WEEK NO. 5

METABOLISM

DOCTOR 2019 | MEDICINE | JU

DONE BY :

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1-Following an early-morning run, a 29-year-old man consumes an allAmerican breakfast consisting of cereal, eggs, bacon, sausage, pancakes with maple syrup, doughnuts, and coffee with cream and sugar. Which of the following proteins will most likely be activated in his liver after breakfast?

A)Cytoplasmic PEP carboxykinase
B)Plasma membrane GLUT-4 transporter
C)Cytoplasmic phosphofructokinase-2
D)Mitochondrial carnitine transporter
E)Cytoplasmic glycogen phosphorylase

2-Which one of the following Is a regulatory mechanism employed by muscle for glycolysis?

(A) Inhibition of PFKI by AMP
(B) Inhibition of hexokinase by Its product
(C) Activation of pyruvate kinase when glucagon levels are elevated
(D) Inhibition of aldolase by fructose-l,6-bisphospbate
(E) Inhibition of glucokinase by F-2,6-P

3-The immediate degradation of glycogen under normal conditions gives rise to which one of the following?

(A) More glucose than glucose-l-phosphate
(b) More glucose-l-phosphate than glucose
(C) Equal amounts of glucose and glucose-l-phosphate
(D) Neither glucose nor glucose-l-phosphate
(E) Only glucose-l-phosphate

4-Which one of the following metabolites is used by all cells for glycolysis, glycogen synthesis pathway?

(A) Glucose-l-phosphate
(B) Glucose-6-phosphate
(C) UDP-glucose
(D) Fructose-6-phosphate
(E) PEP

Questions 5+6 are based on the following case:
A patient presented with a bacterial infection that produced an endotoxin that was found, after extensive laboratory analysis, to inhibit PBPCK.

5-Administration of a high dose of glucagon to this patient 2 to 3 hours after a high-carbohydrate meal would result in which one of the following?
(A) A substantial increase in blood glucose levels
(B) A decrease in blood glucose levels
(C) Have little effect on blood glucose levels

6-Administration of a high dose of glucagon to this patient 30 hours after a high-carbohydrate meal would result in which one of the following?
(A) A substantial increase in blood glucose levels
(B) A decrease in blood glucose levels
(C) Have little effect on blood glucose levels

Questions 7and 8 refer to the following case:
A type I diabetic patient who is taking insulin experiences tremors, a rapid heartbeat, difficulty concentrating, and dizziness. An emergency medical technician administers glucagon and the symptoms dissipate.

7. What is leading to the patient's symptoms?
(A) Hyperglycemia
(B) Hypoglycemia
(C) Fatty acid release
(D) Cortisol release
(E) Overeating

8. Why does glucagon administration help to relieve the symptoms of this patient?

(A) It stimulates liver glycogenolysis.
(B) It stimulates muscle glycolysis.
(C) It works through cGMP as a second messenger.
(D) It stimulates conversion of glucose l-phosphate to UDP-glucose.
(E) It stimulates conversion of glucose 6-phosphate to glucose-l-phosphate.

9-A patient with type I diabetes self-injected insulin prior to their evening meal, but then was distracted and forgot to eat A few hours later, the individual fainted, and after the paramedics arrived, they did a STAT blood glucose level and found it to be 45 mg/dL. The blood glucose level was so low because which one of the following tissues assimilated most of it under these conditions?

(A) Brain
(B) Liver
(C) Red blood cells
(D) Adipose tissue
(E) Intestinal epithelial cells

10-Which of the following will provide the main fuel for muscle contraction during short-term maximum exertion?

A. Muscle glycogen
B. Muscle reserves of triacylglycerol
C. Plasma glucose
D. Plasma nonesterified fatty acids
E. Triacylglycerol in plasma very low density lipoprotein

11-Which one of following statements about glycogen metabolism is correct?

A. Glycogen synthase activity is increased by glucagon.
B. Glycogen phosphorylase is an enzyme that can be activated by phosphorylation of serine residues.
C. Glycogen phosphorylase cannot be activated by calcium ions.
D. cAMP activates glycogen synthesis.

E. Glycogen phosphorylase breaks the α1-4 glycosidic bonds by hydrolysis.

12- Which one of following statements about carbohydrate metabolism is correct?

A. A key step in the biosynthesis of glycogen is the formation of UDP-glucose.
B. Glycogen can be broken down to glucose-6-phosphate in muscle, which then releases free glucose by the action of the enzyme glucose-6-phosphatase.
C. Glycogen is stored mainly in the liver and brain.
D. Insulin inhibits the biosynthesis of glycogen.
E. Phosphorylase kinase is an enzyme that phosphorylates the enzyme glycogen phosphorylase and thereby decreases glycogen breakdown.

13-Which one of following statements about gluconeogenesis is correct?

