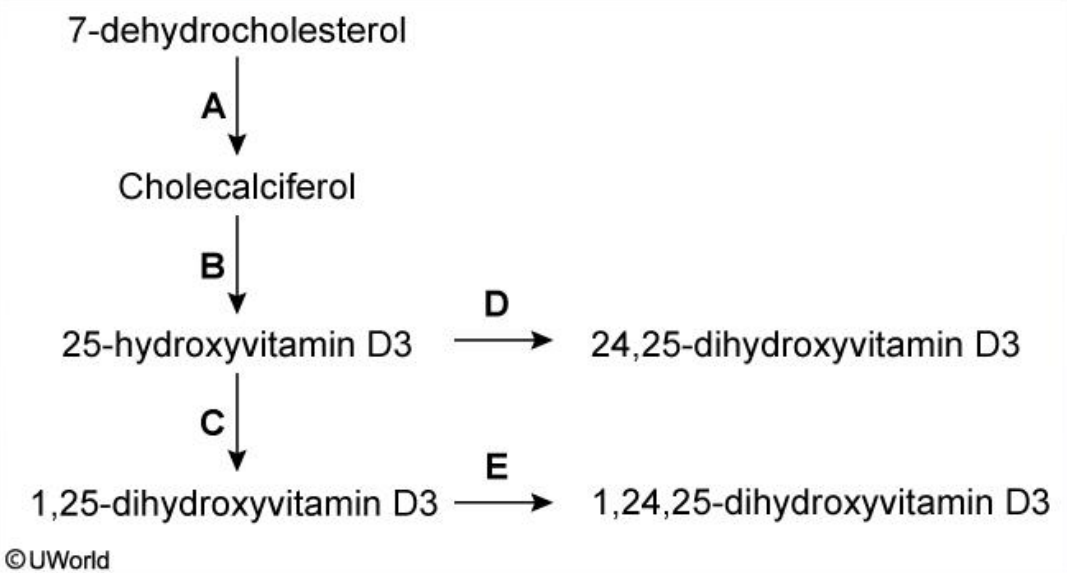
Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 1 of 16
Question Id: 991

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

A 34-year-old man with type 1 diabetes mellitus comes to the office due to achy pain in the shoulders, elbows, and thighs over the past several months. The patient was diagnosed with diabetes 15 years ago and has had difficulty adequately controlling it. He currently takes multiple daily injections of insulin. Vital signs are within normal limits. Physical examination shows mild pedal edema. Serum creatinine is 2.2 mg/dL, up from 1.6 mg/dL six months ago. Additional laboratory results show low serum calcium and elevated parathyroid hormone levels. Inhibition of which of the following enzymatic steps is most likely responsible for this patient's current symptoms?



A. A
B. B

Block Time Remaining: 00:00:03
TUTOR

Feedback | Suspend | End Block

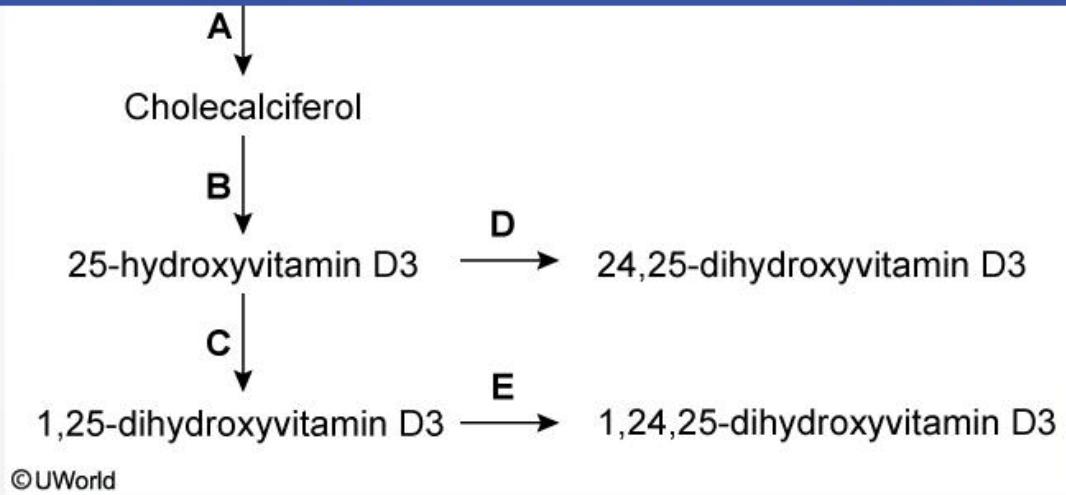
2:10 PM
2/12/2019

Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 1 of 16
Question Id: 991

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



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

Submit

Block Time Remaining: 00:00:05
TUTOR

0 | Feedback | Suspend | End Block

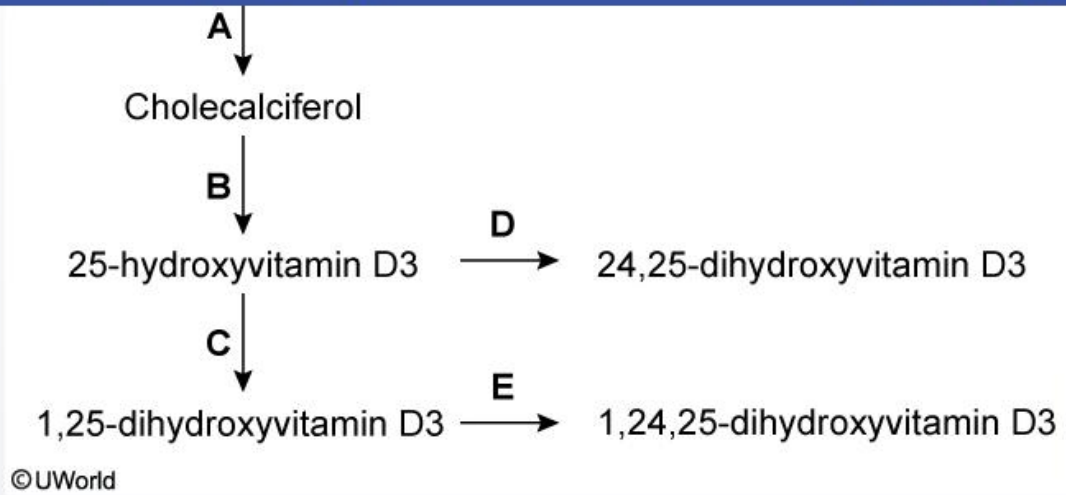
2:10 PM
2/12/2019

Settings

Item 1 of 16
Question Id: 991

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

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16



©UWorld

- A. A [1%]
- B. B [5%]
- ✔ C. C [82%]
- D. D [3%]
- E. E [6%]

Omitted
Correct answer

82%
Answered correctly

9 Seconds
Time Spent

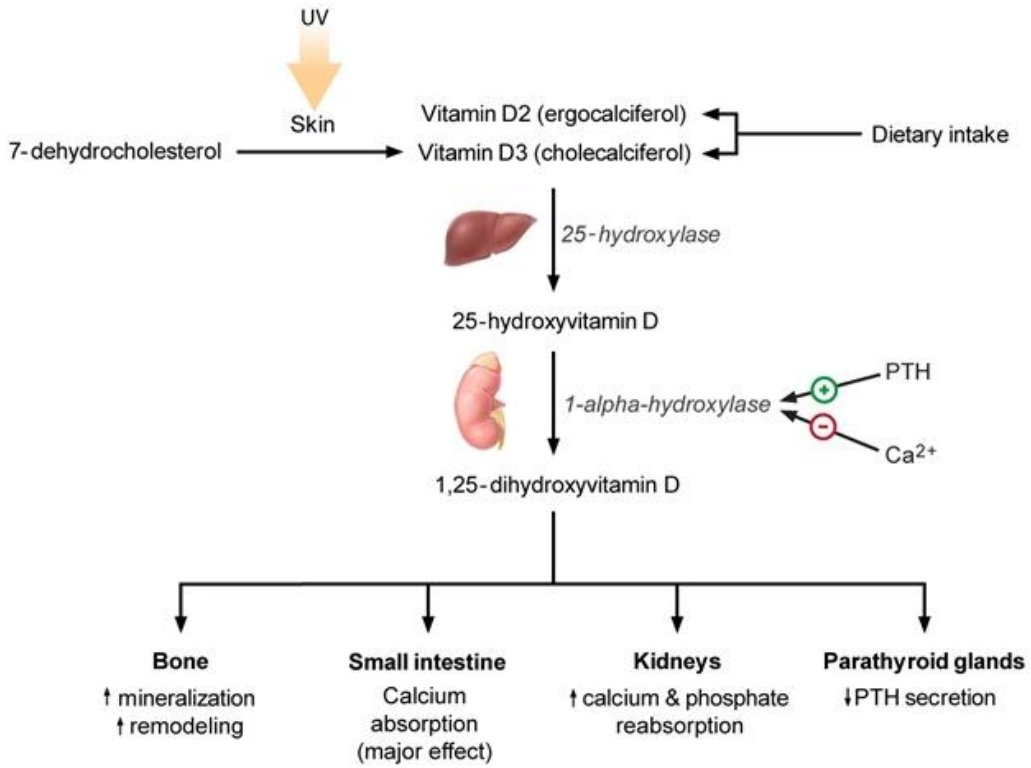
10/16/2018
Last Updated

Block Time Remaining: 00:00:09
TUTOR

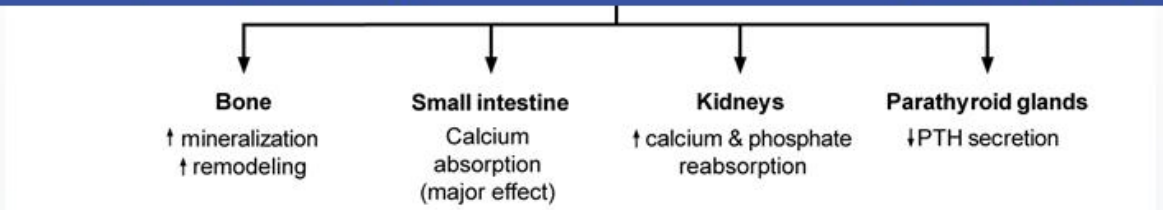
0 | Feedback | Suspend | End Block

2:10 PM
2/12/2019

Normal vitamin D metabolism



PTH = parathyroid hormone.



PTH = parathyroid hormone.
©UWorld

Synthesis of vitamin D begins in the skin with the conversion of 7-dehydrocholesterol to cholecalciferol (vitamin D3) by ultraviolet light. Cholecalciferol is subsequently converted to 25-hydroxyvitamin D (the primary body store of vitamin D) by 25-hydroxylase in the liver. Finally, **25-hydroxyvitamin D** is filtered by renal glomeruli (with vitamin D-binding protein) and delivered to proximal tubule cells, where 1-alpha-hydroxylase converts it to **1,25-dihydroxyvitamin D**, the physiologically active form. The activity of 1-alpha-hydroxylase is upregulated by parathyroid hormone (PTH) and inhibited by fibroblast growth factor 23 (FGF23), a peptide secreted by osteocytes in response to high levels of 1,25-dihydroxyvitamin D.

Chronic kidney disease (CKD) results in impaired conversion of 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D due to the following factors:

- FGF23 levels increase early in CKD, causing direct inhibition of 1-alpha-hydroxylase
- Reduced glomerular filtration limits the delivery of 25-hydroxyvitamin D to proximal tubule cells
- Reduced functional renal mass limits production of 1-alpha-hydroxylase

Inadequate production of 1,25-dihydroxyvitamin D causes reduced intestinal absorption of calcium. This, along with increased phosphate retention (due to impaired glomerular and tubular function), leads to a compensatory increase in parathyroid hormone secretion (**secondary hyperparathyroidism**). Chronically increased PTH levels have a deleterious effect on bone metabolism (**renal osteodystrophy**), and can cause weakness, bone and muscle pain, defective bone mineralization, and an increased risk of fractures.

(Choice A) The initial step in vitamin D synthesis is driven by ultraviolet exposure in the skin. Factors that can lead to vitamin D deficiency

- Reduced functional renal mass limits production of 1-alpha-hydroxylase

Inadequate production of 1,25-dihydroxyvitamin D causes reduced intestinal absorption of calcium. This, along with increased phosphate retention (due to impaired glomerular and tubular function), leads to a compensatory increase in parathyroid hormone secretion (**secondary hyperparathyroidism**). Chronically increased PTH levels have a deleterious effect on bone metabolism (**renal osteodystrophy**), and can cause weakness, bone and muscle pain, defective bone mineralization, and an increased risk of fractures.

(Choice A) The initial step in vitamin D synthesis is driven by ultraviolet exposure in the skin. Factors that can lead to vitamin D deficiency include inadequate sunlight exposure (eg, institutionalized elders, living at extreme latitudes), use of high-grade sunblock, nocturnal occupations, and heavily pigmented skin.

(Choice B) 25-Hydroxyvitamin D deficiency due to inadequate 25-hydroxylase activity can be seen in patients with liver disease, but is uncommon and primarily seen in those with advanced cirrhosis.

(Choices D and E) Vitamin D-24-hydroxylase converts 25- and 1,25-dihydroxyvitamin D into inactive 24-hydroxylated metabolites; it functions to degrade excess levels of vitamin D. Although it is expressed predominantly in the kidneys and may be impaired in chronic kidney disease, loss of this enzyme would lead to higher 1,25-dihydroxyvitamin D levels and so would reduce, rather than worsen, the patient's symptoms.

Educational objective:
In chronic kidney disease, conversion of 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D is impaired. In addition, failure of glomerular and tubular function results in phosphate retention and hypocalcemia. This leads to a compensatory rise in parathyroid hormone (secondary hyperparathyroidism) that can present with weakness, muscle and joint pain, defective bone mineralization, and increased fracture risk.

References

- Impaired vitamin D metabolism in CKD.

Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 2 of 16
Question Id: 954

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

A 22-year-old primigravida who recently emigrated from the Dominican Republic has a normal vaginal delivery. The infant is phenotypically male but has hypospadias and a small phallus. The testes are well developed but reside in the inguinal area. His physical examination, including blood pressure, is otherwise normal. Serum testosterone level is within normal limits. A karyotype is performed and shows 46,XY. Which of the following enzymes is most likely deficient in this patient?

A. 5α-reductase
B. 17-hydroxylase
C. 21-hydroxylase
D. Aromatase
E. DHEA sulfatase

Submit

Block Time Remaining: 00:00:10
TUTOR

0 | Feedback | Suspend | End Block

2:11 PM
2/12/2019

Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 2 of 16
Question Id: 954

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

A 22-year-old primigravida who recently emigrated from the Dominican Republic has a normal vaginal delivery. The infant is phenotypically male but has hypospadias and a small phallus. The testes are well developed but reside in the inguinal area. His physical examination, including blood pressure, is otherwise normal. Serum testosterone level is within normal limits. A karyotype is performed and shows 46,XY. Which of the following enzymes is most likely deficient in this patient?

- A. 5α-reductase [71%]
- B. 17-hydroxylase [8%]
- C. 21-hydroxylase [6%]
- D. Aromatase [6%]
- E. DHEA sulfatase [6%]

Omitted
Correct answer
A

71%
Answered correctly

4 Seconds
Time Spent

01/30/2019
Last Updated

Explanation

5α-reductase deficiency

Cholesterol

Activate Windows
Go to Settings to activate Windows.

Block Time Remaining: 00:00:14
TUTOR

0 | Feedback | Suspend | End Block

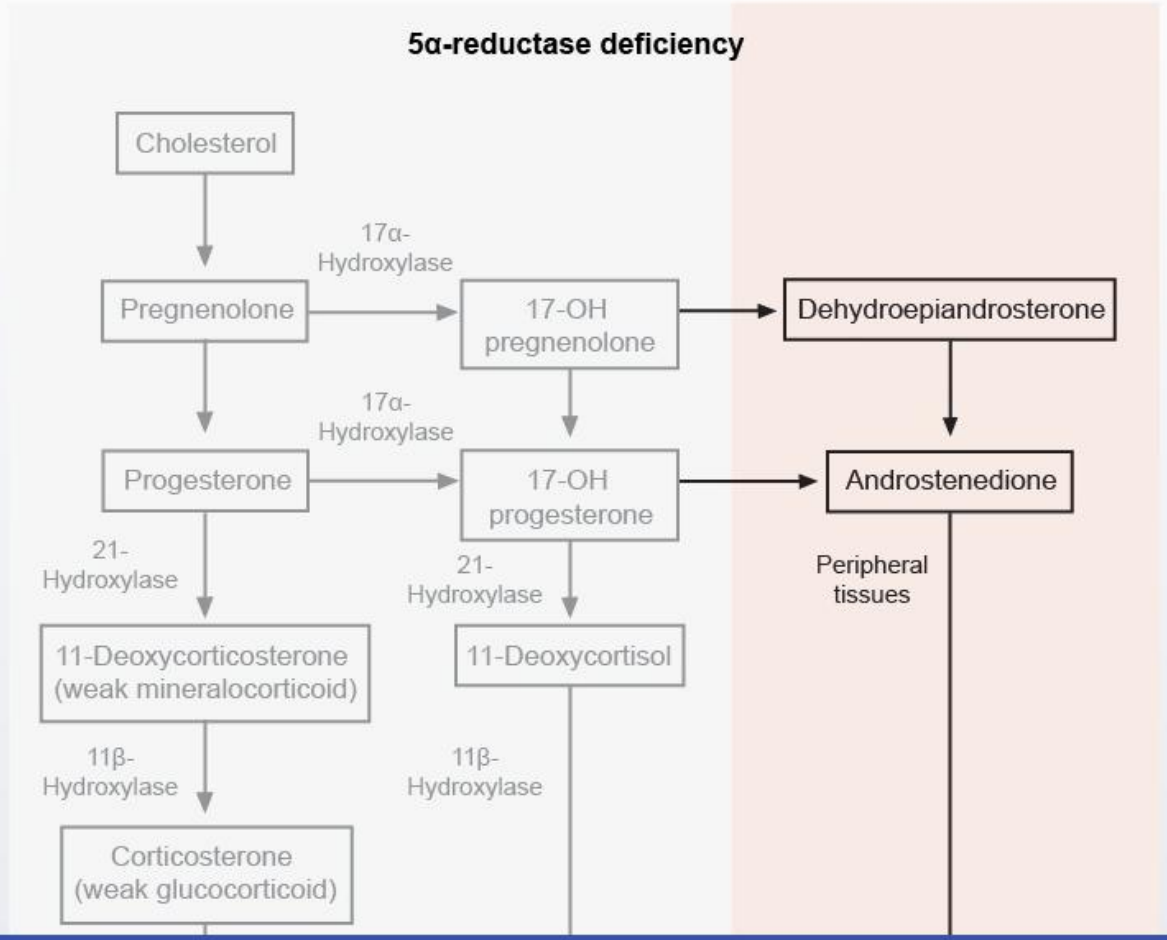
2:11 PM
2/12/2019

Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 2 of 16
Question Id: 954

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



Block Time Remaining: 00:00:14
TUTOR

0 | Feedback | Suspend | End Block

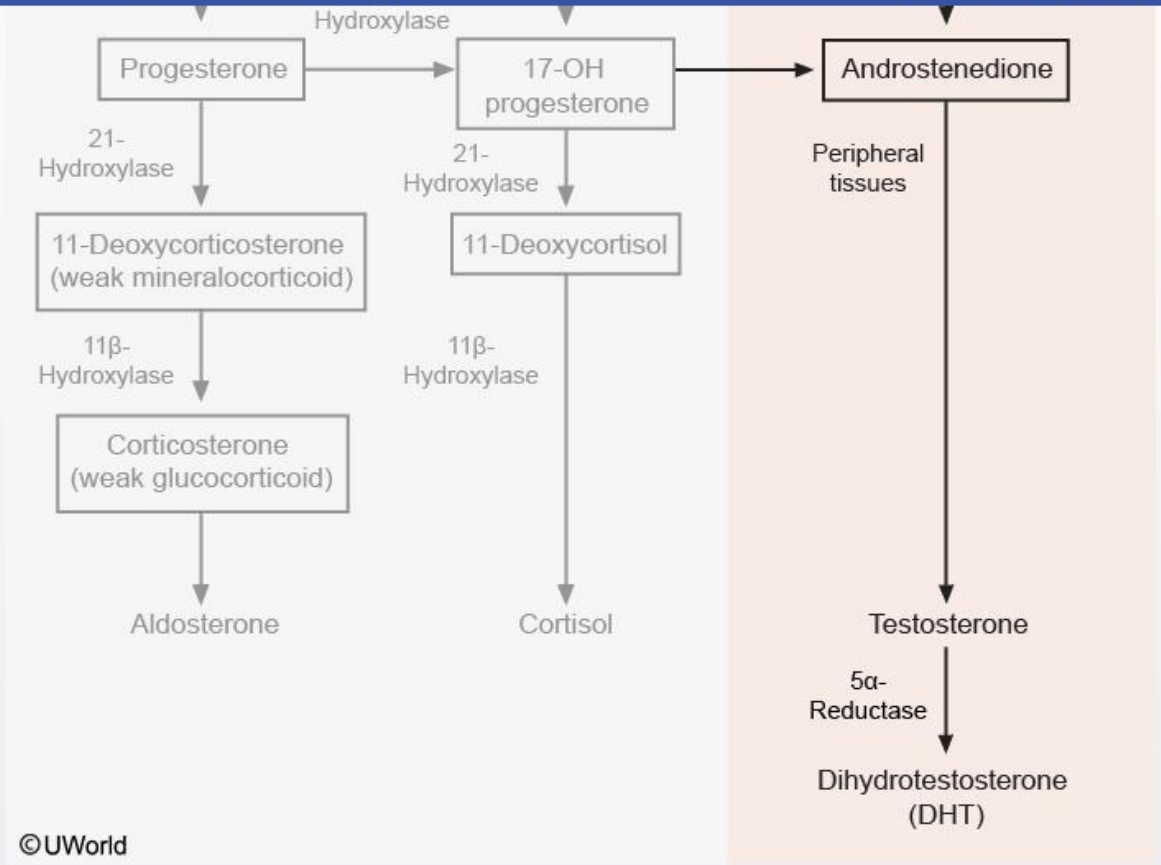
2:11 PM
2/12/2019

Settings

- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10
- 11
- 12
- 13
- 14
- 15
- 16

