Settings

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28

Item 1 of 29
Question Id: 8531

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 43-year-old woman comes to the office due to episodic confusion, blurred vision, tremors, and sweating. The symptoms have increased in intensity in the past few months. The episodes occur any time during the day and are relieved by drinking orange juice. During an episode, her blood glucose level was 32 mg/dL as measured by her husband's home glucose meter. Past medical history includes major depression and irritable bowel syndrome. Laboratory studies are performed during the patient's next episode of symptoms and show the following:

Glucose	35 mg/dL	
Insulin	18 µU/mL	(normal: <3 µU/mL)
C-peptide	4.01 ng/mL	(normal: <0.6ng/mL)

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

A. Alpha-cell tumor
B. Insulin administration
C. Somatostatinoma
D. Sulfonylurea use
E. VIP-secreting tumor

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4 Feedback Suspend End Block

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Settings

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28

Item 1 of 29
Question Id: 8531

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 43-year-old woman comes to the office due to episodic confusion, blurred vision, tremors, and sweating. The symptoms have increased in intensity in the past few months. The episodes occur any time during the day and are relieved by drinking orange juice. During an episode, her blood glucose level was 32 mg/dL as measured by her husband's home glucose meter. Past medical history includes major depression and irritable bowel syndrome. Laboratory studies are performed during the patient's next episode of symptoms and show the following:

Glucose	35 mg/dL	
Insulin	18 µU/mL	(normal: <3 µU/mL)
C-peptide	4.01 ng/mL	(normal: <0.6ng/mL)

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

- A. Alpha-cell tumor [7%]
- B. Insulin administration [10%]
- C. Somatostatinoma [7%]
- ✔ D. Sulfonylurea use [61%]
- E. VIP-secreting tumor [13%]

Omitted
Correct answer
D

61%
Answered correctly

28 Seconds
Time Spent

01/18/2019
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2/12/2019

Evaluation of hypoglycemia			
	Serum insulin	**C-peptide**	**Hypoglycemic drug assay**
Exogenous insulin	Normal/increased	**Low**	Negative
Oral hypoglycemic agents	Normal/increased	Normal/elevated	**Positive**
Insulinoma	Normal/increased	Normal/elevated	Negative

Symptomatic **hypoglycemia** is confirmed by **Whipple's triad**:

- Symptoms of hypoglycemia (eg, tremor, diaphoresis, confusion)
- Low blood glucose level
- Relief of hypoglycemic symptoms when the blood glucose level is increased

True hypoglycemia in nondiabetic patients is uncommon, but can occur due to surreptitious injection of insulin, ingestion of insulin secretagogues (eg, sulfonylurea medications), or an insulin-secreting pancreatic tumor (insulinoma).

Insulin is initially synthesized as preproinsulin and sequentially cleaved into insulin and C-peptide, which are then packaged into secretory granules and secreted together in equimolar amounts. Normally, when blood glucose is low, endogenous insulin secretion stops, and blood levels of insulin and C-peptide will be negligible. In the setting of hypoglycemia, an elevated insulin level with **undetectable C-peptide** suggests

- Low blood glucose level
- Relief of hypoglycemic symptoms when the blood glucose level is increased

True hypoglycemia in nondiabetic patients is uncommon, but can occur due to surreptitious injection of insulin, ingestion of insulin secretagogues (eg, sulfonylurea medications), or an insulin-secreting pancreatic tumor (insulinoma).

Insulin is initially synthesized as preproinsulin and sequentially cleaved into insulin and C-peptide, which are then packaged into secretory granules and secreted together in equimolar amounts. Normally, when blood glucose is low, endogenous insulin secretion stops, and blood levels of insulin and C-peptide will be negligible. In the setting of hypoglycemia, an elevated insulin level with **undetectable C-peptide** suggests injection of **exogenous insulin** (which does not contain C-peptide) **(Choice B)**, whereas elevation of both **insulin and C-peptide** suggests excess **endogenous insulin** due to a sulfonylurea medication or insulinoma. Surreptitious administration of oral hypoglycemics or insulin is typically seen in health care workers and family members of diabetic patients using these medications. It is usually associated with depression or personality disorders. Sulfonylurea or meglitinide abuse can be confirmed by testing the urine or blood for hypoglycemic agents.

(Choice A) Glucagonoma is a rare tumor of pancreatic alpha cells that secretes excessive amounts of glucagon. This results in hyperglycemia, anemia, and necrolytic migratory erythema (a raised erythematous rash affecting the face, groin, and extremities).

(Choice C) Somatostatinoma is a rare tumor of pancreatic delta cells that is associated with diabetes mellitus, steatorrhea, chololithiasis, and hypochlorhydria. These manifestations are due to somatostatin-induced inhibition of insulin, gastrin, secretin, and cholecystokinin secretion, as well as inhibition of gastrointestinal motility.

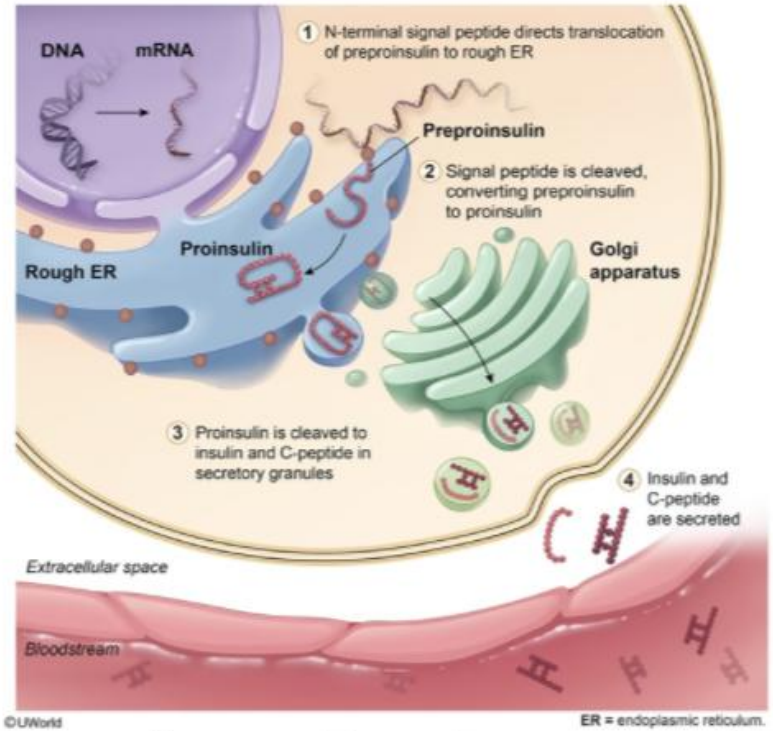
(Choice E) VIPomas are non-beta cell pancreatic islet cell tumors that hypersecrete vasoactive intestinal polypeptide (VIP). Features include watery diarrhea, hypokalemia, and impaired gastric acid secretion.

Educational objective:
Hypoglycemia is characterized by tremor, diaphoresis, or confusion, associated with a low blood glucose level and resolution of symptoms when the blood glucose level is corrected. Hypoglycemia with an elevated insulin level and low C-peptide level suggests exogenous insulin injection, whereas elevated C-peptide suggests an insulin secretagogue or insulin-secreting tumor.

- Low blood glucose level

Exhibit Display

Insulin synthesis and secretion



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Settings

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28

Item 2 of 29
Question Id: 1996

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 55-year-old man with a 6-year history of type 2 diabetes mellitus comes to the office for a follow-up appointment. He says he feels healthy and has no new medical problems. His only medication is metformin. The patient does not use tobacco or alcohol. He consumes a balanced diet rich in complex carbohydrates and jogs for 40 minutes every morning. Review of his blood glucose journal over the last few months shows fasting glucose levels of 150-180 mg/dL. Laboratory analysis shows a hemoglobin A1c level of 3.7%. Further evaluation with hemoglobin electrophoresis shows a hemoglobin A2 level of 7.5% (normal: 1.5%-3.5%). Which of the following is the most likely explanation for this patient's lower-than-expected hemoglobin A1c level?

A. Beta thalassemia trait
B. Folate deficiency
C. Iron deficiency
D. Low erythropoietin
E. Poor glycemic control
F. Sickle cell trait

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Settings

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28

Item 2 of 29
Question Id: 1996

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 55-year-old man with a 6-year history of type 2 diabetes mellitus comes to the office for a follow-up appointment. He says he feels healthy and has no new medical problems. His only medication is metformin. The patient does not use tobacco or alcohol. He consumes a balanced diet rich in complex carbohydrates and jogs for 40 minutes every morning. Review of his blood glucose journal over the last few months shows fasting glucose levels of 150-180 mg/dL. Laboratory analysis shows a hemoglobin A1c level of 3.7%. Further evaluation with hemoglobin electrophoresis shows a hemoglobin A2 level of 7.5% (normal: 1.5%-3.5%). Which of the following is the most likely explanation for this patient's lower-than-expected hemoglobin A1c level?

- A. Beta thalassemia trait [78%]
- B. Folate deficiency [1%]
- C. Iron deficiency [3%]
- D. Low erythropoietin [4%]
- E. Poor glycemic control [2%]
- F. Sickle cell trait [10%]

Omitted
Correct answer
A

78%
Answered correctly

3 Seconds
Time Spent

08/28/2018
Last Updated

Explanation

Block Time Remaining: 00:00:31
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Long-term glycemic control in patients with diabetes can be assessed by measuring **glycated hemoglobin** (**HbA1c**). Glucose freely diffuses across the red blood cell membrane and attaches irreversibly to HbA inside erythrocytes, forming HbA1c. The degree of HbA1c elevation is directly correlated to average blood glucose levels over the erythrocyte life-span. Both **higher glucose** levels and **longer exposure** of red cells to glucose will **increase HbA1c** values. As such, conditions that alter red blood cell survival time affect HbA1c levels.

This patient's elevated **hemoglobin A2** (HbA2) percentage is suggestive of coexisting **beta thalassemia**. HbA2 becomes elevated in beta thalassemia to compensate for beta globin chain underproduction, but the resulting microcytic red cells are prone to **hemolysis**. The increase in red cell turnover causes **falsely low HbA1c levels**.

(Choices B and C) Nutrient deficiencies involving iron, folate, and vitamin B_{12} can reduce the production of new red cells, leading to a preponderance of older erythrocytes in the circulation and falsely elevated HbA1c levels. In contrast, treatment of vitamin deficiency anemias causes young red cells to be rapidly released into the circulation, falsely lowering HbA1c levels.

(Choice D) Diabetic nephropathy that has progressed to chronic renal failure may cause reduced erythropoietin production. The resulting decrease in red cell production may lead to falsely high HbA1c levels (similar to nutrient deficiencies).

(Choice E) Chronically elevated glucose levels due to poor glycemic control are the primary mechanism driving the increase in HbA1c levels in individuals with diabetes.

(Choice F) Sickle cell trait is a benign condition characterized by increased hemoglobin S percentage and reduced HbA levels on hemoglobin electrophoresis. However, the HbA2 percentage remains near normal and HbA1c levels are relatively unchanged due to normal erythrocyte turnover.

Educational objective:
Glycated hemoglobin (HbA1c) forms within circulating red blood cells as hemoglobin A is exposed to glucose, and HbA1c levels are a useful indicator of average glycemic control over the erythrocyte life-span. HbA1c levels are affected by alterations in red blood cell survival; conditions that increase red blood cell turnover (eg, hemolytic anemia) can cause falsely low HbA1c levels.

Exhibit Display

Hemoglobin electrophoresis patterns in sickle cell & beta-thalassemia				
Condition	**Hemoglobin A**	**Hemoglobin A2**	**Hemoglobin F**	**Hemoglobin S**
Normal	95%-98%	~2.5%	<1%	Absent
Beta-thalassemia minor	↓	↑	Near normal	Absent
Beta-thalassemia major	Absent	↑↑	↑↑	Absent
Sickle cell trait	↓↓	Near normal	Near normal	↑
Sickle cell disease	Absent	Near normal	↑↑	↑↑

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Long-term glycemic control in p…uses across the red blood cell memb…h is directly correlated to average bl…ed cells to glucose will **increase HbA1c** v…

This patient's elevated **hemogl**…ta thalassemia to compensate for …rease in red cell turnover causes **falsely**…

(Choices B and C) Nutrient de… preponderance of older erythro…mias causes young red cells to be ra…

(Choice D) Diabetic nephropat…g decrease in red cell production …

(Choice E) Chronically elevate…vels in individuals with diabetes.

(Choice F) Sickle cell trait is a…globin electrophoresis. However, the …yte turnover.

Educational objective:
Glycated hemoglobin (HbA1c) forms within circulating red blood cells as hemoglobin A is exposed to glucose, and HbA1c levels are a useful indicator of average glycemic control over the erythrocyte life-span. HbA1c levels are affected by alterations in red blood cell survival; conditions that increase red blood cell turnover (eg, hemolytic anemia) can cause falsely low HbA1c levels.

Settings

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28

Item 3 of 29
Question Id: 585

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 46-year-old woman comes to the office with a painful rash involving her groin and legs that has been worsening over the last 2 weeks. She was diagnosed with diabetes mellitus 6 months ago but has no other medical problems other than occasional loose stools. Physical examination shows coalescing erythematous plaques with crusting and scaling at the borders and central areas of brownish induration. Biopsy of the lesions reveals superficial necrolysis. Which of the following laboratory abnormalities is most likely to be present in this patient?

A. Elevated amino acids
B. Elevated gastrin
C. Elevated glucagon
D. Elevated somatostatin
E. Elevated vasoactive intestinal polypeptide
F. Low insulin
G. Low zinc

Submit

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Settings

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Item 3 of 29
Question Id: 585

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 46-year-old woman comes to the office with a painful rash involving her groin and legs that has been worsening over the last 2 weeks. She was diagnosed with diabetes mellitus 6 months ago but has no other medical problems other than occasional loose stools. Physical examination shows coalescing erythematous plaques with crusting and scaling at the borders and central areas of brownish induration. Biopsy of the lesions reveals superficial necrolysis. Which of the following laboratory abnormalities is most likely to be present in this patient?

A. Elevated amino acids [3%]
B. Elevated gastrin [2%]
✔ C. Elevated glucagon [30%]
D. Elevated somatostatin [4%]
E. Elevated vasoactive intestinal polypeptide [9%]
F. Low insulin [10%]
G. Low zinc [38%]

Omitted
Correct answer
C

30%
Answered correctly

3 Seconds
Time Spent

09/10/2018
Last Updated

Explanation

Block Time Remaining: 00:00:34
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2/12/2019

Features of glucagonoma	
Clinical presentation	• **Necrolytic migratory erythema** • Erythematous papules/plaques on face, perineum & extremities • Lesions enlarge & coalesce, leaving a central indurated area with peripheral blistering & scaling • **Diabetes mellitus**/hyperglycemia • Gastrointestinal symptoms (diarrhea, anorexia, abdominal pain)
Diagnosis	• Markedly elevated glucagon levels

This patient most likely has a **glucagonoma**, a rare tumor arising from the **alpha cells** of the pancreatic islets of Langerhans. Glucagonomas secrete large quantities of glucagon, so affected patients often have **hyperglycemia** or overt **diabetes mellitus**. A characteristic skin finding is **necrolytic migratory erythema**, an elevated painful and pruritic rash typically affecting the face, groin, and extremities. Over time, small erythematous papules coalesce to form large, indurated plaques with a central clearing that often appears brown or bronze-colored. Diagnosis is made by detecting elevated levels of **glucagon** in the serum.

(Choice A) Glucagon acts on the liver to promote amino acid oxidation and gluconeogenesis from amino acids. Circulating levels of amino acids are low in glucagonoma and thought to contribute to development of necrolytic migratory erythema.

(Choice B) Elevated gastrin levels in patients with gastrinoma are associated with hypersecretion of gastric acid and resultant gastrointestinal ulceration. The peptic ulcers that occur with gastrinomas are often in unusual areas, such as the jejunum. Patients with gastrinomas can also have diarrhea and abdominal pain.

(Choice D) Excess somatostatin secretion from a somatostatinoma typically presents with abdominal pain, gallbladder stones, constipation, hyperglycemia, and steatorrhea. These manifestations result from somatostatin-induced inhibition of insulin, glucagon, gastrin, secretin, and cholecystokinin secretion, and inhibition of gastrointestinal motility.

(Choice E) High levels of vasoactive intestinal polypeptide (VIP) are seen in patients with a VIPoma, which typically presents with intractable

(Choice A) Glucagon acts on the liver to promote amino acid oxidation and gluconeogenesis from amino acids. Circulating levels of amino acids are low in glucagonoma and thought to contribute to development of necrolytic migratory erythema.

(Choice B) Elevated gastrin levels in patients with gastrinoma are associated with hypersecretion of gastric acid and resultant gastrointestinal ulceration. The peptic ulcers that occur with gastrinomas are often in unusual areas, such as the jejunum. Patients with gastrinomas can also have diarrhea and abdominal pain.

(Choice D) Excess somatostatin secretion from a somatostatinoma typically presents with abdominal pain, gallbladder stones, constipation, hyperglycemia, and steatorrhea. These manifestations result from somatostatin-induced inhibition of insulin, glucagon, gastrin, secretin, and cholecystokinin secretion, and inhibition of gastrointestinal motility.

(Choice E) High levels of vasoactive intestinal polypeptide (VIP) are seen in patients with a VIPoma, which typically presents with intractable diarrhea, hypokalemia, and achlorhydria. Patients are usually hypotensive due to dehydration and the vasodilatory effects of VIP.

(Choice F) Diabetes mellitus is present in the majority of patients with glucagonoma, most likely due to excessive hepatic glucose production. Insulin levels tend to be normal but can be elevated secondary to hyperglycemia and glucagon-induced stimulation of the pancreatic beta cells.

(Choice G) Zinc deficiency causes erythematous skin lesions (mainly around body orifices) that are predominantly vesicular and pustular. Other features include hypogonadism, impaired taste and smell, night blindness, and impaired wound healing. Although the skin lesions in zinc deficiency can resemble necrolytic migratory erythema, this patient's lack of additional findings and her recent diabetes mellitus diagnosis make glucagonoma more likely.

Educational objective:
Glucagonoma presents with hyperglycemia (often as newly diagnosed diabetes mellitus) and necrolytic migratory erythema (blistering erythematous plaques with central clearing) affecting the groin, face, and extremities. The diagnosis is made by detecting elevated glucagon levels.

References

Settings

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28

Item 4 of 29
Question Id: 1844

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 14-year-old boy is brought to the office due to painless nodules on his lips and tongue. The lesions appeared several months ago and have been progressively enlarging. The patient underwent total thyroidectomy 5 years ago following the discovery of a thyroid mass and takes thyroid hormone replacement. On physical examination, the patient is tall and slender with disproportionately long arms and legs. His fingers are also long and thin, and joint laxity is present. Eye examination is normal and oral inspection reveals several small, soft, flesh-colored papules on his lips and tongue. Serum TSH is within normal limits. This patient most likely has which of the following conditions?

A. Ehlers-Danlos syndrome
B. Marfan syndrome
C. Multiple endocrine neoplasia type 1
D. Multiple endocrine neoplasia type 2B
E. Neurofibromatosis type 1
F. Neurofibromatosis type 2

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4 | Feedback | Suspend | End Block

Settings

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28

Item 4 of 29
Question Id: 1844

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

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A. Ehlers-Danlos syndrome [4%]
B. Marfan syndrome [6%]
C. Multiple endocrine neoplasia type 1 [1%]
✔ D. Multiple endocrine neoplasia type 2B [83%]
E. Neurofibromatosis type 1 [2%]
F. Neurofibromatosis type 2 [1%]

Omitted
Correct answer
D

83%
Answered correctly

3 Seconds
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11/22/2018
Last Updated

Explanation

Classification of multiple endocrine neoplasia

Block Time Remaining: 00:00:37
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4 Feedback Suspend End Block

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2/12/2019

Classification of multiple endocrine neoplasia	
Type 1	• **Primary hyperparathyroidism** (parathyroid adenomas or hyperplasia) • Pituitary tumors (prolactin, visual defects) • Pancreatic tumors (especially gastrinomas)
Type 2A	• **Medullary thyroid cancer** (calcitonin) • Pheochromocytoma • Primary hyperparathyroidism (parathyroid hyperplasia)
Type 2B	• **Medullary thyroid cancer** (calcitonin) • Pheochromocytoma • Mucosal neuromas/marfanoid habitus

This patient has a **marfanoid habitus**—a tall and slender build with disproportionately long arms, legs, and fingers. The **flesh-colored nodules** on his lips and tongue are likely **mucosal neuromas**, which are unencapsulated, thickened proliferations of neural tissue. This patient also has a history of total thyroidectomy, which was likely due to **medullary thyroid cancer** (MTC). This combination of clinical findings is consistent with **multiple endocrine neoplasia type 2B** (MEN 2B), which is due to an autosomal dominant germ-line mutation in the *RET* proto-oncogene. Other possible manifestations of MEN 2B include pheochromocytoma and intestinal ganglioneuromas (which may cause constipation). The earliest manifestations of the disease often appear in childhood or adolescence. Early recognition of MEN 2B is important as almost all patients develop MTC and prophylactic thyroidectomy can be life-saving.

(Choice A) Ehlers-Danlos syndrome is a heritable connective tissue disorder characterized by skin hyperextensibility, joint hypermobility, tissue fragility, poor wound healing, and easy bruising. There is no known association between Ehlers-Danlos syndrome and thyroid cancer or perioral nodules.

This patient has a **marfanoid habitus**—a tall and slender build with disproportionately long arms, legs, and fingers. The flesh-colored nodules on his lips and tongue are likely **mucosal neuromas**, which are unencapsulated, thickened proliferations of neural tissue. This patient also has a history of total thyroidectomy, which was likely due to **medullary thyroid cancer** (MTC). This combination of clinical findings is consistent with **multiple endocrine neoplasia type 2B** (MEN 2B), which is due to an autosomal dominant germ-line mutation in the *RET* proto-oncogene. Other possible manifestations of MEN 2B include pheochromocytoma and intestinal ganglioneuromas (which may cause constipation). The earliest manifestations of the disease often appear in childhood or adolescence. Early recognition of MEN 2B is important as almost all patients develop MTC and prophylactic thyroidectomy can be life-saving.

(Choice A) Ehlers-Danlos syndrome is a heritable connective tissue disorder characterized by skin hyperextensibility, joint hypermobility, tissue fragility, poor wound healing, and easy bruising. There is no known association between Ehlers-Danlos syndrome and thyroid cancer or perioral nodules.

(Choice B) Although this patient has a marfanoid habitus, the remainder of his presentation is more consistent with MEN 2B than Marfan syndrome. In addition, unlike true Marfan syndrome, patients with MEN 2B do not develop aortic malformations (eg, dilation) or ocular malformations (eg, ectopia lentis).

(Choice C) Multiple endocrine neoplasia type 1 (MEN 1) is an autosomal dominant condition characterized by parathyroid adenomas with hyperparathyroidism, anterior pituitary gland tumors, and pancreatic endocrine tumors (the "3 Ps"). MEN 1 is not associated with thyroid cancer or perioral nodules.

(Choices E and F) Neurofibromatosis type 1 is characterized by café au lait spots, **cutaneous neurofibromas**, axillary or inguinal freckling, optic glioma, and iris hamartomas. Neurofibromatosis type 2 (the more central form) is characterized by bilateral acoustic neuromas, brain meningiomas, and schwannomas of the dorsal roots in the spinal cord. Although this patient has (mucosal) neuromas, the remainder of his presentation is more consistent with MEN 2B.

Educational objective:
Multiple endocrine neoplasia type 2B is characterized by medullary thyroid cancer, pheochromocytoma, marfanoid habitus, and oral and intestinal mucosal neuromas.

Settings

Item 4 of 29
Question Id: 1844

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
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- **Primary hyperparathyroidism** (parathyroid adenomas or

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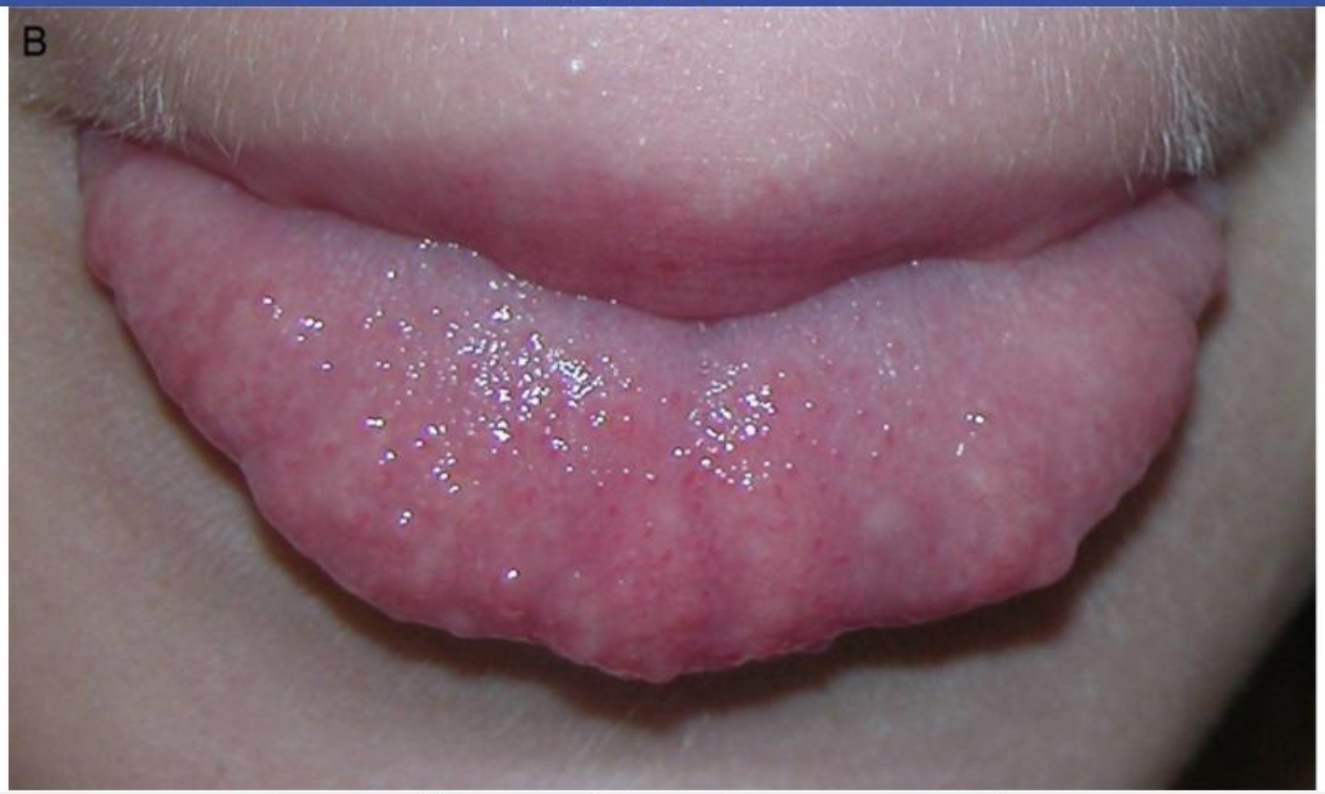

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malformations (eg, ectopia lentis).

