**Exam #3 BMB 514 – Medical Biochemistry 10/24/11**

**STEP 1 - NAME (*Print clearly*)** _____ _____
*(first)* *(last)*

**Circle your college and campus:**

**301 --- CHM-EL**
**302 --- CHM-GR**
**303 --- COM-EL**
**304 --- COM-DMC**
**305 --- COM-MUC**

**STEP 2 – Fill in your answer sheet with a #2 scoring pencil, as follows:**

- ☑ Code in your last name and first initial (F.I.)
- ☑ Code in your Student Number (PID)
- ☑ Code in your section as corresponds to the above list.
- ☑ Code in the correct FORM ..... This is Form **A**
- ☑ Sign your name in the signature box. By signing the answer sheet for this exam, the student certifies that he/she has adhered to the policies of academic honesty in the performance of this exam.

**STEP 3 - Read these instructions:**

- ☑ Page 2 of this exam contains information that may be useful to you: (a) abbreviations for the amino acids; (b) pKa values of functional groups; (c) table of logarithms; and (d) CDC weight classes related to Body Mass Index.
- ☑ A simple calculator is supplied for your use during this exam. No other electronic or computational devices are to be used. Turn off cell phones; keep them out of sight.
- ☑ The proctors have the authority/responsibility to assign any student a different seat at any time, without implication and without explanation, before or during the examination, as they deem necessary. Accomplish any relocation quietly and without discussion.
- ☑ Make sure your exam has 64 questions.
- ☑ We will not answer questions of clarification. However, if you think there is an error on your exam, summon an exam proctor.
- ☑ Read each question very carefully. Choose the single, best answer and mark this answer on your answer sheet. No points will be added for correct answers which appear on the exam page but not on the answer sheet.
- ☑ When you finish, carefully follow the instructions at the end of the exam. When you leave the exam room, please turn in your answer sheet AND your exam to the proctors standing by the doors INSIDE the auditorium. Once you exit the auditorium, please leave the building. Hallway conversations disturb those still taking the exam.
- ☑ There will be answer keys to this exam posted on the course website by 5:00 p.m. the day of the exam. You may wish to copy your responses from your answer sheet onto the answer grid on the LAST page of this exam so that you can check your results. You can tear off the last page and take it with you.
- ☑ You have 130 minutes to complete this exam. No additional time will be allowed for transfer of answers from the exam to the answer sheet. We will close the exam promptly at 10:10 a.m. Once we withdraw the boxes for the answer sheets from the doors, no additional answer sheets will be accepted.

***STEP 4 – Wait until instructed to proceed with the exam!***

# INFORMATION THAT MAY BE USEFUL FOR THE EXAM

| Abbreviations for Amino Acids | | | |
|---|---|---|---|
| Amino Acid | 3-Letter Abbreviation | Amino Acid | 3-Letter Abbreviation |
| Alanine | Ala | Leucine | Leu |
| Arginine | Arg | Lysine | Lys |
| Asparagine | Asn | Methionine | Met |
| Aspartic Acid | Asp | Phenylalanine | Phe |
| Cysteine | Cys | Proline | Pro |
| Glutamine | Gln | Serine | Ser |
| Glutamic Acid | Glu | Threonine | Thr |
| Glycine | Gly | Tryptophan | Trp |
| Histidine | His | Tyrosine | Tyr |
| Isoleucine | Ile | Valine | Val |

| Ionizable Group | pKa |
|---|---|
| α-COOH of any aa | 2 |
| β-COOH of Asp | 4 |
| γ-COOH of Glu | 4 |
| imidazole of His | 6 |
| SH of Cys | 8 |
| α-$NH_2$ of any aa | 9 |
| phenolic OH of Tyr | 10 |
| ϵ-$NH_2$ of Lys | 10 |
| guanidino of Arg | 12 |

## Tables of Logarithmic Relationships

| | Decimal | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Number | .0 | .1 | .2 | .3 | .4 | .5 | .6 | .7 | .8 | .9 |
| 1. | .00 | .04 | .08 | .11 | .15 | .18 | .20 | .23 | .26 | .28 |
| 2. | .30 | .32 | .34 | .36 | .38 | .40 | .41 | .43 | .45 | .46 |
| 3. | .48 | .49 | .51 | .52 | .53 | .54 | .56 | .57 | .58 | .59 |
| 4. | .60 | .61 | .62 | .63 | .64 | .65 | .66 | .67 | .68 | .69 |
| 5. | .70 | .71 | .72 | .72 | .73 | .74 | .75 | .76 | .76 | .77 |
| 6. | .78 | .79 | .79 | .80 | .81 | .81 | .82 | .83 | .83 | .84 |
| 7. | .85 | .85 | .86 | .86 | .87 | .88 | .88 | .89 | .89 | .90 |
| 8. | .90 | .91 | .91 | .92 | .92 | .93 | .93 | .94 | .94 | .95 |
| 9. | .95 | .96 | .96 | .97 | .97 | .98 | .98 | .99 | .99 | 1.00 |
| 10. | 1.00 | | | | | logs | | | | |