Item 2 of 16
Question Id: 954

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



Sexual development is influenced predominantly by 3 hormones:

- **Testosterone**: Development of internal male genitalia, spermatogenesis, male sexual differentiation at puberty (muscle mass, libido)

Block Time Remaining: 00:00:14
TUTOR

0 | Feedback | Suspend | End Block

2:11 PM
2/12/2019

Settings

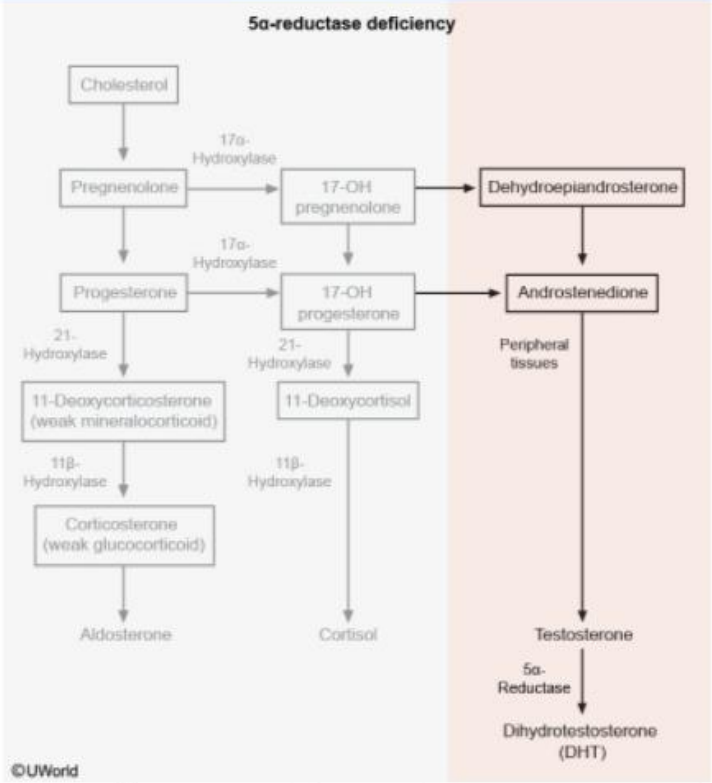
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 2 of 16
Question Id: 954

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

Hydroxylase

Exhibit Display



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

- **Testosterone**: Development of internal male genitalia, spermatogenesis, male sexual differentiation at puberty (muscle mass, libido)

Block Time Remaining: 00:00:14
TUTOR

0 | Feedback | Suspend | End Block

2:11 PM
2/12/2019

(DHT)

Sexual development is influenced predominantly by 3 hormones:

- **Testosterone**: Development of internal male genitalia, spermatogenesis, male sexual differentiation at puberty (muscle mass, libido)
- **Dihydrotestosterone** (DHT): Development of external male genitalia, growth of prostate, male-pattern hair growth; also amplifies effects of testosterone due to high affinity for testosterone receptor.
- **Estrogen**: Endometrial proliferation, development of ovarian granulosa cells, breast development

5α-reductase converts testosterone to DHT. There are 2 types of 5α-reductase; type 1 is present in postpubescent skin, whereas type 2 is found predominantly in the genitals. Deficiency of **5α-reductase type 2** results in diminished conversion of testosterone to DHT in the male urogenital tract. In the male fetus with this genetic defect, the internal genitalia develop normally under the influence of testosterone, but the external genitalia do not develop properly due to the lack of DHT, resulting in **male pseudohermaphroditism**. The genitalia at birth can range from a small phallus with hypospadias to ambiguous or female-type genitalia. Such children are often raised as females until they reach puberty, when high levels of testosterone and the action of 5α-reductase type 1 result in masculinization with male-pattern muscle mass, voice deepening, penile and scrotal growth, and testicular descent.

(Choice B) Deficiency of 17-hydroxylase results in decreased secretion of cortisol and sex steroids and an increased level of mineralocorticoids. This deficiency manifests clinically with sodium retention, leading to hypertension and undervirilization of male infants (female-type genitalia).

(Choice C) 21-hydroxylase converts 17-hydroxyprogesterone to 11-deoxycortisol, and progesterone to 11-deoxycorticosterone. Deficiency of 21-hydroxylase causes corticosteroid precursors to be shunted toward androgen production, resulting in virilization of the female fetus and salt wasting. Male children have salt wasting and normal genitalia.

(Choice D) Aromatase catalyzes the conversion of androgens to estrogens in the gonads and peripheral tissues. Aromatase deficiency presents with virilization of female infants; male patients are not affected phenotypically.

(Choice E) Dehydroepiandrosterone (DHEA) sulfate is a weak androgen produced by the adrenal cortex. Deficiency of DHEA sulfatase does not

genitalia do not develop properly due to the lack of DHT, resulting in **male pseudohermaphroditism**. The genitalia at birth can range from a small phallus with hypospadias to ambiguous or female-type genitalia. Such children are often raised as females until they reach puberty, when high levels of testosterone and the action of 5α-reductase type 1 result in masculinization with male-pattern muscle mass, voice deepening, penile and scrotal growth, and testicular descent.

(Choice B) Deficiency of 17-hydroxylase results in decreased secretion of cortisol and sex steroids and an increased level of mineralocorticoids. This deficiency manifests clinically with sodium retention, leading to hypertension and undervirilization of male infants (female-type genitalia).

(Choice C) 21-hydroxylase converts 17-hydroxyprogesterone to 11-deoxycortisol, and progesterone to 11-deoxycorticosterone. Deficiency of 21-hydroxylase causes corticosteroid precursors to be shunted toward androgen production, resulting in virilization of the female fetus and salt wasting. Male children have salt wasting and normal genitalia.

(Choice D) Aromatase catalyzes the conversion of androgens to estrogens in the gonads and peripheral tissues. Aromatase deficiency presents with virilization of female infants; male patients are not affected phenotypically.

(Choice E) Dehydroepiandrosterone (DHEA) sulfate is a weak androgen produced by the adrenal cortex. Deficiency of DHEA sulfatase does not result in undervirilization of the male fetus.

Educational objective:
5α-reductase converts testosterone to dihydrotestosterone, which mediates development of the external genitalia in the male fetus. Male neonates with 5α-reductase deficiency are born with feminized external genitalia that typically masculinize at puberty. A small phallus and hypospadias are common.

References

- 5-Alpha reductase deficiency: a 40-year retrospective review.

Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 3 of 16
Question Id: 217

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

A 21-year-old man undergoes a routine pre-employment physical examination. During testicular examination, he is found to have only 1 testis in his scrotum. Further evaluation reveals an elevated serum FSH level and a normal serum LH level. Production of which of the following substances is likely to be impaired in this patient?

A. Testosterone
B. Dihydrotestosterone
C. DHEA
D. Inhibin B
E. Cortisol

Submit

Block Time Remaining: 00:00:15
TUTOR

0 | Feedback | Suspend | End Block

Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 3 of 16
Question Id: 217

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

A 21-year-old man undergoes a routine pre-employment physical examination. During testicular examination, he is found to have only 1 testis in his scrotum. Further evaluation reveals an elevated serum FSH level and a normal serum LH level. Production of which of the following substances is likely to be impaired in this patient?

A. Testosterone [10%]
B. Dihydrotestosterone [6%]
C. DHEA [3%]
✔ D. Inhibin B [78%]
E. Cortisol [0%]

Omitted
Correct answer
D

78%
Answered correctly

4 Seconds
Time Spent

11/30/2018
Last Updated

Explanation

Gonadotropin regulation

Hypothalamus

Block Time Remaining: 00:00:17
TUTOR

0 | Feedback | Suspend | End Block

2:11 PM
2/12/2019

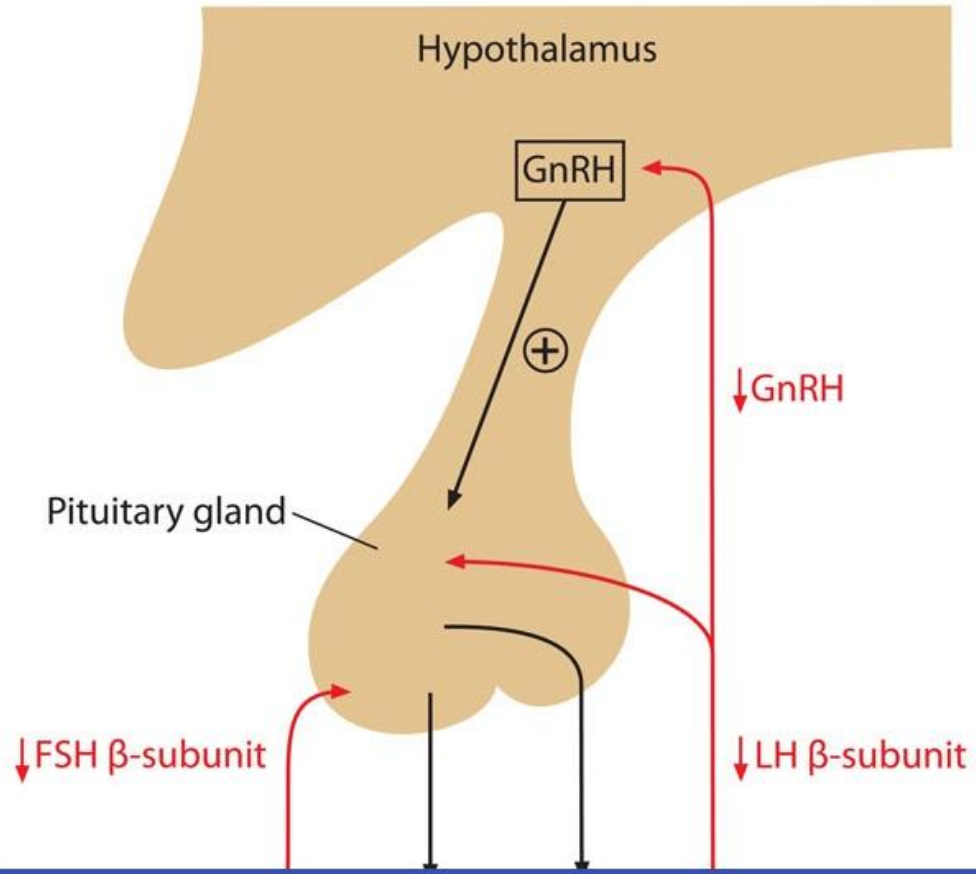
Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 3 of 16
Question Id: 217

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

Gonadotropin regulation



Block Time Remaining: 00:00:17
TUTOR

Feedback | Suspend | End Block

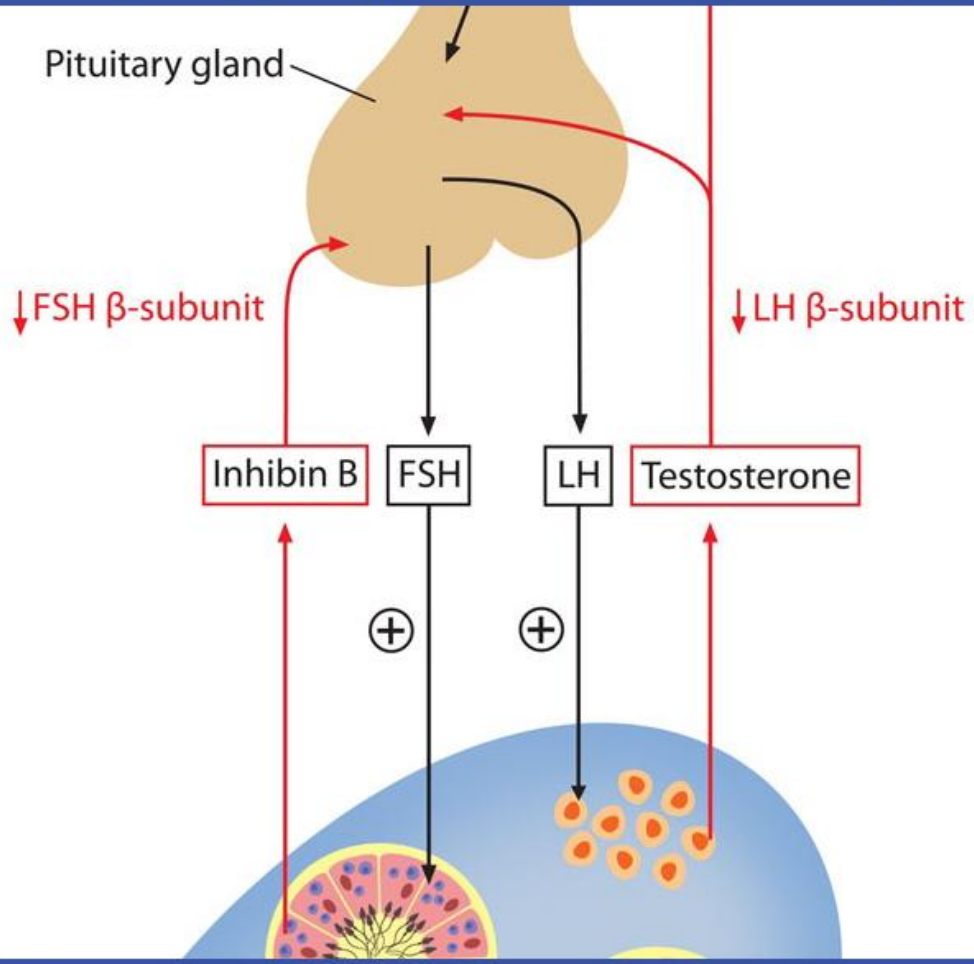
2:11 PM
2/12/2019

Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 3 of 16
Question Id: 217

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



Block Time Remaining: 00:00:17
TUTOR

Feedback | Suspend | End Block

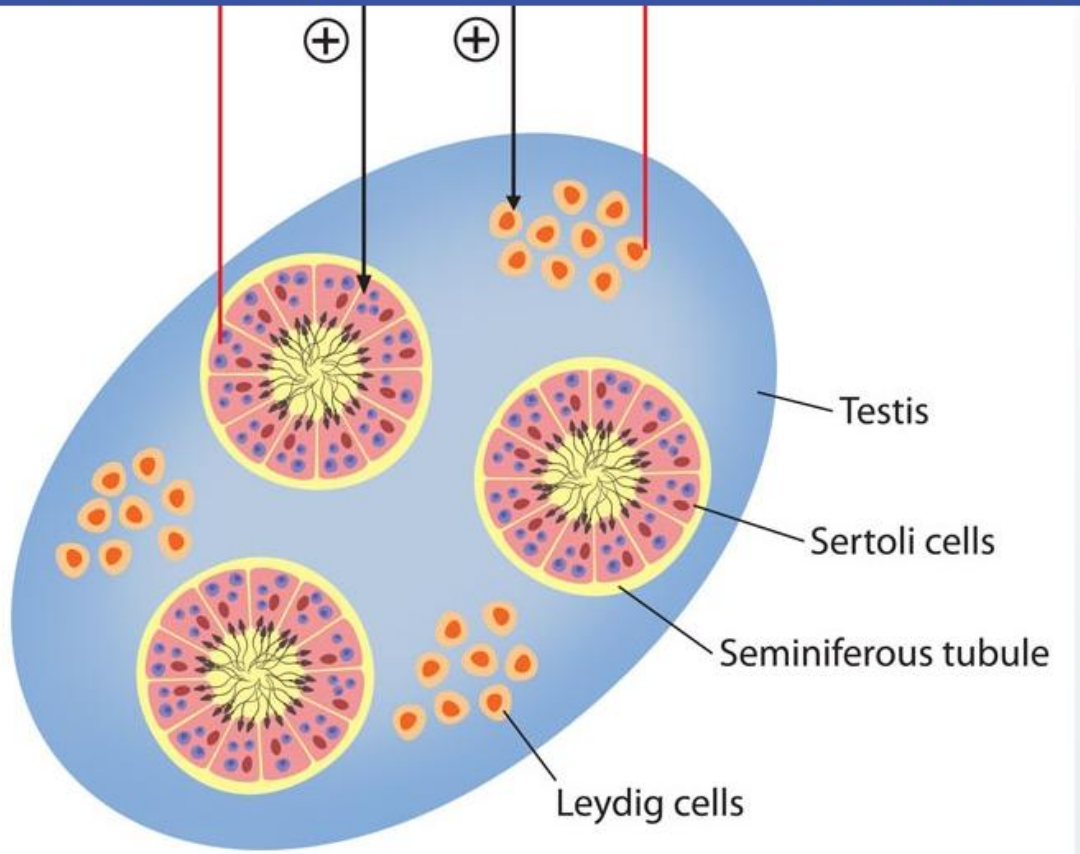
2:11 PM
2/12/2019

Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 3 of 16
Question Id: 217

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



Pulsatile secretion of gonadotrophin-releasing hormone (GnRH) from the hypothalamus stimulates the release of follicle-stimulating hormone

Block Time Remaining: 00:00:17
TUTOR

0 | Feedback | Suspend | End Block

2:11 PM
2/12/2019

Settings

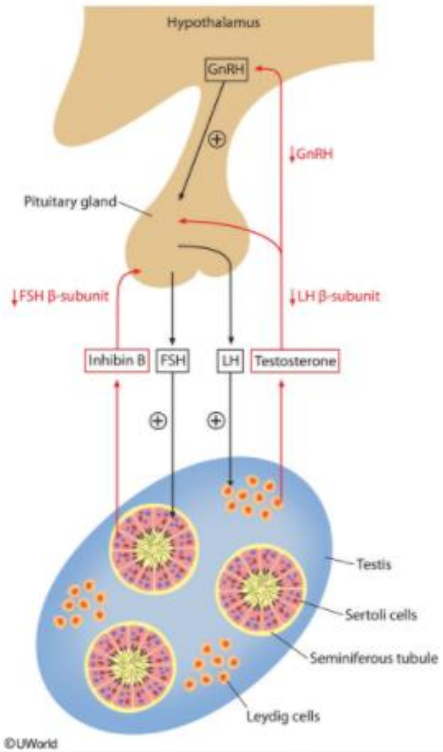
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 3 of 16
Question Id: 217

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

Exhibit Display

Gonadotropin regulation



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

Block Time Remaining: 00:00:17
TUTOR

Feedback | Suspend | End Block

2:11 PM
2/12/2019

Pulsatile secretion of gonadotrophin-releasing hormone (GnRH) from the hypothalamus stimulates the release of follicle-stimulating hormone (FSH) and luteinizing hormone (LH). Both FSH and LH are produced by the gonadotroph cells of the anterior pituitary. LH stimulates the release of testosterone from the Leydig cells of the testes; FSH stimulates the release of inhibin B from the Sertoli cells of the testes. Testosterone has a negative feedback effect on LH and GnRH secretion, and inhibin B suppresses FSH secretion.