A. Because they form acetyl CoA, fatty acids can be a substrate for gluconeogenesis.
B. If oxaloacetate is withdrawn from the citric acid cycle for gluconeogenesis then it can be replaced by the action of pyruvate dehydrogenase.
C. The reaction of phosphoenolpyruvate carboxykinase is important to replenish the pool of citric acid cycle intermediates.
D. The use of GTP as the phosphate donor in the phosphoenolpyruvate carboxykinase reaction provides a link between citric acid cycle activity and gluconeogenesis.
E. There is a greater yield of ATP in anaerobic glycolysis than the cost for synthesis of glucose from lactate.

14-Which one of following statements about glycogen metabolism is correct?

A. Glycogen is synthesized in the liver in the fed state, then exported to other tissues in low density lipoproteins.

B. Glycogen reserves in liver and muscle will meet energy requirements for several days in prolonged fasting.

C. Liver synthesizes more glycogen when the hepatic portal blood concentration of glucose is high because of the activity of glucokinase in the liver.

D. Muscle synthesizes glycogen in the fed state because glycogen phosphorylase is activated in response to insulin.

E. The plasma concentration of glycogen increases in the fed state.

15-Which one of following statements about this step in glycolysis catalyzed by phosphofructokinase and in gluconeogenesis by fructose 1,6-bisphosphatase is correct?

A. Fructose 1,6-bisphosphatase is mainly active in the liver in the fed state.

B. Fructose 1,6-bisphosphatase is mainly active in the liver in the fed state.

C. If phosphofructokinase and fructose 1,6-bisphosphatase are both equally active at the same time, there is a net formation of ATP from ADP and phosphate.

D. Phosphofructokinase is inhibited more or less completely by physiological concentrations of ATP.

E. Phosphofructokinase is mainly active in the liver in the fasting state.

16-Which one of following statements about glycolysis and gluconeogenesis is correct?

A. All the reactions of glycolysis are freely reversible for gluconeogenesis.

B. Fructose cannot be used for gluconeogenesis in the liver because it cannot be phosphorylated to fructose-6phosphate.

C. Glycolysis can proceed in the absence of oxygen only if pyruvate is formed from lactate in muscle.

D. Red blood cells only metabolize glucose by anaerobic glycolysis (and the pentose phosphate pathway).
E. The reverse of glycolysis is the pathway for gluconeogenesis in skeletal muscle.

17-A 25-year-old man visits his GP complaining of abdominal cramps and diarrhea after drinking milk. What is the most likely cause of his problem?
A. Bacterial and yeast overgrowth in the large intestine
B. Infection with the intestinal parasite Giardia lamblia
C. Lack of pancreatic amylase
D. Lack of small intestinal lactase
E. Lack of small intestinal sucrase-isomaltase

18-Which one of following statements about the fed and fasting metabolic states is correct?
A. Fatty acids and triacylglycerol are synthesized in the liver in the fasting state.
B. In the fasting state the main fuel for the central nervous system is fatty acids released from adipose tissue.
C. In the fasting state the main metabolic fuel for most tissues comes from fatty acids released from adipose tissue.
D. In the fed state muscle cannot take up glucose for use as a metabolic fuel because glucose transport in muscle is stimulated in response to glucagon.
E. Plasma glucose is maintained in starvation and prolonged fasting by gluconeogenesis in adipose tissue from the glycerol released from triacylglycerol.

19-Which one of following statements about the fed and fasting metabolic states is correct?
A. In the fed state muscle can take up glucose for use as a metabolic fuel because glucose transport in muscle is stimulated in response to glucagon.
B. In the fed state there is decreased secretion of glucagon in response to increased glucose in the portal blood.

C. In the fed state, glucagon acts to increase the synthesis of glycogen from glucose.
D. Plasma glucose is maintained in starvation and prolonged fasting by gluconeogenesis from ketone bodies.
E. There is an increase in metabolic rate in the fasting state.

20-Which one of following statements about metabolism of sugars is correct?
A. Fructokinase phosphorylates fructose to fructose-6phosphate.
B. Fructose is an aldose sugar like glucose.
C. Fructose transport into cells is insulin dependent.
D. Galactose is phosphorylated to galactose-1-phosphate by galactokinase.
E. Sucrose can be biosynthesized from glucose and fructose in the liver.

21-A liver biopsy is done on a child with hepatomegaly and mild fasting hypoglycemia. Hepatocytes show accumulation of glycogen granules with single glucose residues remaining at the branch points near the periphery of the granule. The most likely genetic defect is in the gene encoding a(n):
(A)α-1,4 phosphorylase
(B)α-1,4:α-1,4 transferase
(C)phosphoglucomutase
(D)α-1,6 glucosidase
(E)lysosomal α-1,4 glucosidase

22-A breast-fed infant begins to vomit frequently and lose weight. Several days later she is jaundiced, her liver is enlarged, and cataracts are noticed in her lenses. These symptoms are most likely caused by a deficiency of:
(A)galactose 1-P uridyltransferase
(B)lactase
(C)glucose-6-phosphatase
(D)galactokinase
(E)aldolase B

23-A 16-year-old patient with type 1 diabetes mellitus was admitted to the hospital with a blood glucose level of 400 mg/ di... (The reference range for blood glucose is80-l00 mg/dL.) One hour after an insulin infusion was begun, her blood glucose level had decreased to 320 mg/ dL. One hour later, it was 230 mg/ dL. The patient's glucose level decreased because the infusion of insulin led to which one of the following?

