, followed by a daily dose of 100 to 150 □g intravenously

B. Therapy should be instituted with intravenous T3 because it acts much more quickly, with no increase in adverse sequelae

C. She has most likely been hypothyroid for years and noncompliant with her levothyroxine therapy

D. The mortality rate for this condition is low

E. Intravenous hydrocortisone should be avoided, as it will greatly increase the risk of infection

Answer: A. This patient has myxedema coma, which is a medical emergency. The mortality rate is as high as 50%. She should be treated with intravenous levothyroxine urgently. While intravenous T3 will act more quickly, it is also associated with greater myocardial oxygen demand. This could lead to ischemia in this elderly woman. It would be more prudent to start with intravenous levothyroxine first. While this patient may have been hypothyroid for years, she has reasons other than noncompliance with levothyroxine that could have precipitated myxedema coma, including a recent surgical stress and the use of narcotics for pain control. Finally, many patients with autoimmune thyroiditis (most common cause) may also have diminished adrenal reserve. Hydrocortisone is reasonable to administer concurrently. Short-term use (2–3 days) will not increase the risk of infection.

Q.11. Which of the following statements regarding thyroid malignancy is true?

A. Medullary thyroid cancer is most commonly associated with a mutation in the p53 oncogene

B. Follicular cancer is the most common type of thyroid malignancy

C. Anaplastic thyroid cancer has the best prognosis

D. Men are more likely to develop thyroid cancer than women

E. Radioactive iodine is a reasonable initial approach to treating localized papillary cancer

Answer: D. Men are at higher risk of developing thyroid cancer than women. The other statements are all false. Medullary thyroid cancer is most commonly associated with a RET oncogene mutation. Papillary cancer is the most common type of thyroid malignancy, and localized disease should be treated primarily with surgery. Anaplastic thyroid cancer has the worst prognosis of all types.

Q.12. A 56-year-old woman with a history of osteoarthritis and atrial fibrillation presents to your office with mild weight loss and heat intolerance. She otherwise feels well. Her physical examination reveals a diffuse goiter with no discrete nodules. You run thyroid tests and find her TSH to be less than 0.01 m U/L and her free T4 to be 2.1 ng/dL (normal 0.8–1.8 ng/dL). An ECG shows normal sinus rhythm. A subsequent thyroid radioiodine uptake test shows diffusely decreased uptake. The best course of action is to

A. Discontinue amiodarone and switch to another antiarrhythmic medication

B. Check a toxicology screen for surreptitious use of levothyroxine

C. Start methimazole

D. Perform an oophorectomy for struma ovarii

E. Start suppressive doses of levothyroxine

Answer: A. This woman has symptomatic and biochemical evidence of thyrotoxicosis. Her examination is notable for a diffuse goiter, but no discrete nodules. Her radioactive iodine uptake test shows decreased uptake diffusely. All of these findings are consistent with a diagnosis of thyrotoxicosis secondary to amiodarone therapy. It should be discontinued. Surreptitious ingestion of levothyroxine may show decreased radioiodine uptake, but should not produce a goiter. Methimazole would be appropriate to start for Graves' disease, but this diagnosis should demonstrate increased radioiodine uptake. Struma ovarii (ectopic thyroid tissue in the ovaries) could be treated with oophorectomy, but is unlikely, given the goiter on exam. It is also quite rare in comparison with common causes, such as amiodarone. Finally, suppressive doses of levothyroxine would be more appropriate for a toxic nodule or nodular goiter with increased radioiodine uptake. This diagnosis is not supported by this woman's thyroid exam or radioiodine uptake results.

CHAPTER 40: CALCIUM DISORDERS AND METABOLIC BONE DISEASE

Q.1. A 72-year-old Australian man presents to the office with pain in his right leg for one year. He has no prior medical problems and denies trauma to the leg. Physical examination shows lateral bowing of the femur. Labs reveal a calcium of 8.4, phosphorus of 3.6, AST of 22, total bilirubin of 0.9, and alkaline phosphatase of 740. Possible long-term complications of his disease include all of the following except

A. Renal failure

B. Congestive heart failure

C. Osteosarcoma

D. Hearing loss

E. Bone fractures

Answer: A. The first step is to recognize that this patient most likely has Paget's disease as evidenced by his ethnicity, unilateral extremity pain, femoral bowing, and high alkaline phosphatase. All of the above answers are fairly well recognized complications of Paget's disease except renal failure. Congestive heart failure stems from a high-output state from numerous vascular shunts in the bone, osteosarcoma from high-turnover, hearing loss from impingement of nerves in the inner ear, and bone fractures from increased fragility.

Q.2. A 72-year-old woman with a history of lung cancer and type 2 diabetes presents to the emergency room with nausea, vomiting, polydipsia, polyuria, and change in mental status. Laboratories reveal glucose of 248 mg/dL, creatinine of 1.4 mg/dL, calcium of 13.9 mg/dL, and bicarbonate of 19 mg/dL. Which of the following is the most appropriate *first* step in management?

