Cell Metabolism

Chapter Outline

I. Metabolism

- Metabolism is the sum of all chemical reactions occurring in a cell
- Energy metabolism is the set of reactions that invlove energy exchange.

Types of Metabolic Reactions

- Anabolism
  - Small molecules are used to make large ones for example the use amino acids to synthesize protein
  - Energy consuming
- Catabolism is the opposite of anabolism

Chemical Reactions

- Reactants (or substrates) → Products
  A + B → C + D
- Direction of reaction
  - Forward →
  - Reverse ←

Hydrolysis and Condensation

- **Hydrolysis** (Hydro= water; lysis=splitting) breaks a larger molecule to smaller ones.
  - A-B + H_2O → A-OH + H-B
- **Condensation (synthesis)** is the reverse of hydrolysis.

Phosphorylation and Dephosphorylation

- **Phosphorylation** - the addition of a phosphate group

  $A + P_i \rightarrow A\text{-}P$

- **Dephosphorylation** - the removal of a phosphate group

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Oxidation-Reduction Reactions

- **Oxidation**—removal of electrons (or H)

  $C_6H_{12}O_6 + 6\ O_2 \rightarrow 6\ CO_2 + 6\ H_2O$

  $HA\text{-}BH \rightarrow A{=}B + 2\ H$

  $H_2 \rightarrow 2\ H^+ + 2\ e^-$

- **Reduction**—addition of electrons (or H)

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II. Metabolic Reactions and Energy

- **Energy** is the ability to do work
- **Potential energy** is stored energy.
- **Kinetic energy** is the energy of movement

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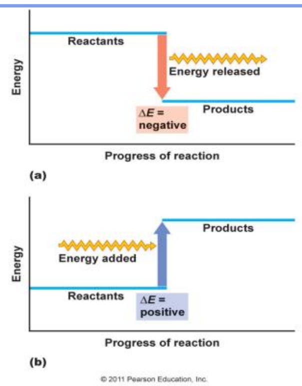
Energy Changes in Reactions

Figure 3.1

- Exergonic reaction (a) is the reaction that goes forward spontaneously
- Endergonic reaction (b): does NOT go forward spontaneously



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The Law of Mass Action

- An increase in the concentration of reactions relative to products tends to push a reaction forward.

  $A + B \rightarrow C + D$

- An increase in the concentration of products relative to the reactants tends to push a reaction in reverse.

  $A + B \leftarrow C + D$

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Activation Energy

- The activation energy is required to overcome the initial burden of a reaction.

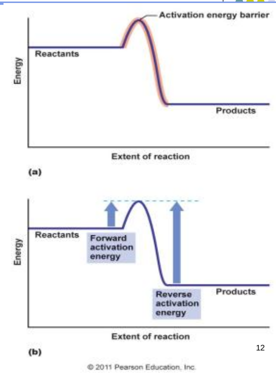

Figure 3.3

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III Reaction Rates

- The reaction rate is a measure of how fast products are made per unit time.

Factors Affecting Reaction Rates

- Reactant and product concentration
  - ↑ reactant concentration → faster forward reaction rate
  - ↑ product concentration → slower forward reaction rate
- Environmental
  - Temperature
    - ↑ temperature → faster reaction rate
  - pH: optimal
- Enzyme and Activation energy barrier
  - ↓ activation energy barrier → faster reaction rate

The Role of Enzymes in Chemical Reactions

- Are proteins that function as catalysts for reactions in biological systems. They speed up reaction.
- Are identified by the suffix *–ase.*
- Are not changed nor consumed in the reaction.
- Can be denatured by extreme temperature or pH.