(A) The stimulation of the transport of glucose across the cell membranes of the liver and brain

(B) The stimulation of the conversion of glucose to glycogen

(c) The stimulation of glycogenolysis in the liver

(d) The inhibition of the conversion of muscle glycogen to blood glucose

24-A 3-month-old infant was cranky and irritable, became quite lethargic between feedings, and began to develop a potbelly. A physical examination demonstrated an enlarged liver, while blood work taken between feedings demonstrated elevated lactate and uric acid levels, as well as hypoglycemia. This child most likely has a mutation in which one of the following enzymes?

(A) Llver glycogen phosphorylase

(B) Glycogen synthase

(C) Glucose-6-phosphatase

(D) Muscle glycogen phosphorylase

(E) Pyruvate kinase

25-In a glucose tolerance test, an individual in the basal metabolic state ingests a large amount of glucose. If an individual displays a normal response, this ingestion results in which one of the following?

(A) Enhanced glycogen synthase activity in the liver

(B) An increased ratio ofphosphorylase a to phosphorylase b in the liver

(C) An increased rate oflactate formation by erythrocytes

(D) Inhibition of PP-1 activityin the liver

(E) Increased activity of CREB

26-A pregnant woman who has a lactase deficiency and cannot tolerate milk in her diet is concerned that she will not be able to produce milk of sufficient caloric value to nourish her baby. The best advice to her is which one of the following?

(A) She must consume pure galactose in order to produce the galactose moiety of lactose.

(B) She will not be able to breastfeed her baby because she cannot produce lactose.

(C) The production of lactose by the mammary gland does not require the ingestion of milk or milk products.

(D) She can produce lactose directly by degrading a-lactalbumin.

(E) A diet rich in saturated fats will enable her to produce lactose.

27-A l-year-old child, on a routine well child visit, was discovered to have cataract formation in both eyes. Blood test demonstrated elevated galactose and galactitol levels. In order to determine which enzyme might be defective in the child, which intracellular metabolite should be measured?

(A) Galactose

(B) Fructose

(C) Glucose

(D) Galactose-1-phosphate

(E) Fructose-l-phosphate

(F) Glucose-6-phosphate

28-A 3-year-old girl has been a fussy eater since being weaned, particularly when fruit is part of her diet She would get cranky, sweat, and display dizziness, and lethargy, after eating a meal with fruit Her mother noticed this correlation, and as long as fruit was withdrawn from her diet, the child did not display such symptoms. The problems the girl exhibits when eating fruit is most likely due to which one of the following?

(A) Decreased levels of fructose in the blood

(B) Elevated levels of glyceraldehyde in liver cells

(C) High levels of sucrose in the stool

(D) Elevated levels of fructose-l-phosphate in liver cells

(E) Decreased levels of fructose in the urine

29-Phosphorylase kinase can be best described by which one of the following?

	Activated in Response to:	Target of Enzyme Activity:	Active in the Presence of Caffeine?	Required Substrate for Enzymatic Activity
(A)	Insulin	Glycogen phosphorylase	Yes	ATP
(B)	Insulin	Glycogen phosphorylase	Yes	GTP
(C)	Insulin	Branching enzyme	No	ATP
(D)	Epinephrine	Branching enzyme	No	GTP
(E)	Epinephrine	Glycogen phosphorylase	Yes	ATP
(F)	Epinephrine	Glycogen phosphorylase	Yes	GTP

30) Under conditions of glucagon release, the degradation of liver glycogen normally produces which one of the following?

A. More glucose than glucose 1-P
B. More glucose 1-P than glucose
C. Equal amounts of glucose and glucose 1-P
D. Neither glucose nor glucose 1-P
E. Only glucose 1-P

31) A patient has large deposits of liver glycogen, which, after an overnight fast, had shorter-than-normal branches. This abnormality could be caused by a defective form of which one of the following proteins or activities?