A. Begin an insulin drip at 1 to 2 units per hour with frequent dexisticks

B. Administer mithramycin to inhibit osteoclast function

C. Institute aggressive hydration with IV fluids, followed by diuresis with furosemide

D. Institute aggressive hydration with IV fluids, followed by diuresis with hydrochlorthiazide

E. Begin high-dose prednisone at 60 mg per day

Answer: C. This patient presents with symptoms of hypercalcemia, which mimic those of diabetic ketoacidosis. However, her calcium level is more worrisome than is her glucose level and should be the focus of treatment. The appropriate first step is administration of aggressive IV fluids, followed by diuresis when the volume is replete. Loop diuretics are preferable because thiazides may further increase the calcium level. The first choice in additional pharmacologic therapy of hypercalcemia (after volume resuscitation) would be calcitonin or pamidronate, not mithramycin. Likewise, steroids are most useful for the subset of patients with granulomatous disease and hypercalcemia. This patient probably has hypercalcemia of malignancy.

Q.3. A 50-year-old, perimenopausal Caucasian woman presents to your office for the first time for a routine physical. Her last menses was 12 months ago. She is not eager to pursue hormone therapy because she read in the newspaper that every woman on estrogen develops breast cancer. She has no chronic medical conditions or endocrine disorders. She is on no medications. Her mother had a hip fracture at age 70 years, but she has no family history of breast cancer. The patient is a former 20-year, pack-a-day smoker but quit 10 years ago. Her physical examination reveals a thin body habitus but is otherwise normal. Which of the following is recommended?

A. The patient is probably not at high risk for osteoporosis because she does not suffer from endocrine diseases such as hyperthyroidism or hyperparathyroidism; nothing further should be done at this time

B. The patient should take calcium and vitamin D and consider screening for osteoporosis in five years once she is completely through menopause

C. The patient should begin hormone replacement therapy and have a screening study in five years once her menopause is complete

D. The patient should undergo screening for osteoporosis now

E. The patient has a complicated clinical picture for osteoporosis and should be referred to an endocrinologist

Answer: D. This woman has numerous osteoporosis risk factors including being thin, Caucasian, postmenopausal, a former smoker, and a positive family history. She should be screened for osteoporosis now. Waiting five years without therapy may result in excessive bone loss, particularly in the perimenopause, when rate of bone loss is most rapid. Even starting calcium and vitamin D or hormone replacement therapy now would not preclude the need to obtain baseline bone mineral measurements (to assess risk for fracture). Osteoporosis screening can be easily accomplished by an internist; referral to an endocrinologist is not necessary at this point.

Q.4. A 55-year-old menopausal woman undergoes bone mineral density testing (DXA scan) because of a strong family history of osteoporosis. Her scores are as follows: hip T-score of −2.6 and Z-score of −1.2; L-spine T-score of −2.5 and Z-score of −1.0. Her only medications are calcium and a multivitamin that contains vitamin D. Which one of the following statements concerning her treatment is true?

A. The bisphosphonates tend to be less potent than other therapies and lack randomized, controlled trials that determine efficacy

B. Her bone mineral density scores are concerning; she should start additional therapy (other than calcium and vitamin D)

C. Estrogen, although useful in the prevention of osteoporosis, will not increase bone density in women with osteoporosis

D. Increasing bone mineral density by as little as 5% is not enough to decrease vertebral fracture risk

E. Her bone density scores are somewhat reassuring; she should continue her calcium supplementation for now

Answer: B. This patient has frank osteoporosis as documented by her bone density T-score of less than −2.5. She should be started on additional therapy (e.g., bisphosphonates or raloxifene). A is incorrect because the bisphosphonates are the most potent inhibitors of bone resorption available and have proven

efficacy in fracture risk reduction. C is incorrect because estrogen will increase bone density in osteoporotic patients, although it is currently not FDA-approved for treatment because of the lack of large, prospective trials. Various drugs approved for treatment of osteoporosis increase bone mineral density in the first several years by varying amounts (ranging from 2% to 8%), yet all decrease vertebral fracture risk. Finally, E is incorrect because her scores are not at all reassuring; calcium and vitamin D therapy alone is not sufficient.

Q.5. A 77–year-old woman who has been living in a nursing home for the past five years is brought to your office by her daughter. The daughter reports that the patient has "not been right" and describes vague total body pains and fatigue. It is difficult for the daughter to provide more specific symptoms. To her knowledge, the patient has not had fevers, nausea, vomiting, or other symptoms. Her physical examination is unremarkable other than very mild diffuse weakness. Her labs show the following:

Sodium 135

Calcium 9.0

Potassium 3.8

Phosphorus 1.8

AST 25

Alkaline phosphatase 330

A DXA perfomed a year ago had shown mild osteopenia. After confirming the diagnosis with another test, what therapy should be instituted?

A. Start calcium 650 mg twice a day and ergocalciferol 50,000 IU twice per week; reassess in three months

B. Start calcium 650 mg twice a day and potassium phosphate 500 mg twice a day; reassess in three months

C. Start calcium 650 mg twice a day and alendronate 70 mg once a week; repeat a DXA scan in one year

D. Start calcium 650 mg twice a day and vitamin D 800 IU once a day; reassess in three months

E. Start calcium 650 mg twice a day, potassium phosphate 500 mg twice a day, and risedronate 35 mg once a week; repeat DXA in one year

Answer: A. This patient presents with osteomalacia, a disorder of inadequate mineralization of the bone matrix due to calcium +/− phosphate deficiency. Her diffuse body pains and lethargy are typical of the vague symptoms patients have. Living in a nursing home with decreased sunlight exposure leading to decreased vitamin D synthesis puts a patient at particularly high risk. Lab findings are often notable for low-normal calcium, low phosphorus, and mildly elevated alkaline phosphatase. The diagnosis is confirmed by a low 25 (OH) vitamin D level (<30

ng/mL). Therapy consists of repletion of vitamin D by ergocalciferol in a dose of 50,000 IU once or twice per week. Over-the-counter cholecalciferol will not be adequate to replenish a patient's stores. Patients should also be prescribed calcium. After three months of therapy, it is reasonable to repeat a 25 (OH) vitamin D level to assess adequacy of therapy. If replete, patients can then be converted to over-the-counter vitamin D. This patient has only mild osteopenia on her DXA scan. She does not require bisphosphonates (alendronate or risedronate). Likewise, potassium phosphate supplements are not needed.