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2/12/2019

Settings

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28

Item 5 of 29
Question Id: 220

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 24-year-old woman, gravida 1 para 1, comes to the office for postpartum follow-up 2 weeks after a term vaginal delivery. Her baby is doing well, but she is concerned because she has not yet lactated. The patient knew she would lose weight and be tired after the baby was born, but she feels excessive fatigue and has had significant weight loss. She also has nausea, loss of appetite, and postural dizziness. The patient has no headaches, visual problems, cold intolerance, constipation, or polyuria. On examination, she appears fatigued and has mild pallor. Laboratory tests are drawn the next morning at 8:00 AM, with the following results:

Hemoglobin	9.6 g/dL
Sodium	130 mEq/L
Cortisol, serum	4 µg/dL
Free T_4	1.0 ng/dL
TSH	0.2 µU/mL

Which of the following pathologic processes is most likely responsible for this patient's symptoms?

A. Glandular hemorrhage
B. Inflammation
C. Ischemic necrosis
D. Malignant infiltration
E. Non-malignant infiltration

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but she is concerned because she has not yet lactated. The patient knew she would lose weight and be tired after the baby was born, but she feels excessive fatigue and has had significant weight loss. She also has nausea, loss of appetite, and postural dizziness. The patient has no headaches, visual problems, cold intolerance, constipation, or polyuria. On examination, she appears fatigued and has mild pallor. Laboratory tests are drawn the next morning at 8:00 AM, with the following results:

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Sodium	130 mEq/L
Cortisol, serum	4 µg/dL
Free T_4	1.0 ng/dL
TSH	0.2 µU/mL

Which of the following pathologic processes is most likely responsible for this patient's symptoms?

- A. Glandular hemorrhage [21%]
- B. Inflammation [1%]
- ✔ C. Ischemic necrosis [72%]
- D. Malignant infiltration [1%]
- E. Non-malignant infiltration [2%]

Omitted
Correct answer

72%
Answered correctly

6 Seconds
Time Spent

01/15/2019
Last Updated

Hypopituitarism	
Etiology	**Pituitary causes** • Mass lesions (primary or metastatic) • Infiltration (eg, lymphocytic hypophysitis) • Hemorrhage (pituitary apoplexy) • Ischemic infarction (Sheehan syndrome) **Hypothalamic lesions** (eg, sarcoidosis, infection, radiation therapy)
Clinical presentation	**ACTH deficiency** • Hypotension, weight loss, hypoglycemia **Hypothyroidism** • Fatigue, cold intolerance, slowed deep-tendon reflexes **Gonadotropins** • Women: Amenorrhea, infertility • Men: Infertility, loss of libido

This patient has signs of **panhypopituitarism** with failure of lactation, central hypothyroidism, and adrenal insufficiency. In the setting of a recent delivery, this most likely represents **ischemic necrosis** of the **pituitary gland** (Sheehan syndrome). During pregnancy, the pituitary enlarges due to estrogen-induced hyperplasia of the lactotrophs. However, the blood supply to the pituitary does not increase proportionally. As a result, the

This patient has signs of **panhypopituitarism** with failure of lactation, central hypothyroidism, and adrenal insufficiency. In the setting of a recent delivery, this most likely represents **ischemic necrosis** of the **pituitary gland** (Sheehan syndrome). During pregnancy, the pituitary enlarges due to estrogen-induced hyperplasia of the lactotrophs. However, the blood supply to the pituitary does not increase proportionally. As a result, the enlarged pituitary is vulnerable to ischemia in case of systemic hypotension due to **peripartum hemorrhage** (which this patient likely experienced given her low hemoglobin).

The most common manifestation of Sheehan syndrome is failure of lactation due to prolactin deficiency. It also commonly causes hypocortisolism and hypothyroidism. Manifestations of thyroid deficiency may take a few weeks to develop due to the long circulating half-life of thyroxine (5-7 days) and peripheral conversion of thyroxine (T4) to T3. Cortisol deficiency manifests rapidly, however, with nausea, postural hypotension, fatigue, and weight loss.

(Choice A) Pituitary apoplexy is due to sudden hemorrhage into the pituitary, usually in the setting of a preexisting pituitary adenoma. It usually presents with acute severe headache, ophthalmoplegia, and altered sensorium.

(Choice B) Lymphocytic hypophysitis is the most common inflammatory condition of the pituitary and typically occurs during late pregnancy or the early postpartum period. In contrast to Sheehan syndrome, the presentation is acute with severe headaches and visual field defects.

(Choice D) Primary pituitary cancer is extremely rare, although the pituitary is prone to metastases due to its rich vascular supply. These patients typically present with tumor mass effects (eg, headache, bitemporal hemianopsia).

(Choice E) Non-malignant infiltrative lesions such as sarcoidosis and histiocytosis X mainly involve the suprasellar region, where they compress the hypothalamus and pituitary stalk. This disrupts the normal hypothalamic dopaminergic suppression of prolactin secretion, leading to increased prolactin levels and possible galactorrhea. Central diabetes insipidus may also be seen with resulting hypernatremia.

Educational objective:
High estrogen levels during pregnancy cause enlargement of the pituitary gland without a proportional increase in blood supply. Peripartum hypotension can cause ischemic necrosis of the pituitary leading to panhypopituitarism (Sheehan syndrome). Patients commonly develop failure of lactation due to deficiency of prolactin.

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Item 6 of 29
Question Id: 221

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 7-year-old boy is being evaluated for growth retardation. Brain MRI shows a 4 cm multiloculated, cystic, suprasellar lesion, which is bulging into the floor of the third ventricle and base of the brain. Calcifications are present. From which of the following structures is this mass most likely derived?

A. Prolactin secreting cells of the anterior pituitary
B. Remnants of the Rathke pouch
C. Astrocytes
D. Arachnoid cap cells
E. Posterior pituitary cells

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2/12/2019

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Item 6 of 29
Question Id: 221

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 7-year-old boy is being evaluated for growth retardation. Brain MRI shows a 4 cm multiloculated, cystic, suprasellar lesion, which is bulging into the floor of the third ventricle and base of the brain. Calcifications are present. From which of the following structures is this mass most likely derived?

A. Prolactin secreting cells of the anterior pituitary [6%]
B. Remnants of the Rathke pouch [80%]
C. Astrocytes [7%]
D. Arachnoid cap cells [2%]
E. Posterior pituitary cells [3%]

Omitted
Correct answer
B

80%
Answered correctly

3 Seconds
Time Spent

11/29/2018
Last Updated

Explanation

Craniopharyngiomas are tumors arising from remnants of Rathke's pouch. The anterior pituitary is formed from an out-pouching of the pharyngeal roof and is called Rathke's pouch. The posterior pituitary gland arises from an extension of the hypothalamic neurons. Together, the anterior and posterior pituitary glands lie in the sella turcica at the skull base.

During the time of pituitary development, remnants of Rathke's pouch cells can remain in the diencephalon (the posterior region of the forebrain).

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Craniopharyngiomas are tumors arising from remnants of Rathke's pouch. The anterior pituitary is formed from an out-pouching of the pharyngeal roof and is called Rathke's pouch. The posterior pituitary gland arises from an extension of the hypothalamic neurons. Together, the anterior and posterior pituitary glands lie in the sella turcica at the skull base.

During the time of pituitary development, remnants of Rathke's pouch cells can remain in the diencephalon (the posterior region of the forebrain). Neoplastic transformation of these "pouch cells" is called a craniopharyngioma. Typically, craniopharyngiomas have three components: solid, comprised of the actual tumor cells; cystic, filled with "machinery oil" liquid; and a calcified component. Any suprasellar mass with three components is highly suggestive of craniopharyngioma. Craniopharyngioma symptoms include headaches, visual field defects, and hypopituitarism, evidenced by the growth retardation of this child. Ultimately, compression of the pituitary stalk by craniopharyngioma leads to hyperprolactinemia by loss of dopaminergic inhibition. Craniopharyngiomas are usually tumors of childhood, being most frequently discovered between the ages of 5 and 10 years of age.

(Choice A) Prolactinomas are uncommon in young children. They typically appear as a homogenous mass when imaged.

(Choice C) Gliomas can occur in the suprasellar region if they arise from the optic apparatus, but do not appear on imaging with the three components described above. Gliomas typically presents with visual symptoms, hypothalamic dysfunction, and hypopituitarism.

(Choice D) Meningiomas are tumors of the leptomeninges, which is the lining of the brain. Hence, meningiomas can occur in any "lined" part of the brain including sellar and suprasellar regions. Meningiomas are usually homogeneous appearance on MRI and can be seen "sticking" to leptomeninges.

Educational Objective:

1. The anterior pituitary is formed from an out-pouching of the pharyngeal roof and is called Rathke's pouch. The posterior pituitary gland arises from an extension of the hypothalamic neurons.
2. Craniopharyngiomas are tumors arising from Rathke's pouch remnants in the anterior pituitary. They characteristically have three components: solid, cystic, and calcified. They present during childhood, usually, with mass effect and visual deficits.

Settings

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28

Item 7 of 29
Question Id: 1011

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 53-year-old woman comes to the physician for a routine check-up. She has no current complaints. Her past medical history is significant for osteoarthritis of the right knee. Her mother suffered from hypertension and was diagnosed with breast cancer at age 68, from which she died 4 years later. Her father had diabetes mellitus and died in a motor vehicle accident at age 56. The patient's blood pressure is 140/85 mm Hg and heart rate is 80/min. Physical examination is normal. Laboratory testing is significant for a fasting blood glucose level of 140 mg/dL on more than 2 occasions. This patient is most likely to die from which of the following conditions?

A. Breast cancer
B. Hyperosmolar nonketotic coma
C. Myocardial infarction
D. Renal failure
E. Stroke

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2/12/2019

Settings

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28

Item 7 of 29
Question Id: 1011

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 53-year-old woman comes to the physician for a routine check-up. She has no current complaints. Her past medical history is significant for osteoarthritis of the right knee. Her mother suffered from hypertension and was diagnosed with breast cancer at age 68, from which she died 4 years later. Her father had diabetes mellitus and died in a motor vehicle accident at age 56. The patient's blood pressure is 140/85 mm Hg and heart rate is 80/min. Physical examination is normal. Laboratory testing is significant for a fasting blood glucose level of 140 mg/dL on more than 2 occasions. This patient is most likely to die from which of the following conditions?

- A. Breast cancer [6%]
- B. Hyperosmolar nonketotic coma [3%]
- ✔ C. Myocardial infarction [61%]
- D. Renal failure [23%]
- E. Stroke [5%]

Omitted
Correct answer
C

61%
Answered correctly

3 Seconds
Time Spent

10/10/2018
Last Updated

Explanation

Risk factors for coronary heart disease

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Risk factors for coronary heart disease	
Highest risk factors (coronary heart disease equivalents)	• Noncoronary atherosclerotic disease • Diabetes mellitus • Chronic kidney disease
Major risk factors	• Hypertension • Hyperlipidemia (↑LDL & triglycerides) • Cigarette smoking • Advanced age • Obesity • Physical inactivity

Several studies have shown that diabetes mellitus is one of the strongest risk factors for coronary heart disease. Cardiovascular mortality is increased by 2- to 4-fold in patients with type 2 diabetes mellitus, and approximately 40% of patients die secondary to coronary heart disease. For a person with type 2 diabetes mellitus, the risk of dying from coronary heart disease exceeds the risk of dying from any of the other listed causes, even in the absence of other major risk factors for coronary heart disease.

(Choice A) The risk of breast cancer is not increased in patients with diabetes mellitus. Although this patient has a family history of breast cancer, her risk is not significantly increased since her mother was at an advanced age when the cancer occurred.

(Choice B) Diabetic ketoacidosis (DKA) and hyperosmolar coma are acute complications of untreated diabetes mellitus. Hyperosmolar coma is seen mainly with type 2 diabetes mellitus and is characterized by very high blood sugar levels without ketoacidosis. The mortality of hyperosmolar coma is higher than DKA; however, very few patients with diabetes die directly from DKA or hyperosmolar coma

	• Obesity • Physical inactivity

Several studies have shown that diabetes mellitus is one of the strongest risk factors for coronary heart disease. Cardiovascular mortality is increased by 2- to 4-fold in patients with type 2 diabetes mellitus, and approximately 40% of patients die secondary to coronary heart disease. For a person with type 2 diabetes mellitus, the risk of dying from coronary heart disease exceeds the risk of dying from any of the other listed causes, even in the absence of other major risk factors for coronary heart disease.

(Choice A) The risk of breast cancer is not increased in patients with diabetes mellitus. Although this patient has a family history of breast cancer, her risk is not significantly increased since her mother was at an advanced age when the cancer occurred.

(Choice B) Diabetic ketoacidosis (DKA) and hyperosmolar coma are acute complications of untreated diabetes mellitus. Hyperosmolar coma is seen mainly with type 2 diabetes mellitus and is characterized by very high blood sugar levels without ketoacidosis. The mortality of hyperosmolar coma is higher than DKA; however, very few patients with diabetes die directly from DKA or hyperosmolar coma.

(Choice D) Diabetes mellitus is the leading cause of end-stage renal disease (ESRD), followed by hypertension. However, approximately 50% of patients with ESRD die due to cardiovascular disease, with infections being the next most common cause.

(Choice E) The risk of stroke is increased in patients with diabetes mellitus. However, cerebrovascular accidents account for about 10% of total mortality in patients with type 2 diabetes mellitus versus 40% from coronary heart disease.

Educational objective:
Patients with **noncoronary atherosclerotic disease**, **diabetes mellitus**, or **chronic kidney disease** are at the same risk of cardiovascular events (eg, myocardial infarction, stroke) as patients with known coronary heart disease. Coronary heart disease is the most common cause of death in patients with diabetes mellitus.

Settings

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28

Item 8 of 29
Question Id: 848

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 65-year-old man comes to the physician because of a non-healing ulcer on his right foot. His past medical history is significant for recurrent high blood glucose readings for the last several years, because he has failed to comply with appropriate treatment. His BMI is 37 kg/m^2. Physical examination is significant for a bilateral symmetric decrease in vibration sensation over the feet and ankles. Which of the following is most likely to be associated with this patient's condition?

A. Pancreatic islet infiltration with leukocytes
B. Pancreatic islet amyloid deposition
C. Circulating anti-islet antibodies
D. Strong linkage with HLA class II gene makeup
E. Episodic ketoacidosis that requires insulin therapy

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4 Feedback | Suspend | End Block

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1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28

Item 8 of 29
Question Id: 848

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 65-year-old man comes to the physician because of a non-healing ulcer on his right foot. His past medical history is significant for recurrent high blood glucose readings for the last several years, because he has failed to comply with appropriate treatment. His BMI is 37 kg/m^2. Physical examination is significant for a bilateral symmetric decrease in vibration sensation over the feet and ankles. Which of the following is most likely to be associated with this patient's condition?

- A. Pancreatic islet infiltration with leukocytes [4%]
- ✔ B. Pancreatic islet amyloid deposition [67%]
- C. Circulating anti-islet antibodies [3%]
- D. Strong linkage with HLA class II gene makeup [16%]
- E. Episodic ketoacidosis that requires insulin therapy [7%]

Omitted
Correct answer
B

67%
Answered correctly

3 Seconds
Time Spent

11/08/2018
Last Updated

Explanation

The patient described in this vignette has type 2 diabetes mellitus (advanced age, obesity, prolonged non-compliance with treatment without immediate life-threatening consequences). The two cardinal defects involved in the pathophysiology of type 2 diabetes mellitus are increased insulin resistance and defective insulin secretion. Although still controversial, many researchers believe that increased insulin resistance is the primary abnormality in type 2 diabetes mellitus. Early in the pathogenesis of type 2 diabetes, glucose tolerance is thought to remain normal

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The patient described in this vignette has type 2 diabetes mellitus (advanced age, obesity, prolonged non-compliance with treatment without immediate life-threatening consequences). The two cardinal defects involved in the pathophysiology of type 2 diabetes mellitus are increased insulin resistance and defective insulin secretion. Although still controversial, many researchers believe that increased insulin resistance is the primary abnormality in type 2 diabetes mellitus. Early in the pathogenesis of type 2 diabetes, glucose tolerance is thought to remain normal because of a compensatory increase in insulin secretion from beta cells. This compensatory insulin response by beta cells ultimately fails, causing poor glucose tolerance. A number of genetic and acquired factors are implicated in the beta-cell dysregulation of type 2 diabetes. Islet amyloid polypeptide (amylin) is one factor thought to be responsible for this beta cell dysfunction. Amylin is stored in insulin secretory granules and is co-secreted with insulin from pancreatic beta cells. Deposits of amylin are universally seen in the pancreatic islets of patients with type 2 diabetes mellitus. Amylin may play a causative role in beta cell apoptosis and defective insulin secretion; however, this theory is still controversial.

Type 1 and type 2 diabetes mellitus have very strong genetic components. Twin studies have shown a concordance rate of 50% in identical twins for diabetes mellitus type 1, and around 80% for diabetes mellitus type 2. The genes involved in the pathogenesis of diabetes mellitus type 2 remain largely unknown. Gene polymorphism within the major histocompatibility complex contributes to type 1 diabetes mellitus disease in humans. HLA-DQ and -DR are the most important determinants of type 1 diabetes mellitus. In the general population, DR3 and DR4 are seen in approximately 40% of subjects; however, in patients with type 1 diabetes mellitus, DR3 and DR4 haplotypes are seen in more than 90% of subjects.

(Choices A, C, D & E) These are features of type 1 diabetes mellitus. Type 1 diabetes occurs when an autoimmune response is triggered by an environmental insult in genetically susceptible individuals. Patients with type 2 diabetes retain at least some beta cell function, but patients with type 1 diabetes mellitus develop absolute deficiency of insulin secondary to immune destruction of pancreatic beta cells. These patients need insulin for survival. Discontinuation of insulin treatment results in ketoacidosis.

Educational objective:
Pancreatic islet amyloid deposition is characteristic of type 2 diabetes mellitus. A strong linkage with HLA class II gene makeup, pancreatic islet infiltration with leukocytes (insulitis), and antibodies against islet antigens are frequently seen in type 1 diabetes.

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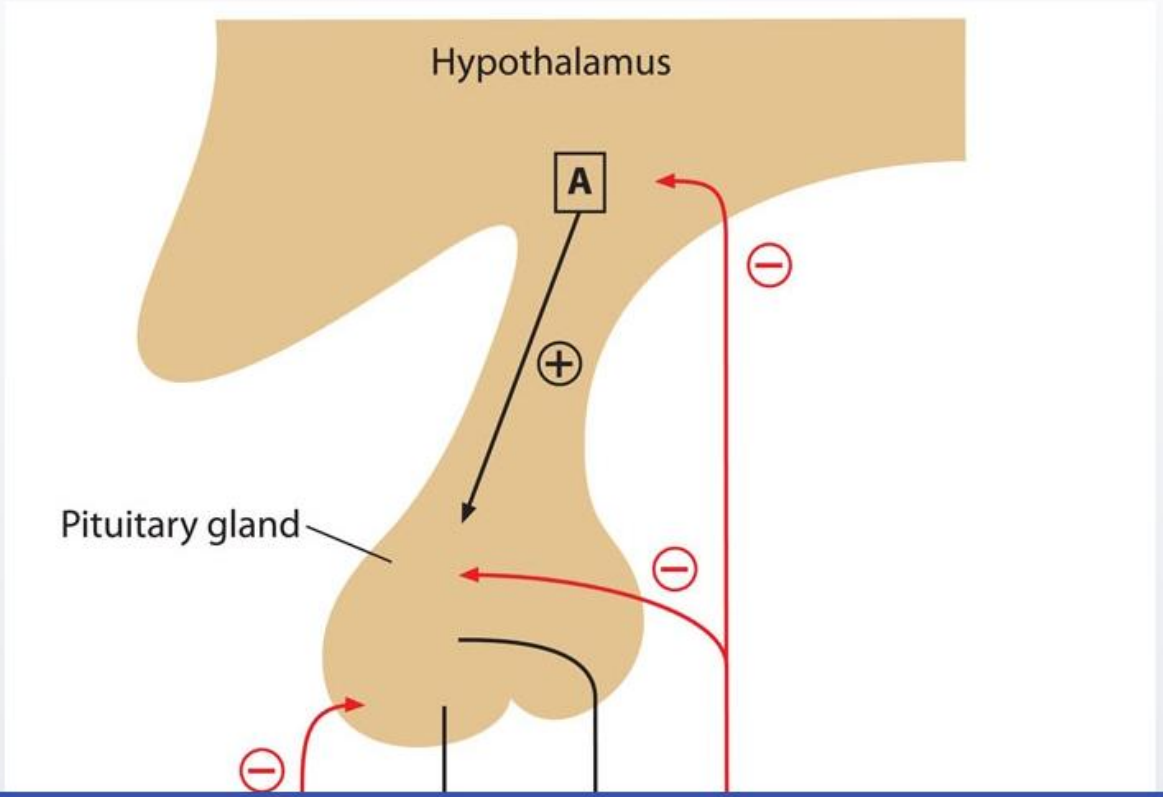
Item 9 of 29
Question Id: 579

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 14-year-old boy is brought to the physician by his mother. She is concerned because although tall, her son looks much younger than his peers and shows no signs of "masculinity." On physical examination, the boy has poorly developed secondary sexual characteristics. He is unable to distinguish smells but has good visual acuity. Which of the following pathways is most likely defective in this patient?



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Settings

Item 9 of 29
Question Id: 579

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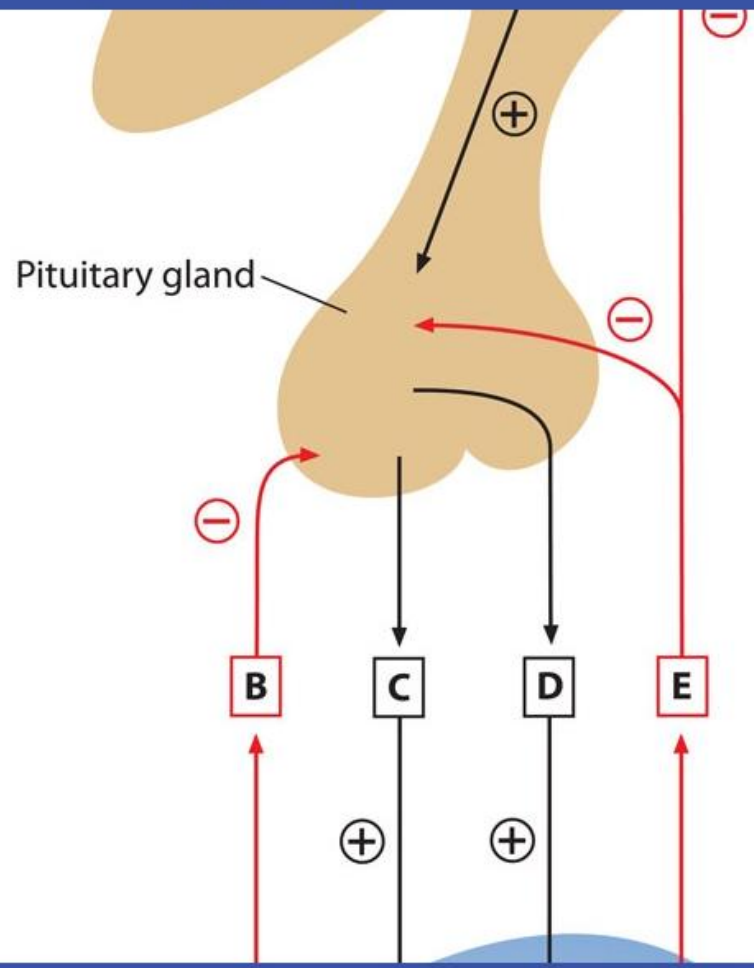

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Item 9 of 29
Question Id: 579

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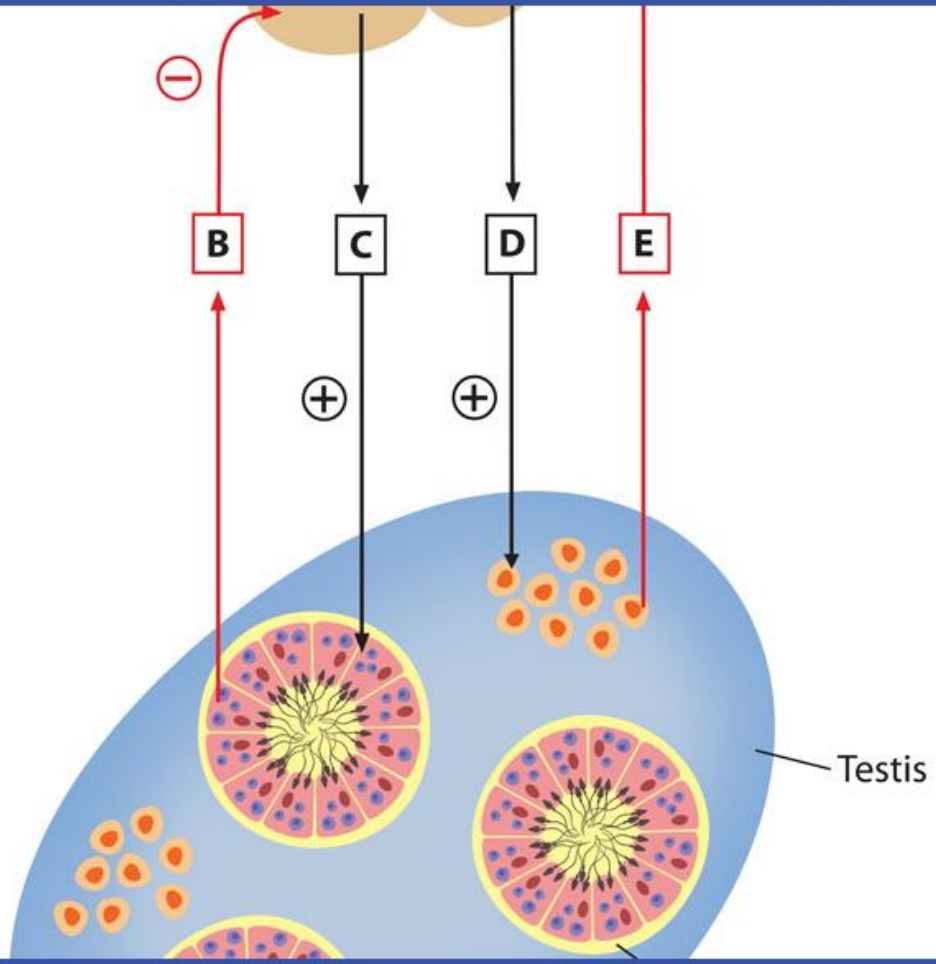

