1. A 50-year-old man consults his physician because he vomited blood immediately after lifting some heavy boxes. He was about 15 lb underweight, dehydrated, and had a history of alcohol abuse. He was hospitalized and a number of tests were done. The liver felt enlarged and a subsequent biopsy revealed a fatty liver. His urine specimen was tea-colored. Results from blood tests indicated elevated LDH, normal creatine kinase (MM), low total protein, and a serum bilirubin level of 6 mg/dl. The serum transferrin was one-fifth saturated.

A. Biochemically describe the enzymatic reactions by which humans metabolize alcohol.

\[
\text{CH}_3\text{-CH}_2\text{OH} \xrightarrow{\text{NAD}^+} \text{CH}_3\text{-CHO} \xrightarrow{\text{NAD}^+} \text{CH}_3\text{-COOH}
\]

B. Biochemically explain why the urine specimen was tea-colored.

The tea-color indicated that conjug bilirubin is spilling into the urine. The alcohol caused necrosis of the liver. The liver can still conjugate bilirubin, but it has a hard time exporting it into bile duct because of liver damage.

C. Biochemically explain why the patient had a fatty liver.

1. Ethanol stimulates lipolytic hormones. They set turn mobilize to breakdown of glycerol. Increasing FA into liver.

2. ↑ NADH (from #1) ⇒ ↑ FA Syn.

3. ↑ CH3COCOH causes impairment of VLC synthesis. Therefore, to back up in liver and cannot get out.

D. Biochemically explain why the patient had a low total serum protein.

Liver makes most of proteins in serum (i.e., albumin, clotting factors, etc.).

∴ ↓ liver function ⇒ ↓ proteins in blood.
E. Biochemically explain the significance of the serum transferrin levels in this patient.

Normally transferrin is $\frac{1}{5}$ saturated. This patient's transferrin is $\frac{1}{5}$ indicating that it is not carrying proper amount of iron. This is due to fact that ceruloplasmin ($Fe^{3+} \rightarrow Fe^{2+}$ to allow iron to be carried by transferrin) is not being made as it should by the defective liver.

F. Biochemically explain why the patient had elevated LDH.

LDH is a liver enzyme (muscle too). ↑ LDH in blood indicates lysis of some liver cells (due to cirrhosis).

G. Biochemically explain what you would expect blood levels of lactate to be relative to a healthy person if this patient were to exercise.

Lac would be higher than in a healthy person. In exercising, lac is being produced by muscle, spilled in blood, and handled by liver to conduct gluconeogenesis. This is the Cori cycle. A cirrhotic liver indicates the patient cannot conduct part of Cori cycle ($lac \rightarrow pyruvate \rightarrow C_{6}H_{12}O_{6}$)

$\Delta LDH (amyotic) \Rightarrow \Delta \text{lactate} \rightarrow [\text{lactate}]$

$\therefore$ ↑ lac in blood during exercise.
2. The two major lipids in the diets of humans are TGs and cholesterol. Humans can synthesize both molecules. Biochemically explain how the biosynthesis of TGs and cholesterol are regulated (include relevant enzymes, their organ location, and cellular location) to ensure that not much is biosynthesized when adequate amounts of each are present in the diet.

1. Key req. enzyme in chol. syn.: HMG-CoA Reductase
   Which is in the ER of all ER-containing cells. The highest amount is in liver. Dietary chol is delivered to liver via chylomicron remnant. The incoming chol inhibits HMG CoA Reductase allosterically.

2. Key enz in fatty syn + hydrox to syn is Acetyl CoA Carboxylase
   The enz in in cyto of all cells (except RBC) + especially the liver and adipose

↑ TO \( \Rightarrow \) ↑ FA \( \Rightarrow \) \( \sqrt{\text{Acetyl CoA Carboxylase (allosterically)}} \)

3. The activation of protein kinase A results in the phosphorylation of a number of enzymes, thereby regulating pathways. For each of the following enzymes below, circle the “yes” or “no” as to whether active protein kinase A directly phosphorylates the respective enzyme. If yes, then state whether the enzyme’s activity “increases” or “decreases”.

   a. Glycogen synthase \( \text{yes} / \text{no} \) \( \downarrow \)
   b. Triglyceride lipase \( \text{yes} / \text{no} \) \( \uparrow \)
   c. Pyruvate dehydrogenase yes / no
   d. ACAT yes / no
   e. HMG CoA reductase yes / no
   f. Muscle Phosphorylase yes / no
   g. Reductase kinase \( \text{yes} / \text{no} \) \( \uparrow \)
   h. Pyruvate carboxylase yes / no
   i. Acetyl CoA carboxylase \( \text{yes} / \text{no} \) \( \downarrow \)
   j. ALA synthase yes / no
4. The action of LCAT on 1-palmitoyl-2-oleoyl-PC and cholesterol results in the products (draw structures):

\[
\text{CH}_2 - \text{CH} = \text{CH} - \text{CH}_2 - \text{C} - 0
\]

A specific activator of this enzyme is \textit{Apo A}.

