BB 422/622

OUTLINE:

Review of 421
Goals of 422
Review of chemical principles
- Thermodynamics
- C/O cycles
- Overview of Metabolism
- ATP cycles

Energy Coupling
Chemical Reactivity
Bioenergetics
Membrane Transport
- Review of membrane structure, dynamics, and proteins
- Mediated/non-mediated
- Energetics
- Facilitative Diffusion
  - ionophores
  - GLUT1
  - Aquaporins
  - Potassium channel
- Active Transport
  - Primary
    - Na/K pump
    - ABC transporters
  - Secondary
    - Glc import
    - Bicarbonate/Cl
    - Lactose/H+

Catabolism of Glucose

Glycogenolysis
- phosphorylase
- debranching enzyme
- phospho-gluco-mutase (PGM)

Glycolysis
- Introduction & overview;
- Phase I
  - hexokinase- phosphotransferase-coupling
  - phospho-gluco-isomerase (PGI)- endiol
  - phospho-fructo-kinase (PFK-1)-
  - Aldolase- Schiff base
    - (electron sink to stabilize a carbanion)
  - triose-phosphate isomerase (TPI)- endiol

Exam 1

- Phase II
  - **GAPDH**- oxidation
  - PG kinase- return on investment- substrate-level phosphorylation
  - **PG mutase**- acid/base; phospho-enzyme
  - **Enolase**- enolate
  - Pyruvate Kinase- phosphotransferase
- Summary: labeling studies, logic, energetics

Catabolism of Other sugars
Pasteur: Anaerobic vs Aerobic
Fermentations- Anaerobic
- Lactate
  - lactate dehydrogenase
- Acetoacetate decarboxylase
- Ethanol
  - pyruvate decarboxylase
  - alcohol dehydrogenase

Aerobic
- Pyruvate
  - pyruvate dehydrogenase complex

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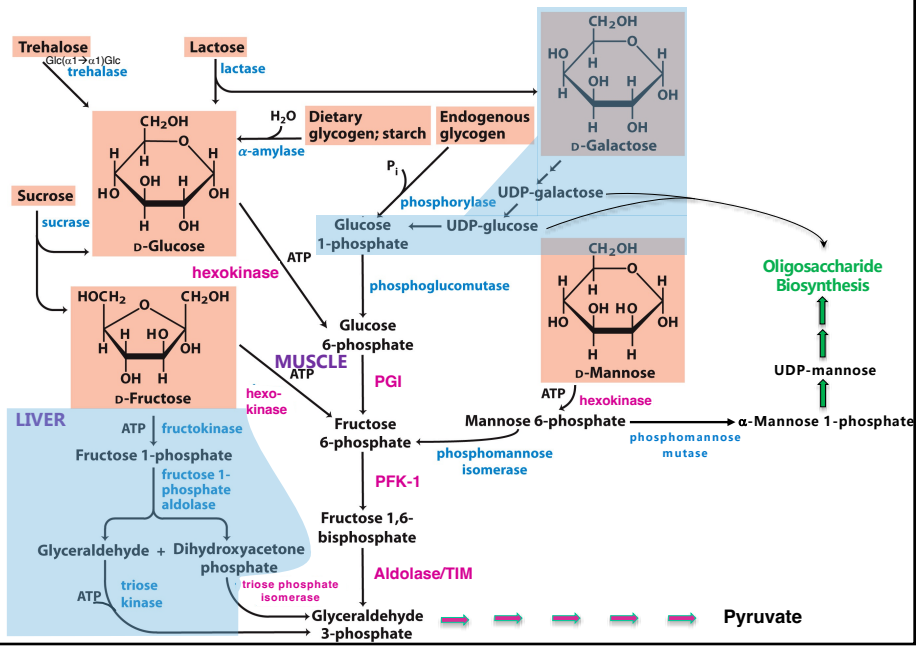
Catabolism of Other Sugars



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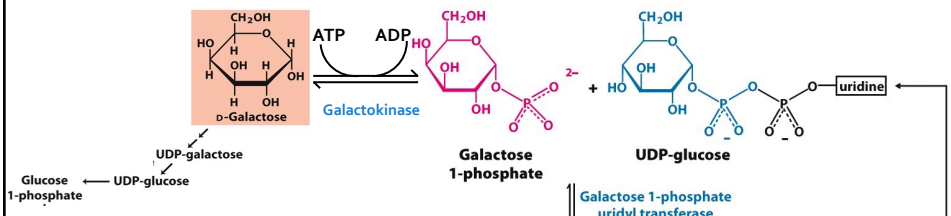
Catabolism of Other Sugars



- Use of nucleotide sugars discovered by Argentinian biochemist Luis Leloir in 1940 for which he received the Nobel Prize.
- Defects in the human genes for these enzymes causes what are called inborn errors in metabolism.
- The cause of one of these due to galactose ingestion was one of the first discovered in 1956 by Herman Kalckar.
- Galacotsemia causes enlarged liver, cirrhosis, kidney failure, cataracts, hypoglycemia, lethargy, and brain damage. Without treatment, mortality is about 75%.
- Defects in transferase are the underlying cause, with incidence of about 1:60,000 births.