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Item 9 of 29
Question Id: 579

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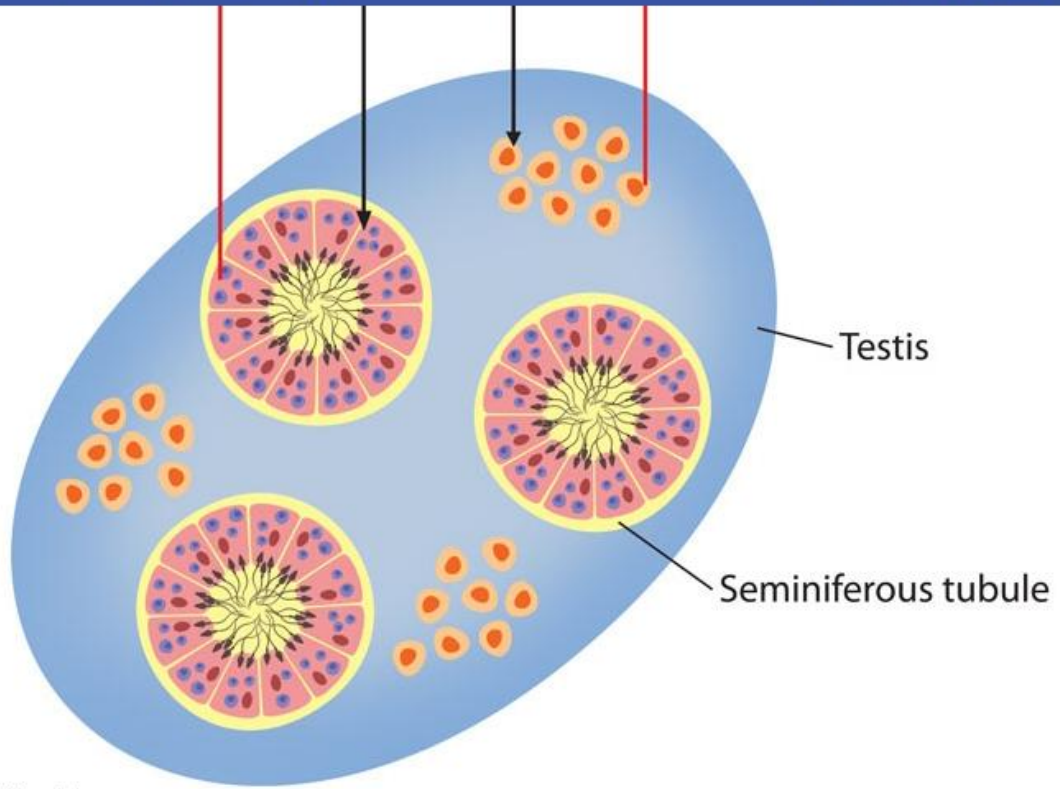

A. A

B. B

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Item 9 of 29
Question Id: 579

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

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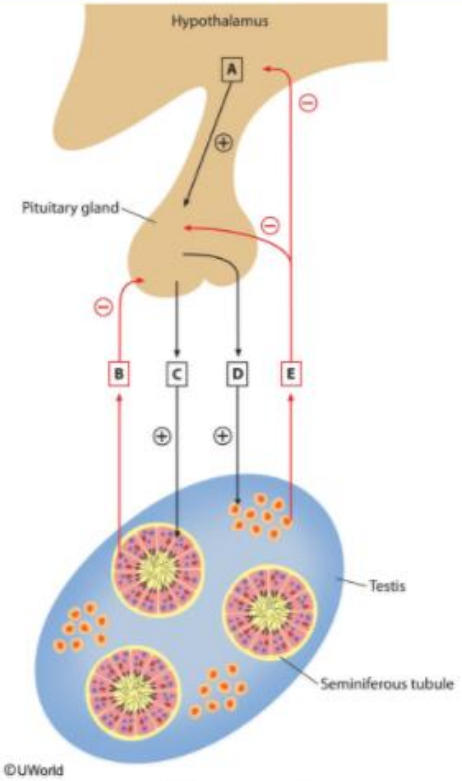

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B. B

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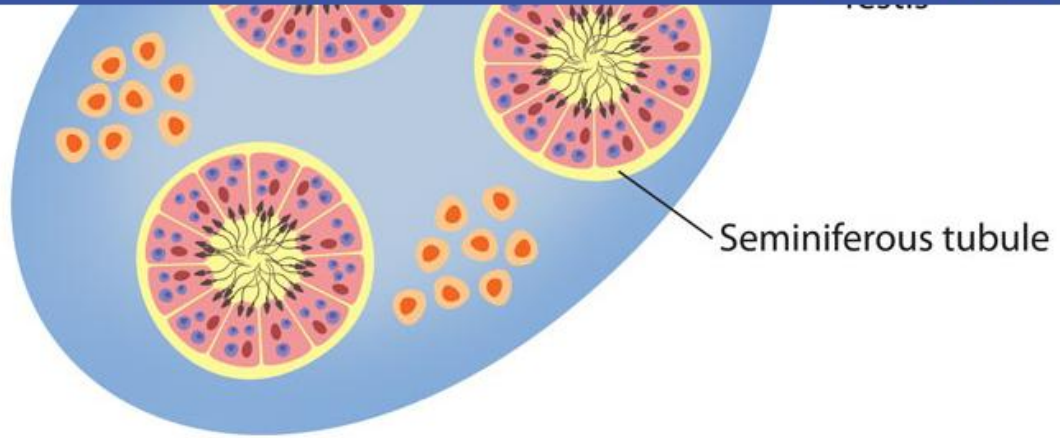
Item 9 of 29
Question Id: 579

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom



- A. A
- B. B
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- D. D
- E. E

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Item 9 of 29
Question Id: 579

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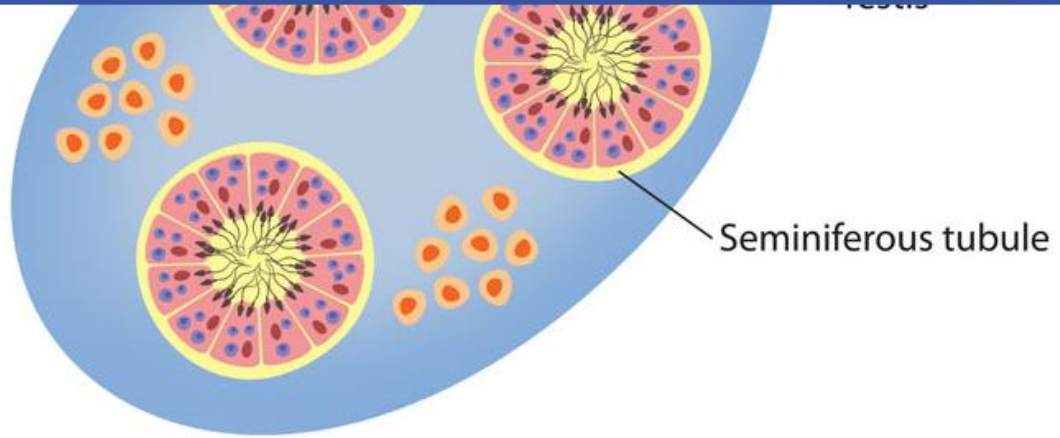

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- A. A [57%]
- B. B [4%]
- C. C [8%]
- D. D [20%]
- E. E [8%]

Omitted
Correct answer

57%
Answered correctly

23 Seconds
Time Spent

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Last Updated

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Explanation

This patient has delayed puberty plus anosmia, consistent with a diagnosis of Kallmann syndrome. Kallmann syndrome results from a failure of GnRH-secreting neurons to migrate from their origin in the olfactory placode (situated outside the central nervous system) to their normal anatomic location in the hypothalamus. Most often, the cause is a mutation in the KAL-1 gene or the fibroblast growth factor receptor-1 gene, which code for proteins required in this migration.

Patients with Kallmann syndrome classically have central hypogonadism and anosmia, although there may be other midline defects as well (eg, cleft lip or cleft palate). Most often, these patients present with delayed puberty. On physical examination, the testes are often just 1-2 mL in volume. There is usually some pubic hair because adrenarche occurs normally.

In the United States, delayed puberty is defined as the absence or incomplete development of secondary sexual characteristics by age 14 in boys and by age 12 in girls. Testicular enlargement is the first sign of puberty in boys, and breast enlargement is the first sign in girls. The initiation of puberty and the maintenance of secondary sexual characteristics and fertility require the coordinated efforts of the hypothalamus, pituitary, and gonads. Delayed puberty can result from a derangement anywhere in this axis.

(Choices B, C, D, and E) These pathways represent **normal feedback loops** between the testes and the hypothalamus and pituitary. Pituitary follicle-stimulating hormone (FSH) stimulates proliferation of the seminiferous tubules and spermatogenesis. The seminiferous tubules produce inhibin, which feeds back to inhibit pituitary FSH secretion. Luteinizing hormone from the pituitary stimulates the interstitial Leydig cells to produce testosterone, which also participates in feedback inhibition.

Educational objective:
In Kallmann syndrome, there is an absence of GnRH secretory neurons in the hypothalamus due to defective migration from the olfactory placode. These patients have central hypogonadism and anosmia, and often present with delayed puberty.

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Item 10 of 29
Question Id: 191

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 42-year-old woman comes to the physician for a routine check-up. She has no current complaints and no significant past medical history. On physical examination, the physician notes lesions on her eyelids that are pictured below.

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

Block Time Remaining: 00:01:17
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Settings

Item 10 of 29
Question Id: 191

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

- 1
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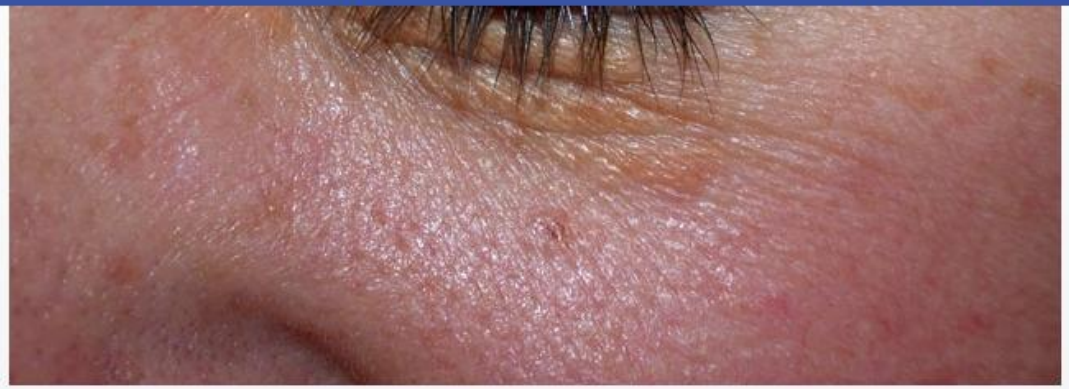

Which of the following is the best next step in the management of this patient?

A. ECG and serum cardiac enzymes
B. Serum lipids and blood glucose level
C. Liver function tests and abdominal ultrasonography
D. Complete blood count and stool guaiac test
E. Slit lamp exam and ophthalmoscopy
F. Lesion biopsy and surgeon referral

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Settings

Item 10 of 29
Question Id: 191

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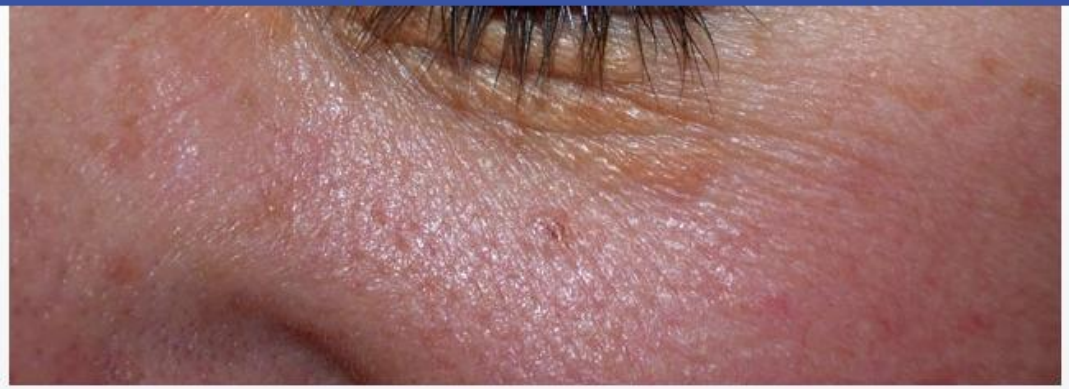

Which of the following is the best next step in the management of this patient?

- A. ECG and serum cardiac enzymes [0%]
- ✔ B. Serum lipids and blood glucose level [93%]
- C. Liver function tests and abdominal ultrasonography [3%]
- D. Complete blood count and stool guaiac test [0%]
- E. Slit lamp exam and ophthalmoscopy [0%]
- F. Lesion biopsy and surgeon referral [0%]

Omitted
Correct answer

93%
Answered correctly

8 Seconds
Time Spent

10/06/2018
Last Updated

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The lesion pictured is a xanthelasma, a type of xanthoma usually found on the medial eyelids. Hyperlipidemia and/or dyslipidemia can result in xanthomas (including xanthelasmas). Xanthelasmas are dermal accumulations of benign-appearing macrophages with abundant, finely vacuolated (foamy) cytoplasm containing cholesterol (free and esterified), phospholipids, and triglycerides. Due in part to insulin resistance promoting increased VLDL production, diabetics may develop a secondary Type IV or V hyperlipidemia (increased VLDL, chylomicrons) and/or a secondary diabetic dyslipidemia with elevated LDL cholesterol and low HDL cholesterol. Thus, in order to determine the type of this patient's lipid disorder and to rule out underlying diabetes, her serum lipids and blood glucose should be measured.

(Choice A) Although this patient may be at increased risk for coronary artery disease due to hyperlipidemia or dyslipidemia, she does not currently have symptoms of myocardial infarction. Her current management should be focused on treating her lipid disorder.

(Choice C) The first step in managing this patient is to establish what type of lipid abnormality she has based upon her serum lipid levels and lipoprotein profile. If the results are consistent with an obstructive liver and/or biliary system lesion producing cholestasis and hypercholesterolemia, then liver function tests and abdominal ultrasonography may be warranted.

(Choice D) A CBC and stool guaiac test are performed when searching for occult GI bleeding.

(Choice E) Slit lamp examination and funduscopy could reveal ocular findings associated with this patient's lipid disorder, such as a corneal arcus (lipid deposit) or lipemia retinalis. However, a serum lipid profile should be obtained next in order to establish the type of hyperlipidemia or dyslipidemia in this patient.

(Choice F) Xanthelasmas are usually diagnosed based on clinical appearance. Biopsy is not required. Treatment is primarily medical and directed at the underlying lipid abnormality. Surgical excision is not medically necessary, but may be undertaken electively for cosmetic reasons.

Educational objective:
Xanthelasmas, a type of xanthoma, are yellowish macules/papules found on the medial eyelids. They are dermal accumulations of macrophages containing cholesterol and triglycerides, and are generally associated with a primary or secondary hyperlipidemia or dyslipidemia. An LDL receptor abnormality is the most common cause.

Settings

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21
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28

Item 11 of 29
Question Id: 1262

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 27-year-old woman comes to the office for evaluation of infertility. The patient and her husband have been trying to conceive for the past 2 years but have been unsuccessful. Her husband recently underwent infertility evaluation and was found to have no abnormalities. The patient's menses began at age 13, and her menstrual cycles were regular until the last few years, when they began occurring at intervals of 3-4 months. She has occasional headaches but no other symptoms. The patient has no prior medical conditions and takes no medications. On physical examination, the patient appears normal and has well-developed secondary sexual characteristics. Cardiopulmonary and abdominal examinations are normal. Pelvic examination reveals no adnexal masses. Neurological examination shows diminished vision in the bilateral temporal visual fields. Examination of the other cranial nerves is normal and there is no focal weakness or sensory loss. An abnormality originating in which of the following is the most likely cause of this patient's current condition?

A. Hypothalamic neurons
B. Ovarian granulosa cells
C. Ovarian theca cells
D. Pituitary lactotrophs
E. Pituitary somatotrophs

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2/12/2019

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Item 11 of 29
Question Id: 1262

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A. Hypothalamic neurons [3%]
B. Ovarian granulosa cells [0%]
C. Ovarian theca cells [1%]
✔ D. Pituitary lactotrophs [85%]
E. Pituitary somatotrophs [8%]

Omitted
Correct answer
D

85%
Answered correctly

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Last Updated

Explanation

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Item 11 of 29
Question Id: 1262

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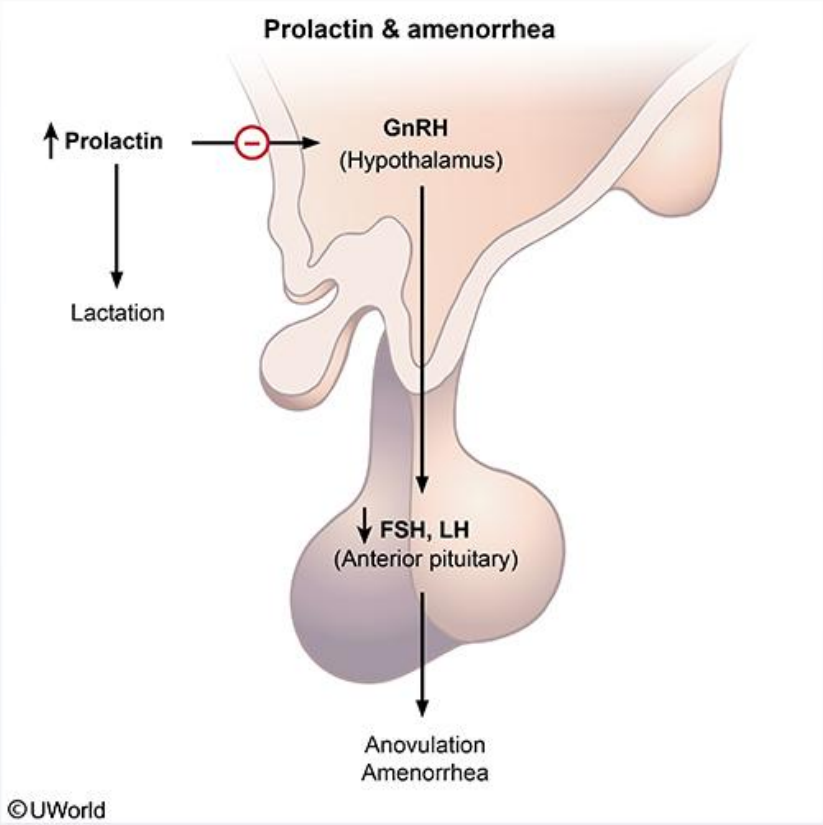

This patient's symptoms are concerning for a **pituitary tumor**. Large pituitary tumors can cause **headaches** due to mass effect, and compression of the optic chiasm by suprasellar extension of the tumor can lead to **bitemporal hemianopsia**.

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Amenorrhea

This patient's symptoms are concerning for a **pituitary tumor**. Large pituitary tumors can cause **headaches** due to mass effect, and compression of the optic chiasm by suprasellar extension of the tumor can lead to **bitemporal hemianopsia**.

The most common type of pituitary adenoma is a **prolactinoma**. Prolactin is a peptide hormone secreted from lactotrophs of the pituitary gland whose primary physiologic action is maintenance of lactation in postpartum women. Hyperprolactinemia also **suppresses GnRH production** in the hypothalamus, leading to **oligomenorrhea/amenorrhea** and infertility. Suppression of ovulation is also seen as a physiologic effect of breastfeeding, which supports elevated prolactin levels for 6 months or more postpartum.

(Choice A) Kallmann syndrome is a disorder involving the GnRH-producing neurons in the hypothalamus. In addition to decreased sense of smell (anosmia/hyposomia), this condition causes hypogonadotropic hypogonadism and presents with short stature and delayed puberty (primary amenorrhea). This patient has secondary amenorrhea (ie, normal initial onset of puberty followed by menstrual dysregulation), and her bilateral temporal visual deficits are more suggestive of a pituitary rather than hypothalamic lesion.

(Choice B) Ovarian granulosa cells produce estrogen, progesterone, and inhibin. Loss of these cells (eg, due to autoimmune disorder) can lead to primary ovarian insufficiency and present with infertility and secondary amenorrhea. However, patients often have hypoestrogenic symptoms (eg, hot flashes), and this disorder would not cause visual field defects.

(Choice C) Ovarian theca cells produce androgens, which provide the substrate for subsequent synthesis of estrogens. Amenorrhea and infertility related to hyperactivity of these cells are typically associated with signs of hyperandrogenism (eg, hirsutism).

(Choice E) Unlike most pituitary hormones, which are under positive regulation by the hypothalamus, prolactin is primarily under negative regulation by hypothalamic dopaminergic neurons via the pituitary stalk. Because of this, any pituitary tumor of significant size that disrupts these dopaminergic pathways can cause moderate hyperprolactinemia. However, somatotroph adenomas typically cause **acromegaly**, with prognathism and bony enlargement of the hands and feet.

Educational objective:

Prolactinomas are the most common pituitary adenoma and can cause galactorrhea, menstrual irregularities, and infertility in premenopausal

the hypothalamus, leading to **oligomenorrhea/amenorrhea** and infertility. Suppression of ovulation is also seen as a physiologic effect of breastfeeding, which supports elevated prolactin levels for 6 months or more postpartum.

(Choice A) Kallmann syndrome is a disorder involving the GnRH-producing neurons in the hypothalamus. In addition to decreased sense of smell (anosmia/hyposomia), this condition causes hypogonadotropic hypogonadism and presents with short stature and delayed puberty (primary amenorrhea). This patient has secondary amenorrhea (ie, normal initial onset of puberty followed by menstrual dysregulation), and her bilateral temporal visual deficits are more suggestive of a pituitary rather than hypothalamic lesion.

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Educational objective:
Prolactinomas are the most common pituitary adenoma and can cause galactorrhea, menstrual irregularities, and infertility in premenopausal women. Large pituitary adenomas can cause headaches from mass effect and bitemporal hemianopsia from compression of the optic chiasm.

References

- Progress in the diagnosis and classification of pituitary adenomas.

Settings

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28

Item 11 of 29
Question Id: 1262

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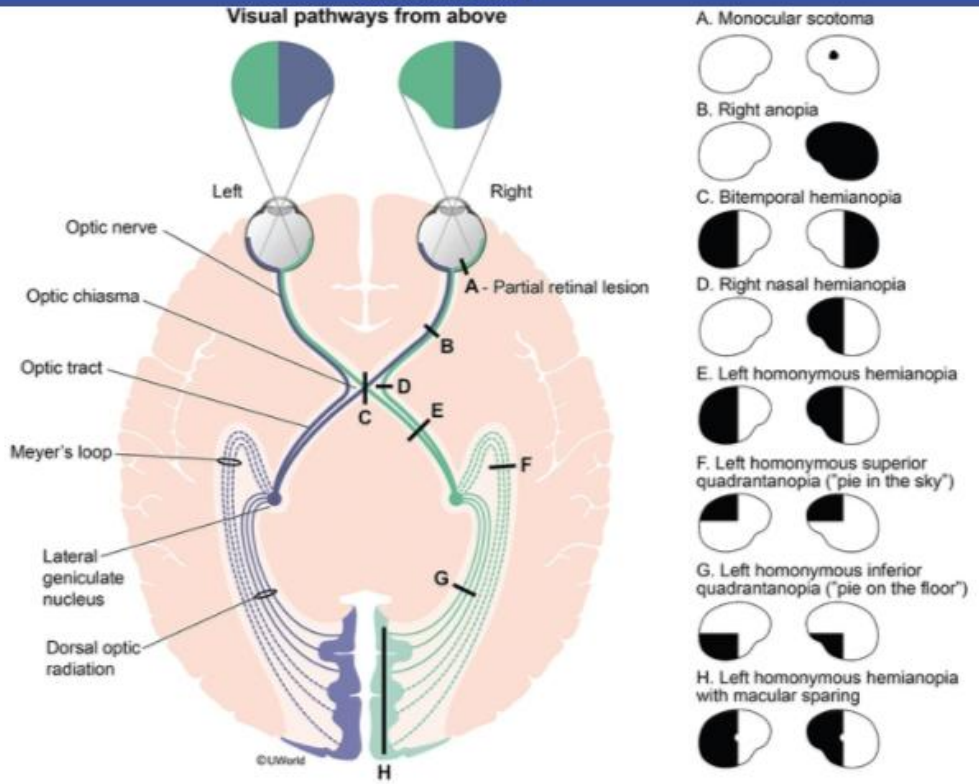

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Item 12 of 29
Question Id: 2080

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The following vignette applies to the next **2** items. The items in the set must be answered in sequential order. Once you click **Proceed to Next Item**, you will not be able to add or change an answer.

A 4-year-old boy is brought to the physician after his mother noticed that he started developing pubic hair. She also says he had a recent growth spurt and is now taller than his 5-year-old brother. In addition, his preschool teacher has noticed axillary odor after he runs or plays. On physical examination, his height corresponds to the 96th percentile and his weight corresponds to the 78th percentile for his age. There is sparse growth of long, pigmented hair at the base of the penis and in both axilla. Laboratory assessment reveals high serum concentrations of 17-hydroxyprogesterone and testosterone.

