BCHM 463 **Your Name:** _____

Biochemistry and Physiology **ID #:** _____

Exam III, April 30, 2003 **Prof. Jason Kahn**

You have 55 minutes for this exam.

Exams written in pencil or erasable ink will not be re-graded under any circumstances.

You may use a calculator for this exam. No other study aids or materials are permitted.

Generous partial credit will be given, *i.e.*, if you don't know, guess.

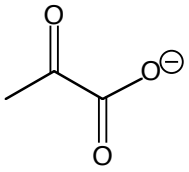
Glucose□ G6P□ F6P□ FBP□ GAP(+DHAP)□ 1,3-BPG□ 3PG□ 2PG□ PEP□ Pyruvate

Explanations should be concise and clear. I have given you more space than you should need.

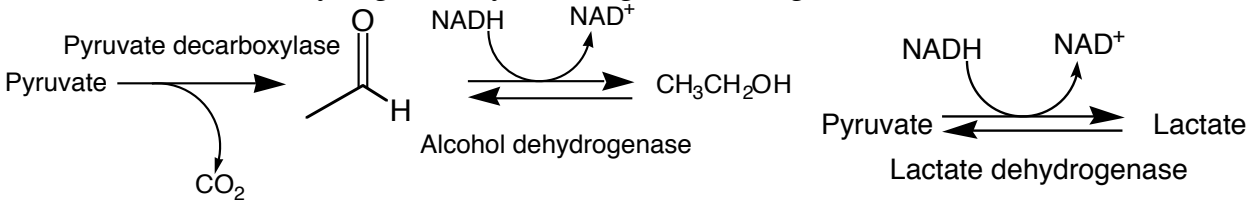
Honor Pledge: Please write out the following sentence and sign it, or talk to me about it:

"I pledge on my honor that I have not given or received any unauthorized assistance on this examination."

1. The Fate of Pyruvate (30 pts):



During anaerobic exercise or fermentation, the pyruvate produced by glycolysis is further processed to give lactate (in muscle) or ethanol and carbon dioxide (in yeast), as shown below. When we ingest ethanol, it is metabolized by liver alcohol dehydrogenase. Pyruvate is given at the right.



(a; 10 pts) Why do these fermentative processes occur (same reason for both)? How does alcoholic fermentation relate to the Pasteur effect? Name the cycle through which liver supports anaerobic glycolysis in muscle.

(b; 6 pts) What are the metabolic effects of alcohol ingestion and metabolism, in terms of redox balance and the pyruvate-lactate equilibrium?

(c; 10 pts) Yet another reason not to drink on an empty stomach…based on your answers above, explain why ethanol inhibits gluconeogenesis in the liver. If glycogen is simultaneously in short supply (the empty stomach), speculate on the physiological consequences. [Note: the question oversimplifies the real situation.]

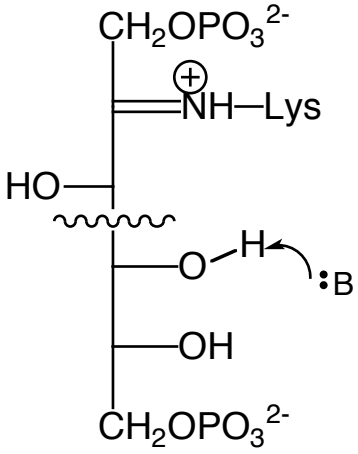
(d; 4 pts) Draw the structure of the nicotinamide ring of NADH.

2. The Aldolase Mechanism and the Logic of Glycolysis (30 pts):

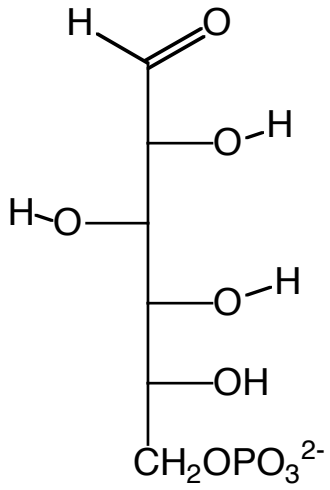
The structure at the right shows a key intermediate in the aldolase reaction. The squiggly line indicates the C-C bond to be broken.