**E.g.** log 3.5 = 0.54

**Reminder: How to form logs of multiples .....**

$\log 35 = \log (3.5 \times 10^1) = (\log 3.5 + \log 10^1) = (0.54 + 1) = 1.54$

$\log 350 = \log (3.5 \times 10^2) = (\log 3.5 + \log 10^2) = (0.54 + 2) = 2.54$

$\log 0.35 = \log (3.5 \times 10^{-1}) = (\log 3.5 + \log 10^{-1}) = (0.54 - 1) = -0.46$

**Body Mass Index = (weight in lbs) x 704/ (height in inches)$^2$**

**CDC Weight Classes**

Underweight: <18.5
Normal: 18.5-24.9
Overweight: 25-29.9
Obese: >30

1) In a patient with severe chronic obstructive pulmonary disease (COPD), COPD "flares" are common and result in an inability to ventilate and the accumulation of carbon dioxide in the body, leading to a primary respiratory acidosis. Of the following mechanisms, which is the most important for management of acid-base status?

A) the carbon dioxide - bicarbonate equilibrium
$CO_2 + H_2O \blacktriangleleft\!\!\longrightarrow\!\! \blacktriangleright H_2CO_3 \blacktriangleleft\!\!\longrightarrow\!\! \blacktriangleright H^+ + HCO_3^-$ ($pK_a$ ~6.1)
B) the ammonia - ammonium ion equilibrium
$NH_4^+ \blacktriangleleft\!\!\longrightarrow\!\! \blacktriangleright H^+ + NH_3$ ($pK_a$ ~9.3)
C) the dissociation of acetic acid
$CH_3COOH \blacktriangleleft\!\!\longrightarrow\!\! \blacktriangleright H^+ + CH_3COO^-$ ($pK_a$ ~4.8)
D) the ionization of β-hydroxybutyric acid
$CH_3CHOHCH_2COOH \blacktriangleleft\!\!\longrightarrow\!\! \blacktriangleright H^+ + CH_3CHOHCH_2COO^-$ ($pK_a$ ~4.4)

2) A medical student suffers an acute anxiety attack the night before the biochemistry final exam and hyperventilates uncontrollably. Which of the following arterial blood gas results would most likely be observed?

| | **pH** | **$pCO_2$ (mmHg)** | **$[HCO_3^-]$ (mM)** |
|---|---|---|---|
| normal | 7.35-7.45 | 35 – 45 | 22 -26 |
| A) | 7.51 | 48 | 38 |
| B) | 7.50 | 29 | 22 |
| C) | 7.40 | 40 | 24 |
| D) | 7.22 | 69 | 27 |
| E) | 7.26 | 26 | 11 |

3) Lipitor (a statin drug) inhibits the enzyme HMG-CoA Reductase in the pathway of cholesterol biosynthesis via competitive inhibition. Normal kinetic parameters for this enzyme with HMG-CoA (without the drug) are: Km = 8.1 μM and Vmax = 330 pmol $min^{-1}$. Which of the following shows the expected changes in the kinetic parameters for HMG-CoA in the presence of the drug?

| | **Km** | **Vmax** |
|---|---|---|
| A) | 8.1 μM | 120 pmol $min^{-1}$ |
| B) | 20.8 μM | 120 pmol $min^{-1}$ |
| C) | 20.8 μM | 330 pmol $min^{-1}$ |
| D) | 8.1 μM | 330 pmol $min^{-1}$ |
| E) | 2.3 μM | 330 pmol $min^{-1}$ |

4) Asparaginase is used to reduce the level of asparagine in the blood in one treatment for leukemia. Which isoform of asparaginase would be most useful if the patient's blood asparagine level is 0.2mM?

| | **Km** | **Vmax** |
|---|---|---|
| A) | 0.1mM; | 0.5 mM/hr |
| B) | 0.2mM; | 0.1 mM/hr |
| C) | 0.2mM; | 0.5 mM/hr |
| D) | 2.0mM; | 0.1 mM/hr |
| E) | 0.1mM; | 0.1 mM/hr |

5) The conversion of proinsulin to insulin requires the activity of two enzymes. Which of the following best represents the classification of these two enzymes?

A) transferases
B) hydrolases
C) lyases
D) isomerases
E) oxidoreductases

6) The mature, active insulin protein contains two peptide chains held together by disulfide bonds. The side chain of which amino acid is capable of forming this covalent linkage?

A) cysteine
B) hydroxyproline
C) isoleucine
D) lysine
E) alanine

7) A 33-year-old farm owner died while using an 11-horsepower gasoline-powered washer to clean the inside of a 3420 cubic-foot swine farrowing area within a larger wooden structure. He had recently insulated this farrowing room. He was working alone, the door was closed, and there was no other ventilation on this very cold day. In the context of this vignette, an investigation by the local medical examiner's office during postmortem analysis must necessarily include a determination of the farmer's level of :

A) 2,3-diphosphoglycerate
B) Hb $A_{IC}$ (Hb=hemoglobin)
C) insulin C-peptide
D) HbCO (Hb=hemoglobin)
E) acetone

8) The reaction Phosphoenolpyruvate (PEP) + ADP + Pi → Pyruvate + ATP is catalyzed in the cell by pyruvate kinase. Which of the ratios given below would result in a $\Delta G' = -4.7$?
Given:
PEP → Pyruvate: $\Delta G^{\circ\prime} = -14.8$
ATP → ADP + Pi: $\Delta G^{\circ\prime} = -7.3$
$\Delta G' = \Delta G^{\circ\prime} + 1.4\log \frac{(\text{Products})}{(\text{Reactants})}$