A. Glycogen phosphorylase
B. Glucagon receptor
C. Glycogenin
D. Amylo-1,6-glucosidase
E. Amylo-4,6-transferase

32) An adolescent patient with a deficiency of muscle phosphorylase was examined while exercising her forearm by squeezing a rubber ball. Compared with a normal person performing the same exercise, this patient would exhibit which one of the following?

a. Exercise for a longer time without fatigue
b. Have increased glucose levels in blood drawn from her forearm
c. Have decreased lactate levels in blood drawn from her forearm

d. Have lower levels of glycogen in biopsy specimens from her forearm muscle
e. E. Hyperglycemia

33) In a glucose tolerance test, an individual in the basal metabolic state ingests a large amount of glucose. If the individual is normal, this ingestion should result in which one of the following?
a. An enhanced glycogen synthase activity in the liver
b. An increased ratio of glycogen phosphorylase a to glycogen phosphorylase b in the liver
c. An increased rate of lactate formation by red blood cells
d. An inhibition of PP-1 activity in the liver
e. An increase of cAMP levels in the liver

34) Consider a person with type 1 diabetes who has neglected to take insulin for
the past 72 hours and also has not eaten much. Which one of the following best describes the activity level of hepatic enzymes involved in glycogen metabolism under these conditions?

	Glycogen Synthase	*Phosphorylase Kinase*	*Glycogen Phosphorylase*
A	Active	Active	Active
B	Active	Active	Inactive
C	Active	Inactive	Inactive
D	Inactive	Inactive	Inactive
E	Inactive	Active	Inactive
F	Inactive	Active	Active

35) Assume that an individual carries a mutation in muscle PKA such that the protein is refractory to high levels of cAMP. Glycogen degradation in the muscle would occur, then, under which one of the following conditions?
A. High levels of intracellular calcium
B. High levels of intracellular glucose
C. High levels of intracellular glucose 6-P
D. High levels of intracellular glucose 1-P
E. High levels of intracellular magnesium

36) Without a steady supply of glucose to the bloodstream, a patient would become hypoglycemic and, if blood glucose levels get low enough, experience seizures or even a coma. Which one of the following is necessary for the maintenance of normal blood glucose?

A. Muscle glucose 6-P
B. Liver glucose 6-P
C. Glycogen in the heart
D. Glycogen in the brain
E. Glycogen in the muscle

37)Glycogen is the storage form of glucose, and its synthesis and degradation is carefully regulated. Which one statement below correctly describes glycogen synthesis and/or degradation?

A) UDP-glucose is produced in both the synthesis and degradation of glycogen.
B) Synthesis requires the formation of α-1,4 branches every 8 to 10 residues.
C) Energy, in the form of ATP, is used to produce UDP-glucose.
D) Glycogen is both formed from and degrades to glucose 1-P.
E) The synthesis and degradation of glycogen use the same enzymes, so they are reversible processes.

38)Mutations in various enzymes can lead to the glycogen storage diseases.
Which one statement is true of the glycogen storage diseases?

A. All except type O are fatal in infancy or childhood.
B. All except type O involve the liver.
C. All except type O produce hepatomegaly.
D. All except type O produce hypoglycemia.
E. All except type O produce increased glycogen deposits.

39)A baby weighing 7.5 lb was delivered at 40 weeks of gestation by normal

spontaneous vaginal delivery. At 1 hour, the baby's blood glucose level was determined to be 50 mg/dL and at 2 hours post-birth was 80 mg/dL. These glucose numbers indicate which process?

A. Maternal malnutrition
B. Glycogen storage disease
C. Normal physiologic change
D. Insulin was given to the baby.
E. IV dextrose 50 was given to the baby.

-SOURCES:
KAPLAN, BRS ,HARPER, MARK'S

-THE ANSWERS AND EXPLANATIONS:

1-Answer: C.
Only PFK-2 will be insulin-activated in the postprandial period.

2-The answer is B.
Hexokinase is inhibited by its product, glucose-6-phosphate. PPKl is activated by AMP and F-2,6-P. F-2.6-P does not inhibit glucokinase, nor is glucokinase present in the muscle. Aldolase is not inhibited by its substrate, fructose-1,6-blsphospbate. Pyruvate kinase is inactivated by glucagon-mediated phosphorylation In the liver but not in the muscle. The muscle isozyme of pyruvate kinase is not a substrate for PKA. In addition, muscle cells do not respond to glucagon because they do not express glucagon receptors.

3-The answer is B.
Phosphorylase produces glucose-l-phosphate from glucose residues linked a-l,4. Free glucose is produced from a-l,6-lmked residues at branch points by an a-l,6-glucosidase activity of the debranching enzyme. Degradation of glycogen produces glucose-l-phosphate and glucose in abouta 1 O:l ratio, which is the ratio of the a-l,4 linkages to a-l,6 linkages.

4-The answer is B.
Glucose-6-phosphate is common to all pathways. It can be converted to glucose-1-phosphate for glycogen synthesis or go directly into the pentose phosphate pathway, or proceed through fructose-6-phosphate in glycolysis. UDP-glucose is formed from glucose-1-phosphate and can be used to form glycogen, lactose, glycoproteins, and glycolipids.