(a; 3 pts) Draw in the three additional electron-pair arrows that will take us to the next step.

(b; 8 pts) Draw and name the two products of the aldolase reaction.



(c; 10 pts) The structure of glucose-6-phosphate is given below. Outline the ß-hydroxy carbonyl moiety hidden within it. Draw the two products we would obtain by carrying out an aldolase-like reaction on glucose-6-phosphate. (In other words, if aldolase worked on G6P instead of on FBP, what would we get?) It may help you to write out the mechanism.

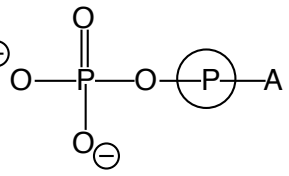


(d; 5 pts) Why do you think glycolysis evolved so that the aldolase reaction is done on fructose (as FBP), rather than glucose or G6P as in part c?

(e; 4 pts) By analogy with one rationale offered for the existence of hexokinase, why do you think the aldolase reaction comes after the PFK-1 reaction rather than before? In other words, why does aldolase operate on FBP rather than F6P?

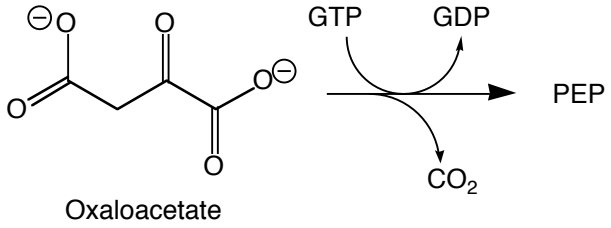
3. High-Energy Molecules (20 pts):

(a; 10 pts) Draw out the pyruvate kinase reaction mechanism: PEP + ADP ⇌ pyruvate + ATP. Assume that catalysis is simply a phosphoryl transfer catalyzed by proximity and orientation, followed by a spontaneous tautomerization (and show both steps). Draw ADP as at the right.



(b; 4 pts) What is the thermodynamic driving force for this substrate-level phosphorylation?

(c; 6 pts) The PK reaction is reversed by pyruvate carboxylase followed by the reaction below. What enzyme catalyzes it (acronym is fine), what process includes this reaction, and what metabolic cycle is linked into glucose metabolism via this reaction?

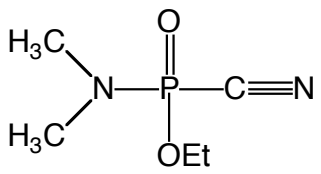


4. Enzyme Kinetics, Inhibition, and Politics (20 pts):

(a; 7 pts) Draw the Lineweaver-Burke double-reciprocal plot for simple Michaelis-Menten kinetics. Label the axes, the *x*-intercept, the *y*-intercept, and the slope.

(b; 3 pts) Explain why a competitive inhibitor does not affect the V_{max} of its target enzyme.

The structure of the nerve agent Tabun is shown at the right. It resembles the structure of acetylcholine, and it is an irreversible inhibitor of acetylcholinesterase.



(c; 6 pts) Give <u>one way you could distinguish experimentally between a pure competitive and an irreversible enzyme inhibitor</u> (there are at least two good possible answers, give one).

(d; 4 pts) <u>Why do chemical warfare agents actually make rather ineffective weapons</u> when used against well-defended countries or troops? (Although, the VX nerve agent is much stickier and more stable than Tabun, and therefore bears a highly unfortunate resemblance to land mines, which have been termed "a weapon of mass destruction in slow motion.")

Score:	1. The Fate of Pyruvate (30 pts):	_____
	2. The Aldolase Mechanism and the Logic of Glycolysis (30 pts):	_____
	3. High-Energy Molecules (20 pts):	_____
	4. Enzyme Kinetics, Inhibition, and Politics (20 pts):	_____
	Total: out of 100	_____