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CONCEPT: THERMODYNAMICS FOR PHYSIOLOGY: THE ENERGETICS OF (BIO)CHEMICAL REACTIONS

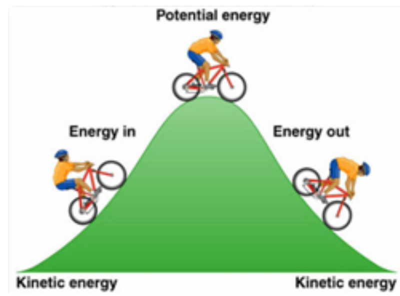
Thermodynamics: Energy and Work:

● **Energy** is the capacity to cause a change in a system.

● There are 2 important kinds of energy:

□ **Kinetic energy** exists in ___________________________.

□ **Potential energy** is stored in something's position.



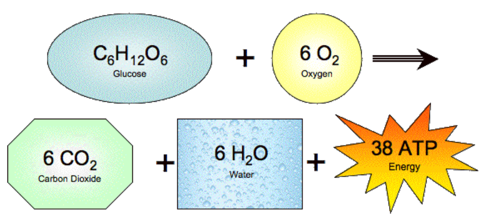
● And 3 important kinds of work:

□ **Chemical work**= making and breaking of chemical ___________________.

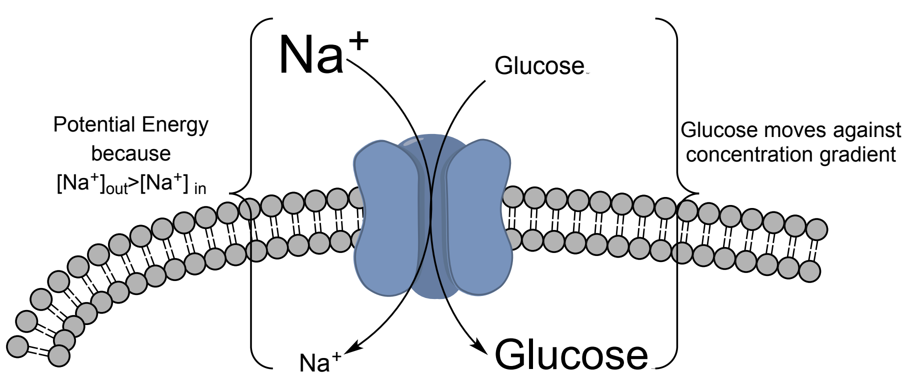
□ **Transport work**= work required to move materials *against* their concentration gradients.

□ **Mechanical work**= work done when physically moving things.

EXAMPLE: Glucose is made of a bunch of carbon, oxygen, and hydrogen atoms bonded together. These bonds hold potential energy. In cells, potential energy stored in these bonds is used to make ATP, an energy source.



EXAMPLE: Sodium Glucose Linked Transporter uses potential energy in Na^+ gradient to move glucose against its concentration gradient.



There is a concentration gradient for Na^+ across cell membranes; $[Na^+]$ is higher on the outside of the cell than the inside that stores potential energy. This PE can be converted to transport work by coupling the movement of Na^+ into the cell to the movement of another molecule—like glucose—against its concentration gradient.

Reaction Energetics:

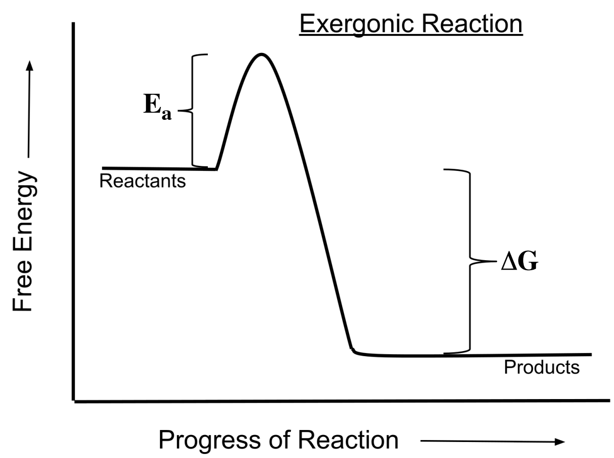
● Chemical reactions occur at a given **rate** ("speed") depending on some conditions

□ ↑*Temperature* and ↑*Reactant Concentration*→↑Rate (because ↑Collisions).

□ **Activation Energy (E_a)**- Reactants must "build up" enough energy to begin a chemical reaction. Lowering E_a speeds up a reaction.

- **Catalysts** speed up reactions by ______________________ activation energy.

● A **reaction coordinate diagram** shows the changes in energy that molecules undergo during a reaction.