Q.6. A 33-year-old African-American woman presents with a dry cough for the past six months. She also notes mild dyspnea on exertion but has attributed that to a weight gain of 10 pounds. Her husband, who accompanies her, also mentions that she has been more fatigued lately. On examination, you note a few scattered crackles in the bilateral lung fields but no wheezing or rhonchi. The remainder of her exam is normal. Labs are notable for a hematocrit of 33, a creatinine of 0.9, an AST of 45, an ALT of 50, and a calcium of 11.2. Her chest x-ray reveals hilar adenopathy and a few bilateral lower lobe infiltrates. What is the best approach to her hypercalcemia?

A. Admit for aggressive hydration with normal saline

B. Arrange infusion of intravenous methylprednisolone in the next several days

C. Arrange infusion of intravenous pamidronate for long-term efficacy

D. Begin oral prednisone at 60 mg per day and taper over 6 to 12 months

E. Prescribe calcitonin, as it will have the quickest onset and the longest duration of action

Answer: D. This patient has a classic case of sarcoidosis. Supporting evidence includes symptoms of dry cough and dyspnea on exertion, hilar adenopathy and infiltrates on chest x-ray, mild anemia, increased liver enzymes, and hypercalcemia. The hypercalcemia is most likely related to unregulated synthesis of 1,25 (OH) vitamin D to its active form by granuloma-associated macrophages. The treatment of choice for this type of hypercalcemia is prednisone, and one can expect an excellent response. The patient's presentation is not acute, and she does not require admission for urgent treatment with normal saline. There is no reason to think intravenous methylprednisolone is more efficacious than oral prednisone. An infusion of pamidronate is probably not necessary, given the odds of a good response to prednisone. Calcitonin is also not necessary and, although it has the quickest onset of the hypercalcemic options, its duration of action is not the longest (bisphosphonates are longer).

Q.7. A 35-year-old woman presents to your office for a routine visit. She has been on prednisone 10 mg a day as treatment for systemic lupus erythematosis for the last six months. Her symptoms included a malar rash, arthralgias, and mild

nephropathy. She is doing much better, although attempts to wean her prednisone below 7.5 mg have been unsuccessful. Should she undergo screening for osteoporosis with a DXA scan?

A. No—her dose of prednisone is not high enough to result in bone density loss

B. No—the duration of steroid therapy has not been long enough in duration to put her at risk

C. Yes—any patient on steroids for longer than three months should be screened

D. Yes—any patient on steroids for longer than 12 months should be screened

E. No—she is still premenopausal and thus her risk for osteoporosis is not that high

Answer: C. Steroid-induced osteoporosis is the most common cause of secondary osteoporosis. Doses as small as 7.5 mg per day for durations of only three months or more can result in significant bone loss. This patient should definitely undergo screening for osteoporosis with a DXA scan. Her dose is large enough and duration long enough for screening to be indicated. Waiting for 12 months of therapy would be too long. Her premenopausal status does not change the need for screening, but may be important in therapeutic considerations.

Q.8. A 35-year-old man presents for a routine physical. He has no significant past medical history and feels well. His physical exam is unremarkable. A set of routine labs reveal the following:

Sodium 141mg/dL

Potassium 4.2 mg/dL

Chloride 108 mg/dL

Creatinine 0.8 mg.dL

Calcium 11.2 mg/dL

Phosphorus 4.0 mg/dL

On further questioning, he has no history of malignancy. His mother underwent neck exploration 10 years ago for unclear reasons but nothing was found. His older sister has hypertension.

A. A sestamibi scan will likely show a single parathyroid adenoma

B. His disorder is hereditary and is usually autosomal recessive

C. A PTH-related peptide level is likely to be elevated

D. A 24-hour urine collection is likely to reveal a calcium excretion of greater than 400 mg per every 24 hours

E. A PTH measurement is likely to be normal

Answer: E. This patient is found to have an incidental slightly elevated calcium level with no other abnormalities. His history and physical examination are unremarkable. The most likely diagnosis is familial hypocalciuric hypercalcemia

(FHH). Another clue is that his mother underwent a negative neck exploration, probably also due to a high serum calcium and subsequent attempt to rule out a parathyroid adenoma. FHH is a benign genetic disorder (autosomal dominant) that gives rise to a mutation in the gene encoding the calcium receptor; neither the kidneys nor parathyroid glands sense calcium appropriately. The result is that the body's "set point" for normal calcium level is higher than average. Patients with FHH have normal life expectancy and no sequelae. PTH levels are usually normal and 24-hour urine calcium levels are classically less than 100 mg/24 hours. In this case, a sestamibi scan looking for a parathyroid adenoma is likely to be negative. Likewise, there is no reason to suspect a malignancy in this patient, and a PTH-related peptide level (often high in patients with squamous cell cancers and hypercalcemia) would not be elevated.