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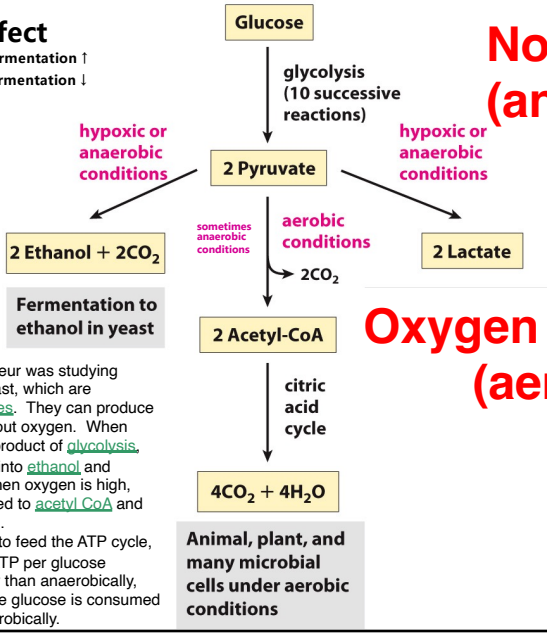
Fates of Pyruvate

Pasteur effect
– O_2→growth ↓ & fermentation ↑
+O_2→growth ↑ & fermentation ↓



No Oxygen (anaerobic)

Oxygen available (aerobic)

In 1857, Louis Pasteur was studying fermentation by yeast, which are facultative anaerobes. They can produce energy with or without oxygen. When oxygen is low, the product of glycolysis, pyruvate, is turned into ethanol and carbon dioxide. When oxygen is high, pyruvate is converted to acetyl CoA and completely oxidized.
Since either needs to feed the ATP cycle, and you get more ATP per glucose oxidized aerobically than anaerobically, about 15 times more glucose is consumed anaerobically as aerobically.

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Fates of Pyruvate: Fermentation

No Oxygen (anaerobic)

Pasteur effect

+O2→growth ↑ & fermentation ↓

Glucose

glycolysis (10 successive reactions)

hypoxic or anaerobic conditions

2 Pyruvate

2 Ethanol + $2CO_2$

Fermentation to ethanol in yeast

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Fates of Pyruvate: Fermentation

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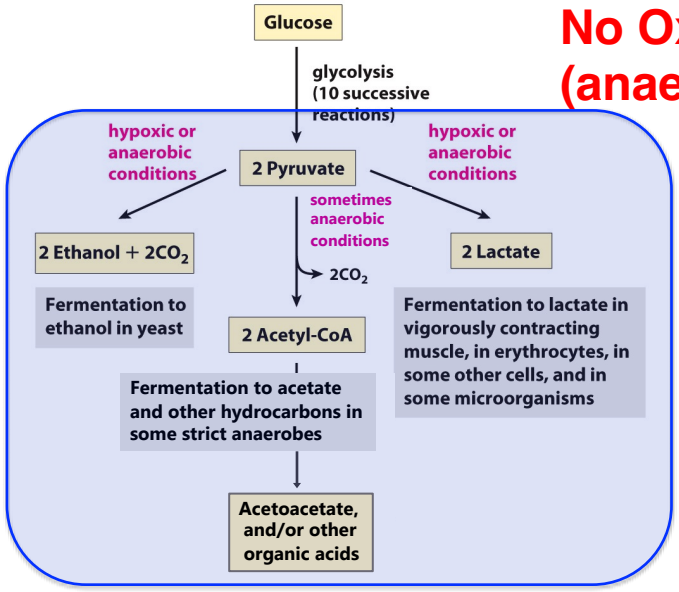

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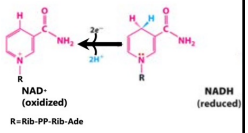
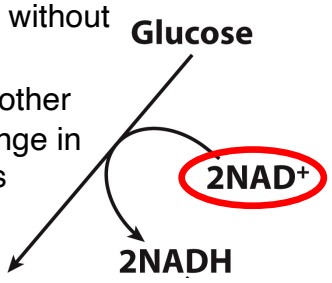
Fates of Pyruvate: Fermentation

Why?