A) $\frac{[\text{Pyruvate}][\text{ATP}]}{[\text{PEP}][\text{ADP}][\text{Pi}]} = 10^2$

B) $\frac{[\text{Pyruvate}]}{[\text{PEP}]} = 10^{-2}$

C) $\frac{[\text{Pyruvate}][\text{ADP}][\text{Pi}]}{[\text{PEP}]\,[\text{ATP}]} = 10^2$

D) $\frac{[\text{Pyruvate}][\text{ATP}]}{[\text{PEP}][\text{ADP}][\text{Pi}]} = 10^{-2}$

E) $\frac{[\text{ATP}]}{[\text{ADP}][\text{Pi}]} = 10^2$

9) A patient presents with poorly functioning Succinate Dehydrogenase, PDH complex E3, and Acyl-CoA Dehydrogenase enzymes (amongst others). You suspect a vitamin deficiency. Which of the following vitamin supplements would be of the most benefit to your patient?

A) Riboflavin (Vit B2)
B) Niacin (Vit B3)
C) Pyridoxal (Vit B6)
D) Biotin (Vit B7)
E) Thiamine (Vit B1)

10) A 40-year-old Caucasian gentleman is admitted to the hospital with a hematocrit of 14 (normal, 37-47). He is noted to have a lemon-yellow waxy pallor. Neurological examination revealed parasthesias (skin sensation of tingling, prickling, or itching), weakness, and an unsteady gait. A peripheral blood smear shows a macrocytic anemia (MCV >100 fl). You suspect a deficiency in **X** and order administration of **Y** to test your hypothesis.

| | **X** | **Y** |
|---|---|---|
| A) | vitamin $B_1$ thiamine | transketolase |
| B) | vitamin $B_3$ niacin | nicotinamide |
| C) | vitamin $B_{12}$ cobalamin | intrinsic factor |
| D) | vitamin C ascorbate | collagen |
| E) | vitamin H biotin | pyruvate carboxylase |

**The next three questions deal with the following case**:

A 2-year-old male born to consanguineous parents (parents are blood related or derived from the same ancestor) is brought into the emergency room suffering from seizures. The patient suffers from episodic bouts of hypoglycemia when he has not eaten. His lab values are below ($PaCO_2$=$pCO_2$):

| | Patient | Normal |
|---|---|---|
| Lactate | 6 mM | 0.5-2.0 |
| Pyruvate | 0.23 mM | 0.03-0.08 |
| Lysine | 89 uM | 88-205 |
| Alanine | 775 uM | 158-393 |
| Proline | 217 mM | 96-272 |

| | Patient | Normal |
|---|---|---|
| pH | 7.24 | 7.35-7.45 |
| $PaCO_2$ | 36 | 38-52 mm Hg |
| $HCO_3$ | 14 | 19-25 mEq/L |
| Na+ | 140 | 135-145 mEq/L |
| K+ | 4.3 | 3.5-5.0 mEq/L |
| Cl- | 111 | 98-108 mEq/L |

11) Knowing that the patient suffers from a detrimental mutation within a key metabolic enzyme and biotin partially corrected this defect, which of the following enzymes is most likely affected by the mutation?

A) Pyruvate kinase
B) Lactate dehydrogenase
C) Citrate synthase
D) Pyruvate dehydrogenase
E) Pyruvate carboxylase

12) What is the best way to describe the patient's metabolic state?

A) Metabolic alkalosis with respiratory compensation
B) Uncompensated metabolic alkalosis
C) Respiratory acidosis with partial metabolic compensation
D) Metabolic acidosis with partial (slight) respiratory compensation
E) Respiratory alkalosis with metabolic compensation

13) Given what you know about metabolism, which of the following would you expect to be elevated in this patient's serum?

A) Oxaloacetate
B) Malate
C) Glucose
D) Linoleic Acid
E) Beta-hydroxybutyrate

14) In a person with a deficiency of fructose 1,6-bisphosphatase, the predominant metabolic consequence is:

A) failure to synthesize glucose from lactic acid
B) failure to split fructose 1,6-bisphosphate into triose phosphates
C) inability to degrade glycogen
D) inability to fix $CO_2$ into organic linkages
E) lowered yield of ATP production per mole of glucose metabolized

15) What is the "activated" form of glucose used during the lengthening of a glycogen primer?

A) ATP- glucose
B) pyrophosphate
C) CDP-glucose
D) malonyl Co-A
E) UDP-glucose

16) The reciprocal regulation between gluconeogenesis and glycolysis involves all of the following EXCEPT:

A) Phosphofructokinase 1
B) Fructose 1,6-bisphosphatase
C) Fructose 2,6-bisphosphate
D) Glucagon
E) Phosphoglucomutase

17) All the following key intermediates in energy metabolism are correctly paired with enzymes that would **directly** consume or produce them **except:**

A) glucose-6-phosphate: glycogen phosphorylase
B) pyruvate: lactate dehydrogenase
C) acetyl CoA: pyruvate dehydrogenase complex
D) pyruvate: pyruvate carboxylase
E) glucose-6-phosphate: hexokinase

18) One hallmark of VonGierke's Disease is hyperuricemia. Which of the following is an explanation for the increased uric acid?