Q.9. A 65-year-old man is hospitalized for a severe lower gastrointestinal bleed. His hematocrit on admission is 17 (baseline around 42). He is given a rapid transfusion of 4 units of packed red blood cells immediately followed by another 4 units within the first 24 hours. Early the next morning, you are called by the nurse to evaluate him due to symptoms of numbness in his hands and feet and difficulty breathing, as well as diffuse muscle twitches on exam. You send stat labs and confirm the diagnosis. Which of the following is likely to be true about his clinical presentation?

A. Inflating the blood pressure cuff above systolic is unlikely to provoke carpopedal spasm

B. His pulmonary exam may reveal diffuse wheezing

C. Tapping on his facial nerve could evoke a Bell's palsy

D. His ECG is likely to show shortening of the QT interval

E. Parasthesias typically are periumbilical in location

Answer: B. This patient has undergone massive transfusion of packed red cells in a short amount of time. The citrate contained in the packed red cells can bind calcium and lead to hypocalcemia of rapid onset. In this patient, stat ionized calcium confirmed the diagnosis. One must be able to recognize the clinical presentation of hypocalcemia to answer this question. It is feasible that his shortness of breath is due to bronchospasm (secondary to the hypocalcemia), resulting in diffuse wheezing on exam (the correct answer). Inflating a blood pressure cuff above systolic may induce carpopedal spasm (Trousseau's sign). Likewise, tapping on his facial nerve could invoke facial spasm (Chvostek's sign), not a Bell's palsy. An ECG is likely to show QT interval prolongation, not shortening. Finally, parasthesias tend to be peri-oral, not peri-umbilical.

Q.10. A 35-year-old man is found to have a routine calcium measurement of 11.1 mg/dL. He has no symptoms and feels well. A 24-hour urine calcium reveals an

excretion of 240 mg per day. A sestamibi scan reveals an isolated left-sided parathyroid adenoma. He wants to know what he should do for treatment. What do you recommend?

A. You recommend conservative medical management, as he is asymptomatic at this time

B. You recommend surgery given his young age and risk of future complications

C. You recommend medical management as he has no history of kidney stones

D. You recommend a thiazide diuretic to increase his urinary excretion of calcium and thus improve his hypercalcemia

E. You recommend surgery with removal of 3 1/2 parathyroid glands and transplantation of the remaining 1/2 gland in the arm.

Answer: B. You recommend surgery due to his young age. There are no absolute rules as to which patients with hyperparathyroidism and an isolated adenoma should proceed to surgery. A consensus panel, however, suggests patients with the following should highly consider surgery: young age (<50), nephrolithiasis, low bone density, serum calcium equal to or greater than 1 mg/dL above the reference range, or a 24-hour urine excretion greater than 400 mg/day. This patient qualifies based on his young age and long-term risk of developing complications, even though he is currently asymptomatic. A thiazide diuretic results in calcium resorption from the proximal tubule and would worsen his hypercalcemia. The appropriate surgery is removal of the adenoma. Excision of 3 1/2 glands is reserved for parathyroid hyperplasia.

Q.11. A 65-year-old woman who underwent a right mastectomy for breast cancer five years ago now presents to the emergency department with new-onset lethargy and polyuria for 4 to 5 days. Her daughter, who accompanies her, tells you she has lost weight and has complained of back pain for the last two months. Physical examination reveals a blood pressure of 115/75 and a heart rate of 110. She is obtunded, but her neurological examination appears nonfocal. Spine films showed diffuse bony metastases. Labs include the following:

Hematocrit 50%

Calcium 13.9 mg/dL

Creatinine 1.5 mg/dL

Phosphorus 3.1 mg/dL

Albumin 3.1g/dL

The most appropriate *initial* management is

A. Intravenous plicamycin

B. Intravenous furosemide

C. Subcutaneous calcitonin

D. Intravenous saline

E. Intravenous pamidronate

Answer: D. All of the above therapies are helpful, but the most crucial first step is aggressive intravenous hydration. This should be followed with intravenous furosemide (once euvolemia has been established) and more long-term therapies such as pamidronate or calcitonin. Intravenous plicamycin is used much less commonly due to side effects (e.g., nausea, local irritation, hepatotoxicity).

Q.12. A 26-year-old male postal worker presents to your office for a pre-employment physical. He feels well and has no symptoms. His past medical history is notable for appendicitis at age 17 resulting in an appendectomy and severe peptic ulcer disease, not well controlled on omeprazole. He continues to use TUMs antacids many times throughout the day. His physical examination is unremarkable. On routine labs, you find a calcium of 11.0 mg/dL. The remainder of his electrolytes and chemistries are normal. Upon further questioning, he does not recall any family history of hypercalcemia, but states his mother underwent trans-sphenoidal pituitary resection 10 years ago. What test should be done next?