5-The answer is A.
By 2 to 3 hours after a high-carbohydrate meal, the patient's glycogen stores would be filled. Glucagon would stimulate glycogenolysis, and blood glucose levels would rise. Gluconeogenesis would still be impaired, but because glycogen levels are high, the liver would be able to export significant amounts of glucose.

6-The answer is C.
Thirty hours after a meal, liver glycogen is normally depleted, and blood glucose level is maintained solely by gluconeogenesis after this time. However, in this case, a key gluconeogenic enzyme is inhibited by an endotoxin. Therefore, gluconeogenesis will not occur at a normal rate, and glycogen stores will be depleted more rapidly than normal. Blood glucose levels will not change significantly if glucagon is administered after 30 hours of fasting.

7-The answer is B.
The patient is having a hypoglycemic episode, most likely caused by too much insulin, or insufficient eating after taking insulin. The insulin is directing the blood glucose to enter the muscle and fat cells, thereby rapidly depleting blood glucose levels. The insulin is also telling the liver to store glucose as glycogen or fatty acids, so the liver is not contributing toward raising blood glucose levels. The symptoms observed in the patient are not because of fatty acid or cortisol release, or overeating.

8-The answer is A.
The patient is having a hypoglycemic episode, and glucagon can be a treatment because it stimulates liver glycogenolysis by using cAMP as a second messenger and releases glucose into the bloodstream. Glucagon does not act on the muscle. Epinephrine acts on both the liver and the muscle. The conversion of glucose-l-phosphate to UDP-glucose and also glucose-6-phosphate to glucose-l-phosphate are steps involved in glycogen synthesis, which is stimulated by insulin but inhibited by the action of glucagon.

9-The answer is D.
Insulin stimulates glucose transport into muscle and adipose cells through mobilization of GLUT 4 transporters from internal vesicles to the cell surface. Insulin does not significantly stimulate glucose transport into tissues such as liver, brain, or red blood cells, which

utilize different variants of the glucose transporters. Only GLUT4 is insulin responsive

10-A
11-B
12-A
13-D
14-C
15-D
16-D
17-D
18-C
19-B
20-D

21-Answer: D.
This activity of the debranching enzyme removes 1,6-linked glucose residues from the branch points during glycogenolysis.

22-Answer: A.
Cataracts + liver disease in a milk-fed infant = classic galactosemia.

23-The answer is B.
Blood glucose decreases because insulin stimulates the transport of glucose into muscle and adipose cells and stimulates the conversion of glucose to glycogen in the liver. Insulin stimulates glycogen synthesis, not glycogenolysis. Muscle glycogen is not converted to blood glucose.

24-The answer is C.
The child has the symptoms ofvon Gierke disease, which is caused by a lack of glucose-6-phosphatase activity. In this disordei; neither liver glycogen nor gluconeogenic precursors (e.g., alanine and glycerol) can be used to maintain normal blood glucose levels. The last step (conversion of glucose-6-phosphate to glucose) is deficient for both glycogenolysis and gluconeogenesis. Muscle

glycogen cannot be used to maintain blood glucose levels because muscle does not contain glucose-6-phosphatase. A defective liver glycogen phosphorylase (Her disease) will not affect the ability of the liver to raise blood glucose levels by gluconeogenesis. In addition, the lack of liver glycogen phosphorylase does not lead to lactic and uric acid accumulation, although mild fasting hypoglycemia can be observed. Defects in liver glycogen synthase (type O glycogen storage disease) will lead to hypoglycemia and hyperketonemia, but not lactate acid or uric acid accumulation. Muscle does not contribute to blood glucose levels, so a defect in muscle glycogen phosphorylase (McArdle disease) will not lead to the observed symptoms, but will lead to exercise intolerance. A defect in pyruvate kinase will lead to hemolytic anemia, but not the other symptoms observed in the patient

25-The answer is A.
After ingestion of glucose, the insulin to glucagon ratio increases, the cAMP phosphodiesterase is activated, cAMP levels drop, and PKA is inactivated. This leads to the activation of glycogen synthase by PP-I. The ratio of phosphorylase a to phosphorylase b is decreased by PP-I as well; thus, glycogen degradation decreases. Red blood cells continue to use glucose and form lactate at their normal rate because glucose is the sole energy source for such cells. CREB is also inactivated under these conditions, thereby reducing the levels of PEPCK (via transcriptional regulation) within the cell.