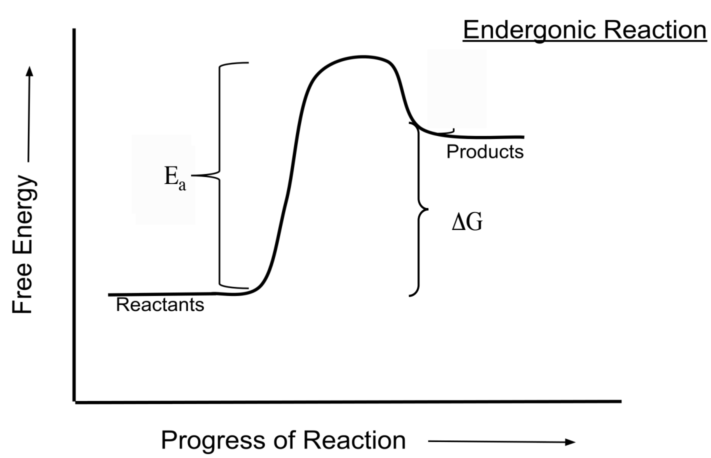


□ **Exergonic** reactions __________________ energy because *the products have less energy than the reactants.*

□ **Endergonic** reactions _________________ energy because *the products have more energy than the reactants.*

● **Enzymes** are biological catalysts—they lower the activation energy so reactions proceed quickly enough to sustain life.

EXAMPLE: The above reaction coordinate diagram is for an *exergonic* reaction. Here's an *endergonic* reaction.



ATP's Role in Reactions:

● **Adenosine Triphosphate** (ATP) is used by the cell as a source of energy for many, many biochemical reactions.

□ The hydrolysis of ATP is exergonic—it releases energy.

□ Endergonic reactions can be **coupled** to the exergonic ATP hydrolysis reaction.

-This makes the entire, net coupled reaction exergonic, allowing it to proceed.

EXAMPLE: The energy for muscle contraction comes from ATP hydrolysis.

Myosin-LE ⇋ Myosin-HE *Endergonic*

ATP ⇋ ADP + P_i *Exergonic*

Myosin-LE+ATP ⇋ Myosin-HE + ADP + P_i ***Exergonic***

For a muscle to contract, proteins in the muscle called myosin must first change from their low-energy conformation (Myosin-LE) to their high-energy conformation (Myosin-HE). This reaction is highly endergonic. Coupling this reaction to ATP hydrolysis allows the reaction to proceed.

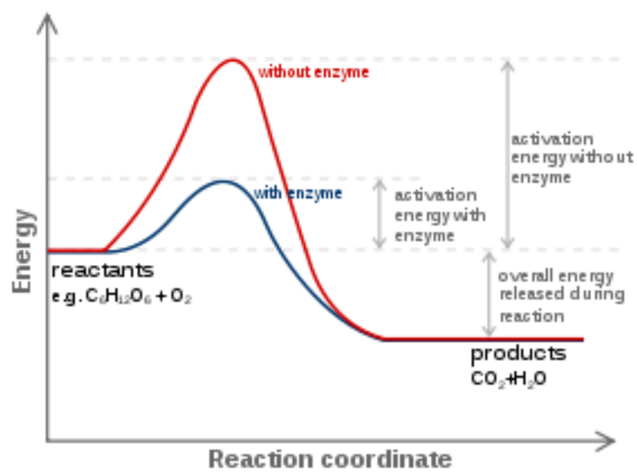
PRACTICE 1: Bringing an amino acid from the inside of the small intestine to the bloodstream requires the use of a Na^+-amino acid cotransporter. The work done by this transporter in moving the amino acid into the cell is an example of which kind of work?

a) Chemical work.
b) Transport work.
c) Mechanical work.

PRACTICE 2: The first reaction in glycolysis is the addition of a phosphate group to glucose, making glucose-6-phosphate. This reaction requires hydrolyzing ATP→ADP. Which of the following describes the energetics of this reaction?

a) Exergonic.
b) Endergonic.

PRACTICE 3: This is a reaction coordinate diagram for a reaction run with or without an enzyme catalyst present.



ΔG (Increased / Decreased / Didn't change)

E_a (Increased / Decreased / Didn't change)

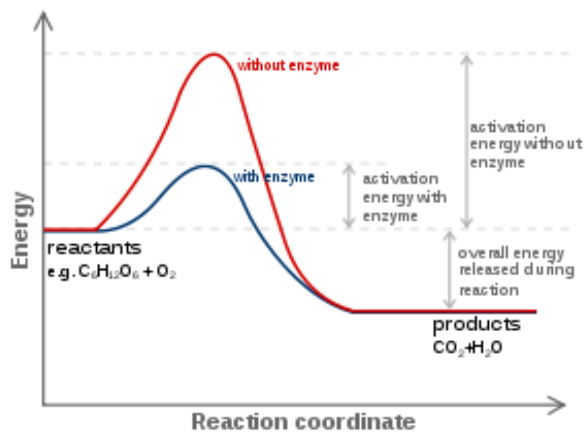
CONCEPT: ENZYMES AND THEIR REGULATION

Enzymes as Catalysts:

● Most important biochemical reactions in the body would proceed far too slowly to maintain life.