A. VIP level and fasting glucose

B. 24-hour urine for metanephrines

C. Serum calcitonin level

D. Serum intact PTH and gastrin level

E. Glucose tolerance test

Answer: D. The key to this question is recognizing that the patient presents with a history consistent with multiple endocrine neoplasia 1 syndrome (MEN 1 or Wermer's syndrome). The MEN 1 syndrome is characterized by the triad of hyperparathyroidism, pituitary tumors, and pancreatic neuroendocrine tumors. His peptic ulcer disease may be representative of an underlying gastrin-secreting pancreatic tumor (Zollinger-Ellison's syndrome), especially given his young age. His hypercalcemia may suggest underlying hyperparathyroidism. The possibility of hereditary MEN 1 is further supported by the family history of possible pituitary tumor in his mother. In order to diagnose the syndrome, an intact PTH and gastrin level should be ordered. He does not have symptoms to suggest a VIPoma, although this can be seen with MEN 1 syndrome. Diabetes is not part of MEN 1, so a fasting glucose or a glucose tolerance test would not be useful. A 24-hour urine for metanephrines and a serum calcitonin level can be used to screen for pheochromocytoma and medullary thyroid cancer, respectively, but these are seen with MEN 2a and 2b, not with MEN 1.

Q.13. Which of the following patients is *not currently* at increased risk for secondary osteoporosis?

A. A 32-year-old woman with seizures on phenytoin for 10 years.

B. A 60-year-old woman with a 20-year history of rheumatoid arthritis treated with etanercept

C. A 24-year-old woman with systemic lupus erythematosis treated with hydroxychloroquine

D. A 19-year-old woman admitted to a psychiatric ward for anorexia nervosa, amenorrhea, and a weight of 88 lbs

E. A 58-year-old man status post lung transplant on cyclosporine

Answer: C. There are many secondary causes of osteoporosis, and this question illustrates several: anti-seizure medication (A), rheumatoid arthritis (independent of steroid therapy) (B), poor nutritional intake and amenorrhea due to relative estrogen deficiency (D), and cyclosporine use (E). Systemic lupus erythematosis alone does not cause osteoporosis. If steroid therapy is required to treat the lupus, the patient would be at increased risk of osteoporosis.

Q.14. Which of the following patients meets diagnostic criteria for osteoporosis?

A. A 57-year-old postmenopausal woman who is found to have osteopenia on a preoperative chest x-ray

B. A 48-year-old perimenopausal woman with a DEXA scan lumbar spine Z-score of +2.5

C. A 70-year-old woman with a history of a traumatic wrist fracture and a DEXA scan T-score of −1.9 in the trochanter

D. A 56-year-old woman with a history of hyperthyroidism and a DEXA scan showing a Z-score of −1.9 and a T-score of −2.6 in the lumbar spine

E. All of the above

Answer: D. The definitive diagnosis of osteoporosis is made through a DEXA scan T-score of −2.5 or lower. Any one anatomical site with such a low score is sufficient for diagnosis. A patient with osteopenia on a routine x-ray should proceed to DEXA scan, but the x-ray is not sufficient for diagnosis. Likewise, an elderly woman with a wrist fracture should also have bone density measurement to evaluate the suspicion of osteoporosis. The woman with the Z-score of +2.5 probably also has an excellent T-score and would not be diagnosed with osteoporosis.

Q.15. You are treating a woman for osteoporosis diagnosed by DEXA scan one month ago. You have both decided on treatment with alendronate 10mg per day. Which one of the following statements about assessing response to therapy is true?

A. A decrease in serum intact-PTH is a good marker of assessment of response to therapy with bisphosphonates

B. The earliest marker for assessment of response to therapy is a 50% decrease in 24-hour urine calcium excretion

C. Urine N-telopeptide levels, if initially high, decrease with treatment of osteoporosis, and serve as a useful early marker for response to treatment

D. A DEXA scan should be repeated at three-month intervals to assess response to treatment

E. A heel ultrasound can be a less expensive way to monitor response at one year

Answer: C. If the urine N-telopeptide measurement is initially high in an osteoporotic patient, checking a subsequent level at 90 days may provide an early indication that the bisphosphonate therapy is effective, and that the patient is compliant. An intact-PTH and a 24-hour urine calcium excretion are less useful markers of response. A follow-up DEXA scan should be obtained, but three months is too early to document a response. The *earliest* interval one can expect to see a response for a follow-up DEXA is at one year. Comparing results from a hell ultrasound and a central DEXA scan is not helpful, as they often do not correlate.

CHAPTER 41: REPRODUCTIVE ENDOCRINOLOGY

Q.1. A 55-year-old disabled firefighter has a history of chronic hip pain caused by trauma in a motor vehicle accident four years ago. He presents to your office with symptoms of decreased libido and erectile dysfunction that began a few months after the accident. He has no other medical history. Medications include oxycontin for pain and a multivitamin. Physical examination reveals a well-virilized man and is notable only for mild testicular atrophy. Testosterone level is 110 ng/dL (normal 300–1000); prolactin level is 32 ng/dL (normal 2–18 ng/dL). Which of the following is most likely *false* regarding his hypogonadism?

A. It is reversible

B. It is caused by normal aging

C. Oxycontin is a likely cause

D. His FSH and LH are low

Answer: B. This man most likely has hypogonadism due to chronic opiate use. Opiates can suppress gonadotropin (FSH and LH) secretion directly leading to low testosterone. In addition, opiates can elevate prolactin, which in turn suppresses gonadotropin release and causes hypogonadism. This would resolve if oxycontin were discontinued. Whereas testosterone levels do decline some with age, a level this low would not be normal.