26-The answer is C.
The woman will be able to breastfeed her baby because she can produce lactose from amino acids and other carbohydrates. She will not have to eat pure galactose, or even lactose, to do so. Glucose, which can be provided by gluconeogenesis or obtained from the diet, can be converted to UDP-galactose (glucose~ glucose-6-phosphate ~ glucose-1-phosphate ~UDP-glucose~ UDP-galactose). UDP-galactose reacts with free glucose to form lactose. a-Lactalbumin is a protein that serves as the modifier of galactosyl transferase, which catalyzes this reaction. The amino

acids of a-lactalbumin can be used to produce glucose, but the immediate products of a-lactalbumin degradation are not lactose. Carbohydrates cannot be synthesized from fats

27-The answer is D.
The child has a form of galactosemia. The elevated galactose enters the lens of the eye, is reduced to galactitol, and is trapped. The difference in osmotic pressure across the lens of the eye leads to cataract formation. Galactose is phosphorylated by galactokinase to galactose-1-phosphate, which reacts with UDP-glucose in a reaction catalyzed by galactose-1-phosphate uridylyl transferase to form UDP-galactose and glucose-1-phosphate. An epimerase converts UDP-galactose to UDP-glucose. Deficiencies in either galactokinase (nonclassical) or galactose-1-phosphate uridylyl transferase (classical) result in galactosemia, with elevated levels of galactose and galactitol (reduced galactose) in the blood. An intracellular measurement of galactose-1-phosphate can allow a definitive diagnosis to be obtained (such levels would be nonexistent if the defect were in galactokinase, and the levels would be greatly elevated if the galactose-1-phosphate uridylyl transferase enzyme were defective).

28-The answer is D.
The patient has HFI, which is caused by a mutation in aldolase B. Sucrose would still be cleaved by sucrase; thus, it would not increase in the stool. Fructose would not be metabolized normally; therefore, it would be elevated in the blood and urine. Aldolase B would not cleave fructose-1-phosphate; thus, its levels would be elevated, and the product, glyceraldehyde, would not be produced.

29-The answer is E.
Glucagon in the liver and epinephrine in both the liver and the muscle cause cAMP levels to rise, activating PKA. PICA phosphorylates and activates phosphorylase kinase, wbic::h, in tum, phosphorylates and activates phosphorylase. These phosphorylation reactions require ATP. Branching enzyme is not a substrate for phosphorylase kinase. Phosphodiesterase inhibitors,

such as caffeine, keep cAMP elevated, which allows P1CA to be active, which keeps phosphorylase kinase active and in its phosphorylated form.

30. The answer is B.
Glycogen phosphorylase produces glucose 1-P; the debranching enzyme hydrolyzes branch points and thus releases free glucose. Ninety percent of the glycogen contains α-(1,4)-bonds, and only 10% are α-(1,6)-bonds, so more glucose 1-P will be produced than glucose.

31. The answer is D.
If, after fasting, the branches were shorter than normal, glycogen phosphorylase must be functional and capable of being activated by glucagon (thus, A and B are incorrect). The branching enzyme (amylo-4,6-transferase) is also normal because branch points are present within the glycogen (thus, E is incorrect). Because glycogen is also present, glycogenin is present in order to build the carbohydrate chains, indicating that C is incorrect. If the debranching activity is abnormal (the amylo-1,6-glucosidase), glycogen phosphorylase would break the glycogen down up to four residues from branch points and would then stop. With no debranching activity, the resultant glycogen would contain the normal number of branches, but the branched chains would be shorter than normal.

32. The answer is C.
The patient has McArdle disease, a glycogen storage disease caused by a deficiency of muscle glycogen phosphorylase. Because she cannot degrade glycogen to produce energy for muscle contraction, she becomes fatigued more readily than a normal person (thus, A is incorrect), the glycogen levels in her muscle will be higher than normal as a result of the inability to degrade them (thus, D is incorrect), and her blood lactate levels will be lower because of the lack of glucose for entry into glycolysis. She will, however, draw on the glucose in her circulation for energy, so her forearm blood glucose levels will be decreased (thus

B is incorrect), and because the liver is not affected, blood glucose levels can be maintained by liver glycogenolysis (thus, E is incorrect).

33. The answer is A.
After ingestion of glucose, insulin levels rise, cAMP levels within the cell drop (thus, E is incorrect), and PP-1 is activated (thus, D is incorrect). Glycogen phosphorylase a is converted to glycogen phosphorylase b by the phosphatase (thus, B is incorrect), and glycogen synthase is activated by the phosphatase. Red blood cells continue to use glucose at their normal rate; hence, lactate formation will remain the same (thus, C is incorrect).

34. The answer is F.
In the absence of insulin, glucagon-stimulated activities predominate. This leads to the activation of PKA, the phosphorylation and inactivation of glycogen synthase, the phosphorylation and activation of phosphorylase kinase, and the phosphorylation and activation of glycogen phosphorylase.

35. The answer is A.
Calcium activates a calmodulin subunit in phosphorylase kinase which will allow phosphorylase kinase to phosphorylate, and activate, glycogen phosphorylase. Glucose is an allosteric inhibitor of glycogen phosphorylase a in liver but has no effect in muscle. Glucose 1-P has no effect on muscle phosphorylase, whereas glucose 6-P is an allosteric inhibitor of muscle glycogen phosphorylase a. The levels of magnesium have no effect on muscle glycogen phosphorylase activity. Normally, glucagon or epinephrine would activate the cAMP-dependent PKA, but this is not occurring under these conditions.