□ **Enzymes**—proteins made by the body—are catalysts; reduce E_a to speed up reactions.

EXAMPLE: Enzyme's effects on a reaction coordinate diagram. ↓E_a (blue) lets the reaction to proceed much more quickly.

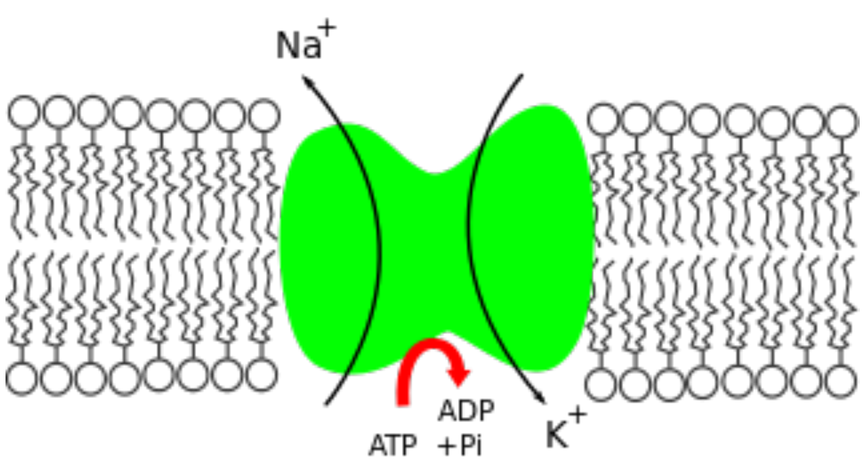


● Enzymes are named with the ending **-ase.**

□ The substrate the enzyme acts on is usually the prefix: e.g. peroxid*ases* break down peroxides.

EXAMPLE: ATPases are a class of enzymes in the body that catalyze the cleavage of energy-storing ATP into ADP+P_i.

The Na^+/K^+ ATPase pump breaks down ATP and uses that energy to pump Na^+ out of the cell and bring K^+ in.



Enzymes as Proteins:

● Most enzymes work by **binding** to the reactants, forcing them into a favorable position to help the reaction along.

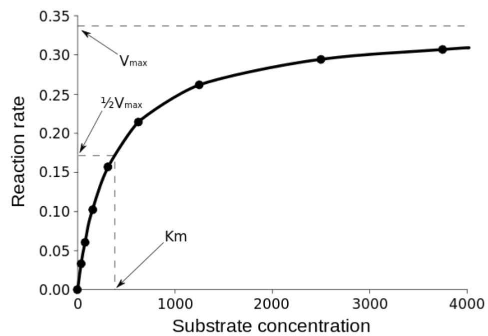
● Enzymes are proteins, which means that all the normal rules with proteins and ligand binding apply.

□ **Saturation**- there's a limited number of binding sites.

□ **Denaturation**- temperature and/or pH fluctuations may compromise enzyme function.

□ **Regulation**- they can be phosphorylated or have allosteric binding to change their activity.

EXAMPLE: Enzymes can saturate. Adding more reactant does increase reaction rate…up to a point.



Enzymes and Multi-Step Pathways:

- Most reactions are a part of long, complicated metabolic pathways.
  - □ Enzymes typically catalyze most or every reaction in a pathway.

EXAMPLE: In this generic metabolic pathway, enzymes W, X, Y, and Z are the catalysts.

$$A + B \underset{W}{\rightleftharpoons} C \underset{X}{\rightleftharpoons} D \underset{Y}{\rightleftharpoons} E \underset{Z}{\rightleftharpoons} F$$

- **End-product feedback inhibition**: *the final product inhibits the first enzyme*
  - □ It is beneficial for the body to not run reactions and pathways needlessly.
  - □ It's efficient to slow or stop the pathway *once there's enough of the final product.*

EXAMPLE: The final product F inhibits the first enzyme in this pathway—W.

$$A + B \underset{W}{\rightleftharpoons} C \underset{X}{\rightleftharpoons} D \underset{Y}{\rightleftharpoons} E \underset{Z}{\rightleftharpoons} F$$

(-)

EXAMPLE: An important early step in glycolysis—a 10-step pathway that breaks down glucose to make ATP and pyruvate—is catalyzed by enzyme phosphofructokinase (PFK). PFK is inhibited by ATP, a product of glycolysis.

$$\text{Glucose} \rightleftharpoons \rightleftharpoons \text{Fructose-6-Phosphate} \xrightarrow[\text{Phosphofructokinase}]{} \text{Fructose-1,6-Bisphosphate} \rightleftharpoons \rightleftharpoons \text{Pyruvate} + \text{ATP}$$

(-)

PRACTICE 1: In a solution with 10 mM of enzyme and 100 mM of substrate, a particular reaction proceeds at a rate of 10 mM/sec. If the concentration of substrate is increased to 300 mM, the reaction continues to proceed at a rate of 10 mM/sec. Which of the following explains this phenomenon?

a) Enzyme saturation.

b) Enzyme denaturation.

c) Enzyme regulation.