- **Regenerates NAD^+ for further glycolysis under anaerobic conditions**
- Generation of energy (ATP) without consuming oxygen
- Reduction of pyruvate to another product, there is no net change in oxidation state of the sugars
- The process is used in the production of food from beer to yogurt to soy sauce. **2 Pyruvate**





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Fates of Pyruvate: Fermentation

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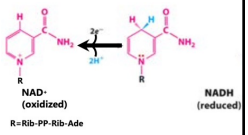

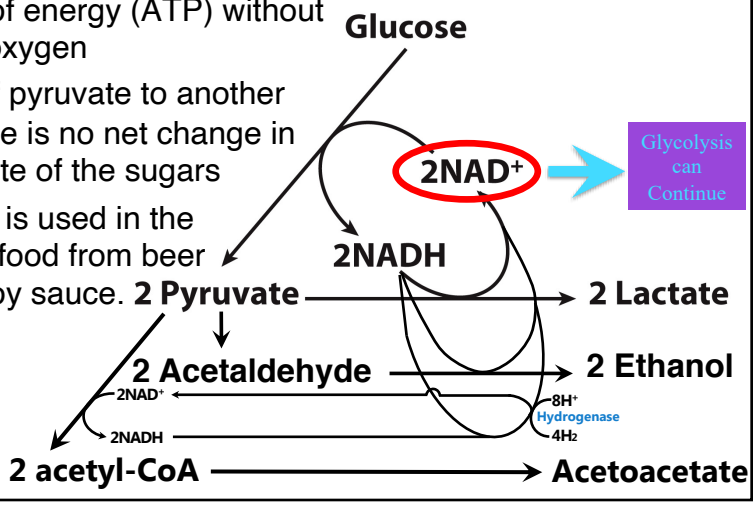

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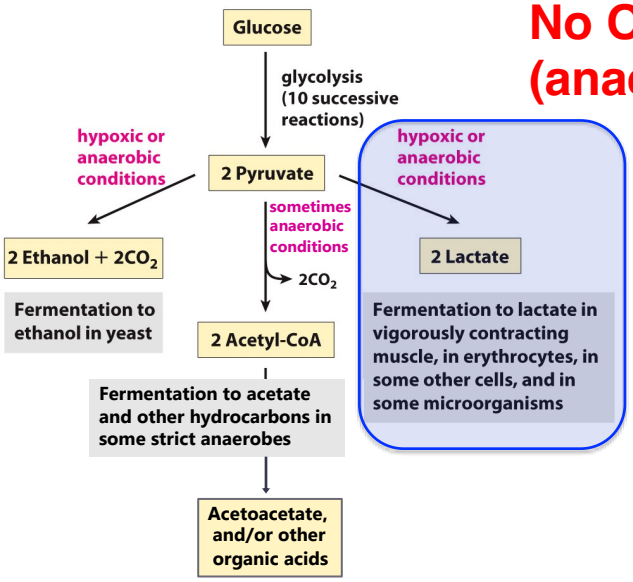
Fates of Pyruvate: Fermentation to Lactate

No Oxygen (anaerobic)



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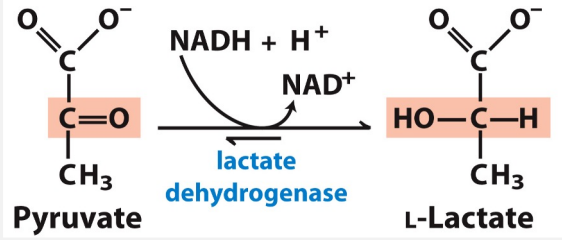
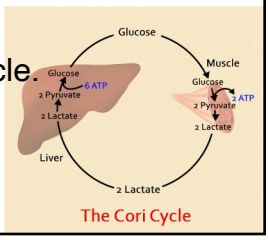
Fates of Pyruvate: Fermentation to Lactate



- Pathway in animals
- Reduction of pyruvate to lactate, reversible
- Highly thermodynamically favorable/reversible ($\Delta G^{\circ\prime} = -6$ kcal/mol)
- During strenuous exercise, lactate builds up in the muscle.
  - generally, less than 1 minute
- The lactate can be transported to the liver and converted to glucose there. Called the Cori cycle.
  - Requires a recovery time
  - high amount of oxygen consumption to fuel gluconeogenesis
  - restores muscle glycogen stores



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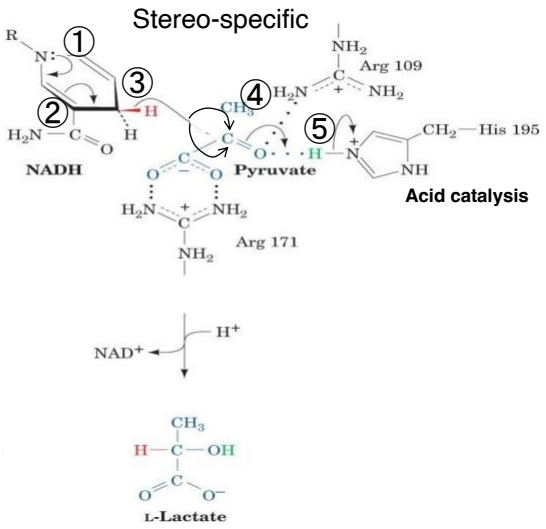
Fates of Pyruvate: Fermentation to Lactate