36. The answer is B. Glycogen in the liver provides glucose for the circulation. Glycogen in the heart, brain, or muscle cannot provide glucose for the circulation. In the liver, glucose 6-phosphatase hydrolyzes glucose 6-P to glucose, which is released into the bloodstream. The liver generates glucose 6-P from either glycogen

degradation or gluconeogenesis. Muscle does not contain glucose 6-phosphatase.

37. The answer is D.
Glycogen is both formed from and degrades to glucose 1-P. A high-energy phosphate bond from UTP is required to produce UDP-glucose in glycogen synthesis, but UDP-glucose is not resynthesized when glycogen is degraded. The pathways of glycogen synthesis and degradation use different enzymes and are not reversible reactions. In this way, the pathways can be regulated independently.

38. The answer is E.
Type O glycogen storage disease is caused by a reduced level of liver glycogen synthase activity, so in this disease, very little liver glycogen is formed so glycogen deposits would not be found in the liver. All of the other glycogen storage diseases are characterized by glycogen deposits. Not all are fatal, some are mild, and some have an adult-onset form. Some glycogen storage disorders involve the liver, whereas others involve the muscle. Only those involving the liver will produce hepatomegaly and hypoglycemia.

39. The answer is C.
At birth, maternal glucose supply to the baby ceases, causing a temporary physiologic drop in glucose even in normal healthy infants. This drop signals glycogenolysis in the newborn liver, returning

-LIPPINCOTT'S QUESTIONS:

1-Which of the following best describes the activity level and phosphorylation state of the listed hepatic enzymes in an individual who consumed a carbohydrate-rich meal about an hour ago?
PFK-1 = phosphofructokinase-1;
PFK-2 = phosphofructokinase-2;

P = phosphorylated.

Choice	PFK-1		PFK-2		Pyruvate Kinase	
	Activity	P	Activity	P	Activity	P
A.	Low	No	Low	No	Low	No
B.	High	Yes	Low	Yes	Low	Yes
C.	High	No	High	No	High	No
D.	High	Yes	High	Yes	High	Yes

2-Use the chart below to show the effect of adenosine monophosphate (AMP) and fructose 2,6-bisphosphate on the listed enzymes of gluconeogenesis and glycolysis.

Enzyme	Fructose 2,6-bisphosphate	AMP
Fructose 1,6-bisphosphatase		
Phosphofructokinase-1		

3-Given that acetyl coenzyme A cannot be a substrate for gluconeogenesis, why is its production in fatty acid oxidation essential for gluconeogenesis?

☆For Questions 6+7, match the deficient enzyme to the clinical finding in selected glycogen storage diseases (GSDs).☆

CHOICE	GSD	DEFICIENT ENZYME
A	Type Ia	Glucose 6-phosphatase
B	Type II	Acid maltase
C	Type III	4:4 Transferase
D	Type IV	4:6 Transferase
E	Type V	Myophosphorylase
F	Type VI	Liver phosphorylase

6》 Generalized accumulation of glycogen, severe hypotonia, and death from heart failure

7》 Severe fasting hypoglycemia, lacticacidemia, hyperuricemia, and hyperlipidemia

8-Epinephrine and glucagon have which one of the following effects on hepatic glycogen metabolism?

A. Both glycogen phosphorylase and glycogen synthase are activated by phosphorylation but at significantly different rates.

B. Glycogen phosphorylase is inactivated by the resulting rise in calcium, whereas glycogen synthase is activated.

C. Glycogen phosphorylase is phosphorylated and active, whereas glycogen synthase is phosphorylated and inactive.

D. The net synthesis of glycogen is increased.

9-In contracting skeletal muscle, a sudden elevation of the sarcoplasmic calcium concentration will result in:

A. activation of cyclic adenosine monophosphate (cAMP)-dependent protein kinaseA

B. conversion of cAMP to AMP by phosphodiesterase.

C. direct activation of glycogen synthase b.

D. direct activation of phosphorylase kinase b.

E. inactivation of phosphorylase kinase a by the action of protein phosphatase-1.

10-Explain why the hypoglycemia seen with Type Ia glycogen storage disease (glucose 6-phosphatase deficiency) is severe, whereas that seen with Type VI (liver phosphorylase deficiency) is mild.