PRACTICE 2: Pepsin is an enzyme in the stomach that digests protein. It works best at a pH of 2. When pepsin gets into the small intestine, where the pH is about 5-6, pepsin stops working. Which of the following explains the decrease in the activity of pepsin in the duodenum?

a) Enzyme saturation.

b) Enzyme denaturation.

c) Enzyme regulation.

CONCEPT: METABOLISM I: OVERVIEW

Metabolism Vocabulary:

● **Metabolism**= catch-all word for the reactions carried out by the body and the rate at which these reactions occur.

□ **Catabolism**= reactions that break down larger molecules to provide parts and energy to make ATP.

-How the body breaks down carbohydrates, fats, and proteins.

□ **Anabolism**= reactions that synthesize larger molecules from parts (usually with ATP as the energy source).

● **Aerobic** reactions and pathways require ____________________ to run; **anaerobic** metabolism can be run *without* O_2.

An Overview of Metabolism:

● Most important metabolic pathway(s) are those that breakdown ____________________.

□ These reactions breakdown glucose into CO_2 and ATP (used for energy).

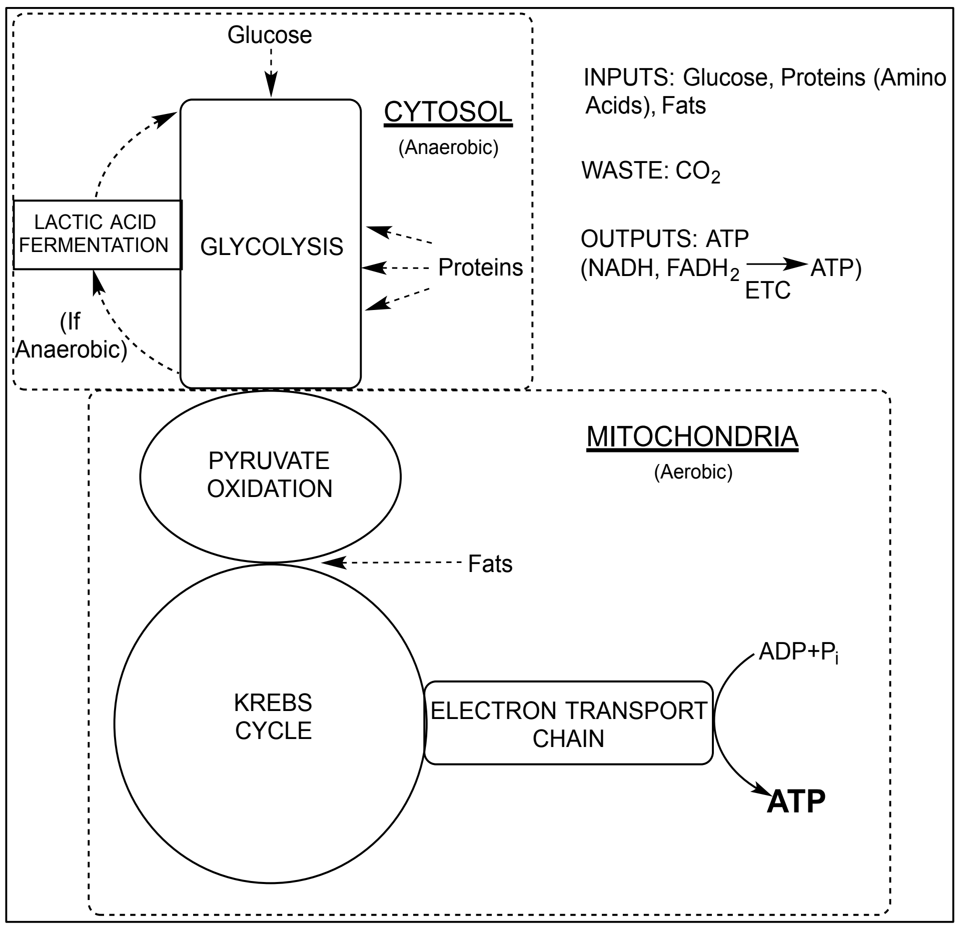
□ Metabolism of other molecules (proteins and fats) feed into these.

● **Glycolysis** is first—a series of 10 reactions that take place in the **cytosol**. It's *anaerobic*!

● **Lactic Acid Fermentation** comes next, but only if the cell is in *anaerobic* conditions.

□ If O_2 present, glycolysis feeds into the rest of *aerobic* metabolism.