Mechanism

Lactate dehydrogenase



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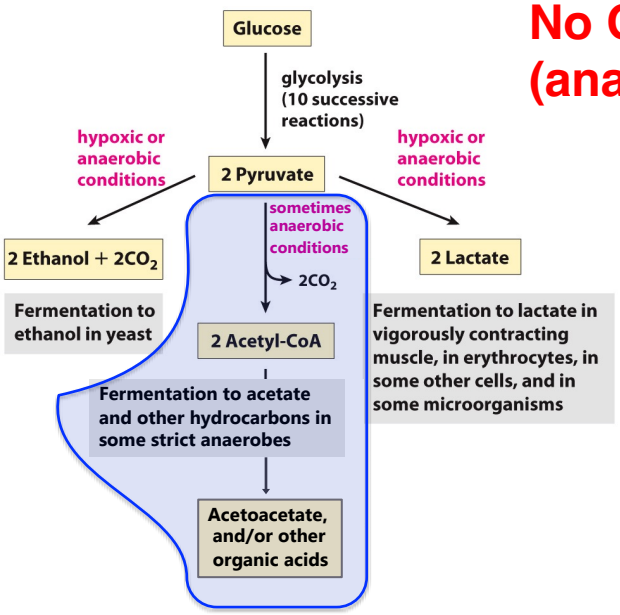
Fates of Pyruvate: Fermentation to Acetate

No Oxygen (anaerobic)



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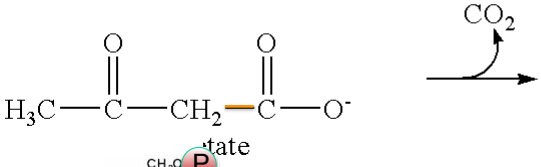
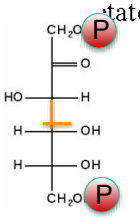
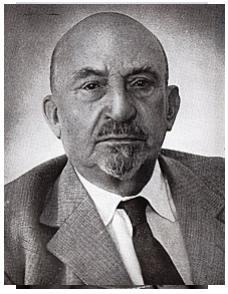
Fates of Pyruvate: Fermentation to Acetoacetate

Acetoacetate Decarboxylase





Strict anaerobe: *Clostridium acetobutylicum*



In 1916, the enzyme, *acetoacetate decarboxylase*, was discovered by Chaim Weizmann….. on to serendipity!

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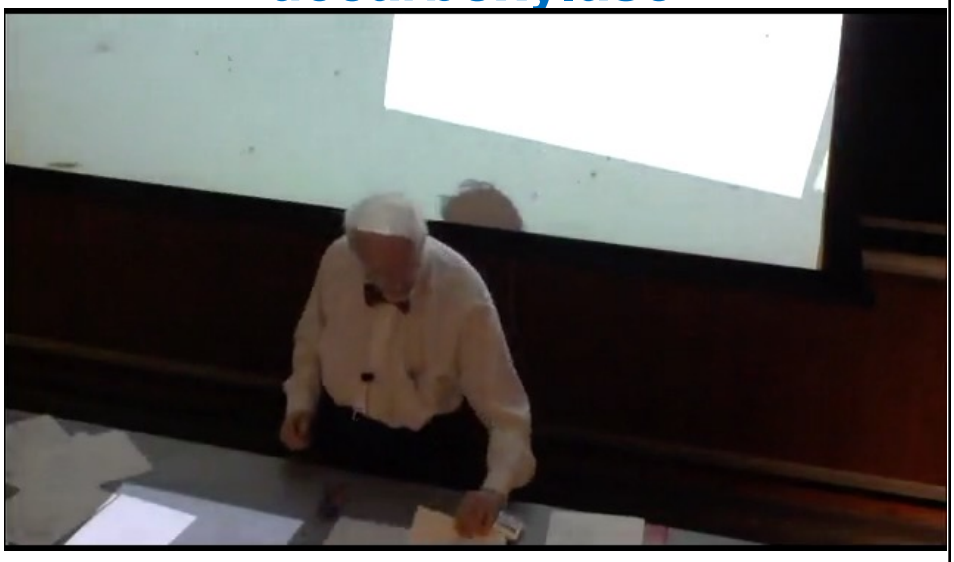
Fermentation: Acetoacetate decarboxylase



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