Item 1 of 2

Which of the following is most likely present in this patient?

A. Adrenal medullary hyperplasia
B. Adrenal cortical hyperplasia
C. Leydig cell hyperplasia
D. Pituitary adenoma
E. Seminoma

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Item 12 of 29
Question Id: 2080

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Item 1 of 2

Which of the following is most likely present in this patient?

A. Adrenal medullary hyperplasia [5%]
✔ B. Adrenal cortical hyperplasia [73%]
C. Leydig cell hyperplasia [11%]
D. Pituitary adenoma [8%]
E. Seminoma [1%]

Omitted
Correct answer
B

73%
Answered correctly

3 Seconds
Time Spent

01/26/2019
Last Updated

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2/12/2019

Clinical phenotypes of 21-hydroxylase deficiency			
	Classic, salt-wasting	**Classic, non-salt-wasting**	**Non-classic, delayed**
Degree of 21-hydroxylase deficiency	Severe	Moderate	Mild
Clinical presentation	Girls present at birth with ambiguous genitalia Boys present at 1-2 weeks with failure to thrive, dehydration, hyperkalemia & hyponatremia	Girls present at birth with ambiguous genitalia Boys present at 2-4 years with signs of early virilization	Premature pubarche or sexual precocity in school-age children Young women can present with acne, hirsutism & menstrual irregularity

21-hydroxylase deficiency is a form of congenital adrenal hyperplasia caused by an autosomal recessive inherited defect in the 21-hydroxylase gene. It can present as 3 distinct syndromes depending on the residual activity of the 21-hydroxylase enzyme. This patient is most likely suffering from the classic, non-salt-wasting form of the disease. Males with this variety typically present during the first few years of life with early virilization and accelerated linear growth due to shunting of corticosteroid precursors toward androgen production in the adrenal cortex. Females with this variety present with ambiguous genitalia at birth. As in all forms of 21-hydroxylase deficiency, patients will have increased serum concentrations of 17-hydroxyprogesterone and androgens.

(Choice A) Adrenal medullary hyperplasia would result in increased production and release of catecholamines. This would have no effect on virilization or linear growth and would not produce the laboratory abnormalities noted.

(Choice C) Leydig cell hyperplasia would result in masculinization due to excessive production of testosterone, androstenedione, and

21-hydroxylase deficiency is a form of congenital adrenal hyperplasia caused by an autosomal recessive inherited defect in the 21-hydroxylase gene. It can present as 3 distinct syndromes depending on the residual activity of the 21-hydroxylase enzyme. This patient is most likely suffering from the classic, non-salt-wasting form of the disease. Males with this variety typically present during the first few years of life with early virilization and accelerated linear growth due to shunting of corticosteroid precursors toward androgen production in the adrenal cortex. Females with this variety present with ambiguous genitalia at birth. As in all forms of 21-hydroxylase deficiency, patients will have increased serum concentrations of 17-hydroxyprogesterone and androgens.

(Choice A) Adrenal medullary hyperplasia would result in increased production and release of catecholamines. This would have no effect on virilization or linear growth and would not produce the laboratory abnormalities noted.

(Choice C) Leydig cell hyperplasia would result in masculinization due to excessive production of testosterone, androstenedione, and dehydroepiandrosterone. However, there would be no excess of the adrenal hormone 17-hydroxyprogesterone.

(Choice D) Pituitary adenomas producing excessive luteinizing hormone and follicle-stimulating hormone can result in increased testosterone levels but would not increase 17-hydroxyprogesterone levels. Pituitary adenomas producing excess adrenocorticotropic hormone (ACTH) can lead to excessive adrenal androgen production. However, the symptoms of excess cortisol production (Cushing's syndrome) would dominate.

(Choice E) A seminoma is a testicular tumor most commonly seen in adults. These tumors are derived from the seminiferous tubules and do not present with virilization or hormonal abnormalities.

Educational objective:
Males with classic, non-salt-wasting 21-hydroxylase deficiency present at age 2-4 years with early virilization, increased linear growth, and elevated levels of 17-hydroxyprogesterone and androgens. Females with classic 21-hydroxylase deficiency (with or without salt-wasting) present with ambiguous genitalia at birth.

Settings

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28

Item 13 of 29
Question Id: 2081

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

Item 2 of 2

After initial assessment, the appropriate interventions are initiated. Treatment of this patient's condition is targeted at directly suppressing which of the following hormones?

- A. Cortisol
- B. Luteinizing hormone
- C. Adrenocorticotropic hormone
- D. Testosterone
- E. Prolactin

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Item 13 of 29
Question Id: 2081

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

Item 2 of 2

After initial assessment, the appropriate interventions are initiated. Treatment of this patient's condition is targeted at directly suppressing which of the following hormones?

- A. Cortisol [3%]
- B. Luteinizing hormone [13%]
- ✔ C. Adrenocorticotropic hormone [47%]
- D. Testosterone [35%]
- E. Prolactin [0%]

Omitted
Correct answer
C

47%
Answered correctly

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Explanation

21-Hydroxylase deficiency

Zona glomerulosa	Zona fasciculata	Zona reticularis

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Settings

Item 13 of 29
Question Id: 2081

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

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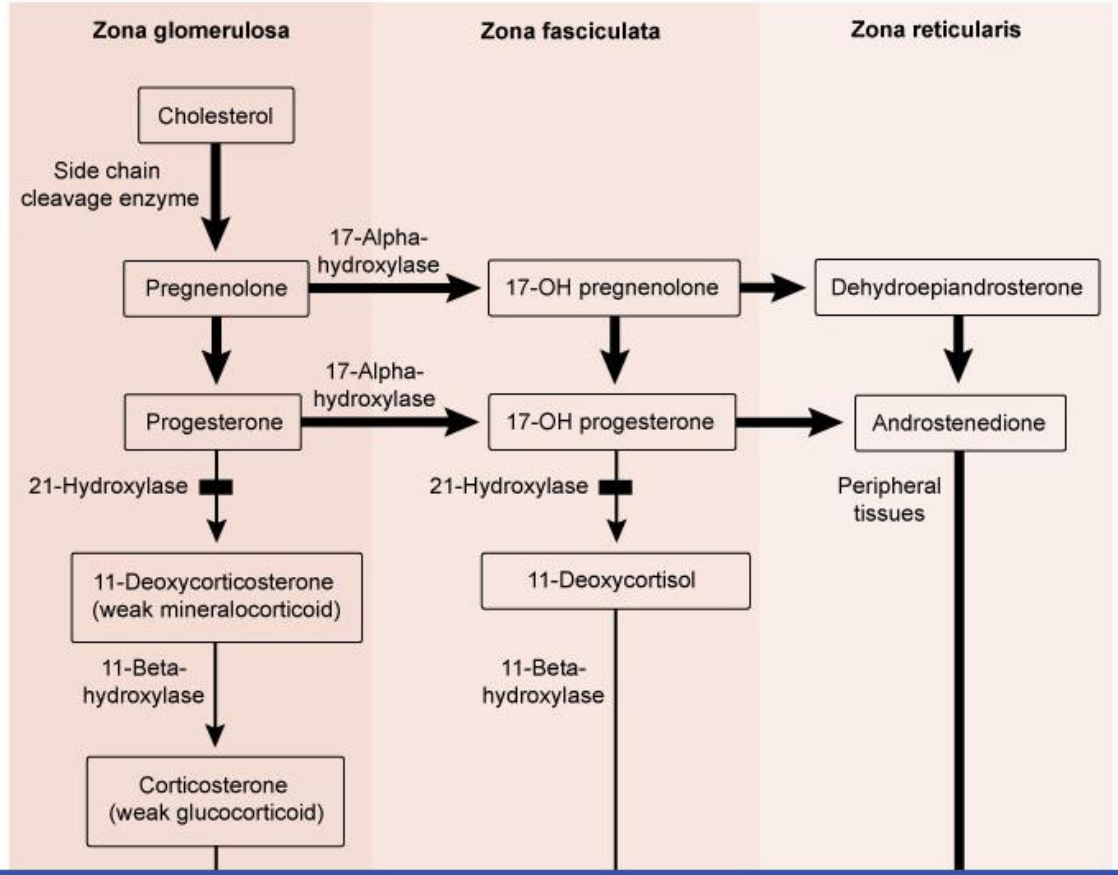
21-Hydroxylase deficiency



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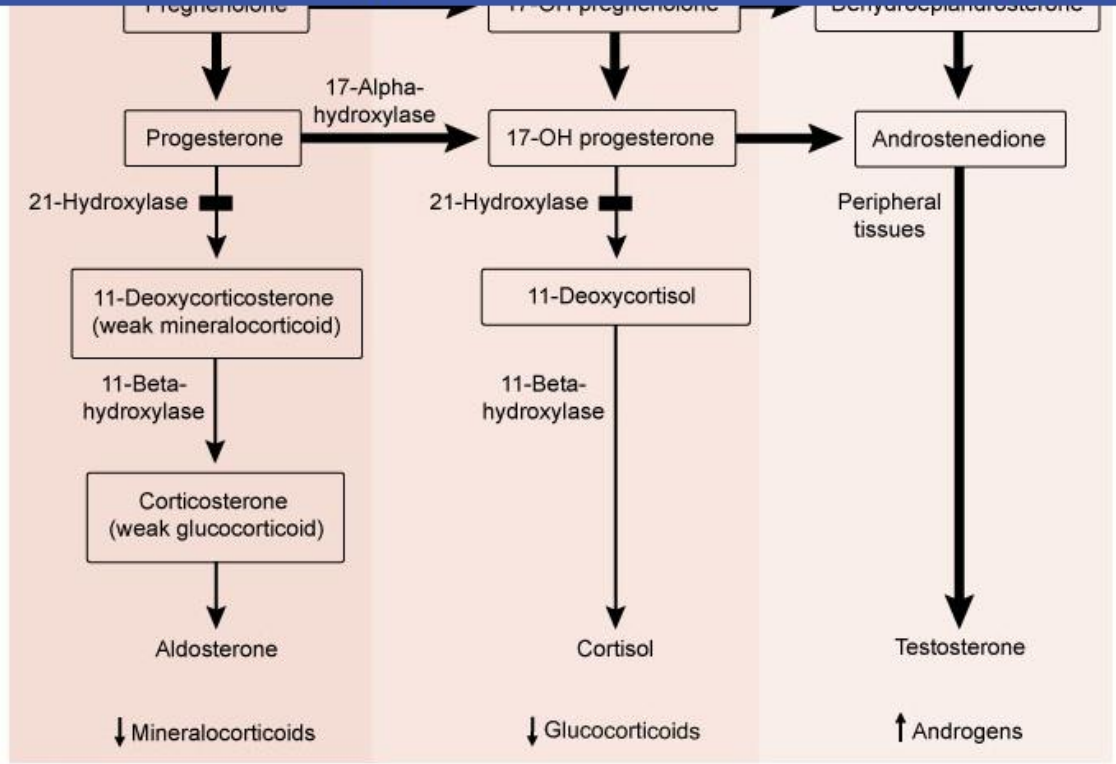

Patients with congenital adrenal hyperplasia due to 21-hydroxylase deficiency have defective conversion of 17-hydroxyprogesterone to 11-deoxycortisol, which impairs cortisol synthesis. Decreased cortisol levels are sensed by the hypothalamus and cause a consequential increase in adrenocorticotropic hormone (ACTH) secretion by the anterior pituitary. This results in stimulation of the adrenal cortex and androgen overproduction.

Patients with congenital adrenal hyperplasia due to 21-hydroxylase deficiency have defective conversion of 17-hydroxyprogesterone to 11-deoxycortisol, which impairs cortisol synthesis. Decreased cortisol levels are sensed by the hypothalamus and cause a consequential increase in adrenocorticotropic hormone (ACTH) secretion by the anterior pituitary. This results in stimulation of the adrenal cortex and androgen overproduction.

Treatment of congenital adrenal hyperplasia involves administering low (ie, physiologic) doses of exogenous corticosteroids to suppress ACTH secretion. By removing excessive ACTH stimulation, exogenous corticosteroids can decrease androgen production by the adrenal cortex.

(Choice A) Failure of cortisol production is the underlying problem in this patient. Further decrease in cortisol production could precipitate adrenal crisis and would be medically dangerous.

(Choice B) Luteinizing hormone (LH) stimulates the testis to produce testosterone. Decreasing LH levels would decrease testosterone production by the testes, but excess testicular testosterone production is not the underlying issue in this patient.

(Choice D) Testosterone is a gonadal androgen that is synthesized only in minimal quantities by the adrenal gland. The virilizing effects seen in this patient are the result of excessive adrenal androgen production (eg, dehydroepiandrosterone and androstenedione). These adrenal androgens undergo peripheral conversion to testosterone, thus explaining the high levels of testosterone found in this patient.

(Choice E) Prolactin excess typically results from a pituitary adenoma. In men, prolactin excess causes hypogonadism, not virilization.

Educational objective:
Treatment of congenital adrenal hyperplasia involves low doses of exogenous corticosteroids to suppress excessive ACTH secretion and reduce stimulation of the adrenal cortex.

A 25-year-old man comes to the office for evaluation of facial acne. He has no significant past medical history and does not use tobacco or alcohol. The patient works as a personal trainer. His family history is significant for diabetes mellitus in his mother and leukemia in his father. His blood pressure is 134/82 mm Hg and pulse is 58/min. On physical examination, there is mild facial acne. The patient's lungs are clear to auscultation. The liver span is 8 cm, and the spleen is not palpable. His testes are soft, and testicular volume is decreased. Laboratory results are as follows:

Hematocrit	60%
White blood cells	7,500/mm^3
Platelets	225,000/mm^3
Erythrocyte sedimentation rate	15 mm/hr
Serum creatinine	1.2 mg/dL
Blood urea nitrogen	18 mg/dL

Which of the following is the most likely explanation for this patient's abnormal laboratory findings?

A. High oxygen affinity hemoglobin
B. Intensive exercise schedule
C. Myeloproliferative disorder
D. Renal artery stenosis
E. Steroid drug abuse
F. Volume depletion due to excessive sweating

are as follows:

Hematocrit	60%
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Erythrocyte sedimentation rate	15 mm/hr
Serum creatinine	1.2 mg/dL
Blood urea nitrogen	18 mg/dL

Which of the following is the most likely explanation for this patient's abnormal laboratory findings?

- A. High oxygen affinity hemoglobin [1%]
- B. Intensive exercise schedule [4%]
- C. Myeloproliferative disorder [3%]
- D. Renal artery stenosis [1%]
- ✔ E. Steroid drug abuse [86%]
- F. Volume depletion due to excessive sweating [3%]

Omitted
Correct answer

86%
Answered correctly

8 Seconds
Time Spent

12/18/2018
Last Updated

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Effects of androgen abuse	
Cardiovascular	• ↑ **Hematocrit** • ↑ LDL, ↓ HDL cholesterol
Dermatologic	• **Acne** • Hirsutism, male-pattern hair loss (♀)
Genitourinary	• Clitoromegaly, oligomenorrhea (♀) • **Testicular atrophy**, ↓ spermatogenesis (♂)
Psychiatric	• Depression, hypomania (♀) • Aggressiveness, mood disorders (♂)
Breast	• Atrophy (♀) • **Gynecomastia** (♂)
Other	• **Deepening of voice** (♀) • Premature epiphyseal closure (adolescents)

This patient has acne, testicular atrophy, and erythrocytosis, findings concerning for **androgenic steroid abuse**. Abuse of androgens, androgen precursors, and agents that increase endogenous androgen production is most common in young adults who engage in competitive athletic activities or for cosmetic purposes.

This patient has acne, testicular atrophy, and erythrocytosis, findings concerning for **androgenic steroid abuse**. Abuse of androgens, androgen precursors, and agents that increase endogenous androgen production is most common in young adults who engage in competitive athletic activities or for cosmetic purposes.

Chronic androgen use may increase muscle mass but has multiple associated risks. Testosterone stimulates red blood cell production, which accounts for the higher hematocrit in normal males compared to normal females. This effect is exaggerated in exogenous androgen abuse, which **increases hematocrit** in a dose-dependent manner. Androgens decrease gonadotropin secretion, which results in **testicular atrophy** and decreased sperm production. Other common findings include **virilization** in women (eg, clitoromegaly, hirsutism) and **acne**.

(Choices A and D) Mutations that cause a high oxygen affinity of hemoglobin reduce the ability of hemoglobin to release oxygen in tissues. Low tissue oxygen levels in the kidneys stimulate erythropoietin release. Renal artery stenosis decreases oxygen delivery to the kidney and also stimulates erythropoietin release. These conditions may produce a compensatory erythrocytosis but would not produce the other clinical signs (eg, acne, testicular atrophy) seen in this patient.

(Choice B) Intensive exercise could result in elevated myoglobin secondary to rhabdomyolysis, but the hematocrit level should not be changed by exercise.

(Choice C) Myeloproliferative disorders, such as polycythemia vera (PV), can lead to erythrocytosis. Patients with PV typically have leukocytosis and thrombocytosis as well. This patient's additional physical findings make steroid abuse more likely.

(Choice F) Heavy sweating may cause a transient increase in hematocrit due to loss of plasma volume but would likely cause other signs of dehydration (eg, tachycardia). This patient's creatinine at the upper limit of normal is typical for patients with increased total muscle mass; hypovolemia also will usually cause a more pronounced rise in blood urea nitrogen.

Educational objective:
Androgenic steroid abuse may lead to erythrocytosis, testicular atrophy, acne, and virilization in women (eg, clitoromegaly, hirsutism).

Settings

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28

Item 15 of 29
Question Id: 1659

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 30-year-old man comes to the office with a neck lump. The patient is otherwise asymptomatic and discovered the nodule incidentally while showering. His medical history is significant for a recently diagnosed pheochromocytoma, which was successfully removed. The patient's father died of thyroid cancer in his 30s. An ultrasound reveals a hypoechoic 3-cm nodule in the right lobe of the thyroid gland. Fine-needle biopsy of the nodule is consistent with a subtype of thyroid cancer. The patient undergoes total thyroidectomy with central neck dissection. Which of the following is the most likely histological finding?

A. Branching structures with interspersed calcified bodies
B. Follicular hyperplasia with tall cells forming intrafollicular projections
C. Nests of polygonal cells with Congo red-positive deposits
D. Pleomorphic giant cell nests with occasional multinucleated cells
E. Sheets of uniform cells forming small follicles

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Item 15 of 29
Question Id: 1659

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- A. Branching structures with interspersed calcified bodies [14%]
- B. Follicular hyperplasia with tall cells forming intrafollicular projections [12%]
- ✔ C. Nests of polygonal cells with Congo red-positive deposits [54%]
- D. Pleomorphic giant cell nests with occasional multinucleated cells [6%]
- E. Sheets of uniform cells forming small follicles [10%]

Omitted
Correct answer
C

54%
Answered correctly

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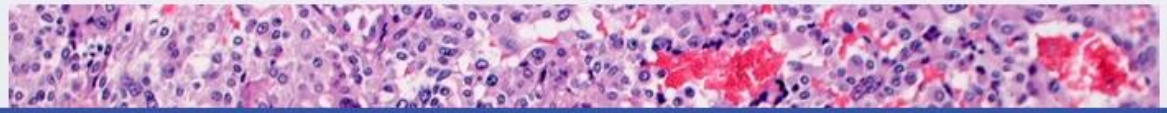
Time Spent

10/01/2018
Last Updated

Explanation



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Item 15 of 29
Question Id: 1659

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

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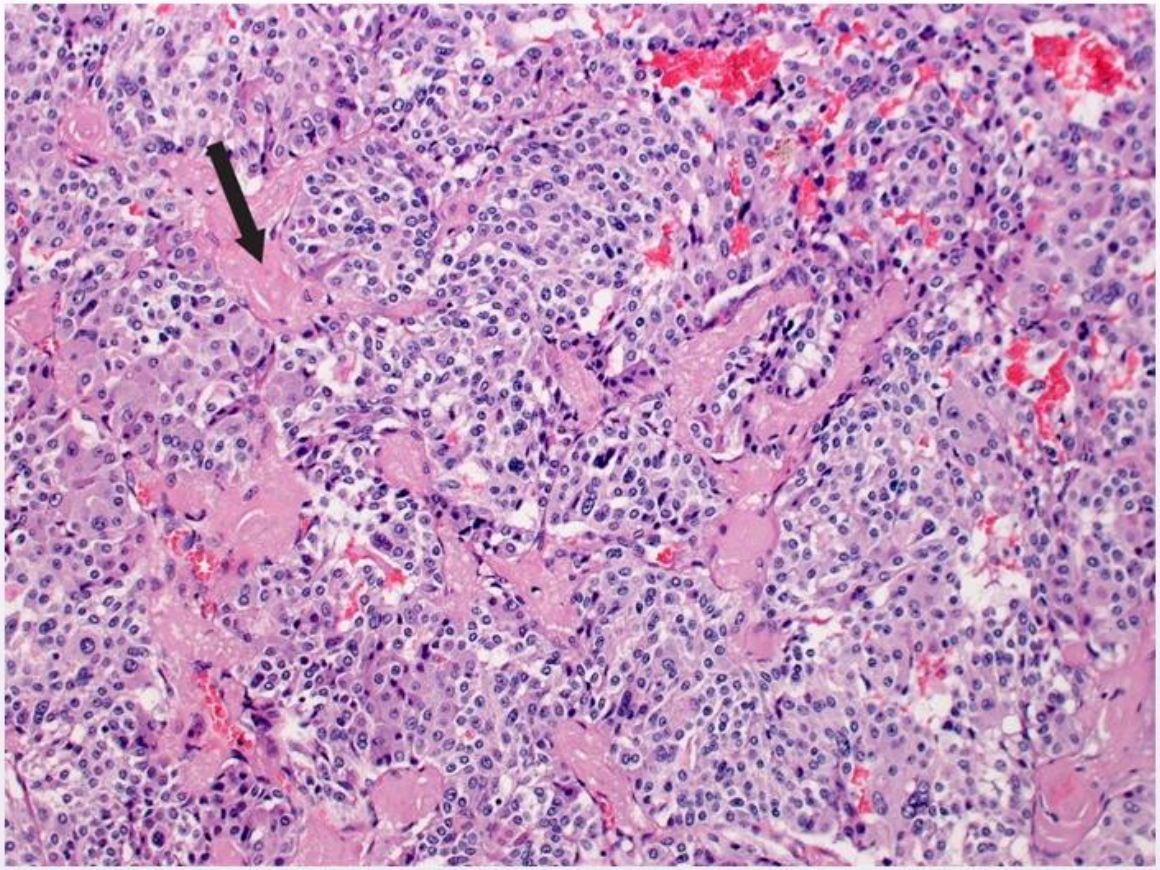

This patient has a personal history of pheochromocytoma and a family history of thyroid cancer. His new thyroid malignancy therefore raises

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2/12/2019

This patient has a personal history of pheochromocytoma and a family history of thyroid cancer. His new thyroid malignancy therefore raises suspicion for **multiple endocrine neoplasia type 2** (MEN2), which is characterized by:

- **Medullary thyroid cancer**
- Pheochromocytoma
- Either parathyroid hyperplasia (type 2A) or marfanoid habitus and mucosal neuromas (type 2B)

Approximately 20% of medullary thyroid cancers are familial, occurring as part of MEN2 or familial medullary thyroid cancer syndrome due to germ-line mutations of the RET proto-oncogene. Medullary thyroid cancer is a neuroendocrine tumor that arises from **parafollicular calcitonin-secreting C cells**. Nests or sheets of polygonal or spindle-shaped cells with extracellular amyloid deposits are seen microscopically. These amyloid deposits (black arrow in the image above) are derived from calcitonin secreted by the neoplastic C cells and stain with Congo red. Despite overproduction of calcitonin, hypocalcemia is not a prominent feature.

(Choice A) Gross inspection of papillary thyroid cancer may reveal formation of visible papillae. Microscopic inspection of papillae shows a fibrovascular core, often with laminar calcifications (**psammoma bodies**). The cells contain **pale nuclei** with finely dispersed chromatin, giving them an empty or ground-glass appearance (Orphan Annie eye nuclei). Intranuclear inclusions and grooves can be seen due to invagination of the nuclear membrane.

(Choice B) The **tall cell variant** of papillary thyroid cancer is characterized by follicular hyperplasia lined by tall epithelial cells; this variant is seen in older individuals and carries a relatively worse prognosis. Tall, crowded cells can also be seen in **Graves disease**, often with hyperactive resorption of colloid leading to scalloping of the colloid edges.

(Choice D) **Anaplastic thyroid cancer** is an aggressive tumor with a very poor prognosis. It is most common in older patients (age >60). Cytologic features include markedly pleomorphic cells, including irregular giant cells and biphasic spindle cells.

(Choice E) The presence of colloid-containing **microfollicles** suggests a benign follicular adenoma. Well-differentiated follicular adenocarcinoma can also contain small follicles but will often show vascular invasion.

secreting C cells. Nests or sheets of polygonal or spindle-shaped cells with extracellular amyloid deposits are seen microscopically. These amyloid deposits (black arrow in the image above) are derived from calcitonin secreted by the neoplastic C cells and stain with Congo red. Despite overproduction of calcitonin, hypocalcemia is not a prominent feature.

(Choice A) Gross inspection of papillary thyroid cancer may reveal formation of visible papillae. Microscopic inspection of papillae shows a fibrovascular core, often with laminar calcifications (**psammoma bodies**). The cells contain **pale nuclei** with finely dispersed chromatin, giving them an empty or ground-glass appearance (Orphan Annie eye nuclei). Intranuclear inclusions and grooves can be seen due to invagination of the nuclear membrane.

(Choice B) The **tall cell variant** of papillary thyroid cancer is characterized by follicular hyperplasia lined by tall epithelial cells; this variant is seen in older individuals and carries a relatively worse prognosis. Tall, crowded cells can also be seen in **Graves disease**, often with hyperactive resorption of colloid leading to scalloping of the colloid edges.

(Choice D) **Anaplastic thyroid cancer** is an aggressive tumor with a very poor prognosis. It is most common in older patients (age >60). Cytologic features include markedly pleomorphic cells, including irregular giant cells and biphasic spindle cells.

(Choice E) The presence of colloid-containing **microfollicles** suggests a benign follicular adenoma. Well-differentiated follicular adenocarcinoma can also contain small follicles but will often show vascular invasion.