A) Excess glucose 6-phosphate causes an increase in purine synthesis that is degraded to uric acid
B) Excess glucose 6-phosphate is converted to alanine that inhibits uric acid secretion
C) High circulating levels of glucagon inhibits the conversion of uric acid to lactate
D) Increased triglycerides are metabolized to uric acid
E) Excess uridine diphosphate not used in glycogen synthesis is excreted as uric acid.

19) You have just eaten some chocolate covered sugar O's for breakfast. Which of the following enzymes serves to protect your system from a dangerous spike in blood sugar after this meal?

A) Fructokinase
B) Glucokinase
C) Hexokinase
D) Galactokinase
E) Phosphofructokinase

**The next <u>two questions</u> deal with the following case:**

A farmer is rushed into the emergency room after collapsing on his farm. Initial and subsequent laboratory data revealed signs of ischemic cardiac injury, abnormal coagulation profile, renal insufficiency, and slight leukocytosis. Lab results (normal ranges in parenthesis):

| *arterial blood gas results:* | *serum chemistry:* |
|---|---|
| pH 7.31 (7.35-7.45) | BUN 43 mEq/L (7-21), |
| $pCO_2$ 44 mm Hg (38-52) | creatinine 2.6 mg/dL (0.5-1.4) |
| $pO_2$ 77 mm Hg (75-100) | Na 135 mEq/L (135-145) |
| oxygen saturation: 95% on inspired oxygen of 35% | K 4.8 mEq/L (3.5-5) |
| | Cl 105 mEq/L (98-108). |

After further tests, you determine that he is not making enough ATP and his mitochondrial oxygen consumption is very low. Using virtual technology you are able to deduce that the addition of 2,4-DNP to his mitochondria does not rescue oxygen consumption. Finally, these purified mitochondria have an excess of reduced cytochrome C.

20) To what mitochondrial poison was the farmer exposed?

A) Oligmycin
B) Amytal
C) Antimycin
D) Hydrogen sulfide
E) Rotenone

21) What is the most likely cause of the acidosis

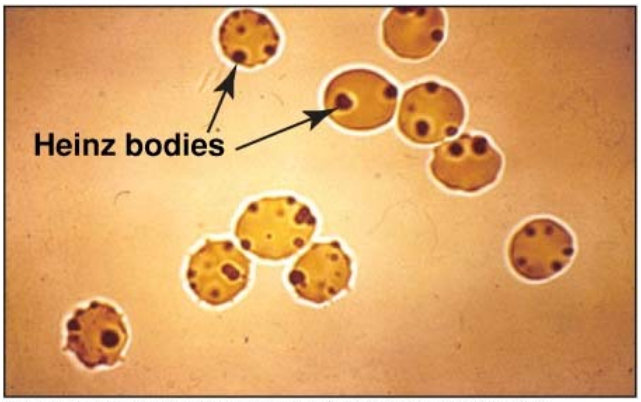
A) Decreased activity of pyruvate kinase leading to excess phosphoenolpyruvate
B) Increased lactic acid caused by inhibition of TCA cycle
C) Decreased production of ketone bodies due to renal dysfunction
D) Excess protons from the mitochondrial inner membrane space being released into circulation
E) Increased activity of alanine transaminase leading to excess alanine

22) A 45-year-old man was treated for pneumonia (Pneumocystis carinii) with trimethoprim-sulfamethoxazole. Two days after the therapy was started, he became slightly jaundiced, with the following blood profile on CBC (complete blood count):

HCT: below normal HGB: below normal RBC: below normal Retic: above normal
Direct bilirubin: ↑ (above normal) Indirect bilirubin: ↑↑↑ (much above normal)

Upon observing his blood smear (see micrograph), you immediately suspect that this patient has a genetic deficiency in which of the following enzymes?

A) glucose 6-phosphate dehydrogenase
B) glycogen phosphorylase
C) phosphofructokinase-1
D) pyruvate kinase
E) cytochrome c oxidase



**The next <u>two questions</u> deal with the following case:**

A 37 year old man is currently being followed in the hematology clinic at Sparrow Hospital. His hemoglobin levels were between 5-7 gm/dl (normal ~13.5 gm/dl in adult males). He occasionally has even more severe decreases in his hemoglobin levels, usually precipitated by viral infections. Because of this and in an effort to decrease hemolysis, he has had a splenectomy. (Erythrocytes are normally removed from the circulation by the spleen.) Subsequently, his hemoglobin levels have ranged 6-9 gm/dl and he is usually asymptomatic from his anemia. Metabolic analyses of his red blood cells show that he maintains less than 50% of the normal level of ATP and has an elevated level of phosphoenolpyruvate in his red blood cells.

23) The patient most likely suffers from a deficiency in what enzyme?