● **Aerobic metabolism**—which takes place in the **mitochondria**—consists of three pathways: **Pyruvate Oxidation,** the **Krebs Cycle**, and the **Electron Transport Chain** (ETC)**.**



□ These use the energy in glucose to make **NADH** and **$FADH_2$**, which carry high-energy electrons.

□ High-energy electrons are then used by the ETC to make ATP.

● Fats enter catabolism at the Krebs Cycle; Proteins enter catabolism as glycolytic intermediates.

PRACTICE 1: Which of the following reactions will proceed if the cell is in anaerobic conditions? (Choose all that apply.)

a) Glycolysis.
b) Lactic Acid Fermentation.
c) Krebs Cycle.
d) Electron Transport Chain.

CONCEPT: METABOLISM II: GLYCOLYSIS

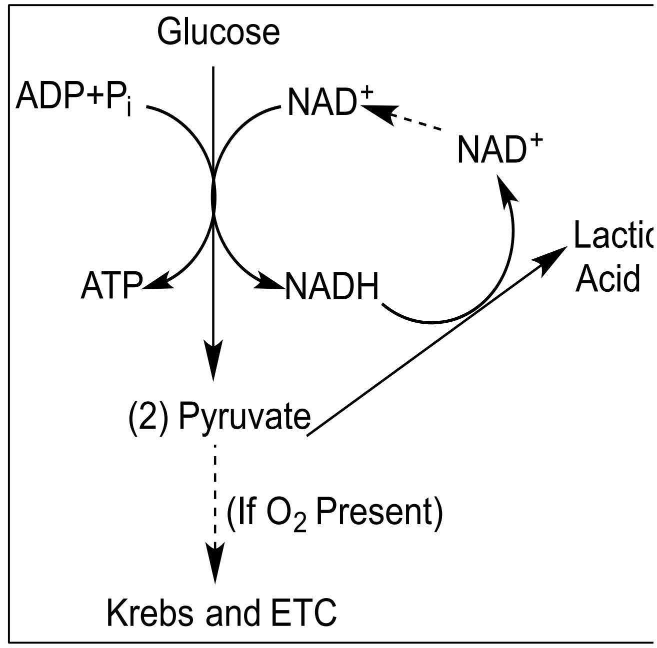
● **Glycolysis** is the beginning of carbohydrate ________________________________.

□ *Very fast* series of 10 reactions that turns 1 glucose→2 pyruvates+2 ATP+ 2 NADH.

-NADH is a high-energy electron carrier; they carry electrons to the mitochondria for later use.

-The ATP can be used immediately by the cell; the NADH are shuttled to the mitochondria (for use in ETC).

□ Glycolysis is anaerobic—none of the reactions require oxygen, so it can be run in times and places of low O_2.



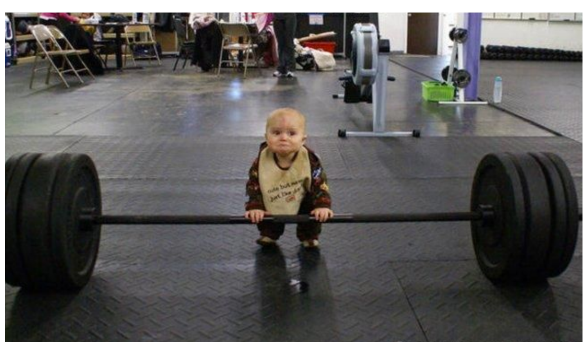
● Glycolysis requires a supply of NAD^+, which is usually regenerated during **aerobic** metabolism (if the cell has O_2).

● If the cell is in **anaerobic** (low O_2) conditions, the cell could quickly run out of NAD^+ → glycolysis stops.

□ **Lactic acid fermentation** lets cell regenerate NAD^+ from NADH, converting pyruvate→lactic acid in the process.

-The lactic acid is a waste product that is cleared by the bloodstream. As an acid, it will decrease blood pH.

EXAMPLE: Glycolysis powers heavy lifts because it delivers ATP very quickly, but also generates lactic acid.



During a lift, the muscles in a powerlifter's arms need to deliver a massive amount of energy in a very short time. This time restriction prevents them from using any aerobic metabolism; they use exclusively glycolysis and lactic acid fermentation to power the lift. As a result, the muscles produce lots of lactic acid, causing ↓pH in the muscles.

PRACTICE 1: A scientist gives a plate full of bacteria a high dose of a drug that irreversibly inhibits the reaction of lactic acid fermentation (i.e. the pyruvate→lactate) reaction. After a while, all the cells are dead. Which of the following explains why the bacteria died?

a) The bacteria could no longer make lactic acid, which they need as food.
b) The bacteria accumulated pyruvate, which is toxic.
c) The bacteria could not regenerate NAD^+, causing glycolysis (and ATP generation) to stop.
d) The bacteria accumulated NADH, which is toxic.