5. Heparin is a highly negatively charged substance which an anti-coagulant and functions to activate anti-thrombin III.

6. In the synthesis of bile acids from cholesterol, the key regulatory step is catalyzed by the enzyme \textit{7 a-hydroxylase}. To carry out this step, the enzyme uses cholesterol as a substrate and also needs oxygen, \textit{O}, \textit{C}, and \textit{NaOH}. The enzyme can be allosterically inhibited by \textit{B}.\textit{A}.

7. A deficiency of the mineral \textit{Ca} would result in an increase in glucose intolerance.

8. In Acute Intermittent Porphyria, the urinary excretion of \textit{ALA} and \textit{PBG} eventually results in the darkening of urine upon standing because (concisely explain):

\[
PBG + ALA
\]

Polymers in light air to red urine colored substance.
9. Statin drugs inhibit the rate-limiting enzyme in cholesterol synthesis. From a Lineweaver-Burk plot, the $K_m$ and $V_{max}$ of this enzyme were calculated to be $4 \times 10^{-3}$ M and $8 \times 10^2$ mmol/hour, respectively. If the above experiment is repeated in the presence of a statin drug, circle the following values that would be obtained.

| A. | 4 x $10^{-3}$ | 3 x $10^2$ |
| B. | 2 x $10^{-3}$ | 1 x $10^2$ |
| C. | 4 x $10^{-3}$ | 9 x $10^2$ |
| D. | 8 x $10^{-3}$ | 8 x $10^2$ |
| E. | 8 x $10^3$  | 9 x $10^5$ |

10. Identify the following with the specific biochemical name:

- 

- 

\[ \text{F} \]

\[ \text{Mevalonate} \]
FOR EACH OF THE MULTIPLE CHOICE QUESTIONS BELOW, CIRCLE THE BEST ANSWER.

11. What is the name of the enzyme that deaminates amino acids to yield an ammonium ion?

   a. Glutamate decarboxylase
   b. Glutamine dehydrogenase
   c. Glutamine decarboxylase
d. Glutamate dehydrogenase
e. Glutamate synthase

12. The cofactor in aminotransferases is...

   a. pyridoxal 5'-phosphate.
b. niacin.
c. biotin.
d. coenzyme B12.
e. tetrahydrofolate.

13. Which amino acids are said to be "ketogenic"?

   a. Alanine, glycine and serine
   b. Aspartate and asparagine
c. Valine, proline and histidine
d. Leucine, phenylalanine and lysine
e. Arginine, glutamate and histidine

14. Argininosuccinate is a common intermediate between...

   a. the urea cycle and glycolysis.
b. the citric acid and the urea cycles.
c. the urea cycle and gluconeogenesis.
d. the citric acid cycle and fatty acid oxidation.
e. gluconeogenesis and the Cori cycle.

15. During amino acid degradation the C3 family of amino acids are converted into...

   a. alpha-ketoglutarate.
   b. pyruvate.
c. oxaloacetate.
d. fumarate.
e. succinyl CoA.
16. Maple syrup disease is caused by the failure of cells to...
   a. oxidatively deaminate amino acids.
   b. breakdown C4 amino acids.
   ☐c. oxidatively decarboxylate alpha-keto acids.
   d. oxidatively decarboxylate acetoacetate.
   e. breakdown C5 amino acids.

17. Alcaptonuria is causes by a failure to...
   ☐a. breakdown homogentisate to 4-maleylacetoacetate.
   b. hydroxylate phenylalanine.
   c. breakdown leucine.
   d. breakdown Isoleucine.
   e. convert methionine to homocysteine.