Sertoli cells are present within the seminiferous tubules of the testes. In patients with 1 testicle, the mass of Sertoli cells is significantly reduced. Therefore, the circulating levels of inhibin B are likely to be low in these patients. Low inhibin B levels will not provide adequate negative feedback on FSH secretion, thus FSH levels will tend to be elevated in males who only have 1 testicle.

A male patient of any age who has only 1 testicle requires further evaluation. Since there is an increased cancer risk in men with an undescended testicle, most of these "abdominal testicles" are either removed (orchiectomy) or receive surgery that allows descent into the scrotum (orchiopexy).

(Choices A, B, and C) Although the number of Leydig cells is reduced when only 1 testicle is present, androgen levels are not affected due to compensation by the remaining Leydig cell mass. Additionally, this patient has a normal LH level, indicating that there is adequate androgenic feedback to the hypothalamus and pituitary. Testosterone, dihydrotestosterone, and DHEA cause LH feedback inhibition, but they are not part of the FSH feedback loop.

(Choice E) Cortisol has no direct relationship with LH and FSH secretion. High circulatory levels of cortisol, however, do produce hypogonadotropic hypogonadism by suppressing the release of gonadotrophin-releasing hormone.

Educational objective:
Inhibin B is produced by the Sertoli cells and is the physiological inhibitor of FSH secretion. LH concentration is controlled primarily by testosterone feedback.

Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 4 of 16
Question Id: 992

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

A 14-year-old boy is brought to the emergency department after accidental ingestion of a chicken bone that lodged in his esophagus. Upper endoscopy is performed and the bone is successfully removed. However, the patient is incidentally found to have mild hypercalcemia on laboratory testing. On follow-up with his primary care provider 2 weeks later, he has no symptoms and clinical examination is unremarkable. Further questioning reveals that several of his family members also have mild hypercalcemia. Subsequent laboratory studies show a borderline high parathyroid hormone concentration, very low urinary calcium level, and normal 25-hydroxyvitamin D level. A mutation in which of the following receptors is most likely responsible for this patient's laboratory abnormalities?

A. Intracellular receptor with a DNA-binding domain
B. Membrane-bound receptor coupled with a G protein
C. Transmembrane ligand-gated ion channel
D. Transmembrane receptor associated with intrinsic tyrosine kinase activity
E. Transmembrane receptor causing activation of Janus kinase/STAT pathway

Submit

Block Time Remaining: 00:00:18
TUTOR

0 | Feedback | Suspend | End Block

2:11 PM
2/12/2019

Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 4 of 16
Question Id: 992

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

A 14-year-old boy is brought to the emergency department after accidental ingestion of a chicken bone that lodged in his esophagus. Upper endoscopy is performed and the bone is successfully removed. However, the patient is incidentally found to have mild hypercalcemia on laboratory testing. On follow-up with his primary care provider 2 weeks later, he has no symptoms and clinical examination is unremarkable. Further questioning reveals that several of his family members also have mild hypercalcemia. Subsequent laboratory studies show a borderline high parathyroid hormone concentration, very low urinary calcium level, and normal 25-hydroxyvitamin D level. A mutation in which of the following receptors is most likely responsible for this patient's laboratory abnormalities?

- A. Intracellular receptor with a DNA-binding domain [7%]
- ✔ B. Membrane-bound receptor coupled with a G protein [55%]
- C. Transmembrane ligand-gated ion channel [20%]
- D. Transmembrane receptor associated with intrinsic tyrosine kinase activity [9%]
- E. Transmembrane receptor causing activation of Janus kinase/STAT pathway [7%]

Omitted
Correct answer
B

55%
Answered correctly

3 Seconds
Time Spent

10/05/2018
Last Updated

Explanation

Calcium homeostasis

Block Time Remaining: 00:00:20
TUTOR

0 | Feedback | Suspend | End Block

2:11 PM
2/12/2019

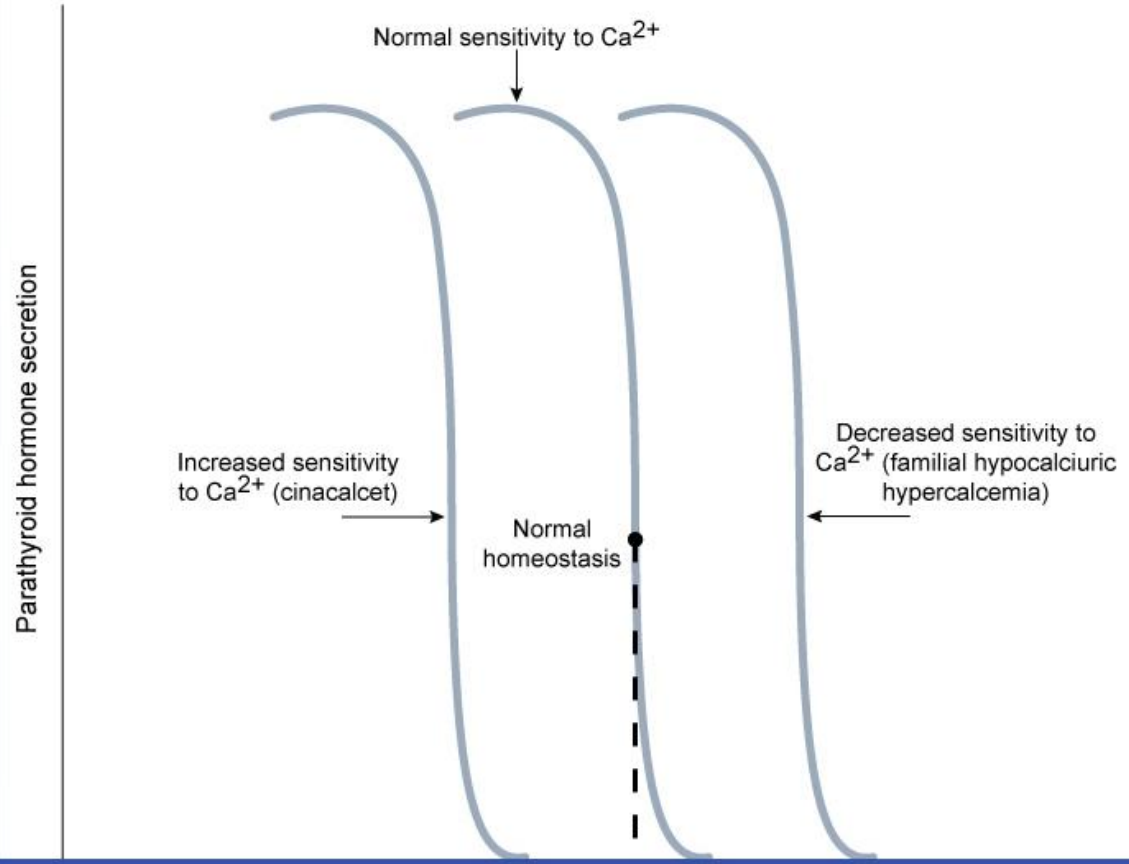
Settings

- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10
- 11
- 12
- 13
- 14
- 15
- 16

Item 4 of 16
Question Id: 992

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

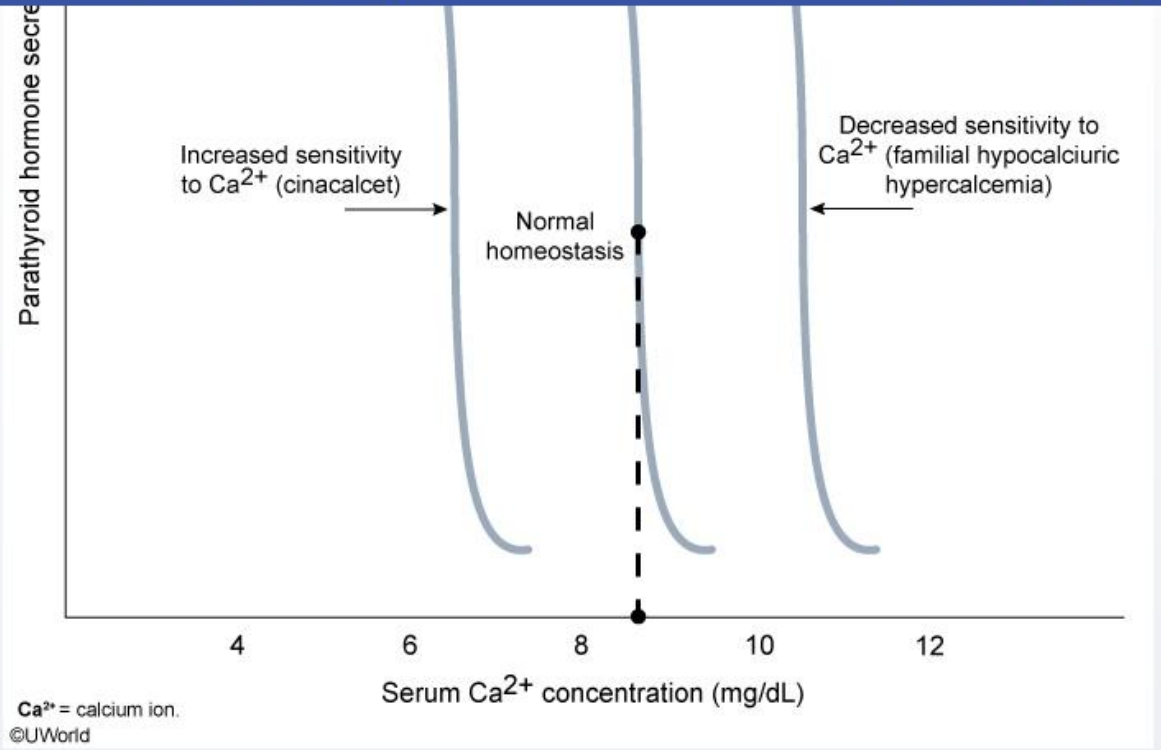
Calcium homeostasis



Block Time Remaining: 00:00:20
TUTOR

0 | Feedback | Suspend | End Block

2:11 PM
2/12/2019



Ca^{2+} = calcium ion.
©UWorld

Calcium-sensing receptors (CaSRs) are transmembrane **G_q protein–coupled** (metabotropic) receptors that regulate the secretion of parathyroid hormone (PTH) in response to changes in circulating calcium levels. Binding of calcium to CaSRs leads to the inhibition of PTH release, whereas low calcium levels allow increased PTH release.

Familial hypocalciuric hypercalcemia (FHH) is a benign autosomal dominant disorder caused by defective CaSRs in the parathyroid gland and kidneys. In FHH, higher serum calcium levels are required to suppress the secretion of PTH. This raises the set point of calcium-induced

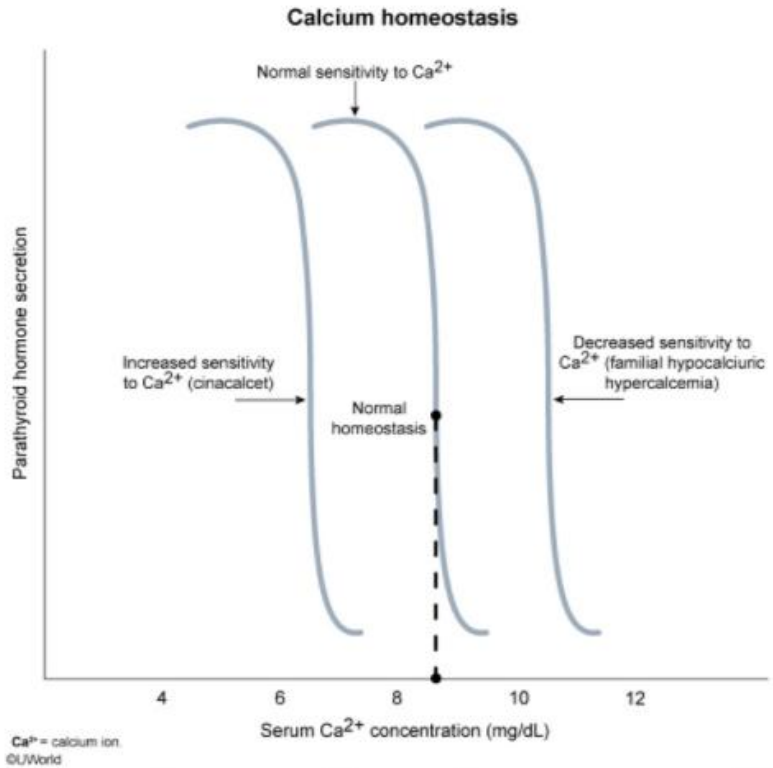
Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 4 of 16
Question Id: 992

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

Exhibit Display



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

kidneys. In FHH, higher serum calcium levels are required to suppress the secretion of PTH. This raises the set point of calcium-induced

Activate Windows
Go to Settings to activate Windows.

Block Time Remaining: 00:00:20
TUTOR

0 | Feedback | Suspend | End Block

2:12 PM
2/12/2019

Calcium-sensing receptors (CaSRs) are transmembrane **G_q protein–coupled** (metabotropic) receptors that regulate the secretion of parathyroid hormone (PTH) in response to changes in circulating calcium levels. Binding of calcium to CaSRs leads to the inhibition of PTH release, whereas low calcium levels allow increased PTH release.

Familial hypocalciuric hypercalcemia (FHH) is a benign autosomal dominant disorder caused by defective CaSRs in the parathyroid gland and kidneys. In FHH, higher serum calcium levels are required to suppress the secretion of PTH. This raises the set point of calcium-induced regulation of PTH secretion. Patients with FHH have mild asymptomatic hypercalcemia, reduced urinary excretion of calcium, and high normal or mildly elevated PTH.

(Choice A) Steroid hormones, thyroid hormone, and vitamin D act by binding to intracellular receptors with DNA-binding domains that interact with the regulatory DNA sequences of target genes.

(Choice C) Transmembrane ligand-gated ion channels (ionotropic receptors) allow a regulated flux of calcium, sodium, potassium, and chloride ions across the cell membrane. Neurotransmitters that work via ion channel–linked receptors include acetylcholine, serotonin, N-methyl-D-aspartate, and gamma-aminobutyric acid.

(Choice D) Insulin and insulin-like growth factor work by stimulating transmembrane receptors with intrinsic tyrosine kinase activity in the intracellular domain, initiating a downstream phosphorylation cascade.

(Choice E) Janus kinase (JAK) is a cytoplasmic protein activated by ligand binding to transmembrane receptors. JAKs activate cytoplasmic transcription factors called signal transducers and activators of transcription (STAT), which enter the nucleus to promote gene transcription. Examples of hormones using a JAK/STAT messenger system include **erythropoietin**, growth hormone, and prolactin.

Educational objective:
Calcium-sensing receptors are G protein–coupled receptors that regulate the secretion of parathyroid hormone in response to changes in circulating calcium levels. Familial hypocalciuric hypercalcemia is a benign autosomal dominant disorder caused by defective calcium-sensing receptors in the parathyroid gland and kidneys.

Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 5 of 16
Question Id: 11660

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

A 45-year-old man comes to the office with hoarseness that began 1 week ago. Physical examination shows a large nodular goiter. Fine-needle aspiration biopsy is diagnostic for papillary thyroid cancer, and the patient is admitted to the hospital for thyroidectomy. On the second postoperative day, he develops muscle cramps in his legs and paresthesias in his fingers and around his lips. Muscle strength and deep tendon reflexes are normal, but he has twitching of his lower facial muscles on percussion below the zygomatic arch. Which of the following is the most likely cause of this patient's current symptoms?

A. Decreased calcium reabsorption from the urine
B. Increased calcium resorption from bone
C. Increased intestinal phosphate absorption
D. Increased phosphate loss in the urine
E. Increased production of calcitriol

Submit

Block Time Remaining: 00:00:21
TUTOR

0 | Feedback | Suspend | End Block

2:12 PM
2/12/2019

Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 5 of 16
Question Id: 11660

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

A 45-year-old man comes to the office with hoarseness that began 1 week ago. Physical examination shows a large nodular goiter. Fine-needle aspiration biopsy is diagnostic for papillary thyroid cancer, and the patient is admitted to the hospital for thyroidectomy. On the second postoperative day, he develops muscle cramps in his legs and paresthesias in his fingers and around his lips. Muscle strength and deep tendon reflexes are normal, but he has twitching of his lower facial muscles on percussion below the zygomatic arch. Which of the following is the most likely cause of this patient's current symptoms?

- ✔ A. Decreased calcium reabsorption from the urine [81%]
- B. Increased calcium resorption from bone [8%]
- C. Increased intestinal phosphate absorption [4%]
- D. Increased phosphate loss in the urine [2%]
- E. Increased production of calcitriol [2%]

Omitted
Correct answer
A

81%
Answered correctly

3 Seconds
Time Spent

09/13/2018
Last Updated

Explanation

PTH, vitamin D & calcium axis

Negative Negative

Block Time Remaining: 00:00:23
TUTOR

0 | Feedback | Suspend | End Block

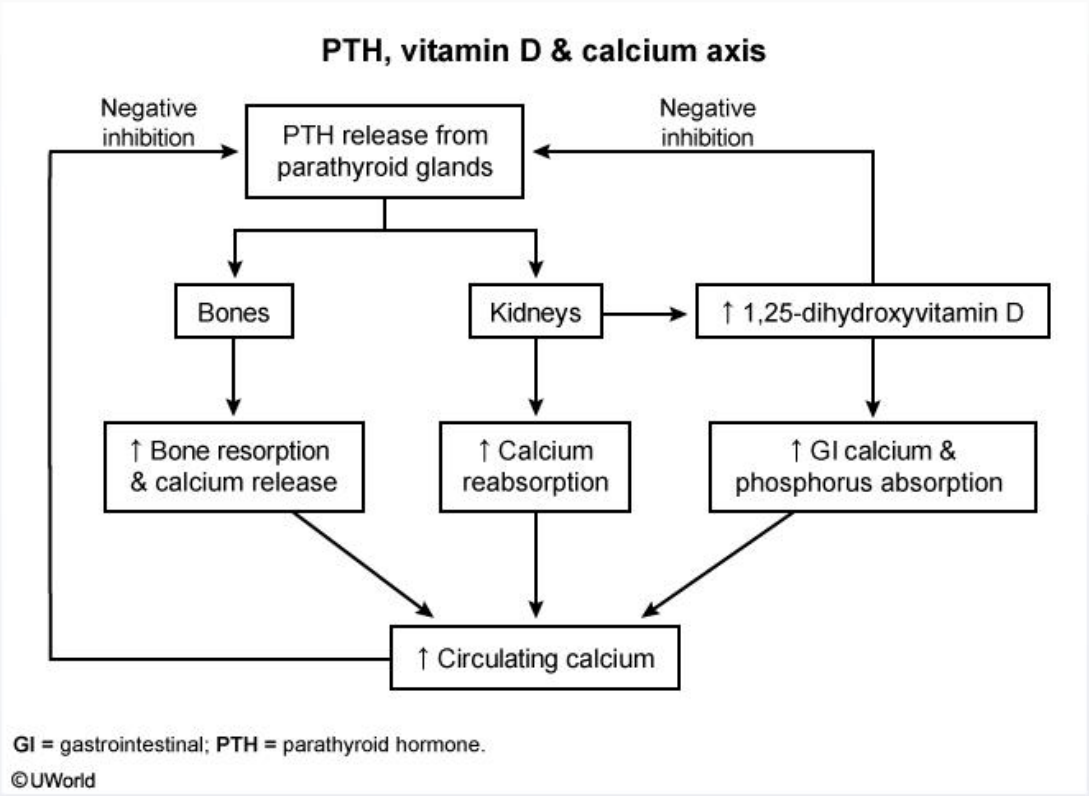
2:12 PM
2/12/2019

Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 5 of 16
Question Id: 11660

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



GI = gastrointestinal; **PTH** = parathyroid hormone.

