Endocrinology

Section 1

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1 Which is TRUE?
a) thyroid gland is essential for life
b) T_3 is more potent than T_4
c) RT_3 is more active than T_4
d) T_3 is the predominant hormone secreted by the thyroid
e) most of T_3 converts to T_4 in peripheral tissue

2 Which of the following proteins has largest capacity to bind with thyroxine?
a) albumin
b) globulin
c) TBG (thyroxine binding globulin)
d) transferrin
e) ferritin

3 Which of the following is NOT PRESENT when the thyroid gland is inactive?
a) abundant colloid
b) large follicles
c) flat cells lining the follicles
d) reabsorption lacunae
e) elevation of TSH

4 Which is TRUE, Insulin:
a) decreases amino acid uptake from the muscle
b) increases ketogenesis
c) increases ketone uptake by muscles
d) decreases protein synthesis in liver
e) increases protein catabolism in muscle

5 All of the following tissues are dependent on insulin for its glucose entry EXCEPT:
a) adipose tissue
b) skeletal muscle
c) smooth muscle
d) cardiac muscle
e) β cells of the pancreas

6 All of the following increase insulin secretion EXCEPT:

a) β adrenergic stimulation
b) acetylcholine
c) glucagon
d) α adrenergic stimulation
e) arginine

7 Which is TRUE?

a) glucagon does not increase insulin secretion
b) somatostatin increases insulin secretion
c) diazoxide stimulates insulin secretion
d) K^+ depletion increases insulin secretion
e) glucagon increases somatostatin secretion

8 Which is TRUE in respect to insulin secretion?

a) dependent on glucose entry to β cells of the pancreas
b) Ca^{2+} is not involved
c) K^+ efflux is essential for insulin secretion
d) metformin increases the insulin secretion from β cells
e) cAMP inhibits its secretion

9 Which of the following increases Ca^{2+} absorption?

a) oxalates
b) phosphates
c) alkalis
d) high Ca^{2+} intake
e) high protein diet

10 Which is TRUE?

a) parathyroid hormone increases Ca^{2+} absorption from PCT (proximal convoluted tubules)
b) PTH inhibits phosphate absorption from proximal convoluted tubule
c) calcitonin stimulates osteoclasts
d) oestrogens stimulates osteoclasts
e) PTH has no effect on osteoblasts

11 Which is TRUE regarding calcitonin?

a) stimulated by decreased gastrin
b) increases Ca^{2+} excretion via kidney
c) decreases Ca^{2+} in the blood but increases phosphate
d) increases bone resorption
e) decreases by CCK2 secretion

12 Somatostatin is secreted from which islet cell?

a) A cell
b) B cell
c) C cell
d) D cell
e) F cell

13 Insulin secretion is inhibited by:

a) CCK
b) amino acids
c) glucagon
d) somatostatin
e) glucose

14 Glucagon secretion is stimulated by:

a) somatostatin
b) glucose
c) insulin
d) ketones
e) exercise

15 Regarding the adrenal glands:

a) the adrenal medulla is essential for life
b) the adrenal cortex constitutes one third of the gland
c) the zona glomerulosa contains 17 α hydroxylase
d) there is severe K^+ depletion in Conn's syndrome

16 Regarding calcium metabolism:

a) high calcium levels leads to tetany
b) 85-90% is in the skeleton
c) high calcium levels activate PTH
d) bone turnover is 80% per year in infants
e) chronic low calcium leads to secondary hyperparathyroidsim?????

17 The greatest reabsorption of calcium in the kidneys occurs in the:

a) proximal convoluted tubule
b) descending loop of Henle
c) ascending loop of Henle
d) distal convoluted tubule
e) collecting duct

18 The net production of ATP per mole of glucose metabolised aerobically is:

a) 8
b) 18
c) 36
d) 38
e) 42

19 The caloric value of protein is:

a) 4.1 Kcal/g
b) 5.3 Kcal/g
c) 6.7 Kcal/g
d) 9.3 Kcal/g
e) 10.1 Kcal/g

20 TSN secretion is stimulated by:

a) dopamine
b) somatostatin
c) cold temperatures
d) stress
e) glucocorticoids

21 Thyroxine (T_4) has great affinity for:

a) thyroxine-binding globulin
b) transthyretin
c) thyroxine-binding pre-albumin
d) albumin
e) triodothyronine

22 GLUT is an example of:

a) simple diffusion
b) facilitated diffusion
c) primary active transport
d) secondary active transport
e) endocytosis

23 The most common cell type of the endocrine pancreas is:

a) A cells
b) B cells
c) C cells
d) D cells
e) F cells

24 Both insulin and somatostatin:
a) are released from extra-pancreatic sites
b) receptors are linked to G proteins
c) inhibit release of glucagons
d) cause K^+ uptake by cells
e) are polypeptides containing two chains linked by disulphide bonds

25 Aldosterone is secreted by:
a) zona reticularis
b) zona fasciculate
c) zona glomerulosa
d) zona fasciculata and reticularis
e) zona glomerulosa and fasciculata

26 Regarding aldosterone:
a) it is released in response to hypokalaemia
b) it has glucocorticoid action
c) it works via G-proteins to increase Na^+ reabsorption
d) its release results in alkaline urine
e) it is highly protein-bound

27 Calcitonin secretion is increased by:
a) gastrin
b) CCK
c) secretin
d) glucagon
e) all of the above

28 All of the following bind to intracellular receptors EXCEPT:
a) cortisol
b) aldosterone
c) 1,25-DHCC
d) parathyroid hormone
e) thyroxine

29 How many trophic hormones does the anterior pituitary produce?
a) 2
b) 3
c) 5
d) 6
e) 8

30 All of the following are high energy phosphate compounds EXCEPT:
a) adenosine triphosphate
b) glucose 6-phosphate
c) creatine phosphate
d) adenosine diphosphate
e) guanosine triphosphate

31 Under aerobic conditions, 1 mol glucose forms:
a) 2 mol ATP
b) 8 mol ATP
c) 16 mol ATP
d) 38 mol ATP
e) 42 mol ATP

32 The approx ratio of fat : CHO energy stores is:
a) 2 : 1
b) 4 : 1
c) 10 : 1
d) 20 : 1
e) 40 : 1

33 Nutritionally essential amino acids include:
a) glycine
b) serine
c) lysine
d) glutamine
e) tyrosin

34 Uric acid is formed by the breakdown of:
a) purines
b) pyrimidines
c) glutamine
d) urea
e) all of the above

35 The LDL contains which aproprotein:
a) A
b) B-48
c) B-100
d) C
e) E

36 Regarding cellular metabolism of cholesterol:

a) it inhibits HMG-CoA redvotase
b) is processed in part to other cholesterol esters by the enzyme acetyl CoA : chol acyltransferase
c) it inhibits the formation of LDL receptors
d) all of the above
e) none of the above

37 Which of the following substances decreases the activity of hormone-sensitive lipase:

a) adrenaline
b) thyroxine
c) serotonin
d) TSH
e) prostaglandin E

38 Chromium deficiency leads to:

a) insulin resistance
b) hypogondal dwarfism
c) anaemia
d) charge in ossification
e) thyroid disorders

39 Vitamin B_1 (thiamine) deficiency leads to:

a) anaemia
b) beri beri
c) convulsions
d) dermatitis
e) pellagra

Endocrinology

Section 1 – Answers

1	B
2	A
3	A
4	C
5	E
6	D
7	E
8	?????
9	E
10	B
11	B
12	D
13	D
14	E
15	D
16	E
17	A
18	D
19	B
20	C
21	A
22	B
23	B
24	C
25	C
26	B
27	E
28	D
29	C
30	B
31	D
32	E
33	C
34	A
35	C
36	D
37	E
38	A
39	B

Section 2

GI/Digestion/Absorption/Metabolism

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1 Vitamins co-transported with Na^+ include all except:
a) thiamine
b) folate
c) niacin
d) riboflavin
e) pyridoxine

2 Fat soluble vitamins include all EXCEPT:
a) vitamin A
b) vitamin C
c) vitamin D
d) vitamin E
e) vitamin K

3 The largest daily volume of secretions in the GIT originates in the:
a) salivary glands
b) stomach
c) gall bladder (bile)
d) pancreas
e) intestine

4 Iron:
a) most dietary iron is in the ferrous state
b) most iron is absorbed in the upper small intestine
c) a ferritin micelle contains 1,000 atoms of iron
d) 90% of body iron is in haemoglobin
e) 10% of dietary iron is normally absorbed

5 Ketone bodies:
a) are not formed under normal conditions
b) are all moderately strong acids
c) are formed when intracellular glucose is deficient
d) are easily metabolised in the liver
e) all of the above

6 Regarding migrating motor complex (MMC), which is TRUE?
a) it occurs mainly during food ingestion
b) it is similar to basic electric rhythm
c) it occurs usually during the fasting between the periods of digestion
d) the gastric acid secretion, bile flow, pancreatic juice secretion decreases during MMC
e) the phase I of the MMC is characterised by co-ordinated electric activity and contraction

7 Regarding cholera; which is TRUE?
a) vibrio cholera organisms enter the enterocytes of the intestine to cause diarrhoea
b) diarrhoea is produced by interference in Cl^- channel by increasing cAMP levels
c) Na^+ / glucose co-transport systems become ineffective in cholera infection
d) the mucosal carrier of Na^+ absorption is ↑↑ed
e) the toxins stimulate the ATPase activity and decrease the ????G protein levels

8 Regarding α amylase of salivary glands, which is TRUE?
a) the activator of salivary (gland) α amylase is Cl^-
b) the optimum pH for its action is pH of 2-3
c) α amylase breaks down carbohydrate to glucose
d) α amylase acts mainly on α-1-6 linkages of carbohydrate
e) α amylase acts on lipids to produce fatty acids and α glycerol

9 Regarding absorption of hexose, which is TRUE?
a) the main absorption site is the terminal part of ileum
b) increased Na^+ concentration in the gut lumen - decreases the hexose absorption
c) glucose and Na^+ share the same co-transport or symport from intestinal lumen to enterocytes
d) glucose is transported from the enterocyte to interstitium by Na^+ dependent glucose transport ($SGLT_2$)
e) the fructose has the same mechanism (which is Na dependent) as hexose

10 Regarding protein digestion and absorption, which is TRUE?
a) the pepsinogens are activated by alkaline pH
b) the chymotrypsin, trypsin, elastase are carboxy peptidase
c) the absorption of tri and di peptides depend on Na^+ dependent transport system
d) the absorption of most amino acids from the intestinal lumen depends on Na^+ dependent transport system
e) the transport of amino acids from enterocyte to blood stream does not depend on Na^+ dependent transport system

11 Which of the following is TRUE?
a) vibrio cholera organism enter the enterocyte to cause diarrhoea
b) colipase: secreted by pancreas activate pancreatic lipase
c) vitamin B_{12} and folic acid absorption depends on Na^+ dependent co transport
d) Ca^{2+} absorption from the gut increases by oxalates and phytates
e) most of the dietary irons are in the ferrous form

12 Which is TRUE:
a) TG cells secrete gastrin 17
b) the hormones of secretin family includes ch???? cystokinins and VIP
c) G_{34} (gastrin) is the principle form, which stimulates the gastric acid secretion
d) gastrin 17 has a longer half-life than G_{34}
e) gastrin stimulates the growth of mucosa in the stomach / small intestine / large intestine

13 Which of the following is FALSE regarding gastrin?
a) gastrin secretion is not inhibited by atropine
b) gastrin secretion is stimulated by amino acids ???? peptides
c) gastrin secretion is stimulated by VIP and GIP and glucagon
d) secretin inhibits gastrin secretion
e) epinephrine increases the gastrin secretion

14 Which of the following is TRUE regarding salivary glands?
a) the parotid gland is the main salivary gland which contributes to total salivary content
b) the submandibular gland is mainly a serous gland
c) the parotid gland is mainly a mucous gland
d) the submandibular gland contributes to 70% of total salivary content
e) the lingual gland is a mixed gland with serous and mucous components

15 Regarding cholecystokinin-pancreozymin, which is TRUE?
a) decreases the gall bladder contraction
b) it secretes pancreatic juice rich in enzymes
c) it secretes pancreatic juice rich in HCO_3^-
d) it decreases the action of secretin on pancrease
e) it increases the gastric emptying time

16 Regarding secretin, which is TRUE?
a) decreases the CCK-P_2 action on the pancreas
b) it secretes pancreatic fluid which are rich in enzymes
c) it increases the acid secretion from the stomach
d) it decreases the gastrin secretion
e) it increases the gastric emptying time

17 VIP:

a) it causes contraction of the intestinal tract including the sphincters
b) it increases the secretion of water and electrolytes from the intestine
c) it increases the acid secretion of the stomach
d) it constricts the blood vessels
e) VIP decreases the action of acetylcholine on salivary glands

18 Which is TRUE, regarding acid secretion?

a) histamine increase acid secretion by increasing intracellular Ca^{2+} level
b) prostaglandins increases adenylcyclase activity and increases ???? a ???secr
c) gastrin increases the acid secretion by increasing the hist??? release from enterochomaffin cells
d) gastrin increases the acid secretion by increasing cAMP
e) acetylcholine acts via histamine receptors

19 What stimulates glucagon secretion?

a) free fatty acids
b) GABA
c) somatostatin
d) α agonists
e) acetylcholine

20 The renal threshold for glycosuria is:

a) 18mg/dL
b) 1.8mg/dL
c) 180mg/dL
d) 80mg/dL
e) 160mg/dL

21 Which effect of insulin occurs in seconds?

a) + protein synthesis
b) - posphorylase
c) increased transport of K^+ into insulin sensitive cells
d) + glycolysis
e) + gluconeogenesis

22 Osteoclasts are derived from:

a) osteocytes
b) fibroblasts
c) basophils
d) osteoblasts
e) monocytes

23 Defective osteoclasts leads to:
a) osteogenesis imperfecta
b) osteopetrosis
c) osteomalacia
d) osteoporosis
e) rickets

24 The total amount of fluid entering the intestine per day is:
a) 200ml
b) 7000ml
c) 2000ml
d) 8800ml
e) 9000ml

25 K^+ is actively reabsorbed from the GIT lumen in the:
a) duodenum
b) jejunum
c) ileum
d) proximal colon
e) distal colon

26 Which part of the GIT does NOT display the basic electrical rhythm?
a) oesophagus
b) antrum of stomach
c) duodenum
d) ileum
e) descending colon

27 What inhibits gastrin secretion?
a) atropine
b) secretin
c) adrenaline
d) amino acids
e) calcium

28 Which GIT hormone stimulates enzyme-rich pancreatic juice secretion?
a) gastrin
b) cholecystokinin
c) secretin
d) VIP
e) glucagon

Section 2 – Answers

GI / Digestion / Absorption / Metabolism

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

Endocrine and Gastrointestinal Tract

Section 1

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1 With regard to carbohydrate digestion:
a) salivary amylase works best at alkaline pH
b) approximately 40% of adult Europeans are lactose intolerant
c) oligosaccharidase deficiency results in osmotic diarrhoea
d) salivary amylase continues to digest carbohydrates in the stomach

2 Carbohydrate absorption:
a) all glucose, galactose and fructose is co-transported with Na by the SGLT-2 transporter into enterocytes
b) all glucose/galactose and fructose is transported across the basolateral membrane by GLUT2
c) fructose absorption is a secondary active transport mechanism
d) absorption is decreased by insulin

3 The liberation of proteins to free amino acids (final digestive step) occur in all of the following EXCEPT:
a) enterocyte cytoplasm
b) brush border
c) small intestine lumen
d) stomach

4 Steatorrhoea occurs with all of the following EXCEPT:

a) gastrinoma
b) congenital defect in gastric lipase
c) ileal disease with failure to reabsorb bile salts
d) exocrine pancreatic disease

5 Which is a water soluble vitamin?
a) D
b) B_{12}
c) A
d) K
e) E

6 Which is not Na^+ dependent for absorption?
a) thiamin
b) riboflavin
c) niacin
d) folate
e) biotin

7 Which is absorbed mainly in the colon?
a) short chain fatty acids
b) calcium
c) vitamin K
d) oligosaccharides

8 Which is INCORRECT regarding nerve supply to the gut?
a) the blood vessels are known to have enteric, parasympathetic and sympathetic innervation
b) the myenteric plexus lies between the longitudinal and circular muscle layers
c) parasympathetic supply is via vagal and sacral nerve
d) sympathetic supply is often inhibitory on cholinergic postganglionic fibres

9 Gastrin secretion is stimulated by all but:
a) luminal peptides
b) vagal discharge
c) luminal acid
d) phenylalanine

10 The actions of gastrin include all but:
a) insulin secretion in response to a carbohydrate meal
b) a trophic effect on colonic mucosa
c) a trophic effect on gastric mucosa
d) pepsin secretion
e) contraction of muscle at the gastro-oesophageal junction

11 Which is NOT an action of CCK?
a) gallbladder contraction
b) increased gastric motility and emptying
c) glucagon secretion
d) secretion of pancreatic juice

12 Which hormone is most important in insulin secretion?

a) gastrin
b) CCK
c) GIP
d) secretin

13 Which produces the majority of salivary volume?

a) lingual glands
b) sublingual
c) parotid
d) submandibular

14 Which nerve is NOT involved in the efferent (motor) swallow reflex?

a) trigeminal
b) vagus
c) facial
d) hypoglossal

15 Which is NOT part of the normal content of gastric juice?

a) HPO_4^{2-}
b) mucus
c) lipase
d) amylase

16 Chief cells secrete:

a) HCl
b) pepsinogen
c) intrinsic factor
d) HCO_3^-

17 Which stimulates parietal cell secretion?

a) prostaglandins
b) aspirin
c) vinegar
d) acetylcholine

18 Regarding bilirubin:

a) unconjugated bilirubin is more soluble than conjugated
b) all conjugated bilirubin is excreted via the intestine
c) bile duct obstruction causes jaundice secondary to unconjugated hyperbilirubinaemia
d) haemolytic anaemia may cause ?????? hyperbilirubinaemia

19 Which form of intestinal smooth muscle contraction does NOT occur in normal health?

a) peristalsis
b) weak antiperistalsis
c) peristaltic rushes
d) tonic contractions
e) segmental contractions

20 In the adrenal medulla:

a) epinephrine is formed by the hydroxylation and decarboxylation of tyrosine
b) 10% of the cells are the epinephrine-secreting type
c) plasma norepinephrine levels are generally unchanged after adrenalectomy
d) catecholamine t1/2 is 10 minutes in the circulation
e) norepinephrine and epinephrine are stored in granules with APT and chromagranin C

21 In the adrenal cortex:

a) the zona glomerulosa has 17 alpha-hydroxylase and no aldosterone synthase
b) all the cholesterol is synthesised from acetate
c) zona fasciculata makes up 10% of the mass of the adrenal gland
d) angiotensin II binds to receptors in the zona reticularis
e) ATCH increases the synthesis of all 5 P450 cytochromes involved in the formation of adrenocortical hormones

22 Regarding the islets of Langerhans:

a) D cells secrete pancreatic polypeptide
b) A cells are the most common
c) they are most plentiful in the body of the pancreas
d) blood from the islets drain into the hepatic portal vein
e) B cell secretion of glucagon occurs by exocytosis

23 Which factor stimulates insulin secretion?
a) thiazide diuretics
b) phenytoin
c) theophylline
d) β blockers
e) epinephrine

24 Thyroid hormones increase the oxygen consumption of:
a) lymph nodes
b) spleen
c) brain
d) anterior pituitary gland
e) liver

25 The action of gastrin includes all EXCEPT:
a) stimulation of insulin secretion after a carbohydrate meal
b) stimulation of gastric acid secretion
c) stimulation of gastric motility
d) contraction of gastro-oesophageal junction musculature
e) stimulation of growth of large intestine mucosa

26 Regarding protein metabolism, which statement is CORRECT?
a) increases the respiratory quotient to values > 1.0
b) has a specific dynamic action (SDA) of approximately 10%
c) endogenous protein breakdown is inhibited by glucagon
d) creatinine excretion is not depressed in starvation
e) NH_4^+ formed during transamination of amino acids is excreted in the urine as urea

27 Regarding fat metabolism, which statement is CORRECT?
a) ketone bodies accumulate in DKA due to a lack of acetyl-CoA substrate
b) fatty acids are transported in the plasma bound to lipoprotein complexes
c) cholesterol is transported from extra-hepatic cells to the liver by high-density lipoproteins (HDLs) in the endogenous pathway
d) eicosanoids are synthesised from cholesterol
e) simvastatin reduces plasma cholesterol levels by increasing hepatic biliary excretion

28 Thyroxine:
a) is mostly bound to albumin in the plasma, since this has the largest capacity
b) is 2-5 times more potent that triiodothyronine (T_3)
c) stimulates TSH release
d) ~33% is deiodinated in the liver to T_3
e) does not cross the placenta

29 Insulin:
a) binds to GLUT 1-5 receptors in the peripheral tissues
b) deficiency results in increased gluconeogenesis
c) has a plasma half-life of 2-3 hours
d) is secreted by the pancreatic A cells
e) average secretion is around 40U/day

30 With respect to calcium metabolism / bone formation:
a) osteoclasts secrete alkaline phosphatase
b) osteoblasts are haemopoietic derivatives of monocyte lineage
c) 1,25$(OH)_2$???D_3 and PTH stimulate both osteoblasts and osteoclasts
d) oestrogens are thought to be protective of osteoporosis as their main effect is osteoblasts stimulation
e) the plasmic calcium may be markedly elevated in “disuse” osteoporosis

31 All of the following, except one, inhibit insulin secretion. Which is it?
a) somatostatin
b) thiazide diuretics
c) propranolol
d) insulin
e) glucagon

32 All but one of the following compounds releases large amounts of energy on breakdown:
a) cAMP
b) ATP
c) creatine phosphate
d) ADP
e) coenzyme A

33 Which is TRUE?
a) adenosine triphosphate is a low energy phosphate
b) reduction involves loss of hydrogen or electrons
c) oxidative phosphorylation occurs in the endoplasmic reticulum
d) ATP is precursor of cyclic AMP
e) ADP has no feedback on oxidative phosphorylation

34 Small intestine:
a) the ligament of Treitz the jejunum becomes the ileum
b) the distance pylorus to ileocecal valve in living humans is 700cm
c) malabsorption syndrome may develop if 25% of the small intestine is removed
d) colonic peristalsis is the first smooth muscle action of the GIT to return after abdominal operation
e) deficiency of gluten hydrolase causes coeliac disease

35 Regarding thyroid hormones:

a) little T_3 is produced peripherally by deiodination T_4
b) albumin has more capacity to bind thyroid hormones than TBG
c) TBG has less affinity for thyroid hormone than albumin
d) thyroid hormones stimulate lipogenesis
e) RT_3 is slightly less active than T_4

36 A calorie is:

a) standard unit of heat energy necessary to raise the temperature of 1L of water 1° from 15-16°C
b) standard unit of heat energy necessary to raise the temperature of 1gm of mercury 1° from 17-18°C
c) the standard unit of heat energy necessary to raise the temperature of 1gm of water 1° from 17-18°C
d) the standard unit of heat energy necessary to raise the temperature of 1gm of water 1° from 15-16°C
e) the standard unit of heat energy necessary to raise the temperature of 1gm of water 1° from 15-16°F

37 Regarding the respiratory quotient:

a) it is the ratio of CO_2 to O_2 at any time
b) RQ of fat is 0.8
c) increases with hyperventilation
d) increases in metabolic alkalosis
e) RQ of carbohydrate is 1.0

38 Regarding basal metabolic rate:

a) it is higher in women
b) it is determined at rest within 12 hours after the last meal
c) increases by 18% for each 1°C of fever
d) is about $40Kcal/m^2/h$ in an average man
e) is about 4,000Kcal/d in an average man

39 Which is NOT a high energy compound?

a) CoA
b) GGP
c) ITP
d) creatine phosphate
e) GTP

40 Regarding the flavoprotein – cytochrome system:
a) cytochrome oxidase is the first step in the chain
b) occurs within the endoplasmic reticulum
c) substrates are pyruvate, water and oxygen and ATP

41 Regarding carbohydrate metabolism:
a) glucokinase is increased in starvation
b) the breakdown of glycogen is called glycolysis
c) the direct oxidative pathway involves the breakdown of glucose through triose
d) the conversion of pyruvate to acetyl-CoA is irreversible
e) conversion of fructose 6-phosphate to fructose 1,6-diphosphate produces 1 ATP

42 Which is NOT produced by the citric acid cycle?
a) NAD^+
b) CO_2
c) GTP
d) $FADH_2$
e) H^+

43 Regarding phosphorylase:
a) it clea???? 1:6α linkages in glycogen
b) it is activated by norepinephrine
c) phosphorylase kinase is directly activated by cyclic AMP
d) activation of protein kinase A inhibits glycogen synthesis
e) α_1 adrenergic receptors in the liver have no part in glycogen breakdown

44 Which amino acid is not found in protein?
a) ornithine
b) arginine
c) valine
d) aspartic acid
e) glycine

45 Which is a nutritionally essential amino acid?
a) taunine
b) leucine
c) glutamate
d) alanine
e) tyrosine

46 Which amino acid is not ketogenic?
a) leucine
b) isoleucine
c) phenylalanine
d) tyrosine
e) alanine

47 Regarding starvation:
a) glycogen provides enough fuel for 48 hours
b) ketoacids derived from fats, are used by the brain and other tissues
c) hypoglycaemia has a protein sparing effect
d) average time until death is 40 days
e) urine creatine levels are unchanged

48 Regarding lipid transport:
a) chylomicrons enter the blood directly from the enterocyte
b) the major aproproteins are apoB, apoD and apo???
c) chylomicrons are broken down to FfA, glycerol and chylomicron remnants by lipoprotein lipase in the liver
d) VLDL provides cholesterol to the tissue
e) LDL is taken up by receptor mediated endocytosis ????

49 Regarding electrolyte absorption:
a) cholera toxin binds to adenosine diphosphate ribose to the subunit of Gs, stimulative ATPase activity
b) active transport of Na^+ into the small intestine enterocytes is coupled with the absorption of glucose
c) magnesium sulphate absorption is coupled with Na^+-K^+-ATPase pump
d) the Na^+-K^+ ATPase pumps are located at the luminal membrane of the enterocyte
e) osmolality in the jejunal lumen is close to that of plasma

50 Regarding calcium:
a) 20% of calcium is absorbed
b) active transport of Ca^{2+} out of the lumen occurs primarily in the lower small intestine
c) 1,25-dihydroxycholecalciferol induces calcium binding protein synthesis in mucosal cell
d) absorption is facilitated by phosphate
e) 1,25-dihydroxycholecalciferol is produced in the skin

51 Regarding iron:
a) it is more readily absorbed in the ferric form
b) men lose about 0.6mg/d
c) average daily iron intake is 40mg
d) ascorbic acid reduces iron absorption

Section 1 – Answers

1	C
2	B
3	D
4	B
5	B
6	D
7	A
8	A
9	C
10	A
11	B
12	C
13	D
14	B
15	D
16	B
17	D
18	D
19	C
20	C
21	E
22	D
23	C
24	E
25	A
26	D

27	C	
28	D	
29	E	
30	C	
31	E	
32	A	
33	D	
34	E	
35	B	
36	D	
37	E	
38	D	
39	B	
40	No answer	
41	D	
42	A	
43	D	
44	E	
45	D	check answers
46	C	don't correspond
47	C	with questions
48		
49	E	
50	No answer	
51	No answer	

Section 2

GI/Digestion/Absorption/Metabolism

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1 Vitamins co-transported with Na^+ include all EXCEPT:
   a) thiamine
   b) folate
   c) niacin
   d) riboflavin
   e) pyridoxine

2 Fat soluble vitamins include all EXCEPT:
   a) vitamin A
   b) vitamin C
   c) vitamin D
   d) vitamin E
   e) vitamin K

3 The largest daily volume of secretions in the GIT originates in the:
   a) salivary glands
   b) stomach
   c) gallbladder (bile)
   d) pancreas
   e) intestine

4 Iron:
   a) most dietary iron is in the ferrous state
   b) most iron is absorbed in the upper small intestine
   c) a ferritin micelle contains 1,000 atoms of iron
   d) 90% of body iron is in haemoglobin
   e) 10% of dietary iron is normally absorbed

5 Ketone bodies:
   a) are not formed under normal conditions
   b) are all moderately strong acids
   c) are formed when intracellular glucose is deficient
   d) are easily metabolised in the liver
   e) all of the above

6 Creatinuria can occur in all EXCEPT:
a) healthy children
b) pregnant women
c) starvation
d) hypothyroidism
e) poorly controlled diabetes mellitus

7 Cations in normal (fasting) gastric juice include all EXCEPT:
a) Na^{+}
b) Ca^{++}
c) K^{+}
d) Mg^{++}
e) H^{+}

8 Human hepatic bile (hepatic bile duct) is largely:
a) water
b) bile salts
c) bile pigment
d) cholesterol
e) lecithin

9 The nutritionally essential amino acids include:
a) alanine
b) cysteine
c) tyrosine
d) methionine
e) glutamine

10 The largest glycogen store in the adult body is in the:
a) liver
b) spleen
c) muscle
d) pancreas
e) circulating red cell mass

11 TSH secretion is stimulated by:
a) dopamine
b) somatostatin
c) cold temperatures
d) stress
e) glucocorticoids

12 Thyroxine (T_4) has greater affinity for:
a) thyroxine-binding globulin
b) transthyretin
c) thyroxine-binding pre-albumin
d) albumin
e) triiodothyronine

13 GLUT is an example of:
a) simple diffusion
b) facilitated diffusion
c) primary active transport
d) secondary active transport
e) endocytosis

14 The most common cell type of the endocrine pancreas is:
a) A cells
b) B cells
c) C cells
d) D cells
e) F cells

15 Both insulin and somatostatin:
a) are released from extra-pancreatic sites
b) receptors are linked to G proteins
c) inhibit release of glucagon
d) cause K^+ uptake by cells
e) are polypeptides containing two chains linked by disulphide bonds

16 Aldosterone is secreted by:
a) zona reticularis
b) zona fasciculata
c) zona glomerulosa
d) zona fasciculata and reticularis
e) zona glomerulosa and fasciculata

17 Regarding aldosterone:
a) it is released in response to hypokalaemia
b) it has glucocorticoid action
c) it works via G proteins to increase Na^+ reabsorption
d) its release results in alkaline urine
e) it is highly protein-bound

18 Calcitonin secretion is increased by:
a) gastrin
b) CCK
c) secretin
d) glucagon
e) all of the above

19 All of the following bind to intracellular receptors EXCEPT:
a) cortisol
b) aldosterone
c) 1,25-DHCC
d) parathyroid hormone
e) thyroxine

20 How many trophic hormones does the anterior pituitary produce?
a) 2
b) 3
c) 5
d) 6
e) 8

21 All of the following are high energy phosphate compounds EXCEPT:
a) adenosine triphosphate
b) glucose 6-phosphate
c) creatine phosphate
d) adenosine diphosphate
e) guanosine triphosphate

22 Under aerobic conditions, 1mol glucose forms:
a) 2mol ATP
b) 8mol ATP
c) 16mol ATP
d) 38mol ATP
e) 42mol ATP

23 The approximate ratio of fat : CHO energy stores is:
a) 2 : 1
b) 4 : 1
c) 10 : 1
d) 20 : 1
e) 40 : 1

24 Nutritionally essential amino acids include:
a) glycine
b) serine
c) lysine
d) glutamine
e) tyrosine

25 Uric acid is formed by the breakdown of:
a) purines
b) pyrimidines
c) glutamine
d) urea
e) all of the above

26 The LDL contains which aproprotein?
a) A
b) B-48
c) B-100
d) C
e) E

27 Regarding cellular metabolism of cholesterol:
a) it inhibits HMG-CoA red???
b) is processed in part to other cholesterol esters by the enzyme acetyl CoA ??? acyltransferase
c) it inhibits the formation of CO_2 receptors
d) all of the above
e) none of the above

28 Which of the following substances decreases the activity of hormone-sensitive lipase?
a) adrenaline
b) thyroxine
c) serotonin
d) TSH
e) prostaglandin E

29 Chromium deficiency leads to:
a) insulin resistance
b) hypogondal dwarfism
c) anaemia
d) changes in ossification
e) thyroid disorder

30 Vitamin B_1 (thiamine) deficiency leads to:

a) anaemia
b) beri beir
c) convulsions
d) dermatitis
e) pellagra

Section 2 – Answers

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

Section 3

Metabolism and Endocrinology

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1 Which of the following phosphate compounds is MOST important in the production of energy?
a) AMP (adenosine monophosphate)
b) ADP (adenosine diphosphate)
c) ATP (adenosine triphosphate)
d) GTP (guanosine triphosphate)
e) CTP (cytidine triphosphate)

2 Which of the following is NOT produced by the citric acid cycle?
a) CO_2
b) H^+ ions
c) NAD^+
d) GTP (guanosine triphosphate)
e) NADH

3 The renal threshold for glucose, the arterial blood level at which glycosuria appears, is approximately:
a) 1.8g/dL
b) 180mg/dL
c) 18mg/dL
d) 80mg/dL
e) 800mg/dL

4 Which of the following amino acids are glucogenic (ie give rise to compounds readily converted to glucose)?
a) alanine
b) leucine
c) isoleucine
d) phenylalanine
e) tyrosine

5 Which of the following lipoproteins is SMALLEST in size?
a) chylomicrons
b) very low density lipoproteins
c) intermediate density lipoproteins
d) low density lipoproteins
e) high density lipoproteins

6 Regarding the respiratory quotient, which of the following is TRUE?
a) it is the ratio of CO_2 and O_2 in the body at any one time
b) can go as high as 2.00 because lactic acid produces more oxygen
c) in acidosis, it goes down
d) in alkalosis it goes up
e) it is possible for it to be negative

7 Regarding body surface area, which of the following statements is TRUE?
a) is calculated using weight/height
b) is calculated using 0.007184 X weight + 0.425 X weight + 0.725
c) it does not affect the basal metabolic rate
d) it does not affect the general metabolic rate
e) it has an effect on the specific dynamic action of foodstuffs

8 Regarding the basal metabolic rate, which of the following is TRUE?
a) it is measured in the absence of disease, at room temperature, within 12 hours of a meal with a Benedict apparatus and the subject asleep
b) it increases 24% per degree Celsius of body temperature above 37°
c) it is decreased during the latter stage of starvation, explaining the initial rapid weight loss than a slowing down of weight loss
d) it declines in pregnancy
e) it correlates closer to weight than to body surface area

9 Biological energy can be derived from all EXCEPT:
a) lactic acid
b) phosphorylcreatine
c) guanosine triphosphate
d) co enzyme A
e) urea

10 Regarding brown fat, which of the following is TRUE?
a) it is fat with a large percentage of melatonin as a constituent
b) it has extensive parasympathetic innervation
c) it is more abundant in adults than in infants
d) heat production is assisted by uncoupling of the H^+/ATP generator system in mitochondria
e) brown fat cells contain multiple droplets of fat

11 Regarding thyroid hormones, which statement is INCORRECT?
a) thyroid hormones bind to receptors in cell nuclei
b) T_3 is less potent than T_4
c) thyroid hormones increase O_2 consumption
d) T_3 promotes nitrogen excretion
e) cerebral glucose consumption is increased by thyroid hormones

12 Regarding thyroxine, which of the following is INCORRECT?

a) increases number of β adrenergic receptors on the heart
b) there is a preferential expression of α myosin in the muscle fibres of the heart in the presence of thyroxine
c) thyroid hormones decrease carbohydrate absorption by the stomach and small bowel
d) hyaluronic acid accumulates in the skin if there is a deficiency of thyroxine
e) large doses can increase body temperature

13 Regarding the respiratory quotient, which of the following is TRUE?

a) it is the ratio of CO_2 produced to the volume of O_2 consumed per unit of time
b) is related to tidal volume
c) is inversely proportioned to pO_2
d) has a value of 2.3 for fats
e) varies with age

14 Which of the following statements is INCORRECT?

a) in a low protein diet, nitrogen excretion by the kidney decreases
b) in a low protein diet, the maximal urine osmolarity is decreased
c) there is a net negative nitrogen balance following the administration of steroids
d) nitrogen balance becomes negative if a single amino acid is missing from the diet
e) insulin spares the breakdown of muscle protein

15 Which of the following is an ESSENTIAL fatty acid?

a) myristic acid
b) palmitic acid
c) stearic acid
d) linolenic acid
e) oleic acid

16 Regarding protein metabolism in starvation, which statement is INCORRECT?

a) glucose has a protein sparing effect by increasing insulin secretion
b) death occurs when protein depletion reaches 50% of normal level
c) total starvation leads to loss of up to 5gms/day of urea nitrogen due to protein catabolism
d) most protein catabolised comes from the liver, spleen and skeletal muscles
e) rapid protein depletion is the terminal phase once fat stores have been almost totally catabolised

17 Which of the following is NOT an unsaturated fatty acid?
a) oleic acid
b) arachidonic acid
c) linoleic acid
d) linolenic acid
e) stearic acid

18 Regarding brown fat, which statement is INCORRECT?
a) fat cells have extensive parasympathetic innervation
b) responsible for part of the post-prandial heat production
c) fat cells contain several droplets of fat
d) prominent between and around the scapulae of infants
e) fat cells contain many mitochondria

19 Regarding carbohydrate metabolism in starvation, which statement is INCORRECT?
a) hepatic glycogenolysis precedes skeletal muscle glycogenolysis
b) blood glucose falls less in women due to greater fat stores
c) glycogen stores are exhausted after half to one day
d) blood glucose level is maintained above a level that would produce symptomatic hypoglycaemia
e) skeletal muscle contains about four times as much glycogen as the liver

20 Regarding lipoproteins, which statement is INCORRECT?
a) VLDL transport cholesterol formed in liver to extrahepatic tissues
b) chylomicrons can cause post-prandial plasma to appear milky
c) LDL are taken up by macrophages
d) oestrogens increase plasma HDL levels
e) elevated IDL levels predispose to atherosclerosis

21 Which of the following does NOT increase the activity of intracellular hormone-sensitive lipase?
a) GH
b) PGE
c) thyroxine
d) glucagon
e) cortisol

22 Which of the following causes a positive nitrogen balance?
a) increased cortisol secretion
b) starvation
c) decreased insulin secretion
d) forced immobilisation
e) increased testosterone secretion

23 Which statement regarding lipoprotein lipase is INCORRECT?
a) it is not hormone sensitive
b) it requires heparin as a co-factor
c) it is confined to adipose tissue
d) its activity is decreased by stress
e) it clears chylomicrons and VLDL from circulation by degradation of triglyceride

24 Regarding uric acid, which statement is INCORRECT?
a) the majority of filtered uric acid is reabsorbed in the proximal tubule
b) xanthine oxidase catalyses its synthesis
c) may be elevated in leukaemia and pre-eclampsia
d) does not undergo renal tubular secretion
e) its excretion rate can be halved by changing to a purine-free diet

25 Regarding ketone bodies, which statement is INCORRECT?
a) formed following ingestion of a high fat/low carbohydrate diet
b) acetoacetate and beta-hydroxybutyrate formation leads to a metabolic acidosis
c) acetone is excreted in the urine
d) readily metabolised by the liver
e) acetone formation leads to ketotic breath

26 Nucleotide breakdown releases purines and pyrimidines. Which of the following is NOT their subsequent fate?
a) re-used to form nucleosides, nucleotides and nucleic acids
b) excreted unchanged in urine
c) directly enter the urea cycle
d) pyrimidines are catabolised to carbon dioxide and ammonia
e) purines are catabolised to uric acid

27 How many ATP molecules are produced from one molecule of a 6-carbon fatty acid metabolised via the TCA cycle to carbon dioxide and water?
a) 36
b) 38
c) 40
d) 42
e) 44

28 Which of the following is NOT a purine?
a) adenine
b) cytosine
c) guanine
d) hypoxanthine
e) xanthine

29 Creatinine appears in the urine in significant amounts in all of the following EXCEPT:
a) normal men
b) thyrotoxicosis
c) post-partum
d) poorly controlled diabetes mellitus
e) children

30 Regarding free fatty acids, which statement is INCORRECT?
a) circulate in plasma bound to globulin
b) they are the major source of energy for cardiac muscle
c) combine with glycerol to form the triglyceride of neutral fat
d) contain an even number of carbon atoms
e) require linkage to carnitine in order to cross mitochondrial membranes prior to oxidation

31 Which amino acid is NOT ketogenic (ie CAN'T be converted into acetoacetate)?
a) leucine
b) isoleucine
c) phenylalanine
d) tyrosine
e) proline

32 Regarding cholesterol, which statement is INCORRECT?
a) dietary cholesterol is absorbed in the intestine and incorporated into chylomicrons formed in the mucosa
b) about 20% is in the plasma, with the remainder intracellular
c) negatively feeds back on its synthetic pathway
d) most hepatic synthesised cholesterol is incorporated into VLDL
e) thyroid hormones decrease the plasma cholesterol level

33 How many ATP molecules are produced from one glucose molecule metabolised aerobically via the Embden-Meyerhof pathway and citric acid cycle?
a) 32
b) 34
c) 36
d) 38
e) 40

34 Which lipoprotein contains the GREATEST proportion of triglyceride?
a) VLDL
b) IDL
c) chylomicrons
d) LDL
e) HDL

35 Basal metabolic rate is GREATER in all of the following circumstances EXCEPT:
a) children compared with adults
b) Caucasians compared with Chinese and Indians
c) females compared with males
d) anxiety compared with depression
e) feeding compared with starvation

36 Which lipoprotein contains the GREATEST proportion of cholesterol and cholesterol esters?
a) VLDL
b) IDL
c) chylomicrons
d) LDL
e) HDL

37 What is the basal metabolic rate of an average sized man per day?
a) 1000 Kcal
b) 2000 Kcal
c) 3000 Kcal
d) 4000 Kcal
e) 5000 Kcal

38 Which lipoprotein contains the GREATEST proportion of protein?
a) VLDL
b) IDL
c) chylomicrons
d) LDL
e) HDL

39 What is the most important factor affecting metabolic rate?
a) muscular exertion
b) recent ingestion of food
c) high or low environmental temperature
d) height, weight and surface area
e) sex

40 Which of the following are NON ESSENTIAL amino acids?
a) valine
b) leucine
c) isoleucine
d) cysteine
e) methionine

41 Regarding plasma protein, all of the following are correct EXCEPT:
a) albumin, globulin and fibrinogen constitute the major plasma proteins in the plasma
b) the fibrinogen polymerises into long fibrin threads during blood coagulation
c) the principal function of albumin is to provide colloid osmotic pressure in the plasma
d) the majority of plasma proteins are formed in the lymphoid tissue
e) rapid loss of plasma proteins may occur during severe burns

42 Factors that predisposes to atherosclerosis includes all of the following EXCEPT:
a) diabetes
b) hypothyroidism
c) smoking
d) male sex
e) female sex hormone

43 Lipoproteins:
a) chylomicrons are themselves very large lipoproteins composed of cholesterol, phospholipids, triglycerides and proteins
b) VLDL contains a higher concentration of triglycerides and a moderate concentration of cholesterol and proteins
c) HDL contains a very higher concentration of cholesterol and a moderate concentration of phospholipids and triglycerides
d) the majority of the lipoproteins are synthesised in the liver
e) the primary function of the lipoproteins are to transport lipids in the blood from liver to adipose tissue

44 Glycogenolysis:
a) is a process of formation of glycogen in the cell
b) is a process of breakdown of glycogen to reform glucose
c) is the conversion of glucose into fructose
d) is the process of breakdown of galactose
e) is the formation of galactose from fructose

45 Regarding ATP:
a) ATP is a combination of adenine, ribose and 3 phosphate radicals
b) ATP are present everywhere in the cytoplasm and nucleoplasm
c) ATP is otherwise called the energy currency of the body
d) ATP becomes GTP after the loss of one phosphate radical
e) ATP is a labile chemical compound that is present in all cells

46 In the body, metabolism of 10gm protein would produce approximately:
a) 1 Kcal
b) 41 Kcal
c) 410 Kcal
d) 4100 Kcal
e) 41 Cal

47 Regarding 1,25 dihydroxycholecalciferol (calcitriol):
a) it is formed by the action of sunlight on pre vitamin D_3
b) it exerts its action via stimulation of adenylcyclase
c) it decreases calcium reabsorption from kidneys
d) its formation is increased with elevated plasma Ca^{++} levels
e) it causes increased formation of calbindin-D proteins

48 The following are active components in the peripheral circulation, EXCEPT:
a) T_3
b) T_4
c) DIT
d) RT_3
e) all of the above

49 Calitriol (1,25-dihydroxycholecalciferol)
a) inhibits Ca^{++} absorption from the gut
b) is formed in the proximal renal tubules from a less active precursor
c) levels rise in response to increase serum PO_4 levels
d) inhibits osteoclasts function
e) inhibits osteoblasts function

50 Stimuli that increase renin secretion include all EXCEPT:
a) hypotension
b) Na^+ depletion
c) cardiac failure
d) lying down
e) diuretics

51 Regarding parathyroid hormone, which is NOT true?
a) it decreases plasma phosphate
b) it is secreted by chief cells of he parathyroid glands
c) it is cleared by Kupffer cells of the liver
d) its secretion is regulated by the level of bound Ca^{++} in plasma
e) it increases bone reabsorption

52 Which of the following reduce insulin secretion?
a) acetylcholine
b) GIP
c) glucagon
d) adrenaline
e) β ketoacids

53 With regard to the effect of thyroid hormone on the cardiovascular system, which of the following are TRUE?
a) level of noradrenaline are increased
b) β adrenergic receptor affinity is decreased in heart muscle
c) circulating adrenaline levels are decreased
d) thyroid hormone levels alter the ratio of cardiac myosin isoform types
e) none of the above

54 Stimuli that increase aldosterone secretion and do not effect glucocorticoid secretion includes all EXCEPT:
a) low Na^+ intake
b) high K^+ intake
c) standing
d) secondary hyperaldosteronism
e) haemorrhage

55 Signs and effects of hyperparathyroidism include all EXCEPT:
a) renal stones
b) demineralization of bones
c) Chvostek's and Trousseau's signs
d) hypercalcaemia
e) hypophosphataemia

56 Glucagon levels are increased by:
a) secretin
b) somatostatin
c) cholecystokinin
d) free fatty acids
e) ketones

57 Insulin release:
a) is inhibited by raised cyclic AMP in pancreatic β cells
b) is not stimulated by blood glucose levels below 6mmol/l
c) is increased by β adrenergic stimulators
d) is inhibited by phosphor diesterase inhibitors
e) is increased by somatostatin

58 Trace elements believed essential to life include all EXCEPT:
a) arsenic
b) cyanide
c) cobalt
d) silicon
e) nickel

59 Mono-iodotyrosin (MIT) and diiodotyrosin (DIT) molecules:
a) are deiodinated before joining to form T_3 and T_4
b) are secreted into plasma alongside T_3 and T_4
c) are the inactive metabolites of T_3 and T_4
d) are cleaved from thyroglobulin by proteases in lysosomes
e) are usually excreted in the urine

60 Calcitonin secretion is stimulated by the following EXCEPT:
a) gastrin
b) somatostatin
c) oestrogen
d) cholecystokinin
e) glucagon

61 With regard to gastric acid secretion, all the following are true EXCEPT:
a) acetylcholine stimulates secretion
b) both G protein and direct calcium channels are involved
c) an H^+ - K^+ antiport transports H^+ into the gastric lumen
d) parietal cells have high levels of carbonic anhydrase
e) acid secretion is maintained at constant levels by local feedback mechanisms

62 Tissues in which insulin does NOT facilitate glucose uptake?
a) red blood cells
b) skeletal muscle
c) cardiac muscle
d) smooth muscle
e) aorta

63 Regarding the “iodide pump” in thyroid cells, which is NOT true?
a) it is stimulated by TSH
b) it depends on Na^+ / K^+ ATPase activity
c) it pumps iodide into the colloid, after entering the cell down an electrical gradient
d) it pumps iodide against an electrical gradient
e) its activity can be measured with trace doses of radioactive iodine

64 Which of the following enzymes are missing in the zona glomerulosa?
a) 17 α hydroxylase
b) 11 β hydroxylase
c) 21 β hydroxylase
d) cholesterol desmolase
e) 3 β hydroxysteroid

65 The effects of hyperthyroidism on the cardiovascular system include all of the following EXCEPT:
a) increased expression of α MHC isoforms in cardiac muscle
b) increased catecholamine plasma levels
c) increased number of β receptors
d) increased affinity of β receptors
e) vasodilation of peripheral vessels

66 Regarding the control of thyroid secretion:
a) free T_3 and T_4 exert feedback control on anterior pituitary
b) free T_3 and T_4 exert feedback control on hypothalamus
c) free T_3 and T_4 exert feedback control on anterior pituitary and hypothalamus
d) free T_3 and T_4 do not affect day to day control of their secretion
e) the basal metabolic rate is the most important determinant of thyroid secretion

67 The following are true of chylomicrons EXCEPT:
a) they are large lipoprotein complexes
b) they are part of the exogenous lipid transport system
c) they enter the circulation via the lymphatic ducts
d) they are cleared from the circulation by lipoprotein lipase on the surface of hepatocytes
e) chylomicron remnants are bound to LDL R and endocytosed

68 All of the following are true regarding chylomicrons EXCEPT:
a) they contain triglycerides, cholesterol and phospholipids
b) they are formed in the intestinal mucosa
c) they are cleared from the circulation by lipoprotein lipase
d) they are transported to the liver by the portal circulation
e) large numbers after a meal give the plasma a milky appearance

69 The tissue or organ with the greatest potential for increasing the metabolic rate of the body is:
a) liver
b) skin
c) adipose tissue
d) skeletal muscle
e) digestive system

70 Triglycerides are transported to cells via:
a) chylomicron remnants
b) HDL
c) LDL
d) VLDL
e) none of the above

71 Regarding vitamin B_{12}
a) it is a fat soluble vitamin
b) its absorption is inhibited by trypsin
c) it is mainly carried in plasma by attachment to albumin
d) it undergoes enterohepatic circulation
e) none of the above are true

72 Regarding HDL:
a) HDL transports ingested cholesterol from the intestine
b) HDL transports triglycerides from peripheral tissues
c) HDL receptors on macrophages are called scavenger receptors
d) elevated HDL levels are associated with increased risk of atherosclerosis
e) none of the above are correct

73 Regarding free fatty acids in plasma, which of the following is NOT true?
a) they account for less than 10% of total fatty acids in plasma
b) they are complexed with a protein carrier
c) they can be metabolised to CO_2 and water in skeletal and cardiac muscle
d) their level in plasma decreases as plasma adrenaline increases
e) they are converted to energy by the citric acid cycle

74 Ubiquitin is:
a) an essential amino acid
b) a polypeptide that tags proteins for degradation
c) a cell membrane glycoprotein
d) a precursor or uric acid
e) none of the above

75 In a fasting adult at rest:
a) skeletal muscle metabolises mainly glucose
b) the brain accounts for approximately 40% of glucose utilised
c) blood glucose concentrations are higher in women than in men
d) blood glucose levels are maintained initially by hepatic glycogenolysis
e) ketones are absent from plasma

76 Uric acid handling by the kidneys involves:
a) filtration only
b) secretion by tubules only
c) filtration and secretion
d) filtration and reabsorption
e) filtration, reabsorption and secretion

77 The following vitamin is fat soluble:
a) niacin
b) B_6
c) K
d) pantothenic acid
e) biotin

78 With regard to the metabolism of carbohydrates:
a) in the absence of liver glycogen stores, glycogen administration does not cause hyperglycaemia
b) glucocorticoids have a minor effect on gluconeogenesis
c) growth hormone causes increased use of glucose for energy
d) glucose is absorbed by most cells by active sodium glucose co-transport
e) during starvation, stores last for less than 24 hours

79 With regard to lipid metabolism:
a) only HDL is formed in the liver
b) fatty acids in the plasma form 1:1 complexes with albumin
c) plasma cholesterol levels rise considerably with an increase in daily ingestion
d) free fatty acids are metabolised in preference to glucose in a non-exercising individual
e) utilisation of fatty acids is stimulated by glucocorticoids

80 With regard to carbohydrate metabolism:
a) the normal fasting glucose is from 3.9 to 11.0mmol/L
b) glucose is phosphylated in cells to glucose-6-phosphate by phosphoenol-pyrunate carboxykinase
c) glycogen, the storage form of glucose, is only in the liver and skeletal muscle
d) glucose can be converted to fats through acetyl CoA which is irreversible
e) none of the above

81 Which statement regarding glucagon is INCORRECT?
a) it is used as an antidote in symptomatic beta blocker overdosage
b) it is synthesised in the A cells of the pancreatic islets and in small intestinal mucosal cells
c) its major site of metabolism is in the plasma
d) it is synthesised in common with glicentin
e) the exogenous glucagon is associated with nausea and vomiting

82 Which of the following is NOT an action of somatostatin?
a) it inhibits glucagon secretion
b) it is a synaptic transmitter in the retina
c) it inhibits insulin secretion
d) it increases contraction of the gallbladder
e) it inhibits pancreatic polypeptide secretion

83 Glucagon increases the secretion of all of the following EXCEPT:
a) catecholamines from a phaeochromocytoma
b) atrial natriuretic peptide
c) growth hormone
d) insulin
e) calcitonin from a medullary carcinoma of the thyroid

84 Regarding the actions of glucagon, which of the following is INCORRECT?
a) it increases blood lactate level
b) it activates hormone-sensitive lipase
c) it has a positive inotropic effect on myocardium
d) large amounts cause intestinal relaxation
e) it decreases renal tubular sodium reabsorption

85 Which of the following does NOT increase pancreatic polypeptide secretion?
a) protein ingestion
b) fasting
c) exercise
d) acute hypoglycaemia
e) intravenous glucose

86 Which iodinated compound is present in GREATEST amounts in the adult thyroid gland?
a) T_4
b) DIT
c) MIT
d) T_3
e) RT_3

87 Regarding the action of glucagon on the liver, which of the following is INCORRECT?
a) it causes glycogenolysis via activation of adenylate cyclase
b) it decreases metabolism of glucose-6-phosphate
c) it causes glycogenolysis via activation of phospholipase C
d) it increases gluconeogenesis from available amino acids
e) it decreases ketone body formation

88 Regarding the synthesis of thyroid hormones, which statement is INCORRECT?
a) iodine undergoes rapid oxidation following entry to thyroid cells
b) the “iodine pump” is the major source of iodine for hormone synthesis
c) TSH increases iodine uptake by the thyroid gland
d) thiocyanate and ouabain decrease iodine uptake by the thyroid gland
e) it involves iodination of thyrosine residues in thyroglobulin

89 Which of the following does NOT inhibit secretion of glucagon?
a) ketones
b) α adrenoceptor agonists
c) secretin
d) amino acids
e) somatostatin

90 Which plasma protein has the greatest thyroxine binding capacity?
a) α 1-acid glycoprotein
b) thyroxine-binding pre-albumin
c) albumin
d) thyroxine-binding globulin
e) orosomucoid

91 Which of the following does NOT increase secretion of glucagon?
a) diabetes mellitus
b) β adrenoceptor agonists
c) GABA
d) starvation
e) exercise

92 Which plasma protein has the greatest thyroxine-binding affinity?
a) α 1-acid glycoprotein
b) thyroxine-binding pre-albumin
c) albumin
d) thyroxine-binding globulin
e) orosomucoid

93 Regarding insulin, which statement is INCORRECT?

a) it consists of two polypeptide chains linked by two disulphide bridges
b) the majority of exogenous insulin is metabolised by the liver
c) it is not the only molecule responsible for insulin-like activity in the blood
d) it increases intracellular potassium concentration
e) exercise increases the affinity of its receptors for insulin

94 Which iodinated compound is present in the SMALLEST amounts in the adult thyroid gland?

a) T_4
b) DIT
c) MIT
d) T_3
e) RT_3

95 Which of the following hormones does NOT increase the hepatic output of glucose?

a) growth hormone
b) adrenaline
c) glucagon
d) noradrenaline
e) cortisol

96 Which thyroid hormone has the longest plasma half-life?

a) T_4
b) DIT
c) MIT
d) T_3
e) RT_3

97 Regarding the action of insulin on adipose tissue, which of the following is INCORRECT?

a) it induces lipoprotein lipase which actively hydrolyses triglyceride from circulating lipoproteins
b) it reduces circulating free fatty acids
c) it promotes triglyceride storage in adipocytes
d) it directly inhibits intracellular lipase
e) its effects appear to involve phosphorylation of lipases

98 Which of the following tissues possess FEW thyroid hormone receptors?

a) liver
b) testis
c) kidney
d) heart
e) skeletal muscle

99 Which glucose transporter is responsible for insulin-mediated glucose uptake in striated muscle and adipose tissue?
a) glut 1
b) glut 2
c) glut 3
d) glut 4
e) glut 5

100 Where are the receptors located by which thyroid hormones mediate most of their effects?
a) cell membrane
b) outer mitochondrial membrane
c) nuclear chromatin
d) inner mitochondrial membrane
e) cytoplasm

101 Regarding the action of insulin in skeletal muscle, which of the following is INCORRECT?
a) it decreases protein catabolism
b) it induces glucogen synthase
c) it decreases ketone uptake
d) it increases amino acid uptake
e) it decreases the release of gluconeogenic amino acids

102 Which thyroid hormone possesses the GREATEST biological activity?
a) T_4
b) DIT
c) MIT
d) T_3
e) RT_3

103 Which glucose transporter is responsible for the facilitated diffusion of glucose into pancreatic B cells?
a) glut 1
b) glut 2
c) glut 3
d) glut 4
e) glut 5

104 Regarding the effects of thyroid hormones, which of the following does NOT occur?
a) it increases metabolic rate
b) it directly stimulates sodium-potassium ATPase
c) it increases protein and fat catabolism
d) it increases body temperature
e) it increases cerebral oxygen consumption

105 Regarding the action of insulin on the liver, which of the following is INCORRECT?
a) it increases gluconeogenesis
b) it decreases glycogenolysis
c) it increases synthesis of triglyceride and VLDL
d) it decreases cyclic AMP
e) it increases phosphate uptake

106 Which statement regarding the thyroid gland and its hormones is INCORRECT?
a) thyroid hyperactivity is associated with an increase in plasma catecholamines
b) iodide trapping by thyroid cells is an active process
c) thyroid hormones enter cells by diffusion across the cell membrane
d) thyroid hormones cause an increase in 2,3 - DPG
e) thyroid hormones increase growth hormone secretion

107 Regarding the secretion of insulin, which statement is INCORRECT?
a) insulin is not required for glucose to enter pancreatic B cells
b) it involves closure of ATP-sensitive potassium channels
c) it is a biphasic process involving two pools of insulin
d) it involves opening of voltage-sensitive calcium channels
e) glucose enters pancreatic B cells by combining with glut 4

108 Which of the following do NOT increase TSH secretion?
a) TRH
b) glucocorticoids
c) infants exposed to cold temperature
d) acute psychosis
e) night time

109 Which of the following does NOT inhibit insulin secretion?
a) somatostatin
b) atropine
c) propranolol
d) gastrin
e) phenytoin

110 Which of the following does NOT increase intestinal calcium absorption?
a) hypocalcaemia
b) parathyroid hormone (PTH)
c) glucocorticoids
d) hypervitaminosis D
e) protein in diet

111 Which of the following does NOT stimulate insulin secretion?

a) acetoacetate
b) glucagon
c) hypokalaemia
d) acetylcholine
e) theophylline

112 Which of the following does NOT decrease intestinal calcium absorption?

a) hypercalcaemia
b) decreased PTH
c) hypovitaminosis D
d) growth hormone
e) phytic acid and oxalate in intestine

113 Regarding the insulin receptor, which statement is INCORRECT?

a) it is present even in cells which do not increase their glucose intake in response to insulin
b) insulin binds to the β subunit on the outer surface of the cell membrane
c) it is a tetramer of two α and two β subunits
d) the binding of insulin decreases the activity of tyrosine kinase on the intracellular end of the receptor
e) the complex of insulin and receptor become internalised by the cell

114 Which of the following does NOT increase plasma calcium?

a) parathyroid hormone
b) vitamin D
c) growth hormone
d) thyroxine
e) calcitonin

115 Which of the following is NOT associated with an increase in erythropoietin secretion?

a) aminophylline
b) renal cell carcinoma
c) cobalt salts
d) thyroxine
e) adenosine

116 Which of the following does NOT increase parathyroid hormone secretion?
a) high plasma magnesium
b) low plasma calcium
c) high plasma phosphate
d) β-adrenergic discharge
e) cyclic AMP

117 Regarding erythropoietin, which statement is INCORRECT?
a) its secretion increases within minutes to hours in response to hypoxia
b) it causes pro-erythroblasts to mature more rapidly into erythrocytes
c) the spleen and salivary glands secrete, but don't synthesise it
d) it inhibits apoptosis in erythroid stem cells
e) the adult liver is able to synthesise enough for normal erythropoiesis in the absence of both kidneys

118 Which statement regarding parathyroid hormone (PTH) is INCORRECT?
a) it is continuously secreted by the parathyroid glands
b) it is synthesised and secreted by the oxyntic cells
c) it is rapidly cleaved in the Kupffer cells of the liver
d) it increases osteoclasts activity in bone
e) it increases formation of 1,25-dihydroxycholecalciferol

119 Regarding endothelins, which statement is INCORRECT?
a) they can cause dose-dependent vasoconstriction in most vascular beds
b) they activate phospholipase C
c) they are structurally similar to vasoactive intestinal contractor
d) they have negative inotropic effect
e) there are low concentrations present in blood

120 Which statement regarding calcitonin is INCORRECT?
a) it is secreted by parafollicular cells of the thyroid gland
b) it inhibits osteoclastic bone resorption
c) total thyroidectomy is usually associated with hypercalcaemia
d) it decreases renal tubular calcium and phosphate reabsorption
e) it is only secreted when plasma calcium concentration exceeds 9.5mg/100ml

121 Regarding atrial natriuretic peptide, which statement is INCORRECT?
a) cardiac innervation is not required for secretion to occur
b) its action is terminated by receptor-mediated endocytosis
c) its filtration fraction is decreased
d) it is secreted by heart, lung and brain
e) glucocorticoids increase its secretion

122 Regarding the role of vitamin D in calcium metabolism, which of the following is INCORRECT?
a) it increases renal tubular calcium and phosphate reabsorption
b) it causes an increase in synthesis of calcium-binding protein
c) it increases bone resorption
d) it decreases bone formation
e) it increases intestinal calcium and phosphate absorption

123 Atrial natriuretic peptide decreases formation of all of the following EXCEPT:
a) aldosterone
b) cyclic GMP
c) renin
d) vasopressin
e) angiotensin III

124 Which of the following does NOT increase aldosterone secretion?
a) constriction of the IVC in the thorax
b) ACTH
c) surgery
d) hyperkalaemia
e) lying supine from the standing position

125 Which of the following does NOT increase secretion of atrial natriuretic peptide?
a) β-adrenoceptor agonists
b) immersion in water up to the neck
c) exercise
d) endothelin
e) changing from erect position to supine

126 Regarding aldosterone, which statement is INCORRECT?
a) it responds to changes in plasma sodium more strongly than changes in plasma potassium
b) it is only synthesised in the zona glomerulosa of the adrenal cortex
c) its main action is to increase the synthesis of sodium-potassium pumps
d) angiotensins II and III have about equal mineralocorticoid stimulating activity
e) it acts via a cytoplasmic receptor that has equal affinity for cortisol

127 A 15-year-old girl suffers from a malabsorption syndrome characterised by the malabsorption of fat. In which vitamin is she MOST likely to be deficient?
a) niacin
b) B_6
c) K
d) pantothenic acid
e) biotin

128 Thyroxine (T_4):

a) secretion is regulated by positive feedback at the hypothalamus
b) is transported principally by albumin in the blood
c) causes increased LDLD in plasma
d) is physiologically more active than T_3
e) increases β receptors in the cardiovascular system

129 Regarding insulin:

a) it increases amino acid uptake
b) its absorption is not affected by the site of injection
c) it causes reduced K^+ uptake by cells
d) it increases protein catabolism
e) it is secreted by the α cells in the islets of Langerhan

130 The content of chylomicrons includes:

a) aproprotein E and aproprotein A
b) cholesterol 30%, protein 20%, triglyceride 50%
c) lethicin 10%, cholesterol 25%, triglyceride 65%
d) protein 2%, cholesterol 5%, triglyceride 90%
e) the enzyme protein phospholipase

131 Regarding calcium metabolism:

a) the adult human body contains 15% of its body mass as calcium
b) calcium is passively absorbed from the intestinal brush border
c) oestrogen inhibits osteoclasts
d) TNF inhibits osteoclasts
e) corticosteroids stimulate osteoblasts

Section 3 - Answers

1	C
2	C
3	B
4	A
5	E
6	E
7	B
8	C
9	E
10	A
11	B
12	C
13	A
14	C
15	D
16	C
17	E
18	A
19	B
20	A
21	B
22	E
23	C
24	D
25	D
26	C
27	E
28	B
29	A
30	A
31	E
32	B
33	D
34	C
35	C
36	D
37	B
38	E
39	A
40	D
41	D
42	E
43	C
44	B
45	D
46	B
47	E
48	C
49	B
50	D
51	D
52	D
53	D
54	E
55	C
56	C
57	C
58	B
59	D
60	B
61	E
62	A
63	C
64	A
65	B
66	C
67	D
68	D
69	D
70	D
71	D
72	C
73	D
74	B
75	D
76	E
77	C
78	E
79	E
80	D
81	C
82	D
83	B
84	A
85	E
86	A
87	E
88	B
89	D
90	C
91	C
92	D
93	B
94	E
95	A
96	A
97	E
98	B
99	D
100	C
101	C
102	D
103	B
104	E
105	A
106	A
107	E
108	B
109	D
110	C
111	C
112	D
113	B
114	E
115	A
116	A
117	E
118	B
119	D
120	C
121	C
122	D
123	B
124	E
125	A
126	A
127	C
128	E
129	A
130	D
131	C

Multichoice Questions

Dr. Vinay Gupta

1. In conn's disease, there is an excess of :
   a) Adrenaline b) Aldosterone
   c) Cortisol d) Noradrenalione
2. Which of the following hormones is released from the posterior pituitary?
   a) ACTH b) Antidiuretic hormone
   c) Growth hormone d) Luetinizing hormone
3. In children, hypothyroidism causes
   a) Acromegaly b) Cretinism
   c) Gigantism d) Myxoedema
4. Which of the following associated with a low concentration of ionized calcium in the serum?
   a) Hypothyroidism
   b) Osteogenesis imperfecta
   c) Paget's disease of the bone
   d) Tetany
5. Which hormone is released when serum calcium decrease:
   a) Parathormone b) Calcitonin
   c) Thyroxine d) Adrenaline
6. A phaeochromocytoma is a tumour of the:
   a) Adrenal cortex b) Parathyroids
   c) Pituitary d) None of the above
7. Due to fear which of the following hormones increases rapidly:
   a) Growth hormones b) Epinephrine
   c) Corticosteroid d) Thyroid hormone
8. Aldosterone
   a) Increases reabsorption of sodium
   b) Increases excretion of potassium
   c) Increases retention of sodium
   d) Both 'A' and 'B'
9. Deficiency of cortisol causes:
   a) Cushing syndrome b) Graves disease
   c) Addison disease d) Acromegaly
10. Vasopressin is synthesized in the:
    a) Anterior pituitary
    b) Hypothalamus
    c) Juxtaglomerular apparatus
    d) Vasomotor centre
11. A child with stunted growth with a stuffedbelly, and short stature with mental retardation is suffering from the deficiency of which of the following:
    a) Thyroxine b) Growth hormone
    c) Rickets d) Parathyroid
12. Trousseau's sign and chovstek's signs are positive in:
    a) Hyperparathyroidism
    b) Hypothyroidism
    c) Hypoparathyroidism
    d) Hyperthyroidism
13. Which hormone, together with the catecholamines, enhances the tone of vascular smooth musle and assists in elevating blood pressure?
    a) Parathyroid hormone
    b) Glucagon
    c) Thyroxine d) Cortisol
14. Iodine is primarily important in the biochemical synthesis of :
    a) ACTH b) Thyroxine
    c) Adrenaline d) Calcitonin
15. Function of ADH is:
    a) Water reabsorption b) Water excretion
    c) Na+ absorption d) K+ secretion
16. Changes in biological activity occuring daily are referred as _______ rhythm:
    a) Circadian b) Circa triginatan
    c) Circa sestin d) Circannual
17. Calcitonin is released by :
    a) Parafollicular cells of thyroid
    b) Chief cells of thyroid
    c) Granular cells of adrenal gland
    d) Stratum fasciculata of adrenal gland
18. Bone metabolism is controlled by:
    a) Vit-D & Calcium b) Parathormone
    c) Calcitonin d) All of the above
19. Which of the following hormones does not affect growth?
    a) Oxytocin b) Somatotropins
    c) Thyroid hormone d) Estrogen
20. Which of the following results due to excessive parathormone secretion:
    a) Increased excretion of phosphates
    b) Increased serum calcium
    c) Decrease excretion of calcium
    d) Increase excretion of calcium
21. Which of the following hormones exerts the least effect on calcium metabolism of bone tissue?
    a) Androgen b) Estrogen
    c) Nor epinephrine d) Thyroid hormone
22. Hormones, which stimulate spermatogenesis are:
    a) Insulin and glucagon
    b) Thyroxine and parathormone
    c) A.D.H. and Oxytocin
    d) Testosterone and F.S.H.
23. Which of the following anterior pituitary hormones is primarily under inhibitory control of hypothalamus.
    a) TSH b) GRH
    c) Somatostatin d) Prolactin
24. Aldosterone production is controlled by:
    a) Anterior pituitary gland
    b) Posterior pituitary gland
    c) Hypothalamus
    d) Adrenal gland
25. Low calcium level will cause:
    a) Hyper excitability of wrist muiscle
    b) Weak heart action
    c) Tetanus
    d) All of the above
26. Hypercalcemia results from the excess production of:
    a) Parathormone b) Calcitonin
    c) Both of the above d) None of the above

27. Edocrine disorder is the primary cause of:
a) Acromegaly b) Albright's syndrome
c) Paget's disease d) Fibrous dysplasia
28. The decreased phosphate levels seen in hyper parathyroidism is due to:
a) Decreased intestinal phosphate absorption
b) Increased calcium excretion
c) Decreased renal phosphate absorption
d) Increased loss of phosphate in urine
29. Enzymes, which play an important role in calcification, are:
a) Enolase and Calcitonin
b) Alkaline phosphatase and catalase
c) Alkaline phosphatase and pyrophophatase
d) Pyrophosphatase and carbonic anhydrase
30. The primary effect of calcitonin is;
a) Bone deposition b) Bone resorption
c) Increases intestinal absorption of calcium
d) Decreases intestinal absorption of calcium
31. Adrenal gland has two parts; cortex and meduall. Which of the following is correct.
a) Cortex is under the control of ACTH
b) Both cortex and medulla are under the control of autonomic nervous system
c) Cortex is exocrine and medulla is endocrine
d) All of the above.
32. Adrenaline used for controlling of bleeding during surgery may result in
a) Syncope
b) Cardiac arrhythmias
c) Drastic fall in blood pressure
d) Production of parathyroid hormone and bone resorption.
34. The blood glucose level in diabetes mellitus is decreased by removal of the:
a) Thyroid b) Parathyroids
c) Anterior pituitary d) Posterior pituitary
35. Excess of cortisol causes:
a) Conn's syndrome b) Cushing's syndrome
c) Acromegaly d) Diabetes insipidus
36. Posterior pituitary insufficiency leads to:
a) Diabetes mellitus b) Diabetes insipidus
c) Dwarfism d) Cretinism
37. Glucocorticoids have all the following actions except:
a) Increase in blood glucose level
b) Increase in protein catabolism
c) Anti-insulin action in peripheral tissues
d) Decrease in glucose uptake by the heart
38. Which of the following is called hunger hormone
a) Epinephrine b) Glucagon
c) Pituitary d) Thyroxine
39. Negative BMR is observed with:
a) Pituitary disturbance
b) Thyroid disturbance
c) Parathyroid
d) All of the above
40. Which of the following hormones increases the sensitivity of heart to epinephrine:
a) Parathyroid b) Insulin
c) Thyroid d) Glucagon
41. Thyroxine causes all the following except:
a) Decreased cell metabolism
b) Increased oxygen consumption
c) Increased pulmonary ventilation
d) Increased basal metabolism
42. The receptors for parathyroid hormone are present in:
a) Osteoblasts b) Osteoclasts
c) Periosteum d) Cartilage
43. Glucagon is secreted by:
a) Alpha cells of pancreas
b) Beta cells of pancreas
c) Gamma cells of pancreas
d) None of the above
44. Parathytoid hormone acts in the body to:
a) Decrease calcium absorption from the intestinal tract
b) Accelerates the removal of the calcium and phosphate from the skeleton but not the teeth.
c) Stimulates liver gluconeogenesis
d) Decreases excretion of sodium and chloride
45. Endocrine glands that are not influenced by the pituitary gland include the:
a) Thyroid gland, testes, and adrenal medulla
b) Adrenal medulla, parathyroids, and the islets of Langerhans
c) Adrenal cortex, parathyroids and ovaries
d) Pancreas, adrenal medulla and thyroid gland
46. The hormone, which stimulates uterus contraction and lets down milk, is:
a) Progesterone b) Prolactin
c) Prostaglandin d) Oxytocin
47. The hormone having the maximum effect on granulation wound healing is:
a) Thyroxine b) Cortisone
c) Parathormone d) Epinephrine
48. The primary site of action of antidiuretic hormone is on the:
a) Distal tubules and collecting ducts in the kidney
b) Afferent arterioles of the glomeruli
c) Thirst center in the hypothalamus
d) Osmoreceptors in the hypothalamus
49. Which of these following is not an effect of insulin?
a) Decreased gluconeogenesis
b) Increased glycogenolysis
c) Increased transport of glucose into cells
d) Induction of lipoprotein lipase
50. Features of hypothyroidism does not include :
a) Obesity
b) Hypertension
c) High TSH levels
d) Increased risk of infections
51. Glucagon is secreted by:
a) Alpha cells of pancreas
b) Liver lobules
c) Spleen
d) Delta cells of pancreas
52. Hormone released during increased stress is:
a) Cortisol b) Thyroxine

c) Growth hormone d) Somatostatin

53. Acromegaly is a disorder of:
a) Excess growth hormone secretion
b) Excess thyroxine secretion
c) Excess ACTH secretion
d) Excess FSH secretion

54. Which of the following statements about the action of the somatomedin is true?
a) They inhibit protein synthesis
b) They antagonize the effect of insulin
c) They promote growth of bone and cartilage
d) They mediate the local effects of somatostatin

55. Steroid hormones are believed to enter target cells via:
a) Facilitated diffusion
b) Carrier-mediated endocytosis
c) Cholesterol lined pores in the plasma membrane
d) Simple diffusion

56. The supraoptic nucleus of the hypothalamus is believed to control secretion of which of the following hormones?
a) Antidiuretic hormone
b) Oxytocin
c) Growth hormone
d) Adreno corticotrophic hormone

57. Epinephrine is most closely related in structure to:
a) Niacin b) Tyrosine
c) Methionine d) Glycerol

58. Glucocorticoids decrease inflammatory reaction by reducing:
a) Activity of histamine
b) Release of histamine
c) Fibroblastic activity
d) Neutrophils

59. Contraceptive action of combined pill is mainly due to:
a) Decrease in tubal motility
b) Prevents the fertlization
c) Prevents the implantation of fertilized egg
d) Inhibits ovulation

60. The following hormones increase the blood glucose level except:
a) Thyroxine b) Parathormone
c) Growth Hormone d) Epinephrine

61. All the following hormones are secreted by adrenal cortex except:
a) Estriol b) Cortisol
c) Corticosterone d) Aldosterone

62. The reabsorption of sodium chloride in kidneys is controlled by the hormones:
a) Adrenaline
b) Aldosterone
c) A.D.H.and vasopressin
d) All of the above

63. Progesterone production in the ovary is primarily by:
a) Stroma b) Corpora albicans
c) Corpora lutea d) Mature follicles

64. Ovulation is associated with sudden rise in
a) Prolactin b) Testosterone
c) L.H. d) Oxytocin

65. In Thyrotoxicosis, there is:
a) Decrease in calcium excretion
b) Increase in serum proteins which bind thyroxine
c) Potentiation of catecholamine action
d) Increase in calcium excretion

66. Not true about T3 and T4 is:
a) T3 more potent than T4
b) T4 binds to prealbumin
c) Absorption of T4 is more than T3
d) Concentration of T4 is more than T3

67. The catecholamines secreted by adrenal medulla:
a) Increases the blood glucose level by favoring glycogenolysis in blood and muscle cells.
b) Decrease the level of free fatty acids and ketone bodies.
c) Increases the splanchnic blood flow
d) Are under the control of parasympathetic nerves.