A) Phosphoenolpyruvate carboxykinase
B) Phosphoglycerate kinase
C) Pyruvate Carboxylase
D) Pyruvate Kinase
E) Glyceraldehyde 3-phosphate dehydrogenase

24) Surprisingly, the patient has an increased exercise tolerance in spite of his chronic anemia. The most likely explanation for this increased tolerance is:

A) Increase phosphoenolpyruvate inhibits gluconeogenesis ensuring the TCA cycle is on
B) Increased phosphoenolpyruvate inhibits fructose 2,6-bisphosphatase ensuring glycoylsis stays active
C) Build up of 2,3-bisphosphoglycerate causes a right shift in hemoglobin-oxygen saturation curve
D) Decreased ATP slows metabolism leading to a decrease in harmful reactive oxygen species.
E) Increased phosphoenolpyruvate inhibits the pentose phosphate pathway, leading to a decrease of NADPH needed for muscle contraction.

25) In the following question the abbreviations used are:

ADP, adenosine 5'-phosphate;
dADP, deoxyadenosine 5'-phosphate;
OMP, orotate monophosphate;
PRA, 5-phosphoribosylamine;
PRPP, 5-phosphoribosyl-1-pyrophosphate
Ribose 5-P, ribose 5-phosphate

Identify the two steps at which feedback inhibition controls *de novo* synthesis of purine nucleotides.

| | **<u>one step</u>** | **<u>another step</u>** |
|---|---|---|
| A) | Ribose 5-P to PRPP | synthesis of carbamoyl phosphate |
| B) | Ribose 5-P to PRPP | PRPP to PRA |
| C) | PRPP to OMP | Ribose 5-P to PRPP |
| D) | PRPP to PRA | ADP to dADP |
| E) | PRPP to OMP | PRPP to PRA |

26) The direct (immediate) precursor of dTMP is:

A) dCMP
B) dCDP
C) dGMP
D) dUMP
E) dAMP

27) A folate deficiency will most directly lead to a **decreased rate of synthesis** of some amino acids, thymidylate AND:

A) glucose
B) palmitate
C) 5-phosphoribosyl-1- pyrophosphate (PRPP)
D) vitamin $B_{12}$
E) adenosine monophosphate (AMP)

28) The inhibition of the synthesis of DNA by methotrexate results from direct inhibition of:

A) the reduction of dihydrofolate to tetrahydrofolate
B) the reduction of ribonucleotides to deoxyribonucleotides
C) the synthesis of S-adenosylmethionine
D) thymidylate synthetase
E) a reaction in the pathway of purine nucleotide biosynthesis

29) Methotrexate is used to treat cancers such as leukemia. If you were to study your patient's cancer cells after they had been exposed to methotrexate, you would find changes in the levels of compounds related to one-carbon metabolism.

| | **overall tetrahydrofolate** | **homocysteine** | **total cobalamin** |
|---|---|---|---|
| A) | increased | decreased | no change |
| B) | decreased | increased | decreased |
| C) | decreased | increased | no change |
| D) | decreased | decreased | decreased |
| E) | increased | increased | increased |

30) A 53-year-old man had adenocarcinoma in his large intestine. While the adenocarcinoma was being surgically removed, nodules of metastatic cancer were found in the liver. After resection (complete removal) of the tumor, therefore, the oncologist began treatment with 5-fluorouracil (5-FU), combined with other chemotherapeutic agents. The 5-FU treatments aided in the killing of the metastatic cancer cells by **decreasing** the intracellular concentration of:

A) deoxythymidine triphosphate (dTTP)
B) deoxyuridine triphosphate (dUTP)
C) ribose 5-phosphate
D) uridine triphosphate (UTP)
E) cytidine triphosphate (CTP)

31) Pyrimidine nucleotides are catabolized ...

A) to the respective bases, which are primarily salvaged
B) to carbon skeletons that are used for other metabolic pathways
C) only down to nucleosides
D) extensively in patients with gout
E) to uric acid, which is excreted

32) A 23-year-old woman was diagnosed with genital herpes. As a part of her treatment, she was prescribed acyclovir (acycloguanosine). This drug works in herpes-infected cells by:

A) activating folate degradation
B) activating reactive oxygen species ($H_2O_2$) production
C) inhibiting DNA synthesis
D) inhibiting ribonucleoside diphosphate reductase (ribonucleotide reductase)
E) activating cAMP synthesis

33) An 18-month-old boy was brought to the clinic because of severe and repeated lip chewing and aggressive tongue biting. A medical history revealed a normal pregnancy with little/no complications. But, a diagnosis of muscular hypotonia (low muscle tone) was made at four months of age. A diagnosis of Lesch-Nyhan syndrome was made on the basis of biochemical analysis and DNA sequencing. Which of the following reactions is most likely to be deficient in this boy?

A) attachment of guanine to 5-phosphoribosyl-1-pyrophosphate (PRPP)
B) condensation of ornithine with carbamoyl phosphate
C) coupling of glycine and succinyl-CoA in initiating heme biosynthesis
D) hydroxylation of phenylalanine
E) removal of phosphate from glucose 6-phosphate

34) A 3-year-old boy is being evaluated for recurrent infections. He is found to be leukopenic and has megaloblastic, hypochromic anemia. He is also noted for developmental retardation. Over the next couple of months, his anemia is found to be unresponsive to iron, folic acid, or vitamin $B_{12}$ supplementation. High levels of orotic acid are found in his urine. What metabolic defect most likely could cause this?