CONCEPT: METABOLISM III: AEROBIC METABOLISM

● ***Aerobic* metabolism** consists of **Pyruvate Oxidation**, **Krebs Cycle** and the **Electron Transport Chain (ETC).**

□ All this aerobic metabolism happens in the **mitochondria.**

□ This series of reactions is much, much more ______________________ than anaerobic metabolism.

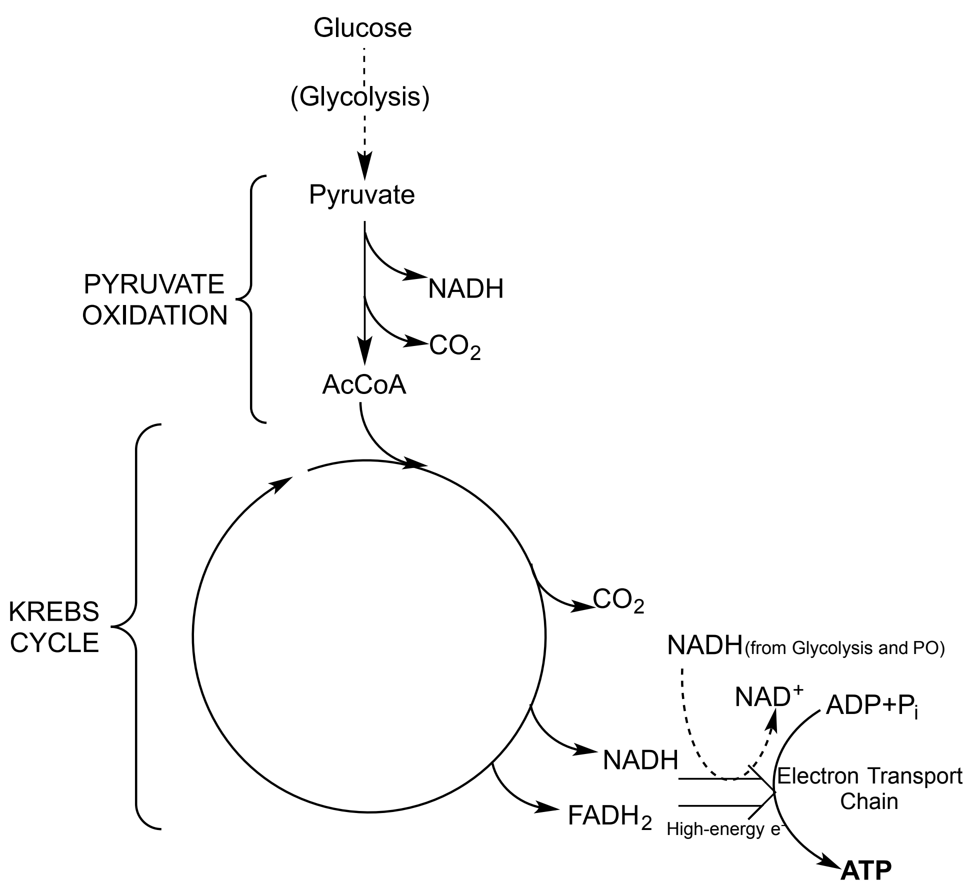
-Glycolysis+Fermentation yield 2 ATP vs. Glycolysis+Krebs+ETC yield ~32 ATP.

□ But, Krebs and ETC *require* O_2 and *take much* ________________ to complete than glycolysis and fermentation.

Summary Table of Aerobic Metabolism:

	Input:	**Output:**
Pyruvate Oxidation	Pyruvate	Useful: NADH, Acetyl CoA (AcCoA) Waste: CO_2
Krebs Cycle (AKA Citric Acid Cycle)	Acetyl CoA	Useful: NADH, $FADH_2$ (another e^- carrier) Waste: CO_2
Electron Transport Chain	NADH, $FADH_2$	Useful: ATP Waste: H_2O

EXAMPLE: A summary schematic of pyruvate oxidation, the Krebs Cycle, and the ETC.



PRACTICE 1: “Burning” fat is the process of breaking stored fat down into free individual units of Acetyl CoA. Which of the following metabolic pathways can be powered by the breakdown of fats? (Choose all that apply).

a) Glycolysis.
b) Pyruvate Oxidation.
c) The Krebs Cycle.
d) The Electron Transport Chain.

PRACTICE 2: The amino acid alanine (among others) can be broken down to pyruvate. Which of the following metabolic pathways can be powered by the breakdown of alanine? (Choose all that apply).

a) Glycolysis.
b) Pyruvate Oxidation.
c) The Krebs Cycle.
d) The Electron Transport Chain.

CONCEPT: METABOLISM IV: PROTEIN AND LIPID CATABOLISM

● Proteins→Glycolysis. Proteins are just a chain of various amino acids. Proteins are broken into amino acids in the gut.

□ Many amino acids are taken up into cells and used to make new proteins.