68. Menopausal hormonal relations are:
a) LH/FSH increase
b) Gonadotropins increase, estrogens decrease
c) Estrogens and gonadotrpins decrease
d) Both increase

69. Regarding Myxoedema the following are true except:
a) Swollen, oedematous look of the face
b) Impotency, amenorrhoea
c) B.M.R. increased by 30%-45%
d) Dullness, loss of memory

70. Reverse T3 is:
a) Synthetic derivative
b) Isomerisation product of T3 and active
c) Isomerisation product of T3 and inactive
d) Reverse of T3

71. Human choronic gonadotrophin hormone (HCG):
a) Acts on the uterus to maintain integrity of endometrium in early pregnancy.
b) Production is greatest in the last three months of pregnancy
c) Can be identified in the urine of pregnant women by immunolgical technique
d) Is a steroid hormone.

72. FSH is secsreted by:
a) Chromophobes b) Basophils
c) Acidophils d) Theca intern cells

73. Which is false regarding insulin:
a) Secreted by Beta cells
b) Glycopeptide
c) Causes lipogenesis
d) Promotes glycogenesis

74. In the adrenal gland, androgens are produced by the cells in the:
a) Zona glomerulosa b) Zona reticularis
c) Zona fasciculata d) Medulla

75. All are seen in cushing's syndrome except:
a) Truncal obesity b) Hypertensiion
c) Hypoglycemia d) Poor wound healing

76. Cortisol levels are maximum during:
a) Sleep b) Early morning
c) Evening d) Have no change

77. Cortisol:
a) Secsretion increases following injury

b) Favours protein synthesis
c) Enhances antigen-antibody reactions
d) Tends to lower blood pressure

78. Oxytocin causes all accept:
a) Lactogenesis
b) Milk ejection
c) Contraction of uterine muscle
d) Myepithelial cell contraction

79. Not a glycoprotein:
a) FSH b) LH
c) TSH d) GH

80. Following are local hormones except:
a) Insulin b) Heparin
c) Bradykinin d) Acetylcholine

81. Insulin facilitates glucose uptake in:
a) Kidney tubules b) Red blood cells
c) Brain d) Skeletal muscle

82. Noradrenaline is differentiated from adrenaline by increasing:
a) Heart rate
b) Cardiac output
c) Peripheral resistance
d) All of the above

83. Hypercalcemia associated with malignancy is most often mediated by:
a) Parathyroid hormone (PTH)
b) Parathyroid hormone related protein (PTHrP)
c) Interleukin-6 (IL-6)
d) Calcitonin

84. A child is below the third percentile for height Growth velocity is normal, but chronologic age is more than skeletal age. The most likely diagnosis is:
a) Constitutional delay in growth
b) Genetic short stature
c) Primordial dwarfism
d) Hypopituitarism

85. Hyjpothyroidism should be treated with daily administration of which of the following thyroid hormone preparations?
a) Thyroid extract b) Thyroglobulin
c) Thyroxine (T4) d) Triodothyronine (T3)

86. Blood coagulation is impaired in
a) Tetany b) Hyperparathyrodism
c) Rickets d) None

87. The hormone which exerts hypoglycemic effect is:
a) Insulin b) Glucagon
c) Growth hormone d) Epinephrine

88. All of the following hormones have cell surface receptors except:
a) Adrenalin b) Growth Hormone
c) Insulin d) Thyroxine

89. Which of the following organs is not involved in calcium homeostasis?
a) Kidneys b) Skin
c) Intestines d) Lungs

90. Osteoclasts are inhibited/modified and regulated by:
a) Parathyroid hormone
b) Calcitonin
c) 1,25-dihydroxycholecalciferol
d) Tumour necrosis factor

91. which one of the following is a precursor of both gonadal and adrenocortical hormones?
a) Progesterone b) Cortisol
c) Testosterone d) Corticosterone

92. Following are the features of cretinism, except
a) Pot-belly
b) Idiotic look
c) Normal intelligence
d) Stunted growth

93. Parathyroid hormone increases the blood level of
a) Copper b) Calcium
c) Iron d) Sodium

94. Paneth cells secrete which of the following?
a) Antibacterial substance
b) Lipase
c) Maltase
d) Secretin

95. Glucose tolerance test is usually done to assess:
a) Acute Pancreatitis
b) Carcinoma of Head of Pancreas
c) Acinar Function of the Pancreas
d) Endocrine Dysfuncres

96. Tetany is characterised by :
a) Hypotonicity of muscles
b) Hypertonicity of muscles
c) Increased serum calcium concentration
d) None of above

97. Which of the following hormiones act via cAMP?
a) Insulin b) Parathormone
c) Vasopressin d) Adrenalin

98. The effect which is seen due to decrease in serum calcium concentration is
a) Relaxation of muscle
b) Excitability of the muscle
c) Increase the renal absorption
d) Depression of Nervous system

ANSWERS

1 (B)	2 (B)	3 (B)	4 (D)	5 (A)
6 (D)	7 (B)	8 (D)	9 (C)	10 (B)
11 (A)	12 (C)	13 (D)	14 (B)	15 (A)
16 (A)	17 (A)	18 (D)	19 (A)	20 (B)
21 (C)	22 (D)	23 (D)	24 (A)	25 (D)
26 (A)	27 (A)	28 (C)	29 (C)	30 (A)
31 (A)	32 (B)	33 (D)	34 (C)	35 (B)
36 (B)	37 (D)	38 (B)	39 (B)	40 (C)
41 (A)	42 (B)	43 (A)	44 (B)	45 (B)
46 (D)	47 (B)	48 (A)	49 (B)	50 (D)
51 (A)	52 (A)	53 (A)	54 (C)	55 (D)
56 (A)	57 (B)	58 (B)	59 (D)	60 (B)
61 (A)	62 (B)	63 (C)	64 (C)	65 (C)
66 (B)	67 (A)	68 (B)	69 (C)	70 (C)
71 (C)	72 (B)	73 (B)	74 (B)	75 (C)
76 (B)	77 A)	78 (A)	79 (D)	80 (A)
81 (D)	82 (C)	83 (B)	84 (A)	85 (C)
86 (A)	87 (A)	88 (D)	89 (D)	90 (B)
91 (A)	92 (C)	93 (B)	94 (A)	95 (D)
96 (B)	97 (B)	98 (B)		

The Endocrine System Quiz

1. Which of the following statements regarding pituitary hormones is false?

A) The hypothalamus makes oxytocin and antidiuretic hormone, which are transported the posterior pituitary for storage.
B) Antidiuretic hormone, released by the posterior pituitary, causes urine volume to increase and blood volume to decrease.
C) Luteinizing hormone, an anterior pituitary hormone, triggers ovulation of an egg from the ovary and causes the ruptured follicle to produce progesterone and some estrogens.
D) Hyposecretion of follicle-stimulating hormone or luteinizing hormone leads to sterility in both males and females.
E) (B) and (C)

2. Androgens are produced by the _______.

A) ovaries.
B) testes.
C) hypothalamus.
D) islets of Langerhans.

3. One of the two hormones made by the pituitary that help regulate reproductive cells is luteinizing hormone. The other hormone is _______.

A) Androgens
B) Follicle stimulating hormone
C) Epinephrine
D) Norepinephrine

4. Calcium level in the blood is regulated by the:

A) Parathyroid and thyroid
B) Adrenal medulla and pancreas
C) Testes
D) Parathyroid and thymus

5. Which one of the following is NOT typical of the changes that follow the binding of a hormone to its target cells:

A) plasma membrane permeability changes
B) cellular mutations occur
C) enzymes are activated or inactivated
D) mitosis is stimulated

6. Being lipid soluble, steroids can do all the following EXCEPT:

A) catalyze cyclic AMP
B) diffuse through the plasma membranes of target cells
C) enter the nucleus
D) activate genes to transcribe mRNA for protein synthesis

7. Estrogens and progesterone are produced by:

A) the testes.
B) the ovaries.
C) the adrenal glands.
D) the hypothalamus.

8. Failure of the pituitary to stop producing growth hormone after body growth is completed results in _______.

A) Gigantism
B) Tetany
C) Kidney failure
D) Acromegaly

9. Most endocrine organs are prodded into action by other hormones; this type of stimulus is called:

A) hormonal stimulus
B) humoral stimulus
C) neural stimulus
D) receptor-mediated stimulus

10. Tropic hormones:

A) stimulate the pineal gland to secrete hormones
B) stimulate the thymus gland to secrete hormones
C) stimulate other endocrines glands to secrete hormones
D) stimulate nervous tissue

11. The body's major metabolic hormone is released from the:

A) Pituitary
B) Thyroid
C) Thymus
D) Hypothalamus

12. Most of the endocrine system is regulated by:

A) negative feedback mechanisms.
B) positive feedback mechanisms.
C) hormone-receptor complexes.
D) hormone-gene complexes.

13. Nervousness, increased body temperature, and increased blood pressure are indications of _______.

A) diabetes mellitus
B) hypoglycemia
C) hypothyroidism
D) hyperthyroidism

14. The alpha cells of the pancreas secrete _______which targets the ________.

A) glucagon; liver
B) melatonin; liver
C) glucagon; kidney
D) calcitonin; thyroid

15. The growth hormone produced by the pituitary gland is known as _______.

A) somatotropin
B) prolactin
C) luteinizing hormone
D) follicle-stimulating hormone

16. The rate of metabolism of all body cells is regulated by _______.

A) parathyroid hormone
B) aldosterone
C) calcitonin
D) thyroid hormone

17. The relatively constant internal environment of the body is maintained by _______.

A) negative feedback.
B) positive feedback.
C) homeostasis.
D) metabolism.

18. The secretions from which of these glands differs between males and females?

A) Adrenal.
B) Parathyroid.
C) Gonadal.
D) Pancreas.

19. The two regulatory systems of the body are the endocrine system and the _______.

A) nervous system
B) immune system
C) circulatory system
D) respiratory system
E) skeletal system

20. Why can a single endocrine hormone produce a wider spread of responses in more of the body than a single nerve cell?

A) A single hormone can target many different responses, whereas a nerve only targets a single response.
B) Blood can carry all the same hormones throughout the body simultaneously, producing responses all over the body; nerve cells can only target a small number of cells.
C) Nerve cells and blood work together. The endocrine has nothing to do with the nervous system.
D) Endocrine hormones only target a very small number of precise responses.

21. Which of the following has both endocrine and exocrine functions?

A) anterior pituitary
B) thyroid
C) adrenal medulla
D) pancreas

22. Which of the following produce antagonistic results?

A) calcitonin and parathryroid hormone
B) FSH and LH
C) ADH and vasopressin
D) oxytocin and prolactin

23. If you drank a liter of water very quickly, the result would be

A) increased secretion of oxytocin
B) decreased secretion of antidiuretic hormone
C) decreased secretion of oxytocin
D) increased secretion of antidiuretic hormone

24. How is hormone secretion regulated?

A) by the nervous system
B) by other hormones
C) by changes in blood composition
D) all of the above

25. Target cells for hypothalamic releasing hormones are in the

A) thyroid
B) hypothalamus
C) anterior pituitary
D) posterior pituitary

26. The posterior pituitary gland stores and secretes

A) oxytocin and antidiuretic hormone
B) human growth hormone and thyroid stimulating hormone
C) prolactin and follicle stimulating hormone
D) glucocorticoids and androgens

27. What stimulates the release of PTH from the parathyroid gland?

A) TSH from the posterior pituitary gland
B) high levels of calcium in the blood
C) calcitonin from the anterior pituitary gland
D) low levels of calcium in the blood

28. The release of cortisol is stimulated by

A) aldosterone
B) angiotensin
C) antidiuretic hormone (ADH)
D) adrenocorticotropic hormone (ACTH)

Answers

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

chapter 6

Endocrine and Reproductive Physiology

CASE 50

Growth Hormone-Secreting Tumor: Acromegaly

Mavis Trippe is a 41-year-old woman who has worked at the cosmetics counter of the local department store for many years. Mavis' colleagues in cosmetics noted that her physical appearance had changed—her features had become coarse, her lower jaw was protruding, and her teeth had separated. They were concerned that Mavis might have a health problem, and one of the colleagues volunteered to have a talk with her. Mavis was a little hurt at their observations, but then opened up and expressed concerns of her own. She disclosed that her menstrual periods had suddenly stopped 5 years ago; that her hat, shoe, and glove size had increased; and that her fingers had enlarged so much that her rings no longer fit. Every night, she had been getting up several times to urinate. Mavis decided to see a physician for evaluation of these strange symptoms.

Physical examination revealed a woman with coarse facial features, a prominent jaw, and large hands and feet. Her blood pressure was elevated at 170/110. The results of laboratory studies are summarized in Table 6–1.

table 6–1 Mavis' Laboratory Values

Glucose, fasting	250 mg/dL	(Normal, 70–100 mg/dL)
Growth hormone, fasting	90 ng/mL	(Normal, 2–6 ng/mL)
IGF-I	Elevated	
FSH	Decreased	
TSH	Normal	
T_4	Normal	
Prolactin	Elevated	

During the administration of glucose in a glucose tolerance test, Mavis' growth hormone levels remained elevated. Magnetic resonance imaging (MRI) of Mavis' brain showed a large intrasellar mass that was pushing upward on the roof of the sella turcica. The physician diagnosed her with acromegaly, caused by a pituitary adenoma that was secreting growth hormone.

Transsphenoidal surgery was performed to remove a large pituitary adenoma. Postoperatively, Mavis' growth hormone and blood glucose levels fell into the normal range. Although her menstrual cycles did not return, the physicians told Mavis that, over time, she could expect improvement in her facial features and reduction in the swelling of her feet and hands.

Questions

1. A significant feature of acromegaly, and one exhibited by Mavis, is widening of bones in the skull, hands, and feet. What is responsible for this widening?

2. Mavis did not exhibit increased *linear* growth of her long bones. Why not?

3. What explanation can you provide for the increased fasting blood glucose level?

4. Why did she have increased urination?

5. Although Mavis' pituitary adenoma secreted growth hormone, her serum prolactin level was also elevated. What explanation can you offer for the increased prolactin level?

6. What was responsible for Mavis' amenorrhea?

7. Based on your knowledge of the feedback control of growth hormone secretion, propose a drug treatment that could have lowered Mavis' growth hormone level prior to surgery?

Answers and Explanations

1. Mavis' pituitary adenoma secreted excessive amounts of **growth hormone**. Growth hormone itself does not have growth-promoting effects on bone. Rather, growth hormone stimulates the production of **insulin-like growth factor I (IGF-I),** or somatomedin, which mediates its growth-promoting effects on bone and soft tissues. IGF-I is synthesized in the target tissues of growth hormone, including liver, kidney, muscle, cartilage, and bone. IGF-I then acts on its target tissues via a tyrosine kinase receptor that is structurally homologous with the insulin receptor.

2. When growth hormone excess occurs *after* puberty, it produces the clinical syndrome of **acromegaly,** which includes progressive thickening of bones and soft tissues; however, because the epiphyseal plates are already closed, the syndrome does not include lengthening of the long bones. When growth hormone excess occurs *before* puberty, it causes a syndrome called **gigantism,** which, because of intense hormonal stimulation of the epiphyseal plates, includes increased linear growth.

3. One of the metabolic actions of growth hormone is inhibition of glucose uptake into muscle and stimulation of gluconeogenesis in liver. These actions are opposite to those of insulin and, consequently, have been termed the "anti-insulin" or **"diabetogenic" effects of growth hormone.** Mavis' high circulating levels of growth hormone resulted in her elevated blood glucose level, resulted in insulin resistance, and could have led to the development of diabetes mellitus.

4. Mavis' polyuria was due to **osmotic diuresis** secondary to her high blood glucose concentration. The high blood glucose led to an increased filtered load of glucose, which exceeded the reabsorptive capacity of the proximal tubule; unreabsorbed glucose was excreted in the urine and acted osmotically to increase Na^+ and water excretion.

5. Normally, **prolactin** secretion by the lactotrophs of the anterior pituitary is under tonic inhibition by **dopamine** secreted from the hypothalamus into the hypothalamic-hypophysial portal blood. One explanation for Mavis' high circulating level of prolactin is that the large pituitary adenoma pushed on the lactotrophs and physically disconnected them from the inhibitory effects of hypothalamic dopamine. Without tonic inhibition by dopamine, prolactin secretion was increased. It is also possible that the pituitary adenoma, in addition to secreting growth hormone, was also secreting prolactin.

6. One reason for Mavis' amenorrhea was encroachment of the pituitary adenoma on other hormone-secreting cells of the anterior pituitary, in this case the gonadotrophs. The gonadotrophs are particularly susceptible to the effects of an expanding intrasellar mass, and as a result, there was decreased secretion of follicle-stimulating hormone (FSH) and luteinizing hormone (LH). The decreased levels of FSH and LH caused decreased secretion of estrogen by the ovaries. Another factor contributing to Mavis' amenorrhea was her elevated serum prolactin; when elevated, prolactin inhibits the secretion of gonadotropin-releasing hormone (GnRH), leading to further suppression of the secretion of FSH and LH.

7. Growth hormone secretion by the anterior pituitary is regulated by two pathways from the hypothalamus, one stimulatory (via **growth hormone-releasing hormone [GHRH]**) and one inhibitory (via **somatostatin**). Growth hormone secretion is controlled by negative feedback as follows (Fig. 6–1). GHRH inhibits its own secretion from the hypothalamus. IGF-I, which is a by-product of growth hormone action on target tissues, inhibits the secretion of growth hormone. And, finally, both growth hormone and IGF-I stimulate the secretion of somatostatin, which then inhibits growth hormone secretion.

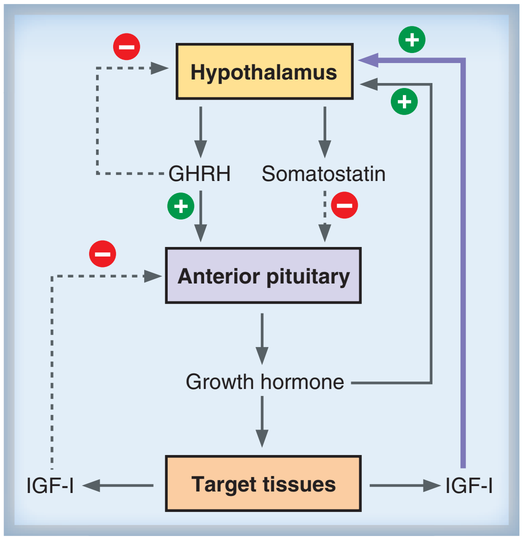

FIGURE 6–1. Regulation of growth hormone secretion. GHRH, growth hormone-releasing hormone; IGF-I, insulin-like growth factor I.

Prior to surgery, Mavis could have been treated with a somatostatin analogue, such as **octreotide,** which, like endogenous somatostatin, inhibits growth hormone secretion.

Key topics

Acromegaly
Dopamine
Gigantism
Growth hormone
Growth hormone-releasing hormone (GHRH)
Insulin-like growth factor I (IGF-I)
Osmotic diuresis
Octreotide
Prolactin
Somatostatin

CASE 51

Galactorrhea and Amenorrhea: Prolactinoma

Meghan Fabrizio is a 39-year-old vice president of an Internet company. She has been married for 10 years and has always used barrier methods for birth control. Meghan's menstrual periods started when she was 12 years old and were regular until 18 months ago. At that time, her periods became irregular and then ceased altogether (amenorrhea). Meghan was very concerned because she and her husband had been talking about trying to have a child. Not only had her periods stopped, but a milky substance was leaking from her breasts.

Meghan made an appointment to see her gynecologist. Findings of the pelvic examination were normal, but the gynecologist was able to express milk from her breasts (galactorrhea). Results of a pregnancy test were negative. Other laboratory results are summarized in Table 6–2.

table 6–2 Meghan's Laboratory Values

Luteinizing hormone, midcycle	5 IU/L (normal, 1–18 IU/L, follicular; 24–100 IU/L, midcycle
Prolactin	86 ng/mL (normal, 5–25 ng/mL)

The laboratory results suggested that Meghan had a prolactinoma. The physician ordered a MRI of her brain. The scan showed a 1.5-cm mass on her pituitary that was believed to be secreting prolactin. While Meghan was awaiting surgery to remove the mass (an adenoma), drug treatment was initiated, which decreased Meghan's serum prolactin level to 20 ng/mL. After the adenoma was removed, Meghan's galactorrhea abated, her menstrual periods resumed, and she is now pregnant with her first child.

Questions

1. How is prolactin secretion regulated?

2. What factors increase prolactin secretion and lead to an increase in the serum prolactin level (hyperprolactinemia)? Which of these factors can be ruled in or ruled out in Meghan's case?

3. Why did Meghan have galactorrhea (increased milk production)?

4. Why were her menstrual cycles irregular? What was the significance of her luteinizing hormone (LH) level?

5. What drug was Meghan given to lower her serum prolactin level? What is its mechanism of action?

6. If Meghan's serum prolactin level had remained elevated, it is unlikely that she could have become pregnant. Why?

7. Meghan had a history of bipolar disorder. While awaiting surgery to remove the adenoma, she experienced a manic phase of her disorder. The physicians considered drug treatment to manage her mania, but were warned by the consulting psychiatrist that risperidone (and other drugs in the same class) was contraindicated. Why would risperidone have been contraindicated before her adenoma was removed?

ANSWERS ON NEXT PAGE

Answers and Explanations

1. **Prolactin** is synthesized and secreted by the **lactotrophs** of the anterior lobe of the pituitary. Its secretion is controlled by the **hypothalamus** (Fig. 6–2) via two regulatory pathways: (i) an inhibitory pathway (through dopamine) and (ii) a stimulatory pathway (through thyrotropin-releasing hormone [TRH]). In persons who are not pregnant or lactating, prolactin secretion by the **anterior pituitary** is **tonically inhibited by dopamine.** In other words, serum prolactin is normally maintained at a low level because inhibition of prolactin secretion by dopamine overrides the stimulation of prolactin secretion by TRH.

   How does this inhibitory dopamine reach the lactotrophs of the anterior pituitary? Dopaminergic neurons secrete dopamine into the median eminence of the hypothalamus. Capillaries in the median eminence drain into **hypothalamic-hypophysial portal vessels** (the direct blood supply from the hypothalamus to the anterior pituitary). These vessels deliver dopamine directly, and in high concentration, to the lactotrophs of the anterior pituitary.

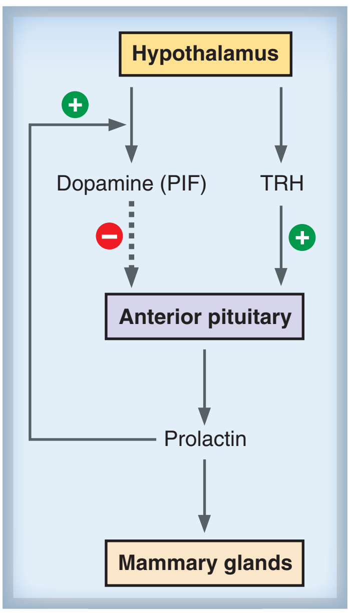

FIGURE 6–2. Control of prolactin secretion. PIF, prolactin-inhibiting factor; TRH, thyrotropin-releasing hormone. (Reprinted, with permission, from Costanzo LS. *BRS Physiology*. 5th ed. Baltimore: Lippincott Williams & Wilkins; 2011:230.)

2. Figure 6–2 shows two mechanisms that potentially could result in increased prolactin secretion: (i) increased TRH secretion and (ii) decreased dopamine secretion. The second possibility, decreased dopamine secretion, suggests an important and intriguing cause of hyperprolactinemia: severing of the hypothalamic-hypophysial tract (e.g., after traumatic head injury). If the connection between the hypothalamus and the anterior pituitary is disrupted, the normal inhibitory control of prolactin secretion by hypothalamic dopamine is lost, and hyperprolactinemia occurs. Other factors that increase prolactin secretion are pregnancy (through increased estrogen levels) and breast-feeding (possibly through increased oxytocin secretion).

   As for the potential causes of Meghan's hyperprolactinemia, pregnancy was ruled out, she was not breast-feeding, and she had no history of traumatic head injury that might have disrupted the blood supply between the hypothalamus and the pituitary. In the absence of other plausible explanations for hyperprolactinemia, it was concluded that the pituitary mass (adenoma) seen on the MRI scan was probably secreting prolactin.

3. Meghan had **galactorrhea** because she was hyperprolactinemic. The major action of prolactin is **lactogenesis** (milk production). Prolactin induces the synthesis of lactose (the carbohydrate of milk), casein (the protein of milk), and lipids. It also promotes the secretion of fluid and electrolytes by the mammary ducts.

4. Meghan's menstrual cycles became irregular and then ceased altogether **(amenorrhea).** In addition to stimulating milk production, prolactin inhibits the secretion of **gonadotropin-releasing hormone (GnRH)** by the hypothalamus. Inhibition of GnRH secretion leads to decreased secretion of **luteinizing hormone (LH),** which normally initiates ovulation at the midpoint of the menstrual cycle. Meghan's LH level was low-normal, even for the preovulatory portion of the menstrual cycle, and much lower than the levels expected at the midcycle surge.

5. Dopamine or **dopamine agonists** (e.g., **bromocriptine**) inhibit prolactin secretion by the anterior pituitary (see Fig. 6–2). Given systemically, bromocriptine acts just like dopamine: it inhibits prolactin secretion. When Meghan was treated with bromocriptine, her serum prolactin level decreased from 86 ng/mL to 20 ng/mL.

6. It is unlikely that Meghan could have become pregnant in her hyperprolactinemic state because prolactin inhibits GnRH secretion (and, consequently, LH secretion). Without an ovulatory surge of LH, ovulation does not occur **(anovulation);** without ovulation, fertilization and pregnancy are impossible. As an aside, fertility is significantly reduced during breast-feeding because the high serum prolactin levels inhibit GnRH and LH secretion. In some parts of the world, breast-feeding is an important mechanism for family spacing, although it is not 100% effective.

7. **Risperidone** is an "atypical" anti-psychotic drug that acts as dopamine antagonist. Thus, had risperidone been administered to Meghan to manage the manic phase of her bipolar disorder, it would have inhibited the tonic inhibition of dopamine on prolactin secretion from the anterior pituitary. The net result of "inhibiting the inhibition" would have been a further increase in serum prolactin levels and worsening of her symptoms.

Key topics

Amenorrhea
Anovulation
Anterior pituitary
Bromocriptine
Dopamine
Galactorrhea
Gonadotropin-releasing hormone (GnRH)
Hypothalamic-hypophysial portal vessels
Hypothalamus
Lactogenesis
Lactotrophs
Luteinizing hormone (LH)
Prolactin
Risperidone

CASE 52

Hyperthyroidism: Graves' Disease

Natasha Schick is a 19-year-old aspiring model who has always dieted to keep her weight in an "acceptable" range. However, within the past 3 months, she has lost 20 lb despite a voracious appetite. She complains of nervousness, sleeplessness, heart palpitations, and irregular menstrual periods. She notes that she is "always hot" and wants the thermostat set lower than her apartment mates.

On physical examination, Natasha was restless and had a noticeable tremor in her hands. At 5 feet, 8 inches tall, she weighed only 110 lb. Her arterial blood pressure was 160/85, and her heart rate was 110 beats/min. She had a wide-eyed stare, and her lower neck appeared full; these characteristics were not present in photographs taken 1 year earlier.

Based on her symptoms, the physician suspected that Natasha had thyrotoxicosis, or increased circulating levels of thyroid hormones. However, it was unclear from the available information *why* her thyroid hormone levels were elevated. Laboratory tests were performed to determine the etiology of her condition (Table 6–3).

table 6–3 Natasha's Laboratory Results

Total T_4	Increased
Free T_4	Increased
TSH	Decreased (undetectable)

T_4, thyroxine; TSH, thyroid-stimulating hormone.

Questions

1. Based on her symptoms, Natasha's physician suspected thyrotoxicosis (elevated levels of thyroid hormone). Why is each of the following symptoms consistent with increased levels of thyroid hormones?

(i) Weight loss
(ii) Heat intolerance
(iii) Increased heart rate
(iv) Increased pulse pressure
(v) Increased arterial blood pressure

2. The physician considered the following possible causes of thyrotoxicosis, based on his understanding of the hypothalamic–anterior pituitary–thyroid axis: (i) increased secretion of **thyrotropin-releasing hormone (TRH)** from the hypothalamus; (ii) increased secretion of thyroid-stimulating hormone (TSH) from the anterior pituitary; (iii) primary hyperactivity of the thyroid gland (e.g., Graves' disease); and (iv) ingestion of exogenous thyroid hormones (factitious hyperthyroidism). Using the laboratory findings and your knowledge of the regulation of thyroid hormone secretion, include or exclude each of the four potential causes of Natasha's thyrotoxicosis.

3. Natasha's physician performed a radioactive I^- uptake test to measure the activity of her thyroid gland. When her thyroid was scanned for radioactivity, I^- uptake was increased uniformly throughout the gland. How did this additional information help refine the diagnosis? Which potential cause of thyrotoxicosis discussed in Question 2 was ruled out by this result?

4. The **triiodothyronine (T_3)** resin uptake test measures the binding of radioactive T_3 to a synthetic resin. In the test, a standard amount of radioactive T_3 is added to an assay system that contains a sample of the patient's serum and a T_3-binding resin. The rationale is that radioactive T_3 will first bind to unoccupied sites on the patient's **thyroid-binding globulin (TBG)** and any remaining, or "leftover," radioactive T_3 will bind to the resin. Thus, T_3 resin uptake is increased when circulating TBG levels are decreased (e.g., liver disease; fewer TBG-binding sites are available) or when endogenous free T_3 levels are increased (endogenous hormone occupies more sites on TBG). Conversely, resin uptake is decreased when circulating TBG levels are increased (e.g., pregnancy) or when endogenous T_3 levels are decreased.

   Natasha's T_3 resin uptake was increased. Using all of the information you have been given thus far, explain this finding.

5. Based on Natasha's symptoms and laboratory findings, Natasha's physicians concluded that she had Graves' disease. Why did they reach this conclusion? Describe the etiology and pathophysiology of this disease.

6. Surgery was scheduled to remove Natasha's thyroid gland (thyroidectomy). While awaiting surgery, Natasha was given two drugs, propylthiouracil (PTU) and propranolol. What was the rationale for giving each of these drugs?

7. Natasha's thyroidectomy was successful, and she was recovering well. Her nervousness and palpitations disappeared, she was gaining weight, and her blood pressure returned to normal. However, she began to experience alarming new symptoms, including muscle cramps, tingling in her fingers and toes, and numbness around her mouth. She returned to her endocrinologist, who noted a positive Chvostek sign (in which tapping on the facial nerve elicits a spasm of the facial muscles). Her total blood Ca^{2+} concentration was 7.8 mg/dL, and her ionized Ca^{2+} concentration was 3.8 mg/dL, both of which were lower than normal (hypocalcemia). What caused Natasha to become hypocalcemic? How did hypocalcemia cause her new symptoms?

8. How was this new problem treated?

Answers and Explanations

1. **Thyrotoxicosis** is a pathophysiologic state caused by elevated circulating levels of free **thyroid hormones.** Natasha's symptoms and physical findings were consistent with thyrotoxicosis: (i) Thyroid hormones **increase the basal metabolic rate (BMR),** O_2 consumption, and nutrient consumption. Thus, Natasha was in a hypermetabolic state and had a voracious appetite; (ii) The increased O_2 consumption resulted in **increased heat production.** The body's normal cooling mechanisms were insufficient to dissipate the extra heat, and Natasha always felt hot; (iii) Thyroid hormones induce the synthesis of a number of proteins, including **β_1 receptors** in the heart. Up-regulation of β_1 receptors in the sinoatrial node produced an increased heart rate, or a positive **chronotropic effect.** (iv) Up-regulation of β_1 receptors in the ventricular muscle produced an increase in **contractility** and **stroke volume,** which was seen as an increase in **pulse pressure.** (v) Both heart rate and contractility were increased; as a consequence, **cardiac output** was increased. The increase in cardiac output produced an **increase in arterial pressure** (arterial pressure [P_a] = cardiac output × total peripheral resistance).

2. Figure 6–3 shows the hypothalamic–anterior pituitary–thyroid axis and the feedback system that regulates the secretion of thyroid hormones. Natasha's laboratory data showed increased levels of free T_4 and total T_4 and decreased levels of TSH. (Total T_4 includes the free and protein-bound components in plasma.)

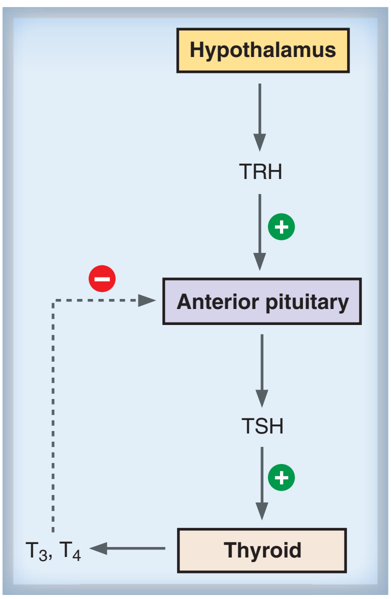

FIGURE 6–3. Control of thyroid hormone secretion. T_3, triiodothyronine; T_4, thyroxine; TRH, thyrotropin-releasing hormone; TSH, thyroid-stimulating hormone. (Reprinted, with permission, from Costanzo LS. *BRS Physiology*. 5th ed. Baltimore: Lippincott Williams & Wilkins; 2011:234.)

(i) Theoretically, but rarely, a hypothalamic tumor can secrete increased levels of TRH. As a result, secretion of TSH by the anterior pituitary is increased, leading to increased secretion of thyroid hormones from the thyroid gland. However, this diagnosis was ruled out by the decreased (undetectable) level of TSH in the blood. If the primary defect was in the hypothalamus, TSH levels would have been increased, not decreased. (ii) By similar reasoning, the anterior pituitary can secrete too much TSH (e.g., from a **pituitary adenoma**), driving increased secretion of thyroid hormones. However, this diagnosis was also ruled out by the finding of undetectable levels of TSH. (iii) If there was primary hyperactivity in the thyroid gland itself, either because the thyroid gland was secreting its hormones autonomously or because a substance with TSH-like actions was driving the thyroid gland, then the laboratory data would be consistent. Levels of both free T_4

(the primary secretory product of the gland) and total T_4 (which includes both free and protein-bound forms in plasma) would be increased. Importantly, TSH levels would be decreased because of negative feedback inhibition of thyroid hormones on the anterior pituitary gland. (iv) If Natasha had ingested synthetic thyroid hormone **(factitious hyperthyroidism),** her levels of free T_4 and total T_4 would have been increased and her TSH level would have been decreased. (Like endogenous thyroid hormone, exogenous thyroid hormone inhibits TSH secretion.)

Thus, on the basis of T_4 and TSH levels alone, primary hyperactivity of the thyroid gland looks just like factitious hyperthyroidism. The physicians were left with the question of whether Natasha had a hyperactive thyroid gland or whether she was ingesting exogenous thyroid hormone (e.g., for weight control). The fullness in her neck suggested an enlarged thyroid gland **(goiter),** but the physicians wanted a more scientific measure of thyroid gland activity (e.g., radioactive I^- scan, as discussed in the next question).

3. The thyroid gland is unique in its requirement for I^-. I^- is taken into the gland by an **Na^+-I^- pump** (or trap), and thyroid hormones are synthesized by the iodination of tyrosines on thyroglobulin (Fig. 6–4).

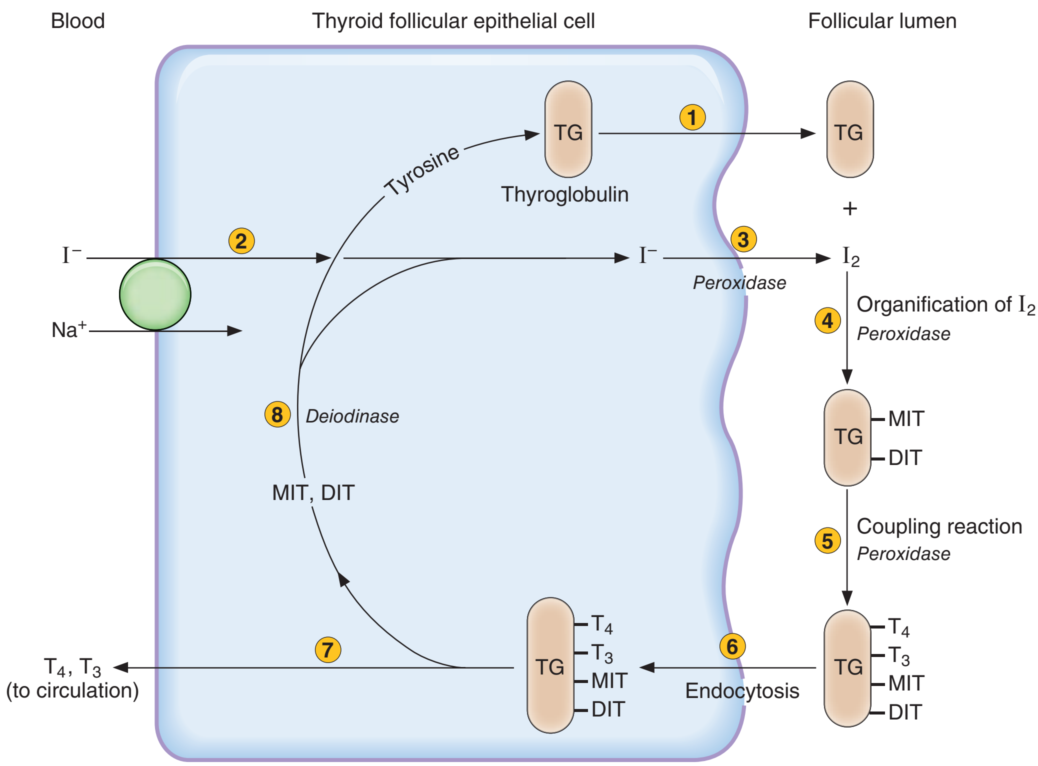

FIGURE 6–4. Steps in the synthesis of thyroid hormones in thyroid follicular cells. DIT, diiodotyrosine; MIT, monoiodotyrosine; TG, thyroglobulin; T_3, triiodothyronine; T_4, thyroxine.

One way to assess thyroid gland activity is to measure **radioactive I^- uptake.** A functional scan of the thyroid can show which areas of the gland are most active, or "hot." In Natasha's case, I^- uptake was increased throughout the gland, suggesting uniform hyperactivity. The functional hyperactivity of the thyroid gland, as demonstrated by the I^- uptake study, ruled out the diagnosis of factitious hyperthyroidism. If Natasha were ingesting exogenous thyroid hormones, her thyroid gland would *not* have shown increased functional activity; in fact, I^- uptake would have been *decreased* because the high levels of thyroid hormone would have suppressed thyroid gland activity (through negative feedback on the anterior pituitary).

4. A finding of increased **T_3 resin uptake** has two possible explanations: (i) TBG levels are decreased or (ii) endogenous levels of thyroid hormones are increased. In Natasha's case, it was the latter: increased endogenous thyroid hormones (from the hyperactive gland) occupied relatively more binding sites on TBG; thus, fewer TBG-binding sites were available to bind radioactive T_3. As a result, uptake of radioactive T_3 by the resin was increased.

5. **Graves' disease,** the most common cause of hyperthyroidism, is an autoimmune disorder caused by the production of abnormal circulating antibodies to TSH receptors on the thyroid gland. These antibodies, called **thyroid-stimulating immunoglobulins (TSIs),** stimulate the thyroid gland, just like **TSH** does. The result is increased synthesis and secretion of thyroid hormones. All of Natasha's symptoms and laboratory findings were consistent with the diagnosis of Graves' disease: increased radioactive I^- uptake, increased T_4 synthesis and secretion, decreased TSH level (by negative feedback), and classic symptoms of thyrotoxicosis.

6. There are three general approaches to the treatment of Graves' disease: (i) removal or destruction of the thyroid gland, (ii) inhibition of thyroid hormone synthesis with drugs, and (iii) blockade of the β_1-adrenergic effects of thyroid hormones that may cause a dangerous increase in arterial pressure.

   Thyroidectomy is a self-evident solution. Alternatively, the thyroid gland can be destroyed with radioactive I^- (much larger amounts than are used for the I^- uptake scan). **Propylthiouracil (PTU)** is an inhibitor of the **peroxidase enzyme** (see Fig. 6–4) that catalyzes all of the steps in thyroid hormone synthesis; **thiocyanate** is a competitive inhibitor of the Na^+-I^- pump in the thyroid gland. Thus, both PTU and thiocyanate decrease the synthesis of thyroid hormones. **Propranolol** is a β-adrenergic antagonist that blocks the positive **inotropic effect** and positive chronotropic effect of thyroid hormones that result from the up-regulation of myocardial β_1 receptors. Thus, propranolol would be expected to offset the increases in cardiac output and arterial pressure that are caused by excess thyroid hormones.

7. Natasha developed **hypocalcemia** because the surgeon must have inadvertently destroyed or removed her parathyroid glands along with her thyroid gland. **Parathyroid hormone (PTH)** increases blood Ca^{2+} concentration by coordinated actions on kidney, bone, and intestine. In the absence of PTH, the blood Ca^{2+} concentration falls. Low blood Ca^{2+} concentration causes muscle cramps, a positive **Chvostek sign** (twitching of facial muscles elicited by tapping on the facial nerve), the **Trousseau sign** (carpopedal spasm after inflation of a blood pressure cuff), and tingling and numbness (by direct effects of low extracellular Ca^{2+} concentration on sensory nerves).

8. **Hypoparathyroidism** is treated with a combination of vitamin D and a high-Ca^{2+} diet. (Although it would seem logical to administer synthetic PTH, such preparations are not available.) Several forms of vitamin D are available, and knowledge of the hormonal regulation of Ca^{2+} homeostasis helps in choosing the appropriate form (Fig. 6–5). PTH stimulates the renal production of **1,25-dihydroxycholecalciferol** (the active form of vitamin D) in the kidney; in hypoparathyroidism, this activation step is diminished. Therefore, Natasha should receive the *active* form of vitamin D (1,25-dihydroxycholecalciferol), along with dietary Ca^{2+} supplementation. Neither cholecalciferol (vitamin D_3) nor 25-hydroxycholecalciferol would correct her hypocalcemia because each substance must be activated in the kidney, which requires PTH.

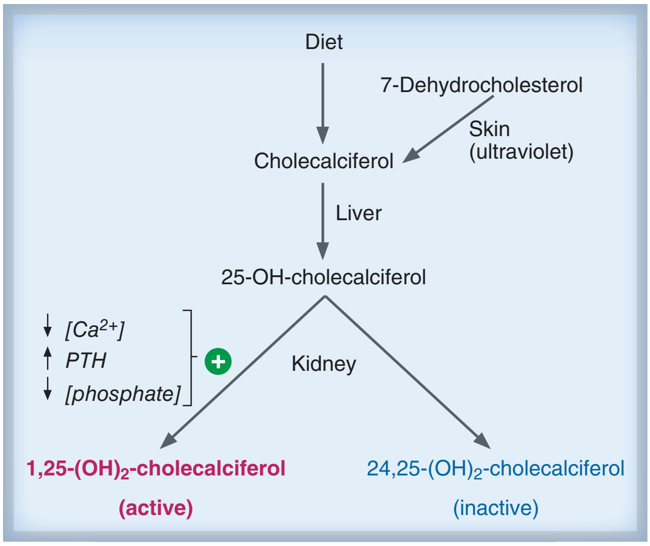

FIGURE 6–5. Steps and regulation of the synthesis of 1,25-dihydroxycholecalciferol. PTH, parathyroid hormone. (Reprinted, with permission, from Costanzo LS. *BRS Physiology*. 5th ed. Baltimore: Lippincott Williams & Wilkins; 2011:249.)

Key topics

Arterial pressure (P_a)
Basal metabolic rate (BMR)
β_1 receptors, or β_1-adrenergic receptors
Cardiac output
Chronotropic effect
Chvostek sign
Contractility
1,25-dihydroxycholecalciferol
Factitious hyperthyroidism
Goiter
Graves' disease
Hypocalcemia
Hypoparathyroidism
I^- uptake by the thyroid gland
Inotropic effect
Na^+-I^- pump
Parathyroid hormone (PTH)
Peroxidase enzyme
Pituitary adenoma
Prophythiouracil (PTU)
Pulse pressure
Stroke volume
T_3 resin uptake

Thiocyanate
Thyroid hormones
Thyroid-binding globulin (TBG)
Thyroid-stimulating hormone (TSH)
Thyroid-stimulating immunoglobulins (TSIs)
Thyrotoxicosis
Thyrotropin-releasing hormone (TRH)
Thyroxine (T_4)
Triiodothyronine (T_3)
Trousseau sign

CASE 53

Hypothyroidism: Autoimmune Thyroiditis

Shirley Tai is a 43-year-old elementary school teacher. At her annual checkup, Shirley complained that, despite eating less, she had gained 16 lb in the past year. Her physician might have attributed this weight gain to "getting older" except that Shirley also complained that she has very little energy, always feels cold (when everyone else is hot), is constipated, and has heavy menstrual flow every month. In addition, the physician noticed that Shirley's neck was very full. The physician suspected that Shirley had hypothyroidism and ordered laboratory tests (Table 6–4).

table 6–4 Shirley's Laboratory Values and Test Results

T_4	3.1 µg/dL (normal, 5–12 µg/dL)
TSH	85 mU/L (normal, 0.3–5 mU/L)
T_3 resin uptake	Decreased
Thyroid antimicrosomal antibodies	Increased

T_4, thyroxine; T_3, triiodothyronine; TSH, thyroid-stimulating hormone.

Based on the physical findings and laboratory results, Shirley's physician concluded that Shirley had autoimmune (Hashimoto) thyroiditis and prescribed oral administration of synthetic T_4 (L-thyroxine). The physician planned to determine the correct dosage of T_4 by monitoring the TSH level in Shirley's blood.

Questions

1. How were Shirley's symptoms of weight gain and cold intolerance consistent with a diagnosis of hypothyroidism?
2. Review the regulation of thyroid hormone secretion by the hypothalamic–anterior pituitary–thyroid axis. List the potential mechanisms that could result in decreased secretion of thyroid hormones. How might you distinguish between these mechanisms as potential causes for her hypothyroidism?
3. Based on the laboratory results, what is the etiology of Shirley's hypothyroidism? Why was her T_4 level decreased?
4. Why was the triiodothyronine (T_3) resin uptake decreased?
5. Why was her thyroid-stimulating hormone (TSH) level increased?
6. Shirley's neck appeared full because she had an enlarged thyroid gland (goiter). If Shirley had *hypo*thyroidism, why was her thyroid gland enlarged?
7. Shirley is receiving hormone replacement therapy in the form of synthetic T_4. How does her body process this T_4? How is synthetic T_4 expected to ameliorate her symptoms?
8. How was Shirley's serum TSH level used to adjust the dosage of synthetic T_4?
9. What symptoms might Shirley experience if the dosage of T_4 is too high?

Answers and Explanations

1. To understand the symptoms of hypothyroidism, we need to review the actions of thyroid hormone and then predict the consequences of hormone deficiency. Like steroid hormones, thyroid hormone acts by inducing the synthesis of new proteins. These proteins are responsible for the various hormone actions, many of which are metabolic. Thyroid hormone increases both the **basal metabolic rate (BMR)** and O_2 consumption (in part because it increases the synthesis of Na^+-K^+ ATPase). Increases in BMR and O_2 consumption lead to increased **heat production.** To provide additional substrates for oxidative metabolism, thyroid hormone increases the absorption of glucose from the gastrointestinal tract and induces the synthesis of key metabolic enzymes, including cytochrome oxidase, NADPH cytochrome C reductase, α-glycerophosphate dehydrogenase, and malic enzyme. To supply more O_2 for aerobic metabolism, thyroid hormone also increases cardiac output and ventilation rate. In adults, thyroid hormone is required for **normal reflexes** and **mentation.** In the perinatal period, thyroid hormone is absolutely required for the normal development of the central nervous system.

Shirley had classic symptoms of **hypothyroidism** (deficiency of thyroid hormones): her BMR was decreased, she had gained weight despite stable caloric intake, she was always cold (when others were hot), and she lacked energy.

2. Refer back to Figure 6–3, which shows how the hypothalamic–anterior pituitary axis regulates thyroid hormone secretion. The hypothalamus secretes a tripeptide **(thyrotropin-releasing hormone, or TRH)** that stimulates the thyrotrophs of the anterior pituitary to secrete **thyroid-stimulating hormone (TSH).** TSH (a glycoprotein) circulates to the thyroid gland, where it has two actions: (i) It increases the synthesis and secretion of thyroid hormones (T_4 and T_3) by stimulating each step in the biosynthetic process; (ii) It causes hypertrophy and hyperplasia of the thyroid gland.

The system is regulated primarily through negative feedback effects of thyroid hormone on TSH secretion. Specifically, T_3 down-regulates TRH receptors on the thyrotrophs of the anterior pituitary, decreasing their responsiveness to TRH. Thus, when thyroid hormone levels are increased, TSH secretion is inhibited. Conversely, when thyroid hormone levels are decreased, TSH secretion is stimulated.

We can use Figure 6–3 to postulate three potential mechanisms for decreased thyroid hormone secretion: (i) primary failure of the hypothalamus to secrete TRH, which would decrease TSH secretion by the anterior pituitary; (ii) primary failure of the anterior pituitary to secrete TSH; and (iii) a primary defect in the thyroid gland itself (e.g., autoimmune destruction or removal of the thyroid).

The three mechanisms that cause hypothyroidism are *not* distinguishable by their effects on circulating thyroid hormone levels or by their symptoms. In each case, circulating levels of T_3 and T_4 are decreased, and symptoms of hypothyroidism occur. However, the mechanisms *are* distinguishable by the circulating levels of TRH and TSH. In **hypothalamic failure** (very rare), secretion of both TRH and TSH is decreased, leading to decreased secretion of thyroid hormones. In **anterior pituitary failure,** secretion of TSH is decreased, leading to decreased secretion of thyroid hormones. In **primary failure of the thyroid gland** (most common), secretion of thyroid hormones is decreased, but secretion of TSH by the anterior pituitary is *increased.* In this scenario, the anterior pituitary gland is normal; TSH secretion is increased because of diminished feedback inhibition by the thyroid hormones.

Thus, the most common cause of hypothyroidism (a primary defect in the thyroid gland) is clearly distinguishable from the second-most common cause (a defect in the anterior pituitary) by their respective TSH levels. If the defect is in the anterior pituitary, TSH levels are decreased; if the defect is in the thyroid, TSH levels are increased.

3. Shirley's laboratory results supported the conclusion that her hypothyroidism was caused by a primary defect in her thyroid gland (decreased T_3 level and increased TSH level). Significantly, she had increased levels of **thyroid antimicrosomal antibodies,** which are antibodies to the **peroxidase enzyme** in the thyroid gland (see Fig. 6–4). The peroxidase enzyme catalyzes the major reactions in the synthesis of thyroid hormones (i.e., reactions involving oxidation of I^- to I_2, organification of I_2 into **monoiodotyrosine [MIT]** and **diiodotyrosine [DIT],** and coupling of MIT and DIT to form T_3 and T_4). Because the circulating antibodies inhibited her peroxidase enzyme, Shirley's thyroid gland did not produce sufficient amounts of thyroid hormones. This form of primary hypothyroidism is called **autoimmune thyroiditis (Hashimoto's thyroiditis).**

4. **T_3 resin uptake** was decreased because Shirley's circulating T_3 levels were decreased. **T_3 resin uptake** is determined by mixing radioactive T_3 with a synthetic binding resin and a sample of the patient's blood. The radioactive T_3 first binds to TBG in the patient's blood; any remaining radioactive T_3 binds to the synthetic resin (i.e., resin uptake). The more radioactive T_3 that is left over, the greater the resin uptake. Thus, T_3 resin uptake is decreased when circulating levels of TBG are increased (more of the patient's TBG-binding sites are available, with less spillover to the resin) or when the patient's T_3 levels are decreased (less of the patient's own T_3 occupies binding sites on TBG; more radioactive T_3 binds to TBG and radioactive T_3 resin uptake is decreased).

5. Earlier, we discussed why Shirley's **TSH** level was increased. Briefly, a primary defect in her thyroid gland led to decreased blood levels of T_4 and T_3. As a result, there was less negative feedback inhibition by thyroid hormones on her anterior pituitary, resulting in increased TSH secretion.

6. Because Shirley had *hypo*thyroidism, perhaps you are surprised that she had a **goiter** (enlarged thyroid gland). In fact, goiter can occur in both hyperthyroidism (hyperactive gland) and hypothyroidism (hypoactive gland). In Shirley's case, decreased secretion of thyroid hormones led to increased secretion of TSH. Through its trophic effects on the thyroid gland, TSH caused hypertrophy, hyperplasia, and enlargement of the gland (even though synthesis and secretion of thyroid hormones was diminished).

7. **Synthetic T_4** (or **L-thyroxine**) is processed in the body just like endogenous T_4. In the target tissues, T_4, whether endogenous or synthetic, is converted either to T_3 or to reverse T_3 (rT_3). T_3 is the most active form of thyroid hormone, and rT_3 is inactive. Therefore, this conversion step in the target tissues modulates how much active hormone is produced.

In Shirley's target tissues, synthetic T_4 was converted to T_3, which then executed all of the physiologic effects of thyroid hormones, including increases in BMR, O_2 consumption, and heat production, and restoration of normal reflexes and central nervous system function.

If T_3 is the active form of thyroid hormone, you may wonder why it isn't administered directly. Patients with hypothyroidism are more often treated with T_4 because it has a much longer half-life than T_3 and, therefore, it can be taken less frequently.

8. The serum TSH level is used to adjust the dosage of synthetic T_4 because TSH secretion is sensitive to feedback inhibition by thyroid hormones. If the replacement dose of T_4 is correct, TSH levels will decrease to normal. If too little T_4 is given, TSH levels will remain elevated. If too much T_4 is given, TSH levels will decrease to below normal.

9. Excessive replacement of T_4 causes the classic symptoms of *hyper*thyroidism: weight loss despite adequate food intake, heat intolerance, nervousness, diarrhea, and amenorrhea.

Key topics

Autoimmune thyroiditis
Basal metabolic rate (BMR)
Diiodotyrosine (DIT)
Goiter
Hashimoto's thyroiditis
Hypothyroidism
Monoiodotyrosine (MIT)
Peroxidase enzyme
T_3 resin uptake
Thyroid antimicrosomal antibodies
Thyroid-stimulating hormone (TSH)
Thyrotropin-releasing hormone (TRH)
Thyroxine (T_4)
Triiodothyronine (T_3)

CASE 54

Adrenocortical Excess: Cushing's Syndrome

Harold Potts is a 48-year-old employee of a local moving company. Over the past 2 years, he had gained 30 pounds, mostly around his "middle," face, and shoulders, although his arms and legs had become very thin. In addition, he had purple stretch marks on his abdomen. His appetite had always been good, but in the past 2 years, it had become enormous! He made an appointment to see his physician because he was having trouble doing the heavy lifting that is required in his job.

In the physician's office, Harold's blood pressure was significantly elevated at 165/105. He had centripetal (truncal) obesity with thin extremities, a buffalo hump (interscapular fat accumulation), a "moon" face, and purple stretch marks (striae) on his abdomen. Table 6–5 summarizes the laboratory results obtained in the fasting state.

table 6–5 Harold's Laboratory Values

Serum Na^+	140 mEq/L (normal, 140 mEq/L)
Serum K^+	3.0 mEq/L (normal, 4.5 mEq/L)
Fasting glucose	155 mg/dL (normal, 70–110 mg/dL)
Serum cortisol	Increased
Serum ACTH	Undetectable

ACTH, adrenocorticotropic hormone.

When a low dose of dexamethasone (a synthetic glucocorticoid) was administered, Harold's serum cortisol level remained elevated. Harold's physician ordered a computed tomography scan, which showed a 7-cm mass (adenoma) on the right adrenal gland. The adenoma was surgically removed 1 week later.

Questions

1. Harold had Cushing's syndrome. He had an adrenal adenoma that secreted large amounts of adrenocortical hormones, primarily cortisol and aldosterone. The increased levels of cortisol were responsible for Harold's **centripetal obesity,** buffalo hump, muscle wasting, striae, and **hyperglycemia** (increased blood glucose concentration). How is each of these abnormalities caused by increased circulating levels of cortisol?

2. Why was Harold's serum adrenocorticotropic hormone (ACTH) level so low? Which etiologies of hypercortisolism were ruled out by his decreased serum ACTH level?

3. How would a healthy person respond to a low-dose dexamethasone test? Was Harold's response normal? If not, why not?

4. Why was Harold's P_a increased?

5. Why was Harold's serum K^+ concentration decreased?

6. In women, Cushing's syndrome causes masculinization, with increased body hair, acne, and irregular menses. Why does Cushing's syndrome have these effects in women?

7. If Harold's surgery had been delayed, his physician could have prescribed a drug that inhibits the synthesis of adrenocortical steroids. What drug might he have prescribed, and what is its mechanism of action?

Answers and Explanations

1. **Cortisol** has diverse actions, several of which are metabolic. One essential role of cortisol is to promote **gluconeogenesis** by altering protein and fat metabolism and directing substrates toward glucose synthesis. Thus, cortisol decreases lipogenesis and stimulates lipolysis, providing gluconeogenic substrates to the liver. Cortisol also increases protein catabolism and decreases new protein synthesis, providing more amino acids to the liver for gluconeogenesis.

Because Harold had **Cushing's syndrome,** his serum cortisol level was increased. In him, each of the normal physiologic actions of cortisol was exaggerated. He was **hyperglycemic** (had a higher than normal fasting blood glucose) because his liver synthesized too much glucose. He had **muscle wasting** (thin arms and legs) because of the protein catabolic effect of excess cortisol. The **striae** were caused by decreased synthesis of collagen proteins (resulting in fragility of subcutaneous tissues). The tendency to accumulate fat around the trunk **(centripetal fat),** face, neck, and back **(buffalo hump)** is characteristic of hypercortisolism. This characteristic is puzzling because cortisol stimulates lipolysis (increased fat breakdown). However, cortisol also stimulates the appetite and, for reasons that are not entirely understood, the increased caloric intake causes fat to be deposited in these specific regions of the body. The centripetal fat distribution is also visually exaggerated because of muscle wasting in the arms and legs.

2. Harold had a very low (undetectable) circulating level of **ACTH** secondary to the high levels of cortisol secreted by the adrenal adenoma. High levels of cortisol inhibit ACTH secretion from the anterior pituitary gland by negative feedback (Fig. 6–6).

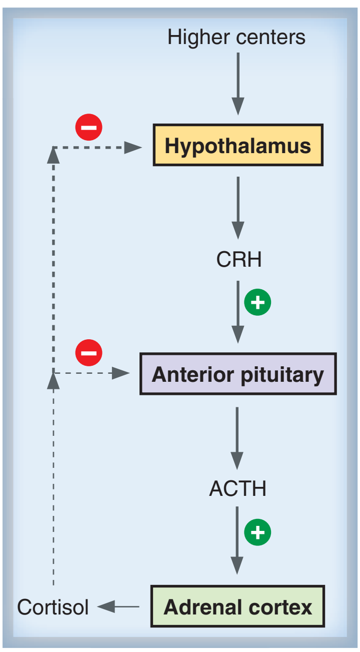

FIGURE 6–6. Control of glucocorticoid secretion. ACTH, adrenocorticotropic hormone; CRH, corticotropin-releasing hormone. (Reprinted, with permission, from Costanzo LS. *BRS Physiology*. 5th ed. Baltimore: Lippincott Williams & Wilkins; 2011:238.)

Harold's decreased ACTH level ruled out three potential causes of hypercortisolism: a hypothalamic tumor that secretes **corticotropin-releasing hormone (CRH),** an anterior pituitary tumor that secretes ACTH, and an ectopic tumor that secretes ACTH. In each of these potential causes of hypercortisolism, circulating levels of ACTH are *increased*. For example, the hypothalamic tumor oversecretes CRH, which drives the anterior pituitary to oversecrete ACTH, which drives the adrenal cortex to oversecrete cortisol. In the case of the anterior pituitary tumor or the ectopic

ACTH-secreting tumor, the high levels of ACTH drive the adrenal cortex to oversecrete cortisol. The bottom line is that none of these potential causes was possible in Harold because his ACTH level was decreased, not increased.

3. **Dexamethasone** is a synthetic glucocorticoid that has all of the effects of cortisol, including inhibition of ACTH secretion from the anterior pituitary. In healthy persons, a low dose of dexamethasone (the **dexamethasone suppression test**) inhibits ACTH secretion, which inhibits endogenous cortisol secretion. Accordingly, in healthy persons, dexamethasone causes both ACTH and cortisol levels in the blood to decrease.

   Harold's response to the low-dose dexamethasone test was *abnormal* (his serum cortisol level remained elevated) because his adrenal adenoma autonomously secreted large amounts of cortisol. These high levels of cortisol completely suppressed ACTH secretion. When more glucocorticoid was added to the blood in the form of synthetic dexamethasone, further inhibition of ACTH secretion did not occur because it was already completely inhibited.

4. Harold's **arterial pressure** was increased (160/105) for two reasons: (i) increased circulating levels of cortisol and (ii) increased circulating levels of aldosterone. **Cortisol** increases arterial pressure by up-regulating β_1-adrenergic receptors on vascular smooth muscle. In this way, cortisol increases the sensitivity of blood vessels, particularly arterioles, to the vasoconstrictor actions of catecholamines (e.g., norepinephrine). **Aldosterone** increases arterial pressure through its effect on renal Na^+ reabsorption. Aldosterone increases Na^+ reabsorption, which leads to increased extracellular fluid volume and blood volume. Increased blood volume leads to increased preload, increased cardiac output, and increased arterial pressure.

5. Harold's serum K^+ concentration was decreased (3.0 mEq/L) because the adrenal adenoma secreted large amounts of **aldosterone.** One major action of aldosterone is to increase K^+ secretion by the renal principal cells, and this increased secretion results in negative K^+ balance and **hypokalemia.**

6. In addition to cortisol and aldosterone, the adrenal cortex secretes the androgens **dehydroepiandrosterone (DHEA)** and **androstenedione** (Fig. 6–7). In women, the adrenal cortex is the major source of androgens. In women who have Cushing's syndrome, the hyperactive adrenal cortex secretes increased amounts of adrenal androgens, which have masculinizing effects (e.g., increased body hair). In men with Cushing's syndrome, secretion of adrenal androgens is increased, but this increase is only a "drop in the (androgen) bucket" because the testes secrete large amounts of their own androgen (testosterone).