18. Humans cannot make the following amino acids:
   a. aspartate, lysine, leucine, histidine and phenylalanine
   ☐b. methionine, threonine, lysine, valine and phenylalanine
   c. histidine, serine, valine, leucine and threonine
   d. tyrosine, phenylalanine, cysteine, histidine and serine
   e. threonine, valine, histidine, tryptophan and asparagine

19. Which vitamin is essential for one-carbon metabolism as in glycine synthesis?
   a. NAD
   b. Polic acid
   c. Pyridoxal 5'-phosphate
   ☐d. Vitamin E
   e. Coenzyme B12

20. Which compound is considered to be the major donor of methyl groups?
   a. N5-methyl-tetrahydrofolate
   b. Homocysteine
   c. Methionine
   d. S-adenosyl-homocysteine
   ☐e. S-adenosyl-methionine

21. The committed step in de novo synthesis of inosine monophosphate uses these substrates:
    ☐a. ribose 5-phosphate and ATP
   b. glycine and ribose 5-phosphate
   c. PRPP and glycine
   d. ribose 5-phosphate and GTP
   ☐e. PRPP and glutamine
22. The proper ratio of ATP to GTP is maintained because they...
   a. stimulate each other's synthesis from IMP.
   b. stimulate conversion of PRPP to the next intermediate in the IMP biosynthesis pathway.
   c. inhibit conversion of PRPP to the next intermediate in the IMP biosynthesis pathway.
   d. inhibit synthesis of IMP.
   e. stimulate synthesis of nucleoside diphosphates.

23. The first step in de novo pyrimidine biosynthesis uses as substrates...
   a. 2ATP, glutamine, water and N5-10 methylene tetrahydrofolate
   b. 2GTP, glutamine, water and HCO3
   c. 2ATP, aspartate, water and HCO3
   d. 2ATP, glutamine, water and HCO3
   e. 2ATP, aspartate, water and N5-10 methylene tetrahydrofolate

24. dTMP is made by which pathway?
   a. UMP → dUMP → dUDP → dTMP
   b. UMP → UDP → dTMP
   c. UMP → dUMP → dUDP → dTDP → dTMP
   d. UMP → UDP → dUDP → dUMP → dTMP
   e. dUTP → dTMP

25. Aminopterin and methotrexate, two anticancer drugs, work by inhibiting...
   a. dihydrofolate reductase.
   b. thymidylate synthase.
   c. xanthine oxidase.
   d. dihydrofolate synthase.
   e. ribonucleotide reductase.

26. Xanthine oxidase catalyzes the conversion of...
   a. IMP to hypoxanthine.
   b. guanosine to hypoxanthine.
   c. xanthine to uric acid.
   d. xanthine to inosine.
   e. xanthine to hypoxanthine

27. In bacteria, the major modification that regulates glutamine synthetase activity is...
   a. glycosylation.
   b. adenylation.
   c. phosphorylation.
   d. prenylation.
   e. ubiquitination.
28. 3-phosphoglycerate is the precursor to which amino acid:
   a. serine
   b. tyrosine
   c. histidine
   d. threonine
   e. methionine

29. Phenylketonuria is caused by a deficiency in...
   a. homogentisate dioxygenase.
   b. phenylalanine hydroxylase.
   c. glutamate dehydrogenase.
   d. aminotransferase.
   e. asparaginase.

30. Isoleucine, methionine and valine are broken down to...
   a. pyruvate.
   b. oxaloacetate.
   c. succinyl-CoA.
   d. alanine.
   e. acetoacetate.

31. The zymogen chymotrypsinogen is convert to its active form (chymotrypsin) by...
   a. HCl.
   b. Enteropeptidase
   c. proelastase.
   d. carboxypeptidase.
   e. trypsin.

32. Which of the following condenses with ornithine to form citrulline?
   a. urea
   b. alpha ketoglutarate
   c. aspartate
   d. carbamoyl phosphate
   e. oxaloacetate

33. The heme breakdown product that gives feces a brown color is called...
   a. urobilin.
   b. stercobilin.
   c. bilirubin.
   d. biliverdin.
   e. urobiilinogen.
34. Guanine and hypoxanthine are recycled by the enzyme called...

a. hypoxanthine-guanine phosphoribosyl kinase
b. hypoxanthine-guanine phosphokinase
\( \text{c. hypoxanthine-guanine phosphoribosyl transferase} \)
d. hypoxanthine-guanine phosphoribosylase
e. hypoxanthine-guanine phosphoribosyl transaminase

35. Describe in detail one of the transport mechanisms for getting amino acids in the intestinal mucosal cells.
36. Describe the committed step in the urea cycle. What compound directly regulates the enzyme and how is this compound synthesized and what regulates its synthesis?

37. Describe in detail how you get dietary amino acids into your body. That is to say, when you are eating, how does your body convert the proteins into amino acids for absorption?