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The Mechanism of Enzyme Action: Lock and Key Model

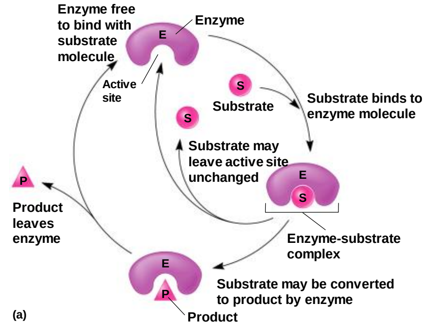

Figure 3.6

The Mechanism of Enzyme Action: Induced-fit Model

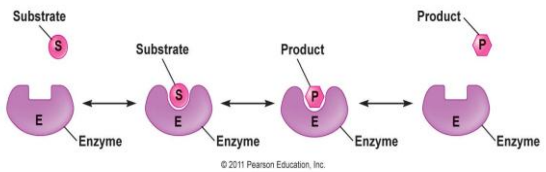

Figure 3.7

Both substrate and product can bind at the active site to allow reverse reaction oocur

How Do Enzymes Speed up Chemical Reactions

- By decreasing activation energy for a specific chemical reaction

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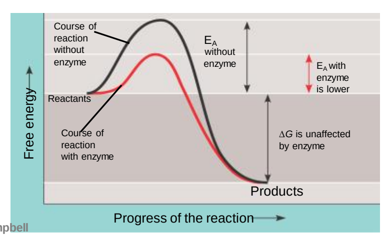


Figure 8.15 Campbell

Enzyme Properties

- **Substrate specificity** : For one set of substrates or a group of similar substrates

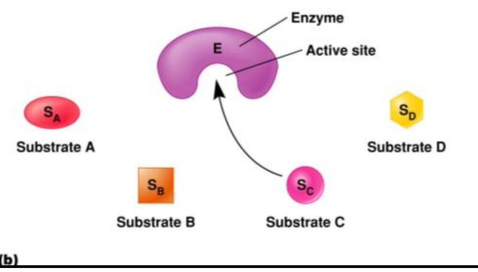
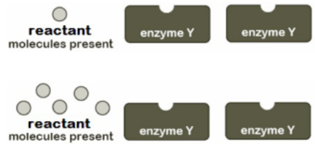


Figure 3.6

Enzyme Properties

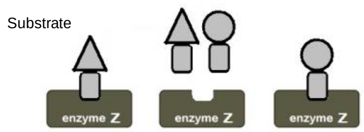
- Saturation: With the increase of substrate concentration, the enzymes reach maximum velocity (Vmax)



Enzyme Properties

- Competition

  Similar shape substrates compete for the same active sites



Cofactors

- Ions or non protein molecules required by an enzyme for the enzyme to be active
  - Organic molecules: Vitamins
  - Trace metals—Mg, Ca, Zn, Fe
    - Allow substrate to bind to active site

Coenzymes

- Organic molecules derived from vitamins that transfer chemical groups during chemical reactions

Coenzyme	Vitamin	Chemical Transferred
NADH	niacin (B_3)	H^+
FAD	riboflavin (B_{12})	H^+
coenzyme A	pantothenic (B_5)	acid acetyl

Factors Affecting Rates of Enzyme-catalyzed Reactions

- Enzyme's catalytic rate
- Concentrations of enzyme and substrate
- Affinity of enzyme for substrate
- Temperature and pH

Enxzyme's Catalytic Rate

- Amount of product produced per unit time
- Assumption: enzyme active site always occupied by substrate
- Some enzymes are inherently faster than others

Concentration of Enzyme and Substrate

Greater enzyme and substrate concentration corresponds to greater reaction rate based on law of mass action

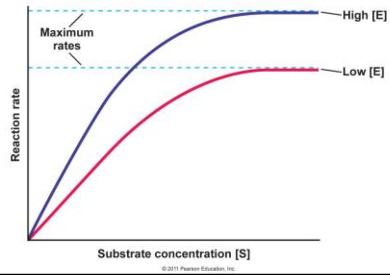


Figure 3.8

Affinity

Measure of strength of binding between substrate and enzyme

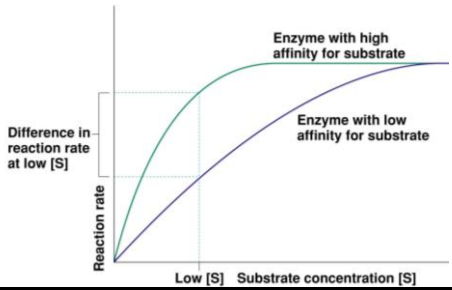
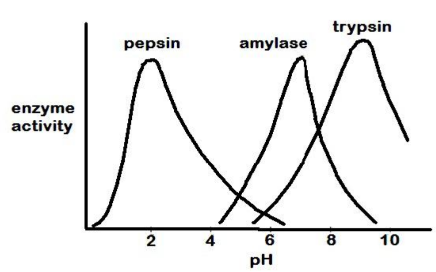