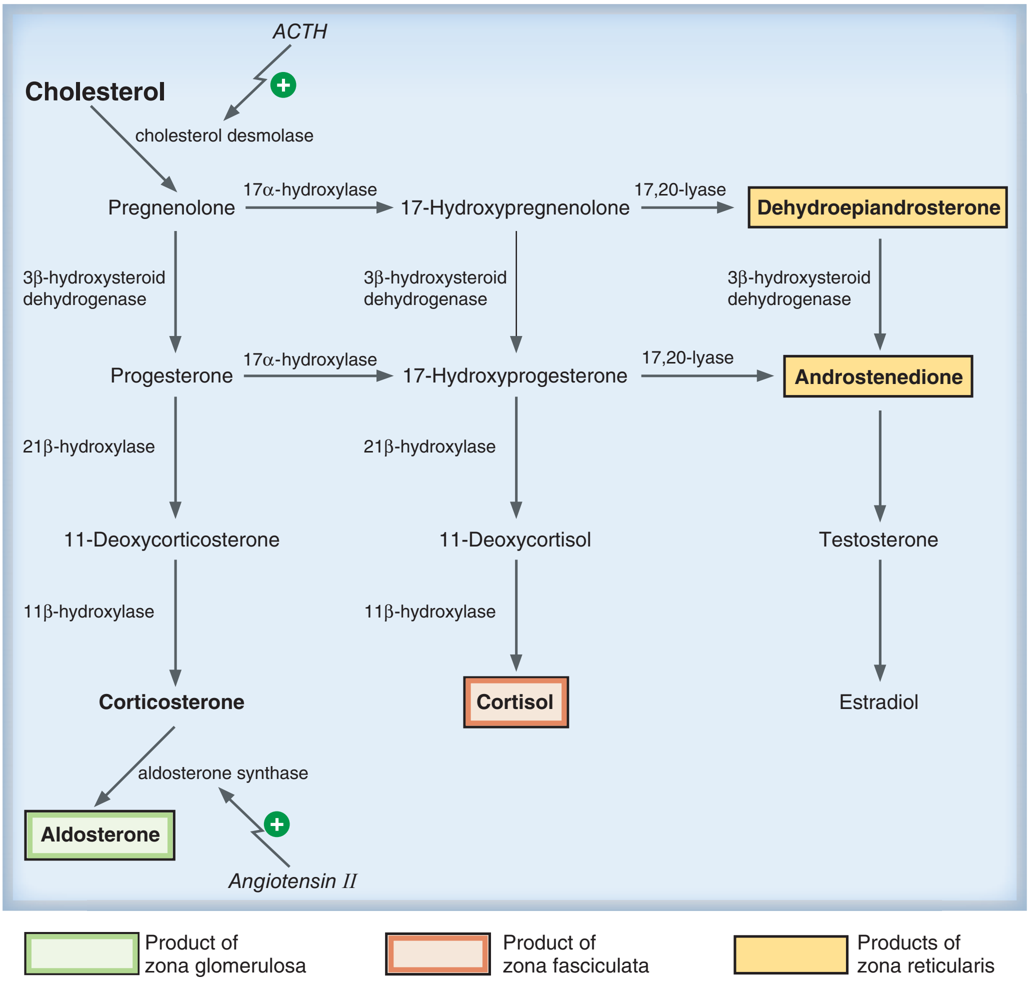

FIGURE 6–7. Synthetic pathways for glucocorticoids, androgens, and mineralocorticoids in the adrenal cortex. ACTH, adrenocorticotropic hormone. (Reprinted, with permission, from Costanzo LS. *BRS Physiology*. 5th ed. Baltimore: Lippincott Williams & Wilkins; 2011:237.)

7. If surgery had been delayed, Harold could have been treated with **ketoconazole,** an inhibitor of **cholesterol desmolase** (the enzyme that catalyzes the first step in the biosynthesis of adrenocortical steroids). Ketoconazole treatment would have decreased the production of cortisol and aldosterone by the adrenal adenoma and decreased the symptoms caused by hypercortisolism and hyperaldosteronism.

Key topics

Adrenocorticotropic hormone (ACTH)
Aldosterone
Androstenedione
Arterial pressure
Buffalo hump
Centripetal obesity
Cholesterol desmolase
Corticotropin-releasing hormone (CRH)
Cortisol
Cushing’s syndrome
Dehydroepiandrosterone (DHEA)
Dexamethasone
Dexamethasone suppression test
Hyperglycemia
Hypokalemia
Ketoconazole
Striae

CASE 55

Adrenocortical Insufficiency: Addison's Disease

Susan Oglesby is a 41-year-old divorced mother of two teenagers. She has always been in excellent health. She recently saw her physician because of several unexplained symptoms, including weight loss of 15 lb, extreme fatigue, and decreased body hair in the axillary and pubic regions. In addition, her skin was very tanned, even though she had not been in the sun. Susan hadn't had a menstrual period in 3 months; she knew she wasn't pregnant and wondered whether she was experiencing early menopause.

In her physician's office, Susan appeared very thin, with sunken eyes and decreased skin turgor. When she was supine (lying), her blood pressure was 90/60 and her pulse rate was 95 beats/min. When she was standing, her blood pressure was 70/35 and her pulse rate was 120 beats/min. Her skin was deeply pigmented, especially her nipples and the creases in the palms of her hands. Susan's physician ordered laboratory tests (Table 6–6).

table 6–6 Susan's Laboratory Values

Venous Blood	
Na^+	126 mEq/L (normal, 140 mEq/L)
K^+	5.7 mEq/L (normal, 4.5 mEq/L)
Osmolarity	265 mOsm/L (normal, 290 mOsm/L)
Glucose (fasting)	50 mg/dL (normal, 70–100 mg/dL)
Cortisol	Decreased
Aldosterone	Decreased
ACTH	Increased
Arterial Blood	
pH	7.32 (normal, 7.4)
HCO_3^-	18 mEq/L (normal, 24 mEq/L).

ACTH, adrenocorticotropic hormone.

Results of an ACTH stimulation test were negative (i.e., there was no increase in the serum level of cortisol or aldosterone). Based on the symptoms, physical examination, laboratory values, and results of the ACTH stimulation test, Susan was diagnosed with primary adrenal insufficiency (Addison's disease). Susan's physician prescribed daily treatment with hydrocortisone (a synthetic glucocorticoid) and fludrocortisone (a synthetic mineralocorticoid). Susan was instructed to take hydrocortisone in two divided doses, with a larger dose at 8 AM and a smaller dose at 1 PM.

At a follow-up visit 2 weeks later, Susan's circulating ACTH level was normal. She had gained 5 lb, her blood pressure was normal (both supine and standing), her tan had started to fade, and she had much more energy.

Questions

1. Why were Susan's serum cortisol, aldosterone, and ACTH levels consistent with primary adrenocortical insufficiency? How did her negative response to the ACTH stimulation test confirm this diagnosis?

2. How did adrenocortical insufficiency cause Susan's decreased arterial pressure? Why did her blood pressure decrease further when she moved from a supine position to a standing position?

3. Why was her pulse rate increased? Why was her pulse rate higher when she was standing than when she was supine?

4. Why was Susan's fasting blood glucose level lower than normal?

5. Why was her serum K^+ concentration elevated (hyperkalemia)?

6. Why was her serum Na^+ concentration decreased (hyponatremia)?

7. What acid–base abnormality did Susan have, and what was its cause? If her P_{CO_2} had been measured, would you expect it to be normal, increased, or decreased? Why?

8. Why did Susan's skin appear tanned (hyperpigmentation)?

9. Why did she have decreased pubic and axillary hair?

10. Why did Susan's ACTH level return to normal within 2 weeks of starting treatment?

11. Why was Susan instructed to take the hydrocortisone in two divided doses, with a larger dose at 8 AM?

Answers and Explanations

1. Susan's decreased serum levels of **cortisol** and **aldosterone** and increased serum level of **adrenocorticotropic hormone (ACTH)** were consistent with primary adrenocortical insufficiency **(Addison's disease).** In this disease, the adrenal cortex is destroyed (usually secondary to an autoimmune process). As a result, the adrenal cortex can no longer secrete its steroid hormones cortisol, aldosterone, and the adrenal androgens DHEA and androstenedione.

   The circulating **ACTH** level can be used to distinguish primary **adrenocortical insufficiency** from secondary adrenocortical insufficiency (refer back to Fig. 6–6 in Case 54). In the *primary* form, the defect is in the adrenal cortex itself; the serum ACTH level is *increased* because the low level of cortisol reduces negative feedback inhibition of ACTH secretion by the anterior pituitary, thereby increasing ACTH levels. In the *secondary* form (hypothalamic or anterior pituitary failure), serum ACTH levels are *decreased* (which leads to decreased cortisol secretion).

   The **ACTH stimulation test** evaluates the responsiveness of cortisol secretion to an injection of exogenous ACTH. The test confirmed that Susan's disease was caused by primary adrenal failure. Even the large amount of ACTH in the injection couldn't stimulate her adrenal cortex to secrete cortisol!

2. Decreased circulating levels of cortisol and aldosterone were responsible for Susan's **decreased arterial pressure** (90/60 supine), as follows: (i) One action of cortisol is up-regulation of β_1-adrenergic receptors on vascular smooth muscle, resulting in increased responsiveness of blood vessels to catecholamines. In the absence of cortisol, the responsiveness of blood vessels to catecholamines is decreased. As a result, there is a decrease in **total peripheral resistance** and arterial pressure; (ii) A major action of aldosterone is increased Na^+ reabsorption by the renal principal cells, leading to increases in extracellular fluid volume and blood volume, venous return, cardiac output, and arterial pressure. In the absence of aldosterone, there is decreased Na^+ reabsorption, decreased extracellular fluid volume and blood volume, and decreased arterial pressure.

   The further decrease in Susan's arterial pressure when she moved from a supine to an upright position **(orthostatic hypotension)** is characteristic of hypovolemia (decreased blood volume). When Susan stood up, blood pooled in the veins of the legs, further compromising venous return, cardiac output, and arterial pressure.

3. Susan's pulse rate was elevated (95 beats/min) because decreases in arterial pressure activate the **baroreceptor reflex.** This reflex directs an increase in sympathetic outflow to the heart and blood vessels. One of these sympathetic responses is an increase in the heart rate mediated by β_1-adrenergic receptors in the sinoatrial node.

   When Susan stood up, her pulse rate increased because her blood pressure had decreased further. The even lower arterial pressure triggered an even stronger response of the baroreceptor reflex.

4. Susan was **hypoglycemic** (fasting blood glucose level, 50 mg/dL) as a result of her decreased cortisol level. One action of cortisol is to increase the blood glucose concentration by promoting gluconeogenesis and decreasing glucose uptake by the tissues. Thus, in cortisol deficiency, gluconeogenesis decreases, glucose uptake by the tissues increases, and as a result, the blood glucose concentration decreases.

5. Susan's serum K^+ concentration was elevated **(hyperkalemia)** secondary to her decreased aldosterone level. In addition to stimulating Na^+ reabsorption, aldosterone stimulates K^+ secretion by the renal principal cells. Thus, in aldosterone deficiency, K^+ secretion is decreased, which leads to positive K^+ balance and hyperkalemia.

6. You may have proposed that Susan was **hyponatremic** because aldosterone deficiency caused her to excrete too much Na^+ in urine. While this explanation seems logical, it is not complete. Susan

was hyponatremic primarily because she had *excess water* in her body relative to Na^+; the excess water diluted her serum Na^+ concentration.

Now we are faced with a more difficult question: Why did Susan retain excess water? There are two major reasons why an increase in body water occurs: (i) the person drinks more water than the kidneys can excrete or (ii) there is increased water reabsorption by the kidneys. The first mechanism (primary polydipsia) is a rare cause of **hyponatremia.** It is much more likely that Susan's kidneys reabsorbed too much water because of a high circulating level of **antidiuretic hormone (ADH).** Recall that ADH secretion is stimulated by both hyperosmolarity and hypovolemia, and that the hypovolemic stimulus will "override" the osmotic stimulus. Thus, Susan's hyponatremia was caused by the following sequence of events: decreased Na^+ reabsorption (as a result of aldosterone deficiency), decreased extracellular fluid volume, decreased blood volume, increased ADH secretion (secondary to hypovolemia), and increased reabsorption of water by the renal collecting ducts.

You may ask whether this high ADH secretion was appropriate given Susan's low serum osmolarity. Shouldn't her low serum osmolarity have turned off ADH secretion? Yes, it should have! Again, the hypovolemic stimulus for ADH secretion overrides the osmotic stimulus.

7. With an arterial pH of 7.32 and an HCO_3^- concentration of 18 mEq/L, Susan had **metabolic acidosis.** (Recall from acid–base physiology that metabolic acidosis begins with a decrease in HCO_3^- concentration, which decreases pH.) If her arterial P_{CO_2} had been measured, it would have been decreased secondary to respiratory compensation for metabolic acidosis (i.e., **hyperventilation**).

The likely cause of Susan's metabolic acidosis is **aldosterone deficiency.** In addition to increasing Na^+ reabsorption and K^+ secretion in the renal principal cells, aldosterone increases H^+ secretion and "new" HCO_3^- reabsorption in the renal intercalated cells. Thus, aldosterone deficiency leads to decreased Na^+ reabsorption (leading to decreased extracellular fluid volume), decreased K^+ secretion (leading to hyperkalemia), and decreased H^+ secretion and new HCO_3^- reabsorption (leading to metabolic acidosis). This form of metabolic acidosis (secondary to aldosterone deficiency) is called **type 4 renal tubular acidosis.** Specifically, aldosterone deficiency causes hyperkalemia, which **inhibits renal NH_3 synthesis;** the decreased supply of NH_3, combined with decreased H^+ secretion, leads to a decrease in NH_4^+ excretion and metabolic acidosis.

8. Susan's **hyperpigmentation** was a consequence of the negative feedback regulation of ACTH secretion. Susan had primary adrenocortical failure, which led to decreased serum levels of cortisol. Decreased levels of cortisol led to decreased negative feedback inhibition of **pro-opiomelanocortin (POMC)** synthesis by the anterior pituitary. POMC, the precursor for ACTH, is a complex molecule that contains **melanocyte-stimulating hormone (MSH)** fragments. Thus, when POMC levels are increased, so are the levels of MSH, which pigments the skin.

9. Susan had decreased pubic and axillary hair because, in addition to deficiencies of cortisol and aldosterone, she had a **deficiency of adrenal androgens.** In women, the adrenal cortex is the major source of androgens (DHEA and androstenedione), which are responsible for body hair and libido.

10. Susan's ACTH level returned to normal within 2 weeks of the initiation of hormone replacement treatment with hydrocortisone (a glucocorticoid) and fludrocortisone (a mineralocorticoid). Like endogenous cortisol, exogenous glucocorticoid has a negative feedback effect on the secretion of ACTH from the anterior pituitary.

11. Susan was instructed to take hydrocortisone (glucocorticoid) in two divided doses, with a larger dose at 8 AM and a smaller dose at 1 PM to replicate the body's **diurnal pattern of cortisol secretion.** Endogenous cortisol secretion is **pulsatile** (occurs in bursts), with the largest burst occurring just before awakening (e.g., at 8 AM). Several smaller bursts occur in the afternoon, and the lowest rates of cortisol secretion occur in the evening and just after falling asleep.

Key topics

Addison's disease
Adrenocortical insufficiency
Adrenocorticotropic hormone (ACTH)
Aldosterone
Antidiuretic hormone (ADH)
Arterial pressure
Baroreceptor reflex
Cortisol
Diurnal pattern (of cortisol secretion)
Hyperkalemia
Hyperpigmentation
Hypoglycemia
Hyponatremia
Melanocyte-stimulating hormone (MSH)
Metabolic acidosis
Orthostatic hypotension
Pro-opiomelanocortin (POMC)
Type 4 renal tubular acidosis

CASE 56

Congenital Adrenal Hyperplasia: 21β-Hydroxylase Deficiency

Lauren and Tim Anderson recently had their second child, a girl whom they named Anne Carter. A day after the delivery, the pediatrician told the Andersons that Anne Carter's clitoris was enlarged. The pediatrician ordered a chromosomal evaluation, which confirmed an XX (female) genotype. Other tests showed that she has ovaries, a uterus, and no testes. Table 6–7 gives the results of the laboratory tests.

table 6–7 Anne Carter's Laboratory Values

Blood glucose	70 mg/dL (normal fasting, 70–100 mg/dL)
Serum cortisol	Low-normal
Serum ACTH	Increased
17-ketosteroid excretion	Increased

ACTH, adrenocorticotropic hormone.

The consulting pediatric endocrinologist made a diagnosis of congenital adrenal hyperplasia secondary to 21β-hydroxylase deficiency. It was recommended that Anne Carter receive hormone replacement therapy and that she undergo surgery to reduce the size of her clitoris.

Questions

1. Using your knowledge of the biosynthetic pathways of the adrenal cortex, predict the consequences of 21β-hydroxylase deficiency. Which adrenocortical hormones will be deficient? Which hormones will be produced in excess?

2. What are the expected physiologic consequences of the hormonal deficiencies you predicted in Question 1?

3. Why was Anne Carter's serum adrenocorticotropic hormone (ACTH) level increased?

4. Anne Carter's blood glucose and serum cortisol levels were both low-normal. Why weren't these values more obviously abnormal?

5. What was the significance of her increased urinary excretion of 17-ketosteroids?

6. Why was Anne Carter's clitoris enlarged at birth?

7. Did she have partial or complete deficiency of 21β-hydroxylase?

8. What hormone replacement therapy did she receive?

9. In terms of later development, what might have happened if Anne Carter's condition had not been diagnosed (and she did not receive hormone replacement therapy)?

Answers and Explanations

1. Refer back to Figure 6–7, which shows the biosynthetic pathways of the adrenal cortex. Briefly, the first step in the pathway is the conversion of cholesterol to pregnenolone, which is catalyzed by the enzyme **cholesterol desmolase.** After pregnenolone is generated, it either proceeds through a series of steps to **aldosterone,** or it is hydroxylated at C-17. 17-Hydroxylated compounds are precursors of cortisol and adrenal androgens as follows. If the two-carbon side chain is cleaved at C-17 (by 17,20 lyase), **adrenal androgens DHEA** and **androstenedione** are generated; if the side chain is not cleaved, **cortisol** is generated.

Figure 6–7 shows that **21β-hydroxylase** is *required for the synthesis of aldosterone and cortisol.* In the aldosterone pathway, it catalyzes the conversion of progesterone to 11-deoxycorticosterone. In the cortisol pathway, it catalyzes the conversion of 17-hydroxyprogesterone to 11-deoxycortisol. If 21β-hydroxylase is absent, both pathways are blocked, and neither aldosterone nor cortisol is synthesized. In addition, steroid intermediates (progesterone, pregnenolone, 17-hydroxypregnenolone, and 17-hydroxyprogesterone) "build up" proximal to the blockage. These intermediates are precursors for, and are shunted toward, the synthesis of adrenal androgens, which are then produced in excess. Therefore, the short answer to the question is that, in addition to a *deficiency* of aldosterone and cortisol, there will be an *excess* of adrenal androgens.

2. The physiologic consequences of aldosterone and cortisol deficiency can be inferred from the established actions of the hormones. The major actions of cortisol are gluconeogenesis, anti-inflammatory effects, immune suppression, and vascular responsiveness to catecholamines (which increases arterial pressure). The major actions of aldosterone are increased Na^+ reabsorption (which leads to increased extracellular fluid volume and increased arterial pressure), increased K^+ secretion, and increased H^+ secretion and "new" HCO_3^- reabsorption. Thus, cortisol deficiency leads to **hypoglycemia** and **hypotension.** Aldosterone deficiency leads to hypotension, **hyperkalemia,** and **metabolic acidosis.**

3. Anne Carter's serum **adrenocorticotropic hormone (ACTH)** level was elevated as a result of her low-normal level of cortisol. Based on the diagnosis of 21β-hydroxylase deficiency, we can presume that, initially, her adrenal cortex produced insufficient amounts of cortisol. Decreased levels of cortisol caused increased secretion of ACTH by reducing negative feedback inhibition on the anterior pituitary (see Fig. 6–6).

4. Initially, it may be puzzling why Anne Carter's blood glucose and cortisol levels were not decreased more significantly. Both values were at the low end of the normal range. However, if she is deficient in 21β-hydroxylase, why weren't these levels even lower? The answer lies in the high levels of ACTH that resulted from her decreased serum cortisol. This increased level of ACTH caused hyperplasia of the adrenal cortex. The hyperplastic adrenal cortex was stimulated to synthesize more cortisol, partially offsetting the original deficiency. (In recognition of this phenomenon, the syndrome is also called **congenital adrenal hyperplasia.**)

5. Adrenal androgens have a ketone group at C-17 that distinguishes them from cortisol, aldosterone, and testosterone. (Cortisol and aldosterone have side chains at C-17. Testosterone, an androgen produced in the testes, has a hydroxyl group at C-17.) Thus, adrenal androgens are called 17-ketosteroids. In Anne Carter's case, increased excretion of **17-ketosteroids** reflected increased synthesis of *adrenal* androgens. This increased synthesis was caused by shunting of steroid intermediates toward androgens and hyperplasia of the adrenal cortex secondary to high levels of ACTH.

6. Anne Carter's clitoris was enlarged because excess adrenal androgens masculinized her external genitalia. In recognition of this masculinizing effect in girls, the disorder is also called **adrenogenital syndrome.** In boys who have 21β-hydroxylase deficiency, the effects of excess adrenal androgens are not obvious at birth; however, these boys may have early masculinization and precocious puberty.

7. Presumably, Anne Carter had a *partial* deficiency of 21β-hydroxylase. This conclusion is supported by the finding that her adrenal cortex maintained low-normal levels of cortisol secretion. *Some* enzyme activity must have been present because her adrenal cortex secreted *some* cortisol. If she had *complete* enzyme deficiency, she would have secreted *no* cortisol and *no* aldosterone. (A complete deficiency of 21β-hydroxylase would have caused a life-threatening crisis with severe hypotension and hypoglycemia at delivery.)

8. Anne Carter was treated with **glucocorticoid replacement** therapy (e.g., hydrocortisone). You may wonder whether this treatment was necessary since her hyperplastic adrenal cortex, driven by the high ACTH levels, was already capable of maintaining cortisol synthesis. Indeed, this treatment *was* necessary because adrenocortical hyperplasia also caused excessive production of androgens (which is undesirable in females). Therefore, the rationale for giving Anne Carter exogenous glucocorticoid treatment was to inhibit ACTH secretion, prevent adrenal hyperplasia, and reduce adrenocortical production of androgens.

Anne Carter may also need **mineralocorticoid replacement** therapy (e.g., fludrocortisone). As with cortisol, she maintained sufficient levels of aldosterone because her adrenal cortex was hyperplastic. However, treatment with exogenous glucocorticoid would be expected to reduce both ACTH secretion and the size of the adrenal cortex. Once the adrenal cortex was reduced in size, it would no longer secrete sufficient quantities of aldosterone (because of the 21β-hydroxylase deficiency) and mineralocorticoid replacement would be required.

9. If not for the clue of clitoromegaly, Anne Carter's condition might not have been diagnosed. If she had not been diagnosed, she would have become further masculinized by continuously high levels of adrenal androgens. In the prepubertal years, she would have had accelerated linear growth, increased muscle mass, and increased body hair. At puberty, she would have experienced irregular menses or even amenorrhea. Finally, because androgens cause closure of the epiphyseal growth plates, her final adult height would have been shorter than average.

Key topics

Adrenocorticotropic hormone (ACTH)
Adrenogenital syndrome
Aldosterone
Androstenedione
Cholesterol desmolase
Congenital adrenal hyperplasia
Cortisol
Dehydroepiandrosterone (DHEA)
21β-hydroxylase
Hyperkalemia
Hypoglycemia
Hypotension
17-ketosteroids
Metabolic acidosis

CASE 57

Primary Hyperparathyroidism

Carl Felicetti is a 53-year-old violinist with a local symphony orchestra. He had always been in excellent health. However, after two sets of tennis on a hot day in July, he suddenly experienced the worst pain of his life. The pain came in waves that started in his right flank and radiated into his groin. When he went to the bathroom, he voided bright red urine. His tennis partner drove him to the emergency room, where an intravenous pyelogram showed several ureteral stones. He was sent home with a prescription for narcotics and instructions to drink lots of water and "wait it out." Fortunately, Carl didn't need to wait long; that evening, he voided more bright red urine and two hard, brown stones. He saved the stones, as instructed, for chemical analysis.

Carl saw his physician the next day. There was nothing unusual in his history, except for constipation and his wife's new "health kick." (She was taking multivitamins and Ca^{2+} supplementation and had convinced Carl that he should take the supplements, too.) Table 6–8 summarizes the results of laboratory tests.

table 6–8 Carl's Laboratory Values

Serum Ca^{2+}	11.5 mg/dL (normal, 10 mg/dL)
Serum phosphate	2 mg/dL (normal, 3.5 mg/dL)
Serum parathyroid hormone	125 pg/mL (normal, 10–65 pg/mL)
Serum albumin	Normal
Alkaline phosphatase	Elevated
Urinary Ca^{2+} excretion	Elevated
Urinary stone composition	Calcium oxalate

Based on the laboratory findings, Carl was diagnosed with primary hyperparathyroidism and scheduled for exploratory neck surgery. While awaiting surgery, he was instructed to discontinue all Ca^{2+} and vitamin supplementation and to drink at least 3 L water each day. At surgery, a single parathyroid adenoma was identified and removed. Carl recovered well; his serum Ca^{2+}, phosphate, and parathyroid hormone (PTH) levels returned to normal, and he had no recurrences of urinary stones.

Questions

1. What are the forms of Ca^{2+} in serum? Which forms are biologically active?

2. What are the physiologic actions of parathyroid hormone (PTH) on bone, kidney, and intestine?

3. Carl's physician made a diagnosis of primary hyperparathyroidism on the basis of Carl's serum Ca^{2+}, phosphate, and PTH levels. How were these values consistent with primary hyperparathyroidism?

4. What was the significance of Carl's elevated alkaline phosphatase level?

5. In making the correct diagnosis, it was important to know that Carl's serum albumin level was normal. Why?

6. Why was Carl's urinary Ca^{2+} excretion elevated (hypercalciuria)?

7. What was the relationship between Carl's recent history of dietary Ca^{2+} supplementation and his hypercalciuria?

ANSWERS ON NEXT PAGE

Answers and Explanations

1. The normal value for total serum Ca^{2+} concentration is 10 mg/dL. This total Ca^{2+} has three components: (i) Ca^{2+} that is bound to albumin (40%), (ii) Ca^{2+} that is complexed to anions (e.g., phosphate, citrate) (10%), and (iii) free, ionized Ca^{2+} (50%). Free, **ionized Ca^{2+}** is the only form that is biologically active.

2. The actions of **parathyroid hormone (PTH)** on bone, kidney, and intestine are coordinated to increase the serum ionized Ca^{2+} concentration and decrease the serum phosphate concentration.

   In **bone,** PTH works synergistically with 1,25-dihydroxycholecalciferol to stimulate **osteoclasts** and increase **bone resorption.** As a result, both Ca^{2+} and phosphate are released from mineralized bone into the extracellular fluid. By itself, this effect on bone would not increase the serum ionized Ca^{2+} concentration because the phosphate that is released from bone complexes with Ca^{2+}.

   In the **kidney,** PTH has two actions, both of which are mediated by the activation of **adenylyl cyclase** and production of **cyclic adenosine monophosphate (cyclic AMP).** (i) In the early proximal tubule, PTH inhibits the **Na^+-phosphate cotransporter** that is responsible for phosphate reabsorption, thus causing an increase in urinary phosphate excretion. This **phosphaturic** effect of PTH is particularly important because the phosphate that was resorbed from bone is then excreted in the urine, thus allowing the serum ionized Ca^{2+} to increase. (ii) PTH stimulates Ca^{2+} reabsorption in the distal tubule.

   In the **intestine,** PTH acts indirectly to increase Ca^{2+} absorption by stimulating renal synthesis of **1,25-dihydroxycholecalciferol,** the active form of vitamin D.

3. The diagnosis of **primary hyperparathyroidism** was consistent with Carl's serum Ca^{2+}, phosphate, and PTH levels. He was hypercalcemic (his serum Ca^{2+} was elevated at 11.5 mg/dL) and **hypophosphatemic** (his serum phosphate was decreased at 2 mg/dL). In addition, he had an elevated circulating level of PTH. The parathyroid adenoma secreted excessive amounts of PTH that had all of the expected actions: increased bone resorption, decreased renal phosphate reabsorption, increased renal Ca^{2+} reabsorption, and increased intestinal Ca^{2+} absorption (through 1,25-dihydroxycholecalciferol). Thus, Carl's **hypercalcemia** resulted from increased bone resorption, increased renal Ca^{2+} reabsorption, and increased intestinal Ca^{2+} absorption. His hypophosphatemia resulted from decreased renal phosphate reabsorption **(phosphaturia)**.

   Primary hyperparathyroidism is sometimes characterized as **"stones, bones, and groans":** "stones" from hypercalciuria (discussed later), "bones" from the increased bone resorption, and "groans" from the constipation caused by hypercalcemia.

   You may wonder why Carl's hypercalcemia didn't inhibit PTH secretion. PTH secretion by normal parathyroid tissue *is* inhibited by hypercalcemia. However, PTH secretion by the adenoma is autonomous and, therefore, is not under negative feedback regulation. Thus, the adenoma continued to secrete PTH unabated, even in the face of hypercalcemia.

4. The major sources of alkaline phosphatase are liver and bone. Increased levels of **alkaline phosphatase** in bone are associated with increased **osteoblastic** activity and high bone turnover (e.g., primary hyperparathyroidism).

5. In considering the etiology of Carl's elevated serum Ca^{2+} concentration, it was important to know that his serum albumin level was normal. From our previous discussion, recall that the total Ca^{2+} concentration is the sum of protein-bound Ca^{2+} (40%), complexed Ca^{2+} (10%), and ionized Ca^{2+} (50%). Although *ionized* Ca^{2+} is the only form that is biologically active, *total* serum Ca^{2+} is more commonly measured. Carl's *total* Ca^{2+} was elevated (11.5 mg/dL). We need to know whether this increase in total Ca^{2+} was simply the result of an increase in serum albumin concentration or whether it was the result of an abnormality in Ca^{2+} homeostasis. Carl's serum albumin level was normal, suggesting that the increase in total Ca^{2+} concentration was caused by an increase in ionized, biologically active Ca^{2+}.

6. Carl's increased urinary Ca^{2+} excretion **(hypercalciuria)** led to the formation of painful urinary calcium oxalate stones. Inevitably, students ask why, if PTH increases renal Ca^{2+} reabsorption, does primary hyperparathyroidism cause increased urinary Ca^{2+} excretion? Shouldn't Ca^{2+} excretion be decreased? It is true that a major action of PTH is to increase Ca^{2+} reabsorption in the distal tubule, which contributes to the development of hypercalcemia. However, as the serum Ca^{2+} concentration increases, the filtered load of Ca^{2+} also increases. Thus, despite increased Ca^{2+} reabsorption, the filtered load of Ca^{2+} eventually overwhelms the reabsorptive capacity of the kidneys. Thus, in primary hyperparathyroidism, both the reabsorption *and* excretion of Ca^{2+} are increased.

7. Carl's primary hyperparathyroidism may have been present (although silent) for several years. Carl could be asymptomatic because, as his serum Ca^{2+} level gradually increased, his filtered load of Ca^{2+} also increased and the excess Ca^{2+} was excreted in the urine. By dumping Ca^{2+} in the urine, his serum was "protected" from dangerous increases in Ca^{2+} concentration. However, when Carl took Ca^{2+} and vitamin D supplements, the Ca^{2+} load to his kidneys sharply increased. The final "precipitating" event was dehydration on the tennis courts. Dehydration stimulated ADH secretion, and Carl's urine became concentrated. Carl's symptoms were caused by an increase in the urinary Ca^{2+} concentration and the precipitation of calcium oxalate stones.

Key topics

Adenylyl cyclase
Alkaline phosphatase
Bone resorption
Cyclic adenosine monophosphate (cyclic AMP)
1,25-dihydroxycholecalciferol
Hypercalcemia
Hypercalciuria
Hypophosphatemic
Na^{+}-phosphate cotransporter
Osteoblastic
Osteoclasts
Parathyroid hormone
Phosphaturia
Primary hyperparathyroidism

CASE 58

Humoral Hypercalcemia of Malignancy

Sam Kessler is a 69-year-old retired businessman. He and his wife had been looking forward to spending more time with their children and grandchildren. Unfortunately, 3 years ago, Mr. Kessler was diagnosed with lung cancer. Despite surgery, radiation therapy, and chemotherapy, his cancer returned. Mr. Kessler told his physicians that he did not want further treatment and preferred to spend his remaining time at home with his family, as pain free as possible. In the past week, Mr. Kessler became very lethargic and had both polyuria (increased urine production) and polydipsia (increased water drinking). He was admitted to the hospital, where laboratory tests were performed (Table 6–9).

table 6–9 Mr. Kessler's Laboratory Values

Serum Ca^{2+}	15.5 mg/dL (normal, 10 mg/dL)
Serum phosphate	1.8 mg/dL (normal, 3.5 mg/dL)
Serum albumin	4.1 g/dL (normal, 3.5–5.5 g/dL)
Serum PTH	4 pg/mL (normal, 10–65 pg/mL)
Serum alkaline phosphatase	Very elevated

PTH, parathyroid hormone.

During a test involving 4 hours of water deprivation, Mr. Kessler's serum osmolarity was 305 mOsm/L (normal, 290 mOsm/L) and his urine osmolarity was 90 mOsm/L.

The physicians concluded that Mr. Kessler had humoral hypercalcemia of malignancy because his lung cancer cells were secreting parathyroid hormone (PTH)-related peptide (PTH-rp). He was treated with a saline infusion and furosemide (a loop diuretic), which caused his serum Ca^{2+} to decrease to 10.8 mg/dL. He returned home with a prescription for pamidronate, an inhibitor of bone resorption that was expected to keep his serum Ca^{2+} in the normal range.

Questions

1. PTH-rp, secreted by certain malignant tumors, is chemically homologous with PTH that is secreted by the parathyroid glands. PTH-rp has all of the biologic actions of PTH on bone and kidney. Given this information, why was Mr. Kessler hypercalcemic (increased serum Ca^{2+}) and hypophosphatemic (decreased serum phosphate)? Why was his alkaline phosphatase level elevated?

2. What was the significance of Mr. Kessler's normal serum albumin level?

3. Why was Mr. Kessler's serum PTH level decreased?

4. After the 4-hour water deprivation test, Mr. Kessler's serum osmolarity was 305 mOsm/L (normal, 290 mOsm/L) and his urine osmolarity was 90 mOsm/L. Administration of an ADH analogue (dDAVP) by nasal spray did not alter his serum or urine osmolarity. The physician concluded that Mr. Kessler had nephrogenic diabetes insipidus. Why? What might be the cause of this condition?

5. Why did Mr. Kessler have polyuria and polydipsia?

6. How did treatment with saline and furosemide decrease his serum Ca^{2+} concentration?

7. How was pamidronate expected to keep Mr. Kessler's serum Ca^{2+} in the normal range?

ANSWERS ON NEXT PAGE

Answers and Explanations

1. **Parathyroid hormone-related peptide (PTH-rp)** is a peptide that is secreted by certain malignant tumor cells (e.g., lung, breast). It is homologous with, and has all of the biologic actions of, **PTH** that is secreted by the parathyroid glands. Therefore, if we know the biologic actions of PTH on bone and kidney, we also know the biologic actions of PTH-rp that caused Mr. Kessler's **hypercalcemia** and **hypophosphatemia.** These actions are as follows: (i) PTH and PTH-rp stimulate **osteoclasts** and increase **bone resorption,** bringing Ca^{2+} and phosphate from the bone into the extracellular fluid; (ii) PTH and PTH-rp inhibit **Na^+-phosphate cotransport** and renal phosphate reabsorption and cause **phosphaturia;** (iii) PTH and PTH-rp stimulate renal Ca^{2+} reabsorption. Together, the effects of PTH-rp on bone and kidney increase the serum Ca^{2+} concentration **(humoral hypercalcemia of malignancy)** and decrease the serum phosphate concentration (hypophosphatemia). Increased **alkaline phosphatase** activity is associated with increased osteoblastic activity in states of high bone turnover.

2. Although Mr. Kessler's serum albumin was normal, his total serum Ca^{2+} was elevated. Therefore, the increase in his total serum Ca^{2+} was not caused by an increase in protein-bound Ca^{2+}, but rather by an increase in serum ionized Ca^{2+}.

3. Mr. Kessler's circulating level of PTH was decreased secondary to his hypercalcemia. PTH secretion by the parathyroid glands is feedback regulated by the serum Ca^{2+} concentration. When serum Ca^{2+} is decreased, PTH secretion is stimulated; when serum Ca^{2+} is increased (in this case, by PTH-rp), PTH secretion is inhibited.

   This question points out a critical difference between hypercalcemia caused by primary hyperparathyroidism (see Case 57) and hypercalcemia of malignancy. In primary hyperparathyroidism, by definition, PTH levels are increased. In humoral hypercalcemia of malignancy, PTH levels are decreased by feedback inhibition on the parathyroid gland.

4. After a **water deprivation test,** Mr. Kessler's **serum osmolarity** was elevated at 305 mOsm/L (normal, 290 mOsm/L). In the face of this elevated serum osmolarity, his **urine osmolarity** was very dilute (hyposmotic) at 90 mOsm/L. Something is wrong with this picture! Shouldn't Mr. Kessler be making concentrated (hyperosmotic) urine when his serum osmolarity is elevated? This abnormal pattern suggests that Mr. Kessler had **diabetes insipidus** caused by ADH deficiency **(central diabetes insipidus)** or by ADH resistance of the collecting ducts (nephrogenic diabetes insipidus).

   Results of the test with **dDAVP** nasal spray (an ADH analogue) confirmed that Mr. Kessler had **nephrogenic diabetes insipidus**—even exogenous ADH couldn't cause his urine to become concentrated. His nephrogenic diabetes insipidus (or ADH resistance) was caused by hypercalcemia. In this condition, Ca^{2+} deposition in the inner medulla of the kidney inhibits ADH-dependent adenylyl cyclase and prevents the ADH action to increase water permeability of the collecting ducts. Thus, even in the presence of exogenous ADH, the urine cannot be concentrated.

5. Mr. Kessler had polyuria (increased urine production) and polydipsia (increased water drinking) secondary to nephrogenic diabetes insipidus. **Polyuria** occurred because his collecting ducts were resistant to the action of ADH and therefore were impermeable to water. Water that was not reabsorbed by the collecting ducts was excreted in the urine. **Polydipsia** occurred because increased urinary water excretion made his body fluids (including the serum) more concentrated. Increased serum osmolarity is a potent stimulus for thirst and drinking behavior through osmoreceptors in the hypothalamus.

6. In the hospital, Mr. Kessler was given saline and furosemide to decrease his serum Ca^{2+} concentration. **Furosemide** inhibits the **Na^+-K^+-$2Cl^-$ cotransporter** in the thick ascending limb and therefore inhibits renal Na^+ reabsorption. Furosemide also inhibits Ca^{2+} reabsorption in the thick ascending limb, which is explained as follows. The Na^+-K^+-$2Cl^-$ cotransporter normally generates a **lumen-positive potential difference** in the thick ascending limb that drives Ca^{2+} reabsorption from the

lumen to the blood through a paracellular route. (The positive charge in the lumen repels the positive charges on Ca^{2+}.) By inhibiting the Na^+-K^+-$2Cl^-$ cotransporter, furosemide eliminates the lumen-positive potential, thereby inhibiting paracellular Ca^{2+} reabsorption. Thus, a portion of the filtered Ca^{2+} that would otherwise have been reabsorbed was excreted in the urine, decreasing Mr. Kessler's serum Ca^{2+} concentration. Saline was administered with the furosemide to prevent extracellular volume contraction.

7. **Pamidronate** is a **bisphosphonate** compound that inhibits osteoclastic bone resorption. This inhibitor of bone resorption was given to offset the osteoclast-stimulating action of PTH-rp.

Key topics

Alkaline phosphatase
Bisphosphonate
Bone resorption
Central diabetes insipidus
dDAVP
Furosemide
Humoral hypercalcemia of malignancy
Hypercalcemia
Hypophosphatemia
Na^+-K^+-$2Cl^-$ cotransporter
Na^+-phosphate cotransport
Nephrogenic diabetes insipidus
Osteoclasts
Pamidronate
Parathyroid hormone-related peptide (PTH-rp)
Parathyroid hormone
Phosphaturia
Polydipsia
Polyuria
Serum osmolarity
Urine osmolarity
Water deprivation test

CASE 59

Hyperglycemia: Type I Diabetes Mellitus

David Mandel was diagnosed with type I (insulin-dependent) diabetes mellitus when he was 12 years old (see Cases 31 and 36). At the time of his diagnosis, David was in middle school. He was an excellent student and had many friends. At a sleepover party, the unimaginable happened: David wet his sleeping bag! He might not have told his parents except that he was worried about other symptoms he was having. He was constantly thirsty and was urinating every 30 to 40 min. Furthermore, despite a voracious appetite, he seemed to be losing weight; all of his pants had become loose in the waist. David's parents panicked because they knew that these were classic symptoms of diabetes mellitus. They took David to see his pediatrician immediately. The pediatrician performed a physical examination and ordered laboratory tests (Table 6–10).

table 6–10 David's Physical Examination and Laboratory Results

Height	5 ft, 3 in
Weight	100 lb (decreased 5 lb from his annual checkup 2 months earlier)
Blood pressure	90/55 (lying down), 75/45 (standing up)
Fasting plasma glucose	320 mg/dL (normal, 70–110 mg/dL)
Plasma ketones	1+ (normal, none)
Urinary glucose	4+ (normal, none)
Urinary ketones	2+ (normal, none)

All of the findings were consistent with a diagnosis of type I (insulin-dependent) diabetes mellitus. David immediately started taking injectable insulin and learned how to monitor his blood glucose level with a fingerstick. He excelled in high school and won a scholarship to the state university, where he is currently a premedical student and is planning a career in pediatric endocrinology. He has periodic checkups with his endocrinologist, who closely monitors his renal function.

Questions

1. How did insulin deficiency lead to an increase in David's blood glucose concentration?

2. How did insulin deficiency lead to the finding of ketones in David's blood and urine?

3. Why did David have glucose in his urine (glucosuria)?

4. Why did David have increased urine production (polyuria)? Why was he drinking so much (polydipsia)?

5. Why was David's blood pressure lower than normal? Why did it decrease further when he stood up?

6. David takes his insulin parenterally (by subcutaneous injection). Why can't he take insulin orally?

7. The endocrinologist closely monitors David's renal function. What is the major nephrologic complication of type I diabetes mellitus?

ANSWERS ON NEXT PAGE

Answers and Explanations

1. David has **type I diabetes mellitus**—his pancreatic β cells do not make sufficient insulin. Two consequences of **insulin deficiency** made David **hyperglycemic:** decreased uptake of glucose by cells and increased gluconeogenesis. These consequences are best understood by reviewing the normal actions of insulin and then considering what happens with insulin deficiency.

(i) One important action of insulin is to direct the insertion of a facilitated transporter for glucose (GLUT4) into cell membranes of muscle and adipose tissue. This transporter causes the uptake of glucose from the blood into the cells. When insulin is deficient, **GLUT4 transporters** are not inserted into cell membranes, glucose is not transported into the cells, and the blood glucose concentration increases.

(ii) Insulin increases the storage of nutrients, including carbohydrates, proteins, and fats. Thus, insulin promotes glycogen formation (and inhibits gluconeogenesis), protein synthesis, and fat deposition (and inhibits lipolysis). When insulin is deficient, both protein catabolism (which generates amino acids) and lipolysis (which generates glycerol and fatty acids) are increased. Thus, insulin deficiency provides more amino acid and glycerol substrates for glucose synthesis (i.e., **increased gluconeogenesis;** Fig. 6–8).

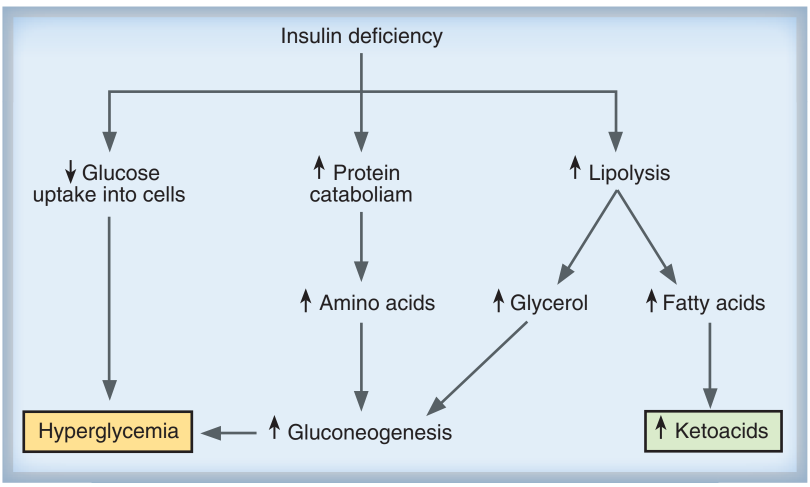

FIGURE 6–8. Metabolic effects of insulin deficiency.

2. David's blood and urine contained ketones because insulin deficiency increased the blood levels of fatty acids, which are the biosynthetic precursors of ketoacids. Insulin deficiency promotes catabolism of all nutrients, including fats (Fig. 6–8). Increased lipolysis leads to increased blood levels of fatty acids that are converted in the liver to **ketoacids,** β-hydroxybutyric acid, and acetoacetic acid. As the concentration of ketoacids increases in the blood, they are filtered across the glomerular capillaries and appear in the urine.

3. David had **glucosuria** (glucose in his urine) because he was hyperglycemic. His blood glucose concentration became so high that the amount of glucose filtered across the glomerular capillaries exceeded the reabsorptive capacity of the renal proximal tubule. Any glucose that was not reabsorbed was excreted in the urine. (For a more complete discussion of renal glucose reabsorption, see Case 31.)

4. David had **polyuria** (increased urine production) because his urine contained glucose. As discussed in the previous question, the filtered load of glucose was greater than the reabsorptive capacity of the proximal tubule and, as a result, glucose was excreted in the urine. The unreabsorbed glucose acted as an **osmotic diuretic,** causing a "back-flux" of Na^+ and water into the proximal tubule. Thus, along with glucose, increased quantities of Na^+ and water were excreted.

David had **polydipsia** because the hyperglycemia caused an increase in his serum osmolarity, which stimulated osmoreceptors in the anterior hypothalamus that increase thirst and promote drinking behavior.

5. David's **arterial pressure** was decreased secondary to the **osmotic diuresis** that was caused by glucose in his urine. Increased excretion of Na^+ and water decreased his extracellular fluid volume and his blood volume. Decreased blood volume led to a decrease in venous return to the heart, decreased cardiac output (by the Frank–Starling mechanism), and decreased arterial pressure. David's arterial pressure decreased further when he stood up **(orthostatic hypotension)** because, as blood pooled in the veins of the legs, venous return and cardiac output were compromised further.

6. Insulin is a protein; therefore, it must be administered parenterally (i.e., by routes other than the gastrointestinal tract). If given orally, it would be digested by intestinal peptidases to amino acids and di- and tripeptides. Once digested, it would no longer be insulin! Subcutaneous injection of insulin bypasses these degradative steps in the gastrointestinal tract.

7. A serious complication of type I diabetes mellitus is **diabetic nephropathy.** This condition can progress to end-stage renal failure that requires dialysis or renal transplantation. Therefore, David's renal function must be monitored for the rest of his life.

   The earliest phase of diabetic nephropathy is characterized by an *increase* in the glomerular filtration rate (GFR) that roughly correlates with the adequacy of glycemic control. In this **hyperfiltration** phase, the better the control of blood glucose concentration with insulin injections, the smaller the increase in GFR. In the next phase of diabetic nephropathy (and a consequence of hyperfiltration), histologic changes occur in the glomerular capillary barrier. The mesangial cells expand, and the basement membrane thickens. Eventually, these changes lead to diffuse glomerular scarring. During this phase, which occurs 5 to 15 years from the onset of type I diabetes mellitus, progressive glomerular changes occur; although the GFR remains elevated and no frank protein is found in the urine, **microalbuminuria** can be detected. Finally, in the later phases of diabetic nephropathy, there is gross proteinuria, decreased GFR, hypertension, and renal failure.

   David will be monitored closely for the presence of the microalbuminuria that signals the beginning of glomerular damage. If microalbuminuria is detected, David will be treated with an **angiotensin-converting enzyme (ACE) inhibitor,** which selectively dilates renal efferent arterioles and reduces glomerular filtration (offsetting the damaging hyperfiltration).

Key topics

Angiotensin-converting enzyme (ACE) inhibitor
Type I diabetes mellitus
Diabetic nephropathy
Gluconeogenesis
Glucosuria
GLUT4 transporters
Hyperfiltration
Insulin deficiency
Ketoacids
Microalbuminuria
Orthostatic hypotension
Osmotic diuresis
Polydipsia
Polyuria

CASE 60

Primary Amenorrhea: Androgen Insensitivity Syndrome

Marcy Maloney is a 17-year-old junior in high school. She seemed to go through **puberty** at the same time as her peers; she had a growth spurt and her breasts developed. However, she has never had a menstrual period. Her mother's menstrual cycles started at age 13, and Marcy's 12-year-old sister recently began to menstruate. Marcy's mother made an appointment for a thorough gynecologic examination.

Marcy's history was unremarkable except for the absence of menstrual cycles **(primary amenorrhea).** On physical examination, Marcy appeared to be a healthy young woman. Her breasts and external genitalia appeared normal. However, she had a short, blind-ending vagina and no visible cervix. On bimanual examination, she had no palpable uterus or ovaries. She had no axillary or pubic hair, and very little hair on her arms and legs.

Marcy had a normal serum cortisol level, normal results on thyroid function tests, and a normal serum prolactin level. A pregnancy test was negative. However, her serum testosterone level was very elevated (even higher than the levels found in normal men).

Because of the findings on physical examination and the elevated serum testosterone level, Marcy's physician ordered a genotype, which was 46, XY. During exploratory surgery, the surgeons found intraabdominal testes, which were removed. Marcy was given estrogen replacement therapy.

The physicians explained to Marcy and her parents that she has androgen insensitivity syndrome (formerly called **testicular feminizing syndrome**). She has a male genotype (XY) and male gonads (testes), but a female phenotype. Marcy was counseled that, because she has no ovaries or uterus, she would never be able to bear children. However, she would continue to look like a woman. The physicians also explained that she could elect to undergo reconstructive surgery on her vagina to permit normal sexual intercourse.

Questions

1. How does a fetus with an XY (male) genotype normally develop into the male phenotype? How does a fetus with an XX (female) genotype normally develop into the female phenotype?

2. Marcy looked like a female, but genetically and gonadally, she was a male. Her disorder (testicular feminizing syndrome) is caused by a deficiency or lack of androgen receptors on target tissues. Which of the following characteristics are explained by the lack of androgen receptors: presence of female external genitalia, absence of a cervix and uterus, absence of body hair, and presence of testes?

3. Why was Marcy's serum testosterone level even higher than that found in normal men?

4. Why did Marcy develop breasts?

5. Marcy's testes were removed because a malignancy can develop in them. Why did she require estrogen replacement therapy after the surgery?

ANSWERS ON NEXT PAGE

Answers and Explanations

1. In the first 5 weeks of gestational life, the gonads are **bipotential** (can develop into either ovaries or testes). In the sixth gestational week, if the fetus is male, the testes begin to develop. In the ninth week, if the fetus is female, the ovaries begin to develop. Thus, genetic sex (either XY or XX) determines gonadal sex, which ultimately determines phenotypic sex (Fig. 6–9).

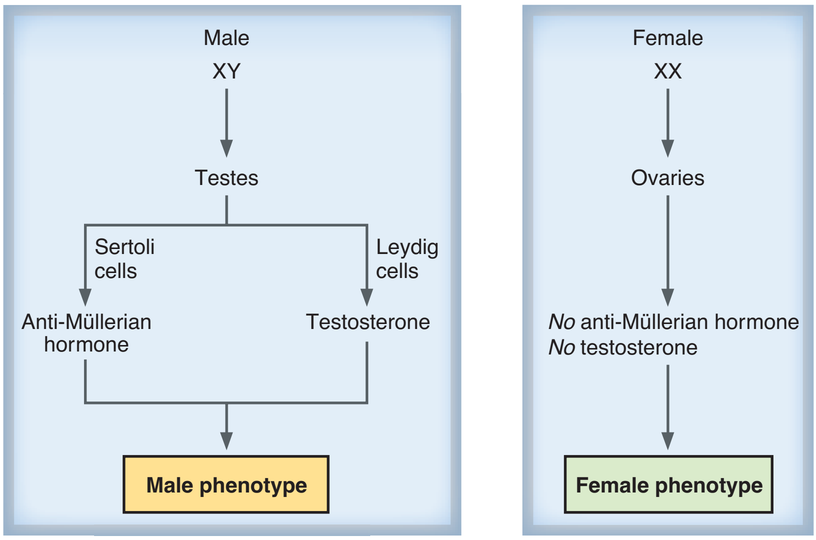

FIGURE 6–9. Sexual differentiation in males and females. (Reprinted, with permission, from Costanzo LS. *BRS Physiology*. 5th ed. Baltimore: Lippincott Williams & Wilkins; 2011:2650.)

A male fetus with an **XY genotype** develops into a gonadal and phenotypic male as follows. During gestational week 6, the SRY gene on the Y chromosome causes differentiation of the bipotential gonads into testes. These fetal testes produce testosterone and anti-Müllerian hormone, both of which are required for the normal development of the male phenotype. **Testosterone,** which is produced by the fetal Leydig cells, stimulates differentiation and growth of the Wolffian ducts. These ducts give rise to the internal male reproductive tract (epididymis, vas deferens, seminal vesicles, and ejaculatory ducts). At the same time, **anti-Müllerian hormone,** which is produced by the fetal Sertoli cells, causes atrophy of the Müllerian ducts that otherwise would develop into the internal female genital tract. Finally, in gestational week 9, there is differentiation and growth of the male external genitalia (penis, scrotum); this process depends on the conversion of testosterone to **dihydrotestosterone** in these target tissues.

A female fetus with an **XX genotype** develops into a gonadal and phenotypic female as follows. At gestational week 9, the bipotential gonads develop into ovaries (because they did not develop into testes earlier). Because there are no testes, there is no secretion of testosterone or anti-Müllerian hormone. Thus, in females, there is *no* testosterone to promote differentiation and growth of the Wolffian ducts into a male internal genital tract, and there is *no* anti-Müllerian hormone to suppress differentiation of the Müllerian ducts into the female internal genital tract. Consequently, the **Müllerian ducts** develop into the internal female genital tract (fallopian tubes, uterus, cervix, and upper one-third of the vagina). In addition, there is differentiation and growth of the external female genitalia (clitoris, labia majora, labia minora, and lower two-thirds of the vagina).

2. **Androgen insensitivity syndrome** is caused by **lack of androgen receptors** and a resultant androgen resistance of target tissues. In utero, Marcy's testes, which were normal, secreted both testosterone and anti-Müllerian hormone. Anti-Müllerian hormone suppressed the differentiation of the

Müllerian ducts into the internal female genital tract. As a result, Marcy has no fallopian tubes, uterus, or upper vagina. Testosterone (which should have caused differentiation of the Wolffian ducts into the male internal genital tract) did not because the target tissues had no androgen receptors. In addition, dihydrotestosterone did not cause differentiation of the external male genitalia because those tissues also lacked androgen receptors. Therefore, by default, Marcy developed female external genitalia.

Only two of the characteristics listed are explained by the lack of androgen receptors: the presence of female external genitalia (which differentiated because the male genitalia did not) and the absence of body hair (one of the biologic actions of androgens in adults). The absence of a cervix and a uterus was caused by anti-Müllerian hormone secreted from Marcy's fetal testes (which suppressed differentiation of the Müllerian ducts). The presence of testes was determined by her genetic sex (XY).

3. Marcy's serum testosterone level was even higher than that found in men because feedback regulation of testosterone secretion involves testosterone receptors in the hypothalamus and anterior pituitary (Fig. 6–10). Although her testes secreted large amounts of testosterone, the testosterone could not feedback regulate its own secretion because her hypothalamus and anterior pituitary had no testosterone receptors.

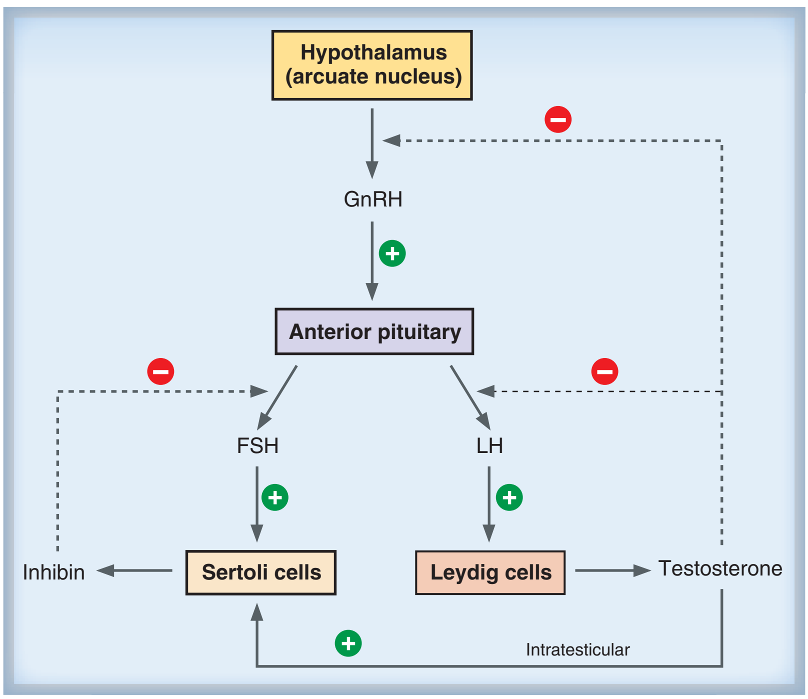

FIGURE 6–10. Control of male reproductive hormones. FSH, follicle-stimulating hormone; GnRH, gonadotropin-releasing hormone; LH, luteinizing hormone. (Reprinted, with permission, from Costanzo LS. *BRS Physiology*. 5th ed. Baltimore: Lippincott Williams & Wilkins; 2011:252.)

4. Marcy developed **breasts** because the testes and adipose tissue contain the **aromatase** enzyme that converts testosterone to **estradiol.** Because Marcy's testosterone levels were so high, sufficient estradiol could be synthesized to cause breast development and female fat distribution. (Remember, the high levels of testosterone *do not* produce masculine characteristics because Marcy lacks androgen receptors.)

5. After the testes were removed, Marcy required **estrogen replacement therapy** to maintain her breasts and female fat distribution. The testes had served as the source of testosterone, which was the precursor for estradiol synthesis.

Key topics

Androgen insensitivity syndrome
Androgen receptors
Anti-Müllerian hormone
Aromatase
Dihydrotestosterone
Estradiol
Primary amenorrhea
Sexual differentiation
Testicular feminizing syndrome
Testosterone

CASE 61

Male Hypogonadism: Kallmann's Syndrome

George Acevedo is the delivery man for a family-owned pharmacy and delicatessen. Although he is 22 years old, he looks more like a 12-year-old. He is still growing at the rate of approximately 0.5 inch per year, his arms appear very long for his body, and he has a prepubertal fat distribution. He has little body or facial hair, does not have erections, and is not sexually active. He has always had a very poor sense of smell. George's parents were concerned and scheduled a checkup with his family physician.

On physical examination, George had a very long arm span, sparse body and facial hair, and a small penis and testes. The results of laboratory tests are summarized in Table 6–11.

table 6–11 George's Laboratory Values

Serum testosterone	120 ng/dL	(normal adult males, 300–1,000 ng/dL)
Serum luteinizing hormone	1.5 mU/mL	(normal adults, 3–18 mU/mL)

A gonadotropin-releasing hormone (GnRH) stimulation test caused a significant increase in George's serum luteinizing hormone (LH) and **testosterone** levels.

George was diagnosed with hypogonadotropic hypogonadism. His physician prescribed pulsatile GnRH treatment, which was delivered through a wearable infusion pump. On a follow-up visit 6 months after the start of treatment, George's height had stabilized, his muscle mass had increased, his facial hair had started to grow, and he looked older. His penis had enlarged, and he was having erections and nocturnal emissions.

Questions

1. George had hypogonadotropic hypogonadism of hypothalamic origin (Kallmann's syndrome). His hypothalamus secreted inadequate amounts of GnRH. How did decreased GnRH secretion cause decreased levels of LH and testosterone?

2. Explain George's prepubertal appearance. Why were his arms so long? Why was he still growing?

3. Decreased testosterone levels can result from a defect in the testes, the anterior pituitary, or the hypothalamus. How did George's physician know that George's low serum testosterone levels were caused by a hypothalamic problem (rather than a primary problem in the testes or in the anterior pituitary)?

4. Why did George have a poor sense of smell?

5. George was treated with pulsatile (rather than continuous or long-acting) GnRH. Why was pulsatile delivery important?

Answers and Explanations

1. **Kallmann's syndrome (hypogonadotropic hypogonadism)** is caused by inadequate secretion of GnRH. In Kallmann's syndrome, which can be hereditary, the hypothalamus does not secrete **gonadotropin-releasing hormone (GnRH),** although other hypothalamic functions are normal. In one hereditary form of the disorder, there is a defect in the **KAL peptide** that plays a role in normal neuronal migration; the neurons that secrete GnRH apparently do not migrate to their proper site in the hypothalamus and, therefore, are nonfunctional.

   George had a deficiency of GnRH that caused decreased secretion of the gonadotropins **luteinizing hormone (LH)** and **follicle-stimulating hormone (FSH)** from the anterior pituitary. LH is responsible for testosterone synthesis in the Leydig cells of the testes. FSH is responsible for spermatogenesis and Sertoli cell functions. Thus, in the absence of GnRH, there was decreased LH and FSH secretion, decreased testosterone secretion, and decreased sperm production.

2. George had a childish appearance (little muscle mass, prepubertal fat distribution, lack of facial and body hair, small penis). Normally, a large increase in testosterone secretion by the testes occurs at puberty and causes the pubertal growth spurt, deepening of the voice, growth of body hair, growth of the penis, and development of libido. Because of his testosterone deficiency, George did not have these **secondary male sex characteristics.** His arms were very long because testosterone is required for the closure of the epiphyseal growth plates (which stops the growth of the long bones). His arms continued to grow because his epiphyseal growth plates had not closed. He continued to grow in height for the same reason (failure of the epiphyseal plates to close, causing sustained growth of the long bones).

3. Because of the results of the **GnRH stimulation test,** George's physician concluded that George's decreased testosterone levels were caused by a problem with *hypothalamic* secretion of GnRH. In the test, administration of GnRH caused an increase in LH and testosterone secretion. Thus, George's anterior pituitary responded normally to GnRH (it secreted LH), and his testes responded normally to LH (they secreted testosterone). These responses implied that the defect resided in the hypothalamus, not in the anterior pituitary or the testes (see Fig. 6–10).

4. Kallmann's syndrome is responsible for George's poor sense of smell. Normally, GnRH-secreting neurons migrate from primordial olfactory tissue into their correct location in the hypothalamus. In Kallmann's syndrome, this migration does not occur. The defect results in a decreased sense of smell (hyposmia) or the complete absence of the sense of smell **(anosmia).**

5. George was treated with **pulsatile GnRH** to initiate puberty. It was expected that continued treatment with pulsatile GnRH would maintain gonadotropin secretion that would in turn maintain testosterone secretion and sperm production. Continuous (or long-acting) GnRH would *not* have been an effective treatment. In normal males (and females), the onset of *pulsatile* GnRH secretion from the hypothalamus initiates puberty by up-regulating GnRH receptors in the anterior pituitary, thus "sensitizing" the reproductive axis. When GnRH is given as a continuous infusion, the GnRH receptors in the anterior pituitary are actually down-regulated, which desensitizes the reproductive axis.

Key topics

Anosmia
Follicle-stimulating hormone (FSH)
GnRH stimulation test
Gonadotropin-releasing hormone (GnRH)
Hypogonadism
KAL peptide
Kallmann's syndrome
Luteinizing hormone (LH)
Secondary male sex characteristics
Puberty
Pulsatile GnRH
Testosterone

CASE 62

Male Pseudohermaphroditism: 5α-Reductase Deficiency

Fourteen years ago, Wally and Wanda Garvey, who live in rural North Carolina, had their first child. The baby was delivered by a general practitioner, who said the baby was a girl. They named her Scarlett, from Wanda's favorite movie. From the beginning, Wally and Wanda felt something was wrong with Scarlett. She did not look like a normal baby girl (she had what looked like a small penis), but it never would have occurred to Wally and Wanda to question a doctor's judgment.

By the time Scarlett was 13 years old, all of her girlfriends had developed breasts and were having periods. Scarlett was experiencing none of these changes and, alarmingly, her voice was deepening and she was becoming very muscular, like the boys. Her small penis (which she had kept secret) was growing larger. She and her girlfriends gossiped about the boys having wet dreams, but to Scarlett's embarrassment, *she* was having something like that. She was starting to feel like a boy, rather than a girl. Wally and Wanda noticed some of these changes, and they were very concerned. The doctor finally admitted that this case was beyond his expertise, and he referred the family to a medical school in another part of the state.

At the medical school, Scarlett was diagnosed with a form of male pseudohermaphroditism caused by a deficiency of 5α-reductase. On physical examination, she had no ovaries, no uterus, a blind vaginal pouch, a small prostate, a penis, descended testes, and hypospadias (urethral opening low on the underside of the penis). She had a male musculature, but no body hair, facial hair, or acne. Her genotype was confirmed as 46,XY, and blood work showed a high-normal level of testosterone and a low level of dihydrotestosterone. Tests on fibroblasts from genital skin showed an absence of 5α-reductase. The physician discussed treatment options, which would be different depending on whether Scarlett wanted to live the rest of her life as a woman or a man.

Questions

1. In males, some androgenic actions depend on testosterone and some depend on dihydrotestosterone. What is the physiologic basis for this difference?

2. Which male target tissues respond to testosterone, and which require dihydrotestosterone?

3. Scarlett had a form of pseudohermaphroditism caused by 5α-reductase deficiency. At birth, which of the following characteristics were (are) a result of the enzyme deficiency, and why? Of the characteristics that were not (are not) a result of the enzyme deficiency, what was (is) their cause?

   (i) 46,XY genotype
   (ii) Presence of testes
   (iii) Absence of uterus
   (iv) Blind-ending vagina
   (v) Small penis

4. At puberty, which of the following characteristics result from Scarlett's high-normal levels of testosterone? Which characteristics result from her inability to produce dihydrotestosterone? Which characteristics are due to neither?

(i) Growth of penis
(ii) Ejaculation
(iii) Deepening of voice
(iv) Lack of body and facial hair
(v) Lack of breast development

5. If Scarlett wishes to continue life as a woman, what is the appropriate treatment?

6. If Scarlett wishes to live the rest of her life as a man, what is the appropriate treatment?

Answers and Explanations

1. The testes synthesize and secrete testosterone, which is converted, in *some* androgenic target tissues, to dihydrotestosterone by the action of the enzyme 5α-reductase. In target tissues that contain **5α-reductase,** dihydrotestosterone is synthesized and is responsible for androgenic activity. In those tissues, testosterone has little or no activity. Other androgenic target tissues do not contain 5α-reductase and do not synthesize dihydrotestosterone. In those tissues, testosterone is the active form.

2. Androgenic actions that utilize **dihydrotestosterone,** and thus *require* **5α-reductase,** include differentiation of the external male genitalia, male-pattern baldness, and growth of the prostate (Fig. 6–11). Androgenic actions that respond directly to **testosterone** and **do *not* require 5α-reductase** are differentiation of internal male genital tract (epididymis, vas deferens, seminal vesicles), muscle mass, pubertal growth spurt, growth of the penis, deepening of the voice, spermatogenesis, and libido.

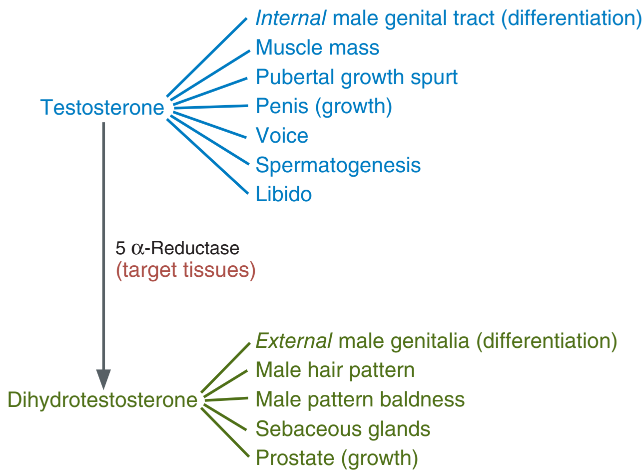

FIGURE 6–11. Androgenic actions mediated by testosterone and dihydrotestosterone.

3. It is helpful to organize your thoughts by considering the characteristics Scarlett did or did not have at birth. She is a genetic and gonadal male, who lacks the enzyme 5α-reductase (a form of **pseudohermaphroditism**). As a **genetic male** (46,XY), the presence of the Y chromosome determines that the bipotential gonads will develop into testes at gestational weeks 6 to 7. Scarlett's **testes are normal,** and thus prenatally, they synthesized both anti-Müllerian hormone and testosterone.

Anti-Müllerian hormone suppresses the development of the **Müllerian ducts** into the internal female genital tract, so Scarlett has no fallopian tubes, uterus, or upper one-third of the vagina. **Testosterone** causes differentiation of the **Wolffian ducts** into the internal male genital tract (epididymis, vas deferens, seminal vesicles), a process that does not require dihydrotestosterone and thus occurs in the absence of 5α-reductase. However, differentiation of the external male genitalia (e.g., penis and scrotum) requires dihydrotestosterone; thus, a **deficiency of 5α-reductase** meant that Scarlett's external genitalia were not normally developed.

Based on this information, Scarlett's characteristics at birth are explained as follows:

(i) The 46,XY genotype is not a result of the enzyme deficiency.
(ii) The presence of testes is determined by the Y chromosome and is not a result of the enzyme deficiency.
(iii) Scarlett does not have a uterus because the normal testes produced anti-Müllerian hormone, which suppressed the development of the Müllerian ducts into an internal female genital tract. Thus, the absence of a uterus is not due to the enzyme deficiency.