A) a defect in carbohydrate metabolism
B) a defect in lipid metabolism
C) a defect in protein metabolism
D) a defect in purine metabolism
E) a defect in pyrimidine metabolism

35) A 3-year-old boy has been diagnosed with systemic carnitine deficiency. Which of the following statements would be **correct**?

A) The patient will show fructose intolerance.
B) After a 24-hour fast, the patient will utilize ketone bodies as fuel.
C) Lipids will accumulate in the cytoplasm of liver cells.
D) During a fasting period of 30 hours, the blood glucose levels will stay constant.
E) The boy most likely has a defect in his liver beta-ketothiolase enzyme.

36) The four repeated steps of beta-oxidation of fatty acids, respectively, are:

A) condensation, reduction, dehydration, reduction
B) dehydrogenation, dehydration, dehydrogenation, cleavage
C) oxidation, hydration, oxidation, cleavage
D) reduction, hydration, reduction, cleavage
E) condensation, hydrogenation, hydration, hydrogenation

37) Which of the following statements **correctly** describes fatty acid synthesis and β-oxidation of fatty acids?

A) Fatty acid synthesis intermediates are covalently linked to coenzyme A (CoA), while β-oxidation intermediates are linked to an acyl carrier protein (ACP).
B) Fatty acid synthesis occurs in the mitochondrial matrix and β-oxidation occurs in the cytosol of all cells.
C) The carboxylation of acetyl CoA to malonyl CoA is the committed step in β-oxidation of fatty acids.
D) The fatty acid chain is elongated by the sequential addition of 3 carbon units during fatty acid synthesis.
E) NADPH is a cofactor used in fatty acid synthesis, while $NAD^+$ and FAD are used in β-oxidation.

38) Which one of the following statements about the absorption of lipids from the intestine is **correct**?

A) Dietary triacylglycerols are partially hydrolyzed and absorbed as free fatty acids and monoacylglycerol.
B) Dietary triacylglycerols must be completely hydrolyzed to free fatty acids and glycerol before absorption.
C) Release of fatty acids from triacylglycerols in the intestine is inhibited by bile salts.
D) Lipoprotein lipase (LPL) degrades the dietary lipids for absorption by the intestinal mucosal cells.
E) Formation of chylomicrons does not require protein synthesis in the intestinal mucosa.

39) What is the "activated" form of a fatty acid used during the synthesis of triacylglycerol from glycerol 3-phosphate?

A) ATP-linked fatty acid
B) acyl-CoA
C) CDP-linked fatty acid
D) acetyl-CoA
E) UDP-linked fatty acid

40) Which of the following is directly involved in the synthesis of phosphatidylcholine from phosphatidylethanolamine?

A) 3-hydroxy-3-methyl-glutaryl CoA (HMG CoA)
B) mevalonate
C) 5-phosphoribosyl-1-pyrophosphate (PRPP)
D) S-adenosylmethionine (SAM)
E) ceramide

**The following 2 questions refer to the clinical scenario below:**
A young girl with a history of severe abdominal pain was taken to her local hospital at 5 AM in severe distress. Blood was drawn, and the plasma appeared milky, with the triacylglyceride (TAG) level in excess of 2000 mg/dl (normal = 4-150 mg/dl). The patient was placed on a diet severely limited in fat, but supplemented with medium-chain length fatty acids.

41) Which of the following lipoprotein particles are most likely responsible for the appearance of the patient's plasma?
A) Very low density lipoproteins (VLDL)
B) Intermediate density lipoproteins (IDL)
C) Low density lipoproteins (LDL)
D) High density lipoproteins (HDL)
E) Chylomicrons

42) Medium-chain length fatty acids are given because they

A) enter directly into the portal blood for metabolism by the liver.
B) are activators of lipoprotein lipase.
C) are more efficiently packed into serum lipoprotein particles.
D) can be converted into a variety of gluconeogenic precursors.
E) provide more calories than long-chain fatty acids.

43) Which of the following statements about bile acids and bile salts is **correct**?

A) Conjugation of the bile salts with taurine or glycine produces bile acids.
B) The addition of taurine or glycine makes these molecules more insoluble in water.
C) Bile acids and bile salts are synthesized in the gall bladder.
D) The majority of bile acids and bile salts are excreted from the body daily.
E) They function as detergents because they are amphipathic.

44) Which of the following conditions would activate the pathway of cholesterol synthesis within a liver cell?

A) Increased concentrations of cholic acid.
B) Increased numbers of LDL receptors at the cell surface.
C) Dephosphorylation of HMG-CoA reductase.
D) Activation of proteases that degrade HMG-CoA reductase.
E) Increased concentrations of malonyl CoA, the substrate of cholesterol synthesis.

45) Lipoprotein lipase is:

A) activated by a protein kinase-driven phosphorylation
B) released from the pancreas to catabolize dietary triacylglycerols in the small intestine.
C) requires co-lipase for activation.
D) an extracellular lipase that catabolizes triacylglycerols in chylomicrons and VLDLs.
E) responsible for releasing fatty acids from adipocyte's stores of triacylglycerols.

**The next two questions relate to the following clinical scenario:** You have an overweight patient with a great deal of adipose tissue (adipocytes). Her diet, though, is mostly carbohydrates with a moderate fat intake.