Educational objective:
Medullary thyroid cancer is a neuroendocrine tumor that arises from parafollicular calcitonin-secreting C cells. It is characterized by nests or sheets of polygonal or spindle-shaped cells with extracellular amyloid deposits derived from calcitonin.

References

- Update on the cytologic and molecular features of medullary thyroid carcinoma.

Settings

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28

Item 16 of 29
Question Id: 782

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 6-year-old boy is brought to the emergency department after a traumatic fall from his bicycle. Physical examination shows a large laceration over his left leg that is irrigated and closed with sutures. While he is receiving care, a routine blood draw shows milky plasma that forms a creamy-appearing supernatant upon standing. Further testing shows that his plasma lipoprotein lipase activity measured after intravenous heparin administration is substantially lower than normal. If his condition remains untreated, this patient is most likely to develop which of the following features?

A. Acute pancreatitis
B. Intellectual disability
C. Myocardial infarction
D. Tendon xanthomas
E. Xanthelasmas

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2/12/2019

Settings

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Item 16 of 29
Question Id: 782

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 6-year-old boy is brought to the emergency department after a traumatic fall from his bicycle. Physical examination shows a large laceration over his left leg that is irrigated and closed with sutures. While he is receiving care, a routine blood draw shows milky plasma that forms a creamy-appearing supernatant upon standing. Further testing shows that his plasma lipoprotein lipase activity measured after intravenous heparin administration is substantially lower than normal. If his condition remains untreated, this patient is most likely to develop which of the following features?

- ✔ A. Acute pancreatitis [38%]
- B. Intellectual disability [1%]
- C. Myocardial infarction [20%]
- D. Tendon xanthomas [24%]
- E. Xanthelasmas [14%]

Omitted
Correct answer
A

38%
Answered correctly

4 Seconds
Time Spent

01/22/2019
Last Updated

Explanation

Important inherited hyperlipoproteinemias

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2/12/2019

Important inherited hyperlipoproteinemias			
Dyslipidemia	**Protein defect**	**Elevated lipoproteins**	**Major manifestations**
Familial chylomicronemia syndrome (Type I)	• Lipoprotein lipase • ApoC-II	Chylomicrons	• **Acute pancreatitis** • Lipemia retinalis • Eruptive skin xanthomas • Hepatosplenomegaly
Familial hypercholesterolemia (Type II A)	• LDL receptor • ApoB-100	LDL	• **Premature coronary artery disease** • Corneal arcus • Tendon xanthomas • Xanthelasmas
Familial dysbetalipoproteinemia (Type III)	• ApoE	Chylomicron and VLDL remnants	• **Premature coronary artery disease** & peripheral vascular disease • Tuboeruptive & palmar xanthomas

			• Hepatosplenomegaly
Familial hypercholesterolemia (Type II A)	• LDL receptor • ApoB-100	LDL	• **Premature coronary artery disease** • Corneal arcus • Tendon xanthomas • Xanthelasmas
Familial dysbetalipoproteinemia (Type III)	• ApoE	Chylomicron and VLDL remnants	• **Premature coronary artery disease** & peripheral vascular disease • Tuboeruptive & palmar xanthomas
Familial hypertriglyceridemia (Type IV)	• ApoA-V	VLDL	• Increased pancreatitis risk • Associated with obesity & insulin resistance

This patient has **familial chylomicronemia syndrome** (type 1 hyperlipoproteinemia), an autosomal recessive condition most often caused by **lipoprotein lipase (LPL) deficiency**. LPL is normally bound to heparan sulfate moieties on the vascular endothelium, allowing it to interact with chylomicrons and VLDL in the circulation and release free fatty acids into the adjacent tissues. Heparin administration releases these

hypertriglyceridemia (Type IV)	• ApoA-V	VLDL	• Associated with obesity & insulin resistance

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This patient has **familial chylomicronemia syndrome** (type 1 hyperlipoproteinemia), an autosomal recessive condition most often caused by **lipoprotein lipase (LPL) deficiency**. LPL is normally bound to heparan sulfate moieties on the vascular endothelium, allowing it to interact with chylomicrons and VLDL in the circulation and release free fatty acids into the adjacent tissues. Heparin administration releases these endothelium-bound lipases, allowing LPL activity to be measured in the laboratory. Without sufficient LPL activity, the body is unable to clear dietary lipid loads due to defective hydrolysis of serum triglycerides (especially **chylomicrons**).

Patients with familial chylomicronemia syndrome present in childhood with marked **hypertriglyceridemia**, recurrent **acute pancreatitis, lipemia retinalis** (milky-appearing retinal vasculature), and eruptive xanthomas (small yellowish papules surrounded by erythema found mainly on extensor surfaces).

(Choice B) The familial hyperlipoproteinemias are not associated with intellectual disability.

(Choices C, D, and E) Accelerated coronary artery disease, tendon xanthomas (nodular lipid deposits in the tendons, particularly the Achilles), and **xanthelasmas** are seen in familial hypercholesterolemia, a condition caused by defects in the LDL receptor or its ligand, ApoB-100. As LDL is mainly cleared from the circulation by receptor-mediated uptake in the liver, individuals with familial hypercholesterolemia have dramatically elevated LDL concentrations.

Educational objective:
Familial chylomicronemia syndrome frequently presents in childhood with recurrent episodes of acute pancreatitis. Patients with this disorder are not usually at increased risk for premature coronary artery disease. Eruptive skin xanthomas may be present in hypertriglyceridemia, but tendon xanthomas and xanthelasmas are primarily seen with hypercholesterolemia.

A 3-year-old boy is brought to the emergency department due to high-grade fever, vomiting, and altered mental status. Physical examination shows hypotension, tachycardia, neck stiffness, and a petechial rash over the trunk and lower extremities. Laboratory results are as follows:

Complete blood count	
Hemoglobin	12.0 g/L
Platelets	80,000/mm^3
Leukocytes	34,500/mm^3
Neutrophils	66%
Band forms	20%
Lymphocytes	14%
Chemistry panel	
Serum sodium	130 mEq/L
Serum potassium	5.6 mEq/L
Blood urea nitrogen	30 mg/dL
Serum creatinine	1.8 mg/dL
Blood glucose	50 mg/dL

While lumbar puncture is being arranged, the patient rapidly develops cardiovascular collapse and bleeding from venipuncture sites. Despite aggressive resuscitation efforts, the child dies. Autopsy would most likely show which of the following?

Lymphocytes	14%

Chemistry panel

Serum sodium	130 mEq/L
Serum potassium	5.6 mEq/L
Blood urea nitrogen	30 mg/dL
Serum creatinine	1.8 mg/dL
Blood glucose	50 mg/dL

While lumbar puncture is being arranged, the patient rapidly develops cardiovascular collapse and bleeding from venipuncture sites. Despite aggressive resuscitation efforts, the child dies. Autopsy would most likely show which of the following?

- A. Adrenal hemorrhage
- B. Cardiac tamponade
- C. Rupture of berry aneurysm
- D. Rupture of coronary artery aneurysm
- E. Saddle pulmonary embolus

Submit

Lymphocytes	14%

Chemistry panel

Serum sodium	130 mEq/L
Serum potassium	5.6 mEq/L
Blood urea nitrogen	30 mg/dL
Serum creatinine	1.8 mg/dL
Blood glucose	50 mg/dL

While lumbar puncture is being arranged, the patient rapidly develops cardiovascular collapse and bleeding from venipuncture sites. Despite aggressive resuscitation efforts, the child dies. Autopsy would most likely show which of the following?

- A. Adrenal hemorrhage [88%]
- B. Cardiac tamponade [2%]
- C. Rupture of berry aneurysm [3%]
- D. Rupture of coronary artery aneurysm [2%]
- E. Saddle pulmonary embolus [3%]

Omitted
Correct answer

88%
Answered correctly

9 Seconds
Time Spent

09/28/2018
Last Updated

Settings

Item 17 of 29
Question Id: 931

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

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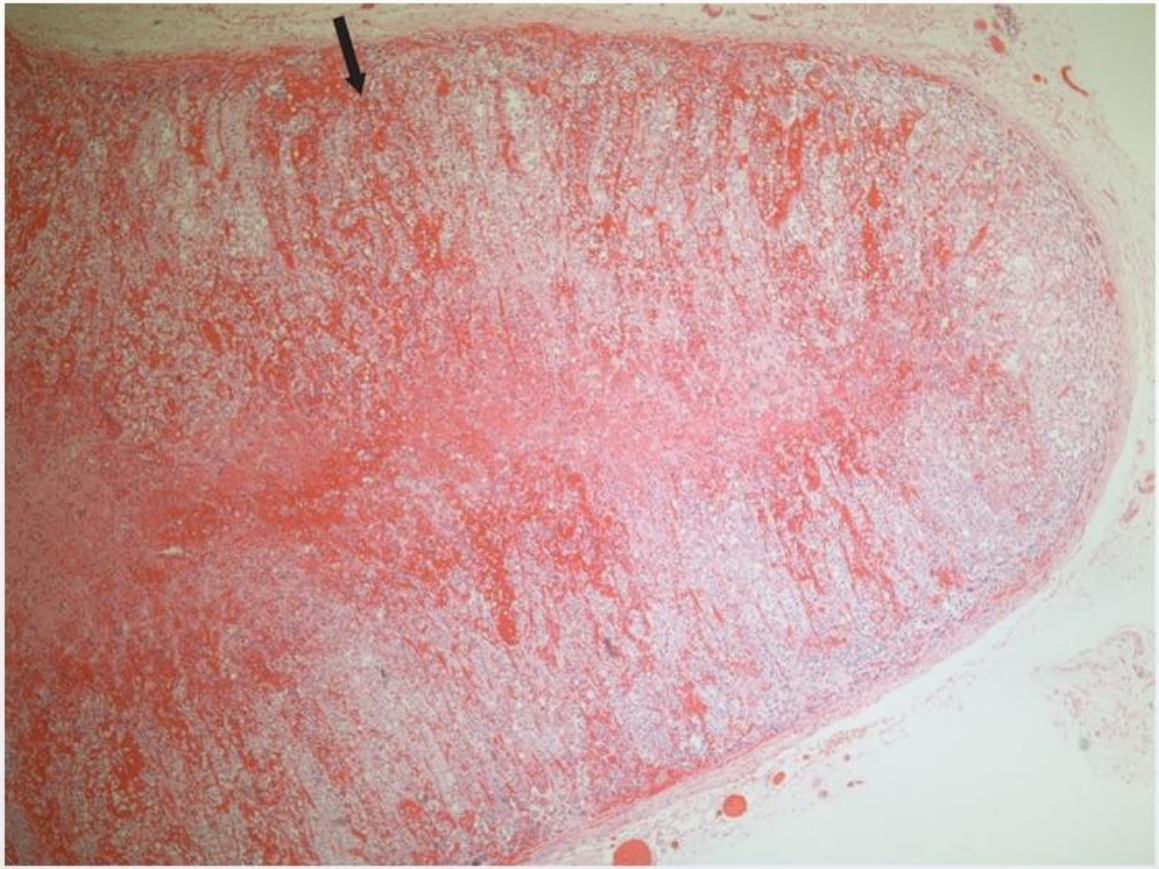

This child has a catastrophic presentation of fever, altered mental status, and nuchal rigidity, consistent with **bacterial meningitis** due to *Neisseria*

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This child has a catastrophic presentation of fever, altered mental status, and nuchal rigidity, consistent with **bacterial meningitis** due to *Neisseria meningitidis*. In addition, the low platelet count, petechial rash, and abnormal bleeding (eg, oozing at venipuncture sites) suggest disseminated intravascular coagulation (DIC) due to **sepsis**. The subsequent shock with hyponatremia, hyperkalemia, and hypoglycemia (due to cortisol deficiency) heralds the onset of adrenal crisis resulting from bilateral hemorrhagic infarction of the adrenal glands (**Waterhouse-Friderichsen syndrome**). Despite systemic infection, organisms are rarely isolated from the adrenal glands at autopsy.

(Choices B, D, and E) Coronary aneurysms can be congenital (eg, polycystic kidney disease) or acquired (eg, Kawasaki disease). In rare instances, these aneurysms can rupture, leading to hemopericardium and cardiac tamponade. Large pericardial effusions can also cause tamponade and mechanically compress the heart, limiting its normal range of motion, venous return, and cardiac output. A massive saddle pulmonary embolus that obstructs flow in both right and left pulmonary arteries can also cause acute cardiovascular collapse. However, shock due to these conditions is not associated with adrenal crisis, and this patient's other clinical features suggest meningitis as the primary cause.

(Choice C) Rupture of a cerebral berry aneurysm causes intracranial hemorrhage, typically characterized by headache, confusion, vomiting, loss of consciousness, and death.

Educational objective:
Meningococcal septicemia can cause bilateral hemorrhagic infarction of the adrenal glands, leading to acute adrenal crisis (Waterhouse-Friderichsen syndrome).

References

- The significance of adrenal hemorrhage: undiagnosed Waterhouse-Friderichsen syndrome, a case series.

Settings

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28

Item 18 of 29
Question Id: 1660

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 45-year-old previously healthy man comes to the office for evaluation of a neck lump. The patient first noticed the swelling a month ago while shaving, and it has progressively enlarged. He has had no fever, neck pain, hoarseness, or difficulty breathing or swallowing. The patient does not use tobacco, alcohol, or illicit drugs. Temperature is 36.7 C (98 F), blood pressure is 110/70 mm Hg, and pulse is 78/min. On physical examination, there is a nontender, firm nodule in the upper portion of the left thyroid lobe. Laboratory studies reveal a normal serum TSH and elevated serum calcitonin levels. Neck ultrasonography shows a 2-cm hypoechoic thyroid nodule with microcalcifications. Fine-needle aspiration of the nodule reveals spindle-shaped cells in an amorphous background. Which of the following gene alterations most likely contributed to this patient's current condition?

A. Activation of *ALK*
B. Activation of *RET*
C. Inactivation of *MEN1*
D. Inactivation of p53
E. Overexpression of *BCL2*
F. Overexpression of *JAK2*

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Settings

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Item 18 of 29
Question Id: 1660

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 45-year-old previously healthy man comes to the office for evaluation of a neck lump. The patient first noticed the swelling a month ago while shaving, and it has progressively enlarged. He has had no fever, neck pain, hoarseness, or difficulty breathing or swallowing. The patient does not use tobacco, alcohol, or illicit drugs. Temperature is 36.7 C (98 F), blood pressure is 110/70 mm Hg, and pulse is 78/min. On physical examination, there is a nontender, firm nodule in the upper portion of the left thyroid lobe. Laboratory studies reveal a normal serum TSH and elevated serum calcitonin levels. Neck ultrasonography shows a 2-cm hypoechoic thyroid nodule with microcalcifications. Fine-needle aspiration of the nodule reveals spindle-shaped cells in an amorphous background. Which of the following gene alterations most likely contributed to this patient's current condition?

A. Activation of *ALK* [0%]
✔ B. Activation of *RET* [76%]
C. Inactivation of *MEN1* [16%]
D. Inactivation of p53 [3%]
E. Overexpression of *BCL2* [1%]
F. Overexpression of *JAK2* [0%]

Omitted
Correct answer
B

76%
Answered correctly

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11/04/2018
Last Updated

Explanation

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Tumors associated with specific oncogenes	
Proto-oncogenes (tumor promoters)	
ABL	Chronic myeloid leukemia
ALK	Large cell lymphoma, non–small cell lung cancer
BRAF	Melanoma
HER1	Squamous cell lung cancer
HER2/neu	Breast cancer, ovarian cancer
MYC	Neuroblastoma (NMYC), small cell lung cancer (LMYC)
RET	Medullary thyroid cancer, pheochromocytoma
Anti-oncogenes (tumor suppressors)	
APC/β catenin	Colorectal cancer, pancreatic cancer
BRCA1, BRCA2	Breast cancer, ovarian cancer
NF1	Neuroblastoma, sarcoma
RB	Retinoblastoma, osteosarcoma
VHL	Renal cell cancer
WT1	Wilms tumor

Anti-oncogenes (tumor suppressors)	
APC/β catenin	Colorectal cancer, pancreatic cancer
BRCA1, BRCA2	Breast cancer, ovarian cancer
NF1	Neuroblastoma, sarcoma
RB	Retinoblastoma, osteosarcoma
VHL	Renal cell cancer
WT1	Wilms tumor

This patient has **medullary thyroid cancer** (MTC) presenting with a palpable nodule and elevated serum calcitonin. MTC is a neuroendocrine tumor that arises from **calcitonin-secreting** C (parafollicular) cells. Microscopy shows nests or sheets of polygonal or spindle-shaped cells, often with extracellular **amyloid deposition** (consisting of full-length calcitonin). MTC is often seen in the context of multiple endocrine neoplasia type 2 (A and B), although the majority of cases are sporadic. Paraneoplastic symptoms (eg, diarrhea, flushing) can occur due to elevated calcitonin levels; however, calcium is usually normal, possibly due to the downregulation of calcitonin receptors.

MTC is associated with activating mutations in the ***RET* proto-oncogene**; mutations are commonly found in sporadic MTC, and germline mutations are present in more than 95% of patients with familial MTC. The *RET* proto-oncogene codes for a membrane-bound **tyrosine kinase receptor** involved in cell cycle regulation. In patients with MTC, **constitutive activation** of the receptor leads to unregulated cellular proliferation.

(Choice A) The anaplastic lymphoma kinase (*ALK*) oncogene codes for a transmembrane receptor tyrosine kinase. Mutations are common in anaplastic large cell lymphoma and non–small cell lung cancer.

(Choice C) The *MEN1* gene codes for a tumor suppressor protein. Mutations are associated with multiple endocrine neoplasia type 1 (pituitary adenomas, primary hyperparathyroidism, pancreatic neuroendocrine tumors) but not type 2.

(A and B), although the majority of cases are sporadic. Paraneoplastic symptoms (eg, diarrhea, flushing) can occur due to elevated calcitonin levels; however, calcium is usually normal, possibly due to the downregulation of calcitonin receptors.

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(Choice C) The *MEN1* gene codes for a tumor suppressor protein. Mutations are associated with multiple endocrine neoplasia type 1 (pituitary adenomas, primary hyperparathyroidism, pancreatic neuroendocrine tumors) but not type 2.

(Choice D) p53 is a tumor suppressor protein involved in DNA repair, apoptosis, and cell cycle control. Inactivating mutations or deletions are present in a large percentage of human tumors, including anaplastic thyroid cancer, but not typically in early-stage MTC.

(Choice E) *BCL2* (B-cell lymphoma 2) is an antiapoptotic gene that enhances cell survival. Its expression is upregulated in many cancer cells. *BCL2* mutations are common in many follicular lymphomas.

(Choice F) Mutations in *JAK2* (Janus kinase 2) are seen in a variety of myeloproliferative disorders such as primary polycythemia and essential thrombocythemia.

Educational objective:
Medullary thyroid cancer is a neuroendocrine tumor that arises from calcitonin-secreting C (parafollicular) cells. It is often seen in the context of multiple endocrine neoplasia type 2 (A and B), although the majority of cases are sporadic. Both sporadic and familial medullary thyroid cancers are associated with mutations in the *RET* proto-oncogene.

References

Settings

Item 18 of 29
Question Id: 1660

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

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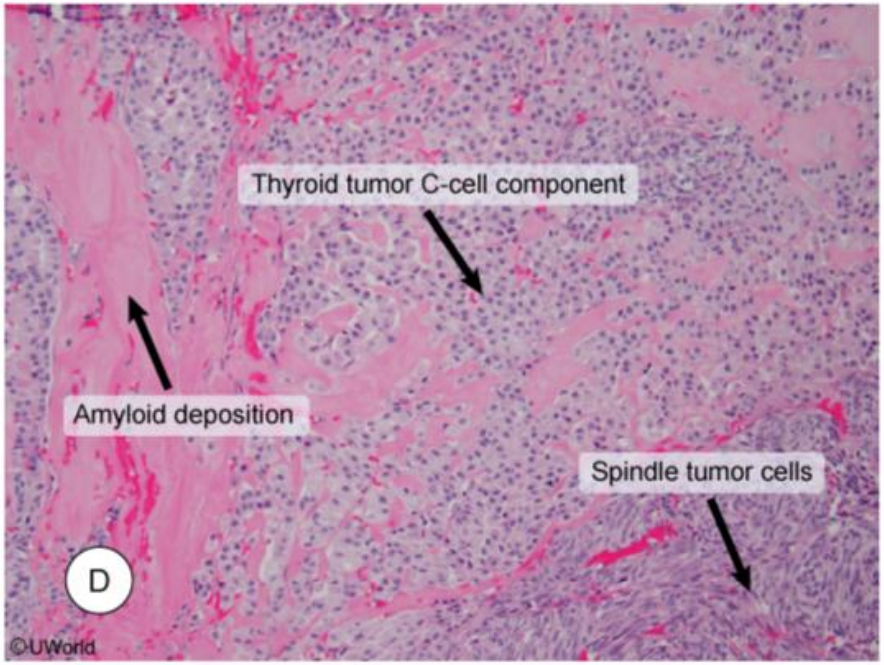

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present in a large percentage of human tumors, including anaplastic thyroid cancer, but not typically in early-stage MTC

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2/12/2019

Settings

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Item 19 of 29
Question Id: 769

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 51-year-old woman comes to the office due to progressively worsening fatigue, weight gain, and constipation for the past 6 months. The patient has had difficulty performing daily activities due to fatigue. She has no significant medical history and takes no medications. The patient has no drug allergies and does not use tobacco, alcohol, or illicit drugs. Blood pressure is 110/80 mm Hg and pulse is 55/min. Physical examination shows mild, diffuse enlargement of the thyroid gland. Cardiopulmonary and abdominal examinations are normal. Biopsy of this patient's thyroid is most likely to show which of the following findings?

A. Branching papillae with cells containing empty-appearing nuclei
B. Dense fibrous tissue extending beyond the thyroid capsule
C. Follicular hyperplasia with tall cells projecting into the follicular lumen
D. Intense lymphoplasmacytic infiltrate with active germinal centers
E. Widespread inflammatory infiltrates, giant cells, and disrupted follicles

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1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28

Item 19 of 29
Question Id: 769

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 51-year-old woman comes to the office due to progressively worsening fatigue, weight gain, and constipation for the past 6 months. The patient has had difficulty performing daily activities due to fatigue. She has no significant medical history and takes no medications. The patient has no drug allergies and does not use tobacco, alcohol, or illicit drugs. Blood pressure is 110/80 mm Hg and pulse is 55/min. Physical examination shows mild, diffuse enlargement of the thyroid gland. Cardiopulmonary and abdominal examinations are normal. Biopsy of this patient's thyroid is most likely to show which of the following findings?

- A. Branching papillae with cells containing empty-appearing nuclei [6%]
- B. Dense fibrous tissue extending beyond the thyroid capsule [5%]
- C. Follicular hyperplasia with tall cells projecting into the follicular lumen [10%]
- ✔ D. Intense lymphoplasmacytic infiltrate with active germinal centers [52%]
- E. Widespread inflammatory infiltrates, giant cells, and disrupted follicles [24%]

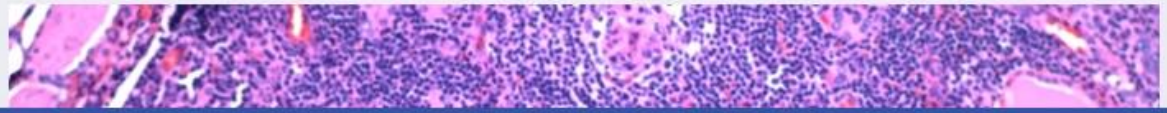
Omitted
Correct answer
D

52%
Answered correctly

3 Seconds
Time Spent

09/20/2018
Last Updated

Explanation



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Settings

Item 19 of 29
Question Id: 769

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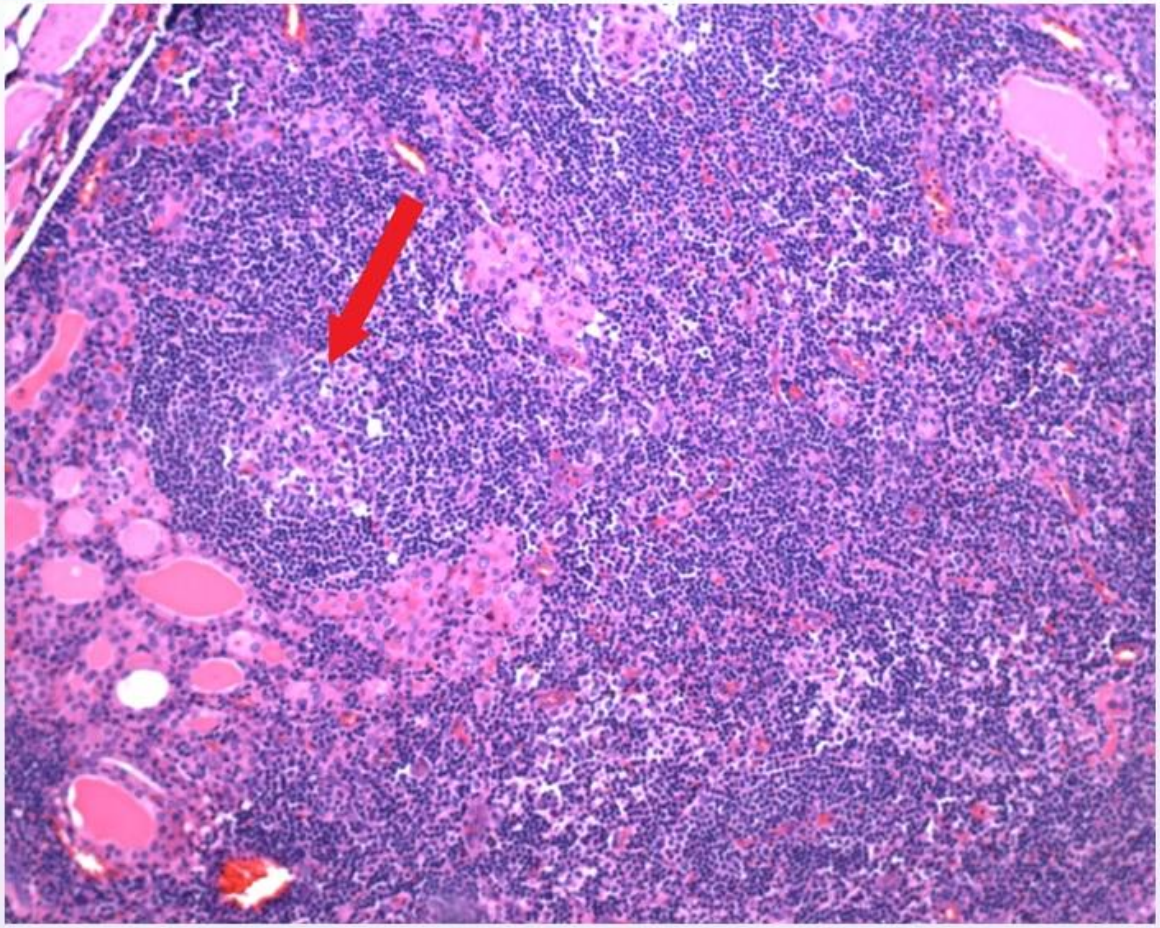

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2/12/2019

This patient has progressive symptoms of hypothyroidism (eg, fatigue, weight gain, constipation) and a diffuse goiter, consistent with **chronic lymphocytic (Hashimoto) thyroiditis**. This disease occurs predominately in women, with a peak incidence at age 45-65, and is the most common cause of hypothyroidism in iodine-sufficient regions such as the United States.