Figure 3.9

Optimal pH

Each enzyme has an optimal pH in which it can function at its maximum rate



Optimal Temperature

Each enzyme has an optimal temperature in which it can function at its maximum rate

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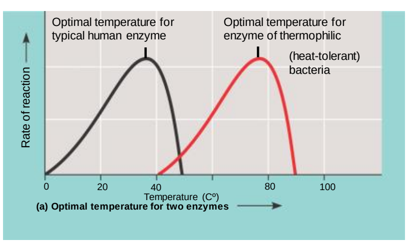


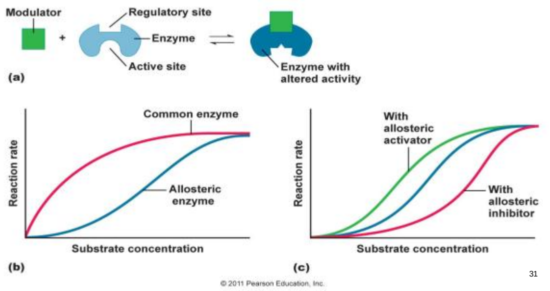
Figure 8.18

Regulation of Enzyme Activity

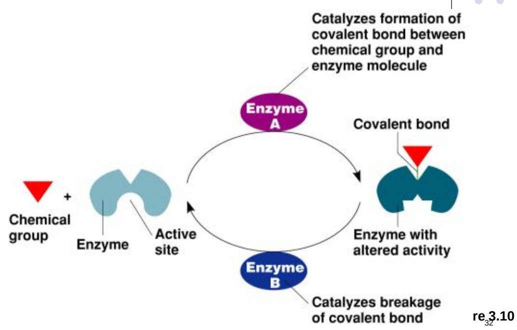
- Allosteric regulation
- Covalent regulation
- Feedback inhibition
- Feedforward activation

Allosteric Regulation

A modulator binds reversibly to the regulatory site on an enzyme to change its conformation and activity (Figure 3.10)



Covalent Regulation



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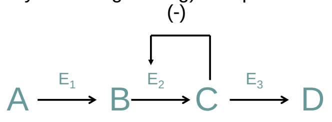
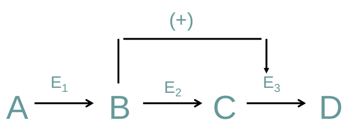
Feedback Inhibition

An intermediate product inhibits the enzyme (frequently the rating-limiting) of a previous step



Feedforward Activation

An intermediate product activates the enzyme of a previous step



Vegetables and Gas

- Humans do not possess the α-GAL enzyme to break raffinose family oligosaccharides (RFOs) in vegetables such as beans.
- RFOs are fermented by bacteria which do possess the α-GAL enzyme and make gases such as CO_2, CH_4 and or H_2

IV. Glucose Oxidation: The Central Reaction of Energy Metabolism

Glucose catabolism = The central reaction of energy metabolism

$C_6H_{12}O_6 + 6\ O_2 + 38\ ADP + 38\ Pi \rightarrow 6\ CO_2 + 6\ H_2O + \text{energy (38 ATP)}$

$\Delta E = -686$ kcal/mole

Complete glucose oxidation = aerobic respiration = cell respiration

ATP: The Medium of Energy Exchange

- ATP hydrolysis
  - ATP + H_2O → ADP + Pi + energy
- ATP synthesis
  - ADP + Pi + energy → ATP + H_2O