Two hormones largely regulate calcium and phosphate homeostasis: parathyroid hormone (PTH), which regulates the minute-to-minute concentrations, and calcitriol, which regulates levels over the longer term. PTH is a polypeptide hormone produced by the chief cells of the parathyroid glands in response to hypocalcemia and has 3 primary effects:

Block Time Remaining: 00:00:23
TUTOR

0 | Feedback | Suspend | End Block

2:12 PM
2/12/2019

GI = gastrointestinal; **PTH** = parathyroid hormone.

Two hormones largely regulate calcium and phosphate homeostasis: parathyroid hormone (PTH), which regulates the minute-to-minute concentrations, and calcitriol, which regulates levels over the longer term. PTH is a polypeptide hormone produced by the chief cells of the parathyroid glands in response to hypocalcemia and has 3 primary effects:

- Increases osteoclastic bone resorption, which releases calcium and phosphate into the circulation
- Increases renal calcium reabsorption and reduces phosphate reabsorption
- Increases formation of 1,25-dihydroxycholecalciferol (by upregulating renal 1-alpha-hydroxylase), which increases intestinal calcium and phosphate absorption

This patient has **symptomatic hypoparathyroidism** following thyroid surgery. Postoperative hypoparathyroidism is common in patients who undergo thyroidectomy for thyroid cancer and can be due to inadvertent surgical removal of or damage to the parathyroid glands. The immediate drop in PTH levels results in decreased calcium and phosphate release from bone **(Choice B)** and **decreased calcium reabsorption** by the kidneys. Inadequate PTH also reduces phosphate excretion by the kidneys **(Choice D)** and decreases the conversion of calcidiol (25-hydroxycholecalciferol) to calcitriol (1,25-dihydroxycholecalciferol) in the renal tubular cells **(Choice E)**. This, in turn, decreases intestinal absorption of calcium and phosphate and lowers total body calcium stores **(Choice C)**.

Educational objective:
Postoperative hypoparathyroidism is common after thyroidectomy. Surgical removal of or damage to the parathyroid glands results in a drop in parathyroid hormone levels, resulting in decreased calcium and phosphate resorption from bone and decreased calcium reabsorption by the kidneys.

References

- Parathyroid disorders.

Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 5 of 16
Question Id: 11660

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

GI = gas
©UWorld

Two hormones largely regulate
concentrations, and calcitriol, w
parathyroid glands in response

- Increases osteoclastic bo
- Increases renal calcium r
- Increases formation of 1,
  phosphate absorption

This patient has **symptomatic**
undergo thyroidectomy for thyro
drop in PTH levels results in de
kidneys. Inadequate PTH also
hydroxycholecalciferol) to calcit
absorption of calcium and phos

Educational objective:
Postoperative hypoparathyroidi
parathyroid hormone levels, res
kidneys.

References

- Parathyroid disorders.

Exhibit Display

Hyperparathyroidism & hypoparathyroidism	
Hyperparathyroidism (↑ PTH)	**Hypoparathyroidism (↓ PTH)**
• ↑ Calcium, ↓ phosphate • Osteoporosis • Nephrolithiasis • Polydipsia, polyuria • Constipation • Bone pain • Muscle pain	• ↓ Calcium, ↑ phosphate • Tingling, numbness • Trousseau & Chvostek signs • Muscle spasms • Seizures

Add To Flash Card

Block Time Remaining: 00:00:23
TUTOR

Feedback | Suspend | End Block

2:12 PM
2/12/2019

Settings

- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10
- 11
- 12
- 13
- 14
- 15
- 16

Item 6 of 16
Question Id: 821

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

A collection of tan fat-containing tissue is found around the kidneys and adrenal glands of a newborn during surgery. Surgical removal of the tissue would most likely contribute to:

A. Fasting hypoglycemia
B. Hypercholesterolemia
C. Fasting ketonemia
D. Lactic acidosis
E. Hypothermia

Submit

Block Time Remaining: 00:00:24
TUTOR

0 | Feedback | Suspend | End Block

2:12 PM
2/12/2019

Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 6 of 16
Question Id: 821

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

A collection of tan fat-containing tissue is found around the kidneys and adrenal glands of a newborn during surgery. Surgical removal of the tissue would most likely contribute to:

A. Fasting hypoglycemia [14%]
B. Hypercholesterolemia [4%]
C. Fasting ketonemia [3%]
D. Lactic acidosis [3%]
✔ E. Hypothermia [74%]

Omitted
Correct answer
E

74%
Answered correctly

3 Seconds
Time Spent

02/06/2019
Last Updated

Explanation

Brown adipose tissue comprises 5% of body mass in neonates. It is also found in hibernating animals, but is present in very small amounts in adult humans. The main function of brown adipose tissue is heat production **(Choice E)**. Neonates have many physiological traits that make them more susceptible to hypothermia, such as an immature nervous system, a high body surface area to volume ratio and a decreased ability to shiver for heat production. Heat production by brown adipose tissue is, therefore, necessary for neonatal survival.

White adipose tissue is composed of cells that contain one intracytoplasmic fat droplet. Unlike white adipocytes, brown adipocytes possess

Block Time Remaining: 00:00:26
TUTOR

0 | Feedback | Suspend | End Block

2:12 PM
2/12/2019

Brown adipose tissue comprises 5% of body mass in neonates. It is also found in hibernating animals, but is present in very small amounts in adult humans. The main function of brown adipose tissue is heat production **(Choice E)**. Neonates have many physiological traits that make them more susceptible to hypothermia, such as an immature nervous system, a high body surface area to volume ratio and a decreased ability to shiver for heat production. Heat production by brown adipose tissue is, therefore, necessary for neonatal survival.

White adipose tissue is composed of cells that contain one intracytoplasmic fat droplet. Unlike white adipocytes, brown adipocytes possess several small intracytoplasmic fat vacuoles and considerably more mitochondria. The drastically increased number of mitochondria in these cells gives brown adipose tissue its tan color. Brown adipose tissue has a higher oxygen requirement and contains more capillaries than white adipose tissue.

In the majority of human cells, mitochondria are the sites of ATP production. In the mitochondria of brown adipose tissue electron transport and phosphorylation are uncoupled. The protons pumped out by electron transport chain return to the matrix via the mitochondrial membrane protein thermogenin, also known as an uncoupling protein. Thus no ATP is synthesized, and the energy released by electron transport is dissipated as heat.

(Choice A) A defect in gluconeogenesis or glycogenolysis would lead to fasting hypoglycemia. These processes primarily occur in the liver.

(Choice B) Hypercholesterolemia is most commonly due to a genetic / familial predisposition for high serum cholesterol levels. It may also be induced by diets high in cholesterol.

(Choice C) Ketonemia occurs when the liver is depleted of glycogen and utilizes body fat for gluconeogenesis. It occurs during sleep, fasting, starvation, and due to metabolic disturbances in diabetes mellitus.

(Choice D) Lactic acidosis results in states of tissue hypoxia or in the presence of defects in oxidative phosphorylation because pyruvate generated by glycolysis is converted to lactate rather than acetyl-CoA in these states.

Educational Objective:
Brown adipose tissue is found in newborns and in hibernating mammals. Brown adipose cells contain several intracytoplasmic fat droplets and

shiver for heat production. Heat production by brown adipose tissue is, therefore, necessary for neonatal survival.

White adipose tissue is composed of cells that contain one intracytoplasmic fat droplet. Unlike white adipocytes, brown adipocytes possess several small intracytoplasmic fat vacuoles and considerably more mitochondria. The drastically increased number of mitochondria in these cells gives brown adipose tissue its tan color. Brown adipose tissue has a higher oxygen requirement and contains more capillaries than white adipose tissue.

In the majority of human cells, mitochondria are the sites of ATP production. In the mitochondria of brown adipose tissue electron transport and phosphorylation are uncoupled. The protons pumped out by electron transport chain return to the matrix via the mitochondrial membrane protein thermogenin, also known as an uncoupling protein. Thus no ATP is synthesized, and the energy released by electron transport is dissipated as heat.

(Choice A) A defect in gluconeogenesis or glycogenolysis would lead to fasting hypoglycemia. These processes primarily occur in the liver.

(Choice B) Hypercholesterolemia is most commonly due to a genetic / familial predisposition for high serum cholesterol levels. It may also be induced by diets high in cholesterol.

(Choice C) Ketonemia occurs when the liver is depleted of glycogen and utilizes body fat for gluconeogenesis. It occurs during sleep, fasting, starvation, and due to metabolic disturbances in diabetes mellitus.

(Choice D) Lactic acidosis results in states of tissue hypoxia or in the presence of defects in oxidative phosphorylation because pyruvate generated by glycolysis is converted to lactate rather than acetyl-CoA in these states.

Educational Objective:
Brown adipose tissue is found in newborns and in hibernating mammals. Brown adipose cells contain several intracytoplasmic fat droplets and many more mitochondria than white adipose cells. They function to produce heat by uncoupling oxidative phosphorylation with the protein thermogenin.

Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 7 of 16
Question Id: 1540

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

A 23-year-old man is brought to the emergency department due to weakness and confusion. Family members report that for the last 2 weeks he has experienced polyuria, polydipsia, and increased appetite. His past medical history is remarkable for an appendectomy at age 12. He also has a brother with hypothyroidism. On examination, the patient is lethargic and confused but responds to basic commands. His breath has a fruity odor. This patient is most likely deficient in a hormone that normally performs which of the following actions?

A. Decreases glucagon secretion
B. Decreases muscle protein synthesis
C. Facilitates the action of glucagon
D. Increases glucagon secretion
E. Increases lipolysis
F. Increases renal glucose reabsorption

Submit

Block Time Remaining: 00:00:27
TUTOR

0 | Feedback | Suspend | End Block

2:12 PM
2/12/2019

Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 7 of 16
Question Id: 1540

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

A 23-year-old man is brought to the emergency department due to weakness and confusion. Family members report that for the last 2 weeks he has experienced polyuria, polydipsia, and increased appetite. His past medical history is remarkable for an appendectomy at age 12. He also has a brother with hypothyroidism. On examination, the patient is lethargic and confused but responds to basic commands. His breath has a fruity odor. This patient is most likely deficient in a hormone that normally performs which of the following actions?

- A. Decreases glucagon secretion [80%]
- B. Decreases muscle protein synthesis [1%]
- C. Facilitates the action of glucagon [3%]
- D. Increases glucagon secretion [7%]
- E. Increases lipolysis [4%]
- F. Increases renal glucose reabsorption [3%]

Omitted
Correct answer
A

80%
Answered correctly

3 Seconds
Time Spent

01/22/2019
Last Updated

Explanation

Insulin effects

Block Time Remaining: 00:00:29
TUTOR

0 | Feedback | Suspend | End Block

2:12 PM
2/12/2019

Insulin effects		
Effect	**Target organs**	**Consequences of inadequate insulin**
↑ Glucose uptake	• Skeletal muscle • Adipose tissue • Liver	**Hyperglycemia** • Polyuria, polydipsia • Lethargy • Polyphagia or anorexia
↑ Glycogen synthesis/ ↓ glycogenolysis	• Liver	
↓ Glucagon secretion	• Pancreas (alpha cells)	
↓ Lipolysis/ ↓ ketogenesis	• Adipose tissue • Liver	Ketosis/ketoacidosis
↑ Protein synthesis	• Muscle	Muscle wasting, weight loss

This patient is exhibiting signs and symptoms of undiagnosed type 1 diabetes mellitus with **diabetic ketoacidosis** (DKA), including polyuria, polydipsia, and abnormal mental state. The fruity breath odor is due to the presence of acetone and indicates increased production of ketone bodies. DKA results from a **deficiency of insulin** coupled with an excess of counter-regulatory hormones (glucagon, cortisol, and growth

↑ Protein synthesis	• Muscle	Muscle wasting, weight loss

This patient is exhibiting signs and symptoms of undiagnosed type 1 diabetes mellitus with **diabetic ketoacidosis** (DKA), including polyuria, polydipsia, and abnormal mental state. The fruity breath odor is due to the presence of acetone and indicates increased production of ketone bodies. DKA results from a **deficiency of insulin** coupled with an excess of counter-regulatory hormones (glucagon, cortisol, and growth hormone).

In normal individuals, blood glucose levels are maintained within a tight range by opposing effects of insulin (secreted by beta cells) and glucagon (secreted by alpha cells). Low blood glucose levels stimulate secretion of glucagon, which acts to increase blood glucose levels by stimulating glycogenolysis and gluconeogenesis in the liver. In contrast, insulin is released in response to high glucose levels and functions to decrease hepatic glucose production and increase glucose uptake by insulin-responsive tissues. Insulin also suppresses glucagon by directly acting on the alpha cells, which prevents glucagon from interfering with the glucose-lowering action of insulin **(Choice D)**.

(Choices B and E) Insulin increases amino acid transport and ribosomal translation efficiency in muscle, adipose, and liver tissue. This causes an overall increase in protein synthesis. Insulin decreases lipolysis in adipose tissue and increases uptake and esterification of fatty acids. In new-onset type 1 diabetes, the lack of insulin induces a catabolic state, and patients typically lose weight despite a normal or increased appetite.

(Choice C) Epinephrine stimulates glucagon release and facilitates the effects of glucagon by increasing release of glucose from the liver and decreasing glucose uptake by peripheral tissues.

(Choice F) Insulin increases renal reabsorption of sodium, leading to increased blood volume and blood pressure. Filtered glucose, however, is almost completely reabsorbed independent of insulin action (unless severe hyperglycemia overwhelms the kidney's glucose-reabsorbing ability).

Educational objective:
Normal blood glucose levels are maintained by opposing effects of insulin and glucagon. Glucagon stimulates hepatic glycogenolysis and gluconeogenesis, whereas insulin increases peripheral glucose uptake and inhibits lipolysis and ketoacid formation. Insulin also suppresses glucagon release.

Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 8 of 16
Question Id: 1355

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

Biochemists working for a national endocrinology institute are investigating the specifics underlying glucose transport across adipose cell membranes. One of their experiments shows that, in the presence of insulin, D-glucose transport across the plasma membrane of adipocytes is much faster than L-glucose transport. Which of the following transport processes best describes the mechanism for glucose entry into these cells?

A. Simple diffusion
B. Receptor-mediated endocytosis
C. Carrier-mediated transport
D. Primary active transport
E. Co-transport

Submit

Block Time Remaining: 00:00:30
TUTOR

0 | Feedback | Suspend | End Block

2:12 PM
2/12/2019

Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 8 of 16
Question Id: 1355

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

Biochemists working for a national endocrinology institute are investigating the specifics underlying glucose transport across adipose cell membranes. One of their experiments shows that, in the presence of insulin, D-glucose transport across the plasma membrane of adipocytes is much faster than L-glucose transport. Which of the following transport processes best describes the mechanism for glucose entry into these cells?

A. Simple diffusion [4%]
B. Receptor-mediated endocytosis [16%]
✔ C. Carrier-mediated transport [60%]
D. Primary active transport [7%]
E. Co-transport [10%]

Omitted
Correct answer
C

60%
Answered correctly

3 Seconds
Time Spent

08/18/2018
Last Updated

Explanation

Classification of transport across cell membranes

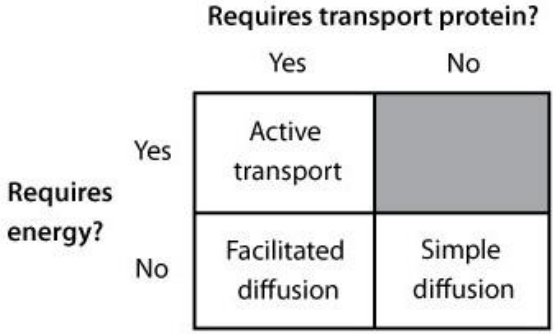
Requires transport protein?

Block Time Remaining: 00:00:32
TUTOR

0 | Feedback | Suspend | End Block

2:12 PM
2/12/2019

Classification of transport across cell membranes



Glucose is the major source of energy for all cells of the body. In the majority of tissues, glucose transport occurs along its concentration gradient, from higher concentrations outside the cell toward lower concentrations inside the cell. However, glucose cannot passively diffuse across the cell membrane in any significant amount and requires carrier proteins to aid its crossing. Transport across the cell membrane by carrier proteins (which undergo conformational changes as the substrate is transported, unlike channel proteins) is termed carrier-mediated transport. Transport that is facilitated by transmembrane proteins without the expenditure of energy is called **facilitated diffusion**.

Transmembrane carrier proteins that belong to the GLUT family transport glucose by facilitated diffusion. These proteins are stereoselective and preferentially catalyze the entrance of D-glucose rather than L-glucose into cells. **GLUT4** is the insulin-sensitive transporter found in skeletal muscle cells and adipocytes. In these cells, the GLUT4 protein is stored in cytoplasmic vesicles. Under the influence of insulin, the transporter protein is incorporated into the cell membrane. An increased number of transporters in the membrane leads to an increased rate of glucose uptake by the cells. Another important glucose transporter is **GLUT2**. It facilitates export of glucose from the liver, small intestine, and kidneys into the circulation and also helps to control insulin secretion in the pancreas.

membrane in any significant amount and requires carrier proteins to aid its crossing. Transport across the cell membrane by carrier proteins (which undergo conformational changes as the substrate is transported, unlike channel proteins) is termed carrier-mediated transport. Transport that is facilitated by transmembrane proteins without the expenditure of energy is called **facilitated diffusion**.

Transmembrane carrier proteins that belong to the GLUT family transport glucose by facilitated diffusion. These proteins are stereoselective and preferentially catalyze the entrance of D-glucose rather than L-glucose into cells. **GLUT4** is the insulin-sensitive transporter found in skeletal muscle cells and adipocytes. In these cells, the GLUT4 protein is stored in cytoplasmic vesicles. Under the influence of insulin, the transporter protein is incorporated into the cell membrane. An increased number of transporters in the membrane leads to an increased rate of glucose uptake by the cells. Another important glucose transporter is **GLUT2**. It facilitates export of glucose from the liver, small intestine, and kidneys into the circulation and also helps to control insulin secretion in the pancreas.

(Choice A) Simple diffusion refers to the movement of particles along their concentration gradient directly through the cell membrane. Transport of gases (O_2 and CO_2) occurs via simple diffusion, as the membrane is very permeable to small, nonpolar molecules.

(Choice B) Endocytosis allows for cellular uptake through the formation of membrane-bound, typically clathrin-coated, vesicles. Uptake of cholesterol by cells occurs by means of receptor-mediated endocytosis (mediated by the LDL receptor).

(Choices D and E) Active transport refers to the movement of a substance against its concentration gradient. This process requires energy as well as transport proteins. In primary active transport, the energy required for transport against the concentration gradient is provided by the hydrolysis of ATP. In secondary active transport, this energy is generated by co-transport of a separate substance down its concentration gradient. Transport of glucose against the concentration gradient occurs via the Na/glucose symporter, which is found in the intestinal and renal tubular epithelium and is used to transfer glucose intracellularly from the lumen.

Educational objective:
Transport of glucose into the cells of most tissues occurs by means of facilitated diffusion. Glucose moves from areas of high concentration to areas of low concentration with the help of transmembrane glucose transporter proteins (GLUT). These carrier proteins are stereoselective and have preference for D-glucose.

Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 9 of 16
Question Id: 770

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

A 32-year-old woman comes to the office due to neck swelling. The patient says her neck has gradually gotten larger, and she does not like how it appears in the mirror. She otherwise feels well and has no hoarseness, trouble swallowing, or shortness of breath. There is no history of head and neck irradiation. The patient has no prior medical conditions and takes no medications. She has a sister with vitiligo. Blood pressure is 110/60 mm Hg and pulse is 75/min. On physical examination, the thyroid is diffusely enlarged with no palpable nodules. There is no tracheal deviation. Serum TSH and free thyroxine levels are normal. Antibodies against thyroid peroxidase are present in high titers. The antigenic target of these antibodies is involved in which of the following processes?

A. Iodide uptake
B. Iodotyrosine deiodination
C. Thyroglobulin iodination
D. Thyroglobulin synthesis
E. Thyroxine to triiodothyronine conversion

Submit

Block Time Remaining: 00:00:33
TUTOR

0 | Feedback | Suspend | End Block

2:13 PM
2/12/2019

Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 9 of 16
Question Id: 770

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

A 32-year-old woman comes to the office due to neck swelling. The patient says her neck has gradually gotten larger, and she does not like how it appears in the mirror. She otherwise feels well and has no hoarseness, trouble swallowing, or shortness of breath. There is no history of head and neck irradiation. The patient has no prior medical conditions and takes no medications. She has a sister with vitiligo. Blood pressure is 110/60 mm Hg and pulse is 75/min. On physical examination, the thyroid is diffusely enlarged with no palpable nodules. There is no tracheal deviation. Serum TSH and free thyroxine levels are normal. Antibodies against thyroid peroxidase are present in high titers. The antigenic target of these antibodies is involved in which of the following processes?