As with all forms of primary hypothyroidism, laboratory studies show low serum thyroxine (T4) levels and an elevated TSH. Elevated antithyroid peroxidase antibody levels can confirm the diagnosis. If the diagnosis is uncertain (eg, thyroid nodularity), a biopsy can be performed to rule out malignancy. Characteristic findings of Hashimoto thyroiditis include an intense **mononuclear infiltrate** consisting of **lymphocytes** and plasma cells, often with **germinal centers** (arrow in image above). Residual follicles are often surrounded by **Hürthle cells** (large oxyphilic cells filled with granular cytoplasm) that represent follicular epithelial cells that have undergone metaplastic change in response to inflammation.

(Choice A) Histopathology in papillary thyroid cancer shows branching papillary structures with concentric calcifications (**psammoma bodies**) and ground-glass or empty-appearing nuclei (**"Orphan Annie eye" nuclei**). However, papillary thyroid cancer typically presents as an enlarging nodule in a clinically euthyroid patient.

(Choice B) Riedel thyroiditis is characterized by extensive fibrosis of the thyroid gland extending into the surrounding structures. The fibrotic thyroid gland in Riedel thyroiditis is typically hard and fixed to surrounding structures, often resembling a malignancy.

(Choice C) Graves disease presents with a diffusely enlarged thyroid gland associated with hyperthyroidism, exophthalmos, and pretibial myxedema. The thyroid **follicular epithelium** is tall and crowded with hyperactive reabsorption, causing scalloping around the edges of the colloid. Follicular hyperplasia with elongated epithelial cells is also seen in the tall-cell variant of papillary thyroid cancer, typically presenting in older adults as an enlarging thyroid mass.

(Choice E) Subacute granulomatous (de Quervain) thyroiditis is characterized by disruption of follicles and a mixed cellular infiltrate with occasional multinuclear giant cells. Patients typically present after a viral upper respiratory infection with fever and a painful, tender thyroid gland.

Educational objective:
Chronic lymphocytic (Hashimoto) thyroiditis is the most common cause of hypothyroidism. Histopathology characteristically shows an intense

malignancy. Characteristic findings of Hashimoto thyroiditis include an intense **mononuclear infiltrate** consisting of **lymphocytes** and plasma cells, often with **germinal centers** (arrow in image above). Residual follicles are often surrounded by **Hürthle cells** (large oxyphilic cells filled with granular cytoplasm) that represent follicular epithelial cells that have undergone metaplastic change in response to inflammation.

(Choice A) Histopathology in papillary thyroid cancer shows branching papillary structures with concentric calcifications (**psammoma bodies**) and ground-glass or empty-appearing nuclei (**"Orphan Annie eye" nuclei**). However, papillary thyroid cancer typically presents as an enlarging nodule in a clinically euthyroid patient.

(Choice B) Riedel thyroiditis is characterized by extensive fibrosis of the thyroid gland extending into the surrounding structures. The fibrotic thyroid gland in Riedel thyroiditis is typically hard and fixed to surrounding structures, often resembling a malignancy.

(Choice C) Graves disease presents with a diffusely enlarged thyroid gland associated with hyperthyroidism, exophthalmos, and pretibial myxedema. The thyroid **follicular epithelium** is tall and crowded with hyperactive reabsorption, causing scalloping around the edges of the colloid. Follicular hyperplasia with elongated epithelial cells is also seen in the tall-cell variant of papillary thyroid cancer, typically presenting in older adults as an enlarging thyroid mass.

(Choice E) Subacute granulomatous (de Quervain) thyroiditis is characterized by disruption of follicles and a mixed cellular infiltrate with occasional multinuclear giant cells. Patients typically present after a viral upper respiratory infection with fever and a painful, tender thyroid gland.

Educational objective:
Chronic lymphocytic (Hashimoto) thyroiditis is the most common cause of hypothyroidism. Histopathology characteristically shows an intense lymphocytic infiltrate, often with germinal centers. Residual follicles may be surrounded by Hürthle cells (large oxyphilic cells filled with granular cytoplasm).

References

- Hashimoto thyroiditis: clinical and diagnostic criteria.

Settings

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28

Item 20 of 29
Question Id: 1012

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 16-year-old boy is brought to the emergency department because of confusion, fatigue, and abdominal pain. He has also experienced excessive thirst and polyuria during the last 3 weeks. His past medical history is insignificant. Family history is unremarkable. Urine dipstick is positive for glucose and ketones. Which of the following factors most likely contributed to the development of this patient's condition?

A. Abdominal fat distribution
B. Excessive body weight
C. Genetic defects in insulin secretion
D. Islet amyloid deposition
E. Islet leukocytic infiltration

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4 | Feedback | Suspend | End Block

5:02 PM
2/12/2019

Settings

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28

Item 20 of 29
Question Id: 1012

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 16-year-old boy is brought to the emergency department because of confusion, fatigue, and abdominal pain. He has also experienced excessive thirst and polyuria during the last 3 weeks. His past medical history is insignificant. Family history is unremarkable. Urine dipstick is positive for glucose and ketones. Which of the following factors most likely contributed to the development of this patient's condition?

A. Abdominal fat distribution [1%]
B. Excessive body weight [2%]
C. Genetic defects in insulin secretion [19%]
D. Islet amyloid deposition [5%]
✔ E. Islet leukocytic infiltration [71%]

Omitted
Correct answer
E

71%
Answered correctly

4 Seconds
Time Spent

08/16/2018
Last Updated

Explanation

Progression of type 1 diabetes mellitus

100%

Block Time Remaining: 00:02:07
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5:02 PM
2/12/2019

Settings

1
2
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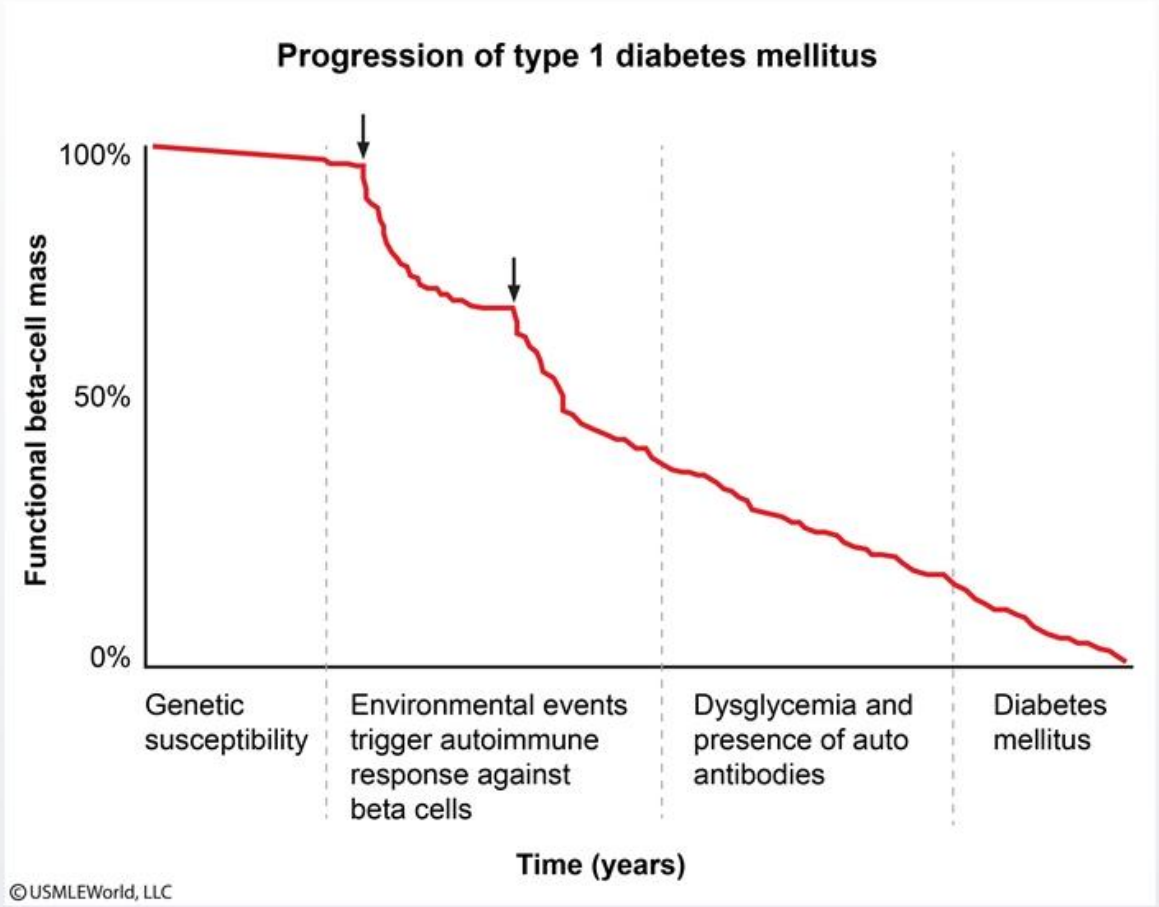
Item 20 of 29
Question Id: 1012

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom



This patient is presenting with diabetic ketoacidosis, a condition that most commonly affects patients with **type 1 diabetes mellitus** due to their

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2/12/2019

response against beta cells | antibodies

Time (years)

This patient is presenting with diabetic ketoacidosis, a condition that most commonly affects patients with **type 1 diabetes mellitus** due to their absolute insulin deficiency. Type 1 diabetes mellitus occurs in genetically susceptible individuals who are exposed to triggering environmental factors (eg, viral infections, environmental toxins, dietary components). This results in an **autoimmune response** against **pancreatic beta cells** that leads to progressive loss of beta cell mass. Overt manifestations of diabetes mellitus tend to develop once >90% of beta cells are destroyed. Although antibodies against islet antigens are detected in a large number of patients, they are thought to play a permissive role in disease pathogenesis; the destruction of beta cells occurs primarily through **cell-mediated immunity**. Infiltration of islets by inflammatory cells is called **insulitis** and is more prominent during the early stages of disease.

(Choices A and B) Abdominal fat deposition and excessive body weight are important contributors to insulin resistance and development of type 2 diabetes mellitus. Intra-abdominal visceral fat is more strongly related to insulin resistance than is subcutaneous fat.

(Choice C) Maturity-onset diabetes of the young is an autosomal dominant disease caused by mutations that impair glucose sensing and insulin secretion by pancreatic beta cells. It presents as non-insulin-dependent diabetes at a young age (<25) and accounts for <5% of all cases of diabetes mellitus.

(Choice D) Islet amyloid polypeptide is secreted along with insulin from pancreatic beta cells. Amyloid deposition occurs in the islets of patients with type 2 diabetes mellitus, although its role as a causative agent of beta cell dysfunction remains unknown. Patients with type 1 diabetes mellitus have low circulating levels of islet amyloid polypeptide due to extensive beta cell destruction.

Educational objective:
Autoimmune insulitis with progressive beta cell loss is the most common cause of type 1 diabetes mellitus. Insulin resistance accompanied by relative insulin deficiency is the main cause of type 2 diabetes mellitus.

Settings

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15
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19
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21
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25
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27
28

Item 21 of 29
Question Id: 225

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 50-year-old man is brought to the emergency department due to a severe, sudden-onset headache that started an hour ago. The patient reports that he has had mild headaches and decreased libido over the past 3 months. He has no other medical conditions and takes no medications. Physical examination reveals bilateral deficits involving the temporal visual fields and impaired extraocular eye movements. Shortly after being admitted to the hospital, he becomes acutely hypotensive and loses consciousness. The patient dies despite aggressive resuscitation efforts. Which of the following is most likely to be found on autopsy?

A. Acute hemorrhage in the pituitary gland
B. Bleeding within the putamen
C. Dissection of the internal carotid artery
D. Inflamed temporal arteries
E. Ischemic necrosis of the pituitary gland
F. Ruptured intracranial aneurysm
G. Thrombus in the venous sinuses

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Block Time Remaining: 00:02:08
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4 | Feedback | Suspend | End Block

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2/12/2019

Settings

Item 21 of 29
Question Id: 225

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 50-year-old man is brought to the emergency department due to a severe, sudden-onset headache that started an hour ago. The patient reports that he has had mild headaches and decreased libido over the past 3 months. He has no other medical conditions and takes no medications. Physical examination reveals bilateral deficits involving the temporal visual fields and impaired extraocular eye movements. Shortly after being admitted to the hospital, he becomes acutely hypotensive and loses consciousness. The patient dies despite aggressive resuscitation efforts. Which of the following is most likely to be found on autopsy?

- ✔ A. Acute hemorrhage in the pituitary gland [61%]
- B. Bleeding within the putamen [1%]
- C. Dissection of the internal carotid artery [1%]
- D. Inflamed temporal arteries [1%]
- E. Ischemic necrosis of the pituitary gland [12%]
- F. Ruptured intracranial aneurysm [19%]
- G. Thrombus in the venous sinuses [2%]

Omitted
Correct answer
A

61%
Answered correctly

3 Seconds
Time Spent

02/12/2019
Last Updated

Explanation

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2/12/2019

Pituitary apoplexy	
Pathogenesis	• Acute pituitary hemorrhage • Usually occurs in preexisting adenoma
Clinical presentation	• Severe headache • Bitemporal hemianopsia (optic chiasm) & ophthalmoplegia (CN III) • Hemodynamic instability & altered sensorium
Complications	• Panhypopituitarism (acute & chronic) • Severe hypotension (central adrenal failure) • Coma & death

This patient had typical features of acute pituitary hemorrhage (**pituitary apoplexy**), including a severe **headache**, **bitemporal hemianopsia** (due to compression of the optic chiasm), and **ophthalmoplegia** (due to compression of the oculomotor nerve [CN III]). Pituitary apoplexy usually occurs in a preexisting **pituitary adenoma**, as in this patient with chronic headaches and low libido (likely due to hyperprolactinemia). The diagnosis can be confirmed on cross-sectional imaging (CT or MRI scan).

Patients with pituitary apoplexy can develop cardiovascular collapse due to ACTH deficiency and subsequent **adrenocortical insufficiency**. Pituitary apoplexy is a medical emergency that requires urgent neurosurgical consultation and treatment with **glucocorticoids** .

(Choice B) Hemorrhage into the putamen (basal ganglia) causes neurologic deficits that gradually worsen over minutes to hours. Typical features include contralateral hemiparesis and hemianesthesia due to disruption of the corticospinal and somatosensory tracts. It is most often seen in chronic hypertensive vasculopathy.

(Choice C) Carotid dissection typically presents with unilateral headache, transient vision loss, ptosis, and miosis (partial Horner syndrome). It usually occurs following trauma, or can occur spontaneously in patients with chronic hypertension, connective tissue disease, or history of

Pituitary apoplexy is a medical emergency that requires urgent neurosurgical consultation and treatment with **glucocorticoids** .

(Choice B) Hemorrhage into the putamen (basal ganglia) causes neurologic deficits that gradually worsen over minutes to hours. Typical features include contralateral hemiparesis and hemianesthesia due to disruption of the corticospinal and somatosensory tracts. It is most often seen in chronic hypertensive vasculopathy.

(Choice C) Carotid dissection typically presents with unilateral headache, transient vision loss, ptosis, and miosis (partial Horner syndrome). It usually occurs following trauma, or can occur spontaneously in patients with chronic hypertension, connective tissue disease, or history of smoking.

(Choice D) Typical symptoms of giant cell (temporal) arteritis include headaches, jaw claudication, and visual disturbances (eg, amaurosis fugax, anterior ischemic optic neuropathy). Patients frequently also have systemic symptoms (eg, fever, fatigue) and proximal muscle pain (polymyalgia rheumatica).

(Choice E) Ischemic necrosis of the pituitary (Sheehan syndrome) most commonly occurs due to hypoperfusion of the enlarged pituitary during childbirth. It presents with chronic hypopituitarism (eg, failure to lactate). Severe headaches and visual field defects do not occur.

(Choice F) Rupture of a saccular aneurysm near the optic chiasm can present similarly to pituitary apoplexy. However, this patient's chronic history of decreased libido and acute cardiovascular collapse is more suggestive of a pituitary etiology.

(Choice G) Cerebral venous sinus thrombosis is most common in patients with underlying thrombophilia, pregnancy, oral contraceptive use, malignancy, or infection. Presenting features include headaches, vomiting, seizures, and focal neurologic deficits.

Educational objective:
Acute pituitary hemorrhage (pituitary apoplexy) is characterized by severe headaches, bitemporal hemianopsia (compression of the optic chiasm), and ophthalmoplegia (compression of the oculomotor nerve). It usually occurs in a preexisting pituitary adenoma. Pituitary apoplexy is a medical emergency that requires urgent treatment with glucocorticoids to prevent acute adrenal crisis and circulatory collapse.

References

Settings

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28

Item 22 of 29
Question Id: 980

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 55-year-old man comes to the office for follow-up of abnormal serum chemistries found on routine laboratory testing. He has a history of hypertension, for which he is being treated with pharmacologic therapy, weight loss, and dietary salt restriction. Blood pressure is 130/80 mm Hg and pulse is 80/min. BMI is 27 kg/m^2. Physical examination reveals no abnormalities. Laboratory studies are as follows:

Serum chemistry	
Sodium	134 mEq/L
Potassium	3.8 mEq/L
Blood urea nitrogen	18 mg/dL
Creatinine	0.8 mg/dL
Calcium	11.0 mg/dL
Glucose	98 mg/dL
Albumin	4 g/dL
Parathyroid hormone	decreased

Which of the following is most likely responsible for these findings?

A. Familial hypocalciuric hypercalcemia
B. Hypothyroidism
C. Medication effect
D. Primary hyperparathyroidism

Block Time Remaining: 00:02:12
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Settings

Item 22 of 29
Question Id: 980

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

Sodium	134 mEq/L
Potassium	3.8 mEq/L
Blood urea nitrogen	18 mg/dL
Creatinine	0.8 mg/dL
Calcium	11.0 mg/dL
Glucose	98 mg/dL
Albumin	4 g/dL
Parathyroid hormone	decreased

Which of the following is most likely responsible for these findings?

A. Familial hypocalciuric hypercalcemia
B. Hypothyroidism
C. Medication effect
D. Primary hyperparathyroidism
E. Secondary hyperparathyroidism

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5:03 PM
2/12/2019

Settings

Item 22 of 29
Question Id: 980

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

Sodium	134 mEq/L
Potassium	3.8 mEq/L
Blood urea nitrogen	18 mg/dL
Creatinine	0.8 mg/dL
Calcium	11.0 mg/dL
Glucose	98 mg/dL
Albumin	4 g/dL
Parathyroid hormone	decreased

Which of the following is most likely responsible for these findings?

- A. Familial hypocalciuric hypercalcemia [20%]
- B. Hypothyroidism [1%]
- ✔ C. Medication effect [63%]
- D. Primary hyperparathyroidism [4%]
- E. Secondary hyperparathyroidism [9%]

Omitted
Correct answer

63%
Answered correctly

7 Seconds
Time Spent

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Last Updated

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Settings

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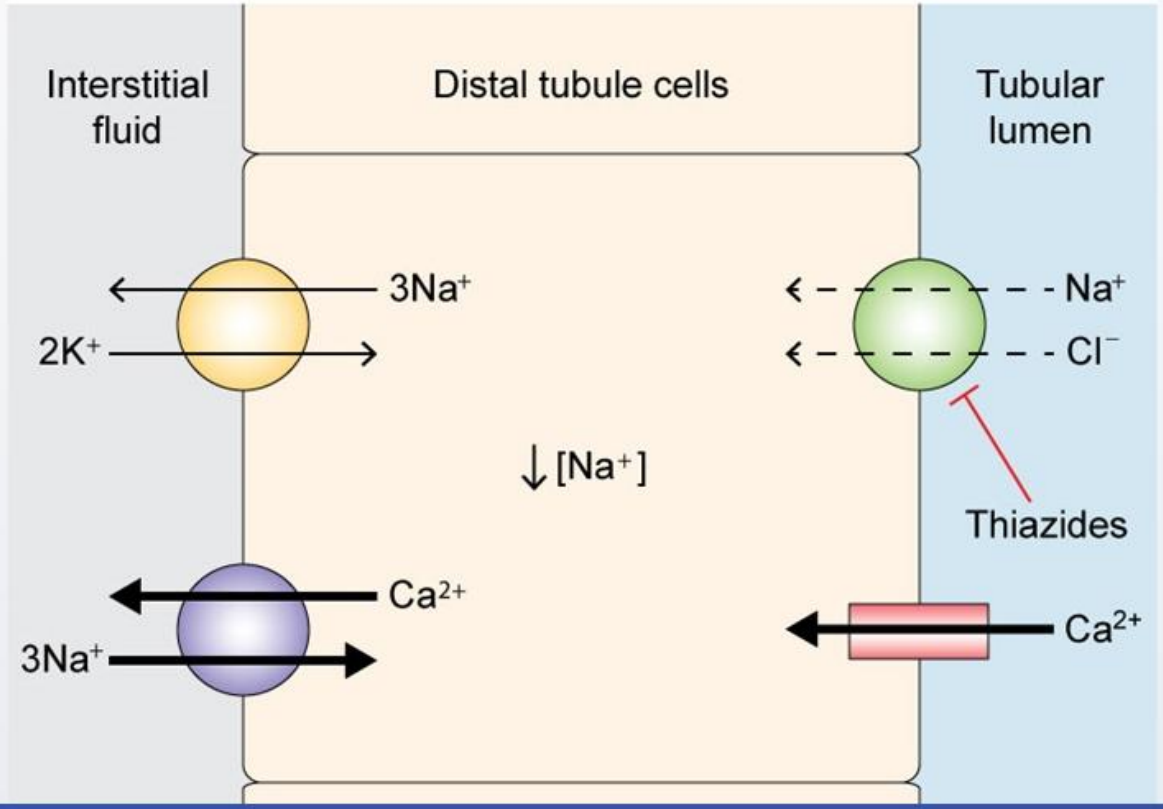
Item 22 of 29
Question Id: 980

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

Effect of thiazide diuretics on distal tubular calcium reabsorption



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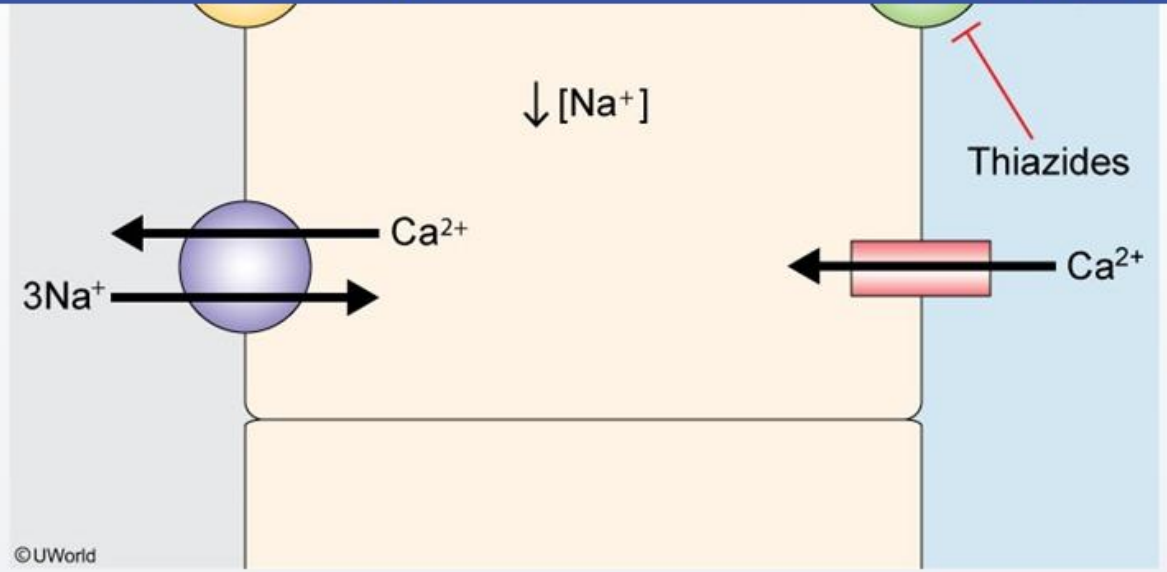

Thiazide diuretics (eg, chlorthalidone, hydrochlorothiazide) are some of the most widely used agents for treatment of hypertension. However, thiazides, especially in higher doses, can cause a variety of metabolic complications, including hypercalcemia, hyperglycemia, hyperlipidemia, hyponatremia, and hypokalemia. The incidence of the individual side effects is relatively low, and, patients rarely experience all of the potential adverse effects.

Thiazides increase renal Ca^{2+} reabsorption, leading to **hypercalcemia** and **hypocalciuria**. This occurs through 2 major mechanisms:

1. Thiazides **inhibit the Na^+/Cl^- cotransporter** on the apical side of distal convoluted tubule cells, which decreases intracellular Na^+ concentration. This activates the basolateral **Na^+/Ca^{2+} antiporter**, which pumps Na^+ into the cell in exchange for Ca^{2+}. The resulting decrease in intracellular Ca^{2+} enhances luminal Ca^{2+} reabsorption across the apical membrane.
2. **Hypovolemia** induced by thiazides increases Na^+ and H_2O reabsorption in the proximal tubule, leading to a passive increase in paracellular

adverse effects.