(iv) Scarlett has a blind-ending vagina for the same reason she does not have a uterus—the testes produced anti-Müllerian hormone, which suppressed the development of the internal female genital tract, including the upper one-third of the vagina.
(v) The small penis is the result of the enzyme deficiency, because differentiation of the male external male genitalia is mediated by dihydrotestosterone.

4. Use the summary information from Answer 3 again to explain Scarlett's characteristics at puberty.

(i) The penis grew at puberty because of the high-normal circulating level of testosterone, which apparently is sufficient to activate the androgen receptors that mediate the growth of the external genitalia.
(ii) Both spermatogenesis and production of many components of the ejaculate are mediated by testosterone and do not require conversion to dihydrotestosterone.
(iii) Deepening of the voice is also mediated by testosterone and does not require conversion to dihydrotestosterone.
(iv) At puberty, despite acquiring many masculine characteristics, Scarlett did not develop body and facial hair. Specifically, the hair follicles require dihydrotestosterone.
(v) At puberty, Scarlett did not develop breasts because she did not have ovaries. In females, the ovaries are the source of the estrogen that is needed for breast development.

5. If Scarlett chooses to continue life as a woman, it will be necessary to remove her testes, which are producing the testosterone that is causing her to be selectively masculinized (growth of penis, deepening of voice, etc.). In addition, because she lacks ovaries, Scarlett has no endogenous source of the estrogen that is needed for breast development and female fat distribution; thus, she will receive treatment with supplemental estrogen. She may elect to have surgical correction of the introitus; however, even with the surgery, she will not be able to bear children because she lacks ovaries and an internal female genital tract.

6. If Scarlett chooses to live the rest of her life as a man, she will be treated with androgenic compounds that do not require 5α-reduction for activity. The supplemental androgens will complete the masculinization process, including the development of male body and facial hair, sebaceous gland activity, growth of the prostate, and in later life, male-pattern baldness.

Key topics

Anti-Müllerian hormone

Dihydrotestosterone

Müllerian ducts

Pseudohermaphroditism

5α-reductase

Testosterone

Wolffian ducts

Chapter 10
Endocrine System

The organs of the endocrine system produce hormones. A hormone is a messenger molecule, made in small quantities by endocrine cells/glands and released into the blood circulation to coordinate cellular activities in distant tissues. Hormone molecules elicit a response in the target cells by attaching to a receptor on the cell's plasma membrane (or inside the cell) that is specific for that molecule.

The hypothalamus is a region of the brain that controls the endocrine system and integrates the activities of the nervous and endocrine systems in 3 ways. (1) The hypothalamus produces and secretes regulatory hormones that control the secretion of 6 or 7 hormones from the endocrine cells in the anterior pituitary gland. In turn, the hormones released by the anterior pituitary, stimulate their target endocrine organs to produce and release hormones which go onto to influence the behaviour of the body cells which have receptors for these hormones. (2) The hypothalamus produces ADH and oxytocin which are transported to the posterior pituitary to be stored and released into the blood following appropriate stimuli. (3) The hypothalamus contains "autonomic centres" that exert neural control over endocrine cells of the medullae of the adrenal glands. When activated, the adrenal medullae release hormones into the bloodstream.

Many organs participate in the production of hormones and you should know (or know of) most of them. The hypothalamus and the anterior pituitary have already been mentioned. The thyroid gland produces thyroxine and calcitonin. The latter decreases the concentration of Ca ions in the blood. The four parathyroid glands produce parathyroid hormone (PTH) which increases the concentration of Ca ions in the blood. The adrenal glands produce many hormones. More than 24 corticosteroid hormones are produced from cholesterol by the adrenal cortex. These include "mineralocorticoids" (e.g. aldosterone), "glucocorticoids" (e.g. cortisol, corticosterone) and "gonadocorticoids" (e.g. estrodiol and the weak androgens androstenedione, dehydroepiandrosterone). The adrenal medullae produce epinephrine and norepinephrine. The pancreas contains regions of cells (called Islets of Langerhans) that produce insulin (the beta cells), and glucagon (the alpha cells). The testes produce testosterone and inhibin while the ovaries produce estrogens, inhibin and

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progesterone. The pineal gland produces melatonin. The kidneys produce erythropoietin, calcitriol ("vitamin D3") and the enzyme renin. The liver (not regarded as an endocrine organ) produces the prohormone angiotensinogen which is converted by renin and then by "angiotensin converting enzyme" to the hormone angiotensin II. The atria of the heart produce atrial natriuretic hormone (ANP) which blocks the secretion of renin.

1. Which statement below about hormones is true?

   A. Hormones are enzymes that catalyse reactions
   B. Hormones are released into the blood circulation
   C. Hormones affect all cells of the body
   D. Hormones are released by neurones at synapses

   Answer is B: Hormones are circulating messengers that are transported in blood. A particular hormone does not necessarily affect every cell in the body. Some (but not all) hormones are released by neurones, for example in the hypothalamus.

2. Which hormones are soluble in blood?

   A. Steroid hormones
   B. Hormones produced by the adrenal cortex
   C. The sex hormones
   D. Those released by the pituitary gland

   Answer is D: The pituitary gland releases peptide hormones which are soluble in blood. The other choices refer to steroid hormones which are insoluble in blood. They require transport via plasma proteins.

3. Which statement about the hypothalamus is correct?

   A. The hypothalamus is connected to the brain by the infundibulum
   B. The hypothalamus is composed of glandular epithelial tissue
   C. The hypothalamus secretes "releasing hormones"
   D. The hypothalamus secretes epinephrine and norepinephrine

   Answer is C: The hypothalamus is part of the brain so is composed of neural tissue. Epinephrine and norepinephrine are released from the adrenal medulla.

4. What hormone does the thyroid produce?

   A. thyroid stimulating hormone
   B. calcitriol
   C. thyroxine
   D. parathyroid hormone

   Answer is C: Thyroxine (or tetra-iodothyronine) is converted to tri-iodothyronine in target tissues.

5. What hormone(s) does the adrenal medulla produce?

   A. aldosterone
   B. epinephrine and norepinephrine
   C. corticosteroids
   D. glucocorticoids

   Answer is B: Epinephrine and norepinephrine are produced in the adrenal medulla (the deep or inside part). Aldosterone is a mineralocorticoid, which like corticosteroids & glucocorticoids, as the "cortico" in the name suggests, are all produced in the adrenal cortex.

6. What is produced by the beta cells of the pancreas?

   A. angiotensin converting enzyme
   B. glucocorticoids
   C. glucagon
   D. insulin

   Answer is D: Beta cells of the pancreatic islets produce insulin. The alpha cells produce glucagon.

7. Which gland or organ releases erythropoietin?

   A. The kidneys
   B. The adrenal glands
   C. The anterior pituitary
   D. The pancreas

   Answer is A: Kidneys produce erythropoietin (EPO) – which signals red bone marrow to increase production of rbc.

8. What effect does parathyroid hormone have?

   A. It increases plasma Ca^{2+} concentration
   B. It decreases plasma Ca^{2+} concentration
   C. It increases the rate of ATP formation
   D. It stimulates the thyroid gland to produce thyroxine

   Answer is A: PTH increases plasma Ca^{2+}. (calcitonin aids in lowering blood calcium).

9. Which one of the following is **NOT** part of the endocrine system?

   A. the islets of Langerhans (pancreatic islets)
   B. the thyroid gland
   C. the acini cells of the pancreas
   D. the parathyroid glands

   Answer is C: The acini cells produce digestive enzymes.

10. What is the difference between an exocrine gland and an endocrine gland?

    A. An endocrine gland secretes neurotransmitters (an exocrine gland does not).
    B. An endocrine gland secretes via a tube to the destination (an exocrine gland does not).
    C. An exocrine gland secretes into the blood (an endocrine gland does not).
    D. An endocrine gland secretes into the blood (an exocrine gland does not).

    Answer is D: Endocrine glands secrete "circulating" hormones, that is secrete into the blood.

11. By what term are hormones derived from tyrosine also known?

    A. amino acid derivatives
    B. peptide hormones
    C. steroid hormones
    D. corticosteroids

    Answer is A: Catecholamines (adrenaline, noradrenaline), dopamine and thyroid hormone are all derived from tyrosine.

12. Which hormones have their receptors inside their target cell?

    A. amino acid based hormones
    B. hormones with a membrane carrier mechanism or that are lipid soluble
    C. steroid hormones and peptide hormones of less than 50 amino acids
    D. lipid soluble hormones

    Answer is B: Choice D is also correct but B is the better answer as thyroid hormones cross membrane by a carrier mechanism.

13. Where in the body is the hypothalamus located?

    A. On the inferior surface of the brain
    B. In the cortex of the adrenal gland
    C. In the anterior pituitary gland
    D. On the dorsal surface of the thyroid gland

    Answer is A: The hypothalamus is below the thalamus, more or less on the "floor" of the brain, but above the pituitary gland.

14. From where are antidiuretic hormone and oxytocin released?

    A. the anterior pituitary
    B. the posterior pituitary
    C. the adrenal cortex
    D. the adrenal medulla

    Answer is B: ADH & OT are produced in the hypothalamus and transported to the posterior pituitary.

15. Which hormone has the element iodine as part of its molecule?

    A. calcitonin
    B. haemoglobin
    C. thyroxine
    D. parathyroid hormone

    Answer is C: Thyroxine or thyroid hormone contains iodine.

16. What effect does aldosterone have?

    A. It causes glucose to be absorbed from the blood
    B. It cause Na^+ to be absorbed in the kidneys
    C. It causes Ca^{++} to be absorbed from the gut
    D. It causes K^+ to be absorbed from the filtrate.

    Answer is B: Aldosterone cases reclamation of sodium ions from the filtrate, and potassium to be secreted in exchange.

17. Which of the following is a part of the endocrine system?

    A. the thalamus
    B. the pancreatic islets (islets of Langerhans)
    C. the renal glands
    D. the salivary glands

    Answer is B: The pancreatic islets secrete the hormones insulin and glucagon.

18. Which of the following is an amino acid derivative hormone?

    A. epinephrine
    B. tyrosine
    C. testosterone
    D. prostaglandin

    Answer is A: Epinephrine is derived from the amino acid tyrosine (so tyrosine is a wrong answer)

19. Which statement below is true of steroid hormones?

    A. they do not have a specific receptor to bind with.
    B. they are not lipid soluble do bind to receptor proteins on the cell membrane.
    C. they are lipid soluble so diffuse through the cell membrane.
    D. they cross the cell membrane via a carrier mechanism.

    Answer is C: Steroids are lipid soluble so diffuse through the plasma membrane to bind to a receptor within the cell.

20. Which structure controls the endocrine system and integrates the activities of the nervous and endocrine systems?

    A. the infundibulum
    B. the pituitary gland

C. the thalamus
D. the hypothalamus

Answer is D: Hypothalamus secretes regulatory hormones that control endocrine cells in the ant.pit. gland; produces ADH & oxytocin; contains "autonomic centres" that exert neural control over endocrine cells of the adrenal medullae.

21. One of the statements below is true. Which one?

A. the anterior pituitary produces testosterone from cholesterol and releases it when releasing hormones arrive from the hypothalamus.
B. the hypothalamus produces ADH and oxytocin which are stored in the posterior pituitary.
C. the posterior pituitary contains autonomic centres that exert neural control over the adrenal glands.
D. the thalamus produces ADH and oxytocin which are stored in the anterior pituitary

Answer is B: Testosterone is not produced in the pituitary, nor does the pituitary contain autonomic centres.

22. Iodine is an essential component of which hormone?

A. thyroid hormones
B. aldosterone
C. thyroid stimulating hormones
D. parathyroid hormone

Answer is A: Thyroid hormones T3 and T4 contain 3 & 4 iodine atoms respectively.

23. Which hormone(s) increases the reabsorption of Ca^{++} from the filtrate in the kidney tubule?

A. calcitonin
B. mineralocorticoids
C. parathyroid hormone
D. aldosterone

Answer is C: PTH causes increased calcium absorption and hence increases blood calcium level.

24. What effect does aldosterone have? It causes:

A. angiotensin to be formed from angiotensinogen
B. Na^+ to be absorbed from the filtrate
C. Na^+ and Ca^{++} to be absorbed from the filtrate and K^+ to be secreted into the filtrate
D. Na^+ to be absorbed from the filtrate and K^+ to be secreted into the filtrate

Answer is D: Aldosterone promotes the absorption of sodium from the filtrate while potassium (also a positively charged ion) is secreted to maintain electrical neutrality.

25. Which of the following is **NOT** part of the endocrine system?

    A. The thymus
    B. The pineal gland
    C. The acini cells of the pancreas
    D. The posterior pituitary gland

    Answer is C: The acini cells produce digestive enzymes.

26. Peptide hormones are produced (and/or released) by which structure?

    A. The adrenal cortex
    B. The gonads
    C. The hypothalamus
    D. The kidneys

    Answer is C: The hypothalamus produces peptide hormones.

27. Which statement applies to steroid hormones?

    A. They are transported dissolved in blood
    B. They bind to receptor proteins on the outside of the plasma membrane
    C. They cross the plasma membrane by using a protein carrier mechanism.
    D. They bind to receptors in the cell cytoplasm or nucleus

    Answer is D: As steroid hormones are lipid soluble, their receptors are inside the cell as they can cross the plasma membrane.

28. Which endocrine organ produces "releasing hormones" and "inhibitory hormones"?

    A. thyroid
    B. anterior pituitary
    C. hypothalamus
    D. thalamus

    Answer is C: The hypothalamus controls the secretion of the anterior pituitary by the use of "releasing hormones" and "inhibitory hormones".

29. What hormone is produced by the parafollicular cells of the thyroid gland?

    A. Parathyroid hormone
    B. Calcitonin
    C. Thyroid hormone
    D. Thyroxine

    Answer is B: Parafollicular (or "C") cells of the thyroid produce calcitonin which aids in lowering of blood calcium.

30. What hormones are produced by the adrenal medulla?

    A. Epinephrine and norepinephrine
    B. Insulin and glucagon

C. Aldosterone and erythropoietin
D. Testosterone and estrogen

Answer is A: The medulla is the deeper part if the adrenal gland.

31. What is one mechanism of hormone action?

A. They act as second messengers in the cytoplasm
B. They act as enzymes for reactions
C. They act as receptor proteins
D. They activate genes in the nucleus

Answer is D: Some hormones (corticosteroids) determine which genes are transcribed in the nucleus.

32. What is the effect of ADH (antidiuretic hormone)?

A. allows walls of collecting duct to become permeable to water
B. inhibits the reabsorption of Na^+
C. causes an increase in the volume of urine produced
D. it promotes diuresis

Answer is A: ADH causes more aquaporins to be inserted into the collecting duct walls which allow water molecules to pass through along the osmotic gradient.

33. Which one of the following is **NOT** true of peptide hormones?

A. they are water soluble
B. they are derived from amino acids
C. their receptors are located in the cell cytoplasm
D. they are transported dissolved in blood

Answer is C: The receptors for peptide hormones are located on the plasma membrane as they are unable to penetrate the plasma membrane.

34. Which hormones are produced by the adrenal medulla?

A. gonadocorticoids
B. steroid hormones
C. mineralocorticoids
D. catecholamines

Answer is D: Epinephrine and norepinephrine (=catecholamines) are produced in the adrenal medulla.

35. How do steroid hormones differ from amino acid-based hormones?

A. steroid hormones are water soluble whereas amino acid based hormones are not.
B. the receptors for steroid hormones are only in the cytoplasm or the nucleus (and amino acid-based hormones are not)

C. steroid hormones are made only in the adrenal glands, while amino acid-based hormones are produced by a variety of glands.
D. steroid hormones activate a G-protein and exert their effect via "second messengers", but the action of amino acid-based hormones results directly on binding to their receptor.

Answer is B: Steroid hormones are lipid soluble so can enter the cell to bind to receptors located inside the cell. Amino acid-based hormones are not lipid soluble so their receptors are located outside the cell on the plasma membrane.

36. Which structure integrates the activities of the endocrine system and the nervous system?

A. the hypothalamus
B. the thalamus
C. the posterior pituitary
D. the anterior pituitary

Answer is A: The hypothalamus is located in the brain and also produces regulatory hormones.

37. Which structure produces ADH and oxytocin?

A. the thalamus
B. the anterior pituitary
C. the hypothalamus
D. the posterior pituitary

Answer is C: ADH and OT are then transported to the posterior pituitary for storage and release.

38. Which structure is composed of glandular epithelial tissue?

A. the thalamus
B. the anterior pituitary
C. the posterior pituitary
D. the hypothalamus

Answer is B: The anterior pituitary produces and releases 6 hormones.

39. Which hormone is the one made in greatest quantity by the thyroid gland?

A. calcitonin
B. thyroid stimulating hormone
C. tri-iodothyronine
D. thyroxine

Answer is D: thyroxine is about 90 % tetra-iodothyronine and 10 % tri-iodothyronine

40. Which of the following organ(s) are **NOT** endocrine organs?

A. renal
B. adrenal

C. thyroid
D. parathyroid

Answer is A: Renal gland is another name for the kidney.

41. To which group of hormones does aldosterone belong?

A. catecholamines
B. glucocorticoids
C. mineralocorticoids
D. gonadocorticoids

Answer is C: As aldosterone is concerned with the absorption of sodium ions, a "mineral" and it is produced by the adrenal **cort** ex, it is termed a mineralocorticoid.

42. Where are the receptors for almost all of the amino acid derived hormones located?

A. on the mitochondria
B. in the nucleus
C. on the outside of the plasma membrane
D. on the inside of the plasma membrane

Answer is C: Amino acid-derived hormones cannot get through the plasma membrane so they attach to receptors located on the outside of the membrane.

43. Which structure produces the hormones ADH and oxytocin?

A. the posterior pituitary
B. the anterior pituitary
C. the thalamus
D. the hypothalamus

Answer is D: ADH & OT are produced in the hypothalamus and are then transported to the posterior pituitary for release.

44. The hypothalamus produces "releasing hormones". What do these releasing hormones do?

A. They direct the posterior pituitary to release hormones.
B. They direct the anterior pituitary to release hormones.
C. They direct the gonads to release hormones.
D. They act as "second messengers" when hormones bind to their receptor site.

Answer is B: The anterior pituitary produces hormones that stimulate other endocrine organs, but the ant pit dos not release hormones until directed to the hypothalamus.

45. What is the role of glucagon and insulin?

A. glucagon raises blood glucose level and inhibits gluconeogenesis.
B. glucagon lowers blood glucose level and stimulates glycogenolysis.

C. insulin raises blood glucose level and stimulates gluconeogenesis
D. insulin lowers blood glucose level inhibits glycogenolysis.

Answer is D: Insulin promotes the uptake of glucose into cells from the blood. Hence it lowers blood glucose. It also inhibits glycogenolysis so less glucose is released from the glycogen store.

46. Which of the following hormones **CANNOT** cross the plasma membrane?

A. sex hormones
B. amino acid based hormones
C. thyroid hormones
D. steroids

Answer is B: amino acid-based hormones are water soluble but not lipid soluble, so cannot cross the plasma membrane.

47. Which of the following "controls" the endocrine system?

A. the posterior pituitary
B. the thalamus
C. the anterior pituitary
D. the hypothalamus

Answer is D: The hypothalamus secretes releasing h. & inhibitory hormones that stimulate the anterior pituitary gland to secrete hormones which in turn control the activities of endocrine cells in the thyroid; cortex of adrenal glands; & reproductive organs. The hypothalamus produces ADH & oxytocin which are stored and released into blood from post.pit. The hypothalamus exerts neural control over the adrenal medullae.

48. Which part of the pituitary gland is comprised of neural tissue?

A. the posterior pituitary
B. the pars intermedia
C. the adenohypophysis
D. the anterior pituitary

Answer is A: The posterior pituitary is part of the brain.

49. Complete the sentence correctly. Parathyroid hormone:

A. is produced by the parafollicular cells of the thyroid gland
B. decreases the concentration of Ca^{++} in the blood
C. releases Ca^{++} from the sarcoplasmic reticulum
M increases the concentration of Ca^{++} in the blood.

Answer is D: When the level of calcium in the blood is lower than required, PTH is released and causes the calcium concentration to increase.

50. The adrenal medulla produces which of the following?

A. weak androgens
B. mineralocorticoids

C. testosterone and oestrogen
D. epinephrine and norepinephrine

Answer is D: The adrenal cortex produces weak androgens and mineralocorticoids.

51. What effect does insulin have?

A. it increases metabolic rate
B. it causes the breakdown of glycogen to glucose
C. it lowers blood sugar level
D. it stimulates gluconeogenesis

Answer is C: Glucose stimulates enhanced membrane transport of glucose into body cells, and inhibits glycogenolysis and gluconeogenesis. This lowers blood glucose level.

52. Which of the following is a substantial difference between amino acid based hormones and steroid hormones?

A. endocrine glands release steroid hormones while amino acid hormones are released from exocrine glands.
B. amino acid hormones are circulating hormones while steroid hormones are local hormones.
C. amino acid hormones are fat soluble while steroid hormones are not.
D. steroid hormones can pass through the plasma membrane while amino acid hormones cannot.

Answer is D: Steroid hormones are fat soluble, AA-based hormones are water soluble (& not fat soluble).

53. What type of molecule is cAMP, or what role does it play?

A. a second messenger
B. an amino acid based hormone
C. a catecholamine
D. a steroid hormone

Answer is A: Cyclic AMP is a second messenger. That is, it is released from the inside of the plasma membrane when an AA-based hormone binds to its receptor.

54. Which one is **NOT** a mode of action of hormones on their target cell?

A. a hormone may stimulate the synthesis of an enzyme in the target cell.
B. a hormone may activate an enzyme by altering its shape.
C. a hormone may deactivate an enzyme by altering its structure.
D. some hormones are enzymes that promote a chemical reaction in a cell.

Answer is D: Hormones are not enzymes (but may cause enzymes to be formed).

55. What may be correctly said about oxytocin and antidiuretic hormone?

    A. they are made and released from the posterior pituitary
    B. they are made in the hypothalamus and stored and released from the posterior pituitary
    C. they are made in the hypothalamus and stored and released from the anterior pituitary
    D. they are made and released from the anterior pituitary

    Answer is B: The hypothalamus produces ADH & OT. The posterior pituitary releases them.

56. Which hormones are produced by the adrenal medulla?

    A. glucocorticoids
    B. mineralocorticoids
    C. adrenalin and noradrenalin
    D. gonadocorticoids

    Answer is C: Adrenalin and noradrenalin (also known as epinephrine and nor epinephrine). The other three choices all have "cortico" in their name indicating their adrenal cortex origin.

57. Which cells produce insulin?

    A. the acini cells of the pancreas
    B. parafollicular cells of the thymus
    C. alpha cells of the islets of Langerhans
    D. beta cells of the islets of Langerhans

    Answer is D: Islets of Langerhans = pancreatic islets. Alpha cells produce glucagon.

58. What are the two parts of the pituitary gland known as?

    A. the thalamus and the hypothalamus
    B. anterior and posterior
    C. alpha and beta cells
    D. cortex and medulla

    Answer is B: Anterior pituitary (epithelial tissue) and posterior pituitary (neural tissue)

59. Which of the following could be a definition of a hormone?

    A. chemicals released to communicate between adjacent cells in contact.
    B. a chemical messenger released into blood to coordinate activities in distant tissues.
    C. a chemical messenger released by a neurone at a synapse.
    D. a chemical messenger in the extracellular fluid between cells of a single tissue.

    Answer is B: Hormones are also known as circulating hormones, meaning they are transported in the blood.

60. One of the following groups of hormones has their receptor inside the cell. Which one?

    A. steroid hormones
    B. catecholamines
    C. adrenalin and noradrenalin
    D. peptide hormones

    Answer is A: steroids are lipids, hence are lipid soluble so can enter the cell.

61. Which two hormones are stored in the posterior pituitary prior to their release?

    A. luteinising hormone and follicle stimulating hormone
    B. adrenalin and noradrenalin
    C. calcitonin and calcitriol
    D. oxytocin and antidiuretic hormone

    Answer is D: OT & ADH are produced in the hypothalamus before being transported to the posterior pituitary.

62. What is a function of calcitonin?

    A. accelerating Ca^{2+} release from bone
    B. stimulating Ca^{2+} excretion by the kidneys
    C. reducing Ca^{2+} deposition in bone
    D. stimulating the formation of calcitriol in the kidneys

    Answer is B: Calcitonin decreases the blood calcium concentration. B is the only choice compatible with this.

63. The hormones thyroxine and tri-iodothyronine contain which element?

    A. cobalt
    B. iron
    C. iodine
    D. manganese

    Answer is C: These thyroid hormones require iodine in their molecule.

64. What is produced in the adrenal cortex?

    A. cholesterol
    B. catecholamines
    C. adrenalin and noradrenalin
    D. corticosteroids

    Answer is D: "Cortico"steroids are made in the adrenal cortex. Choice B and C are the same – these hormones are made in the adrenal medulla.

65. What is the function of insulin?

    A. enhance the transport of glucose through the plasma membrane into the cell
    B. promote glycogenolysis

C. promote gluconeogenesis
D. to raise blood sugar level

Answer is A: Insulin lowers the level of glucose in the blood. The other three choices are about increasing the blood glucose level.

66. Which of the following statements about endocrine hormones is always true?

A. They are secreted by neurones
B. They are derived from amino acids
C. They are produced by exocrine glands
D. They are released into the bloodstream

Answer is D: Endocrine hormones are also known as circulating (in blood) hormones.

67. Which of the following statements about corticosteroids is true?

A. They may also act as neurotransmitters
B. They are transported dissolved in blood
C. They are produced by the adrenal gland
D. They are amino acid derivatives

Answer is C: They are produced by the adrenal cortex.

68. Which structure produces epinephrine and norepinephrine?

A. adrenal pelvis
B. the anterior pituitary
C. adrenal medulla
D. adrenal cortex

Answer is C: The medulla (interior) of the adrenal gland.

69. Which cells produce insulin?

A. the acini
B. the alpha cells
C. the beta cells
D. the islets of Langerhans

Answer is C: The beta cells of the islets of Langerhans.

70. What is the function of erythropoietin (EPO)?

A. stimulate bone marrow to produce red blood cells
B. decrease the plasma concentration of Ca^{++}
C. increase the plasma concentration of Ca^{++}
D. to raise blood sugar level

Answer is A: EPO is produced in the kidneys and stimulates active (red) marrow to produce blood cells.

71. Finish the sentence so that it is correct: A hormone may be defined as a chemical messenger that:

    A. is released into circulation in small quantities.
    B. facilitates communication between adjacent cells.
    C. moves through extracellular fluid between cells of a single tissue
    D. crosses the synaptic cleft and binds to a receptor.

    Answer is A: Hormones travel through the blood to all parts of the body and only small quantities are required.

72. Endocrine communication involves hormones of two types

    A. first messengers and second messengers
    B. steroid hormones and amino acid based hormones
    C. amino acid derivatives and peptide hormones
    D. peptide hormones and corticosteroids

    Answer is B: Hormones are of two structural types and this determines whether they are lipid soluble (can pass through the plasma membrane) or not.

73. Which of the following statements is **FALSE**?

    A. peptide hormones are not able to penetrate the cell membrane
    B. thyroid hormone can cross the membrane
    C. steroid hormones bind to receptors on the outside of the cell membrane
    D. catecholamines are not lipid soluble

    Answer is C: Steroid hormones are lipid soluble so their receptors are inside the cell as they can pass through the plasma membrane.

74. The posterior pituitary does which one of the following?

    A. produces growth hormone, prolactin and tropic hormones
    B. secretes regulatory hormones that control endocrine cells in the anterior pituitary
    C. exerts neural control over other endocrine glands
    D. stores and releases oxytocin and antidiuretic hormone

    Answer is D: OT & ADH are made in hypothalamus and passed along neurones to the posterior pituitary.

75. What does insulin do?

    A. it lowers blood sugar level
    B. it causes the breakdown of glycogen to glucose
    C. it increases metabolic rate
    D. it hydrolyses glucose into ATP

    Answer is A: Insulin stimulates the uptake of glucose into cells from the blood.

76. An amino acid based hormone binds to its receptor. This has the effect of:

    A. activating an enzyme to produce cAMP
    B. causing it to diffuse through the cell to trigger a cascade of reactions

C. activate a G-protein
D. allowing it to move along the membrane

Answer is C: After a hormone binds to its receptor, a G (for guanine) protein is activated as the first effect. The G-protein then moves along the membrane to activate an enzyme that produces – for example – cAMP, which is a "second messenger".

77. The structure that secretes regulatory hormones that control the pituitary gland is known as the:

A. hypothalamus
B. hypophysis
C. hypothyroid
D. hypothymus

Answer is A: Hypothalamus is structure. Hypophysis is another name for the pituitary gland.

78. Why are the receptors for amino acid-based hormones on the outside surface of the cell membrane?

A. cells can respond faster when the hormone does not need to enter the cell.
B. amino acid-based hormones cannot penetrate cell membranes.
C. lysosomes in the intracellular fluid digest amino acid-based hormones.
D. amino acid-based hormones have no role in activating genes in the nucleus.

Answer is B: Amino acid-based hormones are not lipid soluble.

79. What is the difference between endocrine glands and exocrine glands?

A. endocrine glands produce hormones whereas exocrine glands do not.
B. exocrine glands secrete into the blood stream whereas endocrine glands do not.
C. endocrine glands are controlled by the autonomic nervous system whereas exocrine glands are not.
D. exocrine glands secrete steroid hormones whereas endocrine glands secrete amino acid-based hormones.

Answer is A: By definition endocrine glands are part of the endocrine system and they produce hormones.

80. The pituitary gland has an anterior portion and a posterior portion. One difference between the two is:

A. the anterior portion releases hormones following a nervous stimulus while the posterior portion releases hormones following a hormonal stimulus.
B. the posterior portion is able to produce hormones while the anterior portion merely stores hormones made elsewhere.

C. the anterior portion releases antidiuretic hormone (ADH) while the posterior portion does not.
D. the posterior portion is neural tissue while the anterior portion is glandular tissue.

Answer is D: Choices A, B & C are the reverse of the true situation.

81. By what other name is adrenaline also known?

A. noradrenaline
B. epinephrine
C. androgen
D. ANP

Answer is B: Perhaps to diminish the perception that the adrenal gland only produces adrenaline.

82. Which hormones does the pancreas produce?

A. epinephrine and norepinephrine.
B. oxytocin and antidiuretic hormone.
C. glucagon and insulin.
D. glucocorticoids and aldosterone

Answer is C: The pancreatic islets produce these hormones which manage the concentration of glucose in the blood.

83. Which statement is **NOT CORRECT** about hormones:

A. They are chemical substances that alter cell activity
B. They regulate metabolic function of other cells in the body
C. Steroid hormones are amino acid-based and are synthesized from cholesterol
D. They are produced in glands and transported via the blood stream

Answer is C: Steroid hormones are not based on amino acids. They are lipids.

84. What does the anterior lobe of the pituitary gland synthesise and release?

A. Growth hormone-releasing hormone
B. Corticotropin-releasing hormone
C. Thyroid-stimulating hormone
D. Gonadotropin-releasing hormone

Answer is C: All the releasing hormones are produced in the hypothalamus.

85. How do calcitonin or parathyroid hormone control blood calcium levels?

A. Calcitonin acts to increase blood calcium levels
B. Parathyroid hormone release is inhibited by increased calcium levels
C. Parathyroid hormone stimulates bone resorbing cells to take up calcium
D. Calcitonin inhibits parathyroid hormone

Answer is B: PTH acts to increase blood calcium levels. Hence less is required when blood calcium level is high.

86. What controls the blood glucose level?

A. The action of insulin
B. The action of glucagon
C. The action of insulin and glucagon
D. The action of insulin, glucagon and glycogen

Answer is C: Insulin increases blood glucose, while glucagon decreases blood glucose. Glycogen is not a hormone, so it does not affect the level of glucose in the blood.

87. Complete the following sentence correctly: The hypothalamus:

A. Is the major link between the nervous and the endocrine systems.
B. Is situated in the brain superior to the thalamus.
C. Produces a hormone that stimulates the thyroid gland.
D. Does not produce anti-diuretic hormone (ADH).

Answer is A: The hypothalamus integrates the nervous and endocrine systems of body control.

88. Which of the following secretes growth hormone?

A. the adrenal glands
B. The thyroid gland
C. The posterior lobe of the pituitary gland
D. The anterior lobe of the pituitary gland

Answer is D: The anterior lobe produces and releases GH.

89. Blood calcium levels are controlled by hormones from which structures?

A. The parathyroid glands and the thyroid gland
B. The anterior lobe of the pituitary gland and the thyroid gland
C. The parathyroid glands and the anterior lobe of the pituitary gland
D. The adrenal cortex and the hypothalamus.

Answer is A: Parathyroid glands secrete parathyroid hormone (to increase blood Ca level) while the parafollicular cells of the thyroid produce calcitonin which aids in lowering blood Ca.

90. Which statement is **NOT CORRECT**?

A. Males and females produce testosterone and oestrogen respectively in their gonads.
B. Both male and females produce follicle stimulating hormone and luteinizing hormone.

C. Oxytocin is produced and released from the anterior lobe of the pituitary gland.
D. Production of testosterone and oestrogen inhibits the release of gonadotrophin releasing hormone from the hypothalamus.

Answer is C: Oxytocin is produced in the hypothalamus and released from the posterior lobe of the pituitary gland.

91. The hormones known as "catecholamines" (adrenaline, noradrenaline and dopamine) are not lipid soluble. Therefore their receptor sites are:

A. On the inside of the plasma membrane.
B. On the outside of the plasma membrane.
C. In the cell cytoplasm.
D. In the cell nucleus.

Answer is B: With the receptors on the outside of the membrane, catecholamines do not need to be able to penetrate the membrane.

Chapter 7 Endocrine Physiology

For additional ancillary materials related to this chapter, please visit thePoint.

I. OVERVIEW OF HORMONES

A. See Table 7.1 for a list of hormones, including abbreviations, glands of origin, and major actions.

table **7.1** Master List of Hormones

Hormone	Abbreviation	Gland of Origin	Major Actions*
Thyrotropin-releasing hormone	TRH	Hypothalamus	Stimulates secretion of TSH and prolactin
Corticotropin-releasing hormone	CRH	Hypothalamus	Stimulates secretion of ACTH
Gonadotropin-releasing hormone	GnRH	Hypothalamus	Stimulates secretion of LH and FSH
Growth hormone–releasing hormone	GHRH	Hypothalamus	Stimulates secretion of growth hormone
Somatotropin release–inhibiting hormone (somatostatin)	SRIF	Hypothalamus	Inhibits secretion of growth hormone
Prolactin-inhibiting factor (dopamine)	PIF	Hypothalamus	Inhibits secretion of prolactin
Thyroid-stimulating hormone	TSH	Anterior pituitary	Stimulates synthesis and secretion of thyroid hormones
Follicle-stimulating hormone	FSH	Anterior pituitary	Stimulates growth of ovarian follicles and estrogen secretion Promotes sperm maturation (testes)
Luteinizing hormone	LH	Anterior pituitary	Stimulates ovulation, formation of corpus luteum, and synthesis of estrogen and progesterone (ovary) Stimulates synthesis and secretion of testosterone (testes)
Growth hormone	GH	Anterior pituitary	Stimulates protein synthesis and overall growth
Prolactin		Anterior pituitary	Stimulates milk production and breast development
Adrenocorticotropic hormone	ACTH	Anterior pituitary	Stimulates synthesis and secretion of adrenal cortical hormones
Melanocyte-stimulating hormone	MSH	Anterior pituitary	Stimulates melanin synthesis (? humans)
Oxytocin		Posterior pituitary	Milk ejection; uterine contraction
Antidiuretic hormone (vasopressin)	ADH	Posterior pituitary	Stimulates H_2O reabsorption by renal collecting ducts and contraction of arterioles
L-thyroxine Triiodothyronine	T_4 T_3	Thyroid gland	Skeletal growth; ↑ O_2 consumption; heat production; ↑ protein, fat, and carbohydrate use; maturation of nervous system (perinatal)
Glucocorticoids (cortisol)		Adrenal cortex	Stimulates gluconeogenesis; anti-inflammatory; immunosuppression
Estradiol		Ovary	Growth and development of female reproductive organs; follicular phase of menstrual cycle
Progesterone		Ovary	Luteal phase of menstrual cycle
Testosterone		Testes	Spermatogenesis; male secondary sex characteristics
Parathyroid hormone	PTH	Parathyroid gland	↑ serum [Ca^{2+}]; ↓ serum [phosphate]
Calcitonin		Thyroid gland (parafollicular cells)	↓ serum [Ca^{2+}]
Aldosterone		Adrenal cortex	↑ renal Na^+ reabsorption; ↑ renal K^+ secretion; ↑ renal H^+ secretion
1,25-Dihydroxycholecalciferol		Kidney (activation)	↑ intestinal Ca^{2+} absorption; ↑ bone mineralization
Insulin		Pancreas (beta cells)	↓ blood [glucose]; ↓ blood [amino acid]; ↓ blood [fatty acid]
Glucagon		Pancreas (alpha cells)	↑ blood [glucose]; ↑ blood [fatty acid]
Human chorionic gonadotropin	HCG	Placenta	↓ estrogen and progesterone synthesis in corpus luteum of pregnancy
Human placental lactogen	HPL	Placenta	Same actions as growth hormone and prolactin during pregnancy

*See text for more complete description of each hormone.

B. Hormone synthesis

1. Protein and peptide hormone synthesis

- **Preprohormone** synthesis occurs in the **endoplasmic reticulum** and is directed by a specific mRNA.
- **Signal peptides are cleaved** from the preprohormone, producing a **prohormone**, which is transported to the Golgi apparatus.
- Additional peptide sequences are cleaved in the Golgi apparatus to form the **hormone**, which is packaged in secretory granules for later release.

2. Steroid hormone synthesis

- Steroid hormones are **derivatives of cholesterol** (the biosynthetic pathways are described in V A 1).

3. Amine hormone synthesis

- Amine hormones (thyroid hormones, epinephrine, norepinephrine) are **derivatives of tyrosine** (the biosynthetic pathway for thyroid hormones is described in IV A).

C. Regulation of hormone secretion

1. Negative feedback

- is the most commonly applied principle for regulating hormone secretion.
- is self-limiting.
- A hormone has biologic actions that, directly or indirectly, inhibit further secretion of the hormone.
- **For example**, insulin is secreted by the pancreatic beta cells in response to an increase in blood glucose. In turn, insulin causes an increase in glucose uptake into cells that results in decreased blood glucose concentration. The decrease in blood glucose concentration then decreases further secretion of insulin.
- **For example**, parathyroid hormone is secreted by the chief cells of the parathyroid gland in response to a decrease in serum Ca^{2+} concentration. In turn, parathyroid hormone's actions on bone, kidney, and intestine all act in concert to increase the serum Ca^{2+} concentration. The increased serum Ca^{2+} concentration then decreases

further parathyroid hormone secretion.

2. Positive feedback

- is rare.
- is explosive and self-reinforcing.
- A hormone has biologic actions that, directly or indirectly, cause more secretion of the hormone.
- **For example**, the surge of luteinizing hormone (LH) that occurs just before ovulation is a result of positive feedback of estrogen on the anterior pituitary. LH then acts on the ovaries and causes more secretion of estrogen.

D. Regulation of receptors

- Hormones determine the sensitivity of the target tissue by **regulating the number or sensitivity of receptors**.

1. Down-regulation of receptors

- A hormone **decreases the number or affinity of receptors** for itself or for another hormone. For example, in the uterus, progesterone down-regulates its own receptor and the receptor for estrogen.

2. Up-regulation of receptors

- A hormone **increases the number or affinity of receptors** for itself or for another hormone.
- **For example**, in the ovary, estrogen up-regulates its own receptor and the receptor for LH.

II. CELL MECHANISMS AND SECOND MESSENGERS (TABLE 7.2)

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table **7.2** Mechanisms of Hormone Action

cAMP Mechanism	IP_3 Mechanism	Steroid Hormone Mechanism	Other Mechanisms
ACTH	GnRH	Glucocorticoids	**Tyrosine Kinase Mechanism**
LH and FSH	TRH	Estrogen	Insulin
TSH	GHRH	Testosterone	IGF-1
ADH (V_2 receptor)	Angiotensin II	Progesterone	Growth hormone
HCG	ADH (V_1 receptor)	Aldosterone	Prolactin
MSH	Oxytocin	Vitamin D	**cGMP Mechanism**
CRH	α_1 Receptors	Thyroid hormone	ANP
β_1 and β_2 receptors			Nitric oxide
Calcitonin			
PTH			
Glucagon			

ANP = atrial natriuretic peptide; cAMP = cyclic adenosine monophosphate; cGMP = cyclic guanosine monophosphate; IGF = insulin-like growth factor; IP_3 = inositol 1,4,5-triphosphate.

A. G proteins

- are **guanosine triphosphate (GTP)-binding proteins** that couple hormone receptors to adjacent effector molecules. For example, in the cyclic adenosine monophosphate (cAMP) second messenger system, G proteins couple the hormone receptor to adenylate cyclase.
- are used in the adenylate cyclase and **inositol 1,4,5-triphosphate** (IP_3**) second messenger systems**.
- have intrinsic **GTPase activity**.
- have three subunits: α, β, and γ.
- The **α subunit** can bind either guanosine diphosphate (GDP) or GTP. When GDP is bound to the α subunit, the G protein is inactive. When GTP is bound, the G protein is active.
- G proteins can be either stimulatory (G_s) or inhibitory (G_i). Stimulatory or inhibitory activity resides in the α subunits, which are accordingly called α_s and α_i.

B. Adenylate cyclase mechanism (Figure 7.1)

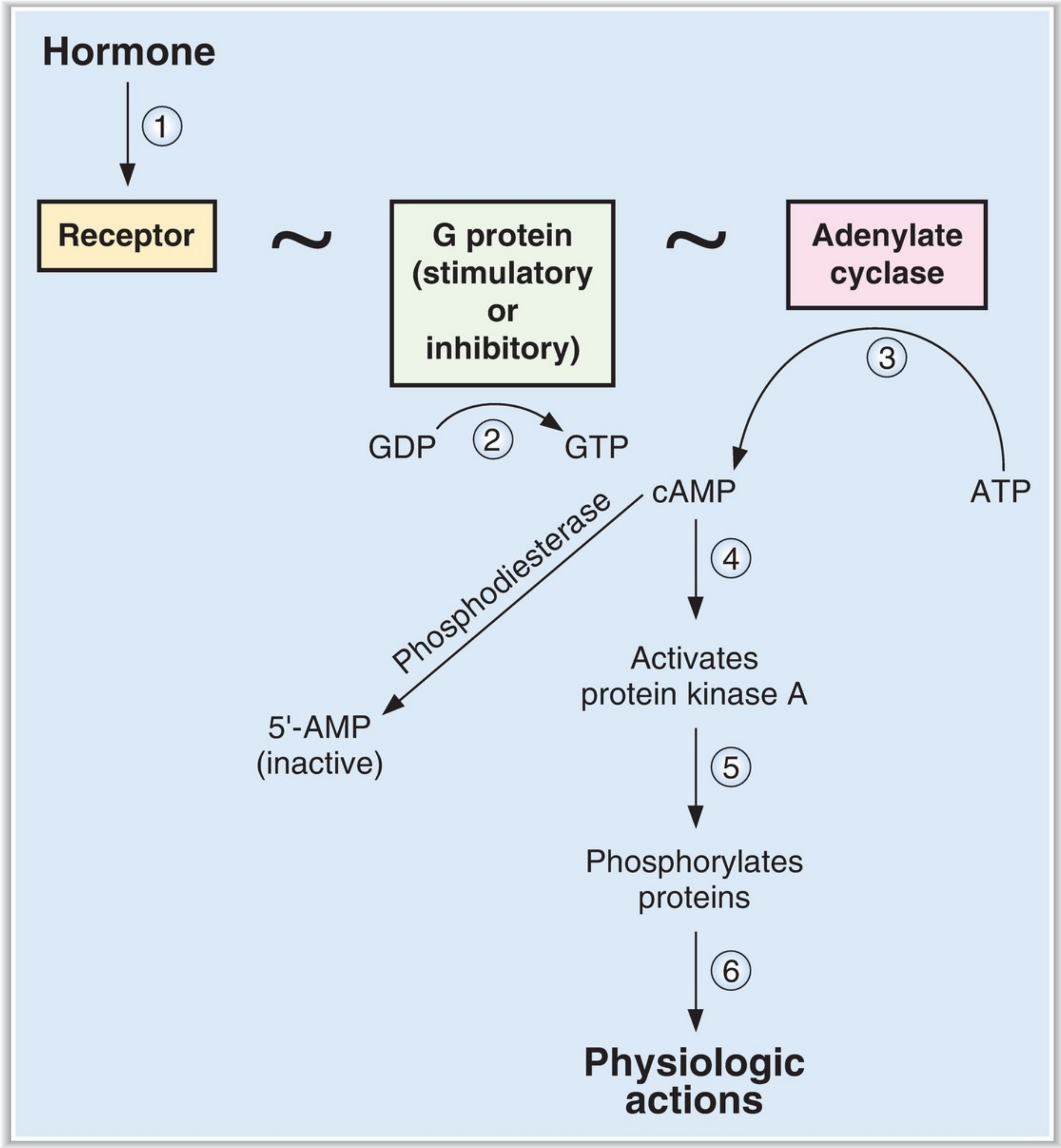


FIGURE 7.1. Mechanism of hormone action—adenylate cyclase. ATP = adenosine triphosphate; cAMP = cyclic adenosine monophosphate; GDP = guanosine diphosphate; GTP = guanosine triphosphate.

1. Hormone binds to a receptor in the cell membrane (step 1).

2. **GDP is released from the G protein and replaced by GTP** (step 2), which activates the G protein. The G protein then activates or inhibits adenylate cyclase. If the G protein is stimulatory (G_s), then adenylate cyclase will be activated. If the G protein is inhibitory (G_i), then adenylate cyclase will be inhibited (not shown). Intrinsic GTPase activity in the G protein converts GTP back to GDP (not shown).
3. **Activated adenylate cyclase** then catalyzes the conversion of adenosine triphosphate (ATP) to cAMP (step 3).
4. **cAMP activates protein kinase A** (step 4), which phosphorylates specific proteins (step 5), producing specific physiologic actions (step 6).
5. **cAMP is degraded to 5′-AMP by phosphodiesterase**, which is inhibited by **caffeine**. Therefore, phosphodiesterase inhibitors would be expected to augment the physiologic actions of cAMP.

C. IP_3 mechanism (Figure 7.2)

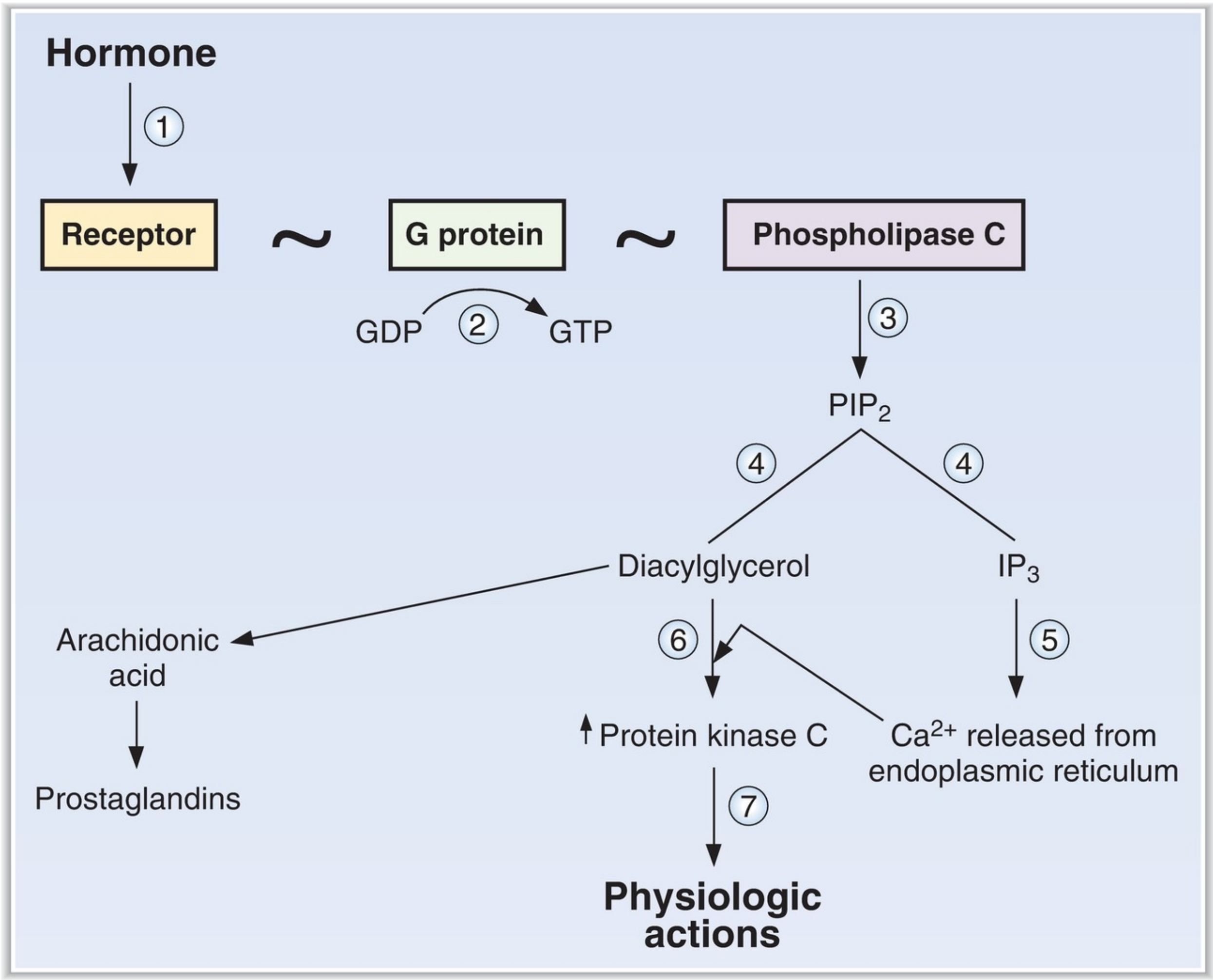


FIGURE 7.2. Mechanism of hormone action—inositol 1,4,5-triphosphate (IP_3)–Ca^{2+}. GDP = guanosine diphosphate; GTP = guanosine triphosphate; PIP_2 = phosphatidylinositol 4,5-diphosphate.

1. **Hormone binds to a receptor** in the cell membrane (step 1) and, via a G protein (step 2), **activates phospholipase C** (step 3).
2. **Phospholipase C liberates diacylglycerol and IP_3** from membrane lipids (step 4).
3. **IP_3 mobilizes Ca^{2+} from the endoplasmic reticulum** (step 5). Together, Ca^{2+} and diacylglycerol **activate protein kinase C** (step 6), which phosphorylates proteins and causes specific **physiologic actions** (step 7).

D. Catalytic receptor mechanisms

- Hormone binds to extracellular receptors that have, or are associated with, enzymatic activity on the intracellular side of the membrane.

1. Guanylyl cyclase

a. Atrial natriuretic peptide (ANP) acts through *receptor* guanylyl cyclase, where the extracellular side of the receptor binds ANP and the intracellular side of the receptor has guanylyl cyclase activity. Activation of guanylyl cyclase converts GTP to cyclic GMP, which is the second messenger.

b. Nitric oxide (NO) acts through *cytosolic* guanylyl cyclase. Activation of guanylyl cyclase converts GTP to cyclic GMP, which is the second messenger.

2. Tyrosine kinases (Figure 7.3)

- Hormone binds to extracellular receptors that have, or are associated with, tyrosine kinase activity. When activated, tyrosine kinase phosphorylates tyrosine moieties on proteins, leading to the hormone's physiologic actions.

a. Receptor tyrosine kinase

- Hormone binds to the extracellular side of the receptor.
- The intracellular side of the receptor has intrinsic tyrosine kinase activity.
- One type of receptor tyrosine kinase is a **monomer** (e.g., receptor for nerve growth factor). Binding of hormone or ligand causes dimerization of the receptor, activation of intrinsic tyrosine kinase, and phosphorylation of tyrosine moieties.
- Another type of receptor tyrosine kinase is a **dimer** (e.g., receptors for **insulin** and **insulin-like growth factor [IGF]**). Binding of hormone activates intrinsic tyrosine kinase, leading to phosphorylation of tyrosine moieties.
- Insulin receptors are also discussed in Section VI C 2.

b. Tyrosine kinase–associated receptor

- is the mechanism of action of **growth hormone**.
- Growth hormone binds to the extracellular side of the receptor.
- The intracellular side of the receptor does *not* have tyrosine kinase activity but is noncovalently *associated with* tyrosine kinase (e.g., Janus family of receptor-associated tyrosine kinase, **JAK**).
- Binding of growth hormone causes dimerization of the receptor and activation of tyrosine kinase in the associated protein (e.g., JAK).

- Targets of JAK include signal transducers and activators of transcription (**STAT**), which cause transcription of new mRNAs and new protein synthesis.

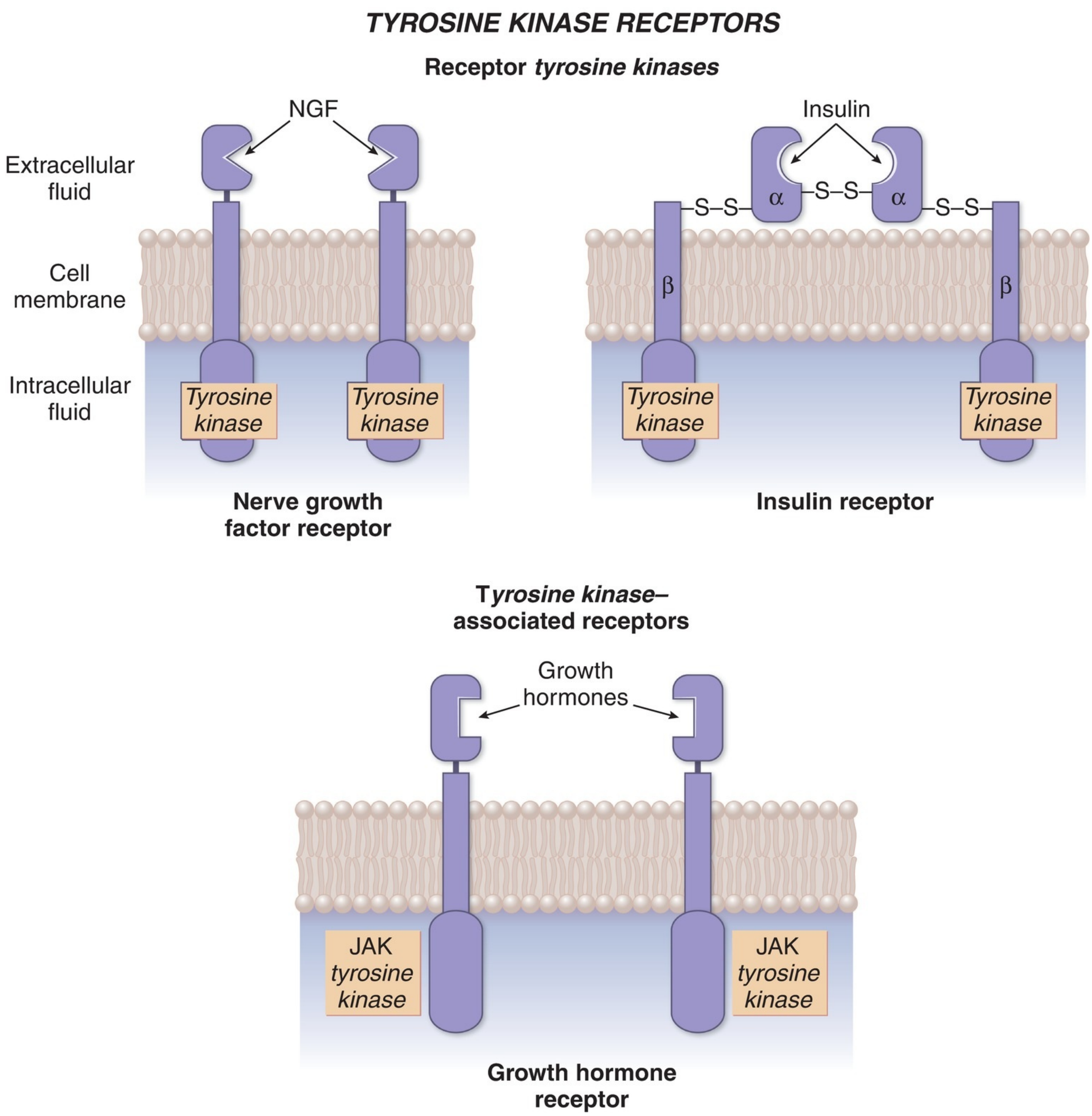


FIGURE 7.3. Tyrosine kinase receptors. Nerve growth factor and insulin utilize receptor tyrosine kinases. Growth hormone utilizes a tyrosine kinase–associated receptor. JAK = Janus family of receptor-associated tyrosine kinase; NGF = nerve growth factor.

E. Steroid hormone and thyroid hormone mechanism (Figure 7.4)

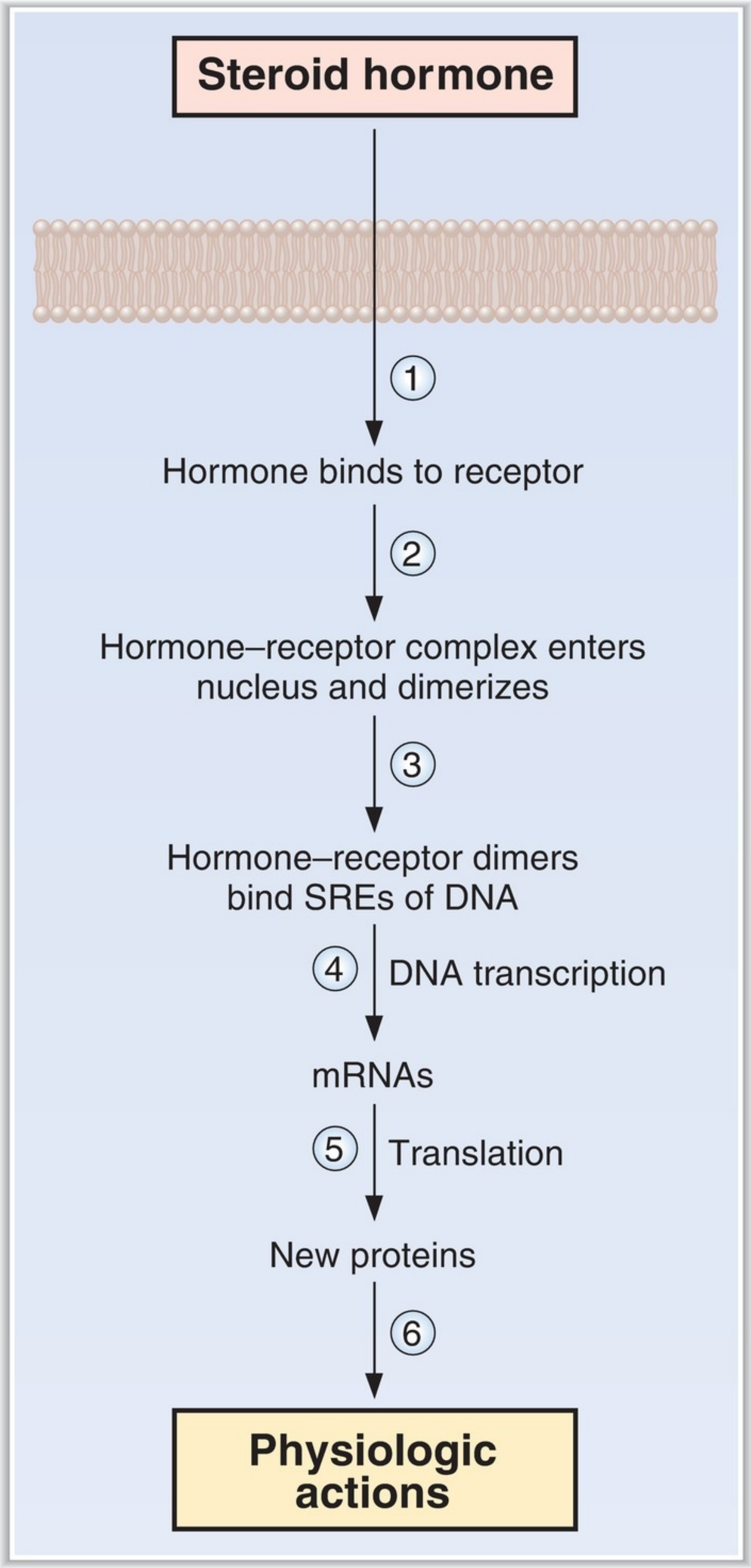

Steroid hormone
1
Hormone binds to receptor
2
Hormone–receptor complex enters nucleus and dimerizes
3
Hormone–receptor dimers bind SREs of DNA
4
DNA transcription
mRNAs
5
Translation
New proteins
6
Physiologic actions

FIGURE 7.4. Mechanism of hormone action—steroid hormones and thyroid hormone. SREs = steroid-responsive elements.

1. Steroid (or thyroid) hormone diffuses across the cell membrane and binds to its **receptor** (step 1).
2. The hormone–receptor complex enters the nucleus and dimerizes (step 2).
3. The **hormone–receptor dimers** are transcription factors that **bind to steroid-responsive elements (SREs)** of DNA (step 3) and initiate DNA transcription (step 4).
4. **New messenger RNA** is produced, leaves the nucleus, and is translated to synthesize new proteins (step 5).
5. The **new proteins** that are synthesized have specific physiologic actions. For example, 1,25-dihydroxycholecalciferol induces the synthesis of calbindin D-28K, a Ca^{2+}-binding protein in the intestine; aldosterone induces the synthesis of Na^+ channels in the renal principal cells.

III. PITUITARY GLAND (HYPOPHYSIS)

A. Hypothalamic–pituitary relationships

1. **The anterior lobe of the pituitary gland** is linked to the **hypothalamus by the hypothalamic–hypophysial portal system**. Thus, blood from the hypothalamus that contains high concentrations of hypothalamic hormones is delivered directly to the anterior pituitary. Hypothalamic hormones (e.g., growth hormone–releasing hormone [GHRH]) then stimulate or inhibit the release of anterior pituitary hormones (e.g., growth hormone).
2. **The posterior lobe of the pituitary gland** is derived from neural tissue. The nerve **cell bodies are located in hypothalamic nuclei**. Posterior pituitary hormones are synthesized in the nerve cell bodies, packaged in secretory granules, and transported down the axons to the posterior pituitary for release into the circulation.

B. Hormones of the anterior lobe of the pituitary

- are growth hormone, prolactin, thyroid-stimulating hormone (TSH), LH, follicle-stimulating hormone (FSH), and adrenocorticotropic hormone (ACTH).

- Growth hormone and prolactin are discussed in detail in this section. TSH, LH, FSH, and ACTH are discussed in context (e.g., TSH with thyroid hormone) in later sections of this chapter.

1. TSH, LH, and FSH

- belong to the same glycoprotein family. Each has an α subunit and a β subunit. The **α subunits are identical**. The β subunits are different and are responsible for the unique biologic activity of each hormone.

2. ACTH, melanocyte-stimulating hormone (MSH), β-lipotropin, and β-endorphin (Figure 7.5)

- are derived from a single precursor, **proopiomelanocortin (POMC)**.
- **α-MSH and β-MSH** are produced in the intermediary lobe, which is rudimentary in adult humans.

3. Growth hormone (somatotropin)

- is the most important hormone for normal growth to adult size.
- is a single-chain polypeptide that is **homologous with prolactin** and human placental lactogen.

a. Regulation of growth hormone secretion (Figure 7.6)

- Growth hormone is released in **pulsatile** fashion.
- **Secretion is increased** by sleep, stress, hormones related to puberty, starvation, exercise, and hypoglycemia.
- **Secretion is decreased** by somatostatin, somatomedins, obesity, hyperglycemia, and pregnancy.

1. *Hypothalamic control—GHRH and somatostatin*

- **GHRH** stimulates the synthesis and secretion of growth hormone.
- **Somatostatin** inhibits secretion of growth hormone by blocking the response of the anterior pituitary to GHRH.

2. *Negative feedback control by somatomedins*

- Somatomedins are produced when growth hormone acts on target tissues. Somatomedins **inhibit the secretion of growth hormone** by acting directly on the anterior pituitary and by stimulating the secretion of somatostatin from the hypothalamus.

3. *Negative feedback control by GHRH and growth hormone*

- **GHRH** inhibits its own secretion from the hypothalamus.
- **Growth hormone** also inhibits its own secretion by stimulating the

secretion of somatostatin from the hypothalamus.

b. Actions of growth hormone

- In the liver, growth hormone generates the production of **somatomedins (IGFs)**, which serve as the intermediaries of several physiologic actions.
- The **IGF receptor** has **tyrosine kinase activity**, similar to the insulin receptor.

1. *Direct actions of growth hormone*

a. ↓ glucose uptake into cells **(diabetogenic)**.

b. ↑ lipolysis.

c. ↑ protein synthesis in muscle and ↑ lean body mass.

d. ↑ production of **IGF**.

2. *Actions of growth hormone via IGF*

a. ↑ protein synthesis in chondrocytes and ↑ **linear growth (pubertal growth spurt)**.

b. ↑ protein synthesis in muscle and ↑ **lean body mass**.

c. ↑ protein synthesis in most organs and ↑ **organ size**.

c. Pathophysiology of growth hormone

1. *Growth hormone deficiency*

- in children causes **dwarfism**, failure to grow, short stature, mild obesity, and delayed puberty.
- can be caused by

a. lack of anterior pituitary growth hormone.

b. hypothalamic dysfunction (↓ GHRH).

c. failure to generate IGF in the liver.

d. growth hormone receptor deficiency.

2. *Growth hormone excess*

- Hypersecretion of growth hormone causes **acromegaly**.

a. Before puberty, excess growth hormone causes increased linear growth **(gigantism)**.

b. After puberty, excess growth hormone causes increased periosteal bone growth, increased organ size, and glucose intolerance.

- can be treated with **somatostatin analogues (e.g., octreotide)**, which inhibit growth hormone secretion.

4. Prolactin

- is the major hormone responsible for **lactogenesis**.
- participates, with estrogen, in breast development.
- is structurally **homologous to growth hormone**.

a. Regulation of prolactin secretion (Figure 7.7 and Table 7.3)

1. *Hypothalamic control by dopamine and thyrotropin-releasing hormone (TRH)*

- Prolactin secretion is **tonically inhibited by dopamine** (prolactin-inhibiting factor [PIF]) secreted by the hypothalamus. Thus, interruption of the hypothalamic–pituitary tract causes increased secretion of prolactin and sustained lactation.
- TRH increases prolactin secretion.

2. *Negative feedback control*

- Prolactin inhibits its own secretion by stimulating the hypothalamic release of dopamine.

b. Actions of prolactin

1. stimulates **milk production** in the breast (casein, lactalbumin).

2. stimulates **breast development** (in a supportive role with estrogen).

3. **inhibits ovulation** by decreasing synthesis and release of gonadotropin-releasing hormone (GnRH).

4. inhibits spermatogenesis (by decreasing GnRH).

c. Pathophysiology of prolactin

1. *Prolactin deficiency* (destruction of the anterior pituitary)

- results in the **failure to lactate**.

2. *Prolactin excess*

- **results from hypothalamic destruction** (due to loss of the tonic “inhibitory” control by dopamine) or from prolactin-secreting tumors **(prolactinomas)**.
- causes **galactorrhea** and decreased libido.
- causes **failure to ovulate** and **amenorrhea** because it inhibits GnRH secretion.
- can be treated with **bromocriptine**, which reduces prolactin secretion by acting as a **dopamine agonist**.

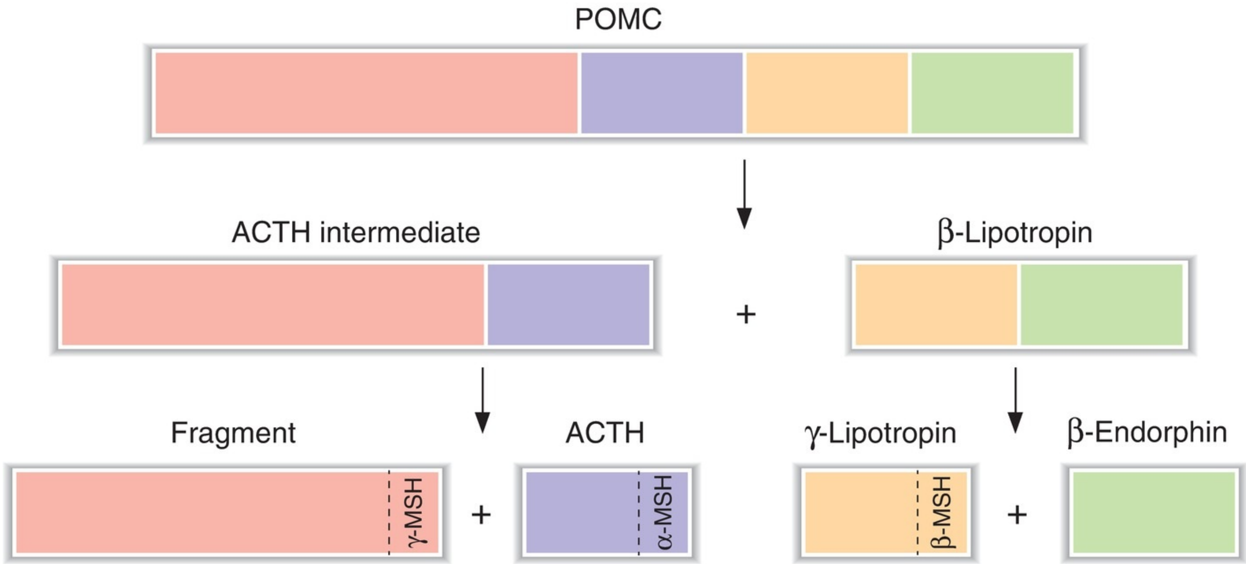


FIGURE 7.5. Proopiomelanocortin (POMC) is the precursor for adrenocorticotropic hormone (ACTH), β-lipotropin, and β-endorphin in the anterior pituitary. MSH = melanocyte-stimulating hormone.