A. Iodide uptake [4%]
B. Iodotyrosine deiodination [5%]
✔ C. Thyroglobulin iodination [69%]
D. Thyroglobulin synthesis [8%]
E. Thyroxine to triiodothyronine conversion [11%]

Omitted
Correct answer
C

69%
Answered correctly

3 Seconds
Time Spent

09/13/2018
Last Updated

Explanation

Thyroid hormone synthesis

Block Time Remaining: 00:00:35
TUTOR

0 | Feedback | Suspend | End Block

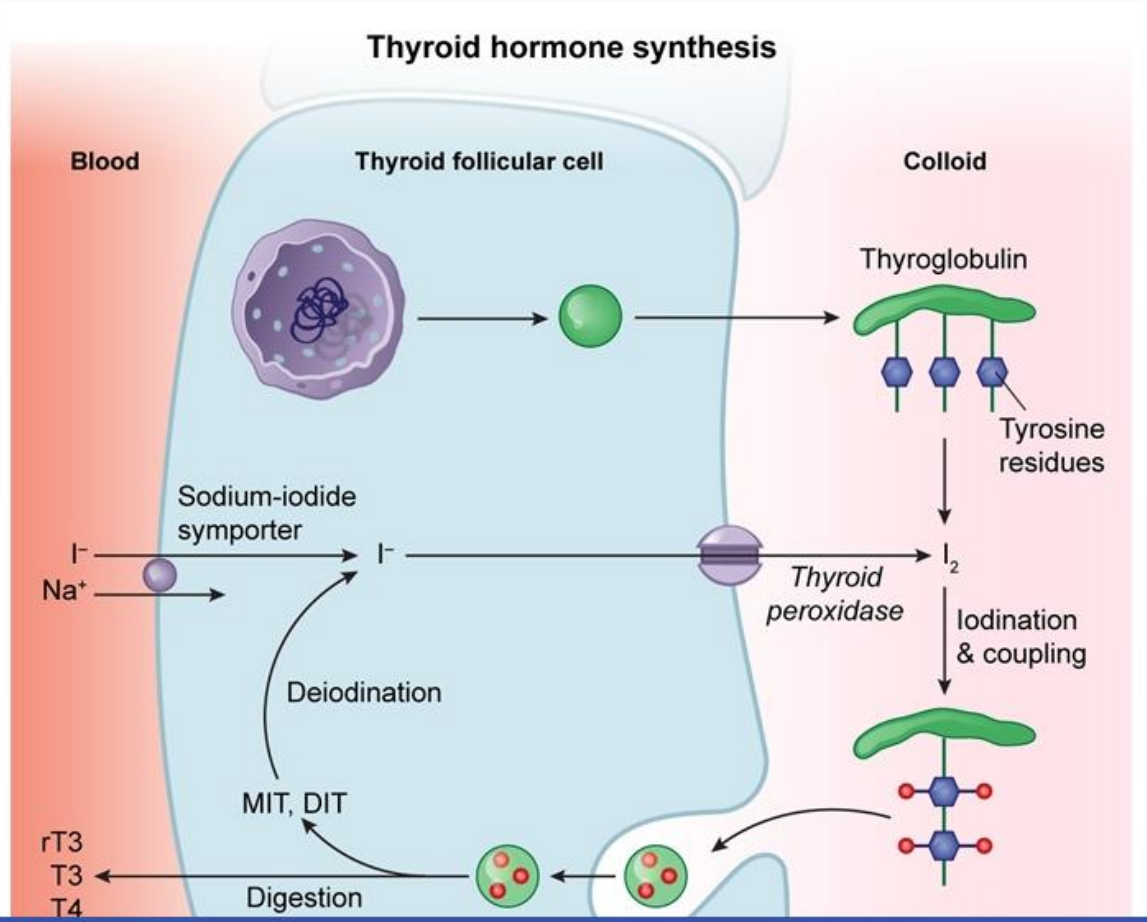
2:13 PM
2/12/2019

Settings

- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10
- 11
- 12
- 13
- 14
- 15
- 16

Item 9 of 16
Question Id: 770

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



Block Time Remaining: 00:00:35
TUTOR

Feedback | Suspend | End Block

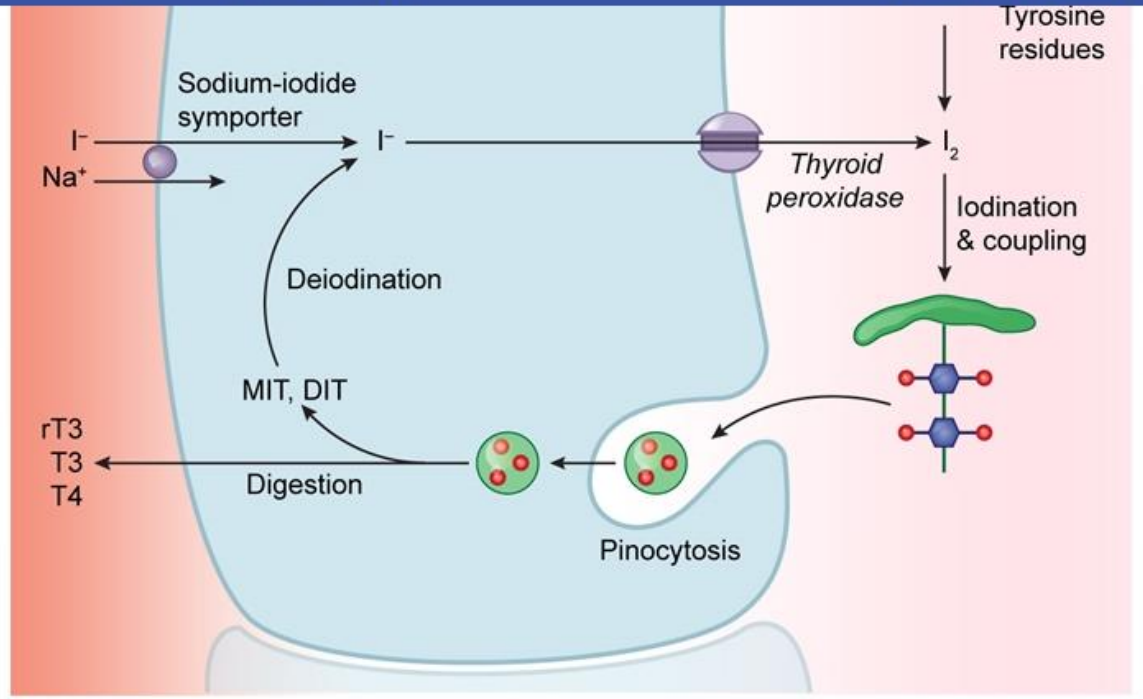
2:13 PM
2/12/2019

Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 9 of 16
Question Id: 770

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



DIT = diiodotyrosine; **rT3** = reverse triiodothyronine; **T3** = triiodothyronine; **T4** = thyroxine; **MIT** = monoiodotyrosine.

Thyroid follicular cells take up iodide (I^-), which is then transported into the thyroid follicular lumen, where it is oxidized to iodine (I_2). Following oxidation, in a process referred to as organification, iodine reacts with tyrosine residues in thyroglobulin to form monoiodotyrosine (MIT) and diiodotyrosine (DIT) (iodination). While still attached to thyroglobulin, DIT and MIT participate in 2 coupling reactions: The coupling of 2 DITs results in formation of **thyroxine** (T4); the combination of 1 DIT and 1 MIT leads to the formation of **triiodothyronine** (T3). Subsequently, thyroglobulin, which is now attached to multiple iodinated tyrosine compounds (ie, MIT, DIT, T3, T4), is engulfed by the thyroid follicular cells and

Block Time Remaining: 00:00:35
TUTOR

0 | Feedback | Suspend | End Block

2:13 PM
2/12/2019

Settings

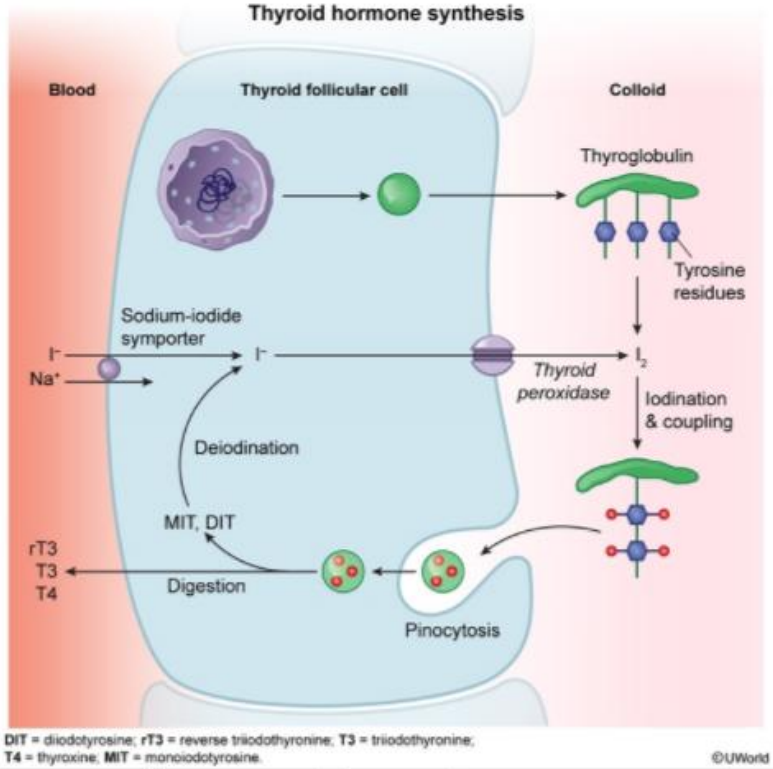
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 9 of 16
Question Id: 770

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

Tyrosine

Exhibit Display



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

thyroglobulin, which is now attached to multiple iodinated tyrosine compounds (ie, MIT, DIT, T3, T4), is engulfed by the thyroid follicular cells and

Block Time Remaining: 00:00:35
TUTOR

0 | Feedback | Suspend | End Block

2:13 PM
2/12/2019

Thyroid follicular cells take up iodide (I^-), which is then transported into the thyroid follicular lumen, where it is oxidized to iodine (I_2). Following oxidation, in a process referred to as organification, iodine reacts with tyrosine residues in thyroglobulin to form monoiodotyrosine (MIT) and diiodotyrosine (DIT) (iodination). While still attached to thyroglobulin, DIT and MIT participate in 2 coupling reactions: The coupling of 2 DITs results in formation of **thyroxine** (T4); the combination of 1 DIT and 1 MIT leads to the formation of **triiodothyronine** (T3). Subsequently, thyroglobulin, which is now attached to multiple iodinated tyrosine compounds (ie, MIT, DIT, T3, T4), is engulfed by the thyroid follicular cells and digested within lysosomes, releasing T3 and T4 into the circulation. Free DIT and MIT are also produced, but only small amounts are secreted because iodotyrosine deiodinase removes the iodine groups from MIT and DIT for recycling **(Choice B)**.

Thyroid peroxidase (TPO) is a multifunctional enzyme that catalyzes the oxidation of iodide, the iodination of thyroglobulin, and the coupling reaction between 2 iodized tyrosine residues. Antibodies against TPO can be seen in a variety of autoimmune thyroid disorders, most commonly chronic lymphocytic (Hashimoto) thyroiditis (90% of patients). Hashimoto thyroiditis is a common cause of diffuse goiter, as in this patient. Although most patients develop residual hypothyroidism (low T4, elevated TSH), early in the disease they may be euthyroid (normal T4, normal TSH) or briefly hyperthyroid (elevated T4, suppressed TSH).

(Choice A) Uptake of iodide from the blood against its concentration gradient is an energy-dependent process carried out by the sodium-iodide symporter and stimulated by TSH. TPO is not involved in iodide uptake.

(Choice D) Thyroglobulin is a high-molecular-weight, glycosylated protein that is the major component of colloid in the thyroid follicle. TPO is involved in iodination, but not synthesis of thyroglobulin.

(Choice E) As noted above, the thyroid produces both T3 and T4, although most is in the form of T4. T3, the more active form of thyroid hormone, is produced primarily in peripheral tissues by deiodination of T4. This reaction is catalyzed by iodothyronine deiodinase, not by TPO.

Educational objective:
Thyroid peroxidase (TPO) catalyzes the oxidation of iodide to iodine, the iodination of thyroglobulin tyrosine residues, and the iodotyrosine coupling reaction that forms T3 and T4. Antibodies against TPO are present in >90% of patients with chronic lymphocytic (Hashimoto) thyroiditis.

Settings

- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10
- 11
- 12
- 13
- 14
- 15
- 16

Item 10 of 16
Question Id: 1325

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

A 27-year-old man comes to the office to follow up type 1 diabetes mellitus. He was diagnosed 15 years ago and has been on a stable insulin regimen for the last 4 years. He currently takes long-acting insulin glargine once daily and short-acting regular insulin with each meal. Since his last visit, the patient has experienced frequent episodes of disorientation, palpitations, tremulousness, and excessive sweating, all of which resolve quickly after drinking some honey dissolved in water. Which of the following factors most likely precipitated this patient's symptoms?

- A. Exercise
- B. Moderate to severe pain
- C. Respiratory infection
- D. Sleep deprivation
- E. Weight gain

Submit

Block Time Remaining: 00:00:36
TUTOR

0 | Feedback | Suspend | End Block

2:13 PM
2/12/2019

Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 10 of 16
Question Id: 1325

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

A 27-year-old man comes to the office to follow up type 1 diabetes mellitus. He was diagnosed 15 years ago and has been on a stable insulin regimen for the last 4 years. He currently takes long-acting insulin glargine once daily and short-acting regular insulin with each meal. Since his last visit, the patient has experienced frequent episodes of disorientation, palpitations, tremulousness, and excessive sweating, all of which resolve quickly after drinking some honey dissolved in water. Which of the following factors most likely precipitated this patient's symptoms?

- A. Exercise [82%]
- B. Moderate to severe pain [0%]
- C. Respiratory infection [10%]
- D. Sleep deprivation [2%]
- E. Weight gain [4%]

Omitted
Correct answer
A

82%
Answered correctly

3 Seconds
Time Spent

08/17/2018
Last Updated

Explanation

Effects of exercise on insulin & glucose

Normal patients | **Insulin-treated diabetic patients**

Block Time Remaining: 00:00:38
TUTOR

0 | Feedback | Suspend | End Block

2:13 PM
2/12/2019

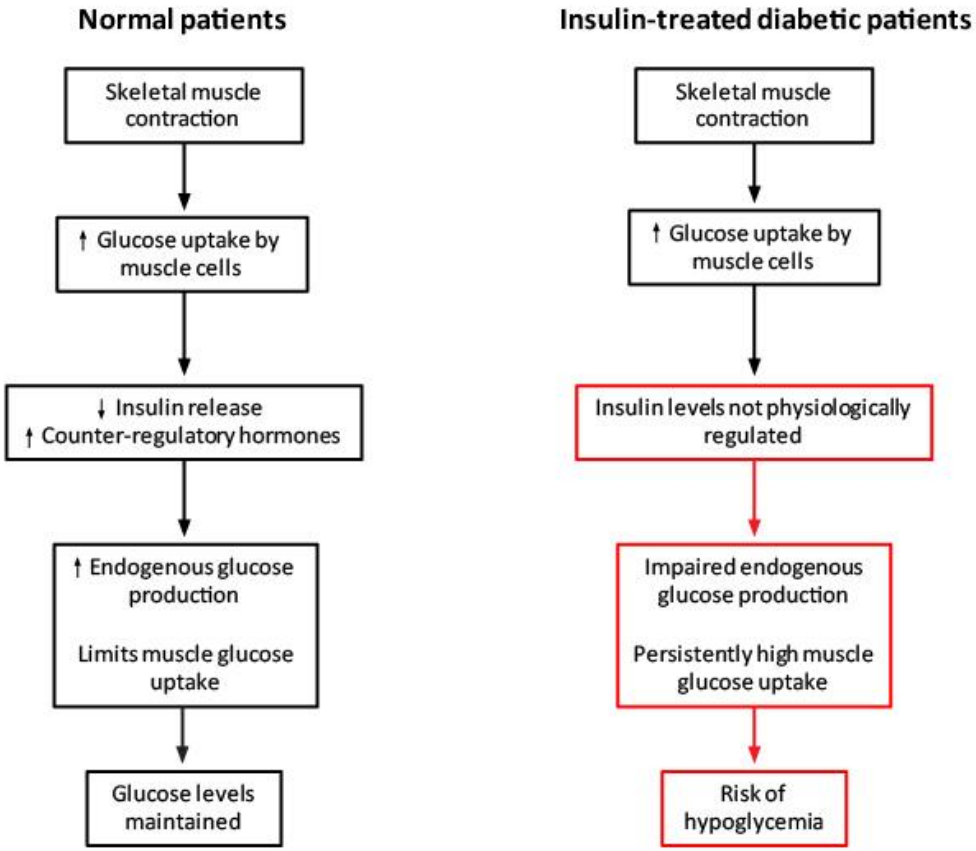
Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 10 of 16
Question Id: 1325

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

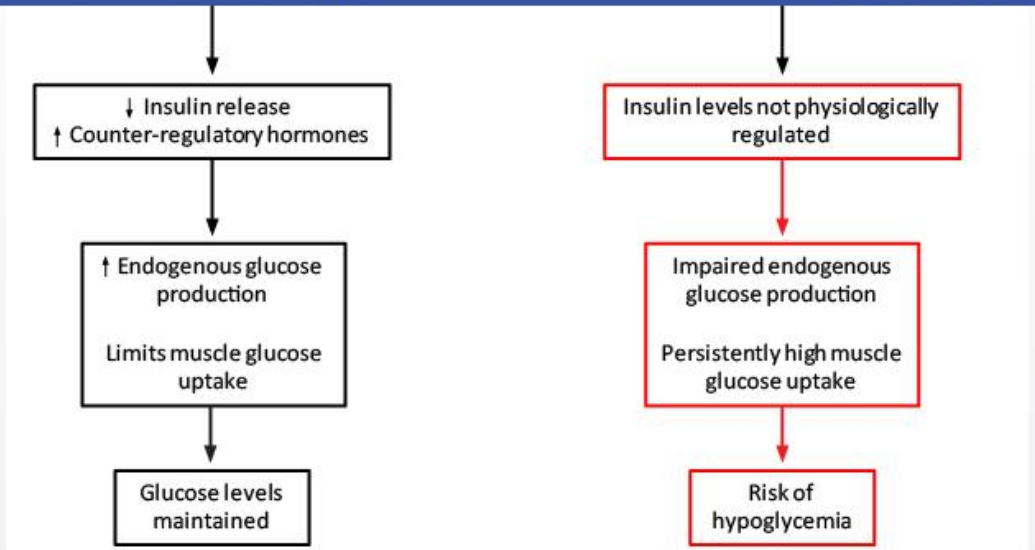
Effects of exercise on insulin & glucose



Block Time Remaining: 00:00:38
TUTOR

0 | Feedback | Suspend | End Block

2:13 PM
2/12/2019



This patient has typical symptoms of **hypoglycemia** (eg, disorientation, sweating, tremors, palpitations), which are relieved by intake of glucose. The 3 most important predisposing factors for hypoglycemia in patients with type 1 diabetes are excessive insulin dose, inadequate food intake, and physical activity/exercise.

Glucose uptake by skeletal muscle cells is mediated by glucose transporter type 4 (**GLUT-4**). GLUT-4 is translocated to cell membranes and transverse tubules (deep invaginations in the cell membrane) in response to **insulin**. GLUT-4 translocation also occurs during **muscle contraction** by an insulin-independent mechanism, which is mediated by several cellular factors, including AMP-activated kinase, nitric oxide, and calcium-calmodulin-activated protein kinase.