Q.2. You are the only physician in a rural community. A 13-year-old boy presents to you with complaints of breast enlargement. His growth and development to date

have been normal. His school performance is above average. He is on no medications. Physical examination reveals a young man in the 60th percentile for height with age-appropriate genital development and secondary sex characteristics. What should be your recommendation?

A. Bromocriptine once daily

B. Testosterone injections twice weekly

C. Referral for pituitary surgery

D. Reassurance

Answer: D. Most likely this boy has physiologic pubertal gynecomastia. This resolves in most cases within several months.

Q.3. A 38-year-old woman is referred for hirsutism since age 17 years. She shaves twice a day to control hair in the beard area, as well as on the midchest, abdomen below the umbilicus, and inner thighs. She reports menses only twice in her life until three months prior, when she began to have regular monthly menses. Her primary physician diagnosed her with diabetes six months ago and started metformin. She is on no other medications. Physical examination reveals BP of 155/85, hair distribution as the patient described, acanthosis nigricans, and no signs of virilization. Labs show total testosterone of 55 ng/dL (normal is 15 to 60), free testosterone of 2.5 ng/dL (normal is 0.1–2.0), and prolactin of 28 ng/dL (normal is 2–20). What is the most likely diagnosis?

A. Polycystic ovary syndrome (PCOS)

B. Testosterone-producing ovarian mass

C. Hyperprolactinemia caused by metformin

D. Adult-onset congenital adrenal hyperplasia

Answer: A. The history of long-term hirsutism and amenorrhea is most consistent with PCOS. The resumption of menses with metformin use is typical in a PCOS patient and not in a patient with congenital adrenal hyperplasia. A virilizing tumor of the ovary would result in a higher testosterone level (possibly >200 ng/dL) and would have induced signs of virilization by now.

Q.4. A 53-year-old obese man presents with a two- to three-year history of erectile dysfunction. He is able to achieve only a partial erection, which he is unable to sustain. His interest in sex has diminished. He has no other medical problems, including hypertension, cardiovascular disease, or diabetes mellitus. On physical examination, he has a BMI of 33 kg/m^2 and a blood pressure of 138/82 mm Hg. With the exception of generalized obesity, the remainder of the physical examination is normal. What is the next step in his management?

A. Prescribe sildenafil 25 mg before sexual activity

B. Measure an 8 AM testosterone concentration

C. Recommend a hypocaloric diet and increase in physical activity to reduce weight by one to two pounds per week

D. Refer for psychiatric evaluation

Answer: B. Hypogonadism should be ruled out prior to starting therapy for erectile dysfunction. If the testosterone is normal, a phosphodiesterase-5 inhibitor, such as sildenafil, would be first-line therapy. Weight loss through diet and exercise can improve erectile function in obese men and should also be recommended. An investigation into a possible treatable underlying cause of erectile dysfunction, however, should be done first. There is no indication that an underlying psychogenic cause exists.

Q.5. A 32-year-old woman presents with oligomenorrhea and hirsutism. She has had irregular menses since puberty, which were regulated in the past on oral contraceptives. She discontinued her oral contraceptive one year ago as she is interested in becoming pregnant. Physical exam reveals an overweight female. Terminal hairs are present on the chin, cheeks, upper lips, and sternal areas. Laboratory examination includes a fasting glucose concentration of 102 mg/dL, a total testosterone of 75 ng/mL, and an LH:FSH ratio of 3:1. Which is the best treatment for this patient?

A. Spironolactone

B. Clomiphene citrate

C. Metformin

D. Weight loss

Answer: D. This patient has all the characteristics of polycystic ovary disease (menstrual dysfunction, biochemical and clinical evidence of androgen excess, evidence of glucose dysregulation). Because she is primarily interested in fertility, most experts would recommend weight loss as first-line treatment. Ovulation induction can often be achieved with a relatively small loss in weight (5%–10%). If weight loss is unsuccessful, a trial of a medication to induce ovulation (clomiphene), with or without metformin, is generally used. Thiazolidenediones (rosiglitazone or pioglitazone) can also be an effective adjunct, but concerns about hepatotoxicity and possible teratogenic effects have limited the use of these medications. If fertility is not the goal of treatment, weight loss, oral contraceptives, and insulin sensitizers have been used alone or in combination. For women with troublesome hirsuitism, anti-androgens such as spironolactone may be a useful adjunct.

Q.6. A 19-year-old man presents to his university’s health clinic with breast discomfort. He has noticed that, over the past three months, a painful swelling has appeared under the areola bilaterally. In addition, he has noted some fatigue and weakness. He has had normal development and is 5' 11" tall. Libido and erectile

function have been normal. He is on no medications, but reports occasional marijuana use. Physical examination shows a weight of 165 pounds, pulse of 95, and blood pressure of 135/55. His thyroid exam is notable for mild enlargement. There is firm, tender tissue about 3 cm in diameter underlying each nipple. Genital exam is normal. What is the next best step in his management?

A. Check an 8 AM testosterone

B. Instruction to stop marijuana use

C. Check a TSH

D. Check a prolactin

Answer: C. Hyperthyroidism should be considered in any man with gynecomastia. Sex hormone binding globulin (SHBG) production is increased by thyroid hormone. Because androgens bind more tightly than estrogens to SHBG, there is a relative excess of free estrogen compared to free androgens in hyperthyroid men. In about 10% of hyperthyroid men, this results in gynecomastia. There is no clear evidence for hypogonadism in this case, but part of the usual workup should include a total testosterone level. A low testosterone should also prompt an investigation for hyperprolactinemia. Marijuana use has been associated with gynecomastia, perhaps due to estrogenic compounds in the inhaled smoke. Other etiologies, however, should be investigated first.