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1. Thiazides **inhibit the Na^+/Cl^- cotransporter** on the apical side of distal convoluted tubule cells, which decreases intracellular Na^+ concentration. This activates the basolateral **Na^+/Ca^{2+} antiporter**, which pumps Na^+ into the cell in exchange for Ca^{2+}. The resulting decrease in intracellular Ca^{2+} enhances luminal Ca^{2+} reabsorption across the apical membrane.
2. **Hypovolemia** induced by thiazides increases Na^+ and H_2O reabsorption in the proximal tubule, leading to a passive increase in paracellular Ca^{2+} reabsorption.

The increase in circulating calcium suppresses parathyroid hormone (PTH) release, leading to a new steady state with a mildly elevated serum calcium concentration and low serum PTH.

(Choice A) Familial hypocalciuric hypercalcemia is a benign disorder caused by mutations in the calcium-sensing receptor in the parathyroid gland and kidneys. Higher calcium levels are required to suppress secretion of PTH, leading to mild hypercalcemia and hypocalciuria. However, unlike in patients taking thiazide diuretics, PTH is high-normal or mildly elevated.

(Choice B) Hyperthyroidism can cause hypercalcemia due to increased osteoclastic bone resorption, but serum calcium in hypothyroidism is usually normal.

(Choices D and E) Primary hyperparathyroidism is caused by parathyroid hyperplasia or adenoma; it is characterized by hypercalcemia with elevated or inappropriately normal PTH levels. Secondary hyperparathyroidism is usually seen in patients with chronic kidney disease and is due to phosphate retention and decreased production of 1,25-dihydroxyvitamin D; these disturbances lead to decreased intestinal calcium absorption, hypocalcemia, hyperphosphatemia, and a compensatory increase in PTH secretion. This patient has a decreased PTH level.

Educational objective:
Thiazide diuretics cause hypercalcemia by increasing the distal tubular reabsorption of Ca^{2+}. The increased circulating calcium levels result in suppression of parathyroid hormone, which distinguishes this effect from hyperparathyroidism.

Settings

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28

Item 23 of 29
Question Id: 1921

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 54-year-old man comes to the office due to worsening fatigue, generalized weakness, and an unintentional 7-kg (15.4-lb) weight loss over the past several weeks. The patient has no prior medical conditions and takes no medications. He has a 40-pack-year history of smoking and does not use alcohol or illicit drugs. Blood pressure is 160/100 mm Hg and pulse is 80/min. Physical examination shows darkening of the skin in sun-exposed areas. There are scattered ecchymoses on the extremities. Mild proximal muscle weakness is present. Chest imaging reveals a 6-cm, irregular right lung mass with mediastinal lymphadenopathy. Which of the following is most likely responsible for the patient's current symptoms?

A. ACTH production from an ectopic site
B. Excess cortisol release from the lung mass
C. Excessive ACTH secretion from the pituitary
D. Hypothalamic dysfunction from metastatic process
E. Malignant invasion of the adrenal cortex

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Block Time Remaining: 00:02:18
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4 Feedback Suspend End Block

5:03 PM
2/12/2019

Settings

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28

Item 23 of 29
Question Id: 1921

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

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- ✔ A. ACTH production from an ectopic site [85%]
- B. Excess cortisol release from the lung mass [3%]
- C. Excessive ACTH secretion from the pituitary [3%]
- D. Hypothalamic dysfunction from metastatic process [2%]
- E. Malignant invasion of the adrenal cortex [4%]

Omitted
Correct answer
A

85%
Answered correctly

3 Seconds
Time Spent

10/23/2018
Last Updated

Explanation

Common paraneoplastic syndromes associated with lung cancer

- Syndrome of inappropriate antidiuretic hormone*

Block Time Remaining: 00:02:20
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5:03 PM
2/12/2019

Common paraneoplastic syndromes associated with lung cancer	
Endocrine	• Syndrome of inappropriate antidiuretic hormone* • Parathyroid hormone-related protein secretion (hypercalcemia) • Ectopic ACTH production (Cushing syndrome)*
Neurologic	• Lambert-Eaton myasthenic syndrome* • Paraneoplastic cerebellar degeneration*
Musculoskeletal	• Hypertrophic osteoarthropathy (clubbing)

*Generally associated with small cell lung cancer.

This patient has fatigue, weakness, and weight loss associated with a suspicious **lung mass**. His hypertension, ecchymoses, and hyperpigmentation suggest **paraneoplastic hypercortisolism** (Cushing syndrome) due to **ectopic ACTH** secretion. As with primary adrenal insufficiency, excess ACTH secretion leads to hyperpigmentation, likely due to co-secretion of alpha-melanocyte-stimulating hormone (alpha-MSH) (both ACTH and alpha-MSH are derived from pro-opiomelanocortin) and direct stimulation of the MC2R receptor on melanocytes by ACTH. Although patients with paraneoplastic hypercortisolism may have many of the typical metabolic features of cortisol excess (eg, hypertension, hyperglycemia, edema), **weight loss** is more common than classic Cushingoid central obesity.

Paraneoplastic hypercortisolism is most commonly associated with small cell lung cancer but can also be seen with other neuroendocrine tumors (eg, bronchial or pancreatic carcinoid). ACTH secreted by small cell lung cancer is not inhibited by high-dose exogenous corticosteroids (eg, dexamethasone), whereas pituitary ACTH secretion decreases via negative feedback.

(Choice B) Cortisol is produced by the zona fasciculata of the adrenal cortex, and autonomous cortisol production (ie, ACTH-independent hypercortisolism) is almost always due to a primary adrenal disorder (eg, adrenal adenoma). Regardless of the source, excess cortisol in a patient with intact hypothalamus-pituitary function suppresses ACTH and patients do not develop hyperpigmentation.

(Choice C) Given this patient's large lung mass and associated weight loss (instead of weight gain and central fat deposition), paraneoplastic

This patient has fatigue, weakness, and weight loss associated with a suspicious **lung mass**. His hypertension, ecchymoses, and hyperpigmentation suggest **paraneoplastic hypercortisolism** (Cushing syndrome) due to **ectopic ACTH** secretion. As with primary adrenal insufficiency, excess ACTH secretion leads to hyperpigmentation, likely due to co-secretion of alpha-melanocyte-stimulating hormone (alpha-MSH) (both ACTH and alpha-MSH are derived from pro-opiomelanocortin) and direct stimulation of the MC2R receptor on melanocytes by ACTH. Although patients with paraneoplastic hypercortisolism may have many of the typical metabolic features of cortisol excess (eg, hypertension, hyperglycemia, edema), **weight loss** is more common than classic Cushingoid central obesity.

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(Choice C) Given this patient's large lung mass and associated weight loss (instead of weight gain and central fat deposition), paraneoplastic ACTH secretion is more likely than an ACTH-producing pituitary adenoma (Cushing disease).

(Choice D) Metastasis to the hypothalamus would likely cause endocrine insufficiency resulting from a lack of trophic hormones to the anterior pituitary. Decreased production of corticotropin-releasing hormone would lead to central adrenal insufficiency, not hypercortisolism.

(Choice E) The adrenal glands are a common site of metastasis. If significant destruction of the adrenal cortical tissue occurs bilaterally, adrenal insufficiency may result. A subsequent increase of ACTH may cause hyperpigmentation; however, symptoms of adrenal insufficiency (eg, hypotension) would be expected, as opposed to the symptoms of cortisol excess seen in this patient.

Educational objective:
Paraneoplastic hypercortisolism, most commonly caused by small cell lung cancer, is due to ectopic ACTH secretion. Clinical features include hypertension, hyperglycemia, edema, and hyperpigmentation. Unlike nonparaneoplastic Cushing syndrome, central obesity is uncommon.

Settings

Item 23 of 29
Question Id: 1921

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A

Explanation

Exhibit Display

Clinical features of Cushing syndrome
• **Central obesity** (eg, fat accumulation in the face [ie, moon face] & back of the neck [ie, buffalo hump]) • **Glucose intolerance** • Hypertension • Menstrual changes & decreased libido • Skin atrophy • Easy bruisability • Hirsutism & acne (excess androgens) • Proximal muscle weakness

Add To Flash Card

This patient has fatigue, weakn… hyperpigmentation suggest **par**…drenal insufficiency, excess ACTH sec…bha-MSH) (both ACTH and alpha-MSH ar…H. Although patients with paraneo…on, hyperglycemia, edema), **weigh**…

Paraneoplastic hypercortisolism is most commonly associated with small cell lung cancer but can also be seen with other neuroendocrine tumors (eg, bronchial or pancreatic carcinoid). ACTH secreted by small cell lung cancer is not inhibited by high-dose exogenous corticosteroids (eg, dexamethasone), whereas pituitary ACTH secretion decreases via negative feedback.

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1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28

Item 24 of 29
Question Id: 1839

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 19-year-old woman comes to the office for evaluation of amenorrhea. Onset of menarche was at age 12, and the patient then had menses regularly every 25-28 days. However, for the last year her menstrual periods have been irregular, and her last period was 3 months ago. The patient has no significant past medical history, eats mainly fruits and vegetables, and exercises regularly at a local gym. She does not use tobacco or alcohol. On further questioning, the patient expresses concern about being overweight and asks for suggestions on cutting down her caloric intake. On physical examination, BMI is 18 kg/m^2. The patient is thin and has dry skin covered by fine, downy hair. A pregnancy test is negative. Which of the following patterns of serum hormone levels is most likely in this patient?

	LH	FSH	Estradiol
A.	Increased	Increased	Decreased
B.	Increased	Decreased	Decreased
C.	Decreased	Normal	Normal
D.	Decreased	Decreased	Decreased
E.	Normal	Normal	Decreased

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5:03 PM
2/12/2019

Settings

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28

Item 24 of 29
Question Id: 1839

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 19-year-old woman comes to the office for evaluation of amenorrhea. Onset of menarche was at age 12, and the patient then had menses regularly every 25-28 days. However, for the last year her menstrual periods have been irregular, and her last period was 3 months ago. The patient has no significant past medical history, eats mainly fruits and vegetables, and exercises regularly at a local gym. She does not use tobacco or alcohol. On further questioning, the patient expresses concern about being overweight and asks for suggestions on cutting down her caloric intake. On physical examination, BMI is 18 kg/m^2. The patient is thin and has dry skin covered by fine, downy hair. A pregnancy test is negative. Which of the following patterns of serum hormone levels is most likely in this patient?

	LH	FSH	Estradiol
A. [16%]	Increased	Increased	Decreased
B. [4%]	Increased	Decreased	Decreased
C. [2%]	Decreased	Normal	Normal
✔ D. [74%]	Decreased	Decreased	Decreased
E. [2%]	Normal	Normal	Decreased

Omitted
Correct answer
D

74%
Answered correctly

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11/24/2018
Last Updated

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2/12/2019

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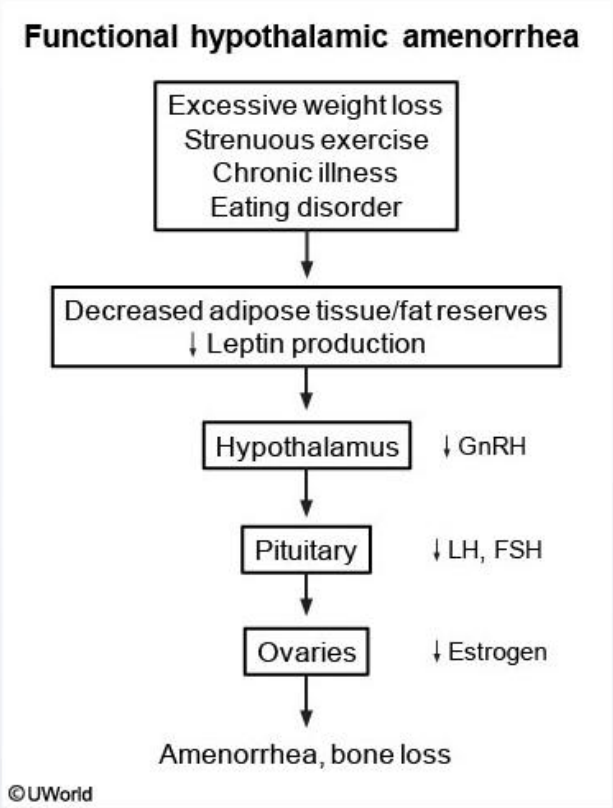
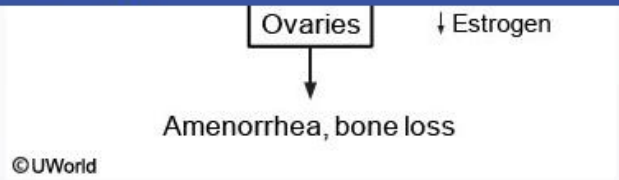
Explanation



Amenorrhea can be categorized as primary (failure of menarche by age 15) or secondary (cessation of menstruation in premenopausal women who have previously had menses). Secondary amenorrhea can be due to hypothalamic, pituitary, ovarian, uterine, or other endocrine (eg, thyroid)



Amenorrhea can be categorized as primary (failure of menarche by age 15) or secondary (cessation of menstruation in premenopausal women who have previously had menses). Secondary amenorrhea can be due to hypothalamic, pituitary, ovarian, uterine, or other endocrine (eg, thyroid) disorders.

This patient's distorted body image, restricted diet, exercise regimen, and physical examination findings (dry skin, lanugo hair) suggest anorexia nervosa with **functional hypothalamic amenorrhea** (FHA). The underlying pathophysiology of FHA appears to involve reduced circulating leptin levels as a result of diminished adipose tissue stores. The decrease in leptin inhibits pulsatile **gonadotropin-releasing hormone (GnRH)** release from the hypothalamus, causing decreased pituitary **LH and FSH** secretion, low circulating **estrogen** levels, and amenorrhea.

In addition to anorexia, FHA can also occur when caloric expenditure is out of proportion to intake, as in thin female athletes (eg, distance runners, dancers) or patients with chronic illness. Potential complications of FHA in young women include reduced peak bone mass, which may lead to early-onset osteoporosis.

Educational objective:
Distorted body image, inadequate diet, dry skin, and lanugo hair in a female suggest anorexia nervosa. Anorexic females commonly have impaired gonadotropin-releasing hormone release from the hypothalamus, leading to low levels of LH, FSH, and estrogen (functional hypothalamic amenorrhea).

References

- Functional hypothalamic amenorrhea: current view on neuroendocrine aberrations.

Settings

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28

Item 25 of 29
Question Id: 768

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 34-year-old woman comes to the office due to a 1 week history of mood swings, difficulty concentrating, and hand tremors. She also has pain at the front of her neck that radiates to her ears and is worse with swallowing. The patient initially attributed her symptoms to a flu-like illness that she had a few weeks earlier. She has no other medical conditions and takes no medications. Blood pressure is 140/80 mm Hg and pulse is 105/min. The thyroid gland is very tender on palpation. After initial laboratory testing, a thyroid scan is performed and reveals diffusely decreased radioiodine uptake. Erythrocyte sedimentation rate is 105 mm/hr. Which of the following pathological changes would be most likely on biopsy of this patient's thyroid gland?

A. Branching papillary structures with interspersed calcified bodies
B. Extensive stromal fibrosis extending beyond the thyroid capsule
C. Follicular hyperplasia with tall cells forming intrafollicular papillary projections
D. Mixed, cellular infiltration with occasional multinucleated giant cells
E. Mononuclear, parenchymal infiltration with well-developed germinal centers

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Item 25 of 29
Question Id: 768

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A 34-year-old woman comes to the office due to a 1 week history of mood swings, difficulty concentrating, and hand tremors. She also has pain at the front of her neck that radiates to her ears and is worse with swallowing. The patient initially attributed her symptoms to a flu-like illness that she had a few weeks earlier. She has no other medical conditions and takes no medications. Blood pressure is 140/80 mm Hg and pulse is 105/min. The thyroid gland is very tender on palpation. After initial laboratory testing, a thyroid scan is performed and reveals diffusely decreased radioiodine uptake. Erythrocyte sedimentation rate is 105 mm/hr. Which of the following pathological changes would be most likely on biopsy of this patient's thyroid gland?

- A. Branching papillary structures with interspersed calcified bodies [4%]
- B. Extensive stromal fibrosis extending beyond the thyroid capsule [9%]
- C. Follicular hyperplasia with tall cells forming intrafollicular papillary projections [10%]
- ✔ D. Mixed, cellular infiltration with occasional multinucleated giant cells [58%]
- E. Mononuclear, parenchymal infiltration with well-developed germinal centers [17%]

Omitted
Correct answer
D

58%
Answered correctly

3 Seconds
Time Spent

09/20/2018
Last Updated

Explanation

Important causes of thyroiditis

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Important causes of thyroiditis		
	Subacute granulomatous thyroiditis	**Hashimoto thyroiditis**
Clinical features	• Onset following a **viral illness** • **Painful** thyroid enlargement • Transient **hyperthyroid** symptoms	• **Autoimmune** etiology • **Painless** thyroid enlargement • Predominant **hypothyroid** features
Diagnostic testing	• ↑ ESR & CRP • ↓ Radioiodine uptake	• Positive **TPO antibody** • Variable radioiodine uptake
Pathology	• Inflammatory infiltrate with macrophages & **giant cells**	• Lymphocytic infiltrate with well-developed **germinal centers** • **Hürthle cells** (eosinophilic epithelial cells)

CRP = C-reactive protein; ESR = erythrocyte sedimentation rate; TPO = thyroid peroxidase.

This patient with **painful** enlargement of the thyroid gland has **subacute granulomatous thyroiditis** (SGT), also called de Quervain thyroiditis. SGT typically follows an acute **viral illness** and is thought to be due to a cross-reacting immune response against viral proteins or tissue antigens released during cellular injury. Patients may experience a **transient hyperthyroid phase** (elevated thyroxine [T4], suppressed TSH) due to release of stored thyroid hormone. Radioiodine uptake is decreased in SGT as the low TSH levels suppress synthesis of new thyroid hormone. The disease is self-limited and resolves in <6 weeks, although patients may have a brief hypothyroid phase before returning to a euthyroid state.

SGT is initially characterized by a neutrophilic infiltrate with microabscess formation, which, as the disease progresses, is replaced by a more generalized inflammatory infiltrate with macrophages and **multinucleated giant cells**. The inflammatory process is reflected by elevated serum acute-phase markers (eg, C-reactive protein, erythrocyte sedimentation rate).

(Choices A and C) Papillary thyroid cancer is characterized by branching papillary structures with concentric calcifications (psammoma

This patient with **painful** enlargement of the thyroid gland has **subacute granulomatous thyroiditis** (SGT), also called de Quervain thyroiditis. SGT typically follows an acute **viral illness** and is thought to be due to a cross-reacting immune response against viral proteins or tissue antigens released during cellular injury. Patients may experience a **transient hyperthyroid phase** (elevated thyroxine [T4], suppressed TSH) due to release of stored thyroid hormone. Radioiodine uptake is decreased in SGT as the low TSH levels suppress synthesis of new thyroid hormone. The disease is self-limited and resolves in <6 weeks, although patients may have a brief hypothyroid phase before returning to a euthyroid state.

SGT is initially characterized by a neutrophilic infiltrate with microabscess formation, which, as the disease progresses, is replaced by a more generalized inflammatory infiltrate with macrophages and **multinucleated giant cells**. The inflammatory process is reflected by elevated serum acute-phase markers (eg, C-reactive protein, erythrocyte sedimentation rate).

(Choices A and C) **Papillary thyroid cancer** is characterized by branching papillary structures with concentric calcifications (psammoma bodies). The **tall-cell variant** of papillary thyroid cancer is characterized by follicular hyperplasia lined by tall epithelial cells. These malignancies would typically present with nodular enlargement rather than acute pain and tenderness. Graves disease can also cause tall cells with **follicular hyperplasia**, but radioiodine uptake is increased due to excessive TSH receptor stimulation.

(Choice B) Riedel thyroiditis is characterized by extensive fibrosis of the thyroid gland that extends into surrounding tissues. The thyroid gland is hard and nontender.

(Choice E) Chronic lymphocytic (Hashimoto) thyroiditis is characterized by diffuse, painless thyroid enlargement, often with symptoms of hypothyroidism (eg, fatigue, cold intolerance). Biopsy reveals diffuse lymphocytic infiltration with formation of **germinal centers**.

Educational objective:
Subacute granulomatous (de Quervain) thyroiditis is characterized by painful thyroid enlargement and usually follows a viral illness. Biopsy shows a mixed inflammatory infiltrate with macrophages and multinucleated giant cells.

References

- Subacute granulomatous (De Quervain's) thyroiditis: Fine-needle aspiration cytology and ultrasonographic characteristics of 21 cases.

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Item 26 of 29
Question Id: 986

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 40-year-old man comes to the office to follow up refractory peptic ulceration. The patient has had persistent upper abdominal pain, nausea, heartburn, and diarrhea for a year despite treatment. Abdominal examination shows mild diffuse tenderness and increased bowel sounds. Laboratory studies show a moderate iron-deficiency anemia, occult blood in the stool, and a markedly elevated serum gastrin level. Upper gastrointestinal endoscopy reveals prominent gastric folds and multiple ulcers in the duodenum. The patient has an otherwise unremarkable past medical history, but multi-organ disease is suspected. This patient should be queried for a family history of which of the following disorders?

A. Multiple endocrine neoplasia type 1
B. Multiple endocrine neoplasia type 2A
C. Multiple endocrine neoplasia type 2B
D. Retinoblastoma and osteosarcoma
E. von Hippel-Lindau syndrome

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Item 26 of 29
Question Id: 986

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

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- ✔ A. Multiple endocrine neoplasia type 1 [75%]
- B. Multiple endocrine neoplasia type 2A [6%]
- C. Multiple endocrine neoplasia type 2B [6%]
- D. Retinoblastoma and osteosarcoma [2%]
- E. von Hippel-Lindau syndrome [9%]

Omitted
Correct answer
A

75%
Answered correctly

3 Seconds
Time Spent

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Explanation

Classification of multiple endocrine neoplasia
• **Primary hyperparathyroidism** (parathyroid adenomas or

Block Time Remaining: 00:02:29
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Classification of multiple endocrine neoplasia	
Type 1	• **Primary hyperparathyroidism** (parathyroid adenomas or hyperplasia) • Pituitary tumors (prolactin, visual defects) • Pancreatic tumors (especially gastrinomas)
Type 2A	• **Medullary thyroid cancer** (calcitonin) • Pheochromocytoma • Primary hyperparathyroidism (parathyroid hyperplasia)
Type 2B	• **Medullary thyroid cancer** (calcitonin) • Pheochromocytoma • Mucosal neuromas/marfanoid habitus

This patient's refractory peptic ulcer associated with an elevated gastrin level is likely due to a gastrin-secreting pancreatic tumor (**Zollinger-Ellison syndrome**). Although most gastrinomas are sporadic, 20%-30% occur in association with **multiple endocrine neoplasia type 1** (MEN 1). This autosomal dominant disorder is most often due to mutations of the MEN1 gene (menin protein) and is characterized by **p**arathyroid adenomas, **p**ituitary tumors, and **p**ancreatic endocrine tumors (the **3 Ps** of MEN 1).

This patient should therefore be queried for symptoms or family history of other MEN 1 tumors. Potential associated conditions include primary hyperparathyroidism (hypercalcemia) and pituitary adenoma (headaches, visual field defects).

(Choices B and C) MEN 2A consists of medullary thyroid cancer, pheochromocytoma, and primary hyperparathyroidism. MEN 2B (also known as MEN 3) is associated with medullary thyroid cancer, pheochromocytoma, mucosal neuromas, and a marfanoid habitus. The MEN 2 syndromes are not associated with pancreatic endocrine tumors.

(Choice D) Retinoblastomas and osteosarcomas can occur due to mutations in the retinoblastoma gene (RB gene), a tumor suppressor gene

This patient's refractory peptic ulcer associated with an elevated gastrin level is likely due to a gastrin-secreting pancreatic tumor (**Zollinger-Ellison syndrome**). Although most gastrinomas are sporadic, 20%-30% occur in association with **multiple endocrine neoplasia type 1** (MEN 1). This autosomal dominant disorder is most often due to mutations of the MEN1 gene (menin protein) and is characterized by **p**arathyroid adenomas, **p**ituitary tumors, and **p**ancreatic endocrine tumors (the **3 Ps** of MEN 1).

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(Choices B and C) MEN 2A consists of medullary thyroid cancer, pheochromocytoma, and primary hyperparathyroidism. MEN 2B (also known as MEN 3) is associated with medullary thyroid cancer, pheochromocytoma, mucosal neuromas, and a marfanoid habitus. The MEN 2 syndromes are not associated with pancreatic endocrine tumors.

(Choice D) Retinoblastomas and osteosarcomas can occur due to mutations in the retinoblastoma gene (RB gene), a tumor suppressor gene involved in regulating the transition of G1 to the S phase of the cell cycle. Gastrinomas do not occur with RB gene mutations.

(Choice E) von Hippel-Lindau disease is an autosomal disorder characterized by multiple tumors, including hemangioblastomas, pheochromocytoma, and renal cell carcinoma.

Educational objective:
Multiple endocrine neoplasia type 1 consists of hyperparathyroidism, endocrine pancreatic tumors (eg, gastrinoma), and pituitary tumors. The genetic defect involves the MEN 1 gene.

References

- Clinical practice guidelines for multiple endocrine neoplasia type 1 (MEN1).

Settings

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28

Item 27 of 29
Question Id: 1658

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 61-year-old woman comes to the office due to a neck lump. She is otherwise in good health and has no other symptoms. Temperature is 36.7 C (98 F), blood pressure is 115/70 mm Hg, and pulse is 78/min. On physical examination, there is a nontender, firm nodule in the left lobe of the thyroid. Laboratory results show a normal serum TSH level. Thyroid ultrasonography reveals a 2-cm, hypoechoic thyroid nodule with increased central blood flow. Fine-needle aspiration biopsy shows clusters of cells with large, overlapping nuclei containing sparse, finely dispersed chromatin. Numerous intranuclear inclusion bodies and grooves are also seen. Which of the following is the most likely diagnosis in this patient?