11-A nursing female with classic galactosemia is on a galactose-free diet. She is able to produce lactose in breast milk because:

A. galactose can be produced from fructose by isomerization.

B. galactose can be produced from a glucose metabolite by epimerization.

C. hexokinase can efficiently phosphorylate galactose to galactose 1-phosphate.

D. the enzyme affected in galactosemia is activated by a hormone produced in the mammary gland.

12-A 5-month-old boy is brought to his physician because of vomiting, night sweats, and tremors. History revealed that these symptoms began after fruit juices were introduced to his diet as he was being weaned off breast milk. The physical exmination was remarkable for hepatomegaly. Tests on the baby's urine were positive for reducing sugar but negative for glucose. The infant most likely suffers from a deficiency of:

A. aldolase B.
B. fructokinase.
C. galactokinase.
D. β-galactosidase.

13-Lactose synthesis is essential in the production of milk by mammary glands. In lactose synthesis:

A. galactose from galactose 1-phosphate is transferred to glucose by galactosyltransferase (protein A), generating lactose.
B. protein A is used exclusively in the synthesis of lactose.
C. α-lactalbumin (protein B) regulates the specificity of protein A by increasing its Km for glucose.
D. protein B expression is stimulated by prolactin.

14-A 3-month-old girl is developing cataracts. Other than not having a social smile or being able to track objects visually, all other aspects of the girl's examination arennormal. Tests on the baby's urine are positive for reducing sugar but negative for glucose. Which enzyme is most likely deficient in this girl?

A. Aldolase B
B. Fructokinase
C. Galactokinase
D. Galactose 1-phosphate uridylyltransferase

-Answers and Explanations:

1- C.

In the period immediately following a meal, blood glucose levels and hepatic uptake of glucose increase. The glucose is phosphorylated to glucose 6-phosphate and used in glycolysis. In response to the rise in blood glucose, the insulin-to-glucagon ratio increases. As a result, the kinase domain of PFK-2 is dephosphorylated

2-

Both fructose 2,6-bisphosphate and adenosine monophosphate downregulate gluconeogenesis through inhibition of fructose 1,6-bisphosphatase and upregulate glycolysis through activation of phosphofructokinase-1. This results in reciprocal regulation of the two pathways.

3-

Acetyl coenzyme A inhibits the pyruvate dehydrogenase complex and activates pyruvate carboxylase, pushing pyruvate to gluconeogenesis and away from oxidation.

6- B.

Acid maltase [a(1→4)-glucosidase] deficiency prevents degradation of any glycogen brought into lysosomes. A variety of tissues are affected, with the most severe pathology resulting from heart damage.

7- A.

Glucose 6-phosphatase deficiency prevents the liver from releasing free glucose into the blood, causing severe fasting hypoglycemia, lacticacidemia, hyperuricemia, and hyperlipidemia.

8-C.

Epinephrine and glucagon both cause increased

glycogen degradation and decreased synthesis in the liver through covalent modification (phosphorylation) of key enzymes of glycogen metabolism. Glycogen phosphorylase is phosphorylated and active (“a”form), whereas glycogen synthase is phosphorylated and inactive (“b”form). Glucagon does not cause a rise in calcium.

9-D.

Ca2+ released from the sarcoplasmic reticulum during exercise binds to the calmodulin subunit of phosphorylase kinase, thereby allosterically activating the “b” form of this enzyme. The other choices are not caused by an elevation of cytosolic calcium.

10-

With Type Ia, the liver is unable to generate free glucose either from glycogenolysis or gluconeogenesis because both processes produce glucose 6-phosphate. With Type VI, the liver is still able to produce free glucose from gluconeogenesis, but glycogenolysis is inhibited.

11-B.

Uridine diphosphate (UDP)-glucose is converted to UDP-galactose by UDP-hexose 4-epimerase, thereby providing the appropriate form of galactose for lactose synthesis. Isomerization of fructose to galactose does not occur in the human body. Galactose is not converted to galactose 1-phosphate by hexokinase. A galactose□free diet provides no galactose. Galactosemia is the result of an enzyme deficiency.

12-A.

The symptoms suggest hereditary fructose intolerance, a deficiency in aldolase B. Deficiencies in fructokinase or galactokinase result in relatively benign conditions characterized by elevated levels of fructose or galactose in the blood and urine. Deficiency in β-galactosidase (lactase) results in a decreased ability to degrade lactose (milk sugar). Congenital

lactase deficiency is quite raren and would have presented much earlier in this baby (and with different symptoms). Typical lactase deficiency (adult hypolactasia) presents at a later age.

13-D.

The expression of α-lactalbumin (protein B) is increased by the hormone prolactin. Uridine diphosphate–galactose is the form used by the galactosyltransferase (protein A). Protein A is also involved in the synthesis of the amino sugar, N-acetyllactosamine.Protein B increases the affinity of protein A for glucose and, so,decreases the Km.

14-C.

The girl is deficient in galactokinase and is unable to appropriately phosphorylate galactose. Galactose accumulates in the blood (and urine). In the lens of the eye, galactose is reduced by aldose reductase to galactitol, a sugar alcohol, which causes osmotic effects that result in cataract formation. Deficiency of galactose 1-phosphate uridylyltransferase also results in cataracts but is characterized by liver damage and neurologic effects. Fructokinase deficiency is a benign condition. Aldolase B deficiency is severe, with affects on several tissues. Cataracts are not typically seen.