46) Which of the following statements is the **best** information that you can tell your patient?

A) She should completely eliminate sugar from her diet to force her body to convert her fat stores back to sugar.
B) She should continue eating her high carbohydrate diet because that is not causing her weight gain.
C) You are going to prescribe her 2,4-dinitrophenol (2,4-DNP) to help her lose the weight by uncoupling her mitochondria.
D) Her liver is converting the excess carbohydrate in her diet to fatty acids for storage as triacylglycerols (TAG), which is the cause of her weight gain.
E) Her increased amount of fat cells (adipocytes) results in a decreased amount of circulating leptin, which is continually making her hungry.

47) Under the conditions of excess carbohydrate intake by your patient, which of the following regulatory effects would be occurring in liver cells?

A) The acetyl CoA formed from the pyruvate dehydrogenase (PDH) complex would activate pyruvate carboxylase for gluconeogenesis to occur.
B) Carnitine acyl transferase I (CAT I) would be inhibited by high concentrations of malonyl CoA.
C) All 8 enzymes of the TCA cycle would be active to generate oxaloacetate (OAA) for shuttling acetyl CoA units to the cytosol.
D) Glycogenolysis (glycogen breakdown) would occur to run glycolysis for ketone body production.
E) NADPH production by the pentose phosphate pathway is necessary to run the electron transport chain for a continual supply of ATP needed for fatty acid synthesis.

48) Enteropeptidase deficiency is an inborn error of metabolism that causes malabsorption of protein. The most likely explanation for protein malabsorption is that in the absence of this enzyme, the only **active** protease is

A) pepsin
B) carboxypeptidase
C) trypsin
D) chymotrypsin
E) elastase

49) Digestion and absorption of proteins

A) occurs only in the presence of bile salts
B) is more effective if the protein has a high content of essential amino acids
C) occurs by hydrolysis of peptide bonds by proteases that are stored as zymogens
D) occurs only by removal of amino acids from the ends of chains (N-terminal or C-terminal)
E) does not occur in the stomach.

50) Which of the following statements regarding protein degradation of **endogenous** proteins is **correct**?

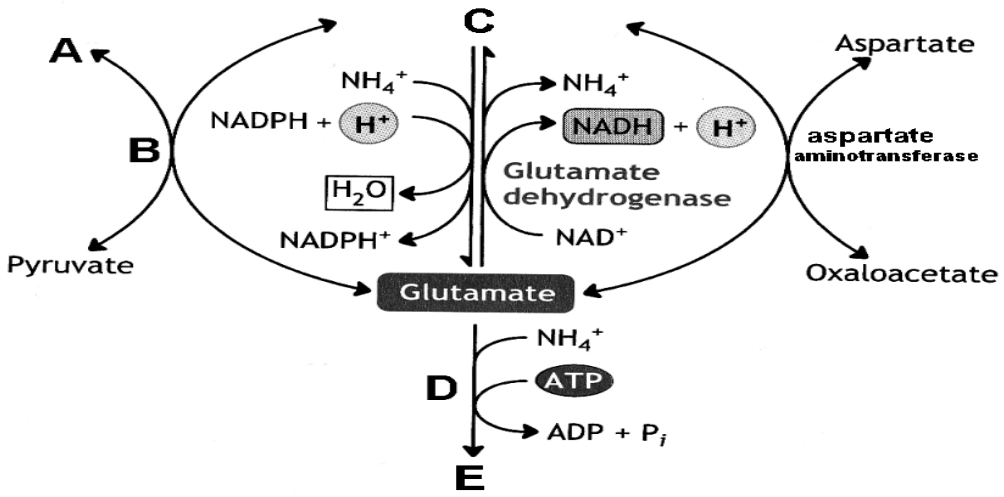
A) The lysosomal pathway primarily degrades proteins taken up by a cell via endocytosis.
B) The attachment of ubiquitin to a protein does not require ATP.
C) Enzymes targeted for destruction require the attachment of only one molecule of ubiquitin.
D) Lysosomes degrade ubiquitin-labeled proteins to peptide fragments.
E) The lysosomal pathway degrades the peptides generated by the proteasome complex.

51) A 2-year-old girl, daughter of a recently immigrated African family, is admitted to the pediatric ward owing to an increase in abdominal girth and failure to thrive. She was breast-fed until 1 year of age, at which time her mother ran out of milk. The mother then fed her bottles of liquid gelatin and believed that she was getting enough calories. On physical examination, hepatomegaly was evident as was depigmentation of both skin and hair: thinning of hair; dry skin. Height and weight in the fifth percentile. Loss of muscle in appearance, confirmed by lab data indicating hypoproteinemia and hypoalbuminemia. She is apathetic and irritable and has been having frequent episodes of diarrhea. Pathology lab reports intestinal mucosal atrophy with loss of brush border enzymes; also atrophy of pancreatic islet cells that secrete digestive enzymes. This girls suffers from:

A) Scurvy
B) Pellagra
C) Marasmus
D) Hypercholesterolemia
E) Kwashiorkor

**For the next three questions, identify the chemical or enzyme name corresponding to the letters A, B, C, D, and E in the diagram below. Then, choose the letter that best fills the blanks (with Question Number) in the following paragraph.**

Processing of the amino groups of the amino acids produces ammonia, which is toxic in its free form. In most tissues, **Question 52**, combines free ammonia with glutamate to produce nontoxic **Question 53**; while muscle cells will export their amino groups as **Question 54** to the liver.