In normal individuals, overt hypoglycemia does not occur with exercise because a drop in blood glucose will stop insulin release from the beta

This patient has typical symptoms of **hypoglycemia** (eg, disorientation, sweating, tremors, palpitations), which are relieved by intake of glucose. The 3 most important predisposing factors for hypoglycemia in patients with type 1 diabetes are excessive insulin dose, inadequate food intake, and physical activity/exercise.

Glucose uptake by skeletal muscle cells is mediated by glucose transporter type 4 (**GLUT-4**). GLUT-4 is translocated to cell membranes and transverse tubules (deep invaginations in the cell membrane) in response to **insulin**. GLUT-4 translocation also occurs during **muscle contraction** by an insulin-independent mechanism, which is mediated by several cellular factors, including AMP-activated kinase, nitric oxide, and calcium-calmodulin-activated protein kinase.

In normal individuals, overt hypoglycemia does not occur with exercise because a drop in blood glucose will stop insulin release from the beta cells and counter-regulatory hormones (eg, glucagon) will increase endogenous glucose production via glycogenolysis and gluconeogenesis. However, patients taking **exogenous insulin** are vulnerable to exercise-induced hypoglycemia as insulin will **continue to be released** from the injection site despite falling glucose levels. In addition, strenuous exercise may cause changes in skin perfusion that can lead to increased insulin absorption (especially if the insulin is injected into an exercising limb rather than the abdominal area).

(Choices B, C, and D) Infection, pain, and sleep deprivation tend to cause hyper- rather than hypoglycemia. Stressful situations increase catecholamine release, which raises glucose by decreasing pancreatic insulin secretion and by increasing glycogenolysis and gluconeogenesis.

(Choice E) Weight gain is associated with insulin resistance. Insulin-treated patients who gain weight usually develop hyperglycemia and require increased doses of insulin to maintain control of glucose.

Educational objective:
Hypoglycemia can be precipitated by exercise in patients with insulin-treated diabetes. Uptake of glucose by skeletal muscle is mediated by the glucose transporter type 4, which is translocated to the cell membrane in response to insulin and muscle contraction.

References

Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 11 of 16
Question Id: 1615

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

A 43-year-old woman comes to the office due to increasing fatigue and weight gain despite decreased food intake. She states, "I have not been feeling like myself lately." The patient asks to be referred to a dermatologist as she has always had "nice" skin that has now become dry. Her hair has been thinning and she hopes that a dermatologist can help with that too. Laboratory evaluation shows high serum TSH, low triiodothyronine (T3), and low thyroxine (T4) levels. The patient has a family member with fatigue whose energy level increased after liothyronine (T3) supplementation, and she asks to try this medication. Administering this therapy would most likely result in which of the following hormone level changes in this patient?

	TSH	T3	Reverse T3	T4
A.	No change	Increase	Increase	Decrease
B.	No change	Increase	Decrease	Decrease
C.	Decrease	Increase	Increase	Decrease
D.	Decrease	Increase	Decrease	Decrease
E.	Decrease	Increase	Decrease	Increase

Submit

Block Time Remaining: 00:00:39
TUTOR

0 | Feedback | Suspend | End Block

2:13 PM
2/12/2019

Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 11 of 16
Question Id: 1615

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

A 43-year-old woman comes to the office due to increasing fatigue and weight gain despite decreased food intake. She states, "I have not been feeling like myself lately." The patient asks to be referred to a dermatologist as she has always had "nice" skin that has now become dry. Her hair has been thinning and she hopes that a dermatologist can help with that too. Laboratory evaluation shows high serum TSH, low triiodothyronine (T3), and low thyroxine (T4) levels. The patient has a family member with fatigue whose energy level increased after liothyronine (T3) supplementation, and she asks to try this medication. Administering this therapy would most likely result in which of the following hormone level changes in this patient?

	TSH	T3	Reverse T3	T4
A. [3%]	No change	Increase	Increase	Decrease
B. [4%]	No change	Increase	Decrease	Decrease
C. [26%]	Decrease	Increase	Increase	Decrease
✔ D. [48%]	Decrease	Increase	Decrease	Decrease
E. [17%]	Decrease	Increase	Decrease	Increase

Omitted
Correct answer

48%
Answered correctly

3 Seconds
Time Spent

08/17/2018
Last Updated

Block Time Remaining: 00:00:41
TUTOR

0 | Feedback | Suspend | End Block

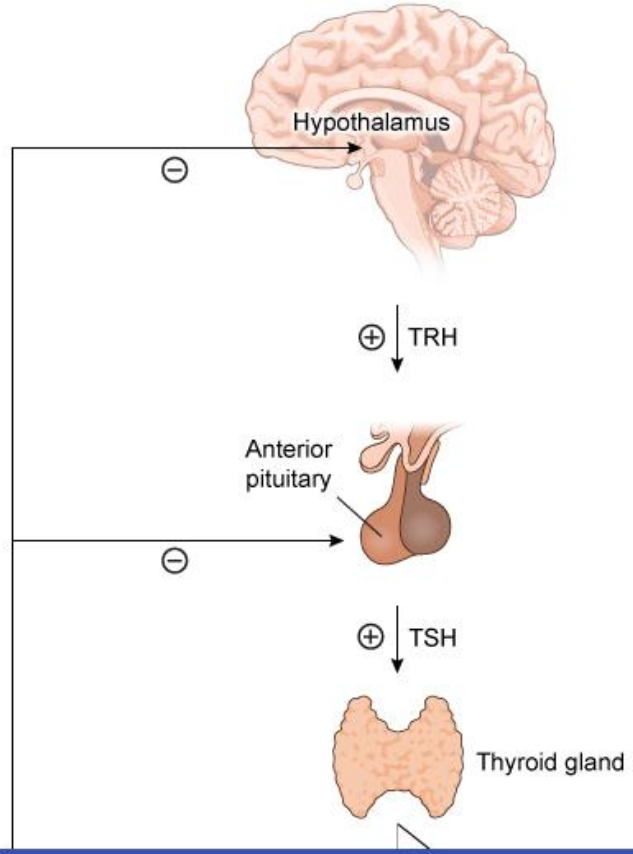
Settings

- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10
- 11
- 12
- 13
- 14
- 15
- 16

Item 11 of 16
Question Id: 1615

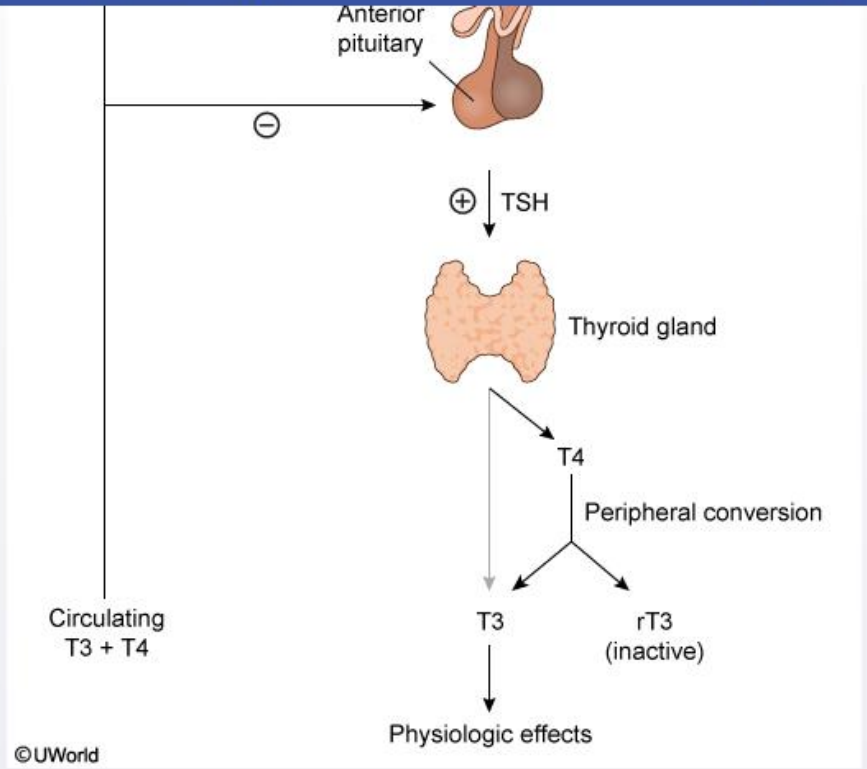
Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

Hypothalamic-pituitary-thyroid axis



Block Time Remaining: 00:00:41
TUTOR

0 | Feedback | Suspend | End Block



Circulating thyroid hormone exists in 3 primary forms:

1. **T4 (thyroxine)** is the major secretory product of the thyroid gland.
2. **T3 (triiodothyronine)** is the most active form of thyroid hormone; a small amount is released by the thyroid gland, but the majority arises from peripheral deiodination of T4.

Circulating thyroid hormone exists in 3 primary forms:

1. **T4 (thyroxine)** is the major secretory product of the thyroid gland.
2. **T3 (triiodothyronine)** is the most active form of thyroid hormone; a small amount is released by the thyroid gland, but the majority arises from peripheral deiodination of T4.
3. **Reverse T3 (rT3)** is an inactive form that is generated almost entirely from the peripheral conversion of T4.

The hypothalamus-pituitary-thyroid axis is regulated via **negative feedback** by thyroid hormone on thyrotropin-releasing hormone–secreting neurons in the hypothalamus and thyrotrophs of the anterior pituitary. In the normal state, most of the circulating thyroid hormone is in the form of T4, which provides most of the feedback suppression of TSH release. However, T3 also suppresses TSH.

This patient has primary hypothyroidism, with low thyroid hormone (T3 and T4) and elevated TSH levels. Exogenous T3 supplementation **rapidly suppresses TSH** levels by increasing negative feedback, which in turn decreases T4 secretion from the thyroid gland. Furthermore, rT3 also decreases because less T4 is available for conversion (T3 cannot be converted into rT3).

However, synthetic T3 (liothyronine) is not recommended for the routine treatment of hypothyroidism, as it has a short half-life and patients can experience wide fluctuations in plasma T3 levels. T4 (levothyroxine) supplementation provides a more physiologic effect and is preferred.

Educational objective:
TSH from the anterior pituitary stimulates the thyroid to produce thyroxine (T4) and a small amount of triiodothyronine (T3). T4 is converted in peripheral tissues to T3 (active form) and reverse T3 (inactive form). TSH secretion is under negative feedback by thyroid hormone on the hypothalamus and pituitary.

References

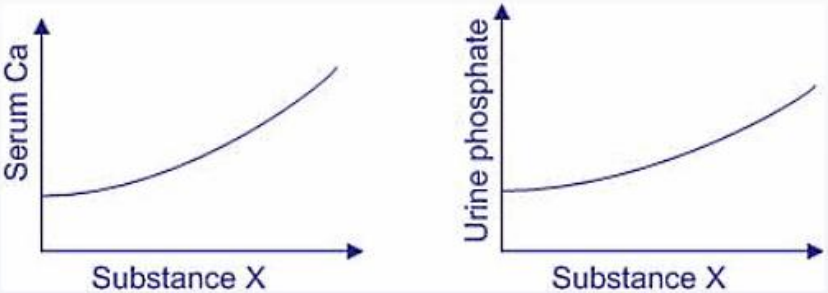
Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 12 of 16
Question Id: 641

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

A group is studying the bone growth and mineralization process in humans. They are testing a new substance, Substance X that exhibits the following metabolic effects with continuous, high-dose infusion (see the graph below).



Substance X has metabolic effects that most closely resemble which of the following chemicals?

A. Calcitriol
B. Calcitonin
C. PTH
D. Somatomedin C
E. Triiodothyronine

Submit

Block Time Remaining: 00:00:42
TUTOR

Feedback | Suspend | End Block

2:13 PM
2/12/2019

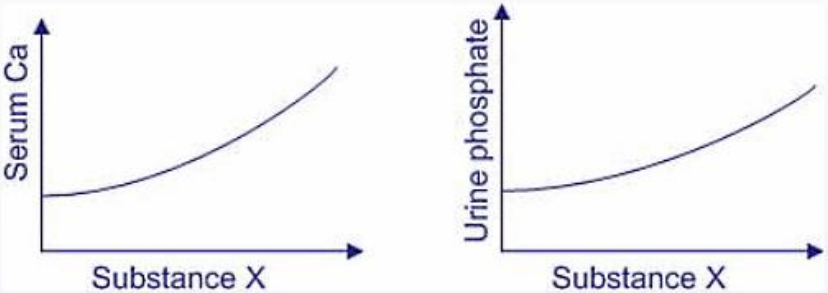
Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 12 of 16
Question Id: 641

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

A group is studying the bone growth and mineralization process in humans. They are testing a new substance, Substance X that exhibits the following metabolic effects with continuous, high-dose infusion (see the graph below).



Substance X has metabolic effects that most closely resemble which of the following chemicals?

A. Calcitriol [7%]
B. Calcitonin [4%]
✔ C. PTH [86%]
D. Somatomedin C [0%]
E. Triiodothyronine [0%]

Omitted
Correct answer
C

86%
Answered correctly

3 Seconds
Time Spent

12/29/2018
Last Updated

Block Time Remaining: 00:00:44
TUTOR

0 | Feedback | Suspend | End Block

2:13 PM
2/12/2019

Substance X causes an increase in serum calcium and urine phosphate. Consider PTH, an 84-amino-acid polypeptide secreted by the parathyroid gland. PTH receptors are predominantly present on bone and kidney tubules. PTH stimulates the formation of cyclic AMP via the G-protein/adenylyl-cyclase pathway. The main action of PTH on bone is increased bone resorption. PTH acts on osteoclasts by an indirect method. It is osteoblasts, not osteoclasts that have PTH receptors. PTH causes osteoblasts to increase the production of RANK-ligand and monocyte colony-stimulating factor (M-CSF); these two factors stimulate osteoclastic precursors to differentiate into bone-resorbing, mature osteoclasts.

PTH functions in another way to increase bone resorption. PTH decreases the release of osteoprotegerin (OPG), which is a decoy receptor for the RANK-ligand. OPG decreases the interaction of RANK-ligand on osteoclasts. Lower levels of OPG allow more interaction between the RANK-ligand and its osteoclastic receptor, causing an increase in bone turnover. As a feedback mechanism, high serum calcium causes less PTH to be produced.

By causing increased bone resorption, PTH increases the efflux of calcium and phosphorus from the bone into circulation. PTH also increases absorption of calcium and decreases absorption of phosphorus from kidney tubules. The graph shown in this vignette shows progressive increase in serum calcium and urinary phosphorus as the concentration of the substance X increases, exactly the effects of PTH.

(Choice A) Calcitriol (1,25-dihydroxy vitamin D) is the active form of vitamin D. It is synthesized from 25-hydroxy vitamin D by the enzyme 1-alpha-hydroxylase of the kidneys. PTH increases the activity of 1-alpha-hydroxylase, ultimately increasing the conversion of 25-hydroxy vitamin-D to 1,25-dihydroxy vitamin D. Calcitriol increases the absorption of calcium and phosphorus from the gastrointestinal tract. It suppresses PTH release by increasing serum calcium, in addition to having a direct effect on the parathyroid glands. It is true that high levels of 1,25-dihydroxy vitamin D will cause hypercalcemia, but phosphaturia will not occur because PTH secretion diminishes when there are high levels of calcium in the blood, meaning that PTH will be less active in discouraging phosphorous resorption in the kidneys.

(Choice B) Calcitonin is produced by the parafollicular C-cells of the thyroid gland. Calcitonin inhibits osteoclasts; it ultimately decreases bone resorption, which can lead to an increase in bone mineral density. The effect of calcitonin is opposite to that of PTH.

(Choice D) Insulin like growth factor (IGF) increases bone formation primarily by acting on osteoblasts. IGF increases osteoblastic activity and promotes collagen synthesis. The effect of IGF on serum calcium and urine phosphorus is minimal.

in serum calcium and urinary phosphorus as the concentration of the substance X increases, exactly the effects of PTH.

(Choice A) Calcitriol (1,25-dihydroxy vitamin D) is the active form of vitamin D. It is synthesized from 25-hydroxy vitamin D by the enzyme 1-alpha-hydroxylase of the kidneys. PTH increases the activity of 1-alpha-hydroxylase, ultimately increasing the conversion of 25-hydroxy vitamin-D to 1,25-dihydroxy vitamin D. Calcitriol increases the absorption of calcium and phosphorus from the gastrointestinal tract. It suppresses PTH release by increasing serum calcium, in addition to having a direct effect on the parathyroid glands. It is true that high levels of 1,25-dihydroxy vitamin D will cause hypercalcemia, but phosphaturia will not occur because PTH secretion diminishes when there are high levels of calcium in the blood, meaning that PTH will be less active in discouraging phosphorous resorption in the kidneys.

(Choice B) Calcitonin is produced by the parafollicular C-cells of the thyroid gland. Calcitonin inhibits osteoclasts; it ultimately decreases bone resorption, which can lead to an increase in bone mineral density. The effect of calcitonin is opposite to that of PTH.

(Choice D) Insulin like growth factor (IGF) increases bone formation primarily by acting on osteoblasts. IGF increases osteoblastic activity and promotes collagen synthesis. The effect of IGF on serum calcium and urine phosphorus is minimal.

(Choice E) Triiodothyronine (T3) increases bone turnover mainly by increasing osteoclastic resorption. T3 increases bone turnover, which causes calcium and phosphorus to efflux from the bone. Some patients with thyrotoxicosis have mild hypercalcemia, although the effect of T3 on calcium homeostasis is considerably less than PTH. As with choice A, the increase in serum calcium will suppress PTH; therefore, the phosphaturic response will not occur.

Educational Objective:

- The main action of PTH on bone is increased bone resorption. PTH acts on osteoclasts by an indirect method. It is osteoblasts, not osteoclasts that have PTH receptors. PTH causes osteoblasts to increase the production of RANK-ligand and monocyte colony-stimulating factor (M-CSF); these two factors stimulate osteoclastic precursors to differentiate into bone-resorbing, mature osteoclasts.
- PTH increases serum calcium level and decreases serum phosphate level (the phosphate is lost to urine).

Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 13 of 16
Question Id: 983

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

A 30-year-old woman comes to the office due to excessive weight gain without any changes in her diet or physical activity. She has also been feeling more tired lately and has had frequent constipation. The patient has no prior medical problems and takes no medications. She has been pregnant once and gave birth to a healthy infant 3 years ago. Family history is significant for a thyroid disorder in her mother. Blood pressure is 116/90 mm Hg and pulse is 58/min. BMI is 28.5 kg/m^2. Physical examination reveals a diffusely enlarged and nontender thyroid with no nodules. There is delayed relaxation of deep tendon reflexes. Her hair is thin and the skin appears dry. Which of the following sets of laboratory findings is most likely to be seen in this patient?

	TSH	Thyroxine (T4)	Triiodothyronine (T3)
A.	Increased	Decreased	Normal
B.	Increased	Normal	Normal
C.	Increased	Increased	Increased
D.	Normal	Normal	Decreased
E.	Decreased	Increased	Increased
F.	Decreased	Normal	Normal

Submit

Block Time Remaining: 00:00:47
TUTOR

0 | Feedback | Suspend | End Block

2:14 PM
2/12/2019

Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 13 of 16
Question Id: 983

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

A 30-year-old woman comes to the office due to excessive weight gain without any changes in her diet or physical activity. She has also been feeling more tired lately and has had frequent constipation. The patient has no prior medical problems and takes no medications. She has been pregnant once and gave birth to a healthy infant 3 years ago. Family history is significant for a thyroid disorder in her mother. Blood pressure is 116/90 mm Hg and pulse is 58/min. BMI is 28.5 kg/m^2. Physical examination reveals a diffusely enlarged and nontender thyroid with no nodules. There is delayed relaxation of deep tendon reflexes. Her hair is thin and the skin appears dry. Which of the following sets of laboratory findings is most likely to be seen in this patient?

