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Consoli and coworkers observed the following data while studying human livers in overnight (14-hour) and long (66-hour) fasting subjects:

	14-hour fast	**66-hour fast**
Plasma glucose concentration (mM)	5.11 (±0.07)	3.15 (±0.09)
Liver glucose output (μmol glucose per minute)	18.8 (±0.8)	11.3 (±0.9)
Percent of liver glucose output derived from phosphoenolpyruvate	28 (±2)	97 (±2)

[Consoli, Kennedy, Miles, and Gerich. (1987) *J. Clin. Invest.* **80**: 1303-1310]

1. Make the assumption that the brain utilizes all of the glucose produced by the liver. How many milligrams of glucose does the brain consume per minute before eating breakfast in the morning?

2. If the average human contains 2.7 L of blood plasma, approximately how many milligrams of glucose do you carry in your blood before eating breakfast in the morning?

3. Circle the appropriate answers for hepatocytes:

<u>14-hour Fast</u>

[insulin] is **INCREASED/DECREASED**
[glucagon] is **INCREASED/DECREASED**
[cAMP] is **HIGH/LOW**
[Fructose-2,6-bisphosphate] is **HIGH/LOW**
Phosphofructokinase-2 is **PHOSPHORYLATED/DEPHOSPHORYLATED**
Phosphofructokinase-2 is **ACTIVE/INACTIVE**
Phosphofructokinase-1 is **ACTIVE/INACTIVE**
Fructose-1,6-bisphosphatase is **ACTIVE/INACTIVE**
Glycogen synthase is **PHOSPHORYLATED/DEPHOSPHORYLATED**
Glycogen synthase is **ACTIVE/INACTIVE**
Glycogen phosphorylase is **PHOSPHORYLATED/DEPHOSPHORYLATED**
Glycogen phosphorylase is **ACTIVE/INACTIVE**

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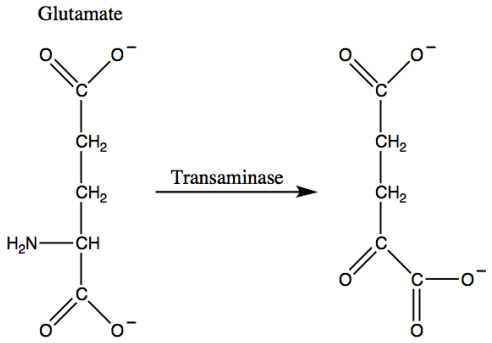
4. Consoli and coworkers observed that the glucose output from the liver decreased by 38% as fasting continued from 14 to 66 hours. During the same increased fasting interval, the amount of glucose derived from phosphoenolpyruvate increased by 246%. Explain what is going on in the liver as fasting increases from 14 to 66 hours.

5. Glutamate is one of the amino acid components of protein. Your liver cells contain a transaminase, which will convert glutamate into α-ketoglutarate. Diagram a pathway that your liver cells might use to turn protein (glutamate) into glucose during a 66-hour fast (i.e. raft, ocean, no land, despair...). Include as much detail as you can.



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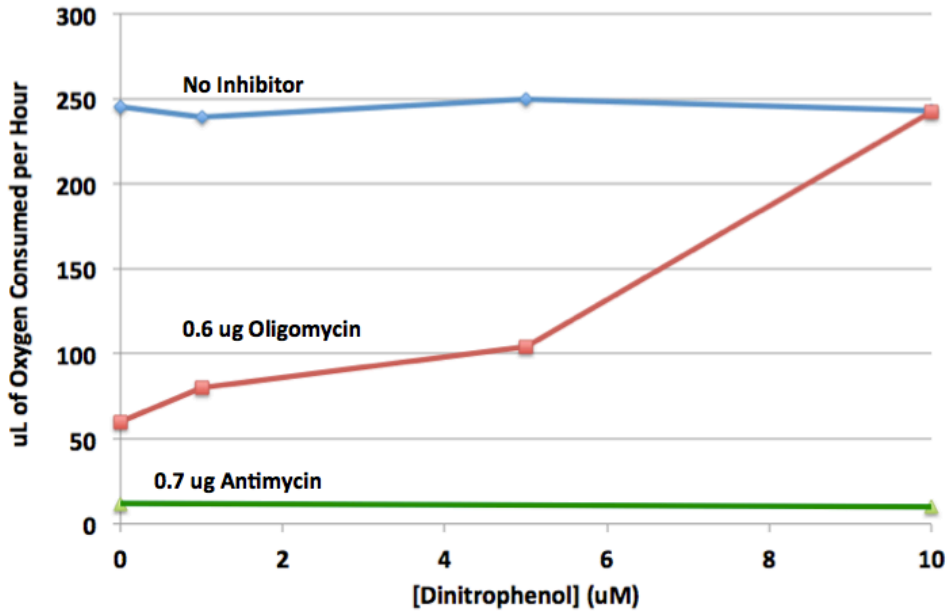
Oligomycin is a potent inhibitor of ATP synthase, while antimycin is a potent inhibitor of Complex III of the electron transport chain in mitochondria. Dinitrophenol is a membrane-soluble molecule that can carry protons across a membrane from high concentration to low concentration in the absence of any enzymes. Dinitrophenol is not thought to interact with any of the complexes of the electron transport chain or ATP synthase.

The following graph summaries the effect of dinitrophenol on purified mitochondria that have been treated with oligomycin or antimycin.



[Adapted from Huijing and Slater. (1961) *J. of Biochemistry* **49**: 493-501]

6. What part of the oxidative phosphorylation pathway consumes oxygen?

7. Explain why the addition of dinitrophenol to oligomycin-inhibited mitochondria resumes oxygen consumption while it has no effect on antimycin-inhibited mitochondria. Be specific.

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1. 10 pts
2. 10 pts
3. 12 pts
4. 13 pts
5. 30 pts
6. 5 pts
7. 20 pts