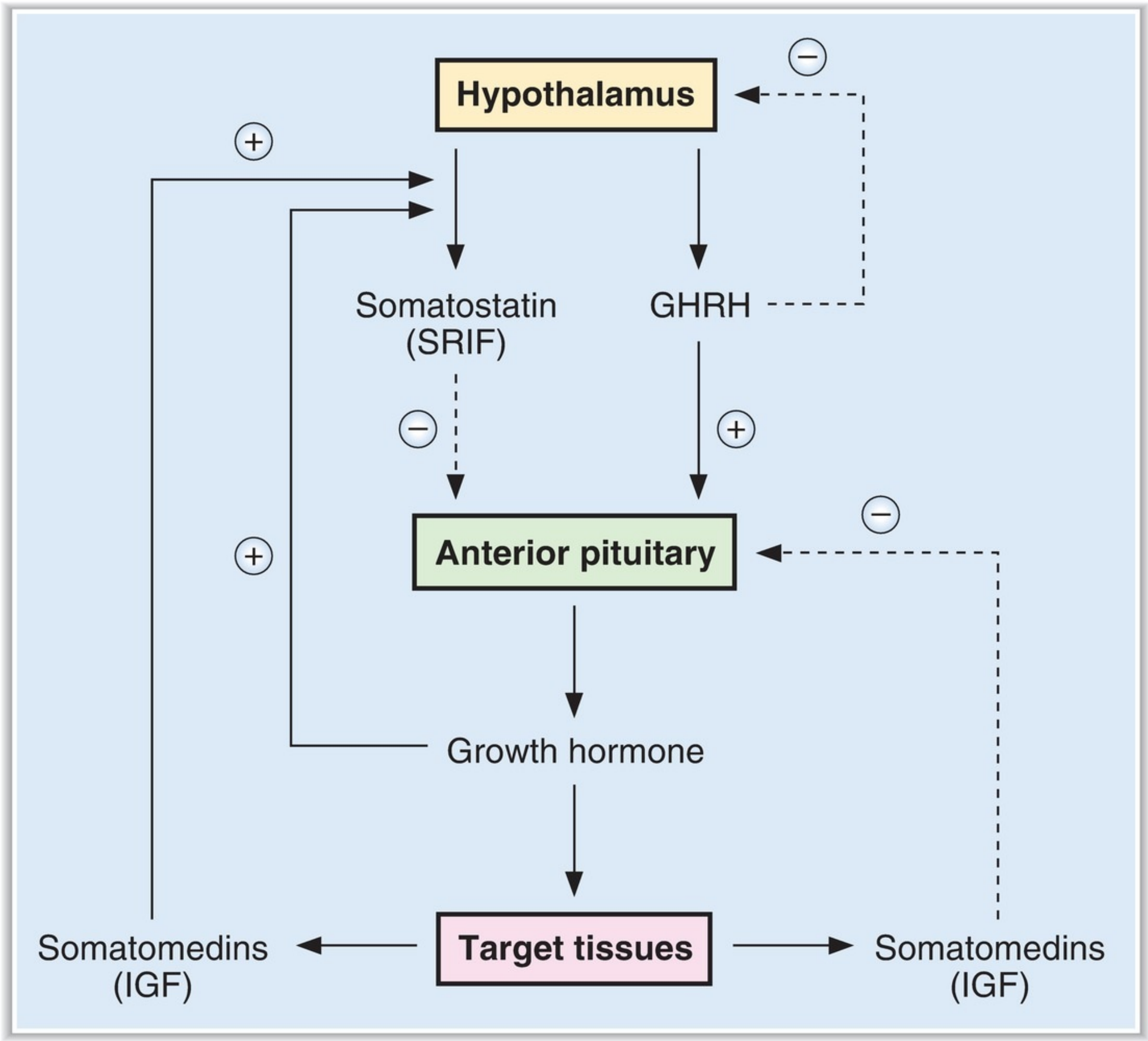


FIGURE 7.6. Control of growth hormone secretion. GHRH = growth hormone–releasing hormone; IGF = insulin-like growth factor; SRIF = somatotropin release–inhibiting factor.

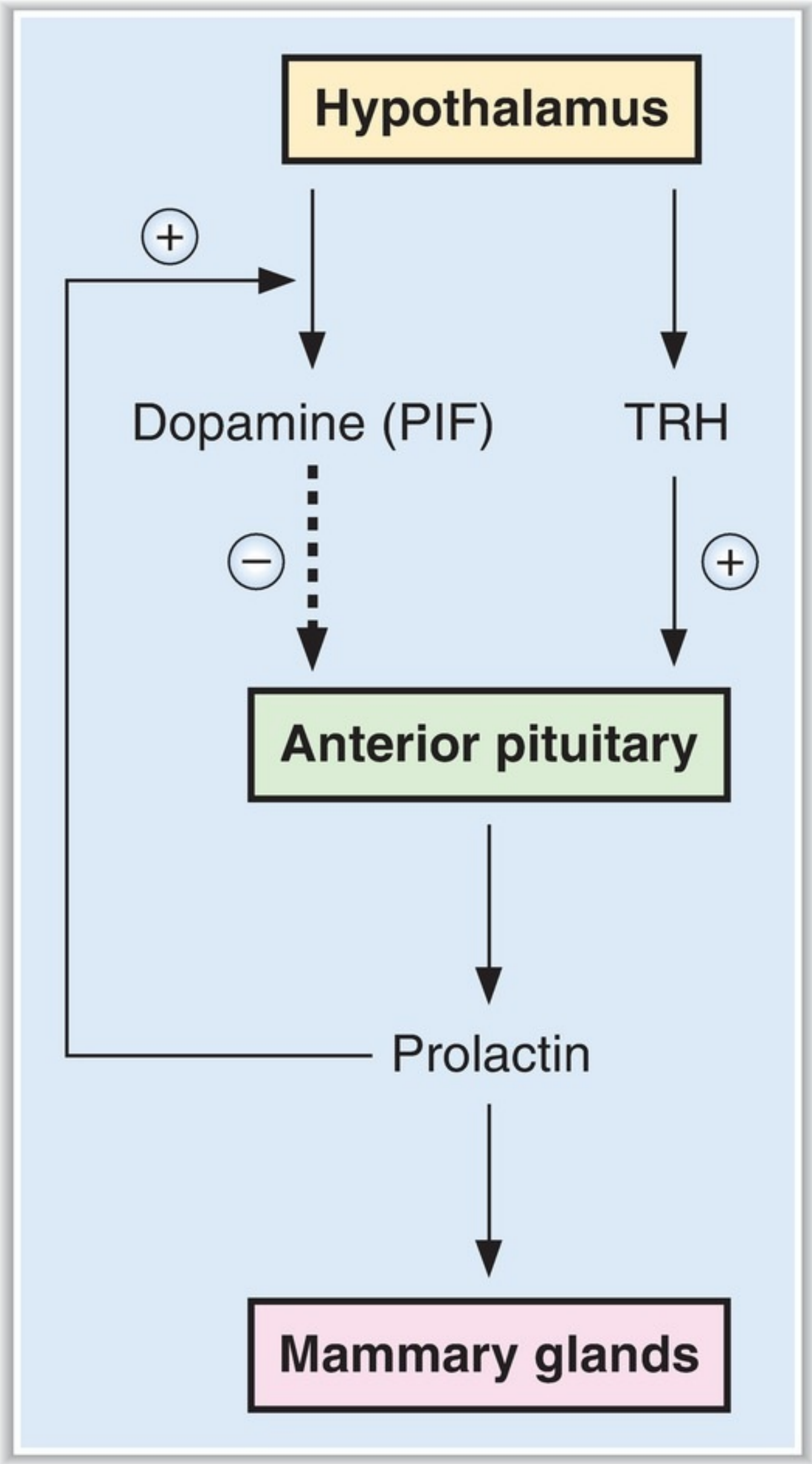

Hypothalamus
Dopamine (PIF)
TRH
Anterior pituitary
Prolactin
Mammary glands

FIGURE 7.7. Control of prolactin secretion. PIF = prolactin-inhibiting factor; TRH = thyrotropin-releasing hormone.

table **7.3** Regulation of Prolactin Secretion

Factors that Increase Prolactin Secretion	Factors that Decrease Prolactin Secretion
Estrogen (pregnancy)	Dopamine
Breast-feeding	Bromocriptine (dopamine agonist)
Sleep	Somatostatin
Stress	Prolactin (by negative feedback)
TRH	
Dopamine antagonists	

TRH = thyrotropin-releasing hormone.

C. Hormones of the posterior lobe of the pituitary

- are antidiuretic hormone (ADH) and oxytocin.
- are homologous nonapeptides.
- are **synthesized in hypothalamic nuclei** and are packaged in secretory granules with their respective **neurophysins**.
- travel down the nerve axons for secretion by the posterior pituitary.

1. ADH (see Chapter 5, VII)

- originates primarily in the **supraoptic nuclei** of the hypothalamus.
- regulates serum osmolarity by increasing the H_2O permeability of the late distal tubules and collecting ducts.

a. Regulation of ADH secretion (Table 7.4)

b. Actions of ADH

1. **↑ H_2O permeability (aquaporin 2, AQP2)** of the principal cells of the late distal tubule and collecting duct (via a **V_2 receptor** and an adenylate cyclase–cAMP mechanism).
2. **constriction of vascular smooth muscle** (via a **V_1 receptor** and an IP_3/Ca^{2+} mechanism).
3. **increased Na^+–$2Cl^-$–K^+ cotransport** in thick ascending limb, leading to

increased countercurrent multiplication and increased corticopapillary osmotic gradient.

4. **increase urea recycling** in inner medullary collecting ducts, leading to increased corticopapillary osmotic gradient.

c. Pathophysiology of ADH (see Chapter 5, VII)

2. Oxytocin

- originates primarily in the **paraventricular nuclei** of the hypothalamus.
- causes **ejection of milk from the breast** when stimulated by suckling.

a. Regulation of oxytocin secretion

1. *Suckling*

- is the major stimulus for oxytocin secretion.
- Afferent fibers carry impulses from the nipple to the spinal cord. Relays in the hypothalamus trigger the release of oxytocin from the posterior pituitary.
- The sight or sound of the infant may stimulate the hypothalamic neurons to secrete oxytocin, even in the absence of suckling.

2. *Dilation of the cervix and orgasm*

- increases the secretion of oxytocin.

b. Actions of oxytocin

1. *Contraction of myoepithelial cells in the breast*

- Milk is forced from the mammary alveoli into the ducts and ejected.

2. *Contraction of the uterus*

- During pregnancy, oxytocin receptors in the uterus are up-regulated as parturition approaches, although the role of oxytocin in normal labor is uncertain.
- Oxytocin can be used to induce labor and **reduce postpartum bleeding**.

---

table **7.4** Regulation of ADH Secretion

Factors that Increase ADH Secretion	Factors that Decrease ADH Secretion
↑ serum osmolarity	↓ serum osmolarity
Volume contraction	Ethanol
Pain	α-Agonists
Nausea (powerful stimulant)	ANP
Hypoglycemia	
Nicotine, opiates, antineoplastic drugs	

ADH = antidiuretic hormone; ANP = atrial natriuretic peptide.

IV. THYROID GLAND

A. Synthesis of thyroid hormones (Figure 7.8)

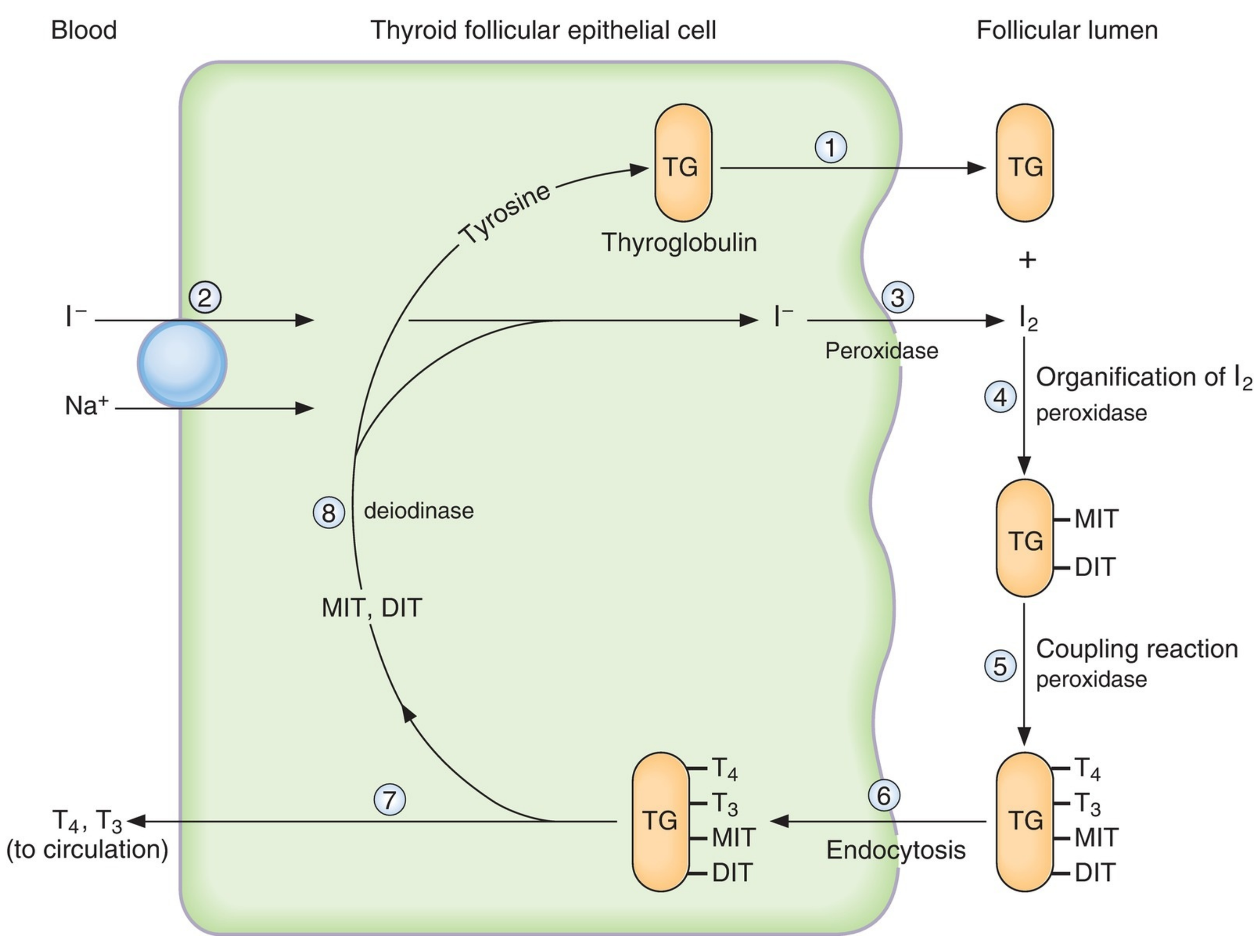


FIGURE 7.8. Steps in the synthesis of thyroid hormones. Each step is

stimulated by thyroid-stimulating hormone. DIT = diiodotyrosine; I^- = iodide; MIT = monoiodotyrosine; T_3 = triiodothyronine; T_4 = thyroxine; TG = thyroglobulin.

- Each step in synthesis is **stimulated by TSH**.

1. **Thyroglobulin** is synthesized from tyrosine in the thyroid follicular cells, packaged in secretory vesicles, and extruded into the follicular lumen (step 1).
2. **The iodide (I^-) pump, or Na^+–I^- cotransport**
   - is present in the thyroid follicular epithelial cells.
   - actively transports I^- into the thyroid follicular cells for subsequent incorporation into thyroid hormones (step 2).
   - is **inhibited by thiocyanate and perchlorate anions**.
3. **Oxidation of I^- to I_2**
   - is catalyzed by a **peroxidase enzyme** in the follicular cell membrane (step 3).
   - **I_2** is the reactive form, which will be "organified" by combination with tyrosine on thyroglobulin.
   - The peroxidase enzyme is **inhibited by propylthiouracil**, which is used therapeutically to reduce thyroid hormone synthesis for the treatment of hyperthyroidism.
   - The same peroxidase enzyme catalyzes the remaining organification and coupling reactions involved in the synthesis of thyroid hormones.
4. **Organification of I_2**
   - At the junction of the follicular cells and the follicular lumen, tyrosine residues of thyroglobulin react with I_2 to form **monoiodotyrosine (MIT) and diiodotyrosine (DIT)** (step 4).
   - High levels of I^- inhibit organification and, therefore, inhibit synthesis of thyroid hormone **(Wolff–Chaikoff effect)**.
5. **Coupling of MIT and DIT**
   - While MIT and DIT are attached to thyroglobulin, two coupling reactions occur (step 5).

a. When two molecules of DIT combine, **thyroxine (T_4)** is formed.

b. When one molecule of DIT combines with one molecule of MIT,

triiodothyronine (T_3) is formed.

- More T_4 than T_3 is synthesized, although T_3 is more active.

b. Iodinated thyroglobulin is stored in the follicular lumen until the thyroid gland is stimulated to secrete thyroid hormones.

6. Stimulation of thyroid cells by TSH

- When the thyroid cells are stimulated, iodinated thyroglobulin is taken back into the follicular cells by endocytosis (step 6). Lysosomal enzymes then digest thyroglobulin, releasing T_4 and T_3 into the circulation (step 7).
- Leftover MIT and DIT are deiodinated by **thyroid deiodinase** (step 8). The I_2 that is released is reutilized to synthesize more thyroid hormones. Therefore, deficiency of thyroid deiodinase mimics I_2 deficiency.

7. Binding of T_3 and T_4

- In the circulation, most of the T_3 and T_4 is bound to thyroxine-binding globulin **(TBG)**.
- In **hepatic failure**, TBG levels decrease, leading to a decrease in total thyroid hormone levels, but normal levels of free hormone.
- In **pregnancy**, TBG levels increase, leading to an increase in total thyroid hormone levels, but normal levels of free hormone (i.e., clinically, euthyroid).

8. Conversion of T_4 to T_3 and reverse T_3 (rT_3)

- In the peripheral tissues, T_4 is converted to T_3 by **5′-iodinase** (or to rT_3).
- **T_3 is more biologically active than T_4.**
- rT_3 is inactive.

B. Regulation of thyroid hormone secretion (Figure 7.9)

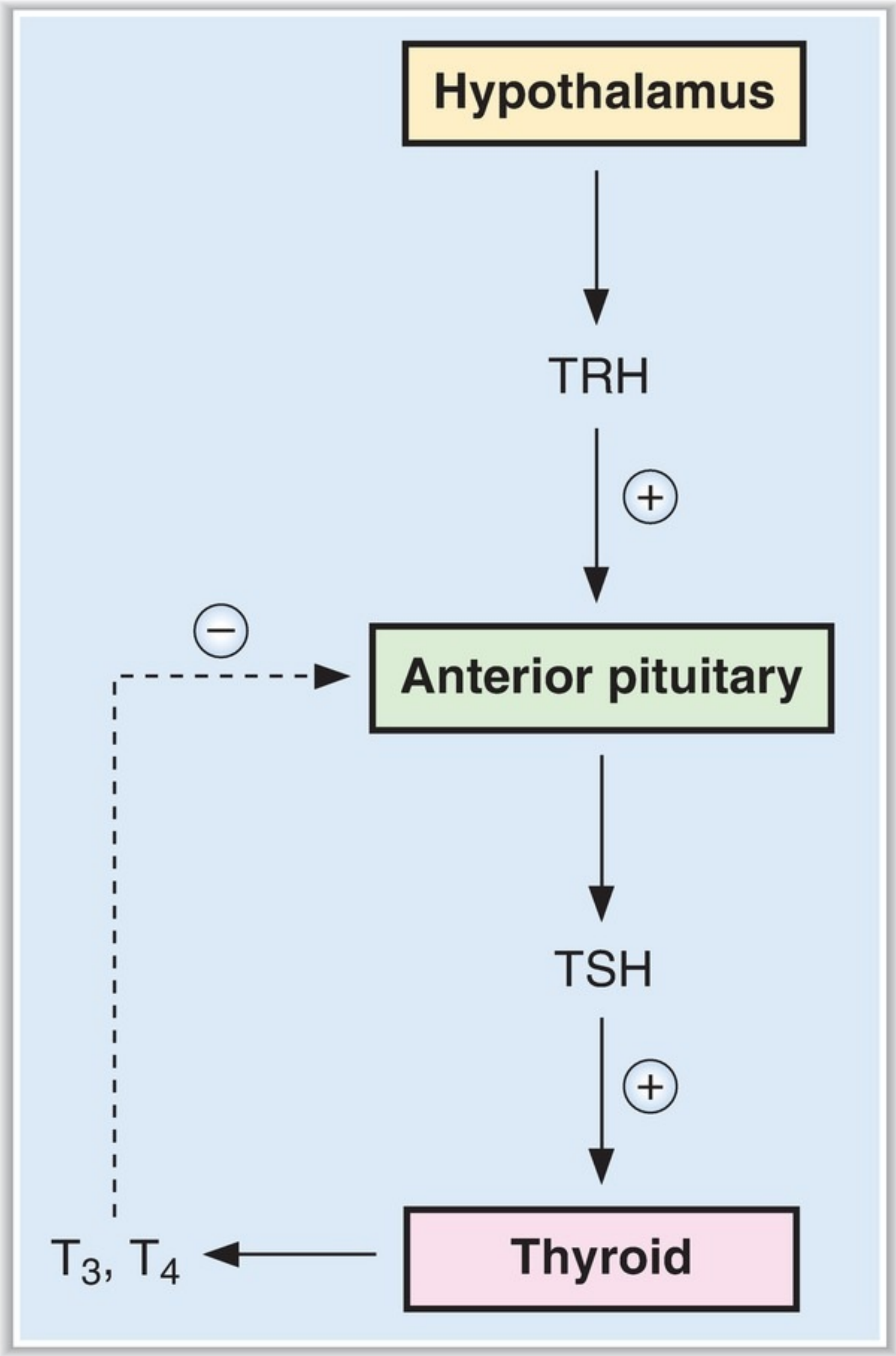

Hypothalamus
TRH
+
−
Anterior pituitary
TSH
+
Thyroid
T_3, T_4

FIGURE 7.9. Control of thyroid hormone secretion. T_3 = triiodothyronine; T_4 = thyroxine; TRH = thyrotropin-releasing hormone; TSH = thyroid-stimulating hormone.

1. Hypothalamic–pituitary control—TRH and TSH

a. TRH is secreted by the hypothalamus and stimulates the secretion of TSH by the anterior pituitary.

b. TSH increases both the synthesis and the secretion of thyroid hormones by the follicular cells via an **adenylate cyclase–cAMP** mechanism.

- Chronic elevation of TSH causes **hypertrophy** of the thyroid gland.

c. T_3 down-regulates TRH receptors in the anterior pituitary and thereby inhibits TSH secretion.

2. Thyroid-stimulating immunoglobulins

- are components of the immunoglobulin G (IgG) fraction of plasma proteins and are **antibodies to TSH receptors** on the thyroid gland.
- bind to TSH receptors and, like TSH, **stimulate the thyroid gland to secrete T_3 and T_4**.
- circulate in high concentrations in patients with **Graves disease**, which is characterized by high circulating levels of thyroid hormones and, accordingly, low concentrations of TSH (caused by feedback inhibition of thyroid hormones on the anterior pituitary).

C. Actions of thyroid hormone

- **T_3 is three to four times more potent than T_4**. The target tissues convert T_4 to T_3 (see IV A 8).

1. Growth

- Attainment of adult stature requires thyroid hormone.
- Thyroid hormones act synergistically with growth hormone and somatomedins to promote **bone formation**.
- Thyroid hormones stimulate **bone maturation** as a result of ossification and fusion of the growth plates. **In thyroid hormone deficiency, bone age is less than chronologic age.**

2. Central nervous system (CNS)

a. Perinatal period

- Maturation of the CNS **requires thyroid hormone in the perinatal period**.
- Thyroid hormone deficiency causes irreversible mental retardation. Because there is only a brief perinatal period when thyroid hormone replacement therapy is helpful, **screening for neonatal hypothyroidism is mandatory**.

b. Adulthood

- **Hyperthyroidism** causes hyperexcitability and irritability.
- **Hypothyroidism** causes listlessness, slowed speech, somnolence, impaired memory, and decreased mental capacity.

3. Autonomic nervous system

- Thyroid hormone has many of the same actions as the sympathetic nervous system because it **up-regulates β_1-adrenergic receptors in the heart**. Therefore, a useful adjunct therapy for hyperthyroidism is treatment with a β-adrenergic blocking agent, such as propranolol.

4. Basal metabolic rate (BMR)

- **O_2 consumption and BMR are increased** by thyroid hormone in all tissues except the brain, gonads, and spleen. The resulting increase in heat production underlies the role of thyroid hormone in temperature regulation.
- Thyroid hormone **increases the synthesis of Na^+, K^+-ATPase** and consequently increases O_2 consumption related to Na^+–K^+ pump activity.

5. Cardiovascular and respiratory systems

- Effects of thyroid hormone on cardiac output and ventilation rate combine to ensure that more O_2 is delivered to the tissues.

a. Heart rate and stroke volume are increased. These effects combine to produce **increased cardiac output**. Excess thyroid hormone can cause **high-output heart failure**.

b. Ventilation rate is increased.

6. Metabolic effects

- Overall, metabolism is increased to meet the demand for substrate associated with the increased rate of O_2 consumption.

a. Glucose absorption from the gastrointestinal tract is increased.

b. Glycogenolysis, **gluconeogenesis**, and **glucose oxidation** (driven by demand for ATP) are increased.

c. Lipolysis is increased.

d. Protein synthesis and degradation are increased. The overall effect of thyroid hormone is **catabolic**.

D. Pathophysiology of the thyroid gland (Table 7.5)

table **7.5** Pathophysiology of the Thyroid Gland

	Hyperthyroidism	Hypothyroidism
Symptoms	↑ metabolic rate Weight loss Negative nitrogen balance ↑ heat production (sweating) ↑ cardiac output Dyspnea Tremor, weakness Exophthalmos Goiter	↓ metabolic rate Weight gain Positive nitrogen balance ↓ heat production (cold sensitivity) ↓ cardiac output Hypoventilation Lethargy, mental slowness Drooping eyelids Myxedema Growth and mental retardation (perinatal) Goiter
Causes	Graves disease (antibodies to TSH receptor) Thyroid neoplasm	Thyroiditis (autoimmune thyroiditis; Hashimoto thyroiditis) Surgical removal of thyroid I^- deficiency Cretinism (congenital) ↓ TRH or TSH
TSH levels	↓ (because of feedback inhibition on anterior pituitary by high thyroid hormone levels)	↑ (because of decreased feedback inhibition on anterior pituitary by low thyroid hormone levels) ↓ (if primary defect is in hypothalamus or anterior pituitary)
Treatment	Propylthiouracil (inhibits thyroid hormone synthesis by blocking peroxidase) Thyroidectomy ^{131}I (destroys thyroid) β-blockers (adjunct therapy)	Thyroid hormone replacement

See Table 7.1 for abbreviations.

V. ADRENAL CORTEX AND ADRENAL

MEDULLA (FIGURE 7.10)

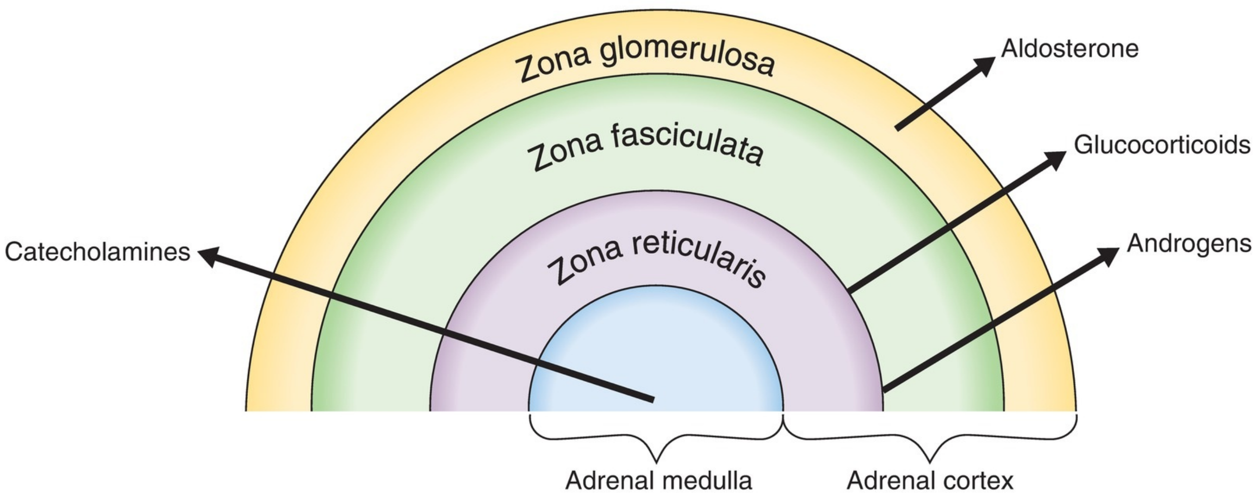


FIGURE 7.10. Secretory products of the adrenal cortex and medulla.

A. Adrenal cortex

1. **Synthesis of adrenocortical hormones** (Figure 7.11)
   - The **zona glomerulosa** produces **aldosterone**.
   - The **zonae fasciculata and reticularis** produce glucocorticoids (**cortisol**) and androgens (**dehydroepiandrosterone** and **androstenedione**).

   a. **21-carbon steroids**
   - include **progesterone, deoxycorticosterone, aldosterone,** and **cortisol**.
   - Progesterone is the precursor for the others in the 21-carbon series.
   - **Hydroxylation at C-21** leads to the production of deoxycorticosterone, which has mineralocorticoid (but not glucocorticoid) activity.
   - **Hydroxylation at C-17** leads to the production of glucocorticoids (cortisol).

   b. **19-carbon steroids**
   - have **androgenic activity** and are precursors to the estrogens.
   - If the steroid has been previously hydroxylated at C-17, the $C_{20,21}$ side

chain can be cleaved to yield the 19-carbon steroids **dehydroepiandrosterone** or **androstenedione** in the adrenal cortex.

- Adrenal androgens have a ketone group at C-17 and are excreted as **17-ketosteroids** in the urine.
- In the testes, androstenedione is converted to testosterone.

c. 18-carbon steroids

- have **estrogenic activity**.
- Oxidation of the A ring **(aromatization)** to produce estrogens occurs in the **ovaries** and **placenta**, but not in the adrenal cortex or testes.

2. Regulation of secretion of adrenocortical hormones

a. Glucocorticoid secretion (Figure 7.12)

- oscillates with a 24-hour periodicity or **circadian rhythm**.
- For those who sleep at night, **cortisol levels are highest just before waking** (≈8 AM) and **lowest in the evening** (≈12 midnight).

1. *Hypothalamic control—corticotropin-releasing hormone (CRH)*

- CRH-containing neurons are located in the **paraventricular nuclei** of the hypothalamus.
- When these neurons are stimulated, CRH is released into hypothalamic–hypophysial portal blood and delivered to the anterior pituitary.
- CRH binds to receptors on corticotrophs of the anterior pituitary and directs them to **synthesize POMC** (the precursor to ACTH) and **secrete ACTH**.
- The second messenger for CRH is **cAMP**.

2. *Anterior lobe of the pituitary—ACTH*

- **ACTH increases steroid hormone synthesis** in all zones of the adrenal cortex by stimulating **cholesterol desmolase** and increasing the conversion of cholesterol to pregnenolone.
- **ACTH also up-regulates its own receptor** so that the sensitivity of the adrenal cortex to ACTH is increased.
- Chronically increased levels of ACTH cause hypertrophy of the adrenal cortex.
- The second messenger for ACTH is **cAMP**.

3. *Negative feedback control—cortisol*

- **Cortisol inhibits the secretion of CRH** from the hypothalamus and the **secretion of ACTH** from the anterior pituitary.
- When cortisol (glucocorticoid) levels are chronically elevated, the

secretion of CRH and ACTH is inhibited by negative feedback.

- The **dexamethasone suppression test** is based on the ability of dexamethasone (a synthetic glucocorticoid) to inhibit ACTH secretion. In normal persons, low-dose dexamethasone inhibits or "suppresses" ACTH secretion and, consequently, cortisol secretion. In persons with **ACTH-secreting tumors**, low-dose dexamethasone does not inhibit cortisol secretion but high-dose dexamethasone does. In persons with **adrenal cortical tumors**, neither low- nor high-dose dexamethasone inhibits cortisol secretion.

b. Aldosterone secretion (see Chapter 3, VI B)

- is under tonic control by ACTH, but is separately regulated by the renin–angiotensin system and by serum potassium.

1. Renin–angiotensin–aldosterone system

a. Decreases in blood volume cause a decrease in renal perfusion pressure, which in turn increases renin secretion. **Renin**, an enzyme, catalyzes the conversion of angiotensinogen to angiotensin I. Angiotensin I is converted to **angiotensin II** by **angiotensin-converting enzyme (ACE)**.

b. Angiotensin II acts on the zona glomerulosa of the adrenal cortex to **increase the conversion of corticosterone to aldosterone**.

c. Aldosterone increases renal Na^+ reabsorption, thereby restoring extracellular fluid (ECF) volume and blood volume to normal.

2. Hyperkalemia increases aldosterone secretion. Aldosterone increases renal K^+ secretion, restoring serum $[K^+]$ to normal.

3. Actions of glucocorticoids (**cortisol**)

- Overall, glucocorticoids are essential for the **response to stress**.

a. Stimulation of gluconeogenesis

- Glucocorticoids increase gluconeogenesis by the following mechanisms:

1. They **increase protein catabolism** in muscle and decrease protein synthesis, thereby providing more amino acids to the liver for gluconeogenesis.

2. They **decrease glucose utilization** and insulin sensitivity of adipose tissue.

3. They **increase lipolysis**, which provides more glycerol to the liver for gluconeogenesis.

b. Anti-inflammatory effects

1. Glucocorticoids **induce the synthesis of lipocortin**, an **inhibitor of phospholipase A_2**. (Phospholipase A_2 is the enzyme that liberates arachidonate from membrane phospholipids, providing the precursor for prostaglandin and leukotriene synthesis.) Because prostaglandins and leukotrienes are involved in the inflammatory response, glucocorticoids have anti-inflammatory properties by inhibiting the formation of the precursor (arachidonate).
2. **Glucocorticoids inhibit the production of interleukin-2** (IL-2) and inhibit the proliferation of T lymphocytes.
3. Glucocorticoids **inhibit the release of histamine and serotonin** from mast cells and platelets.

c. Suppression of the immune response

- Glucocorticoids **inhibit the production of IL-2** and T lymphocytes, both of which are critical for cellular immunity. In pharmacologic doses, glucocorticoids are used to **prevent rejection of transplanted organs**.

d. Maintenance of vascular responsiveness to catecholamines

- Cortisol **up-regulates α_1 receptors** on arterioles, increasing their sensitivity to the vasoconstrictor effect of norepinephrine. Thus, with cortisol excess, arterial pressure increases; with cortisol deficiency, arterial pressure decreases.

4. Actions of mineralocorticoids (aldosterone) (see Chapters 3 and 5)

a. ↑ renal Na^+ reabsorption (action on the principal cells of the late distal tubule and collecting duct).

b. ↑ renal K^+ secretion (action on the principal cells of the late distal tubule and collecting duct).

c. ↑ renal H^+ secretion (action on the α-intercalated cells of the late distal tubule and collecting duct).

5. Pathophysiology of the adrenal cortex (Table 7.6)

a. Adrenocortical insufficiency

1. *Primary adrenocortical insufficiency—Addison disease*
   - is most commonly caused by autoimmune **destruction of the adrenal cortex** and causes acute **adrenal crisis**.
   - is characterized by the following:

a. ↓ **adrenal glucocorticoid, androgen, and mineralocorticoid.**

b. ↑ **ACTH**. (Low cortisol levels stimulate ACTH secretion by negative feedback.)

c. **Hypoglycemia** (caused by cortisol deficiency).

d. Weight loss, weakness, nausea, and vomiting.

e. **Hyperpigmentation**. (Low cortisol levels stimulate ACTH secretion; ACTH contains the MSH fragment.)

f. ↓ pubic and axillary hair in women (caused by the deficiency of adrenal androgens).

g. **ECF volume contraction, hypotension, hyperkalemia,** and **metabolic acidosis** (caused by aldosterone deficiency).

2. *Secondary adrenocortical insufficiency*

- is caused by primary **deficiency of ACTH**.
- **does *not* exhibit hyperpigmentation** (because there is a deficiency of ACTH).
- **does *not* exhibit volume contraction, hyperkalemia,** or **metabolic acidosis** (because aldosterone levels are normal).
- Symptoms are otherwise similar to those of Addison disease.

b. Adrenocortical excess—Cushing syndrome

- is most commonly caused by the administration of **pharmacologic doses of glucocorticoids**.
- is also caused by primary **hyperplasia of the adrenal glands**.
- is called **Cushing disease** when it is caused by overproduction of ACTH.
- is characterized by the following:

1. ↑ **cortisol and androgen levels.**

2. ↓ ACTH (if caused by primary adrenal hyperplasia or pharmacologic doses of glucocorticosteroids); ↑ ACTH (if caused by overproduction of ACTH, as in Cushing disease).

3. **hyperglycemia** (caused by elevated cortisol levels).

4. ↑ protein catabolism and muscle wasting.

5. central obesity (round face, supraclavicular fat, buffalo hump).

6. poor wound healing.

7. **virilization of women** (caused by elevated levels of adrenal androgens).

8. **hypertension** (caused by elevated levels of cortisol and aldosterone).

9. osteoporosis (elevated cortisol levels cause increased bone resorption).

10. striae.

- **Ketoconazole**, an inhibitor of steroid hormone synthesis, can be used to treat Cushing disease.

c. Hyperaldosteronism—Conn syndrome

- is caused by an aldosterone-secreting tumor.
- is characterized by the following:

1. hypertension (because aldosterone increases Na^+ reabsorption, which leads to increases in ECF volume and blood volume).

2. hypokalemia (because aldosterone increases K^+ secretion).

3. metabolic alkalosis (because aldosterone increases H^+ secretion).

4. ↓ **renin** secretion (because increased ECF volume and blood pressure inhibit renin secretion by negative feedback).

d. 21β-Hydroxylase deficiency

- is the most common biochemical abnormality of the steroidogenic pathway (see Figure 7.11).
- belongs to a group of disorders characterized by **adrenogenital syndrome**.
- is characterized by the following:

1. ↓ **cortisol and aldosterone levels** (because the enzyme block prevents the production of 11-deoxycorticosterone and 11-deoxycortisol, the precursors for cortisol and aldosterone).

2. ↑ 17-hydroxyprogesterone and progesterone levels (because of accumulation of intermediates above the enzyme block).

3. ↑ **ACTH** (because of decreased feedback inhibition by cortisol).

4. hyperplasia of zona fasciculata and zona reticularis (because of high levels of ACTH).

5. ↑ **adrenal androgens** (because 17-hydroxyprogesterone is their major precursor) and ↑ **urinary 17-ketosteroids**.

6. virilization in women.

7. early acceleration of linear growth and early appearance of pubic and axillary hair.

8. suppression of gonadal function in both men and women.

e. 17α-Hydroxylase deficiency is characterized by the following:

1. ↓ **androgen and glucocorticoid levels** (because the enzyme block prevents the production of 17-hydroxypregnenolone and 17-hydroxyprogesterone).

2. ↑ **mineralocorticoid levels** (because intermediates accumulate to the left of the enzyme block and are shunted toward the production of mineralocorticoids).

3. lack of pubic and axillary hair (which depends on adrenal androgens) in women.

4. hypoglycemia (because of decreased glucocorticoids).

5. metabolic alkalosis, hypokalemia, and hypertension (because of increased mineralocorticoids).

6. ↑ **ACTH** (because decreased cortisol levels stimulate ACTH secretion by negative feedback).

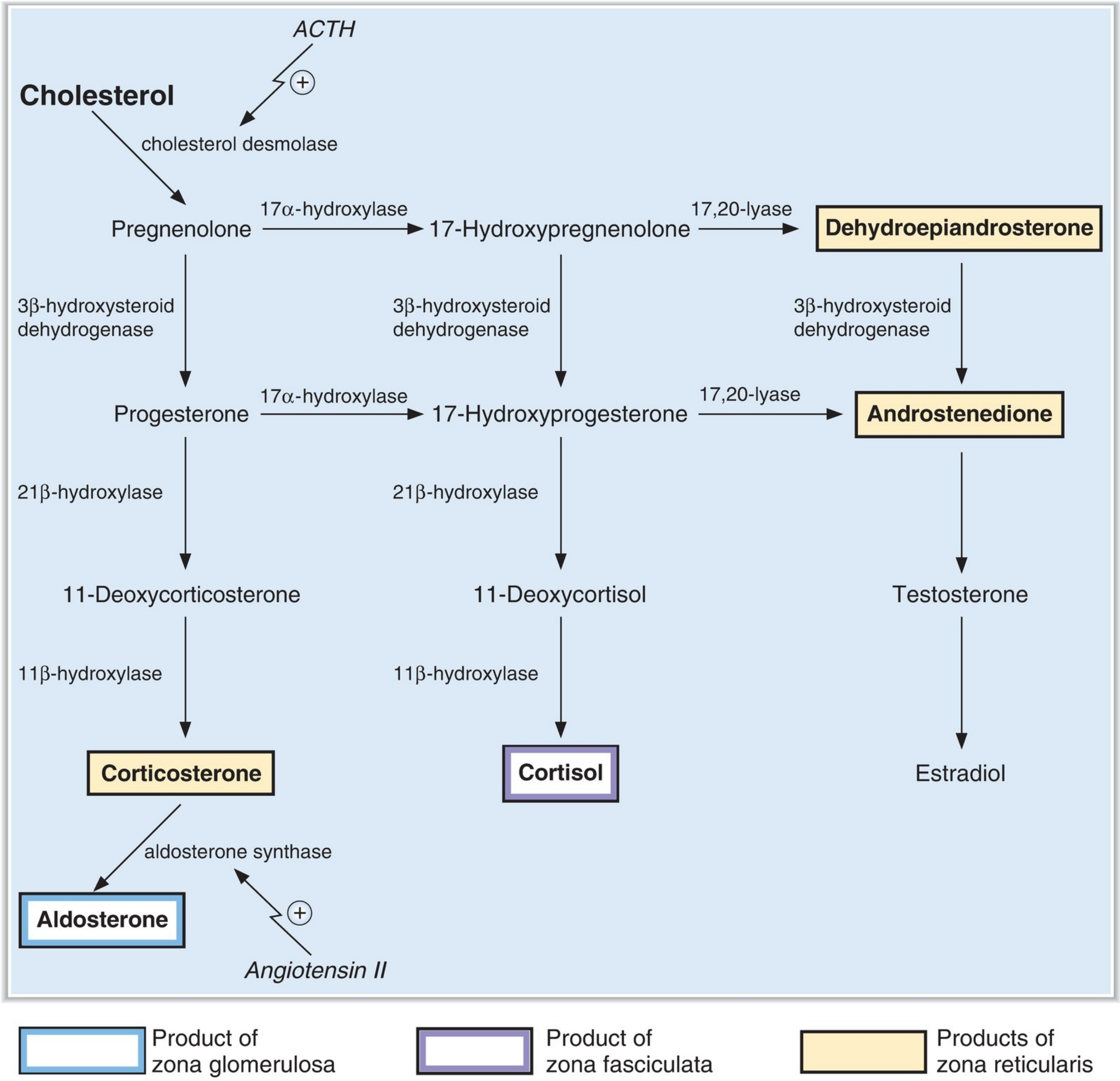
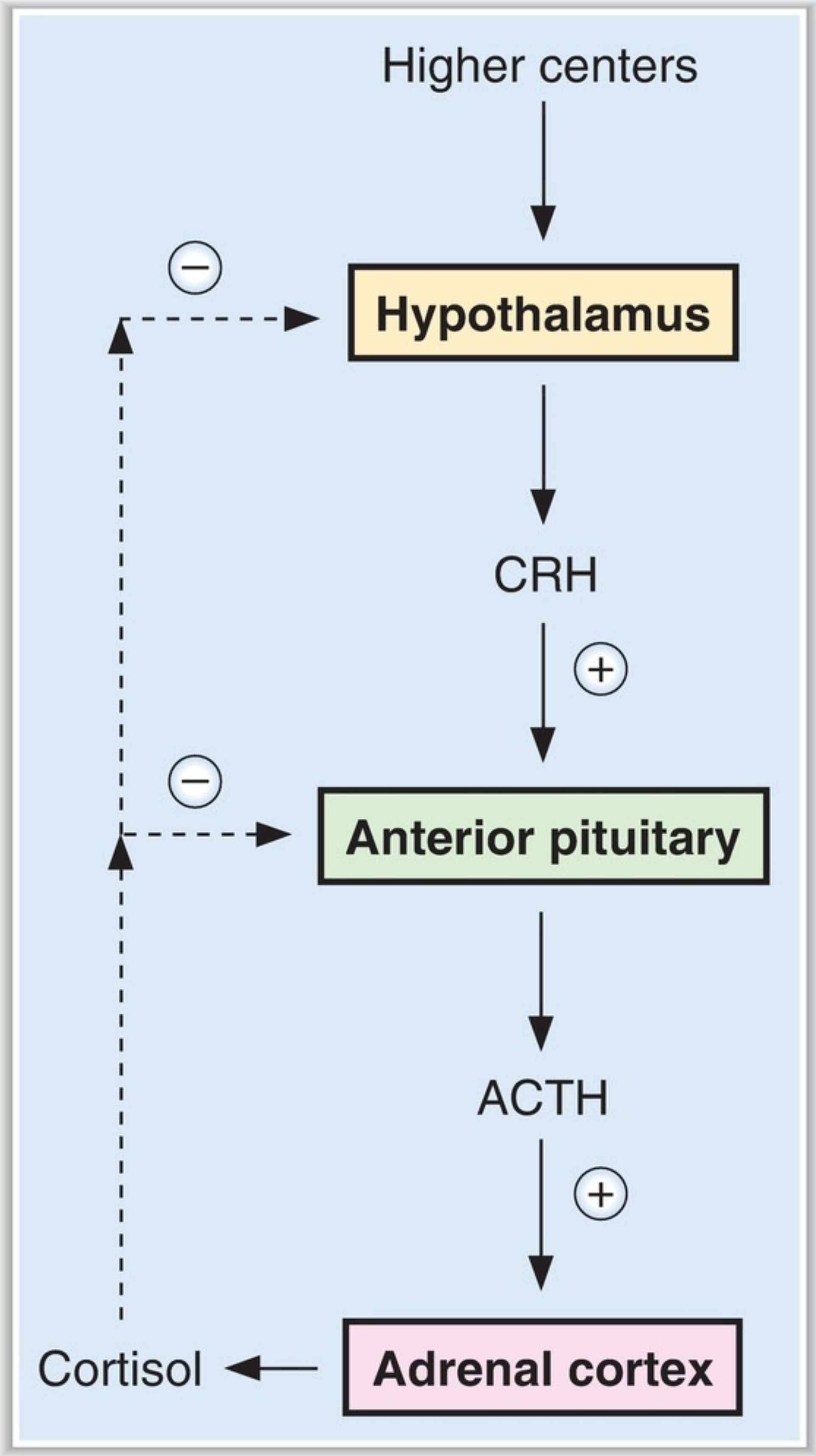


FIGURE 7.11. Synthetic pathways for glucocorticoids, androgens, and mineralocorticoids in the adrenal cortex. ACTH = adrenocorticotropic hormone.



Higher centers
Hypothalamus
CRH
Anterior pituitary
ACTH
Adrenal cortex
Cortisol

FIGURE 7.12. Control of glucocorticoid secretion. ACTH = adrenocorticotropic hormone; CRH = corticotropin-releasing hormone.

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table **7.6** Pathophysiology of the Adrenal Cortex

Disorder	Clinical Features	ACTH Levels	Treatment
Addison disease (e.g., primary adrenocortical insufficiency)	Hypoglycemia Anorexia, weight loss, nausea, vomiting Weakness Hypotension Hyperkalemia Metabolic acidosis Decreased pubic and axillary hair in women Hyperpigmentation	Increased (negative feedback effect of decreased cortisol)	Replacement of glucocorticoids and mineralocorticoids
Cushing syndrome (e.g., primary adrenal hyperplasia)	Hyperglycemia Muscle wasting Central obesity Round face, supraclavicular fat, buffalo hump Osteoporosis Striae Virilization and menstrual disorders in women Hypertension	Decreased (negative feedback effect of increased cortisol)	Ketoconazole Metyrapone
Cushing disease (excess ACTH)	Same as Cushing syndrome	Increased	Surgical removal of ACTH-secreting tumor
Conn syndrome (aldosterone-secreting tumor)	Hypertension Hypokalemia Metabolic alkalosis Decreased renin		Spironolactone (aldosterone antagonist) Surgical removal of aldosterone-secreting tumor
21β-Hydroxylase deficiency (↓ glucocorticoids and mineralocorticoids; ↑ adrenal androgens)	Virilization of women Early acceleration of linear growth Early appearance of pubic and axillary hair Symptoms of glucocorticoid and mineralocorticoid deficiency	Increased (negative feedback effect of decreased cortisol)	Replacement of glucocorticoids and mineralocorticoids
17α-Hydroxylase deficiency (↓ adrenal androgens and glucocorticoids; ↑ mineralocorticoids)	Lack of pubic and axillary hair in women Symptoms of glucocorticoid deficiency Symptoms of mineralocorticoid excess	Increased (negative feedback effect of decreased cortisol)	Replacement of glucocorticoids Aldosterone antagonist

See Table 7.1 for abbreviation.

B. Adrenal medulla (see Chapter 2, I A 4)

VI. ENDOCRINE PANCREAS–GLUCAGON AND INSULIN (TABLE 7.7)

table **7.7** Comparison of Insulin and Glucagon

	Stimulus for Secretion	Major Actions	Overall Effect on Blood Levels
Insulin (tyrosine kinase receptor)	↑ blood glucose ↑ amino acids ↑ fatty acids Glucagon GIP Growth hormone Cortisol	Increases glucose uptake into cells and glycogen formation Decreases glycogenolysis and gluconeogenesis Increases protein synthesis Increases fat deposition and decreases lipolysis Increases K^+ uptake into cells	↓ [glucose] ↓ [amino acid] ↓ [fatty acid] ↓ [ketoacid] Hypokalemia
Glucagon (cAMP mechanism)	↓ blood glucose ↑ amino acids CCK Norepinephrine, epinephrine, ACh	Increases glycogenolysis and gluconeogenesis Increases lipolysis and ketoacid production	↑ [glucose] ↑ [fatty acid] ↑ [ketoacid]

ACh = acetylcholine; cAMP = cyclic adenosine monophosphate; CCK = cholecystokinin; GIP = glucose-dependent insulinotropic peptide.

A. Organization of the endocrine pancreas

- The islets of Langerhans contain three major cell types (Table 7.8). Other cells secrete pancreatic polypeptide.
- **Gap junctions** link beta cells to each other, alpha cells to each other, and beta cells to alpha cells for rapid communication.
- The portal blood supply of the islets allows blood from the beta cells (containing insulin) to bathe the alpha and delta cells, again for rapid cell-to-cell communication.

table **7.8** Cell Types of the Islets of Langerhans

Type of Cell	Location	Function
Beta	Central islet	Secrete insulin
Alpha	Outer rim of islet	Secrete glucagon
Delta	Intermixed	Secrete somatostatin and gastrin

B. Glucagon

1. Regulation of glucagon secretion (Table 7.9)

- The major factor that regulates glucagon secretion is the blood glucose concentration. **Decreased blood glucose stimulates glucagon secretion.**
- Increased blood amino acids stimulate glucagon secretion, which prevents hypoglycemia caused by unopposed insulin in response to a high protein meal.

2. Actions of glucagon

- Glucagon acts on the liver and adipose tissue.
- The second messenger for glucagon is **cAMP**.

a. Glucagon increases the blood glucose concentration.

1. It **increases glycogenolysis** and prevents the recycling of glucose into glycogen.

2. It **increases gluconeogenesis**. Glucagon decreases the production of fructose 2,6-bisphosphate, decreasing phosphofructokinase activity; in effect, substrate is directed toward glucose formation rather than toward glucose breakdown.

b. Glucagon increases blood fatty acid and ketoacid concentration.

- Glucagon **increases lipolysis**. The inhibition of fatty acid synthesis in effect "shunts" substrates toward gluconeogenesis.
- Ketoacids (β-hydroxybutyrate and acetoacetate) are produced from acetyl-coenzyme A (CoA), which results from fatty acid degradation.

c. Glucagon increases urea production.

- Amino acids are used for gluconeogenesis (stimulated by glucagon), and the resulting amino groups are incorporated into urea.

table **7.9** Regulation of Glucagon Secretion

Factors that Increase Glucagon Secretion	Factors that Decrease Glucagon Secretion
↓ blood glucose	↑ blood glucose
↑ amino acids (especially arginine)	Insulin
CCK (alerts alpha cells to a protein meal)	Somatostatin
Norepinephrine, epinephrine	Fatty acids, ketoacids
ACh	

ACh = acetylcholine; CCK = cholecystokinin.

C. Insulin

- contains an A chain and a B chain, joined by two disulfide bridges.
- **Proinsulin is synthesized as a single-chain peptide.** Within storage granules, a connecting peptide (C peptide) is removed by proteases to yield insulin. The **C peptide** is packaged and secreted along with insulin, and its concentration is used to monitor beta cell function in diabetic patients who are receiving exogenous insulin.

1. Regulation of insulin secretion (Table 7.10)

a. Blood glucose concentration

- is the major factor that regulates insulin secretion.
- **Increased blood glucose stimulates insulin secretion.** An initial burst of insulin is followed by sustained secretion.

b. Mechanism of insulin secretion

- Glucose, the stimulant for insulin secretion, binds to the **Glut 2** receptor on the beta cells.
- Inside the beta cells, glucose is oxidized to **ATP**, which closes K^+ channels in the cell membrane and leads to **depolarization** of the beta cells. Similar to the action of ATP, **sulfonylurea drugs** (e.g., tolbutamide, glyburide) stimulate insulin secretion by closing these K^+ channels.
- Depolarization **opens Ca^{2+} channels**, which leads to an increase in intracellular [Ca^{2+}] and then to **secretion of insulin**.

2. Insulin receptor (see Figure 7.3)

- is found on target tissues for insulin.

- is a tetramer, with two α subunits and two β subunits.

a. The α subunits are located on the extracellular side of the cell membrane.

b. The **β subunits** span the cell membrane and have **intrinsic tyrosine kinase activity.** When insulin binds to the receptor, tyrosine kinase is activated and autophosphorylates the β subunits. The phosphorylated receptor then phosphorylates intracellular proteins.

c. The insulin–receptor complexes enter the target cells.

d. Insulin **down-regulates** its own receptors in target tissues.

- Therefore, the number of insulin receptors is **increased in starvation** and **decreased in obesity** (e.g., type 2 diabetes mellitus).

3. Actions of insulin

- Insulin acts on the liver, adipose tissue, and muscle.

a. Insulin decreases blood glucose concentration by the following mechanisms:

1. It **increases uptake of glucose** into target cells by directing the insertion of glucose transporters into cell membranes. As glucose enters the cells, the blood glucose concentration decreases.

2. It **promotes formation of glycogen** from glucose in muscle and liver and simultaneously inhibits glycogenolysis.

3. It **decreases gluconeogenesis**. Insulin increases the production of fructose 2,6-bisphosphate, increasing phosphofructokinase activity. In effect, substrate is directed away from glucose formation.

b. Insulin decreases blood fatty acid and ketoacid concentrations.

- In adipose tissue, insulin **stimulates fat deposition** and **inhibits lipolysis**.
- Insulin **inhibits ketoacid formation** in the liver because decreased fatty acid degradation provides less acetyl-CoA substrate for ketoacid formation.

c. Insulin decreases blood amino acid concentration.

- Insulin stimulates amino acid uptake into cells, increases protein synthesis, and inhibits protein degradation. Thus, insulin is **anabolic**.

d. Insulin decreases blood K^+ concentration.

- Insulin increases K^+ uptake into cells, thereby decreasing blood [K^+].

4. Insulin pathophysiology—diabetes mellitus

- **Case study:** A woman is brought to the emergency room. She is hypotensive and breathing rapidly; her breath has the odor of ketones. Analysis of her blood shows severe hyperglycemia, hyperkalemia, and blood gas values that are consistent with metabolic acidosis.
- **Explanation:**

a. Hyperglycemia

- is consistent with insulin deficiency.
- In the absence of insulin, glucose uptake into cells is decreased, as is storage of glucose as glycogen.
- If tests were performed, the woman's blood would have shown increased levels of both amino acids (because of increased protein catabolism) and fatty acids (because of increased lipolysis).

b. Hypotension

- is a result of ECF volume contraction.
- The high blood glucose concentration results in a high filtered load of glucose that exceeds the reabsorptive capacity (T_m) of the kidney.
- The unreabsorbed glucose acts as an osmotic diuretic in the urine and causes ECF volume contraction.

c. Metabolic acidosis

- is caused by overproduction of ketoacids (β-hydroxybutyrate and acetoacetate).
- The **increased ventilation rate**, or Kussmaul respiration, is the respiratory compensation for metabolic acidosis.

d. Hyperkalemia

- results from the lack of insulin; normally, insulin promotes K^+ uptake into cells.

---

table 7.10 Regulation of Insulin Secretion

Factors that Increase Insulin Secretion	Factors that Decrease Insulin Secretion
↑ blood glucose	↓ blood glucose
↑ amino acids (arginine, lysine, leucine)	Somatostatin
↑ fatty acids	Norepinephrine, epinephrine
Glucagon	
GIP	
ACh	

ACh = acetylcholine; GIP = glucose-dependent insulinotropic peptide.

D. Somatostatin

- is secreted by the delta cells of the pancreas.
- inhibits the secretion of insulin, glucagon, and gastrin.

VII. CALCIUM METABOLISM (PARATHYROID HORMONE, VITAMIN D, CALCITONIN) (TABLE 7.11)

table 7.11 Summary of Hormones that Regulate Ca^{2+}

	PTH	Vitamin D	Calcitonin
Stimulus for secretion	↓ serum [Ca^{2+}]	↓ serum [Ca^{2+}] ↑ PTH ↓ serum [phosphate]	↑ serum [Ca^{2+}]
Action on			
Bone	↑ resorption	↑ resorption	↓ resorption
Kidney	↓ P reabsorption (↑ urinary cAMP) ↑ Ca^{2+} reabsorption	↑ P reabsorption ↑ Ca^{2+} reabsorption	
Intestine	↑ Ca^{2+} absorption (via activation of vitamin D)	↑ Ca^{2+} absorption (calbindin D-28K) ↑ P absorption	
Overall effect on			
Serum [Ca^{2+}]	↑	↑	↓
Serum [phosphate]	↓	↑	

cAMP = cyclic adenosine monophosphate. See Table 7.1 for other abbreviation.

A. Overall Ca^{2+} homeostasis (Figure 7.13)

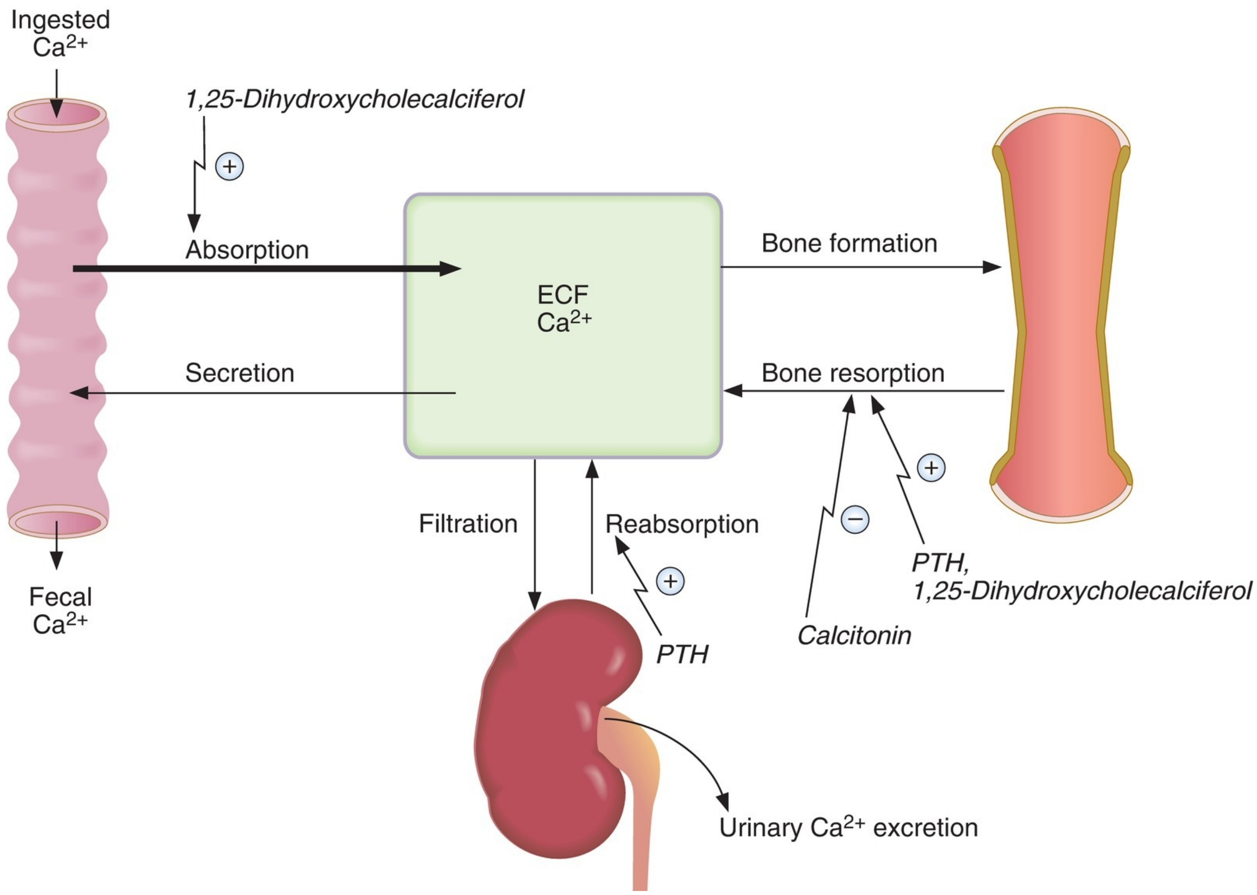

FIGURE 7.13. Hormonal regulation of Ca^{2+} metabolism. ECF = extracellular fluid; PTH = parathyroid hormone.

- 40% of the total Ca^{2+} in blood is **bound to plasma proteins**.
- 60% of the total Ca^{2+} in blood is not bound to proteins and is ultrafilterable. **Ultrafilterable Ca^{2+}** includes Ca^{2+} that is complexed to anions such as phosphate and free, ionized Ca^{2+}.
- **Free, ionized Ca^{2+} is biologically active.**
- Serum [Ca^{2+}] is determined by the interplay of intestinal absorption, renal excretion, and bone remodeling (bone resorption and formation). Each component is hormonally regulated.
- To maintain Ca^{2+} balance, net intestinal absorption must be balanced by urinary excretion.

1. Positive Ca^{2+} balance

- is seen in growing children.
- Intestinal Ca^{2+} absorption exceeds urinary excretion, and the excess is

deposited in the growing bones.

2. Negative Ca^{2+} balance

- is seen in women during pregnancy or lactation.
- Intestinal Ca^{2+} absorption is less than Ca^{2+} excretion, and the deficit comes from the maternal bones.

B. Parathyroid hormone (PTH)

- is the major hormone for the regulation of serum [Ca^{2+}].
- is synthesized and secreted by the **chief cells** of the parathyroid glands.

1. Secretion of PTH

- is controlled by the serum [Ca^{2+}] binding to **Ca^{2+}-sensing receptors** in the parathyroid chief cell membrane. **Decreased serum [Ca^{2+}] increases PTH secretion**, whereas increased serum Ca^{2+} decreases PTH secretion.
- Decreased serum Ca^{2+} causes decreased binding to the Ca^{2+}-sensing receptor, which stimulates PTH secretion.
- Mild decreases in serum [Mg^{2+}] stimulate PTH secretion.
- Severe decreases in serum [Mg^{2+}] inhibit PTH secretion and produce symptoms of hypoparathyroidism (e.g., hypocalcemia).
- The second messenger for PTH secretion by the parathyroid gland is cAMP.

2. Actions of PTH

- are coordinated to produce an **increase in serum [Ca^{2+}]** and a **decrease in serum [phosphate]**.
- The second messenger for PTH actions on its target tissues is **cAMP**.

a. PTH increases bone resorption, which brings both Ca^{2+} and phosphate from bone mineral into the ECF. Alone, this effect on bone would not increase the serum ionized [Ca^{2+}] because phosphate complexes Ca^{2+}.

- Resorption of the organic matrix of bone is reflected in **increased hydroxyproline excretion**.

b. PTH inhibits renal phosphate reabsorption in the **proximal tubule** and, therefore, increases phosphate excretion **(phosphaturic effect)**. As a result, the phosphate resorbed from bone is excreted in the urine, allowing the serum ionized [Ca^{2+}] to increase.

- cAMP generated as a result of the action of PTH on the proximal tubule is excreted in the urine **(urinary cAMP)**.

c. **PTH increases renal Ca^{2+} reabsorption** in the **distal tubule**, which also increases the serum [Ca^{2+}].

d. **PTH increases intestinal Ca^{2+} absorption** indirectly by stimulating the production of 1,25-dihydroxycholecalciferol in the kidney (see VII C).

3. Pathophysiology of PTH (Table 7.12)

a. Primary hyperparathyroidism

- is most commonly caused by **parathyroid adenoma**.
- is characterized by the following:

1. ↑ serum [Ca^{2+}] (hypercalcemia).

2. ↓ serum [phosphate] (hypophosphatemia).

3. ↑ urinary phosphate excretion (phosphaturic effect of PTH).

4. ↑ urinary Ca^{2+} excretion (caused by the increased filtered load of Ca^{2+}).

5. ↑ urinary cAMP.

6. ↑ bone resorption.

b. Humoral hypercalcemia of malignancy

- is caused by **PTH-related peptide (PTH-rp)** secreted by some malignant tumors (e.g., breast, lung). PTH-rp has all of the physiologic actions of PTH, including increased bone resorption, increased renal Ca^{2+} reabsorption, and decreased renal phosphate reabsorption.
- is characterized by the following:

1. ↑ serum [Ca^{2+}] (hypercalcemia).

2. ↓ serum [phosphate] (hypophosphatemia).

3. ↑ urinary phosphate excretion (phosphaturic effect of PTH-rp).

4. ↓ serum PTH levels (due to feedback inhibition from the high serum Ca^{2+}).

- Can be treated with an inhibitor of bone resorption (e.g., etidronate or pamidronate) and furosemide.

c. Hypoparathyroidism

- is most commonly a result of **thyroid surgery**, or it is **congenital**.
- is characterized by the following:

1. ↓ serum [Ca^{2+}] (hypocalcemia) and **tetany**.

2. ↑ serum [phosphate] (hyperphosphatemia).
3. ↓ urinary phosphate excretion.

d. Pseudohypoparathyroidism type Ia—Albright hereditary osteodystrophy

- is the result of **defective G_s protein** in the kidney and bone, which causes end-organ **resistance to PTH**.
- **Hypocalcemia** and **hyperphosphatemia** occur (as in hypoparathyroidism), which are not correctable by the administration of exogenous PTH.
- Circulating **PTH levels are elevated** (stimulated by hypocalcemia).

e. Chronic renal failure

- Decreased glomerular filtration rate (GFR) leads to decreased filtration of phosphate, phosphate retention, and **increased serum [phosphate]**.
- Increased serum phosphate complexes Ca^{2+} and leads to **decreased ionized [Ca^{2+}]**.
- **Decreased production of 1,25-dihydroxycholecalciferol** by the diseased renal tissue also contributes to the decreased ionized [Ca^{2+}] (see VII C 1).
- Decreased [Ca^{2+}] causes **secondary hyperparathyroidism**.
- The combination of increased PTH levels and decreased 1,25-dihydroxycholecalciferol produces **renal osteodystrophy**, in which there is increased bone resorption and osteomalacia.

f. Familial hypocalciuric hypercalcemia (FHH)

- autosomal dominant disorder with decreased urinary Ca^{2+} excretion and increased serum Ca^{2+}.
- caused by **inactivating mutations** of the Ca^{2+}-sensing receptors that regulate PTH secretion.

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table 7.12 Pathophysiology of PTH

Disorder	PTH	1,25-Dihydroxy-cholecalciferol	Bone	Urine	Serum [Ca^{2+}]	Serum [P]
Primary hyper-parathyroidism	↑	↑ (PTH stimulates 1α-hydroxylase)	↑ resorption	↑ P excretion (phosphaturia) ↑ Ca^{2+} excretion (high filtered load of Ca^{2+}) ↑ urinary cAMP	↑	↓
Humoral hyper-calcemia of malignancy	↓	—	↑ resorption	↑ P excretion	↑	↓
Surgical hypo-parathyroidism	↓	↓	↓ resorption	↓ P excretion ↓ urinary cAMP	↓	↑
Pseudohypo-parathyroidism	↑	↓	↓ resorption (defective G_s)	↓ P excretion ↓ urinary cAMP (defective G_s)	↓	↑
Chronic renal failure	↑ (2°)	↓ (caused by renal failure)	Osteomalacia (caused by ↓ 1,25-dihydroxy-cholecalciferol) ↑ resorption (caused by ↑ PTH)	↓ P excretion (caused by ↓ GFR)	↓ (caused by ↓ 1,25-dihydroxy-cholecalciferol)	↑ (caused by ↓ P excretion)

cAMP = cyclic adenosine monophosphate; GFR = glomerular filtration rate. See Table 7.1 for other abbreviation.