	TSH	Thyroxine (T4)	Triiodothyronine (T3)
✔ A. [83%]	Increased	Decreased	Normal
B. [2%]	Increased	Normal	Normal
C. [1%]	Increased	Increased	Increased
D. [8%]	Normal	Normal	Decreased
E. [2%]	Decreased	Increased	Increased
F. [0%]	Decreased	Normal	Normal

Block Time Remaining: 00:00:49
TUTOR

0 | Feedback | Suspend | End Block

2:14 PM
2/12/2019

Settings

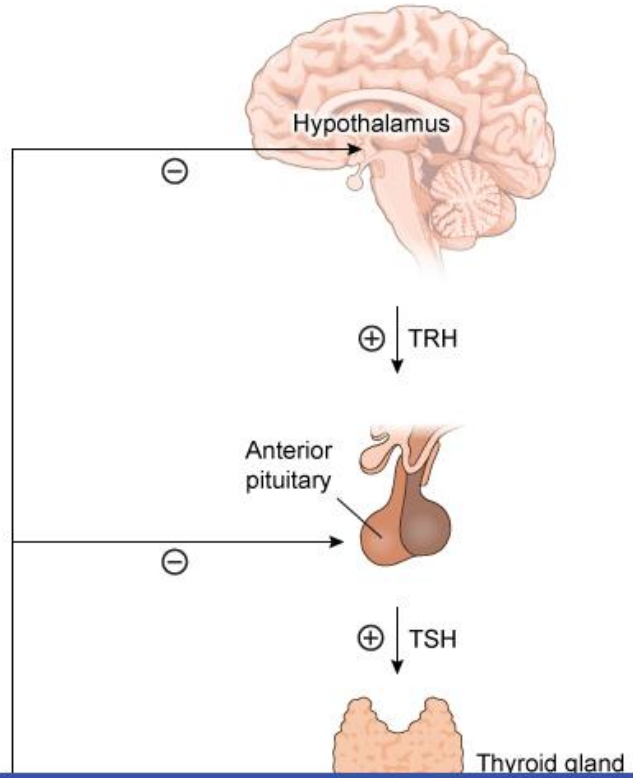
- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10
- 11
- 12
- 13
- 14
- 15
- 16

Item 13 of 16
Question Id: 983

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

Explanation

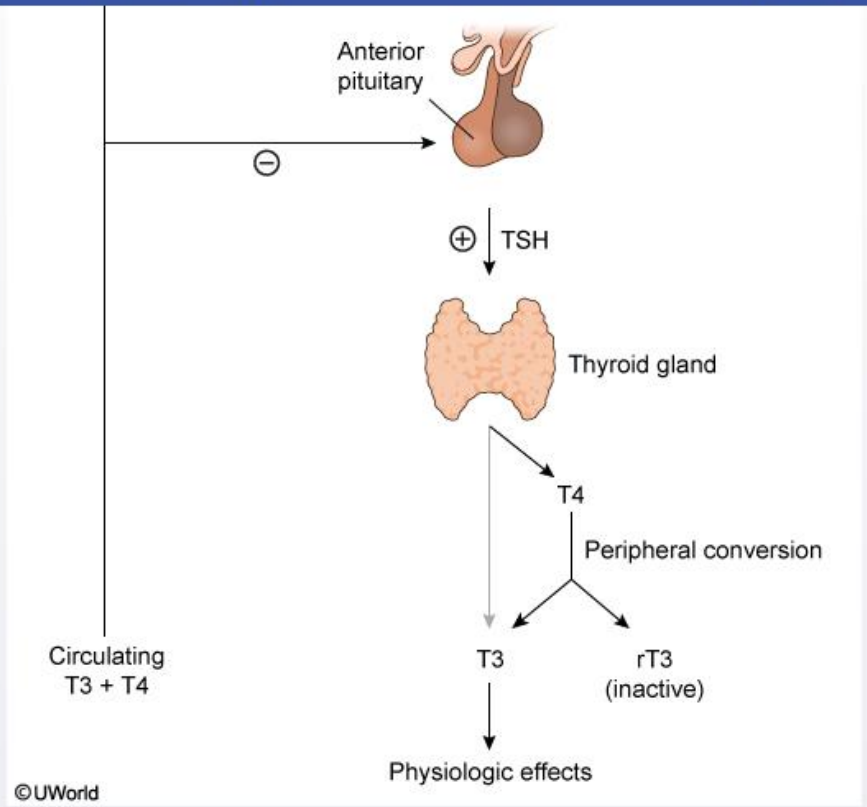
Hypothalamic-pituitary-thyroid axis



Block Time Remaining: 00:00:49
TUTOR

0 | Feedback | Suspend | End Block

2:14 PM
2/12/2019



Regulation of thyroid hormone secretion involves feedback inhibition along the hypothalamic-pituitary-thyroid axis. The hypothalamus releases thyrotropin-releasing hormone (TRH), which triggers release of TSH from the pituitary. TSH stimulates secretion of thyroid hormone from the thyroid, which in turn inhibits release of both TRH and TSH. Thyroid hormone exists in 2 primary forms: T4 (thyroxine), the predominant form secreted by the thyroid, and T3 (triiodothyronine), the more active form produced mainly by deiodination of T4 in peripheral tissues.

Physiologic effects

Regulation of thyroid hormone secretion involves feedback inhibition along the hypothalamic-pituitary-thyroid axis. The hypothalamus releases thyrotropin-releasing hormone (TRH), which triggers release of TSH from the pituitary. TSH stimulates secretion of thyroid hormone from the thyroid, which in turn inhibits release of both TRH and TSH. Thyroid hormone exists in 2 primary forms: T4 (thyroxine), the predominant form secreted by the thyroid, and T3 (triiodothyronine), the more active form produced mainly by deiodination of T4 in peripheral tissues.

This patient has a very typical presentation of **primary hypothyroidism** with weight gain, fatigue, and a delayed relaxation phase of deep tendon reflexes. Her diffuse goiter suggests chronic autoimmune (Hashimoto) thyroiditis, which is the most common cause of hypothyroidism in developed countries. As autoimmune destruction of the gland progresses, thyroid hormone production declines, leading to loss of feedback inhibition of TSH secretion; therefore, patients have **low T4** and **elevated TSH** levels. However, because T3 is produced mainly in peripheral tissues and has a short half-life, serum T3 levels fluctuate widely and correlate poorly with clinical status; **T3 is often normal** in primary hypothyroidism.

(Choice B) TSH secretion is very sensitive to changes in thyroid status and rises in response to even small declines in thyroid hormone production. Subclinical hypothyroidism is a common biochemical state in which an elevated TSH is necessary to maintain normal thyroid hormone levels. However, most patients are asymptomatic.

(Choices C, E, and F) Primary hyperthyroidism (eg, Graves disease) is characterized by elevated thyroid hormone levels and suppressed TSH. Subclinical hyperthyroidism is characterized by suppressed TSH with normal thyroid hormone levels. Central (secondary) hyperthyroidism (eg, TSH-secreting pituitary adenoma) shows elevated levels of both TSH and thyroid hormone. Common clinical features of hyperthyroidism (primary or secondary) include weight loss, heat intolerance, and tachycardia; patients with subclinical hyperthyroidism may be asymptomatic or have mild symptoms. T3 levels correlate with clinical status in hyperthyroidism more closely than in hypothyroidism and are often elevated.

(Choice D) Euthyroid sick syndrome is a constellation of abnormal thyroid tests seen in patients with severe systemic illness (eg, sepsis). Excess cortisol, inflammatory cytokines, starvation, and certain medications (eg, amiodarone) can cause reduced conversion of T4 to T3, leading to low serum T3; reverse T3 (the inactive metabolite of T4) is typically elevated but TSH and T4 are usually normal.

Educational objective:

developed countries. As autoimmune destruction of the gland progresses, thyroid hormone production declines, leading to loss of feedback inhibition of TSH secretion; therefore, patients have **low T4** and **elevated TSH** levels. However, because T3 is produced mainly in peripheral tissues and has a short half-life, serum T3 levels fluctuate widely and correlate poorly with clinical status; **T3 is often normal** in primary hypothyroidism.

(Choice B) TSH secretion is very sensitive to changes in thyroid status and rises in response to even small declines in thyroid hormone production. Subclinical hypothyroidism is a common biochemical state in which an elevated TSH is necessary to maintain normal thyroid hormone levels. However, most patients are asymptomatic.

(Choices C, E, and F) Primary hyperthyroidism (eg, Graves disease) is characterized by elevated thyroid hormone levels and suppressed TSH. Subclinical hyperthyroidism is characterized by suppressed TSH with normal thyroid hormone levels. Central (secondary) hyperthyroidism (eg, TSH-secreting pituitary adenoma) shows elevated levels of both TSH and thyroid hormone. Common clinical features of hyperthyroidism (primary or secondary) include weight loss, heat intolerance, and tachycardia; patients with subclinical hyperthyroidism may be asymptomatic or have mild symptoms. T3 levels correlate with clinical status in hyperthyroidism more closely than in hypothyroidism and are often elevated.

(Choice D) Euthyroid sick syndrome is a constellation of abnormal thyroid tests seen in patients with severe systemic illness (eg, sepsis). Excess cortisol, inflammatory cytokines, starvation, and certain medications (eg, amiodarone) can cause reduced conversion of T4 to T3, leading to low serum T3; reverse T3 (the inactive metabolite of T4) is typically elevated but TSH and T4 are usually normal.

Educational objective:
Primary hypothyroidism is characterized by decreased T4 levels and increased TSH. T3 is primarily produced by conversion from T4 in peripheral tissues; serum levels widely fluctuate due to its short half life, and can often be within the normal range in patients with hypothyroidism.

References

- Pitfalls in the measurement and interpretation of thyroid function tests

Settings

- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10
- 11
- 12
- 13
- 14
- 15
- 16

Item 14 of 16
Question Id: 1562

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

An individual with a point mutation affecting the gene responsible for neurophysin synthesis is most likely to suffer from:

A. Short stature
B. Hyperpigmentation
C. Diabetes insipidus
D. Hypothyroidism
E. Infertility

Submit

Block Time Remaining: 00:00:51
TUTOR

0 | Feedback | Suspend | End Block

Settings

- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10
- 11
- 12
- 13
- 14
- 15
- 16

Item 14 of 16
Question Id: 1562

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

An individual with a point mutation affecting the gene responsible for neurophysin synthesis is most likely to suffer from:

- A. Short stature [8%]
- B. Hyperpigmentation [11%]
- ✔ C. Diabetes insipidus [69%]
- D. Hypothyroidism [4%]
- E. Infertility [5%]

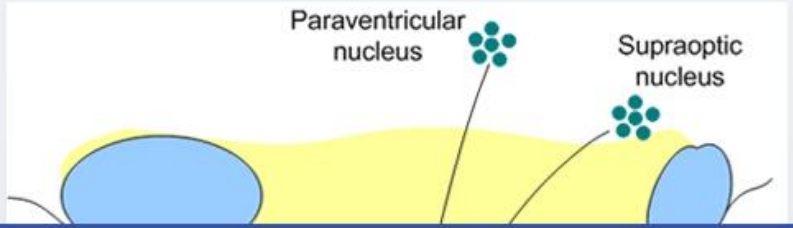
Omitted
Correct answer
C

69%
Answered correctly

3 Seconds
Time Spent

02/06/2019
Last Updated

Explanation



Block Time Remaining: 00:00:52
TUTOR

0 | Feedback | Suspend | End Block

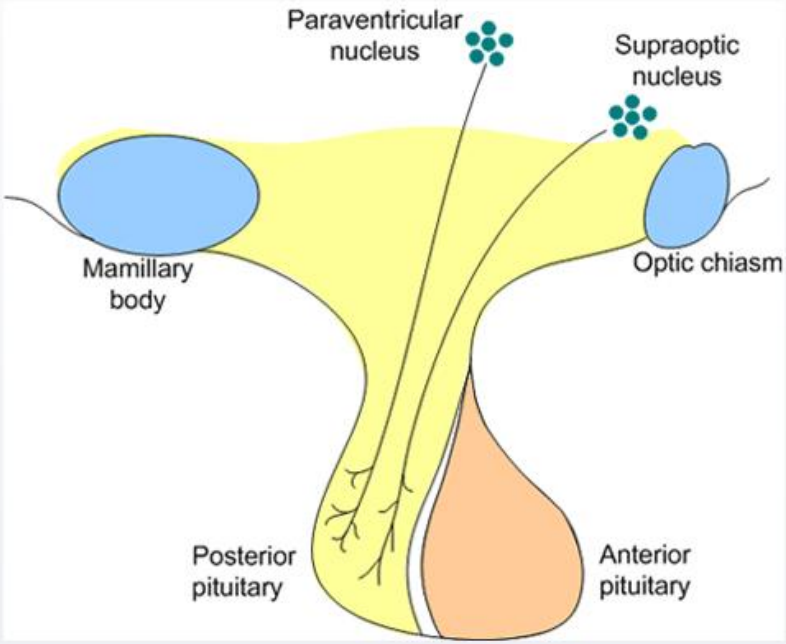
2:14 PM
2/12/2019

Settings

- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10
- 11
- 12
- 13
- 14
- 15
- 16

Item 14 of 16
Question Id: 1562

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



Neurophysins are carrier proteins for oxytocin and vasopressin (antidiuretic hormone, ADH), hormones produced within the paraventricular and supraoptic nuclei, respectively, and released from the posterior pituitary. Like the hormones they accompany, neurophysins are produced within the neuronal cell bodies of hypothalamic nuclei. Neurophysins bind oxytocin and vasopressin and act as chaperone molecules as they are shuttled toward the nerve terminals in the posterior pituitary.

Neurophysin II has a binding site specific for vasopressin and is thought to be involved in the transport and packaging of vasopressin through the endoplasmic reticulum (ER) and Golgi apparatus into neurosecretory granules. A point mutation in neurophysin II could result in abnormal protein

Block Time Remaining: 00:00:52
TUTOR

0 | Feedback | Suspend | End Block

2:14 PM
2/12/2019

Neurophysins are carrier proteins for oxytocin and vasopressin (antidiuretic hormone, ADH), hormones produced within the paraventricular and supraoptic nuclei, respectively, and released from the posterior pituitary. Like the hormones they accompany, neurophysins are produced within the neuronal cell bodies of hypothalamic nuclei. Neurophysins bind oxytocin and vasopressin and act as chaperone molecules as they are shuttled toward the nerve terminals in the posterior pituitary.

Neurophysin II has a binding site specific for vasopressin and is thought to be involved in the transport and packaging of vasopressin through the endoplasmic reticulum (ER) and Golgi apparatus into neurosecretory granules. A point mutation in neurophysin II could result in abnormal protein folding and removal from the ER along with bound vasopressin, thereby decreasing availability of vasopressin for neurosecretory release. Such a mechanism may be responsible for some cases of autosomal dominant hereditary hypothalamic diabetes insipidus.

(Choice A) Short stature may result from a growth hormone deficiency. Neither hypothalamic GHRH release nor anterior pituitary growth hormone secretion involves neurophysins.

(Choice B) Generalized hyperpigmentation is a manifestation of Addison's disease, where a primary defect in adrenal cortisol production reduces feedback inhibition of anterior pituitary pro-opiomelanocortin (POMC) synthesis. As a result, POMC cleavage products, including ACTH and melanocyte-stimulating hormone (MSH), are secreted in excess. High MSH levels cause increased melanin synthesis by melanocytes.

(Choice D) The synthesis and release of TRH and TSH do not involve neurophysins. TRH stimulates the release of both TSH and prolactin. Dopamine tonically inhibits prolactin release.

(Choice E) Infertility can result from inadequate hypothalamic release of GnRH or decreased anterior pituitary production of FSH or LH.

Educational Objective:
Neurophysins are carrier proteins for oxytocin and vasopressin (ADH). Oxytocin and vasopressin are carried by unique neurophysins from their site of production in the cell bodies of the paraventricular and supraoptic nuclei to their site of release in the axon terminals of the posterior pituitary. Point mutations in neurophysin II underlie most cases of hereditary hypothalamic diabetes insipidus, a disorder resulting from insufficient ADH release into the systemic circulation.

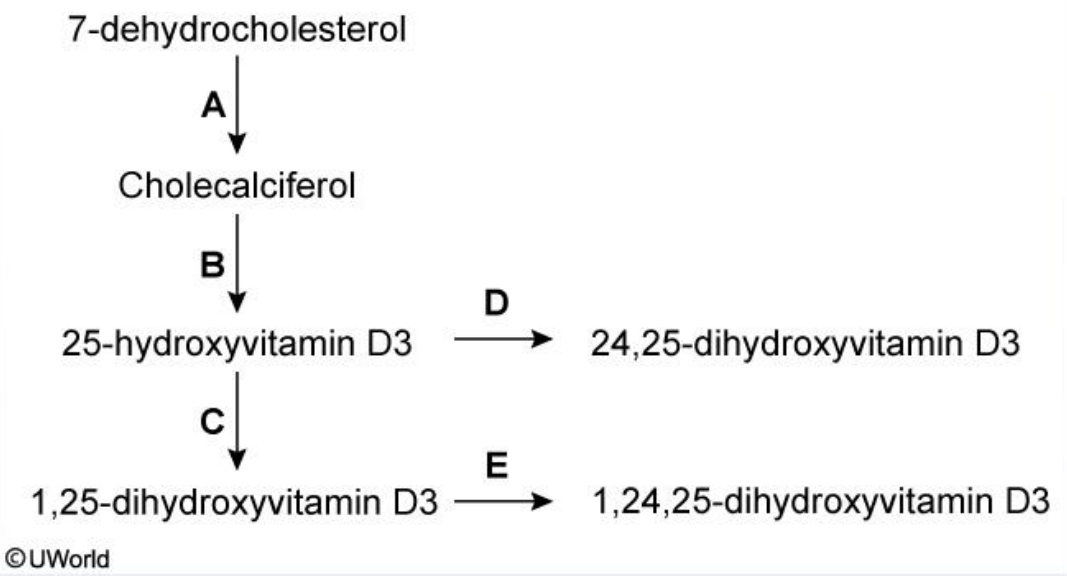
Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 15 of 16
Question Id: 990

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

A 49-year-old man comes to the office due to "aching bones." He has a 2-month history of insidious-onset pain that is most pronounced in the back, pelvis, and lower extremities. The pain is dull and increases after weight-bearing activities. The patient has no prior medical conditions and takes no medications. He emigrated from Central Africa 5 years ago and works overnight shifts as a cab driver. Vital signs are within normal limits. Physical examination shows normal muscle strength in the upper and lower extremities bilaterally. A thorough laboratory evaluation establishes the diagnosis. After discussing the likely cause of his condition, the patient starts spending more time outdoors in the sun. Which of the following enzymatic steps will most likely be affected by this change in activity?