52) Fill in the blank designated as **Question 52** in paragraph above.

53) Fill in the blank designated as **Question 53** in paragraph above.

54) Fill in the blank designated as **Question 54** in paragraph above.

55) Ketone bodies can NOT be used for energy by

A) skeletal muscle cells
B) kidney cells
C) brain cells
D) red blood cells
E) cardiac muscle cells

56) An insulinoma is a type of pancreatic tumor that results in increased insulin production. Which of the following would most likely be seen in an untreated patient with an insulinoma?

A) increased serum fatty acids
B) polyuria (frequent urination)
C) reduced liver glycogen stores
D) ketosis
E) hypoglycemia

57) A long distance runner is several hours into a race. His metabolism is dominated by the influence of epinephrine and glucagon. Which of the following **correctly** describes metabolism occurring in the liver, muscle, and adipose tissue?

A) Concentrations of cAMP are decreased in both the liver and muscle.
B) Muscle tissue increases glucose uptake from the blood.
C) HMG CoA reductase is active in the liver.
D) Glycogen phosphorylase is phosphorylated and active in both liver and muscle.
E) Triacylglycerol breakdown is inhibited in adipose tissue.

58) After five weeks of starvation, which of the following statements would **correctly** describe the changes in levels of circulating fuel compared to the well-fed state?

A) lactate, pyruvate, and alanine are higher
B) glucose is higher
C) overall ATP equivalents of circulating fuel is lower
D) fatty acids are higher
E) ketone bodies are lower

59) A newborn girl appeared normal at birth, but within 24 hours she developed lethargy, hypotonia, and apnea. Initial tests showed that she had low levels of blood urea nitrogen (BUN) and elevated ammonia. A urea cycle defect was suspected, and further tests were performed. Urinalysis results: high glutamine and orotic acid, but undetectable levels of citrulline. The defective enzyme is most likely:

A) carbamoyl phosphate synthetase II
B) argininosuccinate synthetase
C) argininosuccinate lyase
D) arginase
E) ornithine transcarbamoylase

**The next five questions relate to the following clinical scenario:** Sparty has type 1 diabetes mellitus. He has just been admitted to the hospital with symptoms of Kussmaul respirations (rapid and deep breathing), polyuria (frequent urination) and polydipsia (frequent thirst). Initial lab data indicated elevated blood glucose, and the presence of glucose and ketone bodies in the urine.

60) Which of the following statements is most likely the cause of Sparty's abrupt symptoms of polyuria and polydipsia?

A) He injected too much insulin to compensate for a carbohydrate-rich meal.
B) His RBC are lysing, due to lack of glucose uptake, releasing too much water into his plasma.
C) Excess glucose in his urine causes him to excrete excess water, making him drink more for compensation.
D) The increased rate of beta-oxidation causes the electron transport chain to produce excess water.
E) His rapid and deep breathing to blow of excess $CO_2$ causes him to retain water.

61) At the time of Sparty's admission to the hospital, which of the following conditions is most likely **correct**?

A) Protein degradation in his muscle will be inhibited.
B) His ketone body levels will be low.
C) Most of his key regulated enzymes in the liver will be phosphorylated.
D) His $HbA_{1C}$ levels in the blood will be low.
E) His blood pH will be high

62) Which one of Sparty's liver enzyme activities **decreases** when he is treated with insulin?

A) Fructose 1,6-bisphosphatase
B) Pyruvate kinase
C) Pyruvate dehydrogenase complex
D) Phosphofructokinase 1 (PFK1)
E) Glucokinase

63) Why does Sparty's type 1 diabetes cause ketoacidosis, but general starvation conditions would not lead to ketoacidosis?

A) In diabetes, all of the excess glucose is converted to ketone bodies by the liver.
B) In diabetes, tissues do not have to resort to using the ketone bodies produced.
C) In starvation conditions the circulating fatty acids are used by the tissues for fuel, so the liver does not have to make ketone bodies.
D) In starvation conditions, the liver uses the acetyl CoA produced for the TCA cycle rather than ketone body production.
E) In diabetics, muscle tissue also releases ketone bodies to the blood for use by other tissues.

64) Sparty must use a mixture of insulin analogs to maintain his blood glucose due to the lack of production of insulin by his pancreas. Which of the following statements **correctly** describes native human insulin?

A) Insulin is an eicosanoid hormone.
B) Insulin is activated by cleavage of the C-peptide from proinsulin
C) Insulin stimulates phosphorylation of many key regulatory enzymes in metabolism.
D) Insulin binds to G-protein coupled receptors.
E) Insulin is released from α-cells of the pancreas.

END OF EXAMINATION Tear off this sheet and save to check your answers.

**Please remember to:**

- Write the letter corresponding to your **FORM** in the appropriate place on the **answer sheet**.
- **SIGN AND RETURN YOUR EXAMINATION** to an instructor **before leaving the exam room**.

FORM: A

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| 2. _____ | 22. _____ | 42. _____ | 62. _____ |
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