C. Vitamin D

- provides Ca^{2+} and phosphate to ECF for bone mineralization.
- In children, vitamin D deficiency causes **rickets**.
- In adults, vitamin D deficiency causes **osteomalacia**.

1. Vitamin D metabolism (Figure 7.14)

- Cholecalciferol, 25-hydroxycholecalciferol, and 24,25-dihydroxycholecalciferol are inactive.
- The active form of vitamin D is **1,25-dihydroxycholecalciferol**.
- The production of 1,25-dihydroxycholecalciferol in the kidney is catalyzed by the enzyme 1α-hydroxylase.
- **1α-hydroxylase activity is increased** by the following:

1. ↓ serum [Ca^{2+}].

2. ↑ PTH levels.

3. ↓ serum [phosphate].

2. Actions of 1,25-dihydroxycholecalciferol

- are coordinated to **increase both [Ca^{2+}] and [phosphate]** in ECF to

mineralize new bone.

a. **Increases intestinal Ca^{2+} absorption**. Vitamin D–dependent Ca^{2+}-binding protein **(calbindin D-28K)** is induced by 1,25-dihydroxycholecalciferol.

- PTH increases intestinal Ca^{2+} absorption indirectly by stimulating 1α-hydroxylase and increasing production of the active form of vitamin D.

b. **Increases intestinal phosphate absorption.**

c. **Increases renal reabsorption of Ca^{2+} and phosphate**, analogous to its actions on the intestine.

d. **Increases bone resorption**, which provides Ca^{2+} and phosphate from "old" bone to mineralize "new" bone.

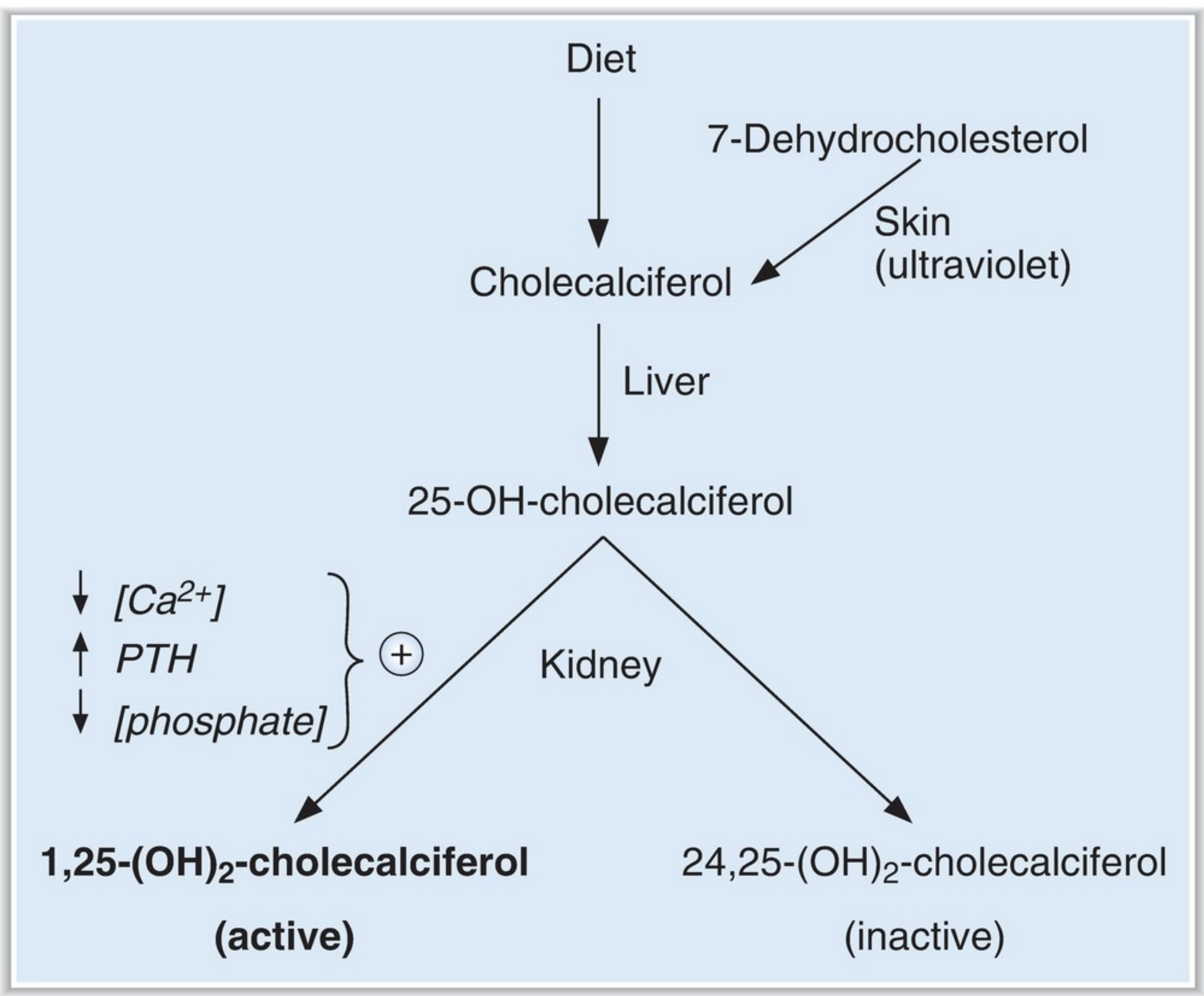


FIGURE 7.14. Steps and regulation in the synthesis of 1,25-dihydroxycholecalciferol. PTH = parathyroid hormone.

D. Calcitonin

- is synthesized and secreted by the **parafollicular cells** of the thyroid.
- secretion is stimulated by an increase in serum [Ca^{2+}].
- acts primarily to **inhibit bone resorption**.
- can be used to **treat hypercalcemia**.

VIII. SEXUAL DIFFERENTIATION (FIGURE 7.15)

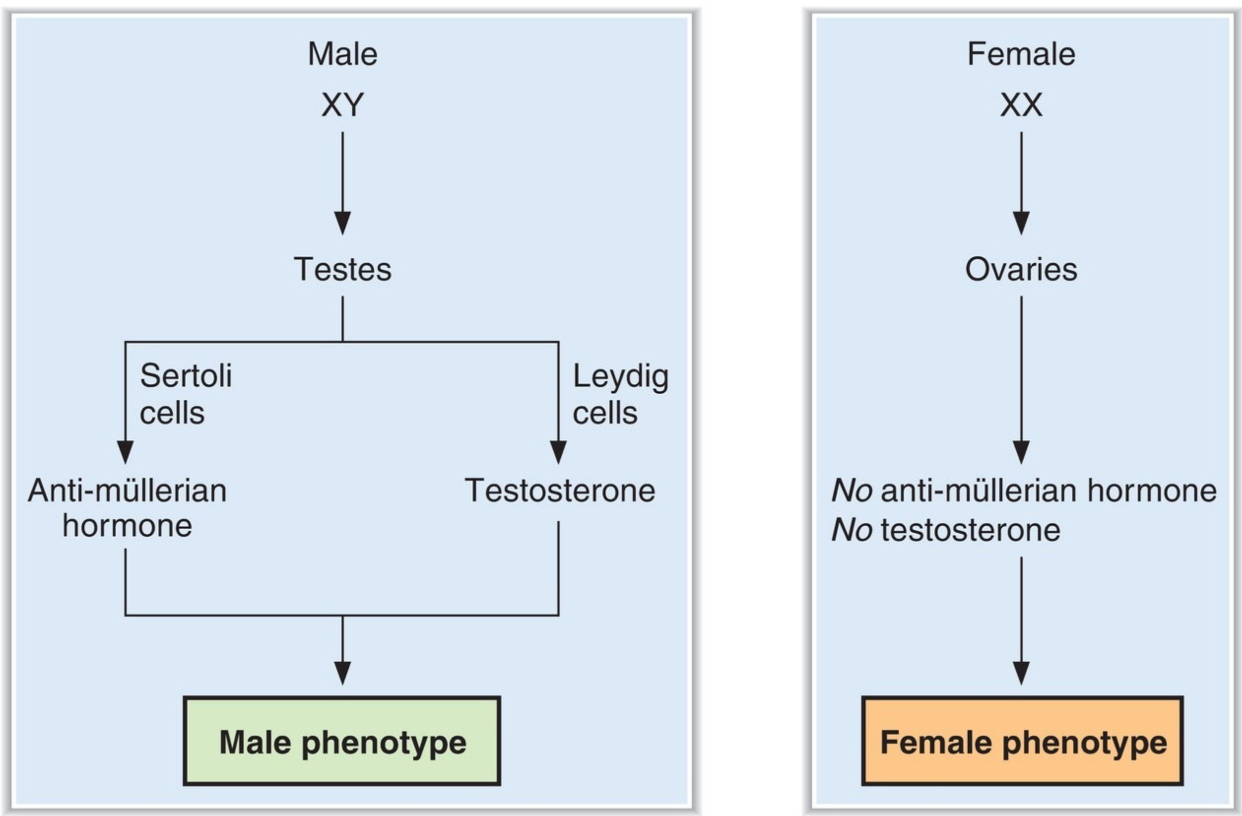


FIGURE 7.15. Sexual differentiation in males and females.

- **Genetic sex** is defined by the sex chromosomes, **XY** in males and **XX** in females.
- **Gonadal sex** is defined by the presence of **testes** in males and **ovaries** in females.
- **Phenotypic sex** is defined by the characteristics of the **internal genital tract** and the **external genitalia**.

A. Male phenotype

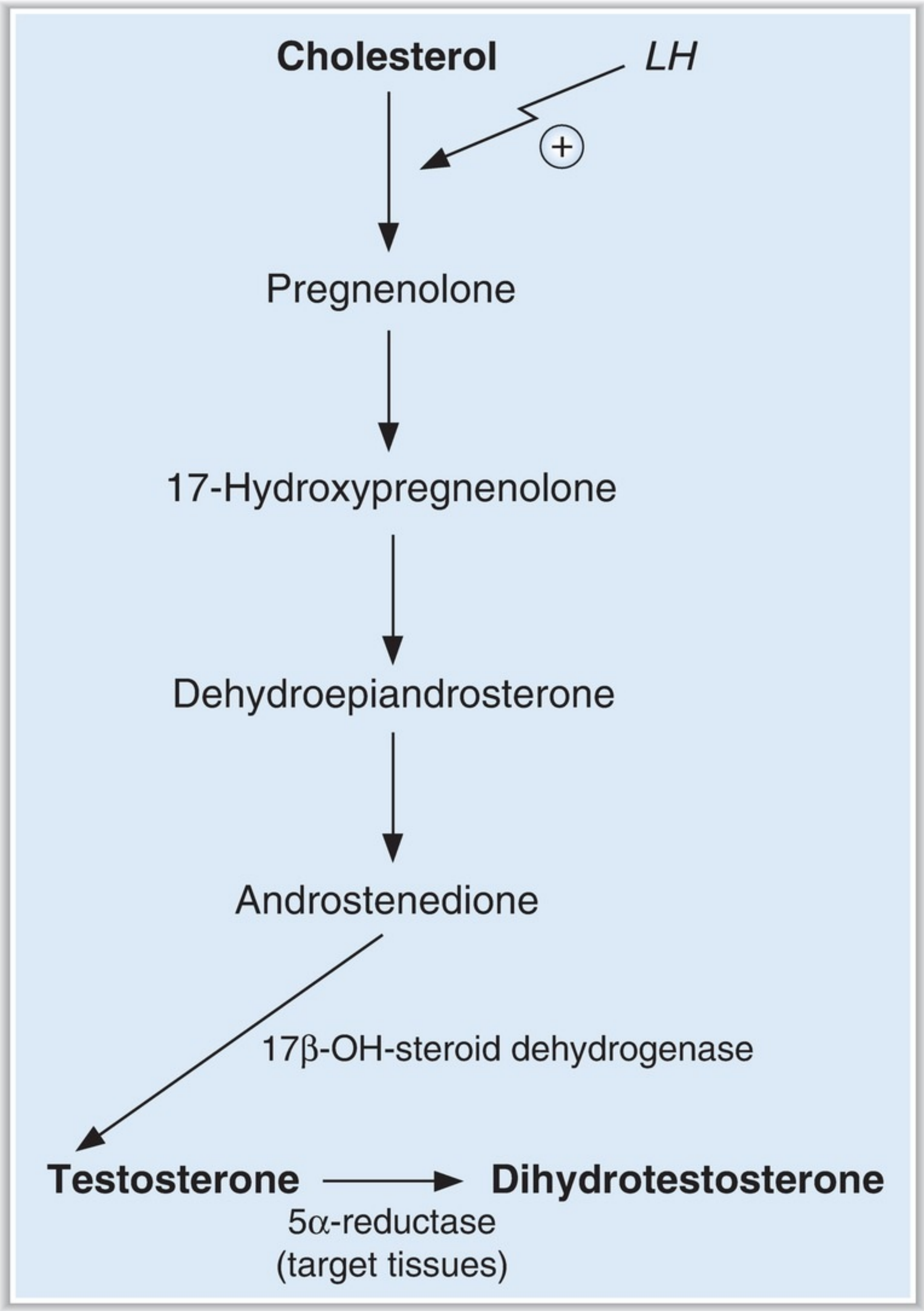
- The testes of gonadal males secrete **anti-müllerian hormone** and **testosterone**.
- Testosterone stimulates the growth and differentiation of the wolffian ducts, which develop into the male internal genital tract.
- Anti-müllerian hormone causes atrophy of the müllerian ducts (which would have become the female internal genital tract).

B. Female phenotype

- The ovaries of gonadal females secrete estrogen, but not anti-müllerian hormone or testosterone.
- Without testosterone, the wolffian ducts do not differentiate.
- Without anti-müllerian hormone, the müllerian ducts are not suppressed and therefore develop into the female internal genital tract.

IX. MALE REPRODUCTION

A. Synthesis of testosterone (Figure 7.16)



Cholesterol
LH
+
Pregnenolone
17-Hydroxypregnenolone
Dehydroepiandrosterone
Androstenedione
17β-OH-steroid dehydrogenase
Testosterone
Dihydrotestosterone
5α-reductase
(target tissues)

FIGURE 7.16. Synthesis of testosterone. LH = luteinizing hormone.

- Testosterone is the major androgen synthesized and secreted by the **Leydig cells**.
- Leydig cells do not contain 21β-hydroxylase or 11β-hydroxylase (in contrast to the adrenal cortex) and, therefore, do not synthesize glucocorticoids or mineralocorticoids.
- LH (in an analogous action to ACTH in the adrenal cortex) increases testosterone synthesis by stimulating cholesterol desmolase, the first step in the pathway.
- Accessory sex organs (e.g., **prostate**) contain **5α-reductase**, which converts testosterone to its active form, dihydrotestosterone.
- **5α-reductase inhibitors (finasteride)** may be used to treat **benign prostatic hyperplasia** because they block the activation of testosterone to dihydrotestosterone in the prostate.

B. Regulation of testes (Figure 7.17)

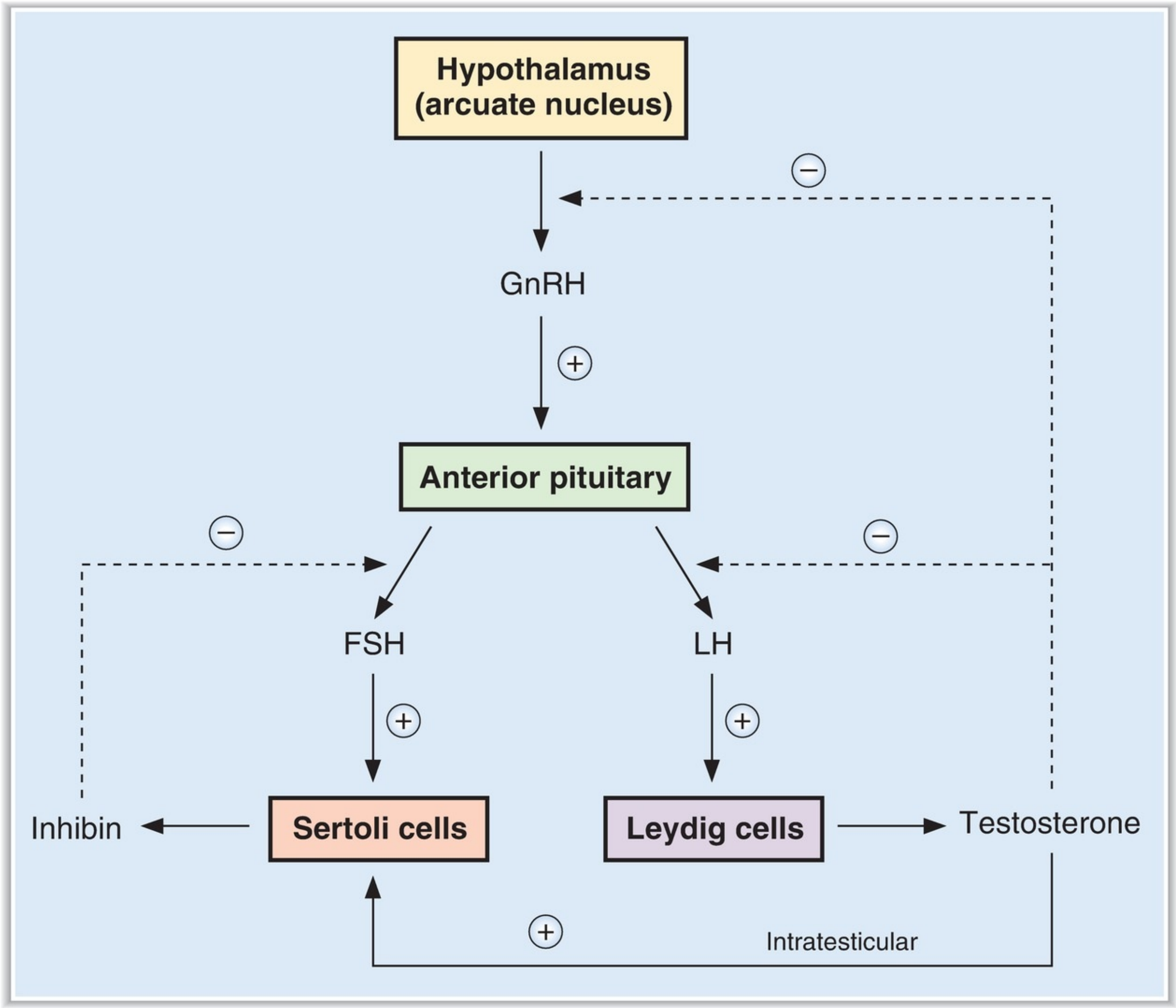


FIGURE 7.17. Control of male reproductive hormones. FSH = follicle-stimulating hormone; GnRH = gonadotropin-releasing hormone; LH = luteinizing hormone.

1. Hypothalamic control—GnRH

- Arcuate nuclei of the hypothalamus secrete GnRH into the hypothalamic–hypophysial portal blood. GnRH stimulates the anterior pituitary to secrete FSH and LH.

2. Anterior pituitary—FSH and LH

- **FSH acts on the Sertoli cells** to maintain **spermatogenesis**. The Sertoli cells also secrete **inhibin**, which is involved in negative feedback of FSH secretion.

- **LH acts on the Leydig cells** to promote **testosterone synthesis**. Testosterone acts via an intratesticular paracrine mechanism to reinforce the spermatogenic effects of FSH in the Sertoli cells.

3. Negative feedback control—testosterone and inhibin

- **Testosterone inhibits the secretion of LH** by inhibiting the release of GnRH from the hypothalamus and by directly inhibiting the release of LH from the anterior pituitary.
- **Inhibin** (produced by the Sertoli cells) **inhibits the secretion of FSH** from the anterior pituitary.

C. Actions of testosterone or dihydrotestosterone

1. Actions of testosterone

- differentiation of epididymis, vas deferens, and seminal vesicles.
- pubertal growth spurt.
- cessation of pubertal growth spurt (epiphyseal closure).
- libido.
- spermatogenesis in Sertoli cells (paracrine effect).
- deepening of voice.
- increased muscle mass.
- growth of penis and seminal vesicles.
- negative feedback on anterior pituitary.

2. Actions of dihydrotestosterone

- differentiation of penis, scrotum, and prostate.
- male hair pattern.
- male pattern baldness.
- sebaceous gland activity.
- growth of prostate.

3. Androgen insensitivity disorder (testicular feminizing syndrome)

- is caused by **deficiency of androgen receptors** in target tissues of males.
- Testosterone and dihydrotestosterone actions in target tissues are absent.
- There are **female external genitalia** ("default"), and there is no internal genital tract.
- Testosterone levels are elevated due to lack of testosterone receptors in the anterior pituitary (lack of feedback inhibition).

D. Puberty (male and female)

- is initiated by the onset of **pulsatile GnRH** release from the hypothalamus.
- FSH and LH are, in turn, secreted in pulsatile fashion.
- GnRH **up-regulates** its own receptor in the anterior pituitary.

E. Variation in FSH and LH levels over the life span (male and female)

1. In childhood, hormone levels are lowest and FSH > LH.
2. At puberty and during the reproductive years, hormone levels increase and LH > FSH.
3. In senescence, hormone levels are highest and FSH > LH.

X. FEMALE REPRODUCTION

A. Synthesis of estrogen and progesterone (Figure 7.18)

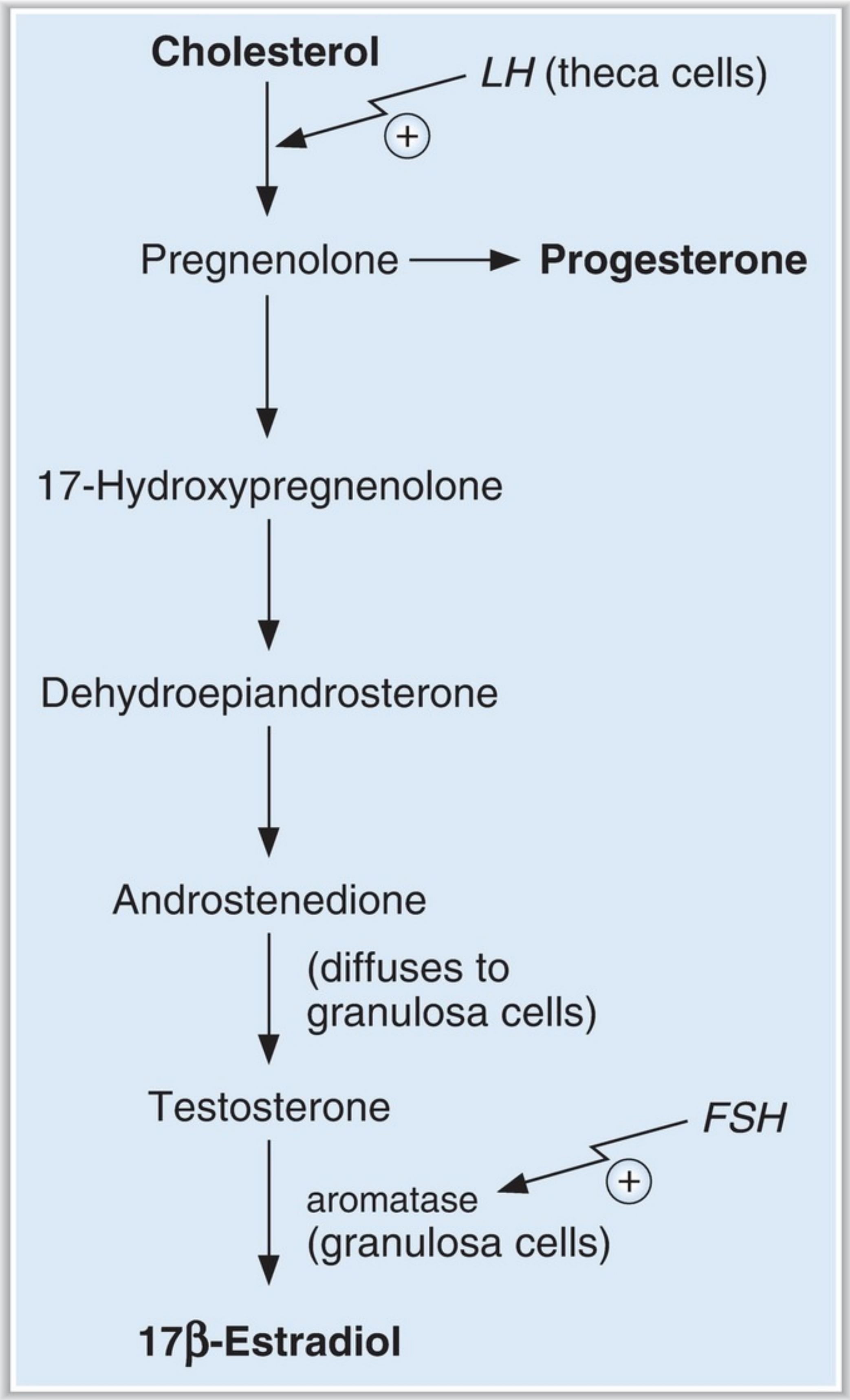

Cholesterol
LH (theca cells)
+
Pregnenolone
Progesterone
17-Hydroxypregnenolone
Dehydroepiandrosterone
Androstenedione
(diffuses to
granulosa cells)
Testosterone
FSH
+
aromatase
(granulosa cells)
17β-Estradiol

FIGURE 7.18. Synthesis of estrogen and progesterone. FSH = follicle-stimulating hormone; LH = luteinizing hormone.

- **Theca cells** produce androstenedione (stimulated at the first step by LH). Androstenedione diffuses to the nearby **granulosa cells**, which contain 17β-hydroxysteroid dehydrogenase, which converts androstenedione to testosterone, and aromatase, which converts testosterone to 17β-estradiol (stimulated by FSH).

B. Regulation of the ovary

1. Hypothalamic control—GnRH

- As in the male, pulsatile GnRH stimulates the anterior pituitary to secrete FSH and LH.

2. Anterior lobe of the pituitary—FSH and LH

- FSH and LH stimulate the following in the ovaries:

a. steroidogenesis in the ovarian follicle and corpus luteum.

b. follicular development beyond the antral stage.

c. ovulation.

d. luteinization.

3. Negative and positive feedback control—estrogen and progesterone (Table 7.13)

- Granulosa cells secrete inhibin, which inhibits FSH secretion.
- Granulosa cells secrete activan, which stimulates FSH secretion.

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table 7.13 Negative and Positive Feedback Control of the Menstrual Cycle

Phase of Menstrual Cycle	Hormone	Type of Feedback and Site
Follicular	Estrogen	Negative; anterior pituitary
Midcycle	Estrogen	Positive; anterior pituitary
Luteal	Estrogen Progesterone	Negative; anterior pituitary Negative; anterior pituitary

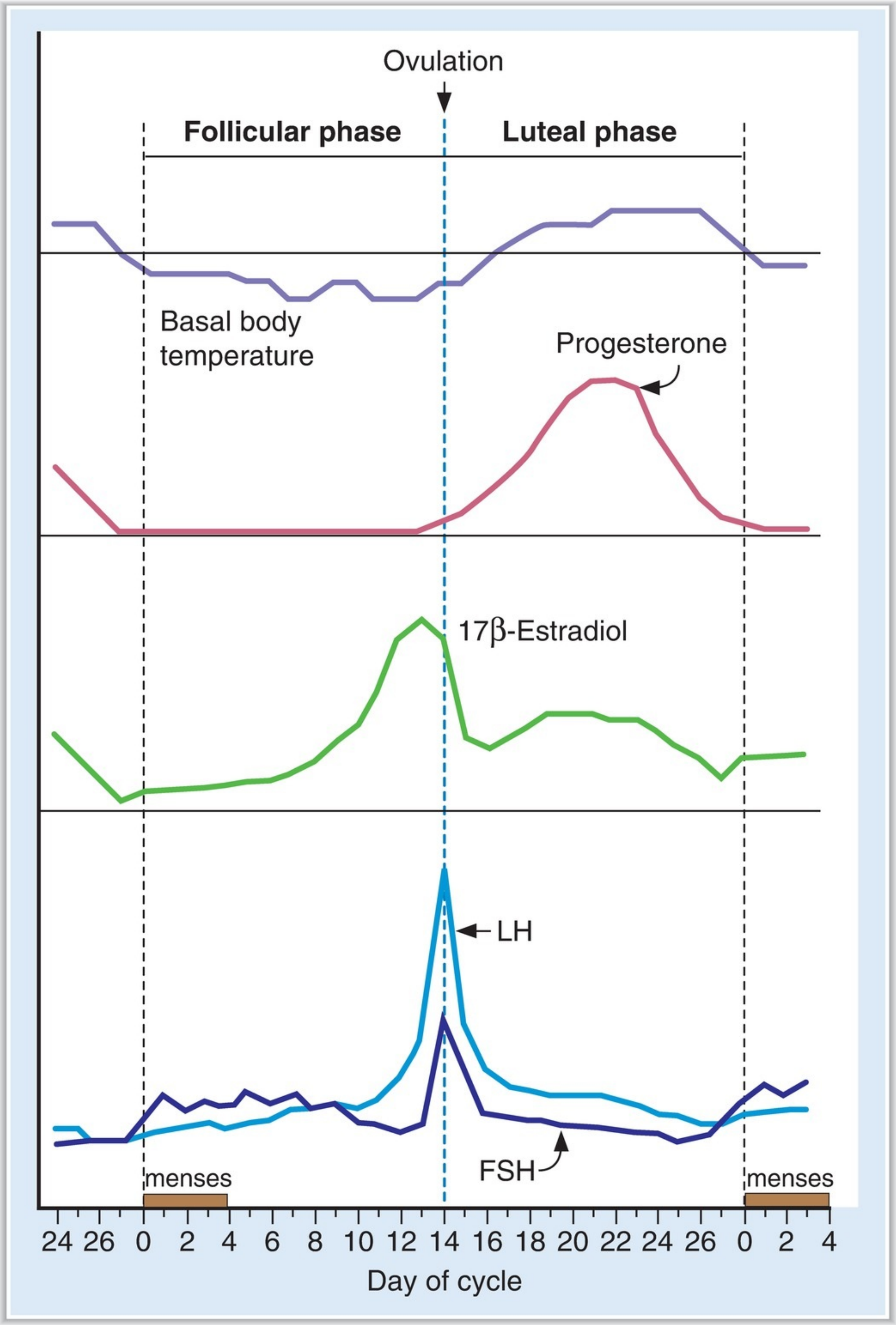
C. Actions of estrogen

1. has both negative and positive feedback effects on FSH and LH secretion.
2. causes maturation and maintenance of the fallopian tubes, uterus, cervix, and vagina.
3. causes the development of female secondary sex characteristics at puberty.
4. causes the development of the breasts.
5. up-regulates estrogen, LH, and progesterone receptors.
6. causes proliferation and development of ovarian granulosa cells.
7. during pregnancy, stimulates growth of myometrium and growth of ductal system in the breast.
8. during pregnancy, stimulates prolactin secretion (but then blocks its action on the breast).
9. increases uterine contractility.

D. Actions of progesterone

1. has negative feedback effects on FSH and LH secretion during luteal phase.
2. maintains secretory activity of the uterus during the luteal phase.
3. during pregnancy, maintains endometrial lining.
4. decreases uterine contractility.
5. participates in development of the breasts.

E. Menstrual cycle (Figure 7.19)



Ovulation
Follicular phase
Luteal phase
Basal body temperature
Progesterone
17β-Estradiol
LH
FSH
menses
menses
24 26 0 2 4 6 8 10 12 14 16 18 20 22 24 26 0 2 4
Day of cycle

FIGURE 7.19. The menstrual cycle. FSH = follicle-stimulating hormone; LH = luteinizing hormone.

1. Follicular phase (days 0 to 14)

- A **primordial follicle develops** to the graafian stage, with atresia of neighboring follicles.
- LH and FSH receptors are up-regulated in theca and granulosa cells.
- **Estradiol levels increase** and cause **proliferation of the uterus**.
- **FSH and LH levels are suppressed** by the negative feedback effect of estradiol on the anterior pituitary.
- Progesterone levels are low.

2. Ovulation (day 14)

- occurs 14 days before menses, regardless of cycle length. Thus, in a 28-day cycle, ovulation occurs on day 14; in a 35-day cycle, ovulation occurs on day 22.
- A burst of estradiol synthesis at the end of the follicular phase has a **positive feedback** effect on the secretion of FSH and LH **(LH surge)**.
- **Ovulation** occurs as a result of the **estrogen-induced LH surge**.
- Estrogen levels decrease just after ovulation (but rise again during the luteal phase).
- **Cervical mucus increases** in quantity; it becomes less viscous and more penetrable by sperm.

3. Luteal phase (days 14 to 28)

- The **corpus luteum** begins to develop, and it **synthesizes estrogen and progesterone**.
- **Vascularity and secretory activity of the endometrium increase** to prepare for receipt of a fertilized egg.
- **Basal body temperature increases** because of the effect of progesterone on the hypothalamic thermoregulatory center.
- If fertilization does not occur, the **corpus luteum regresses** at the end of the luteal phase. As a result, estradiol and progesterone levels decrease abruptly.

4. Menses (days 0 to 4)

- **The endometrium is sloughed** because of the abrupt withdrawal of estradiol and progesterone.

F. Pregnancy (Figure 7.20)

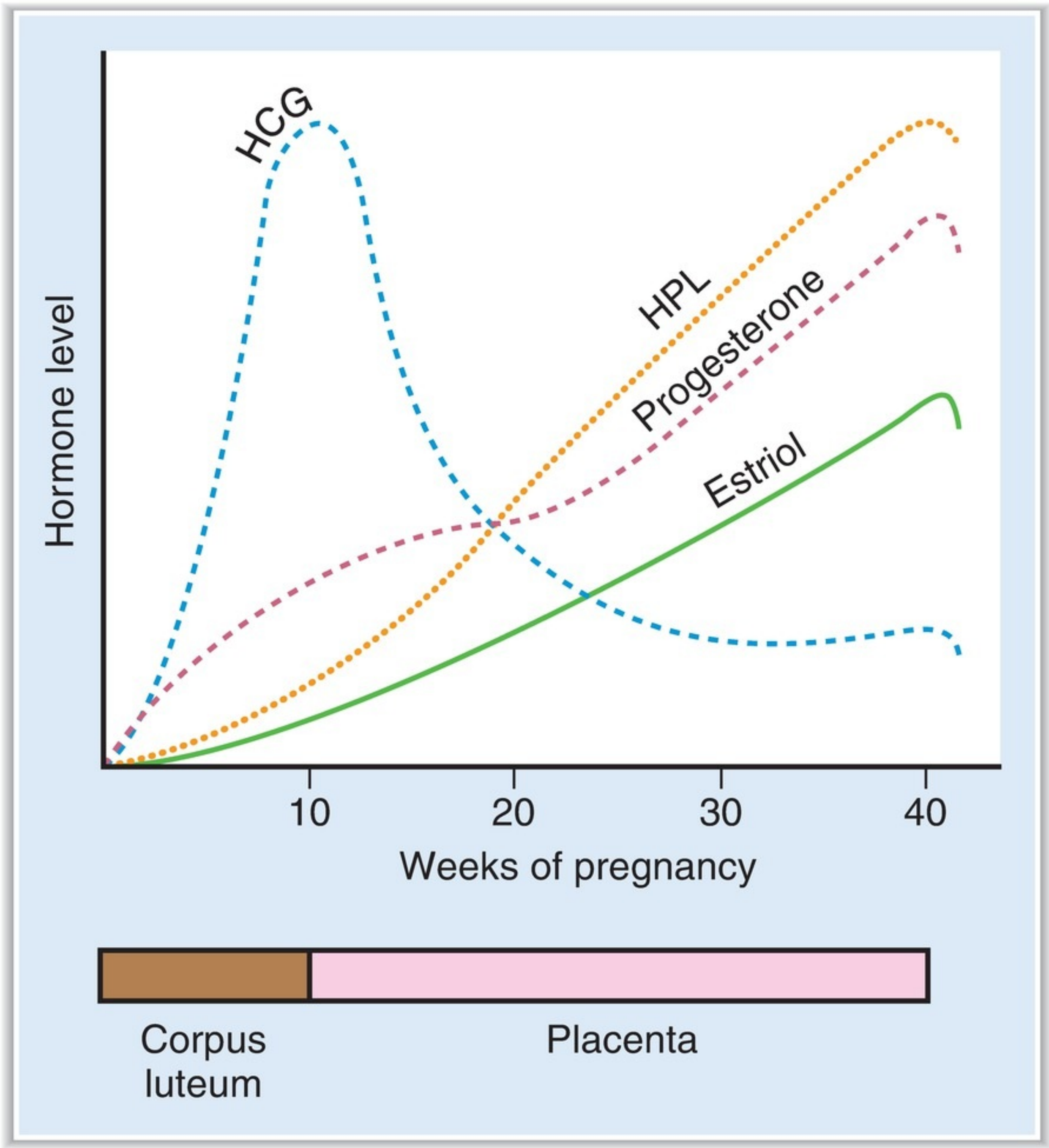


FIGURE 7.20. Hormone levels during pregnancy. HCG = human chorionic gonadotropin; HPL = human placental lactogen.

- is characterized by steadily increasing levels of estrogen and progesterone, which maintain the endometrium for the fetus, suppress ovarian follicular function (by inhibiting FSH and LH secretion), and stimulate development of the breasts.

1. Fertilization

- If **fertilization occurs**, the corpus luteum is rescued from regression by **human chorionic gonadotropin (HCG)**, which is produced by the placenta.

2. First trimester

- The corpus luteum (stimulated by **HCG**) is responsible for the production of estradiol and progesterone.
- Peak levels of HCG occur at gestational week 9 and then decline.

3. Second and third trimesters

- **Progesterone** is produced by the placenta.
- **Estrogens** are produced by the interplay of the **fetal adrenal gland** and the placenta. The fetal adrenal gland synthesizes dehydroepiandrosterone sulfate (DHEA-S), which is then hydroxylated in the fetal liver. These intermediates are transferred to the placenta, where enzymes remove sulfate and aromatize to estrogens. **The major placental estrogen is estriol.**
- **Human placental lactogen** is produced throughout pregnancy. Its actions are similar to those of growth hormone and prolactin.

4. Parturition

- Throughout pregnancy, estrogen increases uterine contractility and progesterone decreases uterine contractility.
- Near term, the estrogen/progesterone ratio increases, which makes the uterus more sensitive to contractile stimuli.
- Near term, increased estrogen levels increase production of local prostaglandins. **Prostaglandins** increase uterine contractility, increase gap junctions between uterine smooth muscle cells, and cause softening, thinning, and dilation of the cervix.
- The **initiating event in parturition is unknown**. (Although oxytocin is a powerful stimulant of uterine contractions, blood levels of oxytocin do not change before labor.)

5. Lactation

- Estrogens and progesterone stimulate the growth and development of the breasts throughout pregnancy.

- **Prolactin levels increase steadily during pregnancy** because estrogen stimulates prolactin secretion from the anterior pituitary.
- **Lactation does not occur during pregnancy because estrogen and progesterone block the action of prolactin on the breast.**
- After parturition, estrogen and progesterone levels decrease abruptly and lactation occurs.
- Lactation is maintained by suckling, which stimulates both oxytocin and prolactin secretion.
- **Ovulation is suppressed** as long as lactation continues because prolactin has the following effects:

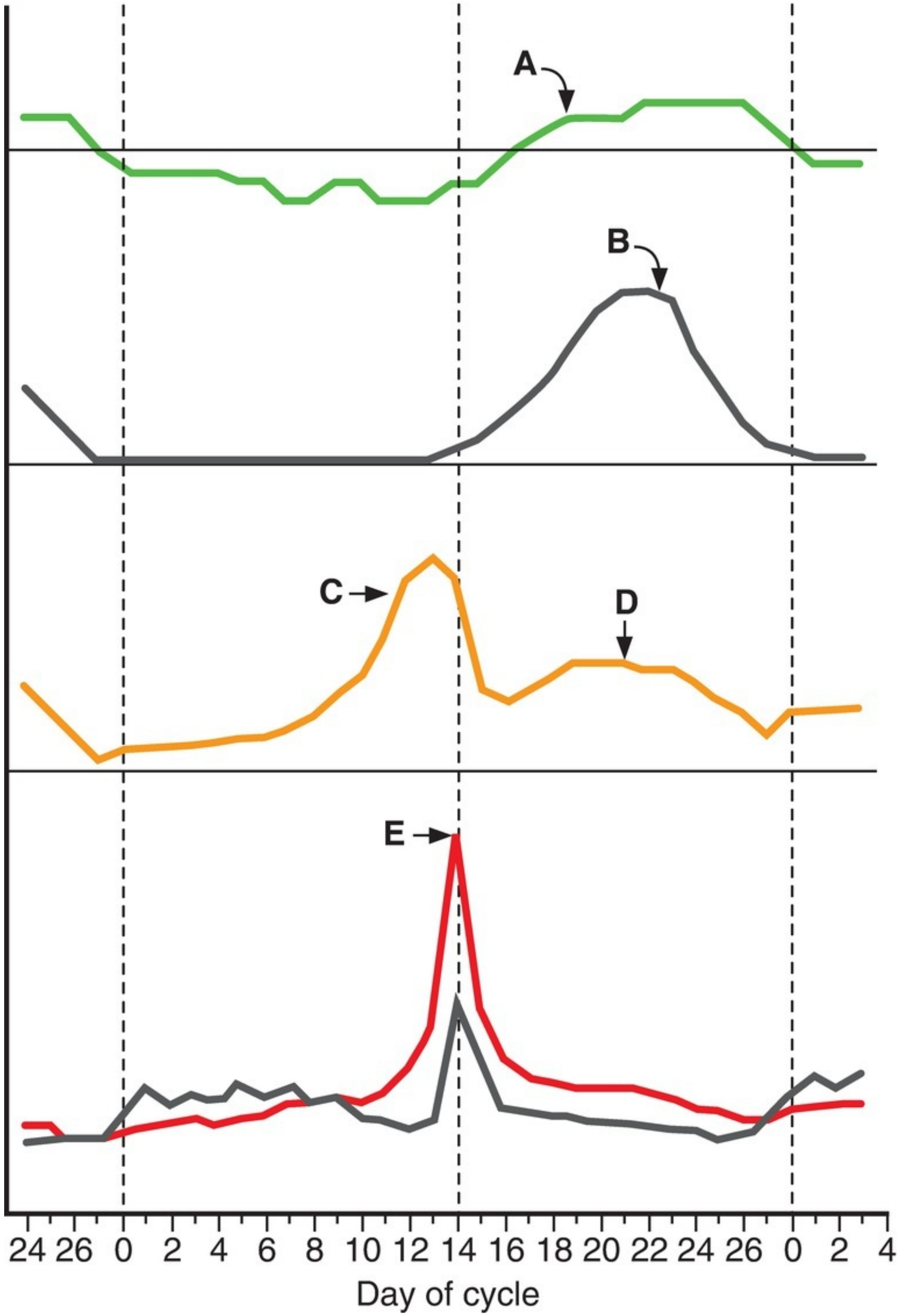
a. inhibits hypothalamic GnRH secretion.

b. inhibits the action of GnRH on the anterior pituitary and consequently inhibits LH and FSH secretion.

c. antagonizes the actions of LH and FSH on the ovaries.

REVIEW TEST

Questions 1–5 Use the graph below, which shows changes during the menstrual cycle, to answer Questions 1–5.



A
B
C
D
E
24 26 0 2 4 6 8 10 12 14 16 18 20 22 24 26 0 2 4
Day of cycle

1. The increase shown at point A is caused by the effect of
(A) estrogen on the anterior pituitary
(B) progesterone on the hypothalamus
(C) follicle-stimulating hormone (FSH) on the ovary
(D) luteinizing hormone (LH) on the anterior pituitary
(E) prolactin on the ovary

2. Blood levels of which substance are described by curve B?
(A) Estradiol
(B) Estriol
(C) Progesterone
(D) Follicle-stimulating hormone (FSH)
(E) Luteinizing hormone (LH)

3. The source of the increase in concentration indicated at point C is the
(A) hypothalamus
(B) anterior pituitary
(C) corpus luteum
(D) ovary
(E) adrenal cortex

4. The source of the increase in concentration at point D is the
(A) ovary
(B) adrenal cortex
(C) corpus luteum
(D) hypothalamus
(E) anterior pituitary

5. The cause of the sudden increase shown at point E is
(A) negative feedback of progesterone on the hypothalamus
(B) negative feedback of estrogen on the anterior pituitary
(C) negative feedback of follicle-stimulating hormone (FSH) on the ovary
(D) positive feedback of FSH on the ovary
(E) positive feedback of estrogen on the anterior pituitary

6. A 41-year-old woman has hypocalcemia, hyperphosphatemia, and decreased urinary phosphate excretion. Injection of parathyroid hormone (PTH) causes an increase in urinary cyclic adenosine monophosphate (cAMP).

The most likely diagnosis is
(A) primary hyperparathyroidism
(B) vitamin D intoxication
(C) vitamin D deficiency
(D) hypoparathyroidism after thyroid surgery
(E) pseudohypoparathyroidism

7. Which of the following hormones acts on its target tissues by a steroid hormone mechanism of action?
(A) Thyroid hormone
(B) Parathyroid hormone (PTH)
(C) Antidiuretic hormone (ADH) on the collecting duct
(D) β_1-adrenergic agonists
(E) Glucagon

8. A 38-year-old man who has galactorrhea is found to have a prolactinoma. His physician treats him with bromocriptine, which eliminates the galactorrhea. The basis for the therapeutic action of bromocriptine is that it
(A) antagonizes the action of prolactin on the breast
(B) enhances the action of prolactin on the breast
(C) inhibits prolactin release from the anterior pituitary
(D) inhibits prolactin release from the hypothalamus
(E) enhances the action of dopamine on the anterior pituitary

9. Which of the following hormones originates in the anterior pituitary?
(A) Dopamine
(B) Growth hormone–releasing hormone (GHRH)
(C) Somatostatin
(D) Gonadotropin-releasing hormone (GnRH)
(E) Thyroid-stimulating hormone (TSH)
(F) Oxytocin
(G) Testosterone

10. Which of the following functions of the Sertoli cells mediates negative feedback control of follicle-stimulating hormone (FSH) secretion?
(A) Synthesis of inhibin
(B) Synthesis of testosterone
(C) Aromatization of testosterone
(D) Maintenance of the blood–testes barrier

11. Which of the following substances is derived from proopiomelanocortin (POMC)?

(A) Adrenocorticotropic hormone (ACTH)
(B) Follicle-stimulating hormone (FSH)
(C) Melatonin
(D) Cortisol
(E) Dehydroepiandrosterone

12. Which of the following inhibits the secretion of growth hormone by the anterior pituitary?

(A) Sleep
(B) Stress
(C) Puberty
(D) Somatomedins
(E) Starvation
(F) Hypoglycemia

13. Selective destruction of the zona glomerulosa of the adrenal cortex would produce a deficiency of which hormone?

(A) Aldosterone
(B) Androstenedione
(C) Cortisol
(D) Dehydroepiandrosterone
(E) Testosterone

14. Which of the following explains the suppression of lactation during pregnancy?

(A) Blood prolactin levels are too low for milk production to occur
(B) Human placental lactogen levels are too low for milk production to occur
(C) The fetal adrenal gland does not produce sufficient estriol
(D) Blood levels of estrogen and progesterone are high
(E) The maternal anterior pituitary is suppressed

15. Which step in steroid hormone biosynthesis, if inhibited, blocks the production of all androgenic compounds but does not block the production of glucocorticoids?

(A) Cholesterol → pregnenolone
(B) Progesterone → 11-deoxycorticosterone
(C) 17-Hydroxypregnenolone → dehydroepiandrosterone

(D) Testosterone → estradiol
(E) Testosterone → dihydrotestosterone

16. A 46-year-old woman has hirsutism, hyperglycemia, obesity, muscle wasting, and increased circulating levels of adrenocorticotropic hormone (ACTH). The most likely cause of her symptoms is
(A) primary adrenocortical insufficiency (Addison disease)
(B) pheochromocytoma
(C) primary overproduction of ACTH (Cushing disease)
(D) treatment with exogenous glucocorticoids
(E) hypophysectomy

17. Which of the following decreases the conversion of 25-hydroxycholecalciferol to 1,25-dihydroxycholecalciferol?
(A) A diet low in Ca^{2+}
(B) Hypocalcemia
(C) Hyperparathyroidism
(D) Hypophosphatemia
(E) Chronic renal failure

18. Increased adrenocorticotropic hormone (ACTH) secretion would be expected in patients
(A) with chronic adrenocortical insufficiency (Addison disease)
(B) with primary adrenocortical hyperplasia
(C) who are receiving glucocorticoid for immunosuppression after a renal transplant
(D) with elevated levels of angiotensin II

19. Which of the following would be expected in a patient with Graves disease?
(A) Cold sensitivity
(B) Weight gain
(C) Decreased O_2 consumption
(D) Decreased cardiac output
(E) Drooping eyelids
(F) Atrophy of the thyroid gland
(G) Increased thyroid-stimulating hormone (TSH) levels
(H) Increased triiodothyronine (T_3) levels

20. Blood levels of which of the following substances is decreased in Graves disease?

(A) Triiodothyronine (T_3)
(B) Thyroxine (T_4)
(C) Diiodotyrosine (DIT)
(D) Thyroid-stimulating hormone (TSH)
(E) Iodide (I^-)

21. Which of the following hormones acts by an inositol 1,4,5-triphosphate (IP_3)-Ca^{2+} mechanism of action?

(A) 1,25-Dihydroxycholecalciferol
(B) Progesterone
(C) Insulin
(D) Parathyroid hormone (PTH)
(E) Gonadotropin-releasing hormone (GnRH)

22. Which step in steroid hormone biosynthesis is stimulated by adrenocorticotropic hormone (ACTH)?

(A) Cholesterol → pregnenolone
(B) Progesterone → 11-deoxycorticosterone
(C) 17-Hydroxypregnenolone → dehydroepiandrosterone
(D) Testosterone → estradiol
(E) Testosterone → dihydrotestosterone

23. The source of estrogen during the second and third trimesters of pregnancy is the

(A) corpus luteum
(B) maternal ovaries
(C) fetal ovaries
(D) placenta
(E) maternal ovaries and fetal adrenal gland
(F) maternal adrenal gland and fetal liver
(G) fetal adrenal gland, fetal liver, and placenta

24. Which of the following causes increased aldosterone secretion?

(A) Decreased blood volume
(B) Administration of an inhibitor of angiotensin-converting enzyme (ACE)
(C) Hyperosmolarity

(D) Hypokalemia

25. Secretion of oxytocin is increased by
(A) milk ejection
(B) dilation of the cervix
(C) increased prolactin levels
(D) increased extracellular fluid (ECF) volume
(E) increased serum osmolarity

26. A 61-year-old woman with hyperthyroidism is treated with propylthiouracil. The drug reduces the synthesis of thyroid hormones because it inhibits oxidation of
(A) triiodothyronine (T_3)
(B) thyroxine (T_4)
(C) diiodotyrosine (DIT)
(D) thyroid-stimulating hormone (TSH)
(E) iodide (I^-)

27. A 39-year-old man with untreated diabetes mellitus type I is brought to the emergency room. An injection of insulin would be expected to cause an increase in his
(A) urine glucose concentration
(B) blood glucose concentration
(C) blood K^+ concentration
(D) blood pH
(E) breathing rate

28. Which of the following results from the action of parathyroid hormone (PTH) on the renal tubule?
(A) Inhibition of 1α-hydroxylase
(B) Stimulation of Ca^{2+} reabsorption in the distal tubule
(C) Stimulation of phosphate reabsorption in the proximal tubule
(D) Interaction with receptors on the luminal membrane of the proximal tubular cells
(E) Decreased urinary excretion of cyclic adenosine monophosphate (cAMP)

29. Which step in steroid hormone biosynthesis occurs in the accessory sex target tissues of the male and is catalyzed by 5α-reductase?
(A) Cholesterol → pregnenolone

(B) Progesterone → 11-deoxycorticosterone
(C) 17-Hydroxypregnenolone → dehydroepiandrosterone
(D) Testosterone → estradiol
(E) Testosterone → dihydrotestosterone

30. Which of the following pancreatic secretions has a receptor with four subunits, two of which have tyrosine kinase activity?
(A) Insulin
(B) Glucagon
(C) Somatostatin
(D) Pancreatic lipase

31. A 16-year-old, seemingly normal female is diagnosed with androgen insensitivity disorder. She has never had a menstrual cycle and is found to have a blind-ending vagina; no uterus, cervix, or ovaries; a 46 XY genotype; and intra-abdominal testes. Her serum testosterone is elevated. Which of the following characteristics is caused by lack of androgen receptors?
(A) 46 XY genotype
(B) Testes
(C) Elevated serum testosterone
(D) Lack of uterus and cervix
(E) Lack of menstrual cycles

Questions 32–34A 76–year-old man with lung cancer is lethargic and excreting large volumes of urine. He is thirsty and drinks water almost constantly. Laboratory values reveal an elevated serum Ca^{2+} concentration of 18 mg/dL, elevated serum osmolarity of 310 mOsm/L, and urine osmolarity of 90 mOsm/L. Administration of an ADH analogue does not change his serum or urine osmolarity.
32. The man's serum ADH level is
(A) decreased because excess water-drinking has suppressed ADH secretion
(B) decreased because his posterior pituitary is not secreting ADH
(C) normal
(D) increased because the elevated serum osmolarity has stimulated ADH secretion
(E) increased because his extreme thirst has directly stimulated ADH secretion

33. The cause of the patient's excess urine volume is

(A) dehydration
(B) syndrome of inappropriate ADH
(C) central diabetes insipidus
(D) nephrogenic diabetes insipidus

34. The most appropriate treatment is
(A) ADH antagonist
(B) ADH analogue
(C) PTH analogue
(D) half-normal saline
(E) pamidronate plus furosemide

Answers and Explanations

1. The answer is B [X E 3; Figure 7.19]. Curve A shows basal body temperature. The increase in temperature occurs as a result of elevated progesterone levels during the luteal (secretory) phase of the menstrual cycle. Progesterone increases the set-point temperature in the hypothalamic thermoregulatory center.

2. The answer is C [X E 3; Figure 7.19]. Progesterone is secreted during the luteal phase of the menstrual cycle.

3. The answer is D [X A, E 1; Figure 7.19]. The curve shows blood levels of estradiol. The source of the increase in estradiol concentration shown at point C is the ovarian granulosa cells, which contain high concentrations of aromatase and convert testosterone to estradiol.

4. The answer is C [X E 3; Figure 7.19]. The curve shows blood levels of estradiol. During the luteal phase of the cycle, the source of the estradiol is the corpus luteum. The corpus luteum prepares the uterus to receive a fertilized egg.

5. The answer is E [X E 2; Figure 7.20]. Point E shows the luteinizing hormone (LH) surge that initiates ovulation at midcycle. The LH surge is caused by increasing estrogen levels from the developing ovarian follicle. Increased estrogen, by positive feedback, stimulates the anterior pituitary to secrete LH and follicle-stimulating hormone (FSH).

6. The answer is D [VII B 3 b]. Low blood [Ca^{2+}] and high blood [phosphate] are consistent with hypoparathyroidism. Lack of parathyroid hormone (PTH) decreases bone resorption, decreases renal reabsorption of Ca^{2+}, and increases renal reabsorption of phosphate (causing low urinary phosphate). Because the patient responded to exogenous PTH with an increase in urinary cyclic adenosine monophosphate (cAMP), the G protein coupling the PTH receptor to adenylate cyclase is apparently normal. Consequently, pseudohypoparathyroidism is excluded. Vitamin D intoxication would cause hypercalcemia, not hypocalcemia. Vitamin D deficiency would cause hypocalcemia and hypophosphatemia.

7. The answer is A [II E; Table 7.2]. Thyroid hormone, an amine, acts on its target tissues by a steroid hormone mechanism, inducing the synthesis of new proteins. The action of antidiuretic hormone (ADH) on the collecting duct (V_2 receptors) is mediated by cyclic adenosine monophosphate (cAMP), although the other action of ADH (vascular smooth muscle, V_1 receptors) is mediated by inositol 1,4,5-triphosphate (IP_3). Parathyroid hormone (PTH), β_1-agonists, and glucagon all act through cAMP mechanisms of action.

8. The answer is C [III B 4 a (1), c (2)]. Bromocriptine is a dopamine agonist. The secretion of prolactin by the anterior pituitary is tonically inhibited by the secretion of dopamine from the hypothalamus. Thus, a dopamine agonist acts just like dopamine—it inhibits prolactin secretion from the anterior pituitary.

9. The answer is E [III B; Table 7.1]. Thyroid-stimulating hormone (TSH) is secreted by the anterior pituitary. Dopamine, growth hormone–releasing hormone (GHRH), somatostatin, and gonadotropin-releasing hormone (GnRH) all are secreted by the hypothalamus. Oxytocin is secreted by the posterior pituitary. Testosterone is secreted by the testes.

10. The answer is A [IX B 2, 3]. Inhibin is produced by the Sertoli cells of the testes when they are stimulated by follicle-stimulating hormone (FSH). Inhibin then inhibits further secretion of FSH by negative feedback on the anterior pituitary. The Leydig cells synthesize testosterone. Testosterone is aromatized in the ovaries.

11. The answer is A [III B 1, 2; Figure 7.5]. Proopiomelanocortin (POMC) is the parent molecule in the anterior pituitary for adrenocorticotropic hormone (ACTH), β-endorphin, α-lipotropin, and β-lipotropin (and in the intermediary lobe for melanocyte-stimulating hormone [MSH]). Follicle-stimulating hormone (FSH) is not a member of this “family”; rather, it is a member of the thyroid-stimulating hormone (TSH) and luteinizing hormone (LH) “family.” MSH, a component of POMC and ACTH, may stimulate melatonin production. Cortisol and dehydroepiandrosterone are produced by the adrenal cortex.

12. The answer is D [III B 3 a]. Growth hormone is secreted in pulsatile fashion, with a large burst occurring during deep sleep (sleep stage 3 or 4). Growth hormone secretion is increased by sleep, stress, puberty, starvation, and hypoglycemia. Somatomedins are generated when growth hormone acts on its target tissues; they inhibit growth hormone secretion by the anterior pituitary, both directly and indirectly (by stimulating somatostatin release).

13. The answer is A [V A 1; Figure 7.10]. Aldosterone is produced in the zona glomerulosa of the adrenal cortex because that layer contains the enzyme for conversion of corticosterone to aldosterone (aldosterone synthase). Cortisol is produced in the zona fasciculata. Androstenedione and dehydroepiandrosterone are produced in the zona reticularis. Testosterone is produced in the testes, not in the adrenal cortex.

14. The answer is D [X F 5]. Although the high circulating levels of estrogen stimulate prolactin secretion during pregnancy, the action of prolactin on the breast is inhibited by progesterone and estrogen. After parturition, progesterone and estrogen levels decrease dramatically. Prolactin can then interact with its receptors in the breast, and lactation proceeds if initiated by suckling.

15. The answer is C [Figure 7.11]. The conversion of 17-hydroxypregnenolone to dehydroepiandrosterone (as well as the conversion of 17-hydroxyprogesterone to androstenedione) is catalyzed by 17,20-lyase. If this process is inhibited, synthesis of androgens is stopped.

16. The answer is C [V A 5 b]. This woman has the classic symptoms of a primary elevation of adrenocorticotropic hormone (ACTH) (Cushing disease). Elevation of ACTH stimulates overproduction of glucocorticoids and androgens. Treatment with pharmacologic doses of glucocorticoids would produce similar symptoms, except that circulating levels of ACTH would be low because of negative feedback suppression at both the hypothalamic (corticotropin-releasing hormone [CRH]) and anterior pituitary (ACTH) levels. Addison disease is caused by primary adrenocortical insufficiency. Although a patient with Addison disease would have increased levels of ACTH (because of the loss of negative feedback inhibition), the symptoms would be of glucocorticoid deficit, not excess. Hypophysectomy would remove the source of ACTH. A pheochromocytoma is a tumor of the adrenal medulla that secretes catecholamines.

17. The answer is E [VII C 1]. Ca^{2+} deficiency (low Ca^{2+} diet or hypocalcemia) activates 1α-hydroxylase, which catalyzes the conversion of vitamin D to its active form, 1,25-dihydroxycholecalciferol. Increased parathyroid hormone (PTH) and hypophosphatemia also stimulate the enzyme. Chronic renal failure is associated with a constellation of bone diseases, including osteomalacia caused by failure of the diseased renal tissue to produce the active form of vitamin D.

18. The answer is A [V A 2 a (3); Table 7.6; Figure 7.12]. Addison disease is caused by primary adrenocortical insufficiency. The resulting decrease in cortisol production causes a decrease in negative feedback inhibition on the hypothalamus and the anterior pituitary. Both of these conditions will result in increased adrenocorticotropic hormone (ACTH) secretion. Patients who have adrenocortical hyperplasia or who are receiving exogenous glucocorticoid will have an increase in the negative feedback inhibition of ACTH secretion.

19. The answer is H [IV B 2; Table 7.5]. Graves disease (hyperthyroidism) is caused by overstimulation of the thyroid gland by circulating antibodies to the thyroid-stimulating hormone (TSH) receptor (which then increases the production and secretion of triiodothyronine [T_3] and thyroxine [T_4], just as TSH would). Therefore, the signs and symptoms of Graves disease are the same as those of hyperthyroidism, reflecting the actions of increased circulating levels of thyroid hormones: increased heat production, weight loss, increased O_2 consumption and cardiac output, exophthalmos (bulging eyes, not drooping eyelids), and hypertrophy of the thyroid gland (goiter). TSH levels will be decreased (not increased) as a result of the negative feedback effect of increased T_3 levels on the anterior pituitary.

20. The answer is D [IV B 2; Table 7.5]. In Graves disease (hyperthyroidism), the thyroid is stimulated to produce and secrete vast quantities of thyroid hormones as a result of stimulation by thyroid-stimulating immunoglobulins (antibodies to the thyroid-stimulating hormone [TSH] receptors on the thyroid gland). Because of the high circulating levels of thyroid hormones, anterior pituitary secretion of TSH will be turned off (negative feedback).

21. The answer is E [Table 7.2]. Gonadotropin-releasing hormone (GnRH) is a peptide hormone that acts on the cells of the anterior pituitary by an inositol 1,4,5-triphosphate (IP_3)-Ca^{2+} mechanism to cause the secretion of follicle-stimulating hormone (FSH) and luteinizing hormone (LH). 1,25-Dihydroxycholecalciferol and progesterone are steroid hormone derivatives of cholesterol that act by inducing the synthesis of new proteins. Insulin acts on its target cells by a tyrosine kinase mechanism. Parathyroid hormone (PTH) acts on its target cells by an adenylate cyclase–cyclic adenosine monophosphate (cAMP) mechanism.

22. The answer is A [V A 2 a (2)]. The conversion of cholesterol to pregnenolone is catalyzed by cholesterol desmolase. This step in the biosynthetic pathway for steroid hormones is stimulated by adrenocorticotropic hormone (ACTH).

23. The answer is G [X F 3]. During the second and third trimesters of pregnancy, the fetal adrenal gland synthesizes dehydroepiandrosterone sulfate (DHEA-S), which is hydroxylated in the fetal liver and then transferred to the placenta, where it is aromatized to estrogen. In the first trimester, the corpus luteum is the source of both estrogen and progesterone.

24. The answer is A [V A 2 b]. Decreased blood volume stimulates the secretion of renin (because of decreased renal perfusion pressure) and initiates the renin–angiotensin–aldosterone cascade. Angiotensin-converting enzyme (ACE) inhibitors block the cascade by decreasing the production of angiotensin II. Hyperosmolarity stimulates antidiuretic hormone (ADH) (not aldosterone) secretion. Hyperkalemia, not hypokalemia, directly stimulates aldosterone secretion by the adrenal cortex.

25. The answer is B [III C 2]. Suckling and dilation of the cervix are the physiologic stimuli for oxytocin secretion. Milk ejection is the *result* of oxytocin action, not the cause of its secretion. Prolactin secretion is also stimulated by suckling, but prolactin does not directly cause oxytocin secretion. Increased extracellular fluid (ECF) volume and hyperosmolarity are the stimuli for the secretion of the other posterior pituitary hormone, antidiuretic hormone (ADH).

26. The answer is E [IV A 2]. For iodide (I^-) to be "organified" (incorporated into thyroid hormone), it must be oxidized to I_2, which is accomplished by a peroxidase enzyme in the thyroid follicular cell membrane. Propylthiouracil inhibits peroxidase and, therefore, halts the synthesis of thyroid hormones.

27. The answer is D [VI C 3; Table 7.7]. Before the injection of insulin, the woman would have had hyperglycemia, glycosuria, hyperkalemia, and metabolic acidosis with compensatory hyperventilation. The injection of insulin would be expected to decrease her blood glucose (by increasing the uptake of glucose into the cells), decrease her urinary glucose (secondary to decreasing her blood glucose), decrease her blood K^+ (by shifting K^+ into the cells), and correct her metabolic acidosis (by decreasing the production of ketoacids). The correction of the metabolic acidosis will lead to an increase in her blood pH and will reduce her compensatory hyperventilation.

28. The answer is B [VII B 2]. Parathyroid hormone (PTH) stimulates both renal Ca^{2+} reabsorption in the renal distal tubule and the 1α-hydroxylase enzyme. PTH inhibits (not stimulates) phosphate reabsorption in the proximal tubule, which is associated with an increase in urinary cyclic adenosine monophosphate (cAMP). The receptors for PTH are located on the basolateral membranes, not the luminal membranes.

29. The answer is E [IX A]. Some target tissues for androgens contain 5α-reductase, which converts testosterone to dihydrotestosterone, the active form in those tissues.

30. The answer is A [VI C 2]. The insulin receptor in target tissues is a tetramer. The two β subunits have tyrosine kinase activity and autophosphorylate the receptor when stimulated by insulin.

31. The answer is C [IX C]. The elevated serum testosterone is due to lack of androgen receptors on the anterior pituitary (which normally would mediate negative feedback by testosterone). The presence of testes is due to the male genotype. The lack of uterus and cervix is due to anti-müllerian hormone (secreted by the fetal testes), which suppressed differentiation of the müllerian ducts into the internal female genital tract. The lack of menstrual cycles is due to the absence of a female reproductive tract.

32. The answer is D [III C 1; also Chapter 7, VII]. The man is excreting large volumes of dilute urine, which has raised his serum osmolarity and made him very thirsty. The increase in serum osmolarity would then cause an increase in serum ADH levels. The fact that exogenous ADH administration did not change his serum or urine osmolarity suggests that the collecting duct of the nephron is unresponsive to ADH. Thirst does not directly increase ADH secretion.

33. The answer is D [III C 1; VII, B 3; Chapter 7, VI]. The man's urine osmolarity is very dilute, while his serum osmolarity is increased. In the face of increased serum osmolarity, there should be increased ADH secretion, which should then act on the collecting duct principal cells to increase water reabsorption and concentrate the urine. The fact that the urine is dilute, not concentrated, suggests that ADH either is absent (central diabetes insipidus) or is ineffective (nephrogenic diabetes insipidus). Administration of an exogenous ADH analogue separates these two possibilities—it was ineffective in changing serum or urine osmolarity; thus, it can be concluded that ADH unable to act on the collecting ducts, that is, nephrogenic diabetes insipidus. One cause of nephrogenic diabetes insipidus is hypercalcemia, which is present in this patent secondary to his lung cancer; he likely has humoral hypercalcemia of malignancy, due to secretion of PTH-rp by the tumor. Dehydration would cause increased ADH secretion and increased urine osmolarity. Syndrome of inappropriate ADH would cause increased urine osmolarity and subsequently decreased serum osmolarity, due to excess water reabsorption.

34. The answer is E [VII, B 3]. The man's nephrogenic diabetes insipidus is caused by hypercalcemia secondary to increased PTH-rp secreted by his lung tumor. PTH-rp has all of the actions of PTH, including increased bone resorption, increased renal Ca^{2+} reabsorption, and decreased renal phosphate reabsorption; all of these actions lead to increased serum Ca^{2+} concentration. The treatment should be directed at lowering serum Ca^{2+} concentration, which can be achieved by giving an inhibitor of bone resorption (e.g., pamidronate) and an inhibitor of renal Ca^{2+} reabsorption (furosemide). Giving an ADH antagonist would be ineffective because the man's nephrogenic diabetes insipidus has made his collecting ducts insensitive to ADH. Giving half-normal saline could lower his serum osmolarity temporarily, but would not address the underlying problem of hypercalcemia.