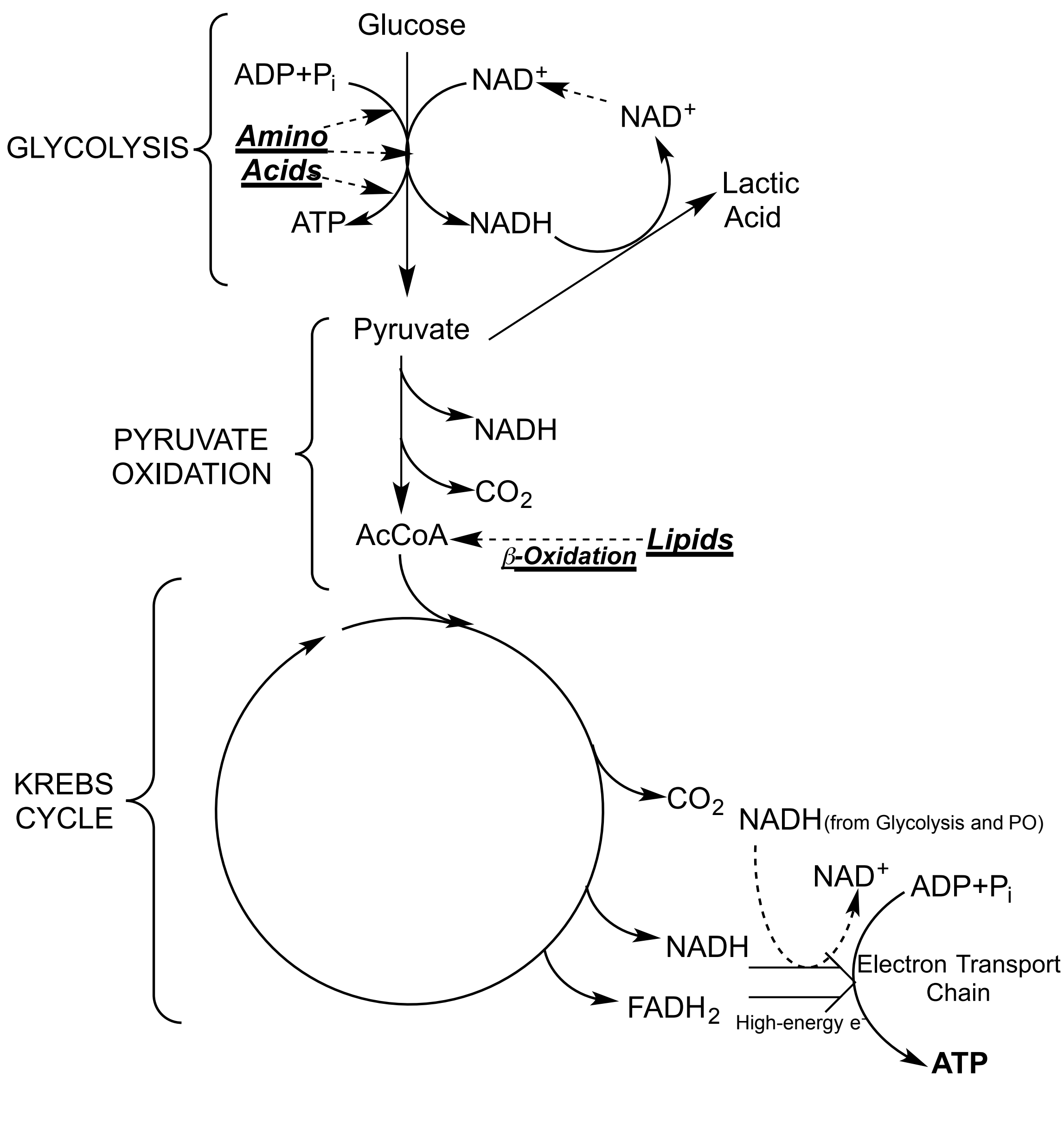
□ Or, amino acids can be modified into glycolytic intermediates (or pyruvate) and fed into glycolysis.

● Lipids→**β-oxidation**. Lipids (fats) are essentially very long hydrocarbon chains. ($CH_3CH_2CH_2CH_2CH_2$…)

□ In the mitochondria, fats' hydrocarbon chains can be chewed up by a series of reactions called **β-oxidation.**

□ β-oxidation yields a series of AcCoA units, which can be fed into the Krebs Cycle to make ATP.

EXAMPLE: Summary schematic of catabolism, including the places of β-oxidation and amino acid catabolism.



PRACTICE 1: Lonidamine is an inhibitor of the enzyme hexokinase, which catalyzes *the first reaction in glycolysis.* Which of the following is *true* regarding cells treated with lonidamine*?*

a) Cells treated with lonidamine will be able to use *fats* as a fuel source.
b) Cells treated with lonidamine will *not* be able to use *fats* as a fuel source.

