

General Concept Review Questions for Exam 4

Note that the questions included here are **not** exam questions as they are too broad and difficult to grade, although I did use questions like this in the oral exams I gave recently. **To do well on my exams, it is very important for you to practice answering actual exam questions which are represented in the study guide problems and the old exams.** The study guide questions and exam questions posted on the course website all come with answers and are the source of about 20-40% of the actual exam questions I use every year. The general concept review questions here are to help you *see the forest through the trees* in preparation for more in depth studying.

To understand metabolism, you need to learn the "how" and "why" of these metabolic pathways (flux and regulation). In my experience, it gives you a better feel for how physiology, nutrition, pharmacology, molecular and cellular biology, and other life science disciplines, interface with the "molecular basis of life," also known as *biochemistry*. The answers to "what" questions can be looked up on the internet using Google, so memorizing "what" info is a poor use of study time.

Here are some examples of questions I may ask on the exam, and ones you definitely won't see:

What is the name of the enzyme that cleaves glycogen to release glucose? *Won't see.*
How is the catalytic activity of glycogen phosphorylase regulated? Could see.

What is the chemical structure of the glycosidic linkage at glycogen branchpoints? *Won't see.*
Why is there a branch point every ten glucose residues in glycogen? Could see.

What is the product of the committed reaction in cholesterol biosynthesis? *Won't see.*
Explain the logic of citrate being an allosteric activator of HMG-CoA reductase? Could see.

If you cannot distinguish between "what" and "why" questions where I give you the "what" in the question, then you should come talk to me so I can help you understand.

Glycogen metabolism:

- What is the biochemical explanation for favism, a condition that affects 400 million people worldwide? (Seems like detail, but in reality, you need to understand PPP to answer it).
- Explain how flux through glycolysis and gluconeogenesis is reciprocally-regulated so that we don't burn up ATP by running both pathways at the same time. (should understand the role of F-2,6-BP, *the* most important regulator in the glycolytic and gluconeogenic pathways).
- How does the "I am hungry" hormone glucagon increase glucose release from liver cells? (Explain signaling through cAMP, PKA, phosphorylation cascade, glycogen phosphorylase enzyme and inorganic phosphate, etc., why does this make sense for glucagon to do this).
- How does the "I just ate" hormone insulin increase glycogen synthesis in liver cells? (Probably a bit more important than glucagon because we are discussing diabetes, nevertheless, the same drill; signaling through dephosphorylation that leads to inactivation of phosphorylase, but activation of glycogen synthase, role of UDP-glucose, cost 1 ATP to add each time, etc.)

Fatty acid metabolism

- Explain why a mole of stearate (C18) has a higher energy potential than three moles of glucose (3 x C6) when each is completely oxidized to CO₂ and H₂O? (you need to know that β oxidation provides more energy intermediates for ATP synthesis than does glucose, the reason is that stearate is completely saturated and carries many more electrons per carbon than does glucose that is at a higher oxidation state, i.e., less reduced).
- Under what metabolic conditions is the ketogenic pathway favored, what purpose does it serve? (you need to first know what the ketogenic pathway is, also that acetyl-CoA backs up because there is not enough carbohydrate to keep the citrate cycle going, and that the energy charge is low which drives the conversion of acetyl-CoA to ketone bodies; the purpose of the ketogenic pathway is to export ketones to the heart muscle to use as metabolic fuel - 10 ATP per acetyl-CoA).
- Explain how eating excess calories of non-fat carbohydrates ends up as stored lipid in adipose tissue. (start in the liver mitochondria where acetyl-CoA is converted to citrate and then shipped out to the cytosol because high energy charge in the cell tells the citrate cycle to slow down, no ATP is needed. So citrate shuttle moves acetyl-CoA units to the cytosol and the rest is up to you to explain; malonyl-CoA, loading up fatty acid synthase, turning the cycle, generating palmitoyl-CoA, making triacylglycerol, shipping it out as LDL, etc.).
- Describe how blood glucose levels and energy charge control the activity of acetyl-CoA carboxylase? (you need to start by describing the allosteric and covalent modification differences of this enzyme and what they do in terms of activity, then you need to explain the role of phosphorylation and dephosphorylation through AMP kinase).
- What is meant by good cholesterol and bad cholesterol in terms of lipoproteins and their function in triacylglycerol and cholesterol homeostasis? (you need to explain the association between cardiovascular disease and the serum levels of LDL and HDL, and then describe the functional role of these lipoproteins, what does LDL do in term of cholesterol and the formation of atherosclerotic plaques, how is this different than the role of HDL, etc.).

Amino acid metabolism

- How is atmospheric N₂ incorporated into the biosphere? (you need to explain that only certain bacteria can carry out nitrogen fixation, it requires lots of ATP and a big enzyme complex that uses a series of redox reactions to convert N₂ to 2 NH₃, the NH₃ is then assimilated into glutamate and glutamine by enzymes in plants and bacteria, most often through the combined action of glutamine synthetase and glutamate synthase, animals eat plants and that is how they get the amino acids and the nitrogen that comes with it).
- Why does increasing arginine levels in the diet provide a treatment for individuals with argininosuccinase deficiency? (first need to describe the urea cycle and what its purpose is, then describe where the nitrogen comes from to make urea, include why an enzyme deficiency in a cycle breaks the cycle but this can be bypassed by increasing arginine which builds up cycle intermediates and keeps a part of the cycle active resulting in excretion of argininosuccinate as the nitrogen carrier; this is a good question because you have to understand the urea cycle, and nitrogen flux to explain the treatment).

- Explain why it makes sense that plants and bacteria make all 20 amino acids and humans only synthesize about half. (need to explain essential and nonessential amino acids, the general rule about structural complexity and number of metabolic steps required, the fact that humans eat protein and so why waste energy making amino acids, plants don't eat and have to be self sufficient.)
- Explain why phenylketonurians are not albinos even though they lack the enzyme phenylalanine hydroxylase. (this is one of my all time favorite questions because you have to understand a lot to answer it correctly, or versions of this question. First off, what is PKU, why do they have symptoms, what does phenylalanine hydroxylase do in terms of tyrosine generation under normal conditions, what is albinism, what does tyrosinase do, and finally, don't forget that humans eat proteins all of the time so tyrosine makes into the pigment synthesis pathway even though phenylalanine hydroxylase is deficient).

Integrated metabolism

- What is the primary role of the liver under normal homeostatic conditions compared to starvation conditions? (need to explain the central role of the liver in exporting fuel and making urea for excretion, the liver is a train depot, things get exchanged after they come in and then get shipped out again - during starvation many things change, most notably ketogenesis, amino acids coming in which are converted to glucose via gluconeogenesis, fat being oxidized to acetyl-CoA for ketone synthesis, etc.).
- How is that an overweight person can be in energy balance and eat less calories per day than a thinner person who is also in energy balance? (what is energy balance, how do you go from positive energy balance to negative energy balance, what is the physical activity of an overweight person compared to a more active person, why doesn't the overweight person lose weight if they eat less than the thin person, i.e., back to the meaning of energy balance.)
- What is meant by "a Calorie is a Calorie, but some Calories are more nutritious than others?" (what is a Calorie, how does food alter insulin and fatty acid signaling, why are some types of fat actually worse than others, what is glycemic index, what are nutrients, etc.).
- Explain how obesity can give rise to type II diabetes and why two groups of Pima Indians that are genetically similar but live in different parts of the southwest display radically different incidences of type II diabetes. (start with the thrifty gene hypothesis, and then explain the relationship between high fat levels and what this does to insulin signaling through intracellular pathways and include how the two groups of Pima Indians are different in terms of daily living).