©UWorld

A. A

Block Time Remaining: 00:00:55
TUTOR

Feedback | Suspend | End Block

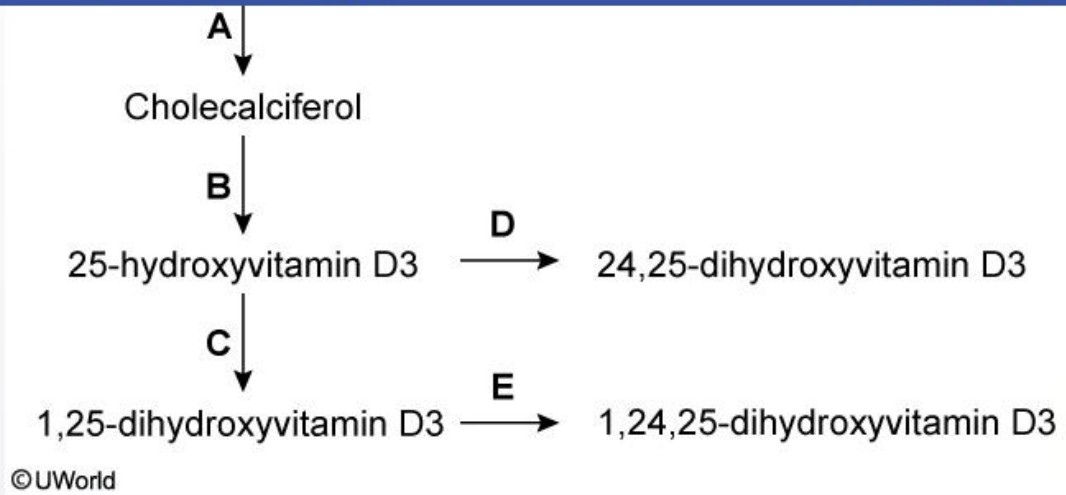
2:14 PM
2/12/2019

Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 15 of 16
Question Id: 990

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



A. A
B. B
C. C
D. D
E. E

Submit

Block Time Remaining: 00:00:58
TUTOR

0 | Feedback | Suspend | End Block

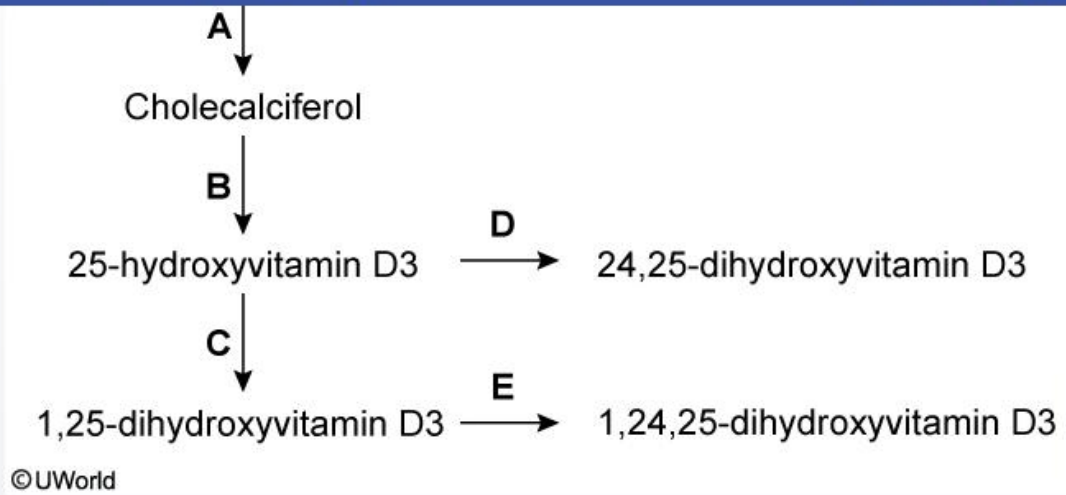
2:14 PM
2/12/2019

Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 15 of 16
Question Id: 990

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



- A. A [63%]
- B. B [17%]
- C. C [13%]
- D. D [3%]
- E. E [1%]

Omitted
Correct answer

63%
Answered correctly

8 Seconds
Time Spent

11/26/2018
Last Updated

Block Time Remaining: 00:01:00
TUTOR

0 | Feedback | Suspend | End Block

2:14 PM
2/12/2019

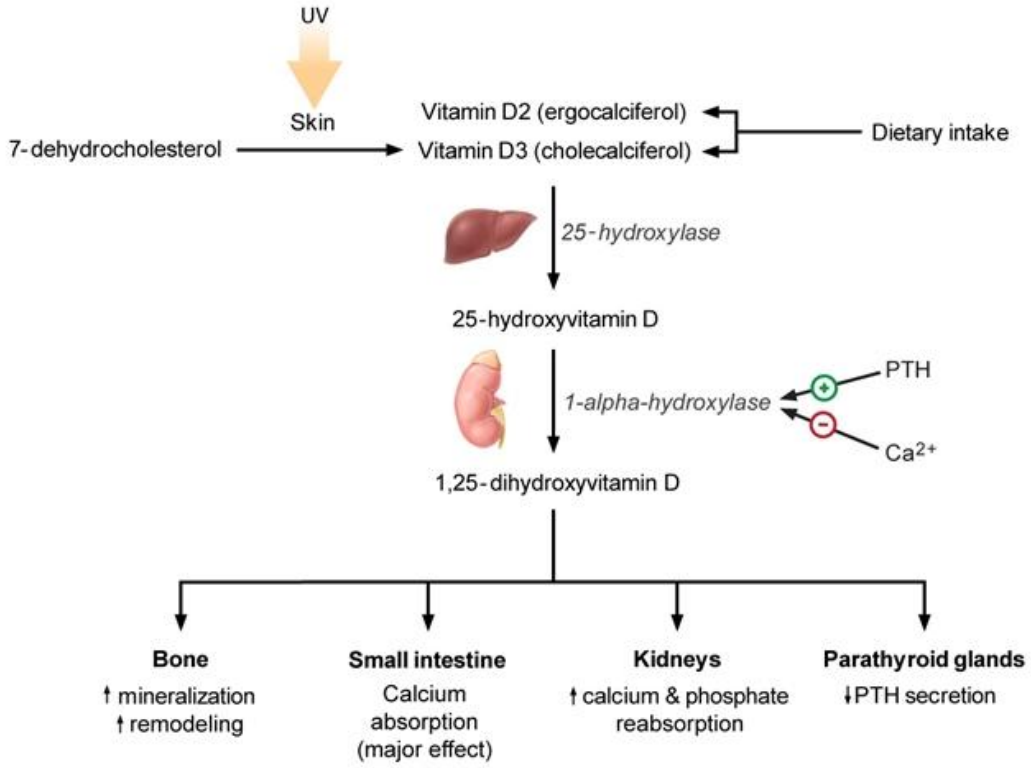
Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 15 of 16
Question Id: 990

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

Normal vitamin D metabolism



PTH = parathyroid hormone.

On exposure to **sunlight**, **7-dehydrocholesterol** (provitamin D3) in the skin absorbs ultraviolet (UV) B rays. This opens the B ring of 7-

Block Time Remaining: 00:01:00
TUTOR

0 | Feedback | Suspend | End Block

2:14 PM
2/12/2019

On exposure to **sunlight**, **7-dehydrocholesterol** (provitamin D3) in the skin absorbs ultraviolet (UV) B rays. This opens the B ring of 7-dehydrocholesterol, forming previtamin D3, which then undergoes thermal isomerization to form **vitamin D3** (cholecalciferol). Vitamin D3 is then hydroxylated in the liver to 25-hydroxyvitamin D and subsequently to 1,25-hydroxyvitamin D (the active form) in the kidneys.

Vitamin D deficiency can lead to osteomalacia with bone pain or tenderness, muscle weakness or cramps, gait abnormalities, and increased fracture risk. Factors associated with limited UV exposure and increased risk of vitamin D deficiency include the following:

- **Reduced time outdoors:** elderly individuals, patients living in residential care or who are frequently hospitalized, people who avoid going outdoors due to high risk of skin cancer
- **Low UV sun exposure:** individuals living at extreme northern or southern latitudes
- **Predominantly nocturnal lifestyle:** shift work or occupations requiring overnight work
- **Blockade of sunlight exposure:** people who use high-grade sunblock or wear full-coverage clothing
- **Reduced UV penetration:** individuals with heavily pigmented skin

(Choices B and C) The conversion of vitamin D2 and D3 to 25-hydroxycholecalciferol by 25-hydroxylase in the liver is primarily regulated by feedback inhibition from 25-hydroxycholecalciferol. The conversion to 1,25-dihydroxycholecalciferol by 1-alpha-hydroxylase in the kidney is primarily regulated by parathyroid hormone (PTH) and plasma calcium levels. Neither of these steps takes place in the skin or is affected by sunlight exposure.

(Choices D and E) 25-hydroxyvitamin D-24-hydroxylase converts 25- and 1,25-dihydroxyvitamin D into inactive 24-hydroxylated metabolites. It is upregulated by 1,25-dihydroxyvitamin D (to prevent excess vitamin D activity) and suppressed by parathyroid hormone (to facilitate replenishment of circulating calcium levels) and thus functions as a counter-regulatory homeostatic enzyme. However, it is not affected by sunlight.

Educational objective:
Sunlight exposure catalyzes conversion of 7-dehydrocholesterol to cholecalciferol (vitamin D3) in the skin. Subsequent 25-hydroxylation in the liver and 1-hydroxylation in the kidneys produce 1,25-dihydroxyvitamin D, the active form. Inadequate exposure to sunlight can lead to vitamin D deficiency.

Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 16 of 16
Question Id: 1009

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

A family is found to have a novel genetic disorder characterized by elevated insulin levels and frequent hypoglycemia brought on by even brief periods of fasting. A group of investigators discovers that they carry a mutation involving a potassium channel expressed in pancreatic beta cells. This abnormality causes hypoglycemia because it makes the potassium channels overly sensitive to their normal, activity-modulating regulatory substance. Which of the following substances binds directly to these channels to regulate their activity?

A. ATP
B. Citrate
C. Fructose-6-phosphate
D. Fumarate
E. Glucose
F. Lactate
G. Malate
H. Pyruvate

Submit

Block Time Remaining: 00:01:01
TUTOR

0 | Feedback | Suspend | End Block

2:15 PM
2/12/2019

Settings

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Item 16 of 16
Question Id: 1009

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

A family is found to have a novel genetic disorder characterized by elevated insulin levels and frequent hypoglycemia brought on by even brief periods of fasting. A group of investigators discovers that they carry a mutation involving a potassium channel expressed in pancreatic beta cells. This abnormality causes hypoglycemia because it makes the potassium channels overly sensitive to their normal, activity-modulating regulatory substance. Which of the following substances binds directly to these channels to regulate their activity?

- A. ATP [69%] ✔
- B. Citrate [2%]
- C. Fructose-6-phosphate [2%]
- D. Fumarate [0%]
- E. Glucose [21%]
- F. Lactate [0%]
- G. Malate [0%]
- H. Pyruvate [1%]

Omitted
Correct answer
A

69%
Answered correctly

3 Seconds
Time Spent

02/04/2019
Last Updated

Explanation

Block Time Remaining: 00:01:03
TUTOR

0 | Feedback | Suspend | End Block

2:15 PM
2/12/2019

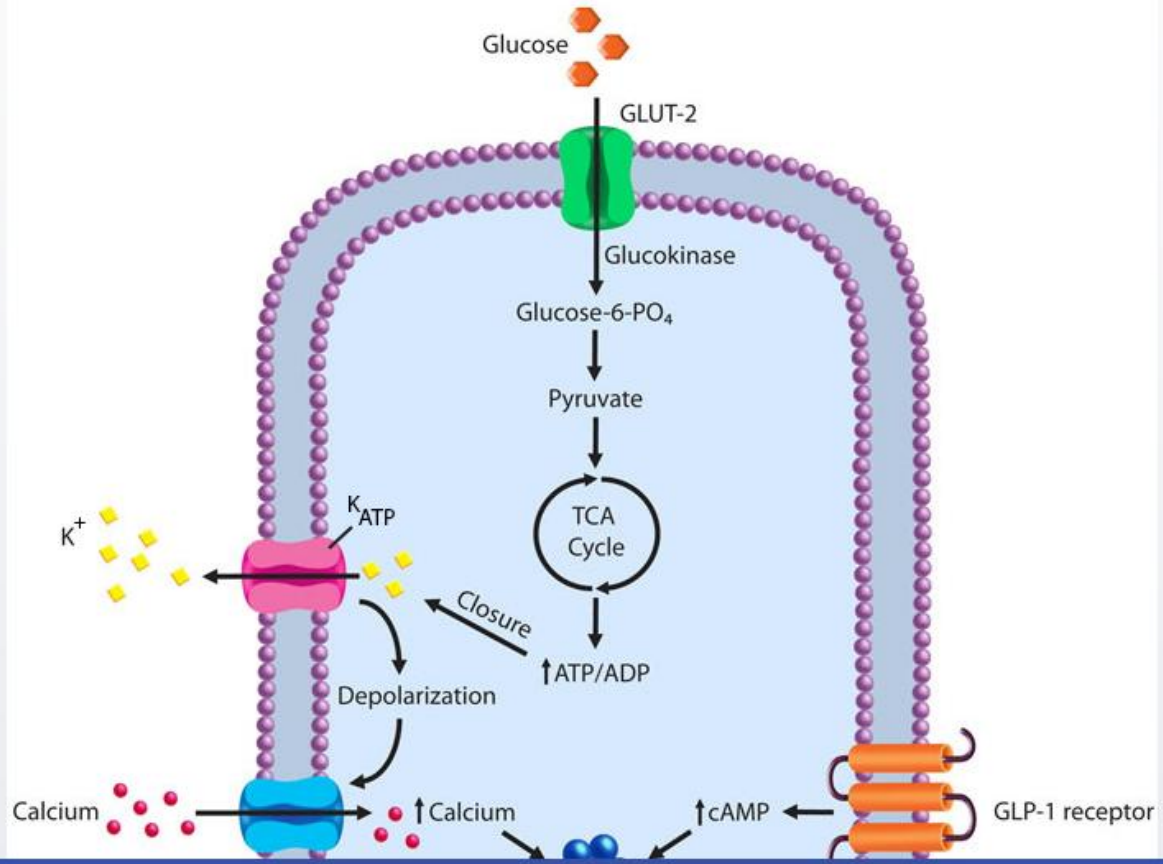
Settings

- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10
- 11
- 12
- 13
- 14
- 15
- 16

Item 16 of 16
Question Id: 1009

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

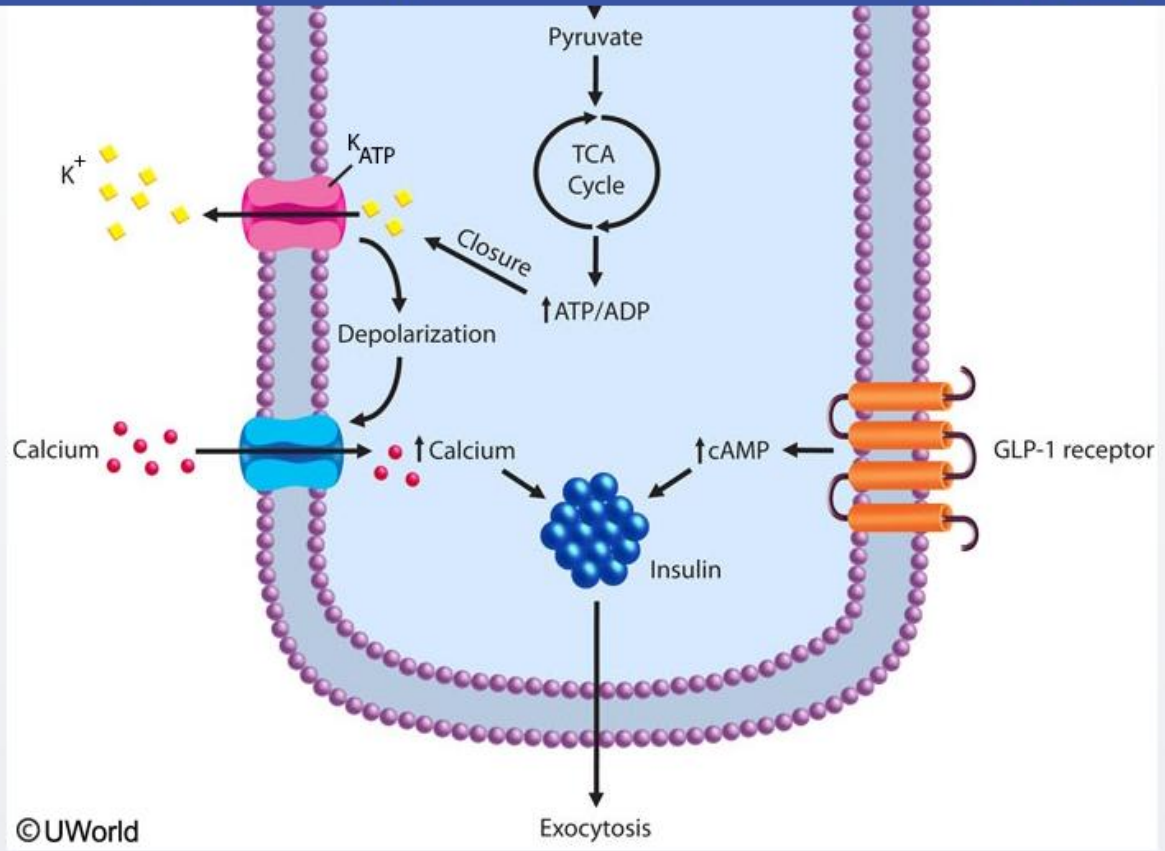
Pancreatic beta cell function



Block Time Remaining: 00:01:03
TUTOR

0 | Feedback | Suspend | End Block

2:15 PM
2/12/2019



Glucose is the most important stimulator of insulin release. Glucose enters beta cells by facilitated diffusion via **glucose transporter 2** (GLUT-2) and undergoes oxidative metabolism through glycolysis and the citric acid cycle, generating **ATP**. ATP then binds to the regulatory subunit of the **ATP-sensitive K+ channel** (K_{ATP} channel). K_{ATP} channels are normally open at rest and maintain membrane polarization by allowing outward

Settings

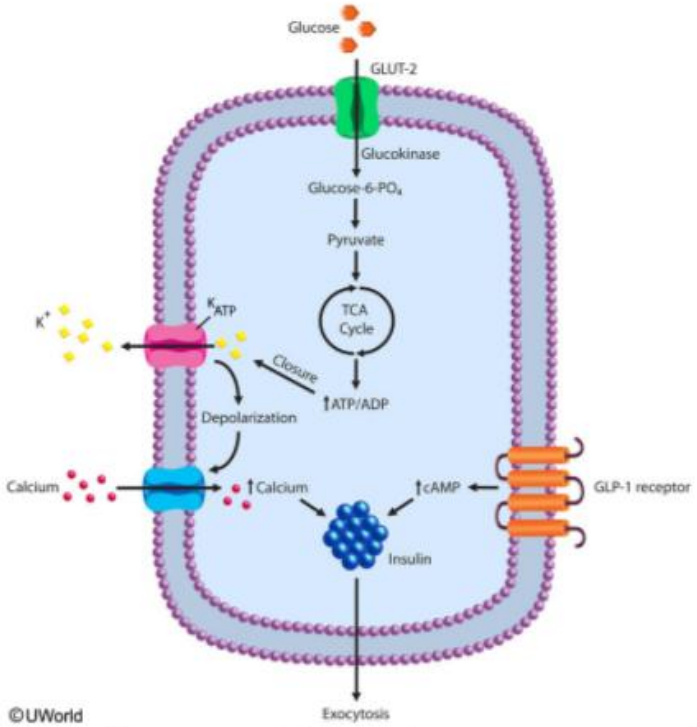
- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10
- 11
- 12
- 13
- 14
- 15
- 16

Item 16 of 16
Question Id: 1009

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

Exhibit Display

Pancreatic beta cell function



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

ATP-sensitive K+ channel (K+ channel). K+ channels are normally open at rest and maintain membrane polarization by allowing outward

Block Time Remaining: 00:01:03
TUTOR

0 | Feedback | Suspend | End Block

2:15 PM
2/12/2019

Exocytosis

Glucose is the most important stimulator of insulin release. Glucose enters beta cells by facilitated diffusion via **glucose transporter 2** (GLUT-2) and undergoes oxidative metabolism through glycolysis and the citric acid cycle, generating **ATP**. ATP then binds to the regulatory subunit of the **ATP-sensitive K^+ channel** (K_{ATP} channel). K_{ATP} channels are normally open at rest and maintain membrane polarization by allowing outward movement of potassium from the beta cells, but on binding ATP, the K_{ATP} channels close. A high ATP/ADP ratio therefore leads to decreased K^+ efflux and **membrane depolarization**. This results in the opening of voltage-dependent calcium channels, increased intracellular calcium levels, and subsequent **insulin release**.

Family studies in patients with neonatal diabetes mellitus have identified mutations of the K_{ATP} channels in which elevated glucose levels do not lead to appropriate depolarization and insulin release. These patients can be treated successfully with sulfonylureas, which bind to K_{ATP} channels and cause closure independent of ATP. Conversely, a mutation causing an increased affinity for ATP and inappropriate closure of the K_{ATP} channels would lead to excessive insulin release and frequent hypoglycemia.

(Choices B, D, and G) Citrate, malate, and fumarate are intermediate products in the citric acid cycle. During this process, energy is stored as NADH and $FADH_2$. ATP is then produced when NADH and $FADH_2$ enter oxidative phosphorylation. However, these intermediates do not have any direct effect on K_{ATP} channels.

(Choices C, F, and H) Fructose 6-phosphate and pyruvate are products of the glycolytic pathway. Lactate is produced from pyruvate during anaerobic glycolysis. Glycolysis raises intracellular ATP levels, but these glycolytic intermediates do not affect K_{ATP} channels directly.

(Choice E) Glucose induces insulin release from beta cells via ATP formation but does not interact with K_{ATP} channels directly.

Educational objective:
Oxidative metabolism of glucose in pancreatic beta cells generates ATP. ATP-induced closure of the ATP-sensitive K^+ channel leads to membrane depolarization and subsequent insulin release.

References

Facebook: https://Facebook.com/MedicalBooksVN
Website: https://MedicalBooksVN.com
Email: MedicalBooksVN@gmail.com