- A. Anaplastic carcinoma
- B. Colloid nodule
- C. Follicular adenoma
- D. Follicular carcinoma
- E. Medullary carcinoma
- F. Papillary carcinoma

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Item 27 of 29
Question Id: 1658

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

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- A. Anaplastic carcinoma [12%]
- B. Colloid nodule [1%]
- C. Follicular adenoma [10%]
- D. Follicular carcinoma [9%]
- E. Medullary carcinoma [9%]
- ✔ F. Papillary carcinoma [55%]

Omitted
Correct answer
F

55%
Answered correctly

3 Seconds
Time Spent

09/26/2018
Last Updated

Explanation

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Item 27 of 29
Question Id: 1658

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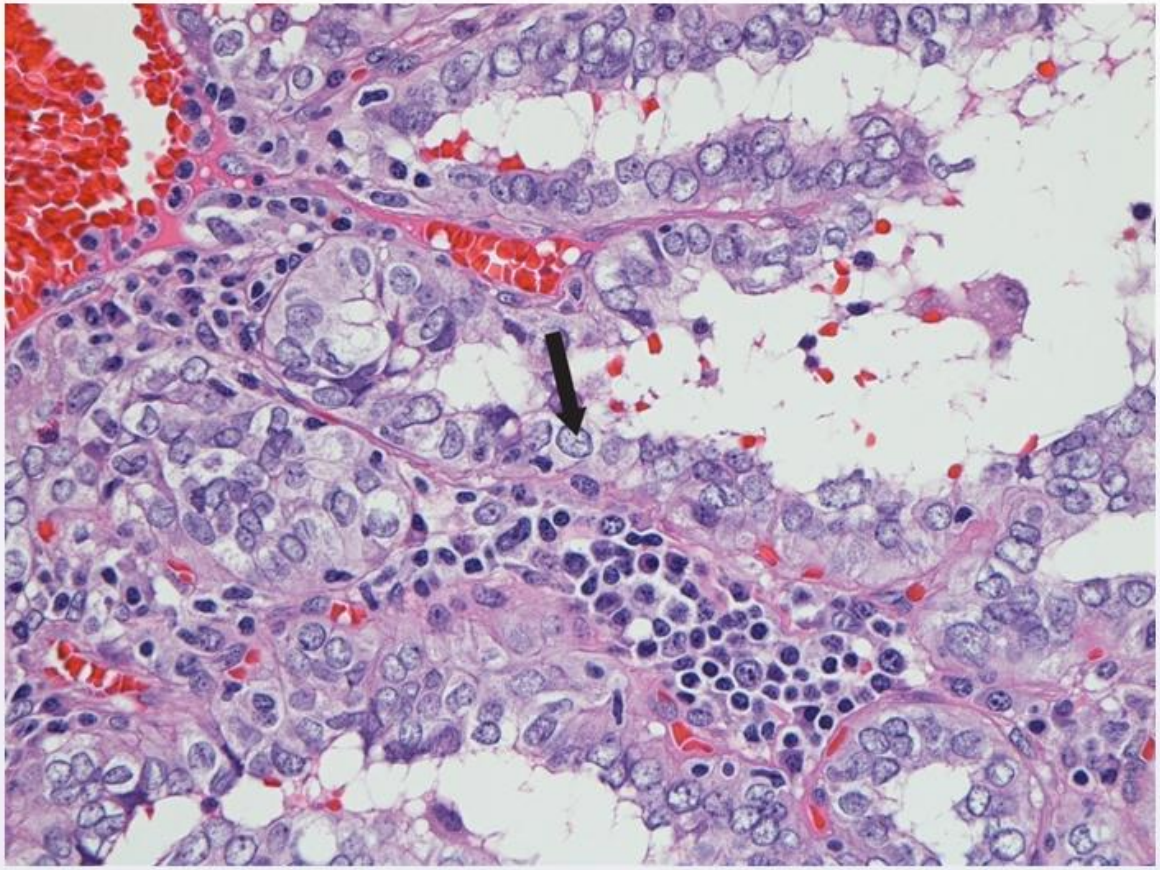

The 4 main types of primary thyroid carcinoma include papillary, follicular, medullary (derived from the parafollicular calcitonin-secreting C cells),

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The 4 main types of primary thyroid carcinoma include papillary, follicular, medullary (derived from the parafollicular calcitonin-secreting C cells), and anaplastic. The papillary type is most common, accounting for >70% of cases. Risk factors include a positive family history of thyroid cancer and radiation exposure (especially during childhood).

Papillary carcinoma cells are characteristically large with overlapping nuclei containing **finely dispersed chromatin**, giving them an empty or ground-glass appearance (sometimes termed **Orphan Annie eye** nuclei after a cartoon character whose eyes were drawn without pupils or irises). Numerous **intranuclear inclusions and grooves** (arrow) can be seen due to invagination of the nuclear membrane. **Psammoma bodies** (laminated calcium deposits) may also be found within the tumor.

(Choice A) **Anaplastic thyroid cancer** is an aggressive tumor with a very poor prognosis. It is most common in older patients (age >60). Cytologic features include markedly pleomorphic cells, including irregular giant cells and biphasic spindle cells.

(Choice B) Most benign thyroid nodules are colloid nodules formed from focal hyperplasia of normal thyroid follicular cells. On cytopathology, a colloid nodule consists of variable-sized thyroid follicles, colloid, and macrophages.

(Choices C and D) Follicular neoplasms lack the characteristic nuclear features and psammoma bodies found in papillary tumors. Distinguishing a benign follicular adenoma from a well-differentiated follicular cancer depends on the presence of vascular and capsular invasion, which cannot be determined on a fine-needle aspiration specimen.

(Choice E) **Medullary thyroid cancer** appears histologically as polygonal or spindle-shaped cells with a slightly granular cytoplasm that stains for calcitonin. Extracellular amyloid deposits (arrow) consisting of calcitonin polypeptide may also be seen. Medullary thyroid cancer is a component of multiple endocrine neoplasia types 2A and 2B.

Educational objective:
Papillary thyroid cancer is the most common type of thyroid cancer. Characteristic findings on histopathology include large cells with nuclei containing finely dispersed chromatin, giving an empty or ground-glass appearance (Orphan Annie eye), and intranuclear inclusions or grooves.

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Item 27 of 29
Question Id: 1658

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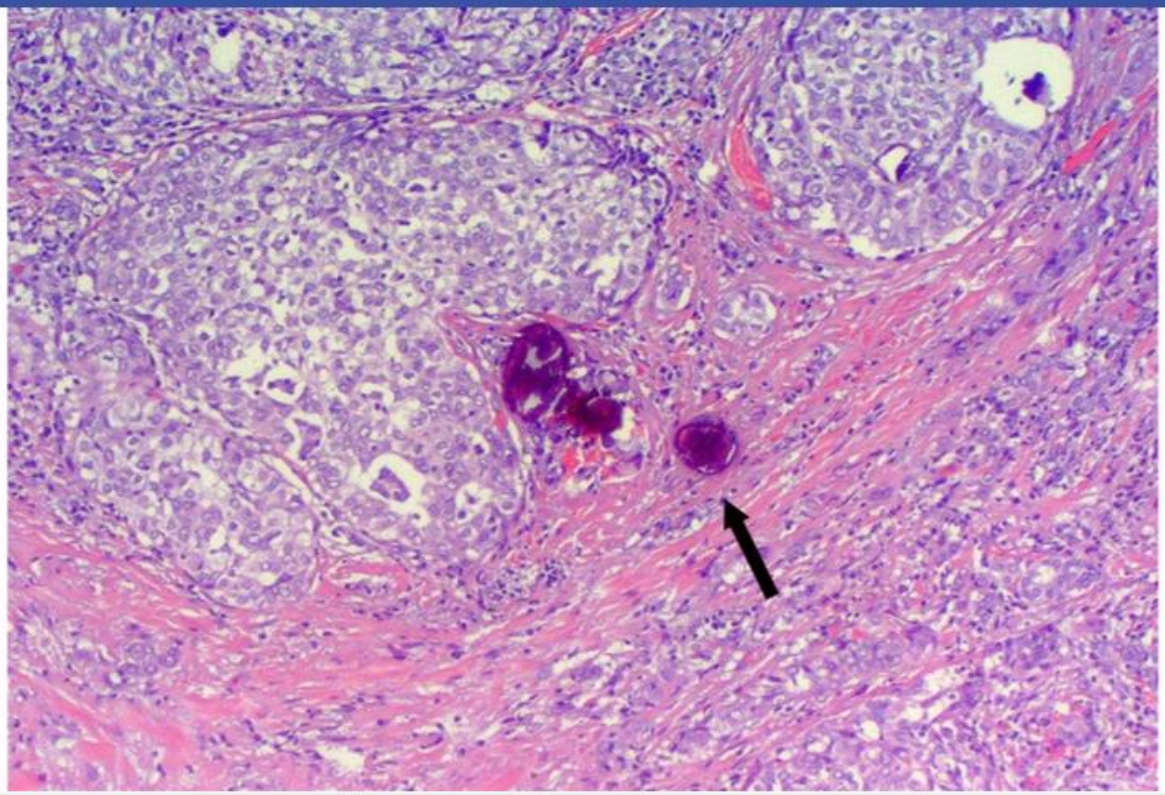

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A 60-year-old woman comes to the office due to difficulty climbing stairs and dyspnea on exertion over the last 6 weeks. The patient has a 40-pack-year smoking history. Blood pressure is 160/90 mm Hg and pulse is 78/min. Auscultation of the chest reveals decreased breath sounds over the right lung base. Proximal muscle strength is 4 on a scale of 0-5. Skin examination shows scattered ecchymoses. Laboratory results show mild hyperglycemia and elevated 24-hour urinary free cortisol. Serum cortisol level is at the upper limit of normal and is not suppressed following administration of low-dose dexamethasone. Serum ACTH level is elevated. Chest x-ray reveals a right lower lobe lung mass. Which of the following changes are most likely to occur after administration of high-dose dexamethasone in this patient?

	ACTH	Cortisol
A.	Decrease	Decrease
B.	Increase	Increase
C.	Increase	No change
D.	No change	Decrease
E.	No change	No change

Submit

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	ACTH	Cortisol
A. [5%]	Decrease	Decrease
B. [2%]	Increase	Increase
C. [1%]	Increase	No change
D. [8%]	No change	Decrease
✔ E. [82%]	No change	No change

Omitted
Correct answer
E

82%
Answered correctly

3 Seconds
Time Spent

10/28/2018
Last Updated

Biochemical findings in Cushing syndrome			
Etiology	**ACTH**	**Cortisol**	**High-dose dexamethasone suppression test**
Pituitary adenoma	↑	↑	↓ Cortisol
Ectopic ACTH secretion	↑	↑	Cortisol remains elevated
Adrenal adenoma/carcinoma	↓	↑	

This patient's hypertension, proximal muscle weakness, and hyperglycemia are suggestive of excess cortisol (ie, **Cushing syndrome** [CS]). Hypercortisolism can be confirmed by finding elevated cortisol levels in a late-night salivary sample or 24-hour urine collection. Additionally, low-dose dexamethasone suppression testing can also be useful for confirming the diagnosis; administration of a small dose of a potent glucocorticoid rapidly **suppresses ACTH** and cortisol secretion in normal individuals, but patients with CS are resistant to low-dose glucocorticoids so serum cortisol remains elevated.

Once the diagnosis is confirmed, the next step is **establishing the cause** of CS, which involves measurement of **serum ACTH levels**:

- Low ACTH levels are seen with autonomous adrenal production of cortisol (eg, adrenal adenoma or carcinoma) or exogenous glucocorticoid exposure due to feedback suppression
- **High ACTH** levels occur with pituitary adenomas (ie, Cushing disease) or ectopic ACTH production by nonpituitary tumors, which can be further distinguished with the **high-dose dexamethasone suppression test**:
  - Pituitary sources of ACTH are only relatively resistant to feedback inhibition, and high doses of dexamethasone will suppress ACTH and cortisol levels **(Choice A)**
  - Nonpituitary **ectopic sources** of ACTH (eg, **small cell lung cancer**) are completely resistant to feedback inhibition, and ACTH and cortisol will remain elevated following high doses of dexamethasone

cortisol remains elevated.

Once the diagnosis is confirmed, the next step is **establishing the cause** of CS, which involves measurement of **serum ACTH levels**:

- Low ACTH levels are seen with autonomous adrenal production of cortisol (eg, adrenal adenoma or carcinoma) or exogenous glucocorticoid exposure due to feedback suppression
- **High ACTH** levels occur with pituitary adenomas (ie, Cushing disease) or ectopic ACTH production by nonpituitary tumors, which can be further distinguished with the **high-dose dexamethasone suppression test**:
  - Pituitary sources of ACTH are only relatively resistant to feedback inhibition, and high doses of dexamethasone will suppress ACTH and cortisol levels **(Choice A)**
  - Nonpituitary **ectopic sources** of ACTH (eg, **small cell lung cancer**) are completely resistant to feedback inhibition, and ACTH and cortisol will remain elevated following high doses of dexamethasone

This patient's rapid symptom onset, heavy smoking history, and lung mass are consistent with paraneoplastic CS, likely due to small cell lung cancer. **ACTH and cortisol production** will likely be **unchanged** following high-dose dexamethasone.

(Choices B and C) In normal individuals, dexamethasone suppresses ACTH release from the pituitary. In patients with abnormal pituitary or ectopic ACTH production, dexamethasone affects ACTH levels as described above. However, dexamethasone does not stimulate ACTH release in any setting.

(Choice D) The fall in cortisol seen in dexamethasone suppression tests is due to feedback suppression causing decreased ACTH release. A fall in cortisol would not be seen without a corresponding fall in ACTH.

Educational objective:
Cushing syndrome caused by a pituitary adenoma or ectopic (paraneoplastic) ACTH secretion is associated with elevated ACTH levels. High-dose dexamethasone suppresses ACTH and cortisol secretion when Cushing syndrome is caused by a pituitary adenoma (Cushing disease) but not when it is caused by ectopic ACTH secretion (eg, small cell lung cancer).

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Item 28 of 29
Question Id: 927

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

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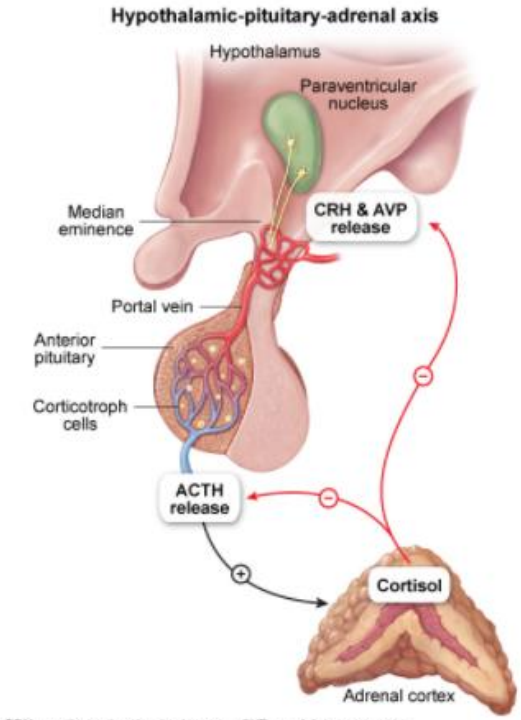

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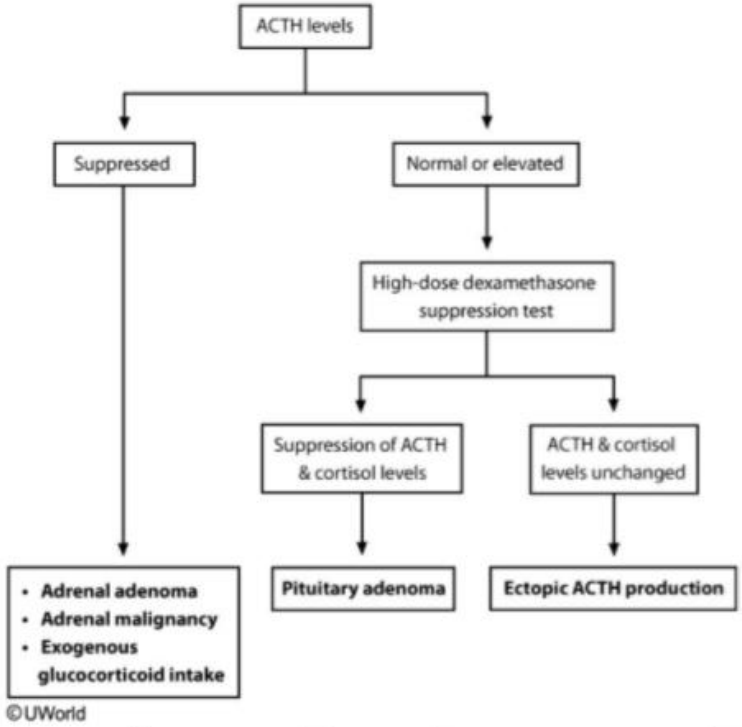
28

Item 28 of 29
Question Id: 927

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

Exhibit Display

Diagnosing the cause of Cushing syndrome



Zoom In | Zoom Out | Reset | Add To Flash Card

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4 | Feedback | Suspend | End Block

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Item 29 of 29
Question Id: 7651

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 45-year-old man comes to the office due to slowly progressive back and joint pain. In particular, his knee and ankle joints are stiff and painful when he walks. Over the past year, the patient has also experienced excessive sweating, and his ring and shoe sizes have increased. He has no prior medical issues and takes no medications. The patient does not use tobacco, alcohol, or illicit drugs. There is no significant family history. Physical examination shows coarse facial features with a prominent forehead, protruding jaw, and widely separated maxillary teeth. There is mild swelling and crepitus of the knees and ankles bilaterally. Which of the following is most likely to be associated with this patient's condition?

- A. Aortic root dilation
- B. Bicuspid aortic valve
- C. Left ventricular hypertrophy
- D. Mitral valve prolapse
- E. Pericardial effusion

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4 | Feedback | Suspend | End Block

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Item 29 of 29
Question Id: 7651

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

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- A. Aortic root dilation [17%]
- B. Bicuspid aortic valve [2%]
- ✔ C. Left ventricular hypertrophy [66%]
- D. Mitral valve prolapse [9%]
- E. Pericardial effusion [2%]

Omitted
Correct answer
C

66%
Answered correctly

3 Seconds
Time Spent

02/09/2019
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Explanation

Acromegaly

Enlarged facial features

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4 | Feedback | Suspend | End Block

5:05 PM
2/12/2019

Settings

Item 29 of 29
Question Id: 7651

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

- 2
- 3
- 4
- 5
- 6
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- 10
- 11
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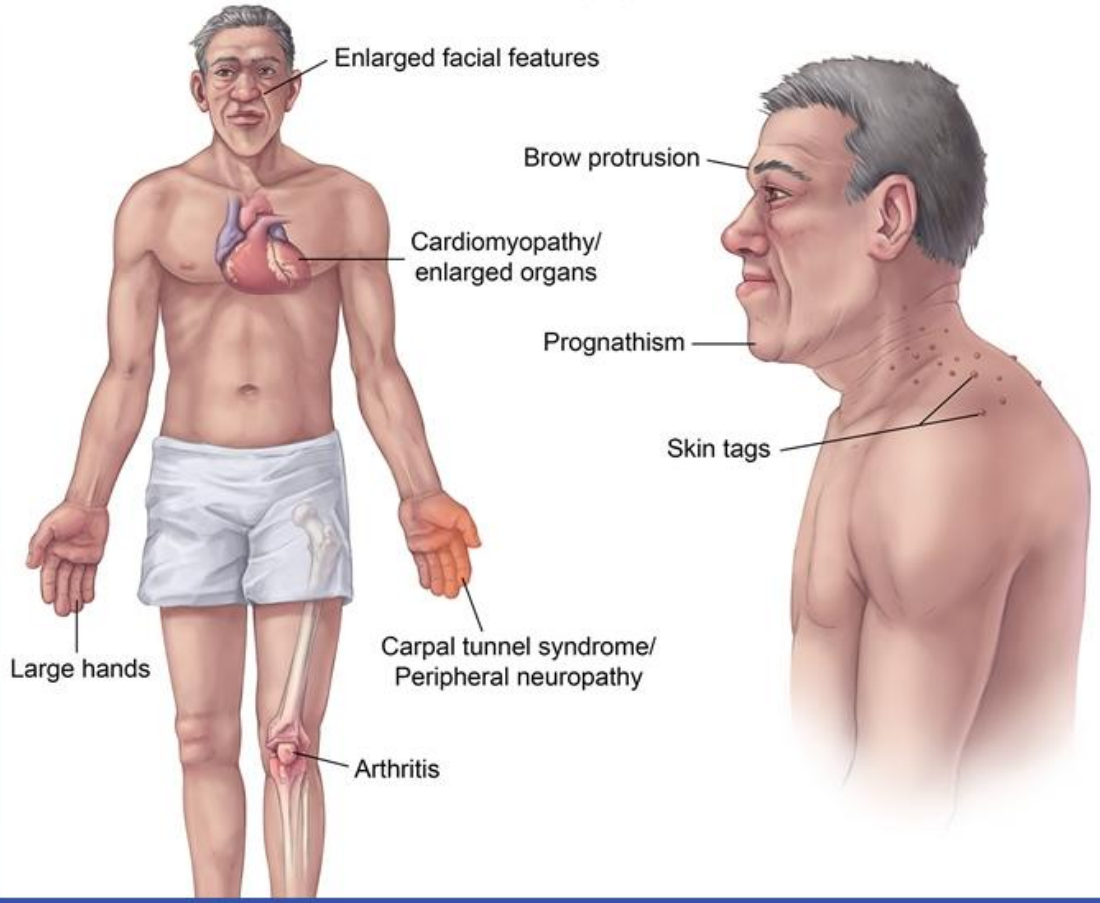
Acromegaly



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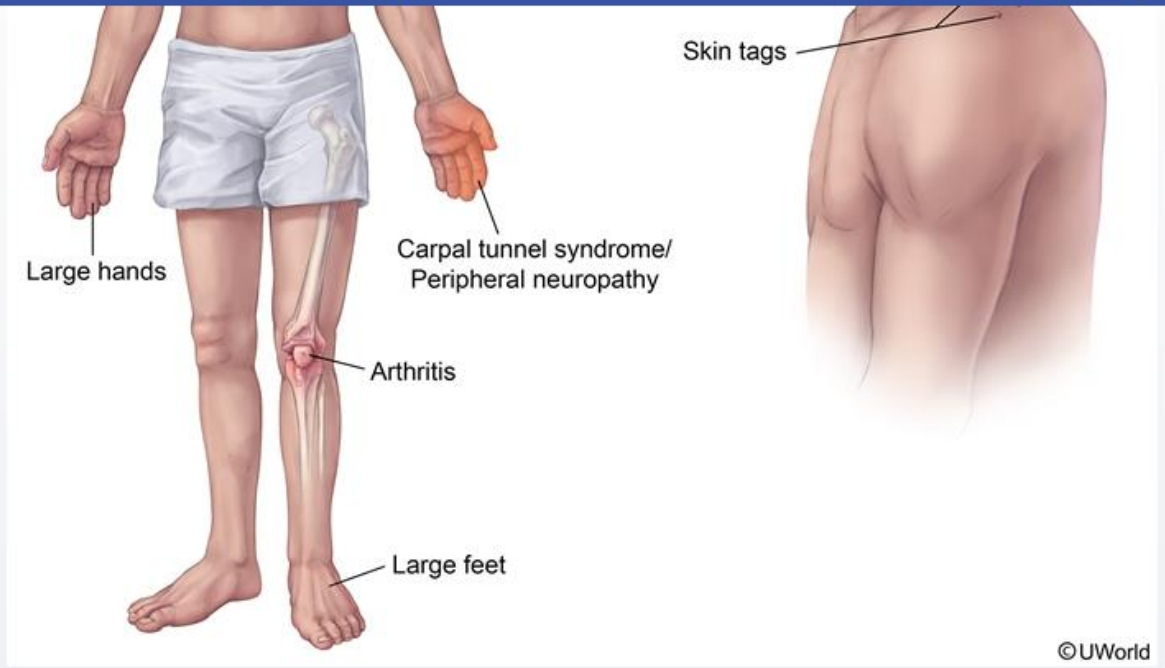

This patient has bony overgrowth (ie, frontal bossing; enlarged jaw, hands, and feet) consistent with acromegaly. **Acromegaly** is caused by excessive production of **growth hormone** (GH) and is most often due to a pituitary somatotroph adenoma. Excess GH both directly and indirectly (via release of insulin-like growth factor 1 from the liver) leads to overgrowth of many tissues, including bone, cartilage, and visceral organs.

In the heart, chronic GH elevation stimulates cardiac growth, causing **left ventricular hypertrophy**, diastolic dysfunction, and possible heart failure. The joints are also frequently involved in acromegaly, as excessive GH causes hyperplasia of articular chondrocytes and synovial hypertrophy, leading to wear and degeneration of articular cartilage and periarticular bone (hypertrophic **arthropathy**). Soft tissue involvement is also common and manifests as macroglossia, deepening of the voice (due to laryngeal soft tissue growth), carpal tunnel syndrome, and peripheral

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(Choices A and D) Marfan syndrome is an inherited condition caused by a defect in fibrillin-1. Cardiovascular complications include cystic medial degeneration of the aorta (with aneurysmal dilation and dissection), aortic regurgitation, and mitral valve prolapse. However, unlike the bony enlargement in acromegaly, the typical **marfanoid habitus** is characterized by a tall, slender build and an increased ratio of limb length-to-height.

(Choice B) Ehlers-Danlos syndrome is due to an autosomal recessive defect in lysyl hydroxylase, which leads to defects in connective tissues (eg, fragile, hyperextensible skin). Musculoskeletal manifestations include hypermobile joints, pectus excavatum, and scoliosis. Valvular heart disease is common and can present as bicuspid aortic valve or mitral/tricuspid valve prolapse.

(Choice E) Patients with untreated hypothyroidism can have a pericardial effusion, and also frequently have nonpitting edema (myxedema) due to excessive deposition of mucopolysaccharides and adipogenesis in the dermis and subcutaneous tissues. However, bony enlargement is not characteristic.

Educational objective:
Acromegaly is caused by excessive production of growth hormone, usually due to a pituitary somatotroph adenoma. Musculoskeletal manifestations include bony hypertrophy (eg, frontal bossing; enlarged jaw, hands, and feet) and osteoarthritis. Left ventricular hypertrophy is often common in acromegaly and may progress to heart failure.

References

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