BI/CH 422/622

OUTLINE:

Review
Bioenergetics
Membrane Transport
Catabolism of Glucose
Glycogenolysis
- phosphorylase
- debranching enzyme
- phospho-gluco-mutase (PGM)

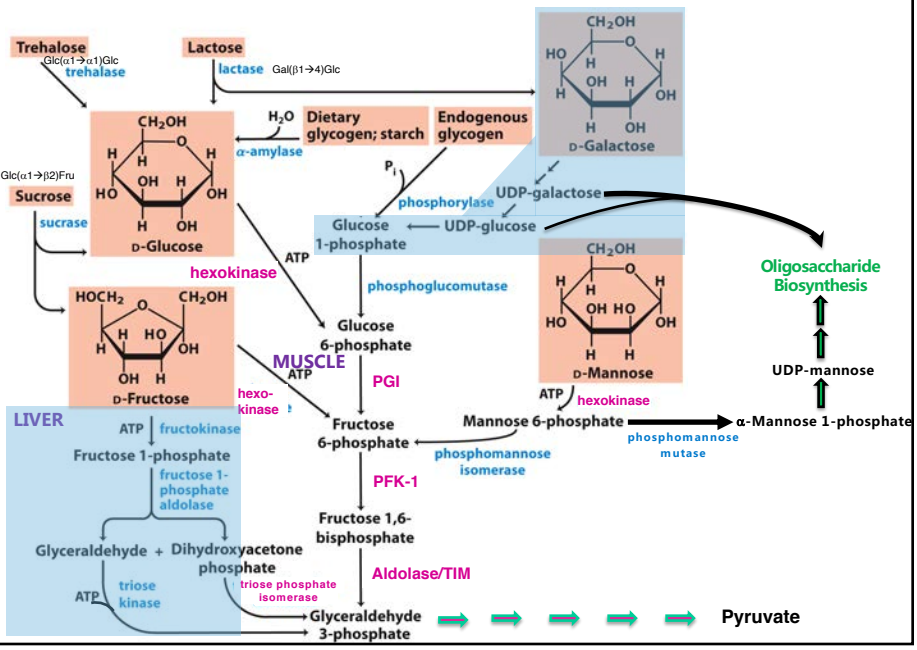
Glycolysis
- Introduction & overview; 2 phases
- Phase I
  - hexokinase
  - phospho-gluco-isomerase (PGI)
  - phospho-fructo-kinase (PFK-1)
  - Aldolase
  - triose-phosphate isomerase (TPI)
- Phase II
  - glyceraldehyde-3-phosphate dehydrogenase
  - PG kinase
  - PG mutase
  - Enolase
  - Pyruvate Kinase
- Summary: labeling studies, logic, energetics

Other sugars

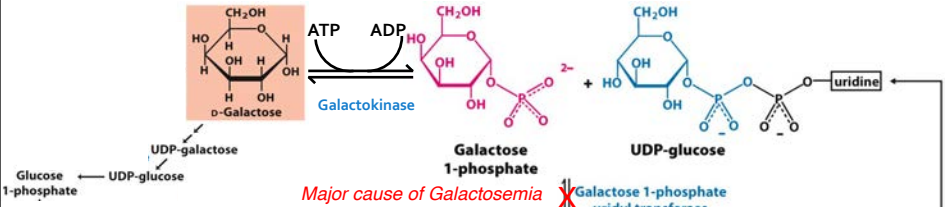
Pasteur: Anaerobic vs Aerobic Fermentations
- Lactate
  - lactate dehydrogenase
- Acetoacetate
  - Acetoacetate decarboxylase
- Ethanol
  - pyruvate decarboxylase
  - alcohol dehydrogenase

Announcements:
Material for Exam 1 ends today

Catabolism of Other Sugars



Catabolism of Other Sugars

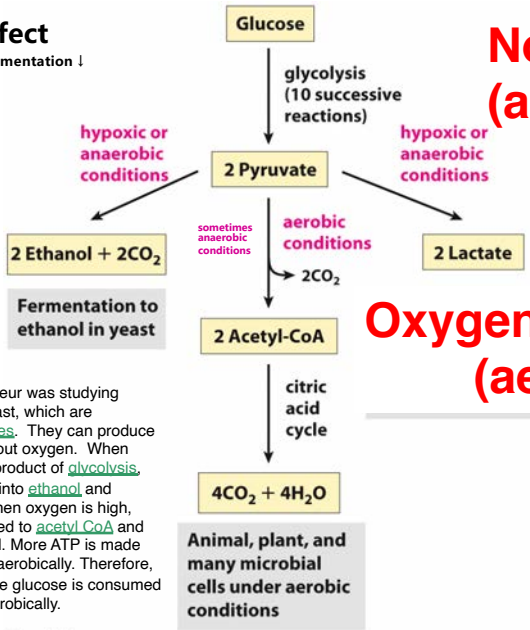


- Use of nucleotide sugars discovered by Argentinian biochemist Luis Leloir in 1940 for which he received the Nobel Prize.
- Defects in the human genes for these enzymes causes what are called inborn errors in metabolism.
- The cause of one of these due to galactose ingestion was one of the first discovered 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.