PRACTICE 2: Lonidamine is an inhibitor of the enzyme hexokinase, which catalyzes *the first reaction in glycolysis.* Which of the following is *true* regarding cells treated with lonidamine*?*

a) Cells treated with lonidamine will be able to use *proteins* as a fuel source.
b) Cells treated with lonidamine will *not* be able to use *proteins* as a fuel source.

CONCEPT: METABOLISM V: ANABOLISM

● The major *anabolic* processes used by the body (mostly the liver) are the synthesis of glycogen and adipose tissue.

● **Glycogen** is a ________ polymer used by the body—primarily skeletal muscle and liver cells—as a way to store glucose.

□ **Glycogenesis**-In well-fed state, liver cells take up glucose from the blood and polymerize it into glycogen.

□ **Glycogenolysis**-In the fasting state, the liver breaks down glycogen and sends the glucose to the body.

● Fats are synthesized in the liver and stored in **adipose tissue** (fat cells).

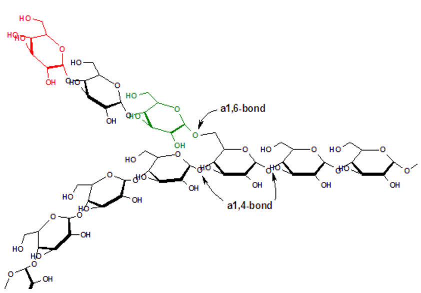
□ **Lipogenesis**- In the well-fed state, synthesis of fats.

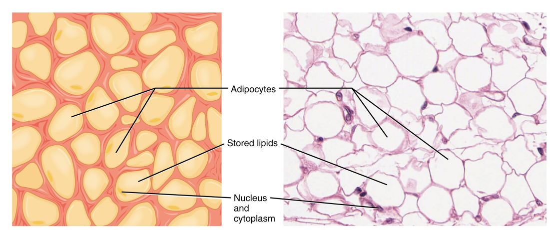
□ **Lipolysis**- In the fasting state, adipose cells break down fats and release **triacylglycerides** (TAGs), which are taken up by cells and undergo β-oxidation in the mitochondria.

● **Gluconeogenesis** is an anabolic process used to make extra _______ from spare parts (basically glycolysis backwards).

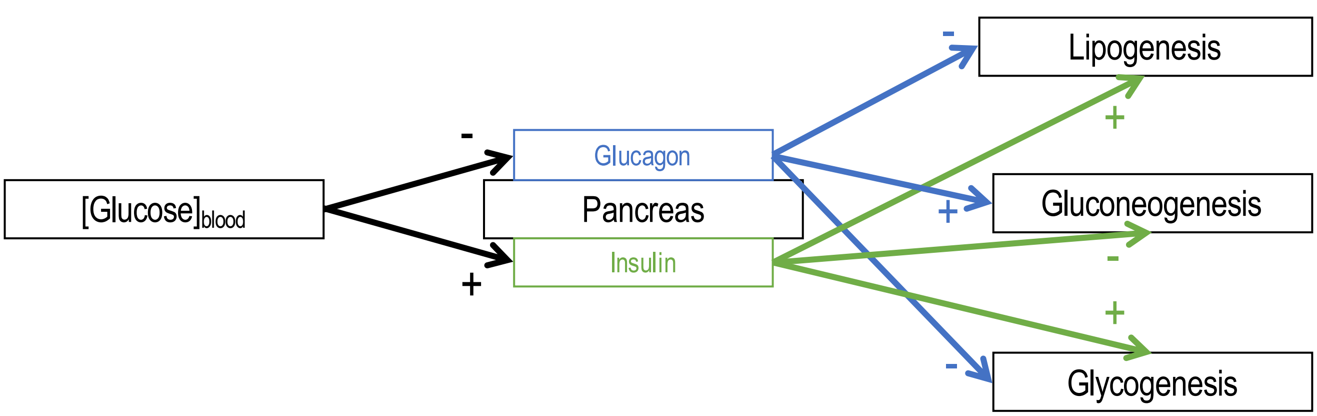
□ Done by the liver during times of low blood glucose.

EXAMPLE: A polymer of glycogen and adipose tissue storing lipids.





EXAMPLE: Insulin (↑insulin when ↑[glucose]) and glucagon (↑glucagon when ↓[glucose]) are involved in regulation of lipogenesis, gluconeogenesis, and glycogenesis.



PRACTICE 1: The livers of patients with Type II Diabetes maintain abnormally high rates of gluconeogenesis and glycogenolysis. Which of the following is the expected effect of elevated gluconeogenesis and glycogenolysis on the blood glucose levels of a diabetic patient?

a) It will cause their blood glucose levels to *increase* (i.e. more glucose in their blood).
b) It will cause their blood glucose levels to *decrease* (i.e. less glucose in their blood).