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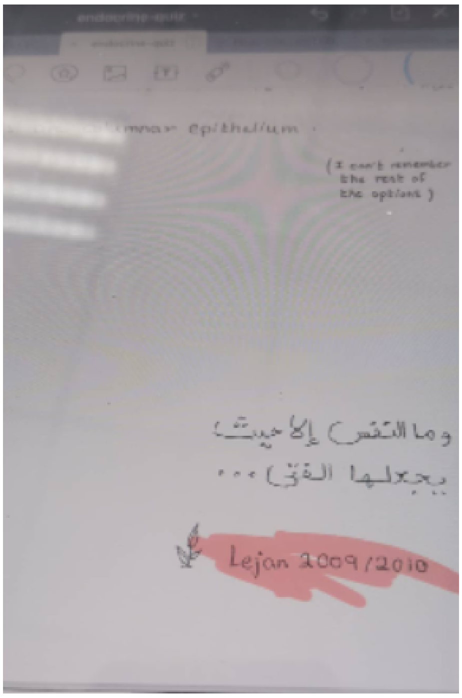


سهري لتنقيح العلوم ألذ لي

من وصل غانية وطيب عناق

وتمايلي طربا لحل عويصة

أشهى وأحلى من مدامة ساق

وصرير أقلامي على أوراقها

أحلى من الدوكاء والعشاق

وألذ من نقر الفتاة لدفها

نقري لالقي الرمل عن أوراقي

أأبيت سهران الدجى وتبيته

نوما وتبغي بعد ذاك لحاقي

31 pages , 6906 word , 197 questions

1.One of the followings is NOT TRUE about the endocrine system:

a. A single endocrine gland may produce more than one hormone
b. A single hormone may be secreted by more than one endocrine gland
c. A single hormone has always one specific target cell the
d. Same chemical substance may be either a hormone or neurotransmitter
e. Some organs of the endocrine system perform non endocrine function

Answer c

2.Which of the following hormones does NOT work mainly via cyclic adenosine monophosphate as a second messenger

a. Insulin
b. ACTH
c. Adrenalin
d. Glucagon
e. TSH

Answer A

3.Which one of the following is the MOST important hyperglycemic hormone?

a. Growth
b. Cortisol
c. Glucagon
d. Adrenaline
e. Thyroxine

Answer c

4.Choose the incorrect answer regards Vitamin D:
a. Increases the intestinal absorption of calcium
b. Is essential for normal calcification in childhood
c. Requires hepatic modification for activation
d. The formation of (D3) structure is sufficient for the Human.
e. Deficiency May Result In Hyperparathyroidism

Answer d

5.Which of the following hormones is the most essential to life
a. Thyroid Hormone
b. Aldosterone
c. Calcitonin
d. Epinephrine
e. Vasopressin

Answer B

6. Cholesterol gives rise to all of the following EXCEPT
a. Aldosterone
b. Catecholamines
c. Estrogen
d. Progesterone
e. Testosterone

Answer b

7.Which of the following hormones is least important in Ca++metabolism
a. PTH
b. Aldosterone
c. 1,25- Dihydroxycholecalciferol
d. GH
e.Insulin

Answer b

8.Which one of the following hormones is hypoglycemic
a. Growth Hormone
b. Glucagon
c. Epinephrine
d. Insulin
e. Cortisol

Answer d

9.Which of the following is a neurohormone ?
a. Vasopressin(ADH)
b. Thyroid
c. Growth hormone
d. Cortisol
e. Luteinizing Hormone

Answer A

10.Which one of the following about osteoporosis is NOT TRUE:
a. The most common of all bone diseases in adults specially in old age
b. Occurs In Females Only
c. It results from diminished organic matrix rather than abnormal bone calcification
d. Lack of physical stress on the bone because of inactivity is one of the causes of osteoporosis
e. It is different disease from osteomalacia

Answer b

11. In ONE of the following conditions growth hormone & insulin secretion is increased
a. Protein Intake
b. Carbohydrate Intake
c. Fasting
d. Obesity
e. Aging

Answer A

12. Inhibition the production of one of the following will lead to hypotension (if severe enough, fatal):
a. Insulin
b. Thyroxin
c. Angiotensin II
d. Cortisol
e. ACTH

Answer C

13. **which of the following tissues does insulin DOES NOT facilitate glucose uptake**
a. Cardiac Muscle
b. Smooth Muscle
c. Leucocytes (WBCS)
d. Erythrocytes (RBCs)
e. Pituitary

Answer d

14. Dwarfism & mental retardation may be the result of a deficiency of :
a. Growth hormone releasing hormone
b. GH
c. Somatomedins
d. Thyroid Hormones
e. Adrenalin Hormone

Answer d

15. All the following stimulate GH secretion EXCEPT
a. Obesity
b. Decrease blood glucose
c. Decrease blood-free fatty acids
d. Fasting

e. Exercise

Answer a

16. Circulating adrenaline: Choose the INCORRECT answer:
a. Is a peptide hormone
b. Tends to raise blood glucose levels
c. Stimulates glucagon secretion
d. Can Cause Case constriction
e. Is more likely to directly increase the heart rate

Answer a

17. Which of the following hormones is very important during the early development of the nervous system
a. Growth Hormone
b. Thyroid Hormone
c. Cortisol
d. Parathyroid Hormone
e. Insulin

Answer b

18. The most abundant product secreted from the thyroid gland is_____most potent thyroid secretory product is ______
a. T4, T4
b. T3, T4
c. T4, T3
d. T4, MIT
e. DIT, T3

Answer c

19. Which of the following hormones does not work mainly via cAMP as a second messenger:
a. Insulin.
b. ACTH.
c. Adrenalin.
d. Glucagon.
e. TSH.

Answer A

19. True about hormone mechanisms:
a. All Steroid Hormones Bound To Cytoplasmic Receptors.
b. Some steroid hormones are bound to cell surface receptors.
c. Protein Hormones Can Cross The Cell Membrane.

Answer b

20. Hormone that is synthesized in endocrine cells and released to the interstitial space binds to a specific receptor of the nearby cell, this hormone is:
a. Neurohormone
b. Paracrine

c. Neurotransmitter

Answer B

21. **Which of the following is NOT a hypothalamic function?**
a. Control Of Anterior Pituitary Hormone Secretion.
b. Control of sleep and wakefulness.
c. Regulation Of Body Water And Urine Osmolality.
d. Regulation of core body temperature.
e. Regulation Of Feeding.

Answer b (memorize)

22. With reference to pituitary function Which one of the following is NOT true?
a. Adrenocorticotropic hormone secretion is inhibited by a rise in blood cortisol.
b. Growth hormone is secreted only before adulthood.
c. The hypothalamus secretes both growth hormone releasing factor and growth hormone-inhibiting factor.
d. Oxytocin migrates in neurons from hypothalamus to posterior pituitary.
e. Storage of anti-diuretic hormone is in the pituitary.

Answer b

23.True about hypothalamic hormones:
a. ADH is produced by hypothalamus stored in anterior pituitary gland.
b. Hypothalamus produces both FSH & LH.
c. All hypothalamic hormones stimulate anterior pituitary gland hormones.
d. GHRH Stimulate (FSH) & (LH) release from anterior pituitary
e. All hypothalamic hormones are either peptides or Catecholamines.

Answer E

24.Which part of the brain controls thirst and urine output, food intake, and body temperature among other things?
a. Basal nuclei.
b. Brain stem.
c. Cerebral cortex.
d. Hypothalamus.
e. Thalamus.

Answer D

25.The hypothalamic-pituitary portal system is important in the regulation of all of the following hormones EXCEPT for
a. GH.
b. ACTH.
c. Vasopressin.
d. Prolactin.
e. TSH.

Answer C

26.Which of the following characterizes type I but not type II diabetes mellitus
a. Hyperglycemia.
b. Lack of insulin.
c. Polyuria Polydipsia.
d. Can usually be successfully managed by dietary control & weight reduction without the necessity of insulin injections.
e. Lack Of Insulin Necessary.

answer B

27.The hormone that, in general is antagonistic to all the others in terms of metabolic effects is
a. Growth Hormone.
b. Glucagon.
c. Epinephrine.
d. Insulin.
e. Cortisol.

Answer D

28.Which one of the following about anti-diuretic hormone (ADH) is NOT true:
a. It Is Synthesized In Neurons.
b. It is carried to the pituitary gland via capillaries.
c. Its Release Into The Blood Is From The Posterior Pituitary.
d. Lack of ADH causes diabetes insipidus.
e. ADH acts on the kidney tubules.

Answer b

29.Which of the following probably triggers the onset of labor?
a. ACTH in fetus.
b. ACTH in the mother.
c. Prostaglandins.
d. Oxytocin.
e. Placental renin.

Answer D

30.Which one of the following is not secreted by pituitary gland?
a. Prolactin.
b. Oxytocin.
c. G.H.
d. Somatomedin.
e. L.H.

Answer d

31.- All of the following are true about GH except:
a. Gigantism Is Related To Overproduction Of Growth Hormone.
b. Another term for Growth hormone is somatotropin.
c. GH and insulin function synergistically.

d. GH decrease glucose uptake by muscle cells.
e. Somatostatin stimulate GH release.

Answer E

32.- All of the following are true about GH except:

حلوه مرتين شكله رح ييجي

a. Gigantism Is Related To Overproduction Of Growth Hormone. b. Another term for Growth hormone is somatotropin.
c. GHandinsulinfunctionsynergistically.
d. GH decrease glucose uptake by muscle cells.
e. Somatostatin stimulate GH release.

Answer E

33. is the part of the brain that controls the anterior pituitary gland secretions
a. Pineal Gland.
b. Thalamus.
c. Hypothalamus.
d. Medulla oblongata.
e. Corpus Callosum.

Answer c

34.If you were to eat four sugar glaze doughnuts and a large soft drink (like Pepsi), which hormone would you expect to be secreted at higher levels:
a. Cortisol.
b. Epinephrine.
c. Glucagon.
d. Insulin.
e. Oxytocin.

Answer D

35.An increase in plasma levels of ACTH leads to?
a. Increased glucagon levels.
b. Increased plasma cortisol levels.
c. Increased plasma epinephrine levels.
d. Increased plasma parathyroid hormone levels.
e. Increased plasma vasopressin levels.

Answer B

36.Physiological cut of the pituitary stalk (infundibulum) that connects hypothalamus to pituitary gland will show an increase in which of the following hormones?
a. Thyroid Stimulating Hormone.
b. Prolactin.
c. OxytocinandADH.
d. Growth hormone.
e. Cortisol.

Answer B

37.ACTH is the major regulator for secretion of which of the following from the adrenal glands?
a. Epinephrine And Norepinephrine
b. Cortisol.
c. Androgens(dihydroepiandrostendione-DHEA). d. Aldosterone.
e. All of the above are correct.

Answer b

38.Series of photographs taken of a middle-aged man over a period of 20 years demonstrates gradual coarsening of facial features and progressive protrusion of the brows. Upon questioning, the patient reports having to wear larger shoes than he did as a young man. Which of the following pair of hormones regulates the hormone responsible for these changes?
a. Thyroid stimulating hormone (TSH) and adrenocorticotropic hormone (ACTH).
b. Somatostatin and growth hormone releasing hormone (GHRH).
c. Prolactin And Follicle Stimulating Hormone(FSH).
d. Luteinizing hormone (LH) and human chorionic gonadotropin (hCG).
e. Dopamine And Norepinephrine.

Answer B

39.The supraoptic and paraventricular nuclei of the hypothalamus control the secretion of which of the following hormones to the posterior pituitary?
a. Oxytocin and prolactin.
b. Growth hormone and prolactin.
c. Follicle stimulating hormone and luteinizing hormone.
d. Antidiuretic hormone and oxytocin. والثنين single peptide 9 A.A
e. Adreno Cortico Trophic Hormone And Oxytocin.

Answer d

40.Hypopituitarism that involves all its hormone is characterized by
a. Weight Gain.
b. Intolerance to heat.
c. Infertility.
d. High levels of cortisol.
e. Excessive Growth Of The Soft Tissue.

Answer C

41.The following statements about Oxytocin is INCORRECT:
a. It Is important in parturition by stimulating uterine contractions.
b. It Is involved in a positive feedback cycle during parturition.
c. It Is secreted by the neurohypophysis.
d. It Stimulates synthesis of milk by glands.
e. Sucklingstimulatesitssecretion.

Answer D

42.The hypothalamus inhibits the release of

a. ACTH.
b. FSH.
c. GH.
d. Prolactin.
e. TSH.

Answer D

43.Synaptic vesicles store
a. Glycogen For Energy Production.
b. Oxygen.
c. Neurotransmitter.
d. Calcium ions.
e. Enzymes For Degrading Neurotransmitter.

Answer C

44.Which type of hormonal interactions is the effect of thyroxine and adrenaline on fat cells?
a. Permissive Effect.
b. Synergistic Effect.
c. Antagonistic Effect.
d. A and B.
e. AandC.

Answer A

Remember (GH and Insulin :synergistically,
from costanzo :Thyroid hormones act synergistically with growth hormone and somatomedins to promote bone formation
Cortisol & glucagon Permissive in glucnoeogenisissssss)

45.The release of somatostatin from islet delta cell & its subsequent action on nearby alpha & beta cells in the same pancreatic islet, this is an example of
a. Autocrine Types Of Hormone Action.
b. Exocrine types of hormone action.
c. Neuroendocrine Types Of Hormone Action. d. Paracrine types of hormone action.
e. Endocrine Types Of Hormone Action.

Answer D

46.Which of the following does NOT stimulate insulin secretion?
a. Elevated Blood Amino Acid Concentration.
b. Gastrointestinal hormones.
c. Big Sandwich.
d. Starvation.
e. Elevated Blood Glucose Concentration.

Answer D

47.Most hormones of the body are classified structurally as:
a. steroids.

b. Amines.
c. Carbohydrates.
d. Peptides and proteins.
e. Lipids.

Answer d

48.Hormone receptors:
a. Respond To A Particular Peptide Hormone Only.
b. Tend to increase in number in response to an increased presence of hormone molecules that bind to them.
c. Are found in the plasmamembranes of cells and the nuclei of other cells depend on the nature of the **hormone**.
d. Are found in the plasma membranes of cells that respond to steroid hormones.
e. None of the above.

Answer C

49.Which of the following secrete hormones
a. Hypothalamus.
b. Testes.
c. Kidneys.
d. Stomach and intestine. e. All of the above.

Answer E

50.Cortisol is an example of:
a. Adenylate Cyclase Mechanism(CAMP)of hormone action.
b. Guanylate cyclase mechanism (CGMP) of hormone action. Phospholipase C mechanism (IP3/Ca++) of hormone action.
c. Steroid Hormone Mechanism Of Hormone Action.
d. Tyrosine kinase mechanism of hormone action.

Answer C

51.All of the following produce hormones EXCEPT:
a. Posterior Pituitary
b. Stomach
c. Liver
d. Thyroid

Answer a

52.Which hormone of the following is the hormone made by liver:
a. Ghrelin
b. Somatomedin c. GH

Answer B

53.Affected in all hypopituitary disorders:
a.
b. Prolactin

c. GH

Answer A

54.Excess GH secretion, what is wrong?
a. Muscle Increases Glucose Uptake
b. Atrophy of pancreatic beta cells

Answer A

55.Which one of the following enhances GH?
a. Aging
b. Obesity
c. Fasting

Answer C

56.Wrong about mechanism of action of hormone:
a. protein hormones can not penetrate cell membranes and their receptors are found on the cell's surface.
b. Protein hormones activate the G-protein in the cell membrane.
c. Amino Acid derivatives hormones are lipid soluble and they can penetrate cell membrane as well as nuclear membrane.
d. All steroid hormones always bind receptors inside the cell of the nucleus.

Answer D

57.True about G protein:
a. G-protein is composed of 3 subunits alpha,beta and delta.
b. the active part of G-protein is the beta subunit; which separates from the G protein when it is activated.
c. Relays on a signal from the first messenger/receptor complex to a membrane protein to activate processes

Answer C

58.True about desensitization:
a. it happens directly when the cells are exposed to a certain hormone for a short duration.
b. heterologous desensitization is characterized by loss of responsiveness only to the particular ligand and maintained responsiveness of the cell to other ligands; and homologous desensitization, in which the cell becomes unresponsive to other ligands as well.
c. desensitization is another term for upregulation.
d. An example on desensitization is type I Diabetes Mellitus.
e. noneoftheabove.

Answer e

59.A lot of hormones contribute in growth, choose the major growth hormones pair that determines growth of post uterine life:
a. Insulin,GH
b. Thyroid hormone, insulin
c. GH,IGF-1

d. Estrogen,androgen

Answer c

60.Hormone that binds cytoplasmic receptor:
a. Calcitonin
b. Insulin
c. Glucagon
d. Progesterone

Answer d

61.What is the second messenger of oxytocin & TRH?
a. IP3.
b. cAMP.
c. cGMP.

Answer A

62.Patient with cardiomegaly and other things, the abnormal hormone is:
a. GH
b. Prolactin
c. ADH
d. Oxytocin
e. TSH

Answer A

63.Acromegaly and gigantism are due to?
a. Insulin Deficiency
b. ACTH overproduction
c. ACTHdeficiency
d. GH overproduction
e. GH deficiency

Answer D

64.Find the odd hormone:
a. Growth Hormone.
B.. prolactin.
c. Somatostatin.
d. Cortisol.
e. Calcitonin.

PAnswer d

65.In Comparison of cortisol and aldosterone, which of the following NOT True:
a. Cortisol has mineralocorticoid activity.
b. Aldosterone has some glucocorticoid activity.
c. The rate of secretion of aldosterone is higher than cortisol.

Ans c

66.Which one of the following about Aldosterone is NOT true:
a. Assists in compensation for depletion of blood volume by hemorrhage.
b. Is secreted by the zona glomerulosa of the adrenal cortex.
c. It contributes in glucocorticoid activity.
d. Output is principally dependent on adrenocorticotropic hormone secretion.
e. Promotes Renal Loss Of Potassium.

Answer d

67.Although the adrenal cortex secretes at least _____ different hormones, about 95% of the mineralocorticoid activity is due to ______.
a. 3,Aldosterone.
b. 2,Cortisol.
c. 4,Gonadocrticoids. d. 5,Epinephrine.
e. 7,Norepinephrine

Answer A

68.A tumor in the adrenal zona glomerulosa can cause hypersecretion of hormones produced in that region. Which of the following might you expect to find in a patient with such a tumor?
a. Decreased blood calcium levels.
b. Increased blood glucose levels.
c. Increased blood sodium levels.
d. Increased Dehydration.
e. Increased Ketoacidosis

Answer c

69.ACTH is the major regulator for secretion of which of the following from the adrenal glands?
a. Epinephrine and norepinephrine.
b. Cortisol.
c. Androgens(dihydroepiandrostendione-DHEA).
d. Aldosterone.
e. All of the above are correct.

مكررر من فوء

Answer b

70.Adrenal cortical hormones essential for sodium and potassium regulation is?
a. Progesterone.
b. Epinephrine and norepinephrine.
c. Cortisol
d. Androgens.
e. Aldosterone.

Answer E

71.Which of the following statements concerning adrenocortical hormones is INCORRECT?
a. Mineralocorticoids are essential for life.
b. They all combine with intracellular receptors.
c. They are all controlled primarily by ACTH.
d. They are all derived from cholesterol.
e. They are all steroids.

Answer c

فشئنا رقم

73.The most important hormone in keeping normal K+ concentration in the body:
a. Cortisol.
b. Vasopressin.
c. Insulin.
d. Aldosterone.

Answer d

74.Wrong about ACTH:
a. Secreted when the median eminence is stimulated.
b. Its secretion is affected by aldosterone.
c. Is a Polypeptide
d. Increases The Release Of Cortisol.

Answer b

75.which of the following doesn't stimulate ALDOSTERONE:
a. Potassium
b. ACTH
c. Sodium
d. Renin

Answer c

76. Cortisol has permissive effect with glucagon in:
a. Gluconeogenesis.
b. Glycogenolysis.
c. Lipolysis.
d. Vasoconstriction

Answer A

77.Which hormone lead to hypertension?
a. Angiotensin 2.
b. Insulin.
c. Glucagon.
d. Thyroid hormone.

Answer a

78.Which one of the following Inhibits ACTH release:
a. Cortisol.
b. Aldosterone.
c. Insulin.
d. Thyroid hormone.
Answer a

79.Wrong about angiotensin II?
a. A maximal amount of aldosterone is needed for fluid balance.
b. Is the main stimulus of aldosterone.
c. Angiotensin I produces angiotensin II under the effect of enzyme/ hormone from the lungs.
d. Affects the reabsorption of sodium directly and indirectly.

Answer A

80.Wrong about direct cortisol functions:
a. Glycogenolysis.
b. Gluconeogenesis.

c. Fat Mobilization.
d. CNSfunction.

Answer A

Primary aldosterone stimulator:
a. Angiotensin II.
b. Changes in plasma potassium.
c. ACTH.
d. TSH.

Answer A

81.Main site of action for aldosterone?
a. Proximaltubule.
b. Distaltubule.
c. Collecting tubules.
d. Loop of Henle.

Answer c

82.All of the following apply to glucocorticoid except:
a. Antidiuretic Effect.
b. Gluconeogenesis.
c. Support vascular response.
d. Fatmobilization.

Answer A

SssssssssSssssssssSssssssssSssssssssSssssssssSssssssssSssssssssSssssssss
F

83.A patient with parathyroid deficiency 10 days after thyroidectomy will show
a. Increased muscular excitability, high plasma Ca and bone resorption.
b. High plasma phosphate, high plasma Ca++ and bone resorption.
c. High plasma Ca++, high level of active vitamin D and tetanus.
d. A low plasma phosphate, high plasma Ca levels and tetanus.
e. A low plasma Ca levels, increased muscular excitability.

Answer E

84. Which of the following is not involved in regulation of plasma Ca++ levels
a. Thyroid.
b. Small intestine.
c. Skin.
d. Lungs.
e. Kidneys.

Answer d

85.Which of the following statements concerning parathyroid hormone's (PTH) actions is INCORRECT?
a. An elevated plasma calcium acts directly on the parathyroid gland to stimulate PTH secretion.
b. PTH helps the kidneys excrete excess phosphate from the body.
c. PTH promotes localized dissolution of bone by stimulating osteoclasts.
d. PTH promotes the rapid movement of Ca from the bone fluid into
the plasma.
e. PTH stimulates the reabsorption of Ca from the kidney.

Answer a

86-Low blood glucose level typically results in the secretion of all of the following EXCEPT:

a. Cortisol.
b. Glucagon.
c. Growth Hormone.
d. PTH.
e. Thyroxine(T4).

Answer d

87.Each of the following hormones is an amino acid derivative EXCEPT:

a. Epinephrine.
b. Melatonin.
c. Norepinephrine.
d. Thyroid stimulating hormone (TSH).
e. Thyroxin(T4).

Answer d

88-Regarding the thyroid hormones;

a. They decrease the basal metabolic rate.
b. They are lipid soluble steroid hormones.
c. T4 is four time more active than T3.
d. In the serum most of the thyroid hormones are in the free form.
e. After birth they stimulate development of the central nervous system

Answer e

89-Hyperthyroidism can be due to all of the following EXCEPT

a. Lack of iodine.
b. Thyroid-stimulating immunoglobulin.
c. TOOmuchT4orT3.
d. TOOmuchTRH.
e. TOO much TSH.

Answer a

90.Which of the following hormones enhances the formation of the active form of vitamin D?

a. Aldosterone.
b. Calcitonin.
c. Cortisol.
d. Parathyroid Hormone.
e. Thyroxine.

Answer d

91-Which one of the following about osteoporosis is not true:

a. The most common of all bone diseases in adults specially in old age
b. Occurs In Females Only.
c. It results from diminished organic matrix rather than abnormal bone calcification.
d. Lack of physical stress on the bone because of inactivity one of the causes of osteoporosis.
e. It is a different disease from osteomalacia.

Answer b

92. Which one of the following factors is the most important in the production of 1,25 (OH)2-D from 25 (OH)D in the kidney:

a. LowplasmaCa++level.

b. Low Plasma Phosphate Level.
c. PTH.
d. Insulin.
e. GH.

Answer C

93. Which of the following is INCORRECT concerning PTH, calcitonin & vitamin D?
a. Vitamin D deficiency is the cause of rickets.
b. PTH is the most important hormone in the control of calcium metabolism.
c. Both calcitonin & PTH are produced in the follicle cells of the thyroid gland.
d. Vitamin D is actually a hormone that increases calcium absorption in the intestine.
e. Parathyroid hormone is essential for life.

Answer C

95. Calcitonin has which of the characteristics?
a. It stimulates the action of osteoclasts.
b. Its absence or its excess can be fatal.
c. The blood iron level directly controls the secretion of calcitonin.
d. It helps maintain the homeostasis of calcium & phosphate in the blood.
e. It is produced by the parathyroid glands.

Answer D

96. Which of the following biochemical events does NOT take place within the thyroid gland during hormone synthesis?
a. Four iodine molecules combine with one tyrosine molecule to form one tetraiodothyronine molecule.
b. Two iodine molecules combine with one tyrosine molecule to form one diiodotyrosine molecule.
c. Two diiodotyrosine molecules combine to form one molecule of thyroxine.
d. One monoiodotyrosine molecule combines with one diiodotyrosine molecule to form one triiodothyronine molecule.
e. Iodiderecyclingoccurswithinthethyroidfollicularcell.

Answer A

97. Which of the following hormones is very important during early development of the nervous system?
a. Growth Hormone.
b. Thyroid Hormone.
c. Cortisol.
d. Parathyroid Hormone.
e. Noneoftheabove Are Correct.

Answer B

98. Iodine is necessary for the formation of
a. ACTH.
b. Calcitonin.
c. Cortisol.
d. Insulin.
e. Thyroid Hormone.

Answer e

99. Which one of the following about the T4 is FALSE:

a. Is quantitatively the major precursor of T3.
b. Is formed by condensation of 2 iodinated tyrosine.
c. Binds directly to DNA in the nucleus of target cells.
d. Is bound to protein in the plasma.
e. Has one-week half-life.

Answer c

100. Which one of the following hormones is least important in bone formation and Ca metabolism:
a. PTH.
b. Aldosterone.
c. 1,25 - dihydroxycholecalciferol.
d. GH.
e. Insulin.

Answer b

101. Which one of the following about T3 is NOT TRUE?
a. Is converted into rT3 in some conditions.
b. Is made up of two iodinated tyrosine molecules.
c. Mainly produced from T4.
d. The Most Active Hormone Of Thyroid Gland.
e. Very little is produced from the thyroid gland.

Answer a

102. Which one of the following hormones most probably is least secreted during stressful conditions?
a. Cortisol.
b. Prolactin.
c. G.H.
d. Somatostatin.
e. Thyroxine.

Answer e

103. The following hormones counteract the hypoglycemic effect of insulin EXCEPT:
a. Thyroxine.
b. Growth Hormone.
c. Glucagon.
d. Cortisol.
e. Adrenaline.

Answer A

104. The hormone that aids in determining the Basal metabolic rate (BMR) is
a. Estrogen.
b. Thyroid Hormone.
c. Insulin.
d. Epinephrine.
e. Testosterone.

Answer b

105. Dwarfism & mental retardation may be the result of a deficiency of
a. Growth-hormone releasing hormone.
b. GH.
c. Somatomedins.
d. Thyroid Hormones.

e. Adrenaline Hormone.

Answer d

106. Hormone that has receptor in almost all cells:

a. Adrenocorticotropin.
b. Thyroxin.
c. Parathyroid.
d. TSH.
e. LH.

Answer b

107. One of the following hormones is not correctly linked to its actions: (x = effective, -- = not effective)

	Process → Hormone ↓	glycogenolysis	lipolysis	gluconeogenesis	Inhibition of Glu intake
a-	Glucagon	x	-	x	-
b-	GH	x	x	-	x
c-	Cortisol	x	x	-	x
d-	Thyroid H	x	-	-	x
e-	epinephrine	x	-	x	x

☐ Picture 1

Answer d

108. One of these hormones when present in excessive amounts results in protein catabolism: -

a. Insulin. b. GH.
c. T3.
d. IGF-1. e. PRL.

Answer c

109. Where is 1,25 (OH)D produced from:

a. Liver.
b. Kidney.
c. Skin.
d. Stomach

Answer b

110. Choose the wrong sentence:

a. Ca,Mg And Phosphate Are Not Important.
b. Vitamin D is the major regulator for Ca.
c. Calcitonin decreases Ca blood level
d. Alkalosis decreases free calcium levels.

Answer a

111. Which pair of the following hormones is the most potent activator of the synthesis of 1,24-(OH)2 vit D3.

a. GH & PRL.
b. GH & insulin.
c. PRL & insulin.
d. PTH,lowP.
e. PTH, low Ca +2.

Answer d

112. About Ca+2 metabolism, which one is Not True:
a. PTH and vit D has synergistic effect.
b. Calcitonin Reduces(Ca)Level.
c. PTH and vit D has the same effect.

Answer c

113.-Which is false about the thyroid:
a. Iodine deficiency doesn't cause goiter
b. Thyroid hormones are amino acid derivatives.

Answer a

114. Which is false about T4:
a. It acts more rapidlythanT3.
b. T4 has longer half-life than T3

Answer A

115-Which is true about thyroglobulin:
a. Contains MIT & DIT.
b. glycoprotein produced by the follicular cells of the parathyroid gland

Answer A

116-True about Thyroxin synthesis:
a. Iodide (I-) is oxidized to Iodine (I2)
b. One tyrosine can carry 3 iodine molecules maximum.

Answer A

117-What happens to most of T4?
a. Converted to T3
b. Converted to reverse T3

Answer A

118- which of the following does not occur in thyroid hormone synthesis:
a. 4 molecules of iodine bind to one molecule of tyrosine to form tetraiodothyronine
b. When one MIT binds with DIT, they produceT3
c. WhentwoDITbindwitheachother,theyproduceT4

Answer A

119-True about T3:
a. promotes growth
b. contains 2 iodine molecules

Answer A

120- Not a symptom of hyperparathyroidism
a. tetany
b. softening of the bones

121-Not made in the liver
a. calcitonin
b. 25(OH)D

Answer A

122. Wrong about Vit. D:
a. making ergocalciferol is sufficient for humans
b. 1,25(OH) D is the most potent form

Answer A

123-Wrong about calcitonin?

a. Deficiency causes hypercalcemia but hypersecretion doesn't cause hypocalcemia
b. Produced by thyroid

Answer A

124-Wrong about endocrine:
a. anterior pituitary hormone directly inhibits parathyroid
b. hypothalamus regulates anterior pituitary gland hormones

ANSWER A

Ssssssssss
No
125. All of the following regulate the excretion of K+ by the kidney EXCEPT ONE
a. Aldosterone.
b. ADH.
c. Insulin.
d. Acid-base balance.
e. [Na+] of tubular fluid.

Answer c

126.Which of the following about the dehydration effects in insulin deficiency is NOT true:
a. Osmotic pressure of tubular fluid increases.
b. Cellular dehydration occurs.
c. Both ECF and ICF dehydration develops.
d. Osmotic diuresis occurs.
e. Tubular reabsorption of fluid increases.

Answer E

127-Which of the following is NOT produced by the exocrine part of the pancreas?
a. Amylase.
b. Carboxypeptidase. c. Lipase.
d. Somatostatin.
e. Trypsinogen.

Answer d

128-Which of the following characterizes type I but not type II diabetes mellitus?
a. Hyperglycemia.
b. Lack of insulin.
c. Polyuria & polydipsia.
d. Can usually be successfully managed by dietary control & weight reduction without the necessity of insulin injections.
e. Lack of insulin necessary.

Answer B

129-The renal threshold in diabetic patients is about:
a. 120mg/100mlplasma.
b. 150mg/100mlplasma.
c. 180 mg/100 ml plasma.
d. 220mg/100mlplasma.
e. 250mg/100mlplasma.

Answer c

130-Which one of the following about obesity is TRUE:

a. Obesity is the most common and most expensive nutritional problem in the industrialized world specifically in the U.S.A.
b. A convenient and reliable indicator of body fat is the (PMI).
c. (EMI) is the body weight (in Kg) divided by the square of the height (in meters).
d. Values above 25 are abnormal, individuals with values of 25-30 are overweight, and those with values > 30 are obese.
e. All Of The Above.

Answer e

131-Type-1 diabetes mellitus is different from type-2 in all of the following EXCEPT
a. Plasma Insulin Level.
b. Plasma Glucose Level.
c. Insulin sensitivity.
d. Age Of Onset.
e. Bodyweight(normally).

Answer b

132-Regarding urine in a normal person in a regular diet, all the following are true EXCEPT:
a. Contains glucose and protein.
b. Contains Urea And Creatinine.
c. Does not contain inulin.
d. Is acidic.
e. Is hyperosmolar.

Answer a

133-Which one of the following hormones is hypoglycemic
a. Growth Hormone
b. Glucagon.
c. Epinephrine.
d. Insulin.
e. Cortisol.

Answer d

134-Which one of the following is the MOST important hyperglycemic hormone?
a. Growth.
b. Cortisol.
c. Glucagon.
d. Adrenaline.
e. Thyroxine.

Answer c

136-Choose the Wrong pair:
a. Epinephrine:increased glycogenolysis in skeletal.
b. Progesterone:increased glucose in plasma.
c. GH: increased glucose in plasma.
d. Glucagon:increased gluconeogenesis.
e. Insulin:increased protein synthesis.

Answer b

137-correct about insulin independent diabetes:
a. Insulin is normal or above normal.
b. Atrophy of beta cells of pancreas.
c. Insulin is below normal level.

Answer a

138.Wrong about glucose homeostasis:
a.The rates of secretion of cortisol and growth hormone are not usually coupled to the absorptive-post-absorptive pattern
b.Glucagon and the sympathetic nervous system are activated during the post absorptive period
c.Their presence in the blood at basal concentrations is necessary for normal adjustment of lipid and carbohydrate metabolism to the post absorptive period
d.Excessive amounts of either hormone do not cause abnormally elevated plasma glucose concentrations
e.Insulin secretion and plasma concentration are increased during the absorptive period and decreased during post-absorption

Answer d

139-Which of the following doesn’t happen in patient with diabetes:
a. Diabetic coma could be caused by dehydration.
b. Increased Osmotic Diuresis.
c. Increased tubular reabsorption.
d. Increased ECF volume.
e. Increased ECF and ICF volume.

Answer c

140-What is the action that needs the least amount of insulin hormone?
a. Inhibiting Hepatic Gluconeogenesis.
b. Lipolysis inhibition.
c. Stimulation of amino acid uptake.

Answer A%

141-Wrong about type 2 diabetes mellitus
a. Not limited to obesity and the limited cause.
b. Treatment being similar to DM1.

Answer b

142-Constant glucose level to?
a. Brain.
b. Liver.
c. Muscles.

Answer a

143-True about insulin
a. Requirement Increases In Obesity.
b. It is a polypeptide containing 4 peptide chains.
c. It is a hyperglycemic hormone.

Answer a

144-True about DM?
a. Type 2 are usually obese and have a family history of the disease.
b. Type 1 is insulin independent.
c. Blood glucose is decreased in type 1 while it is increased in type 2.

Answer a

145-Wrong about DM?
a. Type 2 Has Peripheral Resistance Which Involves.
b. Decreased glucose uptake by skeletal muscles and brain tissue.
c. Type 1 usually affects children
Answer b

146-Is not raised in severely uncontrolled DM
a. Blood Volume.
b. Glucose.
c. Glucagon.

Answer a

147-Regulates potassium within normal range
a. Insulin.
b. Glucagon.
c. Leptin.

Answer a

148-What is the concentration of glucose in diabetic patients?
a. 300.
b. 100.

Answer a

149. correct about insulin independent diabetes
A. Insulin is normal or above normal
B.atrophy of beta cells of pancreas
C. insulin is below normal level

Answer A
المفروض A&B بس الدكتور حسب بي غلطططططط

150. least concentration of insulin causes?
A. inhibition of lipolysis
B. inhibition of hepatic gluconeogenesis
C. increase glucose uptake

Answer B

F

151. 95% of mineralocorticoids are ?
a.deoxycorticosterone
b.Aldosterone
c.progesterone

answer B

All domains in PKC except

G protein

152.Uncontrolled diabetes mellitus?
a.High blood volume
b.low blood volume
not sureeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeeee
answer A

153.A decrease in extracellular fluid volume would be expected to cause increased secretion of all of the following EXCEPT:
a.Estrogen.
b.Renin.

c.Vasopressin.
d.ADH.
e.Cortisol.

Answer A

154-In which of the following thyroid abnormalities goiter DOES NOT occur:
a.Hypothyroidism due to lack of iodine.
b.Hyperthyroidism due to TSI.
c.Hypothyroidism due to primary failure of thyroid gland.
d.Hyperthyroidism due to hypersecreting thyroid tumor.
e.Hyperthyroidism secondary to excess hypothalamic secretion.

Answer d

155.Which one of the following about glucose homeostasis is not true?
a.The rates of secretion of cortisol and growth hormone are not usually coupled to the absorptive-post-absorptive pattern
b.Glucagon and the sympathetic nervous system are activated during the post absorptive period
c.Their presence in the blood at basal concentrations is necessary for normal adjustment of lipid and carbohydrate metabolism to the post absorptive period
d.Excessive amounts of either hormone do not cause abnormally elevated plasma glucose concentrations
e.Insulin secretion and plasma concentration are increased during the absorptive period and decreased during post-absorption

Answer d

156-Which one of the following about amylin and insulin hormones is not true?
a.Patients with type I diabetes have a deficiency of insulin with a normal level of amylin
b.They are co-packaged in the same granules
c.Amylin hormone complements the actions of insulin in post prandial glucose homeostasis via several mechanisms
d.Plasma concentrations of the two hormones display a similar diurnal pattern of low fasting levels and high levels in response to meals
e.Consequently, amylin is normally co-secreted with insulin

Answer A

160.Hormone increases efferent arteriole resistance and increase GFR?
a.ANG II
b.ANG I
c.OXYTOCIN

Answer: ANG II

162.Which of the following doesn’t happen in case of excessive aldosterone?
a. dyhyration and acidosis
b.**lower potassium levels**
c.increase Na+ levels

Answer: dehydration and acidosis

163.Which of the following is not a physiological regulator for aldosterone?
Answer: ANG I

In a patient with lack of ADH, which segment is the most diluted?
a)Thin descending
b)Thin ascending
c)Thick ascending
d) Late distal + Cortical collecting

answer D

164) Which of the following not secreted from kidney ?
A)Renin
B) Erythropoietin
C) ADH
D) Colcitriol

answer C

165.what is the hormone that decreases insulin secretion

a. leptin
b. gh
c. cortisol

answer A

166.Which of the following is incorrect regarding Vitamin D?
Answer: D2, D3 they have the same efficient

Which of the following does not use cAMP as a second messenger?
a. ACTH
b. MSH
c. GLUCAGON
d. insulin

Answer: insulin&oxytocin (both are correct)

167.estrogen hormone dosent contribute with the gh in the protein synthesis

Severe uncontrolled diabetes mellitus leads to : Choose the incorrect answer
a. decrease in PH.
b. increase plasma k+ concentration.
c. increase Blood volume.
d. increase osmotic diuresis of urine

e. increase amino acids.

answer B (n the diabetic, **amino acid catabolism is exaggerated in the fasting state** as reflected by increased uptake of alanine by the liver for gluconeogenesis and accelerated branched-chain amino acid catabolism in muscle.
bssssss brdo
uptake of branched chain amino acids by muscle is reduced and these amino acids accumulate in increased amounts in arterial blood)

168.The activity of the adrenal zona glomerulosa is stimulated mainly by:
a. Cortisol.
b. Hypernatremia.
c. Hypokalemia.
d. Angiotensin II.
e. Atrial natriuretic peptide.

answer D

169.Triiodothyronine (T3): choose the correct answer
a. Binds to plasma membrane receptors
b. Is all protein bound in the circulation
c. Promotes Growth.
d. Is the only biologically active form of thyroid hormone
e. 90% is formed from thyroxine (T4)

answer C

170.Which one of the following about the mechanism of action of hormones is true?
a. Some hormones of steroid types bind with receptors in the cell membrane in certain conditions.
b. Most of the protein hormones have Diacylglycerol and IP3 as a second messengers.
c. All amino acids derivatives hormones bind with receptors inside the cells or nucleus.
d. Once the hormone binds with the receptors for sure it continuous to proceed functioning.
e. All steroid hormones bind always with receptors in the cells or nucleus.

answer A

171.PTH has which of the following primary actions ?
a. It decreases renal tubular calcium reabsorption.
b. It increases bone resorption.
c. It increases gastrointestinal calcium absorption.
d. It increases 24,25-(OH)2-vitamin D synthesis.
e. It decreases urinary phosphate excretion.

answer B

172.Antidiuretic hormone: Choose the correct answer:
a. Is produced by posterior pituitary gland cells
b. Increases the permeability of the cells in the 100p of Henle to water
c. Secretion is little affected by changes in plasma osmolality of less than 10%

d. Secretion increases when plasma volume falls but osmolality is unchanged
e. Causes the osmolality of the plasma to rise

answer C

173. The increased levels of one choice of the following hormones accompany the maternal morning sickness:
a. Progesterone and estrogen
b. Human placental lactogens (HPLS) and prolactin
C. TRH and TSH
d. GnRh and LH
e. hCG and Thyroxine

answer E (haitham proved)

174.The secretion and release of growth hormone: Choose the incorrect answer:
a. Is promoted by hypothalamic GH releasing hormone and is pulsatile in nature
b. Is prompted by IGFS
c. Is increased by exercise and stress
d. Is promoted by acetylcholine indirectly
e. Is strongly inhibited by hypothalamic somatostatin

answer B

175.During sleep there is a fall in the circulating level of: Choose the incorrect answer :
a. cortisol
b. T4.
c. Growth hormone
d. Adrenaline.
e. insulin

answer A

176.The free functional percentage of Aldosterone is:
a. relatively high
b. very low
c. very high
d. high
e. low

answer A

177.ACTH secretion is inhibited by
a. Cortisol.
b. Norepinephrine.
c. Androstenedione.
d. ADH.
e. Testosterone.

answer A

ANATOMY SECTIONNNNNNNNNNNNNNNNNNNNNNNNNNNN

1. Anterior Midline Masses:

A. Thyroglossal duct cyst
B. lateral cervical cyst
C. hyoid cyst

answer A

2. All of the following are true considering Sheehan Syndrome EXCEPT:
A. Lactrotroph hyperplasia
B. Relaxation of infundibular arteries
C. can happen during pregnancy

answer B

3. **Mismatch**:
A. Neuroendocrine - Anterior Pituitary
B. severe headache – pituitary apoplexy

answer A

4. All of the following are TRUE except.
A. Bright Dot on the (MRI) is Vasopressin from the Anterior Pituitary
B. pituitary gland is medial to cavernous sinus and inferior to optic chiasm and superior to sphenoid air sinus
C.Superior hypophyseal arteries supply pars tuberalis D.blood can flow from posterior lobe to anterior lobe of pituitary gland

answer A

5. The superior thyroid artery is initially associated with the _______ and must be ligated _____ during thyroidectomy.
A. External Laryngeal Nerve, away the gland
B. Internal Laryngeal Nerve, away from the gland
C. External Laryngeal Nerve, near from the gland
D. Recurrent Laryngeal Nerve, near the gland
E. Recurrent Laryngeal Nerve, away from the gland

answer C

6. When a mass is associated with the thyroid gland, and you ask the patient to swollow, the mass moves up, because of the:
A.Paratracheal fascia
B. Pretracheal Fascia
C. laryngeal fascia
D. attachment of muscles

answer B

7. Enlarged Thyroid which moves behind the sternum:
A. True capsule of thyroid
B. Retrosternal Goiter
C. Hyoid bone

answer B

8. Thyroid Gland was formed between.
A. Tuberculum Impar - Copula
B. Ultimobrachial bodies- tuberculum impair
C. first and second branchial arches

answer A

9. Wrong about pituitary:
A. Hypothalamohypopheseal tract injury lead to ADH deficiency

B. Posterior pituitary contain neurosecretory granules
C. Anterior lobe give bright spot
D.The gland is inferior to the optic chiasm

answer C

10. Upper Limitation of thyroid gland:
A. Pretracheal fascia
B.The superior belly of the omohyoid
C. The capsule of thyroid

answer A
maybe b

11. Acidophils cells of the pituitary secretes:
A- GH
B- TSH
C- ACTH

answer A

12. Which of the following is WRONG:
A. Inferior parathyroid originate from dorsal wing of 4th pouch
B.The thymus originate from ventral wing of 3th pouch
C.oxyphil cells show low levels of PTH synthesis

answer A

13. Wrong about pituitary gland blood supply?
A.The venous drainage of posterior pituitary lobe is into cavernous sinus
B.lymphatic drainage of thyroid gland is into superior and posterior deep cervical nodes
C. Primary plexus drain into cavernous

answer C

14. Right about branchial fistula?
A.They are midline in position
B. It is formed because of failure of second pharyngeal arch to grow cuadally over the third and fourth arches
C. It is located posterior to sternocleidomastoid muscle

answer B

15. Wrong about thyroid drainage
A. All drain into internal jugular vein
B. Superior thyroid vein drains into the internal jugular vein
C.The inferior thyroid veins of the two sides anastomose with one another as they descend in front of the trachea.

answer A

16. Parathyroid glands: which is incorrect:
a-Superior parathyroid glands receive most of their blood supply from the superior thyroid art.
2> parathyroid glands: which is incorrect:
a - the right parathyroid glands drain into the left internal jugular vein

17. thyroid gland: which is incorrect:
a- the pyramidal represents the inferior part of thyroglossal duct
b- Most of its blood supply is derived from the superior thyroid art

answer: B

18. Pituicytes are most precisely described as :
a- modified neurons
b- Secretory cells in the post pituitary
C- Glial cells in the pars nervosa

answer: C

19. eosinophilic cytoplasm, few rER, no secretory granules and abnormally shaped mitochondria are typical characteristics of:
a- chief cells of the parathyroid
b- Oxyphil cells
c- Cells of the zona glumerulosa
d- Cells of the zona fasciculata
e- Cells of the zona reticularis

answer: B

20. Oxyphil cells (wrong statement):
a- derived from the ultimobranchial body
21. (wrong statement):
a- the adrenal medulla is a modified parasympathetic ganglion.
22.pituitary gland (wrong statement)
a- secretory cells are present near the capillaries in the pars nervosa
b- Rathke's pouch is rudimentary in humans

answer: A

UNIT XIV

Endocrinology and Reproduction

1. Which receptor controls nitric oxide (NO) release to cause vasodilation during penile erection?
   A) Leptin receptor
   B) Angiotensin AT1 receptor
   C) Endothelin ETA receptor
   D) Muscarinic receptor

2. Which statement about antidiuretic hormone (ADH) is true?
   A) It is synthesized in the posterior pituitary gland
   B) It increases salt and water reabsorption in the collecting tubules and ducts
   C) It stimulates thirst
   D) It has opposite effects on urine and plasma osmolality

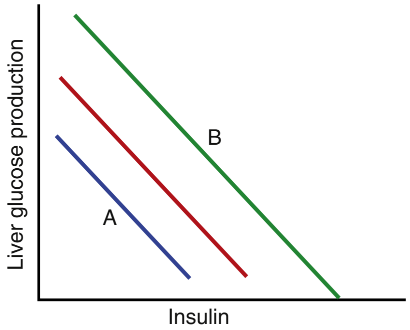
3. After menopause, hormone replacement therapy with estrogen-like compounds is effective in preventing the progression of osteoporosis. What is the mechanism of their protective effect?
   A) They stimulate the activity of osteoblasts
   B) They increase absorption of calcium from the gastrointestinal tract
   C) They stimulate calcium reabsorption by the renal tubules
   D) They stimulate parathyroid hormone (PTH) secretion by the parathyroid gland

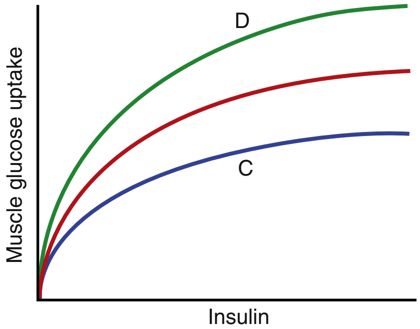
4. A patient has nephrogenic diabetes insipidus. Of the following options, which outcome would be expected or which intervention would be suggested?
   A) Expected outcome: decreased plasma sodium concentration
   B) Expected outcome: increased secretion of ADH from the supraoptic and paraventricular nuclei
   C) Expected outcome: high urine osmolality
   D) Suggested intervention: water restriction
   E) Suggested intervention: ADH antagonists (vaptans)

5. Within minutes after a normal delivery, flow through the foramen ovale decreases dramatically. What is the cause of this change?
   A) Increased formation of prostaglandin E_2 (PGE_2) in the endocardium
   B) Increased rate of flow through the pulmonary artery
   C) Increased left atrial pressure
   D) Increased right atrial pressure
   E) Increased partial pressure of oxygen (Po_2)

6. Which hormones antagonize the effect of NO and cause the penis to become flaccid after orgasm?
   A) Endothelin and norepinephrine
   B) Estrogen and progesterone
   C) Luteinizing hormone (LH) and follicle-stimulating hormone (FSH)
   D) Progesterone and LH

Questions 7–9





The red lines in the above figure illustrate the normal relationships between plasma insulin concentration and glucose production in the liver and between plasma insulin concentration and glucose uptake in muscle. Use this figure to answer Questions 7–9.

7. Which lines most likely illustrate these relationships in a patient with type 2 diabetes?
   A) A and C
   B) A and D
   C) B and C
   D) B and D

8. Which lines most likely illustrate these relationships in a patient with acromegaly?
   A) A and C
   B) A and D
   C) B and C
   D) B and D

9. Line D most likely illustrates the influence of which of the following?
   A) Exercise
   B) Obesity
   C) Growth hormone (GH)
   D) Cortisol
   E) Glucagon

10. Thecal cells in the follicle are not able to produce what sex steroid?
    A) Estradiol
    B) Testosterone
    C) Progesterone
    D) Dihydrotestosterone

11. A baby is born with a penis, a scrotum with no testes, no vagina, and XX chromosomes. This condition is referred to as hermaphroditism. What could cause this abnormality?
    A) Abnormally high levels of human chorionic gonadotropin (HCG) production by the trophoblast cells
    B) The presence of a testosterone-secreting tumor in the mother's right adrenal gland
    C) Abnormally high levels of LH in the maternal blood
    D) Abnormally low levels of testosterone in the maternal blood
    E) Abnormally low rates of estrogen production by the placenta

12. A young woman is given daily injections of a substance beginning on the sixteenth day of her normal menstrual cycle and continuing for 3 weeks. As long as the injections continue, she does not menstruate. The injected substance could be which of the following?
    A) Testosterone
    B) FSH
    C) An inhibitor of progesterone's actions
    D) A PGE_2 inhibitor
    E) HCG

13. Which of the following increases secretion of GH?
    A) Senescence
    B) Insulin-like growth factor-1 (IGF-1)
    C) Somatostatin
    D) Hypoglycemia
    E) Exogenous GH administration

14. Which of the following could inhibit the initiation of labor?
    A) Administration of an antagonist of the actions of progesterone
    B) Administration of LH
    C) Administration of an antagonist of PGE_2 effects
    D) Mechanically dilating and stimulating the cervix
    E) Administration of oxytocin

15. Exposure to ultraviolet light directly facilitates which of the following?
    A) Conversion of cholesterol to 25-hydroxycholicalciferol
    B) Conversion of 25-hydroxycholicalciferol to 1,25-dihydroxycholicalciferol
    C) Transport of calcium into the extracellular fluid
    D) Formation of calcium-binding protein
    E) Storage of vitamin D_3 in the liver

16. Which of the following decreases the pressure in the pulmonary artery after birth?
   A) An increase in systemic arterial pressure
   B) Closure of ductus arteriosus
   C) An increase in left ventricular pressure
   D) A decrease in pulmonary vascular resistance

17. Which of the following is both synthesized and stored in the hypothalamus?
   A) ADH
   B) Thyroid-stimulating hormone (TSH)
   C) LH
   D) Somatostatin
   E) Somatomedin

18. If a radioimmunoassay is properly conducted and the amount of radioactive hormone bound to antibody is low, what would this result indicate?
   A) Plasma levels of endogenous hormone are high
   B) Plasma levels of endogenous hormone are low
   C) More antibody is needed
   D) Less radioactive hormone is needed

19. By which mechanism do LH and FSH return to baseline levels?
   A) LH surge
   B) Negative feedback on gonadotropin-releasing hormone (GnRH) by progesterone
   C) Negative feedback on GnRH by estradiol
   D) Negative feedback on GnRH from testosterone

20. Spermatogenesis is regulated by a negative feedback control system in which FSH stimulates the steps in sperm cell formation. Which negative feedback signal associated with sperm cell production inhibits pituitary formation of FSH?
   A) Testosterone
   B) Inhibin
   C) Estrogen
   D) LH

21. Which of the following is true during the 12-hour period preceding ovulation?
   A) A surge of LH is secreted from the pituitary
   B) The surge occurs immediately after the formation of the corpus luteum
   C) The surge is followed immediately by a fall in the plasma concentration of progesterone
   D) The number of developing follicles is increasing

22. When do progesterone levels rise to their highest point during the female hormonal cycle?
   A) Between ovulation and the beginning of menstruation
   B) Immediately before ovulation
   C) When the blood concentration of LH is at its highest point
   D) When 12 primary follicles are developing to the antral stage

23. What accompanies sloughing of the endometrium during the endometrial cycle in a normal woman?
   A) An increase in progesterone
   B) The LH "surge"
   C) A decrease in both progesterone and estrogen
   D) An increase in estradiol

24. Some cells secrete chemicals into the extracellular fluid that act on cells in the same tissue. Which of the following refers to this type of regulation?
   A) Neural
   B) Endocrine
   C) Neuroendocrine
   D) Paracrine
   E) Autocrine

25. Which of the following pairs is an example of the type of regulation referred to in Question 24?
   A) Somatostatin—GH secretion
   B) Somatostatin—insulin secretion
   C) Dopamine—prolactin secretion
   D) Norepinephrine—corticotropin-releasing hormone (CRH) secretion
   E) CRH—adrenocorticotropic hormone (ACTH) secretion

26. A professional athlete in her mid-20s has not had a menstrual cycle for 5 years, although a bone density scan revealed normal skeletal mineralization. Which fact may explain these observations?
   A) She consumes a high-carbohydrate diet
   B) Her grandmother sustained a hip fracture at age 79 years
   C) Her blood pressure is higher than normal
   D) Her plasma estrogen concentration is very low
   E) She has been taking anabolic steroid supplements for 5 years

27. What is the nongenomic effect of testosterone on vascular smooth muscle?
   A) Vasodilation
   B) Vasoconstriction
   C) Increase in prostaglandins
   D) Increase in estrogen receptors

28. In the circulatory system of a fetus, which of the following is greater before birth than after birth?
   A) Arterial Po_2
   B) Right atrial pressure
   C) Aortic pressure
   D) Left ventricular pressure

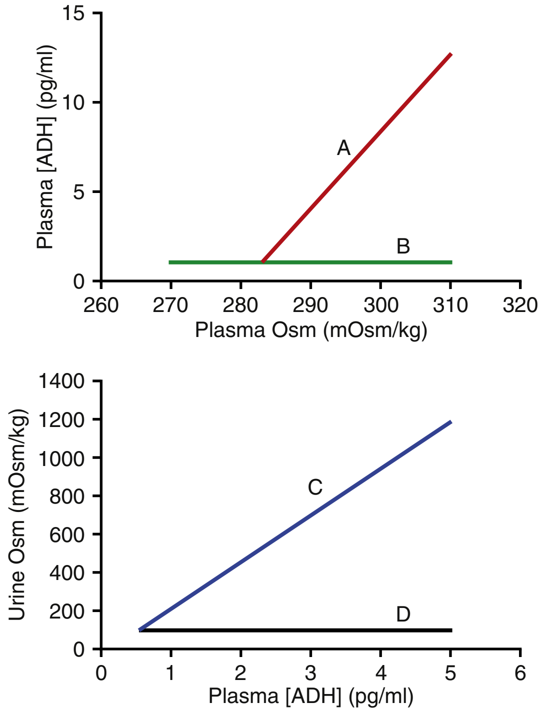
Questions 29 and 30

Match each of the patients described in Questions 29 and 30 with the correct set of plasma values listed in the table below. Normal values are as follows: plasma aldosterone concentration, 10 ng/dl; plasma cortisol concentration, 10 mg/dl; and plasma potassium concentration, 4.5 mEq/L.

	Aldosterone Concentration	Cortisol Concentration	Potassium Concentration
A)	10.0	2.0	4.5
B)	2.0	2.0	6.0
C)	40.0	30.0	2.0
D)	40.0	10.0	4.5
E)	40.0	10.0	2.0

29. A patient with Conn's syndrome.

30. A patient consuming a low-sodium diet.



31. In the above figure, which lines most likely reflect the responses in a patient with nephrogenic diabetes insipidus?
    A) A and C
    B) A and D
    C) B and C
    D) B and D

32. Which enzyme in the cytochrome P450 steroid synthesis cascade is directly responsible for estradiol synthesis?
    A) 17-beta-hydroxysteroid dehydrogenase
    B) 5-alpha reductase
    C) Aromatase
    D) Side chain cleavage enzyme

33. Which of the following is greater after birth than before birth?
    A) Flow through the foramen ovale
    B) Pressure in the right atrium
    C) Flow through the ductus arteriosus
    D) Aortic pressure

34. PTH does what directly?
    A) Controls the rate of 25-hydroxycholicalciferol formation
    B) Controls the rate of calcium transport in the mucosa of the small intestine
    C) Controls the rate of formation of calcium-binding protein
    D) Controls the rate of formation of 1,25-dihydroxycholicalciferol
    E) Stimulates renal tubular phosphate reabsorption

35. Which substances are most likely to produce the greatest increase in insulin secretion?
    A) Amino acids
    B) Amino acids and glucose
    C) Amino acids and somatostatin
    D) Glucose and somatostatin

36. Which of the following would be expected in a child with dwarfism due to pituitary dysfunction?

	Plasma [IGF-1]	Growth-Hormone-Releasing Hormone Secretion	Fasting Plasma [Glucose]
A)	↑	↑	↓
B)	↑	↑	↑
C)	↑	↓	↓
D)	↓	↓	↑
E)	↓	↓	↓
F)	↓	↑	↓

37. For male differentiation to occur during embryonic development, testosterone must be secreted from the testes. What stimulates the secretion of testosterone during embryonic development?
    A) LH from the maternal pituitary gland
    B) HCG
    C) Inhibin from the corpus luteum
    D) GnRH from the embryo's hypothalamus

38. A patient has an elevated plasma thyroxine (T_4) concentration, a low plasma TSH concentration, and her thyroid gland is smaller than normal. What is the most likely explanation for these findings?
    A) A lesion in the anterior pituitary that prevents TSH secretion
    B) The patient is taking propylthiouracil
    C) The patient is taking thyroid extract
    D) The patient is consuming large amounts of iodine
    E) Graves' disease

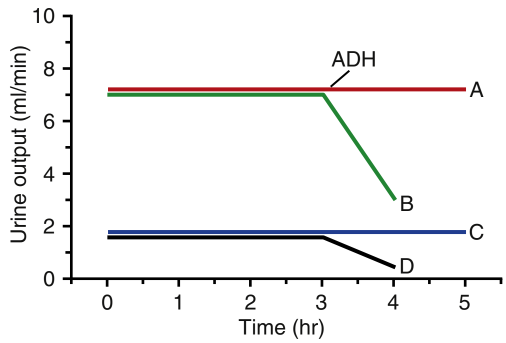
39. Extracellular ionic calcium activity will be decreased within 1 minute by which of the following?
    A) An increase in extracellular phosphate ion activity
    B) An increase in extracellular pH
    C) A decrease in extracellular partial pressure of carbon dioxide (PCO_2)
    D) All the above
    E) None of the above

40. As menstruation ends, estrogen levels in the blood rise rapidly. What is the source of the estrogen?
    A) Corpus luteum
    B) Developing follicles
    C) Endometrium
    D) Stromal cells of the ovaries
    E) Anterior pituitary gland

41. A 30-year-old woman reports to the clinic for a routine physical examination. The examination reveals she is pregnant. Her plasma levels of TSH are high, but her total thyroid hormone concentration is normal. Which of the following best reflects the patient's clinical state?
    A) Graves' disease
    B) Hashimoto's disease
    C) A pituitary tumor secreting TSH
    D) A hypothalamic tumor secreting thyrotropin-releasing hormone (TRH)
    E) The patient is taking thyroid extract

42. Which anterior pituitary hormone plays a major role in the regulation of a nonendocrine target gland?
    A) ACTH
    B) TSH
    C) Prolactin
    D) FSH
    E) LH

43. A female athlete who took testosterone-like steroids for several months stopped having normal menstrual cycles. What is the best explanation for this observation?
    A) Testosterone stimulates inhibin production from the corpus luteum
    B) Testosterone binds to receptors in the endometrium, resulting in the failure of the endometrium to develop during the normal cycle
    C) Testosterone binds to receptors in the anterior pituitary that stimulate the secretion of FSH and LH
    D) Testosterone inhibits the hypothalamic secretion of GnRH and the pituitary secretion of LH and FSH



44. An experiment is conducted in which ADH is administered at hour 3 to four subjects (A to D). In the above figure, which lines most likely reflect the response to ADH administration in a normal patient and in a patient with central diabetes insipidus?

	Normal	Central Diabetes Insipidus
A)	B	A
B)	B	D
C)	D	A
D)	D	B

45. Which of the following decreases the resistance in the arteries leading to the sinuses of the penis?
    A) Stimulation of the sympathetic nerves innervating the arteries
    B) NO
    C) Inhibition of activity of the parasympathetic nerves leading to the arteries
    D) All the above

46. A patient has a goiter associated with high plasma levels of both TRH and TSH. Her heart rate is elevated. This patient most likely has which condition?
    A) An endemic goiter
    B) A hypothalamic tumor secreting large amounts of TRH
    C) A pituitary tumor secreting large amounts of TSH
    D) Graves' disease

47. A man eats a low-carbohydrate meal that is rich in proteins containing the amino acids that stimulate insulin secretion. Which response accounts for the absence of hypoglycemia?
    A) Suppression of GH
    B) Suppression of somatomedin C secretion
    C) Stimulation of cortisol secretion
    D) Stimulation of glucagon secretion
    E) Stimulation of epinephrine secretion

48. A 46-year-old man has "puffy" skin and is lethargic. His plasma TSH concentration is low and increases markedly when he is given TRH. What is the most likely diagnosis?
    A) Hyperthyroidism due to a thyroid tumor
    B) Hyperthyroidism due to an abnormality in the hypothalamus
    C) Hypothyroidism due to an abnormality in the thyroid
    D) Hypothyroidism due to an abnormality in the hypothalamus
    E) Hypothyroidism due to an abnormality in the pituitary

49. Negative feedback on FSH release from the anterior pituitary in men that results in a reduction in estradiol production is due to which hormone?
    A) Progesterone
    B) Estradiol
    C) Testosterone
    D) Inhibin

50. During the first few years after menopause, FSH levels are normally extremely high. A 56-year-old woman completed menopause 3 years ago. However, she is found to have low levels of FSH in her blood. What is the best explanation for this finding?
    A) She has been receiving hormone replacement therapy with estrogen and progesterone since she completed menopause
    B) Her adrenal glands continue to produce estrogen
    C) Her ovaries continue to secrete estrogen
    D) She took birth control pills for 20 years before menopause

51. Blockade of what receptors will prolong erection in the male?
    A) Estrogen receptors
    B) Cholesterol receptors
    C) Muscarinic receptors
    D) Phosphodiesterase-5 receptors

52. Which of the following pairs of hormones and the corresponding action is incorrect?
    A) Glucagon—increased glycogenolysis in liver
    B) Glucagon—increased glycogenolysis in skeletal muscle
    C) Glucagon—increased gluconeogenesis
    D) Cortisol—increased gluconeogenesis
    E) Cortisol—decreased glucose uptake in muscle

53. A large dose of insulin is administered intravenously to a patient. Which set of hormonal changes is most likely to occur in the plasma in response to the insulin injection?

	Growth Hormone	Glucagon	Epinephrine
A)	↑	↓	↔
B)	↔	↑	↑
C)	↑	↑	↑
D)	↓	↑	↑
E)	↓	↓	↔

54. What is a frequent cause of delayed breathing at birth?
    A) Fetal hypoxia during the birth process
    B) Maternal hypoxia during the birth process
    C) Fetal hypercapnia
    D) Maternal hypercapnia

55. Which hormone is largely unbound to plasma proteins?
    A) Cortisol
    B) T_4
    C) ADH
    D) Estradiol
    E) Progesterone

56. What is the mechanism by which the zona pellucida becomes "hardened" after penetration of a sperm cell to prevent a second sperm from penetrating?
    A) A reduction in estradiol
    B) The proteins released from the acrosome of the sperm
    C) An increase in intracellular calcium in the oocyte
    D) An increase in testosterone that affects the sperm

57. Why is milk produced by a woman only after delivery, not before?
    A) Levels of LH and FSH are too low during pregnancy to support milk production
    B) High levels of progesterone and estrogen during pregnancy suppress milk production
    C) The alveolar cells of the breast do not reach maturity until after delivery
    D) High levels of oxytocin are required for milk production to begin, and oxytocin is not secreted until the baby stimulates the nipple

58. Which of the following increases the rate of excretion of calcium ions by the kidney?
    A) A decrease in calcitonin concentration in the plasma
    B) An increase in phosphate ion concentration in the plasma
    C) A decrease in the plasma level of PTH
    D) Metabolic alkalosis

59. A patient has hyperthyroidism due to a pituitary tumor. Which set of physiological changes would be expected?

	Thyroglobulin Synthesis	Heart Rate	Exophthalmos
A)	↑	↑	+
B)	↑	↑	−
C)	↑	↓	+
D)	↓	↓	+
E)	↓	↓	−
F)	↓	↑	−

60. A 25-year-old man is severely injured when hit by a speeding vehicle and loses 20 percent of his blood volume. Which set of physiological changes would be expected to occur in response to the hemorrhage?

	Atrial Stretch Receptor Activity	Arterial Baroreceptor Activity	ADH Secretion
A)	↓	↓	↑
B)	↓	↓	↓
C)	↔	↑	↑
D)	↑	↑	↑
E)	↑	↑	↓

61. If a woman has a tumor that is secreting large amounts of estrogen from the adrenal gland, which of the following will occur?
    A) Progesterone levels in the blood will be very low
    B) Her LH secretion rate will be totally suppressed
    C) She will not have normal menstrual cycles
    D) Her bones will be normally calcified
    E) All the above

62. When compared with the postabsorptive state, which set of metabolic changes would most likely occur during the postprandial state?

	Hepatic Glucose Uptake	Muscle Glucose Uptake	Hormone-Sensitive Lipase Activity
A)	↑	↑	↑
B)	↑	↓	↑
C)	↓	↑	↓
D)	↑	↑	↓
E)	↓	↑	↑

63. Very early in embryonic development, testosterone is formed within the male embryo. What is the function of this hormone at this stage of development?
    A) Stimulation of bone growth
    B) Stimulation of development of male sex organs
    C) Stimulation of development of skeletal muscle
    D) Inhibition of LH secretion

64. Which change would be expected to occur with increased binding of a hormone to plasma proteins?
    A) Increase in plasma clearance of the hormone
    B) Decrease in half-life of the hormone
    C) Increase in hormone activity
    D) Increase in degree of negative feedback exerted by the hormone
    E) Increase in plasma reservoir for rapid replenishment of free hormone

65. A patient arrives in the emergency department apparently in cardiogenic shock due to a massive heart attack. His initial arterial blood sample reveals the following concentrations of ions and pH level:

Sodium	137 mmol/L
Bicarbonate	14 mmol/L
Free calcium	2.8 mmol/L
Potassium	4.8 mmol/L
pH	7.16

To correct the acidosis, the attending physician begins an infusion of sodium bicarbonate and after 1 hour obtains another blood sample, which reveals the following values:

Sodium	138 mmol/L
Bicarbonate	22 mmol/L
Free calcium	2.3 mmol/L
Potassium	4.5 mmol/L
pH	7.34

What is the cause of the decrease in calcium ion concentration?
    A) The increase in arterial pH resulting from the sodium bicarbonate infusion inhibited PTH secretion
    B) The increase in pH resulted in the stimulation of osteoblasts, which removed calcium from the circulation
    C) The increase in pH resulted in an elevation in the concentration of HPO_4^-, which shifted the equilibrium between HPO_4^- and Ca^{++} toward $CaHPO_4$
    D) The increase in arterial pH stimulated the formation of 1,25-dihydroxycholecalciferol, which resulted in an increased rate of absorption of calcium from the gastrointestinal tract

66. A patient presents with tachycardia and heat intolerance. You suspect Graves' disease. Which of the following is not consistent with your diagnosis?
    - A) Increased total and free T_4
    - B) Suppressed plasma [TSH]
    - C) Exophthalmos
    - D) Goiter
    - E) Decreased thyroid radioactive iodine uptake

67. A 30-year-old woman is breastfeeding her infant. During suckling, which hormonal response is expected in the woman?
    - A) Increased secretion of ADH from the supraoptic nuclei
    - B) Increased secretion of ADH from the paraventricular nuclei
    - C) Increased secretion of oxytocin from the paraventricular nuclei
    - D) Decreased secretion of neurophysin
    - E) Increased plasma levels of both oxytocin and ADH

68. A 30-year-old man has Conn's syndrome. Which set of physiological changes is most likely to occur in this patient compared with a healthy person?