Q.7. A 38-year-old African-American man presents with painful swelling under the areola for six months. He has been receiving treatment for HIV over the past four years. He denies erectile dysfunction, weakness, or loss of libido. Other medical problems include mild diabetes mellitus and hypertension. He denies opiate or marijuana use. His medications include tenofovir, lamivudine, efavirenz, trimethoprim/sulfamethoxazole, metformin, and hydrochlorothiazide. Physical examination is normal with the exception of 2 cm of tender tissue below each nipple. Testicular examination is normal. Total testosterone is 435 ng/dL; TSH and prolactin are normal. Which of the following is likely contributing to his gynecomastia?

A. Tenofovir

B. Efavirenz

C. Trimethoprim/sulfamethoxazole

D. Hydrochlorothiazide

Answer: B. Among HIV-infected patients, there are multiple reasons for gynecomastia. Hypogonadism is common in this population and should be ruled out first. There is some evidence that the chronic inflammation associated with HIV disease can also be a factor. Medications likely play a significant role and, among the HIV medications, efavirenz has been cited with the most frequently.

The nucleoside reverse transcriptase inhibitors zidovudine and stavudine have also been associated with gynecomastia.

Q.8. Which of the following medications has *not* been linked to gynecomastia in men?

A. Ketoconazole

B. Atenolol

C. Lisinopril

D. Spironolactone

E. Omeprazole

Answer: B. Ketoconazole, ACE inhibitors (including lisinopril), spironolactone, and omeprazole have all been linked to gynecomastia (to varying degrees). Of the choices listed, only atenolol (and other ☐-blockers) has not been associated with this process.

Q.9. A 39-year-old female attorney presents to your office with concern about facial hair. She has noticed increasing amounts of course, black hair on her chin over the last five years. Her menses began at age 12 and have always been regular. On further questioning, she recalls that her mother would occasionally shave her facial area as well. On examination, she weighs 120 pounds and her blood pressure is 125/85. She has no evidence of virilization, such as clitoromegaly or enhanced musculature. Labs reveal a testosterone of 340 ng/dL (normal is 15–60 ng/dL) and normal free testosterone level. What is the most appropriate next step in diagnosing her condition?

A. No further workup is necessary

B. Check an LH/FSH ratio

C. Check a 17-hydroxyprogesterone level

D. Order a CT of the adrenal glands

E. Order a 24-hour urine for urinary free cortisol

Answer: A. This woman has a family history of facial hirsutism and normal physical examination and laboratory values. She most likely has physiologic (familial) hirsutism, which is common, particularly in women of Mediterranean descent (e.g., Greek, Italian). No further workup is necessary. An LH/FSH ration would be appropriate if you suspected polycystic ovary disease, but her menses have been regular and she has no other symptoms suggesting this (obesity, acne, insulin resistance). A 17-hydroxyprogesterone level is useful for ruling out congenital adrenal hyperplasia. This is unlikely in this case, however, because her hirsutism did not begin at menarche and she has no menstrual irregularities. An adrenal CT would be helpful in visualizing an adrenal tumor, but the biochemical workup does not suggest this. Finally, in a young woman without obesity or

hypertension, Cushing's disease is highly unlikely, and a 24-hour urinary free cortisol would be of low diagnostic yield.

Q.10. A 17-year-old woman presents to your office for a "check-up." During the visit, you learn that her mother is concerned because she has never had the onset of menses. She denies any other symptoms, including headaches, nausea, and weight loss. She has no family history of delayed puberty. On physical examination, she is of normal height and weight. Vital signs are normal. She has a feminine appearance and age-appropriate breast development. On pelvic examination, pubic hair is noticeably absent, and the vagina ends blindly. What is the most likely diagnosis?

A. Constitutional delay of puberty

B. Turner's syndrome

C. Testicular feminization

D. Gonadal dysgenesis

E. Kallman's syndrome

Answer: C. This patient has primary amenorrhea, as she has never had the initial onset of menses. The key to this question is distinguishing primary amenorrhea *with* versus *without* secondary sexual characteristics. This patient has normal breast development and a feminine appearance, suggesting some secondary sexual features. This, together with the blind-ending vagina, makes testicular feminization (karyotype XY with androgen insensitivity) likely. The presence of secondary sexual features (e.g., normal breast development) makes choices A, B, D, and E unlikely. In addition, she has no family history of delay of puberty. Her normal height argues against the diagnosis of Turner's syndrome, and the lack of anosmia renders Kallman's syndrome unlikely.

Q.11. A 20-year-old woman presents to your office with primary amenorrhea and elevated gonadotropin levels. A workup reveals a karyotype of XO. Which of the following physical features is she *not* likely to have?

A. Webbed neck

B. Underdeveloped breasts

C. Valgus deformity of the elbow

D. Pectus excavatum

E. Short stature

Answer: C. The patient's karyotype of XO is consistent with the diagnosis of Turner's syndrome. Her primary amenorrhea and elevated gonadotropin levels support this. Patients with Turner's syndrome usually have a webbed neck, short stature, valgus deformity of the elbow, and lack of sexual maturation (e.g.,

underdeveloped breasts). They often have a shield chest, but not pectus excavatum.