Fates of Pyruvate

Pasteur effect

+O2→growth ↑ & fermentation ↓



No Oxygen (anaerobic)

Oxygen available (aerobic)

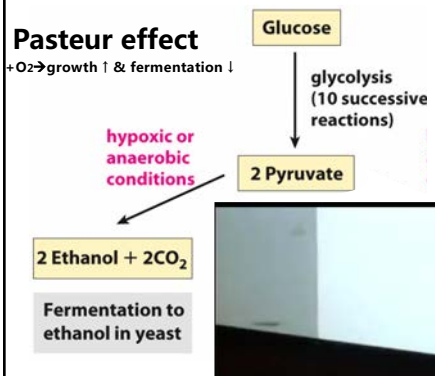
In 1857, Louis Pasteur was studying fermentation by yeast, which are facultative anaerobes. They can produce energy with or without oxygen. When oxygen is low, the product of glycolysis, pyruvate, is turned into ethanol and carbon dioxide. When oxygen is high, pyruvate is converted to acetyl CoA and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

Fates of Pyruvate

No Oxygen (anaerobic)

Pasteur effect

+O2→growth ↑ & fermentation ↓



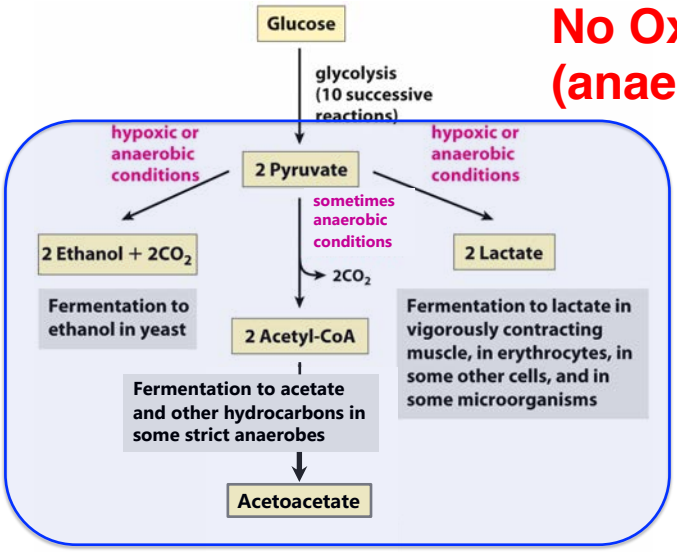
In 1857, Louis Pasteur was studying fermentation by yeast, which are facultative anaerobes. They can produce energy with or without oxygen. When oxygen is low, the product of glycolysis, pyruvate, is turned into ethanol and carbon dioxide. When oxygen is high, pyruvate is converted to acetyl CoA and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

The beginnings of biochemistry……

…

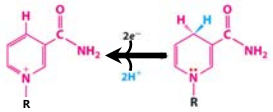
Fates of Pyruvate: Fermentation

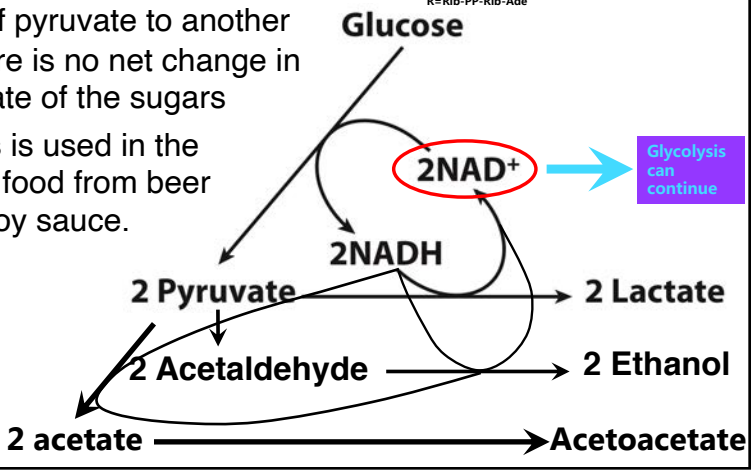
No Oxygen (anaerobic)



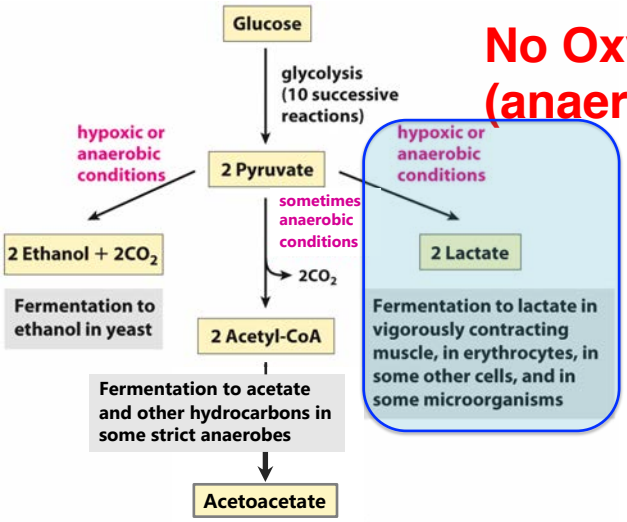
Fermentation: Why?