	Arterial Pressure	Extracellular Fluid Volume	Sodium Excretion
A)	↔	↔	↔
B)	↑	↔	↔
C)	↑	↑	↔
D)	↔	↑	↓
E)	↑	↑	↓

69. Why is it important to feed newborn infants every few hours?
    - A) The hepatic capacity to store and synthesize glycogen and glucose is not adequate to maintain the plasma glucose concentration in a normal range for more than a few hours after feeding
    - B) If adequate fluid is not ingested frequently, the plasma protein concentration will rise to greater than normal levels within a few hours
    - C) The function of the gastrointestinal system is poorly developed and can be improved by keeping food in the stomach at all times
    - D) The hepatic capacity to form plasma proteins is minimal and requires the constant availability of amino acids from food to avoid hypoproteinemic edema

70. Dehydroepiandrosterone sulfate (DHEAS), the precursor for the high levels of estradiol that occur in pregnancy, is made in what tissue?
    - A) Fetal adrenal gland
    - B) Ovary of the mother
    - C) Placenta
    - D) Adrenal gland of the mother

71. What is the consequence of sporadic nursing of the neonate by the mother?
    - A) An increase in prolactin-releasing hormone
    - B) An increase in oxytocin
    - C) Lack of birth control
    - D) Lack of prolactin surge

72. Which of the following would be associated with parallel changes in aldosterone and cortisol secretion?
    - A) Addison's disease
    - B) Cushing's disease
    - C) Cushing's syndrome (adrenal tumor)
    - D) A low-sodium diet
    - E) Administration of a converting enzyme inhibitor

73. A chronic increase in the plasma concentration of thyroxine-binding globulin (TBG) would result in which of the following?
    - A) An increased delivery of T_4 to target cells
    - B) A decrease in plasma free [T_4]
    - C) An increase in the conversion of T_4 to triiodothyronine (T_3) in peripheral tissues
    - D) An increase in TSH secretion
    - E) No change in metabolic rate

74. RU486 causes abortion if it is administered before or soon after implantation. What is the specific effect of RU486?
    - A) It binds to LH receptors, stimulating the secretion of progesterone from the corpus luteum
    - B) It blocks progesterone receptors so that progesterone has no effect within the body
    - C) It blocks the secretion of FSH by the pituitary
    - D) It blocks the effects of oxytocin receptors in the uterine muscle

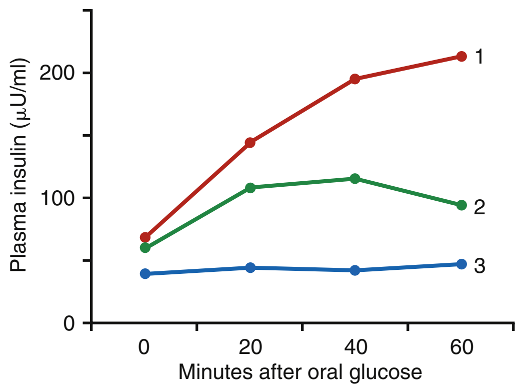
75. A 55-year-old man has developed the syndrome of inappropriate antidiuretic hormone secretion due to carcinoma of the lung. Which physiological response would be expected?
    - A) Increased plasma osmolality
    - B) Inappropriately low urine osmolality (relative to plasma osmolality)
    - C) Increased thirst
    - D) Decreased secretion of ADH from the pituitary gland

76. During pregnancy, the uterine smooth muscle is quiescent. During the ninth month of gestation, the uterine muscle becomes progressively more excitable. What factor contributes to the increase in excitability?
    - A) Placental estrogen synthesis rises to high rates
    - B) Progesterone synthesis by the placenta decreases
    - C) Uterine blood flow reaches its highest rate
    - D) PGE_2 synthesis by the placenta decreases
    - E) Activity of the fetus falls to low levels

77. A 20-year-old woman is not having menstrual cycles. Her plasma progesterone concentration is found to be minimal. What is the explanation for the low level of progesterone?
    A) LH secretion rate is elevated
    B) LH secretion rate is suppressed
    C) FSH secretion rate is suppressed
    D) No corpus luteum is present
    E) High inhibin concentration in the plasma has suppressed progesterone synthesis

78. Before the preovulatory surge in LH, granulosa cells of the follicle secrete which hormone?
    A) Testosterone
    B) Progesterone
    C) Estrogen
    D) Inhibin

Questions 79 and 80



79. Based on the above figure, which set of curves most likely reflects the responses in a healthy individual and in patients with type 1 or type 2 diabetes mellitus (DM)?

	Healthy	Type 1 DM	Type 2 DM
A)	3	2	1
B)	1	2	3
C)	1	3	2
D)	2	1	3
E)	2	3	1

80. Based on the above figure, which set of curves most likely reflects the responses in a healthy person and in a patient in the early stages of Cushing's syndrome?

	Healthy	Cushing's Syndrome
A)	3	2
B)	1	2
C)	1	3
D)	2	1
E)	2	3

81. Which hormone activates enzyme-linked receptors?
    A) ADH
    B) Insulin
    C) ACTH
    D) PTH
    E) Aldosterone

82. Which of the following is produced by the trophoblast cells during the first 3 weeks of pregnancy?
    A) Estrogen
    B) LH
    C) Oxytocin
    D) HCG
    E) None of the above

83. Which of the following is higher in the neonate than in the fetus?
    A) Flow through the foramen ovale
    B) Right atrial pressure
    C) Flow through the ductus arteriosus
    D) Aortic pressure

84. Which finding is most likely in a patient who has myxedema?
    A) Somnolence
    B) Palpitations
    C) Increased respiratory rate
    D) Increased cardiac output
    E) Weight loss

85. At birth, a large, well-nourished baby is found to have a plasma glucose concentration of 17 mg/dl (normal is 80 to 100 mg/dl) and a plasma insulin concentration twice the normal value. What is the explanation for these findings?
    A) The neonate experienced in utero malnutrition
    B) The mother was malnourished during pregnancy
    C) The mother is diabetic, with poorly controlled hyperglycemia
    D) The mother is obese

86. In the fetus, why can normal growth occur despite low P_{O_2} levels?
    A) The concentration of hemoglobin A is increased in the fetus
    B) The hemoglobin of the fetus can carry more oxygen at lower P_{CO_2} levels
    C) The oxyhemoglobin curve in the fetus is shifted to the left
    D) The mother has increased blood volume during pregnancy

87. Which of the following stimulates the secretion of PTH?
   A) An increase in extracellular calcium ion activity above the normal value
   B) An increase in calcitonin concentration
   C) Respiratory acidosis
   D) Increased secretion of PTH-releasing hormone from the hypothalamus
   E) None of the above

88. A 40-year-old woman consumes a high-potassium diet for several weeks. Which hormonal change is most likely to occur?
   A) Increased secretion of DHEA
   B) Increased secretion of cortisol
   C) Increased secretion of aldosterone
   D) Increased secretion of ACTH
   E) Decreased secretion of CRH

89. After implantation into the uterus, nutrition of the blastocyst comes from which structure?
   A) Placenta
   B) Decidua
   C) Glomerulosa cells
   D) Corpus luteum

90. Which hormone is not stored in its endocrine-producing gland?
   A) T_4
   B) PTH
   C) Aldosterone
   D) ACTH
   E) Insulin

91. A young woman comes to the emergency department with a vertebral compression fracture. Radiographs of the spine indicate generalized demineralization. She is vegetarian, does not smoke or drink alcohol, and has a normal plasma potassium concentration of 5.4 mEq/L, a sodium concentration of 136 mEq/L, and a plasma calcium concentration of 7.0 mg/dl. Her vitamin D_3 value is several times greater than normal, although her 1,25-dihydroxycholecalciferol concentration is at the lower limit of detectability. She has been in renal failure for the past 5 years and undergoes hemodialysis three times each week. What is the cause of her low 1,25-dihydroxycholecalciferol level?
   A) Metabolic acidosis
   B) Metabolic alkalosis
   C) She is unable to form 1,25-dihydroxycholecalciferol because of her extensive kidney disease
   D) She is undergoing dialysis with a dialysis fluid that does not contain calcium
   E) She is taking receiving calcium supplements

92. The placenta is incapable of synthesizing which hormones?
   A) Estrogen
   B) Progesterone
   C) Androgens
   D) Estriol

93. A neonate develops jaundice and has a bilirubin concentration of 10 mg/dl on day 2 (normal is 3 mg/dl at 2 days old). The neonatologist can be confident that the condition is not erythroblastosis fetalis if which of the following is true?
   A) The bilirubin concentration rises no further
   B) Hematocrit falls only slightly
   C) The mother, father, and neonate are all Rh-negative
   D) The mother has no history of hepatic dysfunction

94. Which finding would likely be reported in a patient with a deficiency in iodine intake?
   A) Weight loss
   B) Nervousness
   C) Increased sweating
   D) Increased synthesis of thyroglobulin
   E) Tachycardia

95. A 37-year-old woman presents to her physician with an enlarged thyroid gland and high plasma levels of T_4 and T_3. Which of the following is likely to be decreased?
   A) Heart rate
   B) Cardiac output
   C) Peripheral vascular resistance
   D) Ventilation rate
   E) Metabolic rate

96. Before intercourse, a woman irrigates her vagina with a solution that lowers the pH of the vaginal fluid to 4.5. What will be the effect on sperm cells in the vagina?
   A) The metabolic rate will increase
   B) The rate of movement will decrease
   C) The formation of PGE_2 will increase
   D) The rate of oxygen consumption will increase

97. Which hormonal responses would be expected after a meal high in protein?

	Insulin	Glucagon	Growth Hormone
A)	↑	↑	↓
B)	↑	↑	↑
C)	↑	↓	↓
D)	↓	↓	↑
E)	↓	↑	↑

98. Men who take large doses of testosterone-like androgenic steroids for long periods are sterile in the reproductive sense of the word. What is the explanation for this finding?
   A) High levels of androgens bind to testosterone receptors in the Sertoli cells, resulting in overstimulation of inhibin formation
   B) Overstimulation of sperm cell production results in the formation of defective sperm cells
   C) High levels of androgen compounds inhibit the secretion of GnRH by the hypothalamus, resulting in the inhibition of LH and FSH release by the anterior pituitary
   D) High levels of androgen compounds produce hypertrophic dysfunction of the prostate gland

99. Cortisone is administered to a 30-year-old woman for the treatment of an autoimmune disease. Which of the following is most likely to occur?
   A) Increased ACTH secretion
   B) Increased cortisol secretion
   C) Increased insulin secretion
   D) Increased muscle mass
   E) Hypoglycemia between meals

100. In the hypothalamic-pituitary-gonadal axis of the female, what is the follicular cell type that produces inhibin?
   A) Cytotrophoblasts
   B) Synthiotrophoblasts
   C) Granulosa
   D) Thecal

101. The function of which of the following is increased by an elevated parathyroid hormone concentration?
   A) Osteoclasts
   B) Hepatic formation of 25-hydroxycholecalciferol
   C) Phosphate reabsorptive pathways in the renal tubules
   D) All the above

102. Which statement about peptide or protein hormones is usually true?
   A) They have longer half-lives than steroid hormones
   B) They have receptors on the cell membrane
   C) They have a slower onset of action than both steroid and thyroid hormones
   D) They are not stored in endocrine-producing glands

103. Which set of physiological changes would be most likely to occur in a patient with acromegaly?

	Pituitary Mass	Kidney Mass	Femur Length
A)	↓	↓	↑
B)	↓	↑	↑
C)	↑	↔	↔
D)	↑	↑	↔
E)	↑	↑	↑

104. Cortisol and GH are most dissimilar in their metabolic effects on which of the following?
   A) Protein synthesis in muscle
   B) Glucose uptake in peripheral tissues
   C) Plasma glucose concentration
   D) Mobilization of triglycerides

105. Why do infants of mothers who had adequate nutrition during pregnancy not require iron supplements or a diet rich in iron until about 3 months of age?
   A) Growth of the infant does not require iron until after the third month
   B) The fetal liver stores enough iron to meet the infant's needs until the third month
   C) Synthesis of new red blood cells begins after 3 months
   D) Muscle cells that develop before the third month do not contain myoglobin

106. Cortisone is administered to a patient for the treatment of an autoimmune disease. Which of the following would least likely occur in response to the cortisone treatment?
   A) Hypertrophy of the adrenal glands
   B) Increased plasma levels of C-peptide
   C) Decreased CRH secretion
   D) Increased blood pressure
   E) Hyperglycemia

107. Which symptom would least likely be associated with thyrotoxicosis?
   A) Tachycardia
   B) Increased appetite
   C) Somnolence
   D) Increased sweating
   E) Muscle tremor

108. If a male is born without a penis and testes, a defect is likely in which gene on the Y chromosome?
   A) ERE—estrogen response element
   B) ARE—androgen response element
   C) SRY—affecting Sertoli cells
   D) ERG—early response genes

109. Where does fertilization normally take place?
   A) Uterus
   B) Cervix
   C) Ovary
   D) Ampulla of the fallopian tubes

110. Which finding is most likely to occur in a patient who has uncontrolled type 1 DM?
   A) Decreased plasma osmolality
   B) Increased plasma volume
   C) Increased plasma pH
   D) Increased release of glucose from the liver
   E) Decreased rate of lipolysis

111. GH secretion would most likely be suppressed under which condition?
   A) Acromegaly
   B) Gigantism
   C) Deep sleep
   D) Exercise
   E) Acute hyperglycemia

112. Pregnenolone is not in the biosynthetic pathway of which substance?
   A) Cortisol
   B) Estrogen
   C) Aldosterone
   D) 1,25(OH)2D
   E) DHEA

113. Two days before the onset of menstruation, secretions of FSH and LH reach their lowest levels. What is the cause of this low level of secretion?
   A) The anterior pituitary gland becomes unresponsive to the stimulatory effect of GnRH
   B) Estrogen from the developing follicles exerts a feedback inhibition on the hypothalamus
   C) The rise in body temperature inhibits hypothalamic release of GnRH
   D) Secretion of estrogen, progesterone, and inhibin by the corpus luteum suppresses hypothalamic secretion of GnRH and pituitary secretion of FSH

114. Which condition contributes to "sodium escape" in persons with Conn's syndrome?
   A) Decreased plasma levels of atrial natriuretic peptide
   B) Increased plasma levels of angiotensin II
   C) Decreased sodium reabsorption in the collecting tubules
   D) Increased arterial pressure

115. An experiment is conducted in which patients in group 1 are given compound X and patients in group 2 are given compound Y. After 3 weeks, studies show that patients in group 1 have a higher rate of ACTH secretion and a lower blood glucose concentration than those in group 2. Identify compounds X and Y.

	Compound X	Compound Y
A)	Cortisone	Placebo
B)	Cortisol	Placebo
C)	Placebo	Cortisol
D)	ACTH	Placebo
E)	Placebo	ACTH

116. A 30-year-old woman reports to the clinic for a routine physical examination, which reveals she is pregnant. Her plasma levels of TSH are high, but her total T_4 concentration (protein bound and free) is normal. Which of the following best reflects this patient's clinical state?
   A) Graves' disease
   B) Hashimoto's disease
   C) A pituitary tumor that is secreting TSH
   D) A hypothalamic tumor that is secreting TRH
   E) The patient is taking thyroid extract

117. A man has a disease that destroyed only the motor neurons of the spinal cord below the thoracic region. Which aspect of sexual function would not be possible?
   A) Arousal
   B) Erection
   C) Lubrication
   D) Ejaculation

118. Which component of the reproductive system has the most far-reaching effects on the physiology of the organism?
   A) /Y chromosomal effects
   B) X dose—one X chromosome versus two X chromosomes
   C) Gonadal steroid hormones
   D) Prenatal testosterone levels

119. A sustained program of lifting heavy weights will increase bone mass. What is the mechanism of this effect of weightlifting?
   A) Elevated metabolic activity stimulates parathyroid hormone secretion
   B) Mechanical stress on the bones increases the activity of osteoblasts
   C) Elevated metabolic activity results in an increase in dietary calcium intake
   D) Elevated metabolic activity results in stimulation of calcitonin secretion

120. Birth control pills containing combinations of synthetic estrogen and progesterone compounds that are given for the first 21 days of the menstrual cycle are effective in preventing pregnancy. What is the explanation for their efficacy?
   A) Prevention of the preovulatory surge of LH secretion from the pituitary gland
   B) Prevention of development of the ovarian follicles
   C) Suppression of the function of the corpus luteum soon after it forms
   D) Prevention of normal development of the endometrium

121. Which of the following would be expected in a patient with a genetic deficiency of 11-β-hydroxysteroid dehydrogenase type II?
   A) Hyperkalemia
   B) Hypertension
   C) Increased plasma renin activity
   D) Increased plasma [aldosterone]
   E) Hyperglycemia

122. Which physiological response is greater for T_3 than for T_4?
   A) Secretion rate from the thyroid
   B) Plasma concentration
   C) Plasma half-life
   D) Affinity for nuclear receptors in target tissues
   E) Latent period for the onset of action in target tissues

123. A “birth control” compound for men has been sought for several decades. Which substance would provide effective sterility?
   A) A substance that mimics the actions of LH
   B) A substance that blocks the actions of inhibin
   C) A substance that blocks the actions of FSH
   D) A substance that mimics the actions of GnRH

124. For milk to flow from the nipple of the mother into the mouth of the nursing infant, what must occur?
   A) Myoepithelial cells must relax
   B) Prolactin levels must fall
   C) Oxytocin secretion from the posterior pituitary must take place
   D) The baby’s mouth must develop a strong negative pressure over the nipple
   E) All the above

125. Failure of the ductus arteriosus to close is a common developmental defect. Which condition would likely be present in a 12-month-old infant with patent ductus arteriosus?
   A) Below normal arterial Po_2
   B) Below normal arterial Pco_2
   C) Greater than normal arterial blood pressure
   D) Lower than normal pulmonary arterial pressure

126. Which set of physiological changes would be expected in a nondiabetic patient with Cushing’s disease?

	Plasma Aldosterone	Plasma Cortisol	Plasma Insulin
A)	↑	↑	↑
B)	↑	↑	↔
C)	↑	↔	↔
D)	↔	↔	↑
E)	↔	↑	↔
F)	↔	↑	↑

127. When compared with the late-evening values typically observed in normal subjects, plasma levels of both ACTH and cortisol would be expected to be higher in which persons?
   A) Normal subjects after waking in the morning
   B) Normal subjects who have taken dexamethasone
   C) Patients with Cushing’s syndrome (adrenal adenoma)
   D) Patients with Addison’s disease
   E) Patients with Conn’s syndrome

128. Which of the following conditions or hormones would most likely increase GH secretion?
   A) Hyperglycemia
   B) Exercise
   C) Somatomedin
   D) Somatostatin
   E) Aging

129. Which set of findings would be expected in a person maintained on a long-term low-sodium diet?

	Plasma [Aldosterone]	Plasma [Atrial Natriuretic Peptide]	Plasma [Cortisol]
A)	↑	↑	↔
B)	↑	↓	↓
C)	↑	↓	↔
D)	↔	↔	↔
E)	↓	↓	↓
F)	↓	↑	↓

130. What would be associated with parallel changes in aldosterone and cortisol secretion?
   A) Addison’s disease
   B) Cushing’s disease
   C) Cushing’s syndrome (ectopic ACTH-producing tumor)
   D) A high-sodium diet
   E) Administration of a converting enzyme inhibitor

131. Which blood vessel in the fetus has the highest Po_2?
   A) Ductus arteriosus
   B) Ductus venosus
   C) Ascending aorta
   D) Left atrium

132. A 59-year-old woman has osteoporosis, hypertension, hirsutism, and hyperpigmentation. Magnetic resonance imaging indicates that the pituitary gland is not enlarged. Which condition is most consistent with these findings?
   A) Pituitary ACTH-secreting tumor
   B) Ectopic ACTH-secreting tumor
   C) Inappropriately high secretion rate of CRH
   D) Adrenal adenoma
   E) Addison’s disease

133. Which set of findings is an inappropriate hypophysial hormone response to the hypothalamic hormone listed?

	Hypothalamic Hormone Secretion	Hypophysial Hormone
A)	Somatostatin	↓ GH
B)	Dopamine	↑ Prolactin
C)	GnRH	↑ LH
D)	TRH	↑ TSH
E)	CRH	↑ ACTH

134. A patient is administered sufficient T_4 to increase plasma levels of the hormone severalfold. Which set of changes is most likely in this patient after several weeks of T_4 administration?

	Respiratory Rate	Heart Rate	Plasma Cholesterol Concentration
A)	↑	↑	↑
B)	↑	↑	↓
C)	↑	↓	↑
D)	↓	↓	↑
E)	↓	↑	↓

135. During the latter stages of pregnancy, many women experience an increase in body hair growth in a masculine pattern. What is the explanation for this phenomenon?

A) The ovaries secrete some testosterone along with the large amounts of estrogen produced late in pregnancy
B) The fetal ovaries and testes secrete androgenic steroids
C) The maternal and fetal adrenal glands secrete large amounts of androgenic steroids that are used by the placenta to form estrogen
D) The placenta secretes large amounts of estrogen, some of which is metabolized to testosterone

136. What causes menopause?

A) Reduced levels of gonadotropic hormones secreted from the anterior pituitary gland
B) Reduced responsiveness of the follicles to the stimulatory effects of gonadotropic hormones
C) Reduced rate of secretion of progesterone from the corpus luteum
D) Reduced numbers of follicles available in the ovary for stimulation by gonadotropic hormones

137. What does not increase when insulin binds to its receptor?

A) Fat synthesis in adipose tissue
B) Protein synthesis in muscle
C) Glycogen synthesis
D) Gluconeogenesis in the liver
E) Intracellular tyrosine kinase activity

138. Release of which hormone is an example of neuroendocrine secretion?

A) GH
B) Cortisol
C) Oxytocin
D) Prolactin
E) ACTH

139. During the week after ovulation, the endometrium increases in thickness to 5 to 6 millimeters. What stimulates this increase in thickness?

A) LH
B) Estrogen from the corpus luteum
C) Progesterone from the corpus luteum
D) FSH

140. Inhibition of the iodide pump would be expected to cause which change?

A) Increased synthesis of T_4
B) Increased synthesis of thyroglobulin
C) Increased metabolic rate
D) Decreased TSH secretion
E) Extreme nervousness

141. Before implantation, the blastocyst obtains its nutrition from uterine endometrial secretions. How does the blastocyst obtain nutrition during the first week after implantation?

A) It continues to derive nutrition from endometrial secretions
B) The cells of the blastocyst contain stored nutrients that are metabolized for nutritional support
C) The placenta provides nutrition derived from maternal blood
D) The trophoblast cells digest the nutrient-rich endometrial cells and then absorb their contents for use by the blastocyst

142. Which pituitary hormone has a chemical structure most similar to that of ADH?

A) Oxytocin
B) ACTH
C) TSH
D) FSH
E) Prolactin

143. Which option would not be efficacious in the treatment of patients with type 2 diabetes?

A) Glucocorticoids
B) Insulin injections
C) Thiazolidinediones
D) Sulfonylureas
E) Weight loss

144. Which of the following is most likely to occur in the early stages of type 2 diabetes?
 A) Increased insulin sensitivity
 B) Decreased hepatic glucose output
 C) Increased plasma levels of C-peptide
 D) Increased plasma [β-hydroxybutyric acid]
 E) Hypovolemia

145. What is the most common cause of respiratory distress syndrome in neonates born at 7 months' gestation?
 A) Pulmonary edema due to pulmonary arterial hypertension
 B) Formation of a hyaline membrane over the alveolar surface
 C) Failure of the alveolar lining to form adequate amounts of surfactant
 D) Excessive permeability of the alveolar membrane to water

146. Which of the following would be expected to occur during the postprandial period?

	Adipocyte α-Glycerol Phosphate	Plasma [Insulin]	Glycogen Phosphorylase
A)	↑	↑	↓
B)	↑	↑	↑
C)	↑	↓	↑
D)	↓	↓	↑
E)	↓	↓	↓
F)	↓	↑	↓

147. A 45-year-old woman has a mass in the sella turcica that compresses the portal vessels, disrupting pituitary access to hypothalamic secretions. The secretion rate of which hormone would most likely increase in this patient?
 A) ACTH
 B) GH
 C) Prolactin
 D) LH
 E) TSH

148. Which of the following is not produced by osteoblasts?
 A) Alkaline phosphatase
 B) RANK ligand
 C) Collagen
 D) Pyrophosphate
 E) Osteoprotegerin

149. Which set of findings would be expected in a patient with primary hyperparathyroidism?

	Plasma [1,25-(OH)2D3]	Plasma [Phosphate]	Urinary Ca^{++} Excretion
A)	↑	↑	↑
B)	↑	↓	↑
C)	↑	↓	↓
D)	↓	↓	↑
E)	↓	↑	↓
F)	↓	↑	↑

150. A man who has been exposed to high levels of gamma radiation is sterile due to destruction of the germinal epithelium of the seminiferous tubules, although he has normal levels of testosterone. Which of the following would be found in this patient?
 A) A normal secretory pattern of GnRH
 B) Normal levels of inhibin
 C) Suppressed levels of FSH
 D) Absence of Leydig cells

Questions 151 and 152

An experiment was conducted in which rats were injected with one of two hormones or saline solution (control) for 2 weeks. Autopsies were then performed, and organ weights were measured (in milligrams). Use this information to answer Questions 151 and 152.

	Control	Hormone 1	Hormone 2
Pituitary	12.9	8.0	14.5
Thyroid	250	500	245
Adrenal glands	40	37	85
Body weight	300	152	175

151. What is hormone 1?
 A) TRH
 B) TSH
 C) T_4
 D) ACTH
 E) Cortisol

152. What is hormone 2?
 A) TSH
 B) T_4
 C) CRH
 D) ACTH
 E) Cortisol

153. Which of the following would be expected in a patient with vitamin D deficiency?

	Plasma [1,25-(OH)2D3]	Bone Resorption	Intestinal Calbindin
A)	↑	↑	↑
B)	↑	↓	↑
C)	↑	↓	↓
D)	↓	↓	↑
E)	↓	↑	↓
F)	↓	↑	↑

ANSWERS

1. **D)** Parasympathetic postganglionic fibers release acetylcholine that activates muscarinic receptors on endothelium to produce NO and increases cyclic guanosine monophosphate, which activates protein kinase G, causing a reduction in intracellular calcium (also increasing NO by positive feedback) and causing vasodilation.
   TMP13 p. 1027

2. **D)** ADH increases the permeability of the collecting tubules and ducts to water, but not to sodium, which in turn increases water reabsorption and decreases water excretion. As a result, urine concentration increases and the retained water dilutes the plasma. ADH is synthesized in the supraoptic and paraventricular nuclei of the hypothalamus and has no direct effect on the thirst center.
   TMP13 pp. 949-364, 404, 949

3. **A)** Estrogen compounds are believed to have an osteoblast-stimulating effect. When the amount of estrogen in the blood falls to very low levels after menopause, the balance between the bone-building activity of the osteoblasts and the bone-degrading activity of the osteoclasts is tipped toward bone degradation. When estrogen compounds are added as part of hormone replacement therapy, the bone-building activity of the osteoblasts is increased to balance the osteoclastic activity.
   TMP13 pp. 949, 1045

4. **B)** In nephrogenic diabetes insipidus, the kidneys cannot respond to ADH. Consequently, dilute urine and loss of water from the extracellular fluid occurs, resulting in hypernatremia. Hypernatremia stimulates thirst, which attenuates the severity of hypernatremia, whereas water restriction exacerbates hypernatremia. Hypernatremia also stimulates ADH secretion from the magnocellular neurons in the hypothalamus.
   TMP13 p. 949

5. **C)** After birth, systemic arterial resistance increases dramatically due to loss of the placental vasculature. Consequently, arterial pressure, left ventricular pressure, and left atrial pressure all increase. At the same time, pulmonary vascular resistance decreases due to expansion of the lungs, and pulmonary artery pressure, right ventricular pressure, and right atrial pressure all fall. Blood flow through the foramen is a function of the pressure gradient, which after birth favors flow from the left to the right atrium, but most of the flow is blocked by the septal flap on the septal wall of the left atrium.
   TMP13 pp. 1073-1075

6. **A)** Norepinephrine is released from the nerve terminals and endothelin is released from endothelial cells in the vasculature, causing vasoconstriction of the vasculature.
   TMP13 p. 1027

7. **C)** Type 2 DM is characterized by diminished sensitivity of target tissues to the metabolic effects of insulin—that is, there is insulin resistance. As a result, hepatic uptake of glucose is impaired and glucose release is enhanced. In muscle, the uptake of glucose is impaired.
   TMP13 pp. 985-986, 995

8. **C)** In acromegaly, high plasma levels of GH cause insulin resistance. Consequently, glucose production by the liver is increased and glucose uptake by peripheral tissues is impaired.
   TMP13 pp. 943-944, 996-997

9. **A)** During exercise, glucose utilization by muscle is increased, which is largely independent of insulin.
   TMP13 p. 985

10. **A)** Thecal cells do not have the capacity to produce estradiol because they lack aromatase.
    TMP13 pp. 1040, 1043, 1044

11. **B)** A very high concentration of testosterone in a female embryo will induce formation of male genitalia. An adrenal tumor in the mother that synthesizes testosterone at a high, uncontrolled rate could produce the masculinizing effect.
    TMP13 pp. 1043, 1044

12. **E)** HCG has the same stimulatory effect as LH on the corpus luteum. Administration of HCG would cause the corpus luteum to continue to secrete estrogen and progesterone, preventing degradation of the endometrium and the onset of menstruation.
    TMP13 p. 1059

13. **D)** Hypoglycemia is a potent stimulus for GH. GH decreases with aging and in response to the hypothalamic inhibitory hormone somatostatin. GH secretion would decrease in response to both exogenous GH administration and IGF-1 as a result of negative feedback inhibition.
    TMP13 p. 945

14. **C)** Antagonism of progesterone's effects, dilation of the cervix, and oxytocin all increase uterine smooth muscle excitability and facilitate contractions and the onset of labor. LH would have no effect. Prostaglandin

E_2 strongly stimulates uterine smooth muscle contraction and is formed at an increasing rate by the placenta late in gestation.
TMP13 p. 1064, 1066

15. A) Ultraviolet light absorbed by the skin directly facilitates conversion of cholesterol to 25-hydroxycholesterol.
TMP13 p. 1007

16. D) Pulmonary vascular resistance greatly decreases as a result of expansion of the lungs. In the unexpanded fetal lungs, the blood vessels are compressed because of the small volume of the lungs. Immediately upon expansion, these vessels are no longer compressed, and the resistance to blood flow decreases severalfold.
TMP13 pp. 1073, 1074

17. D) The inhibitory hormone somatostatin is both synthesized and stored in the hypothalamus. Both TSH and LH are synthesized and stored in the anterior pituitary gland. ADH is synthesized in the hypothalamus but is stored in the posterior pituitary gland. Somatomedin (IGF-1) is synthesized in the liver.
TMP13 p. 946

18. A) In a radioimmunoassay, there is too little antibody to completely bind the radioactively tagged hormone and the hormone in the fluid (plasma) to be assayed. Thus, there is competition between the labeled and endogenous hormone for binding sites on the antibody. Consequently, if the amount of radioactive hormone bound to antibody is low, this finding would indicate that plasma levels of endogenous hormone are high.
TMP13 p. 936

19. C) Just before the LH surge, estradiol levels increase, which causes negative feedback on GnRH to stop producing LH and FSH, resulting in the decrease in their levels.
TMP13 p. 1039

20. B) The Sertoli cells of the seminiferous tubules secrete inhibin at a rate proportional to the rate of production of sperm cells. Inhibin has a direct inhibitory effect on anterior pituitary secretion of FSH. FSH binds to specific receptors on the Sertoli cells, causing the cells to grow and secrete substances that stimulate sperm cell production. The secretion of inhibin thereby provides the negative feedback control signal from the seminiferous tubules to the pituitary gland.
TMP13 p. 1033

21. B) Ovulation will not take place unless a surge of LH precedes it. Immediately prior to ovulation, the number of follicles is decreasing due to normal attrition of all but one follicle, and consequently estrogen synthesis by the ovary is decreasing. Progesterone synthesis is stimulated by the LH surge.
TMP13 pp. 1039, 1040

22. A) The corpus luteum is the only source of progesterone production, except for minute quantities secreted from the follicle before ovulation. The corpus luteum is functional between ovulation and the beginning of menstruation, during which time the concentration of LH is suppressed below the level achieved during the preovulatory LH surge.
TMP13 pp. 1046-1047

23. C) At the end of the luteal phase, the corpus luteum is resorbed and fails to produce progesterone and estradiol, making levels fall precipitously and causing the endometrium to slough.
TMP13 p. 1039

24. D) Paracrine communication refers to cell secretions that diffuse into the extracellular fluid to affect neighboring cells.
TMP13 p. 925

25. B) The delta cells of the pancreas secrete somatostatin, which inhibits the secretion of insulin and glucagon from the pancreatic beta and alpha cells, respectively. Choice D is an example of neural communication, and the remaining choices are examples of neuroendocrine communication.
TMP13 pp. 925, 993

26. E) Anabolic steroids bind to testosterone receptors in the hypothalamus, providing feedback inhibition of normal ovarian cycling and preventing menstrual cycling as well as stimulation of osteoblastic activity in the bones.
TMP13 pp. 1028, 1031

27. A) Testosterone causes vasodilation by inhibiting L-type calcium channels to inhibit calcium influx into the cells, thus causing vasodilation.
TMP13 p. 1026

28. B) Right atrial pressure falls dramatically after the onset of breathing because of a reduction in pulmonary vascular resistance, pulmonary arterial pressure, and right ventricular pressure.
TMP13 pp. 1073-1075

29. E) Patients with Conn's syndrome have tumors of the zona glomerulosa that secrete large amounts of aldosterone. Consequently, plasma levels of aldosterone are elevated, causing hypokalemia. The secretion of cortisol from the zona fasciculata is normal.
TMP13 p. 981

30. D) Aldosterone secretion is elevated when dietary sodium intake is low, but cortisol secretion is normal. Although aldosterone increases the rate of potassium secretion by the principal cells of the collecting tubules, this effect is offset by a low distal tubular flow rate. Consequently, there is little change in either potassium excretion or plasma potassium concentration.
TMP13 pp. 971-972

31. B) In patients with nephrogenic diabetes insipidus, the kidneys do not respond appropriately to ADH, and the ability to form concentrated urine is impaired. In contrast, there is a normal ADH secretory response to changes in plasma osmolality.
TMP13 pp. 380-381, 949

32. C) Aromatase causes conversion of testosterone to estradiol.
TMP13 p. 1043

33. D) Because of the loss of blood flow through the placenta, systemic vascular resistance doubles at birth, which increases the aortic pressure as well as the pressure in the left ventricle and left atrium.
TMP13 pp. 1073, 1074

34. D) Parathyroid hormone acts in the renal cortex to stimulate the reaction forming 1,25-dihydroxycholicalciferol from 25-hydroxycholicalciferol. It has no effects on other the other reactions.
TMP13 pp. 1007-1008

35. B) Both amino acids and glucose stimulate insulin secretion. Furthermore, amino acids strongly potentiate the glucose stimulus for insulin secretion. Somatostatin inhibits insulin secretion.
TMP13 pp. 990-991, 993

36. F) In this form of dwarfism, there is decreased synthesis and secretion of GH into the circulation. As a result, stimulation of hepatic IGF-1 secretion is decreased and secretion of hypothalamic GnRH is increased due to diminished negative feedback. GH has several actions to increase blood levels of glucose, and when blood levels of GH are inappropriately low, fasting blood glucose concentration tends to fall.
TMP13 pp. 943-947

37. B) HCG also binds to LH receptors on the interstitial cells of the testes of the male fetus, resulting in the production of testosterone in male fetuses up to the time of birth. This small secretion of testosterone is what causes the fetus to develop male sex organs instead of female sex organs.
TMP13 pp. 1033, 1060-1061

38. C) If a subject took sufficient amounts of exogenous thyroid extract to increase plasma levels of T_4 above normal, feedback would cause the secretion of TSH to decrease. Low plasma levels of TSH would result in atrophy of the thyroid gland. In a person with Graves' disease, the same changes in plasma levels of T_4 and TSH would be present, but the thyroid gland would not be atrophied. In fact, goiter is often present in patients with Graves' disease. A lesion in the anterior pituitary that prevents TSH secretion or the taking of propylthiouracil or large amounts of iodine would be associated with low plasma levels of T_4.
TMP13 pp. 959-960

39. D) Choices A to C would all shift the mass action balance toward the side favoring association of ionic calcium with phosphate compounds or other anionic compounds, resulting in reduced levels of free ionic calcium.
TMP13 p. 1001

40. B) In the nonpregnant female, the only significant source of estrogen is ovarian follicles or corpus luteae. Menstruation begins when the corpus luteum degenerates. Menstruation ends when developing follicles secrete estrogen sufficiently to raise circulating concentration to a level that stimulates regrowth of the endometrium.
TMP13 pp. 1039, 1042, 1046-1047

41. B) As a result of negative feedback, plasma levels of TSH are a sensitive index of circulating levels of unbound (free) thyroid hormones. High plasma levels of TSH indicate inappropriately low levels of free thyroid hormones in the circulation, such as are present with autoimmune destruction of the thyroid gland in persons with Hashimoto's disease. However, because elevated plasma levels of estrogen in pregnancy increase hepatic production of TBG, the total amount (bound + free) of thyroid hormones in the circulation is elevated. Plasma levels of thyroid hormones are elevated in persons with Graves' disease and in patients with a pituitary TSH-secreting tumor, as well in patients given thyroid extract for therapy.
TMP13 pp. 954, 958-962

42. C) The major target tissue for prolactin is the breast, where it stimulates the secretion of milk. The other anterior pituitary hormones (ACTH, TSH, FSH, and LH) stimulate hormones from endocrine glands.
TMP13 p. 927

43. D) The cells of the anterior pituitary that secrete LH and FSH, along with the cells of the hypothalamus that secrete GnRH, are inhibited by both estrogen and testosterone. The steroids taken by the woman caused sufficient inhibition to result in cessation of the monthly menstrual cycle.
TMP13 pp. 1033, 1047-1048

44. D) Patients with central diabetes insipidus have an inappropriately low secretion rate of ADH in response to changes in plasma osmolality, but their renal response to ADH is not impaired. Because plasma levels of ADH are depressed, the ability to concentrate urine is impaired, and a large volume of dilute urine is excreted. Loss of water tends to increase plasma osmolality, which stimulates the thirst center and leads to a very high rate of water turnover.
TMP13 p. 949

45. B) NO is the vasodilator that is normally released, causing vasodilation in these arteries.
TMP13 pp. 1027, 1034

46. B) A hypothalamic tumor secreting large amounts of TRH would stimulate the pituitary gland to secrete increased amounts of TSH. As a result, the secretion of thyroid hormones would increase, which would result in an elevated heart rate. In comparison, a patient with either a pituitary tumor secreting large amounts of TSH or Graves' disease would have low plasma levels of TRH because of feedback. Both TRH and TSH levels would be elevated in an endemic goiter, but the heart rate would be depressed because of the low rate of T_4 secretion.
TMP13 pp. 957-962

47. D) Consumption of amino acids stimulates both GH and glucagon secretion. Increased glucagon secretion tends to increase blood glucose concentration and thus opposes the effects of insulin to cause hypoglycemia.
TMP13 pp. 992-993

48. D) Lethargy and myxedema are signs of hypothyroidism. Low plasma levels of TSH indicate that the abnormality is in either the hypothalamus or the pituitary gland. The responsiveness of the pituitary to the administration of TRH suggests that pituitary function is normal and that the hypothalamus is producing insufficient amounts of TRH.
TMP13 pp. 958-962

49. D) Inhibin prevents FSH release from the anterior pituitary, preventing Sertoli cells from causing aromatization to produce estradiol.
TMP13 p. 1032

50. A) After menopause, the absence of feedback inhibition by estrogen and progesterone results in extremely high rates of FSH secretion. Women taking estrogen as part of hormone replacement therapy for symptoms associated with postmenopausal conditions have suppressed levels of FSH as a result of the inhibitory effect of estrogen.
TMP13 pp. 1050, 1051

51. D) Phosphodiesterase-5 receptors prevent hydrolysis of cyclic guanosine monophosphate, thus keeping the levels high and maintaining vasodilation.
TMP13 p. 1034

52. B) Glucagon stimulates glycogenolysis in the liver, but it has no physiological effects in muscle. Both glucagon and cortisol increase gluconeogenesis, and cortisol impairs glucose uptake by muscle.
TMP13 pp. 972-973, 992

53. C) Injection of insulin leads to a decrease in blood glucose concentration. Hypoglycemia stimulates the secretion of GH, glucagon, and epinephrine, all of which have counter-regulatory effects to increase glucose levels in the blood.
TMP13 p. 945, 993-994

54. A) Prolonged fetal hypoxia during delivery can cause serious depression of the respiratory center. Hypoxia may occur during delivery because of compression of the umbilical cord, premature separation of the placenta, excessive contraction of the uterus, or excessive anesthesia of the mother.
TMP13 p. 1073

55. C) In general, peptide hormones are water soluble and are not highly bound by plasma proteins. ADH, a neurohypophysial peptide hormone, is virtually unbound by plasma proteins. In contrast, steroid and thyroid hormones are highly bound to plasma proteins.
TMP13 p. 929-930

56. C) The rise in intracellular calcium in the oocyte triggers the cortical reaction in which granules that previously lay at the base of the plasma membrane undergo exocytosis. That process leads to the release of enzymes that "harden" the zona pellucida and prevent other sperm from penetrating.
TMP13 p. 1025

57. B) Although estrogen and progesterone are essential for the physical development of the breast during pregnancy, a specific effect of both these hormones is to inhibit the actual secretion of milk. Even though prolactin levels are increased 10- to 20-fold at the end of pregnancy, the suppressive effects of estrogen and progesterone prevent milk production until after the baby is born. Immediately after birth, the sudden loss of both estrogen and progesterone secretion from the placenta allows the lactogenic effect of prolactin to promote milk production.
TMP13 pp. 1066-1067

58. C) The concentration of PTH strongly regulates the absorption of calcium ion from the renal tubular fluid. A reduction in hormone concentration reduces calcium reabsorption and increases the rate of calcium excretion in the urine. The other choices either have little effect on or decrease calcium excretion.
TMP13 pp. 1011-1012

59. B) A pituitary tumor secreting increased amounts of TSH would be expected to stimulate the thyroid gland to secrete increased amounts of thyroid hormones. TSH stimulates several steps in the synthesis of thyroid hormones, including the synthesis of thyroglobulin. Increased heart rate is among the many physiological responses to high plasma levels of thyroid hormones. However, high plasma levels of thyroid hormones do not cause exophthalmos. Immunoglobulins cause exophthalmos in Graves' disease, the most common form of hyperthyroidism.
TMP13 pp. 952, 957, 961

60. A) Hemorrhage decreases the activation of stretch receptors in the atria and arterial baroreceptors. Decreased activation of these receptors increases ADH secretion.

TMP13 p. 949

61. E) Choices A to D are true: LH secretion will be suppressed (B) by the negative feedback effect of the estrogen from the tumor; consequently, she will not have menstrual cycles (C), and because she will not have normal cycles, no corpus luteae will develop, so no progesterone will be formed (A). The high levels of estrogen produced by the tumor will provide stimulation of osteoblastic activity to maintain normal bone activity (D).

TMP13 pp. 1044, 1045

62. D) After eating a meal, insulin secretion is increased. As a result, there is an increased rate of glucose uptake by both the liver and muscle. Insulin also inhibits hormone-sensitive lipase, which decreases hydrolysis of triglycerides in fat cells.

TMP13 pp. 985-987, 992

63. B) The primary function of testosterone in the embryonic development of males is to stimulate formation of the male sex organs.

TMP13 pp. 219-220, 364, 383, 405, 949-950

64. E) Protein-bound hormones are biologically inactive and cannot be metabolized. Thus, an increase in protein binding would tend to decrease hormone activity and plasma clearance and increase the half-life of the hormone. Free hormone is also responsible for negative feedback inhibition of hormone secretion. Therefore, a sudden increase in hormone binding to plasma proteins would decrease negative feedback. Protein binding of hormones does, however, provide a reservoir for the rapid replacement of free hormone.

TMP13 pp. 929-930

65. C) The reduction in hydrogen ion indicated by the elevation in pH increases the concentration of negatively charged phosphate ion species available for ionic combination with calcium ions. Consequently, the free calcium ion concentration is reduced.

TMP13 pp. 1011-1012

66. E) In Graves' disease, antibodies against the TSH receptor in the thyroid gland stimulate many of the steps in the synthesis of thyroid hormones, including increased iodine uptake. Due to excessive stimulation of the gland, the thyroid gland hypertrophies and secretes increased amounts of thyroid hormones. High circulating levels of thyroid hormones inhibit TSH secretion due to negative feedback inhibition. The antibodies present in Graves' disease also cause pathological changes in the tissue surrounding the eyes, leading to protrusion of the eyeballs.

TMP13 pp. 960-961

67. C) During suckling, stimulation of receptors on the nipples increases neural input to both the supraoptic and paraventricular nuclei. Activation of these nuclei leads to the release of oxytocin and neurophysin from secretion granules in the posterior pituitary gland. Suckling does not stimulate the secretion of appreciable amounts of ADH.

TMP13 pp. 1066, 1067

68. C) In Conn's syndrome, large amounts of aldosterone are secreted. Because aldosterone causes sodium retention, hypertension is a common finding in patients with this condition. However, the degree of sodium retention is modest, as is the resultant increase in extracellular fluid volume. This occurs because the rise in arterial pressure offsets the sodium-retaining effects of aldosterone, limiting sodium retention and permitting daily sodium balance to be achieved.

TMP13 pp. 970, 981

69. A) Because the liver functions imperfectly during the first weeks of life, the glucose concentration in the blood is unstable and falls to very low levels within a few hours after feeding.

TMP13 pp. 1075, 1076

70. D) DHEA sulfate produced by the fetal adrenal gland diffuses to the placenta and is converted to DHEA and then to estradiol and provides estradiol to the mother.

TMP13 pp. 1060, 1061

71. D) Sporadic nursing of the mother results in a lack of prolactin surge because mechanosensors in the nipple cause prolactin release. Without prolactin release, there is a lack of milk production, and the mother eventually will not be able to provide milk for the baby.

TMP13 pp. 1066, 1067

72. A) Persons with Addison's disease have diminished secretion of both glucocorticoids (cortisol) and mineralocorticoids (aldosterone). In persons with Cushing's disease or Cushing's syndrome, cortisol secretion is elevated but aldosterone secretion is normal. A low-sodium diet is associated with a high rate of aldosterone secretion but a secretion rate of cortisol that is normal. By inhibiting the generation of angiotensin II and thus the stimulatory effects of angiotensin II on the zona glomerulosa, administration of a converting enzyme inhibitor would decrease aldosterone secretion without altering the rate of cortisol secretion.

TMP13 pp. 971-972, 979-980

73. E) In the steady state, high plasma levels of TBG would simply increase the reservoir for hormone and, therefore, the total amount of thyroid hormone in the circulation. However, protein-bound hormone is inactive. The metabolic effects of thyroid hormones and their feedback inhibition on TSH secretion are determined

by the free thyroid hormone and not the total amount of thyroid hormone in the circulation. Both the plasma levels of free thyroid hormone and TSH would be expected to be normal in the steady state. Consequently, the metabolic rate would be unchanged.
TMP13 pp. 929-930, 955-960

74. B) Progesterone is required to maintain the decidual cells of the endometrium. If progesterone levels fall, as they do during the last days of a nonpregnant menstrual cycle, menstruation will follow within a few days, with loss of pregnancy. Administration of a compound that blocks the progesterone receptor during the first few days after conception will terminate the pregnancy.
TMP13 pp. 1060-1061

75. D) An inappropriately high rate of ADH secretion from the lung promotes excess water reabsorption, which tends to produce concentrated urine and a decrease in plasma osmolality. Low plasma osmolality suppresses both thirst and ADH secretion from the pituitary gland.
TMP13 pp. 404, 949

76. B) A very high plasma concentration of progesterone maintains the uterine muscle in a quiescent state during pregnancy. In the final month of gestation the concentration of progesterone begins to decline, increasing the excitability of the muscle.
TMP13 pp. 1027, 971-972

77. D) The corpus luteum is the only source of progesterone. If she is not having menstrual cycles, no corpus luteum is present.
TMP13 p. 1048

78. C) FSH stimulates the granulosa cells of the follicle to secrete estrogen.
TMP13 pp. 1040, 1048

79. E) In response to increased blood levels of glucose, plasma insulin concentration normally increases during the 60-minute period following oral intake of glucose. In type 1 DM, insulin secretion is depressed. In contrast, in type 2 DM, insulin resistance is a common finding and, at least in the early stages of the disease, there is an abnormally high rate of insulin secretion.
TMP13 pp. 995-998

80. D) In Cushing's syndrome, high plasma levels of cortisol impair glucose uptake in peripheral tissues, which tends to increase plasma levels of glucose. As a result, the insulin response to oral intake of glucose is enhanced.
TMP13 pp. 996-998

81. B) In general, protein hormones cause physiological effects by binding to receptors on the cell membrane. However, of the four protein hormones indicated, only insulin activates an enzyme-linked receptor. Aldosterone is a steroid hormone and enters the cytoplasm of the cell before binding to its receptor.
TMP13 p. 932

82. D) HCG is secreted from the trophoblast cells beginning shortly after the blastocyst implants in the endometrium.
TMP13 pp. 1060-1061

83. B) Aortic pressure increases due to the increase in left ventricular pressure. The increase in left atrial pressure causes the foramen ovale to close. The ductus arteriosus also closes within a short time after birth.
TMP13 pp. 1073-1075

84. A) Somnolence is a common feature of hypothyroidism. Palpitations, increased respiratory rate, increased cardiac output, and weight loss are all associated with hyperthyroidism.
TMP13 pp. 957, 962-963

85. C) An infant born of an untreated diabetic mother will have considerable hypertrophy and hyperfunction of the islets of Langerhans in the pancreas. As a consequence, the infant's blood glucose concentration may fall to lower than 20 mg/dl shortly after birth.
TMP13 pp. 1078-1079

86. C) Hemoglobin F levels are higher in the fetus than in the mother, and hemoglobin F in the fetus can carry more oxygen than can hemoglobin in the mother.
TMP13 p. 1058

87. E) Choices A to D would not stimulate PTH secretion. An increase in calcium concentration (A) suppresses PTH secretion; calcitonin has little to no effect on PTH secretion (B); acidosis would increase free calcium in the extracellular fluid, thereby inhibiting PTH secretion (C); and PTH-releasing hormone does not exist (D).
TMP13 pp. 1001, 1011

88. C) Potassium is a potent stimulus for aldosterone secretion, as is angiotensin II. Therefore, a patient consuming a high-potassium diet would exhibit high circulating levels of aldosterone.
TMP13 p. 971

89. B) The decidua and trophoblasts provide the nutrition needed to provide nourishment of the blastocyst.
TMP13 pp. 1057, 1060-1062

90. C) Steroid hormones are not stored to any appreciable extent in their endocrine producing glands. This is true for aldosterone, which is produced in the adrenal cortex. In contrast, there are appreciable stores of thyroid hormones and peptide hormones in their endocrine-producing glands.
TMP13 p. 928

91. C) 1,25-dihydroxycholecalciferol is formed only in the renal cortex. Extensive renal disease reduces the amount of cortical tissue, eliminating the source of this active calcium regulating hormone.
TMP13 p. 1015

92. C) The placenta cannot produce androgens but can only produce DHEA by removal of the sulfate from DHEAS produced in the fetal adrenal glands.
TMP13 p. 1060

93. C) For erythroblastosis fetalis to occur, the baby must inherit Rh-positive red blood cells from the father. If the mother is Rh-negative, she then becomes immunized against the Rh-positive antigen in the red blood cells of the fetus, and her antibodies destroy fetal red blood cells, releasing large quantities of bilirubin into the plasma of the fetus.
TMP13 p. 1076

94. D) Because iodine is needed to synthesize thyroid hormones, the production of thyroid hormones is impaired if iodine is deficient. As a result of feedback, plasma levels of TSH increase and stimulate the follicular cells to increase the synthesis of thyroglobulin, which results in a goiter. Increased metabolic rate, sweating, nervousness, and tachycardia are all common features of hyperthyroidism, not hypothyroidism, due to iodine deficiency.
TMP13 pp. 960-963

95. C) Because of the effects of thyroid hormones to increase metabolism in tissues, tissues vasodilate, thus increasing blood flow and cardiac output. All the other choices increase in response to high plasma levels of thyroid hormones.
TMP13 pp. 956-957

96. B) Sperm cell motility decreases as pH is reduced below 6.8. At a pH of 4.5, sperm cell motility is significantly reduced. However, the buffering effect of sodium bicarbonate in the prostatic fluid raises the pH somewhat, allowing the sperm cells to regain some mobility.
TMP13 p. 1024

97. B) A protein meal stimulates all three hormones indicated.
TMP13 pp. 945, 991, 993

98. C) Testosterone secreted by the testes in response to LH inhibits hypothalamic secretion of GnRH, thereby inhibiting anterior pituitary secretion of LH and FSH. Taking large doses of testosterone-like steroids also suppresses the secretion of GnRH and the pituitary gonadotropic hormones, resulting in sterility.
TMP13 p. 1033

99. C) Steroids with potent glucocorticoid activity tend to increase plasma glucose concentration. As a result, insulin secretion is stimulated. Increased glucocorticoid activity also diminishes muscle protein. Because of feedback, cortisone administration leads to a decrease in adrenocorticotropic hormone secretion and, therefore, a decrease in plasma cortisol concentration.
TMP13 pp. 972-973

100. C) Inhibin is the hormone that has a negative feedback on the anterior pituitary to prevent FSH from being released. Inhibin is produced by the granulosa cells in the ovary.
TMP13 pp. 1040-1041

101. A) An increase in the concentration of PTH results in the stimulation of existing osteoclasts and, over longer periods, increases the number of osteoclasts present in the bone.
TMP13 pp. 1010-1011

102. B) In general, peptide hormones produce biological effects by binding to receptors on the cell membrane. Peptide hormones are stored in secretion granules in their endocrine-producing cells and have relatively short half-lives because they are not highly bound to plasma proteins. Protein hormones often have a rapid onset of action because, unlike steroid and thyroid hormones, protein synthesis is usually not a prerequisite to produce biological effects.
TMP13 pp. 926, 929-932

103. D) A pituitary tumor secreting GH is likely to present as an increase in pituitary gland size. The anabolic effects of excess GH secretion lead to enlargement of the internal organs, including the kidneys. Because acromegaly is the state of excess GH secretion after epiphyseal closure, increased femur length does not occur.
TMP13 p. 947

104. A) GH and cortisol have opposite effects on protein synthesis in muscle. GH is anabolic and promotes protein synthesis in most cells of the body, whereas cortisol decreases protein synthesis in extrahepatic cells, including muscle. Both hormones impair glucose uptake in peripheral tissues and, therefore, tend to increase plasma glucose concentration. Both hormones also mobilize triglycerides from fat stores.
TMP13 pp. 943-944, 972-973

105. B) If the mother has had adequate amounts of iron in her diet, the infant's liver usually has enough stored iron to form blood cells for 4 to 6 months after birth. However, if the mother had insufficient iron levels, severe anemia may develop in the infant after about 3 months of life.
TMP13 pp. 1072, 1077

106. A) High plasma levels of steroids with glucocorticoid activity suppress CRH and, consequently, ACTH secretion. Therefore, the adrenal glands would actually atrophy with chronic cortisone treatment. Increased plasma levels of glucocorticoids tend to cause sodium retention and increase blood pressure. They also tend to increase plasma levels of glucose and, consequently, stimulate insulin secretion and C-peptide, which is part of the insulin prohormone.

TMP13 pp. 972-973, 976-977, 979-980

107. C) Thyrotoxicosis indicates the effects of thyroid hormone excess. Thyroid hormone excites synapses. In contrast, somnolence is characteristic of hypothyroidism. Tachycardia, increased appetite, increased sweating, and muscle tremor are all signs of hyperthyroidism.

TMP13 pp. 956-958, 961

108. C) SRY is the region on the Y chromosome that encodes a transcription factor that causes differentiation of Sertoli cells from precursors in testis. If SRY is not present, granulosa cells in the ovary are produced.

TMP13 p. 1029

109. D) Fertilization of the ovum normally takes place in the ampulla of one of the fallopian tubes.

TMP13 p. 1055

110. D) Because insulin secretion is deficient in persons with type 1 DM, there is increased (not decreased) release of glucose from the liver. Low plasma levels of insulin also lead to a high rate of lipolysis; increased plasma osmolality, hypovolemia, and acidosis are all symptoms of uncontrolled type 1 DM.

TMP13 pp. 995-996

111. E) Under acute conditions, an increase in blood glucose concentration will decrease GH secretion. GH secretion is characteristically elevated in the chronic pathophysiological states of acromegaly and gigantism. Deep sleep and exercise are stimuli that increase GH secretion.

TMP13 pp. 945-946

112. D) All the steroids listed include pregnenolone early in their biosynthetic pathway. 1,25(OH)2D is derived from vitamin D and does not include pregnenolone in its biosynthetic pathway.

TMP13 pp. 965-967, 1007-1008

113. D) Estrogen and, to a lesser extent, progesterone secreted by the corpus luteum during the luteal phase have strong feedback effects on the anterior pituitary gland to maintain low secretory rates of both FSH and LH. In addition, the corpus luteum secretes inhibin, which inhibits the secretion of FSH.

TMP13 p. 1042

114. D) Under chronic conditions, the effects of high plasma levels of aldosterone to promote sodium reabsorption in the collecting tubules are sustained. However, persistent sodium retention does not occur because of concomitant changes that promote sodium excretion. These changes include increased arterial pressure, increased plasma levels of atrial natriuretic peptide, and decreased plasma angiotensin II concentration.

TMP13 pp. 961, 981

115. C) Increased plasma levels of cortisol tend to increase plasma glucose concentration and inhibit ACTH secretion. Therefore, if cortisol were administered to patients in group 2, the patients in group 1 would have lower plasma glucose concentrations and higher plasma levels of ACTH.

TMP13 pp. 972-973, 976-977

116. B) Circulating levels of free T_4 exert biological effects and are regulated by feedback inhibition of TSH secretion from the anterior pituitary gland. Protein-bound T_4 is biologically inactive. Circulating T_4 is highly bound to plasma proteins, especially to TBG, which increases during pregnancy. An increase in TBG tends to decrease free T_4, which then leads to an increase in TSH secretion, causing the thyroid to increase thyroid hormone secretion. Increased secretion of thyroid hormones persists until free T_4 returns to normal levels, at which time there is no longer a stimulus for increased TSH secretion. Therefore, in a chronic steady-state condition associated with elevated TBG, high plasma total T_4 (bound and free) and normal plasma TSH levels would be expected. In this pregnant patient, the normal levels of total T_4, along with high plasma levels of TSH, would indicate an inappropriately low plasma level of free T_4. Deficient thyroid hormone secretion in this patient would be consistent with Hashimoto's disease, the most common form of hypothyroidism.

TMP13 pp. 954, 958-962

117. D) The motor neurons of the spinal cord of the thoracic and lumbar regions are the sources of innervation for the skeletal muscles of the perineum involved in ejaculation.

TMP13 pp. 1026, 1027

118. C) The gonadal steroids, in addition to controlling reproductive function, also control nonreproductive organ function via their estrogen and androgen receptors. For example, estrogens control vascular function due to their ability to increase intracellular calcium in vascular smooth cells causing vasodilation. In addition, estradiol upregulates synthesis of endothelial NO synthase, leading to vasodilation.

TMP13 p. 1034

119. B) Bone is deposited in proportion to the compressional load that the bone must carry. Continual mechanical stress stimulates osteoblastic deposition and calcification of bone.

TMP13 pp. 1006-1007

120. A) Administration of either estrogen or progesterone in appropriate quantities during the first half of the menstrual cycle can inhibit ovulation by preventing the preovulatory surge of LH secretion by the anterior pituitary gland, which is essential for ovulation.
TMP13 pp. 1040, 1041

121. B) In the absence of 11-β-hydroxysteroid dehydrogenase, renal epithelial cells cannot convert cortisol to cortisone and, therefore, cortisol will bind to the mineralocorticoid receptor and mimic the actions of excess aldosterone. Consequently, this would result in hypertension associated with suppression of the renin-angiotensin-aldosterone system, along with hypokalemia.
TMP13 pp. 968-970, 980-981

122. D) In target tissues, nuclear receptors for thyroid hormones have a greater affinity for T_3 than for T_4. The secretion rate, plasma concentration, half-life, and onset of action are all greater for T_4 than for T_3.
TMP13 pp. 953-955

123. C) Blocking the action of FSH on the Sertoli cells of the seminiferous tubules interrupts the production of sperm. Choice C is the only option that is certain to provide sterility.
TMP13 p. 1033

124. C) Oxytocin is secreted from the posterior pituitary gland and carried in the blood to the breast, where it causes the cells that surround the outer walls of the alveoli and ductile system to contract. Contraction of these cells raises the hydrostatic pressure of the milk in the ducts to 10 to 20 mm Hg. Consequently, milk flows from the nipple into the baby's mouth.
TMP13 pp. 1068-1069

125. A) If the ductus arteriosus remains patent, poorly oxygenated blood from the pulmonary artery flows into the aorta, giving the arterial blood an oxygen level that is below normal.
TMP13 p. 1075

126. F) Persons with Cushing's disease have a high rate of cortisol secretion, but aldosterone secretion is normal. High plasma levels of cortisol tend to increase plasma glucose concentration by impairing glucose uptake in peripheral tissues and by promoting gluconeogenesis. However, at least in the early stages of Cushing's disease, the tendency for glucose concentration to increase appreciably is counteracted by increased insulin secretion.
TMP13 pp. 972-973, 979-980

127. A) In healthy patients, the secretory rates of ACTH and cortisol are low in the late evening but high in the early morning. In patients with Cushing's syndrome (adrenal adenoma) or in patients taking dexamethasone, plasma levels of ACTH are very low and are certainly not higher than normal early morning values. In patients with Addison's disease, plasma levels of ACTH are elevated as a result of deficient adrenal secretion of cortisol. The secretion of ACTH and cortisol would be expected to be normal in Conn's syndrome.
TMP13 pp. 977-980

128. B) Exercise stimulates GH secretion. Hyperglycemia, somatomedin, and the hypothalamic inhibitory hormone somatostatin all inhibit GH secretion. GH secretion also decreases as persons age.
TMP13 p. 945

129. C) A low-sodium diet would stimulate aldosterone but not cortisol secretion. Increased atrial stretch associated with volume expansion would stimulate atrial natriuretic peptide secretion but would not be expected during a low-sodium diet.
TMP13 pp. 364, 405, 971-972

130. A) Adrenal gland hypofunction with Addison's disease is associated with decreased secretion of both aldosterone and cortisol. In Cushing's disease and Cushing's syndrome associated with an ectopic tumor, the mineralocorticoid-hypertension induced by high plasma levels of cortisol would suppress aldosterone secretion. Neither a high-sodium diet nor administration of a converting enzyme inhibitor would affect cortisol secretion.
TMP13 pp. 971-972, 979-980

131. B) Blood returning from the placenta through the umbilical vein passes through the ductus venosus. The blood coming from the placenta has the highest concentration of oxygen found in the fetus.
TMP13 p. 1074

132. B) Osteoporosis, hypertension, hirsutism, and hyperpigmentation are all symptoms of Cushing's syndrome associated with high plasma levels of ACTH. If the high plasma ACTH levels were the result of either a pituitary adenoma or an abnormally high rate of corticotropin-releasing hormone secretion from the hypothalamus, the patient would likely have an enlarged pituitary gland. In contrast, the pituitary gland would not be enlarged if an ectopic tumor were secreting high levels of ACTH.
TMP13 pp. 979-980

133. B) Prolactin secretion is inhibited, not stimulated, by the hypothalamic release of dopamine into the median eminence. GH is inhibited by the hypothalamic-inhibiting hormone somatostatin. The secretion of LH, TSH, and ACTH are all under the control of the releasing hormones indicated.
TMP13 p. 942

134. B) Increased heart rate, increased respiratory rate, and decreased cholesterol concentration are all responses to excess thyroid hormone.
TMP13 pp. 956-958

135. C) Estrogen secreted by the placenta is not synthesized from basic substrates in the placenta. Instead, it is formed almost entirely from androgenic steroid compounds that are formed in the adrenal glands of both the mother and the fetus. These androgenic compounds are transported by the blood to the placenta and converted by the trophoblast cells to estrogen compounds. Their concentration in the maternal blood may also stimulate hair growth on the body.
TMP13 pp. 1060-1061

136. D) By age 45 years, only a few primordial follicles remain in the ovaries to be stimulated by gonadotropic hormones, and the production of estrogen decreases as the number of follicles approaches zero. When estrogen production falls below a critical value, it can no longer inhibit the production of gonadotropic hormones from the anterior pituitary. FSH and LH are produced in large quantities, but as the remaining follicles become atretic, production by the ovaries falls to zero.
TMP13 pp. 1050, 1051

137. D) The binding of insulin to its receptor activates tyrosine kinase, resulting in metabolic events leading to increased synthesis of fats, proteins, and glycogen. In contrast, gluconeogenesis is inhibited.
TMP13 pp. 984-989

138. C) The secretion of chemical messengers (neurohormones) from neurons into the blood is referred to as neuroendocrine secretion. Thus, in contrast to the local actions of neurotransmitters at nerve endings, neurohormones circulate in the blood before producing biological effects at target tissues. Oxytocin is synthesized from magnocellular neurons whose cell bodies are located in the paraventricular and supraoptic nuclei and whose nerve terminals terminate in the posterior pituitary gland. Target tissues for circulating oxytocin are the breast and uterus, where the hormone plays a role in lactation and parturition, respectively.
TMP13 pp. 925, 948-950

139. C) Progesterone secreted in large quantities from the corpus luteum causes marked swelling and secretory development of the endometrium.
TMP13 pp. 1046-1047

140. B) Inhibition of the iodide pump decreases the synthesis of thyroid hormones but does not impair the production of thyroglobulin by follicular cells. Decreased plasma levels of thyroid hormones result in a low metabolic rate and lead to an increase in TSH secretion. Increased plasma levels of TSH stimulate the follicular cells to synthesize more thyroglobulin. Nervousness is a symptom of hyperthyroidism and is not caused by thyroid hormone deficiency.
TMP13 pp. 951-952, 956-960

141. D) As the blastocyst implants, the trophoblast cells invade the decidua, digesting and imbibing it. The stored nutrients in the decidual cells are used by the embryo for growth and development. During the first week after implantation, this is the only means by which the embryo can obtain nutrients. The embryo continues to obtain at least some of its nutrition in this way for up to 8 weeks, although the placenta begins to provide nutrition after about the 16th day beyond fertilization (a little more than 1 week after implantation).
TMP13 p. 1056

142. A) Both ADH and oxytocin are peptides containing nine amino acids. Their chemical structures differ in only two amino acids.
TMP13 p. 949

143. A) Because glucocorticoids decrease the sensitivity of tissues to the metabolic effects insulin, they would exacerbate diabetes. Thiazolidinediones and weight loss increase insulin sensitivity. Sulfonylureas increase insulin secretion. If weight loss and the aforementioned drugs are ineffective, exogenous insulin may be used to regulate blood glucose concentration.
TMP13 pp. 991, 996-997

144. C) In the early stages of type 2 diabetes, the tissues have a decreased sensitivity to insulin. As a result, there is a tendency for plasma glucose to increase, in part because decreased hepatic insulin sensitivity leads to increased hepatic glucose output. Because of the tendency for plasma glucose to increase, there is a compensatory increase in insulin secretion, including C-peptide, which is part of the insulin prohormone. Hypovolemia and increased production of ketone bodies, although commonly associated with uncontrolled type 1 diabetes, are not typically present in the early stages of type 2 diabetes.
TMP13 pp. 984, 994-998

145. C) One of the most characteristic findings in respiratory distress syndrome is failure of the respiratory epithelium to secrete adequate quantities of surfactant into the alveoli. Surfactant decreases the surface tension of the alveolar fluid, allowing the alveoli to open easily during inspiration. Without sufficient surfactant, the alveoli tend to collapse, and there is a tendency to develop pulmonary edema.
TMP13 p. 1074

146. A) After eating a meal, insulin secretion increases. Increased plasma levels of insulin inhibit glycogen phosphorylase, the enzyme that causes glycogen to split into glucose. In addition, insulin promotes glucose uptake in adipose tissue, providing α-glycerol phosphate, which is needed to combine fatty acids with triglycerides, the storage form of fat.

TMP13 pp. 985-990

147. C) The primary controllers of ACTH, GH, LH, and TSH secretion from the pituitary gland are hypothalamic-releasing hormones. They are secreted into the median eminence and subsequently flow into the hypothalamic-hypophysial portal vessels before bathing the cells of the anterior pituitary gland. Conversely, prolactin secretion from the pituitary gland is influenced primarily by the hypothalamic inhibiting hormone dopamine. Consequently, obstruction of blood flow through the portal vessels would lead to reduced secretion of ACTH, GH, LH, and TSH, but increased secretion of prolactin.

TMP13 p. 942

148. D) Osteoblasts secrete all of the above except pyrophosphate. Secretions (alkaline phosphatase) from osteoblasts neutralize pyrophosphate, an inhibitor of hydroxyapatite crystallization. Neutralization of pyrophosphate permits the precipitation of calcium salts into collagen fibers.

TMP13 pp. 1004-1006

149. B) In primary hyperparathyroidism, high plasma levels of PTH increase the formation of 1,25-(OH)2D3, which increases intestinal absorption of calcium. This action of PTH, along with its effects to increase bone resorption and renal calcium reabsorption, leads to hypercalcemia. However, because of the high filtered load of calcium, calcium is excreted in the urine. High plasma levels of PTH also decrease phosphate reabsorption and increase urinary excretion, leading to a fall in plasma phosphate concentration.

TMP13 pp. 1009-1012, 1014-1015

150. A) Gamma radiation destroys the cells undergoing the most rapid rates of mitosis and meiosis, the germinal epithelium of the testes. The man described is said to have normal testosterone levels, suggesting that the secretory patterns of GnRH and LH are normal and that his interstitial cells are functional. Because he is not producing sperm, the levels of inhibin secreted by the Sertoli cells would be maximally suppressed, and his levels of FSH would be strongly elevated.

TMP13 p. 1033

151. B) In this experiment, the size of the thyroid gland increased because TSH causes hypertrophy and hyperplasia of its target gland and increased secretion of thyroid hormones. Increased plasma levels of thyroid hormones inhibit the secretion of TRH, which decreases stimulation of the pituitary thyrotropes, resulting in a decrease in the size of the pituitary gland. Higher plasma levels of thyroid hormones also increase metabolic rate and decrease body weight.

TMP13 pp. 955-957, 960

152. C) In this experiment, the size of the pituitary and adrenal glands increased because CRH stimulates the pituitary corticotropes to secrete ACTH, which in turn stimulates the adrenals to secrete corticosterone and cortisol. Higher plasma levels of cortisol increase protein degradation and lipolysis and therefore decrease body weight.

TMP13 pp. 972-974, 976-977

153. E) Vitamin D deficiency leads to rickets in children and osteomalacia in adults. A deficiency in vitamin D leads to reduced synthesis of the active form of the vitamin 1,25-(OH)2D3. In turn, in the presence of low plasma levels of 1,25-(OH)2D3, the synthesis of calbindin in the intestine is reduced, resulting in impaired intestinal absorption of calcium. Impaired intestinal absorption of calcium tends to cause hypocalcemia, which stimulates PTH secretion. Increased PTH secretion contributes to the maintenance of plasma calcium concentration, in part, by increasing bone resorption.

TMP13 pp. 1010-1011, 1015