CHAPTER 42: NEUROENDOCRINE AND ADRENAL DISEASE

Q.1. A 37-year-old female with no significant past medical history is referred to you because, after an MVA with head trauma, she underwent a brain MRI that revealed a 0.5-cm pituitary adenoma. She reports being in good health before the accident. She has 3 children, and the youngest one is 9 months old. She stopped breast-feeding her 3 months ago. Her menses are regular. On physical examination, her BP is 115/80, her weight is 120 pounds, and she stands 5□ 4□□. She has no breast discharge. The rest of the examination is unremarkable. Her prolactin is 14 ng/mL. What should further workup include?

A. Overnight dexamethasone suppression test

B. 24-hour urinary free cortisol

C. IGF-1 level

D. Repeat MRI in 6 to12 months

E. Ophthalmology consultation for formal visual fields test

Answer: D. This patient has a pituitary "incidentaloma." She has no signs or symptoms of pituitary hormone deficit or excess, as indicated by recent pregnancy, normal periods, and normal physical examination. Her prolactin is normal. Less than 10% of these tumors grow over time. Therefore she only needs a follow-up MRI in 6 to 12 months (and less frequently thereafter) to verify that the microadenoma is not growing. Visual field testing is not indicated in a microadenoma.

Q.2. A 27-year-old man is referred to you because of polyuria and polydipsia. He reports drinking about 2 to 3 gallons of water a day. He is not sure how long he has had this problem. He admits to having 0 to 1 micturition per night. He has a history of depression, presently treated with fluoxetine. He is otherwise healthy and has no history of head trauma, weight change, cold intolerance, or impotence. Physical examination is entirely normal. Laboratory evaluation shows normal glucose and calcium, sodium of 134 mEq/L, and uric acid 3.5 mg/dL. What is the most likely diagnosis?

A. Nephrogenic diabetes insipidus

B. Psychogenic polydipsia

C. Central diabetes insipidus

D. Syndrome of inappropriate antidiuretic hormone secretion (SIADH)

E. Glucose intolerance

Answer: B. This patient has no evidence of central nervous system diseases that may cause diabetes insipidus. Furthermore, he has no significant nocturia, and the fact that he cannot recall how long he has had this problem suggests that the onset was gradual. Finally, patients with diabetes insipidus (central or nephrogenic) never present with hyponatremia. Fluoxetine does not cause central or nephrogenic diabetes inspidus. Polyuria is not a feature of SIADH. Glucose intolerance does not cause polyuria. All these clinical data point to psychogenic polydipsia.

Q.3. A 28-year-old woman is diagnosed with medullary thyroid cancer. During the workup, she is found to have primary hyperparathyroidism. She is adopted, and has no information on her biological parents. She has one son, aged 4, in good health. The next step should be

A. Measure calcium in her child

B. Obtain RET-proto-oncogene gene testing

C. Measure prolactin level

D. Obtain brain MRI

E. Measure serum IGF-1

Answer: B. This patient may have MEN-2. The vast majority of MEN-2 cases can be diagnosed by analysis of mutations in the RET proto-oncogene. This is particularly important in this case, since the patient has a child. If she has a mutation, her child should be tested as well, and he should undergo prophylactic thyroidectomy to avoid the development of medullary thyroid cancer. It is unlikely her child would have hyperparathyroidism at age 4. Pituitary adenomas are not part of MEN-2.

Q.4. A 36-year-old woman has a two year history of severe hypertension. She has normal weight, and no other associated symptoms. Her family history is unremarkable. She developed hypokalemia (2.9 mEq/L) when she was treated with HCTZ. After HCTZ was discontinued, hypokalemia resolved (3.7 mEq/L). Her blood pressure is now controlled on maximal dose of a beta-blocker and of a calcium channel-blocker. The next step should be

A. Obtain abdomen CT

B. Obtain abdomen MRI

C. Obtain pituitary MRI

D. Measure serum aldosterone and plasma renin activity

E. No additional workup is required

Answer: D. This young woman has significant hypertension, and no family history. Although hypokalemia developed only while on HCTZ, some patients with primary hyperaldosteronism do not have hypokalemia if they are not exposed to diuretics. Therefore, she should be screened for hyperaldosteronism with an aldosterone/plasma renin ratio. Imaging of the abdomen is not indicated at this point; a functional hormonal abnormality should be established first.

Q.5. A 47-year-old woman is referred to you because during an emergency room visit for right-sided abdominal pain she underwent an abdomen CT that showed a 2.5 cm left adrenal mass. She has normal blood pressure, normal weight, and normal fasting glucose. Her menses are regular. The next step should be

A. No further workup needed. Repeat CT in 6 to 12 months

B. Abdomen MRI

C. Obtain 24-hour urine free cortisol

D. Obtain 24-hour urine for total and fractionated metanephrines

E. 1 mg dexamethasone suppression test

Answer: D. This is an adrenal "incidentaloma." The patient shows no evidence of Cushing's syndrome or of hyperaldosteronism. However, some pheochromocytomas can be clinically silent. As this is a potentially fatal disease, it must be ruled out. If evaluation of pheochromocytoma is negative, she should have a repeat CT scan of her abdomen in 6 to 12 months.