- **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.



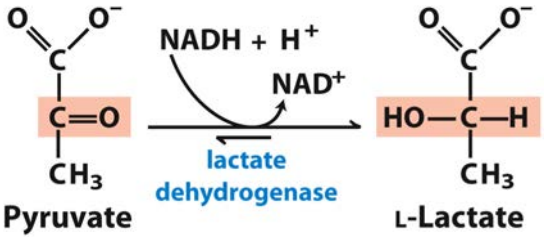


Fates of Pyruvate: Fermentation

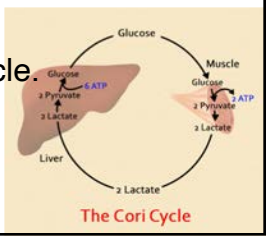


No Oxygen (anaerobic)

Fermentation: Lactic acid



- 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

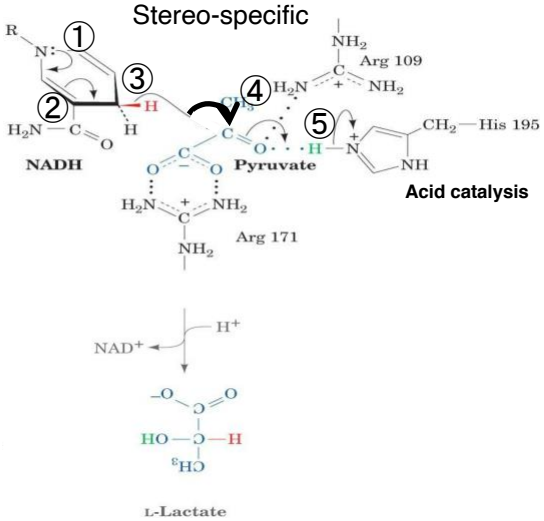


Fermentation: Lactic acid

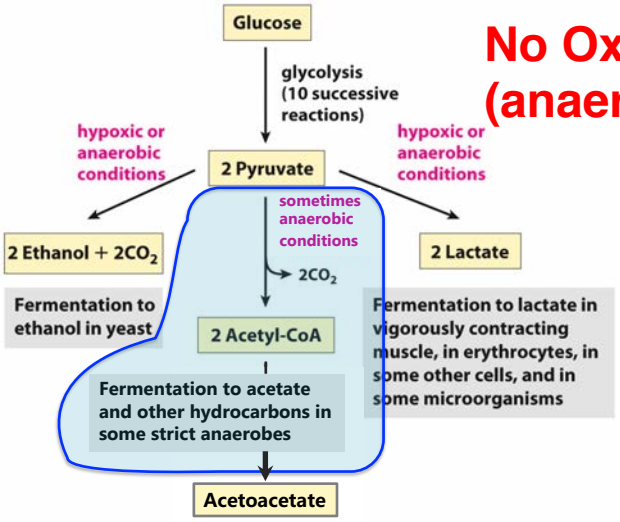
Mechanism

Lactate dehydrogenase

Stereo-specific



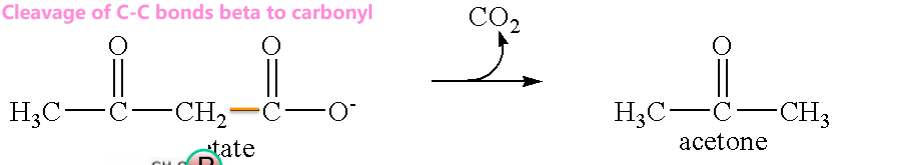
Fates of Pyruvate

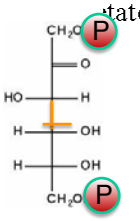


No Oxygen (anaerobic)

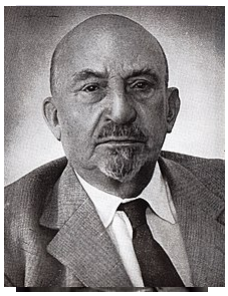
Fermentation: Acetoacetate decarboxylase

Cleavage of C-C bonds beta to carbonyl





Strict anaerobe: *Clostridium acetobutylicum*



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

Fermentation: Acetoacetate decarboxylase

BI/CH 422/622

Material for Exam 1 Ends