Universal Energy Molecule ATP

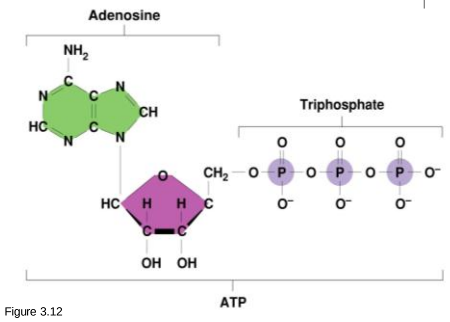


Figure 3.12

ATP in Coupled Reactions

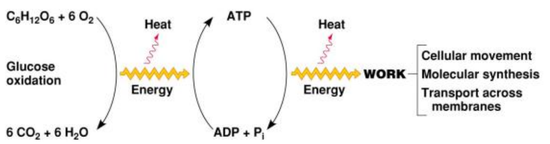
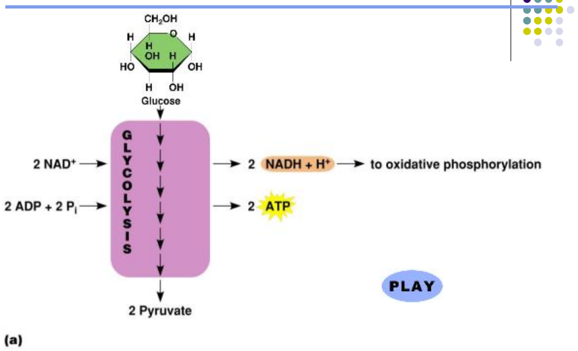


Figure 3.13

V. Stages and Locations of Complete Glucose Oxidation

- Cytosol
  - Glycolysis
- Mitochondria
  - Mitochondrial matrix
    - Acetyl CoA formation
    - Krebs cycle
  - Inner mitochondrial membrane (Cristae)
    - Oxidative phosphorylation

Glycolysis Summary



(b) Overall reaction: Glucose + 2 NAD^+ + 2 ADP + 2 P_i ⟶ 2 Pyruvate + 2 NADH + 2 H^+ + 2 ATP

Step Linking Glycolysis to Krebs Cycle: Acetyl CoA Formation

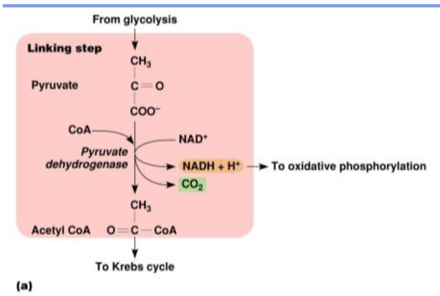
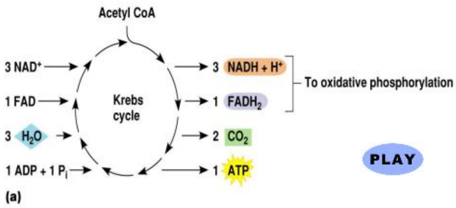


Figure 3.16

(b) Overall reaction: Pyruvate + CoA + NAD^+ ⟶ Acetyl CoA + CO_2 + NADH + H^+

Summary of the Krebs Cycle



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(b) Overall reaction: Acetyl CoA + 3 NAD^+ + FAD + ADP + P_i + 3 H_2O → 2 CO_2 + 3 NADH + 3 H^+ + $FADH_2$ + ATP

Figure 3.18

The Electron Transport Chain: Oxidative Phosphorylation

- Use of movement of electrons down the electron transport chain (ETC) to synthesize ATP requires oxygen
- Oxygen is the final electron acceptor
- Produce most ATPs

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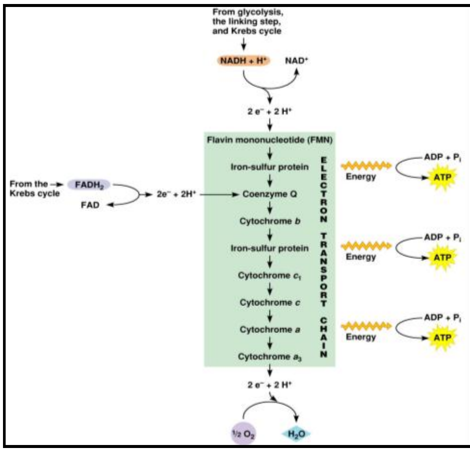


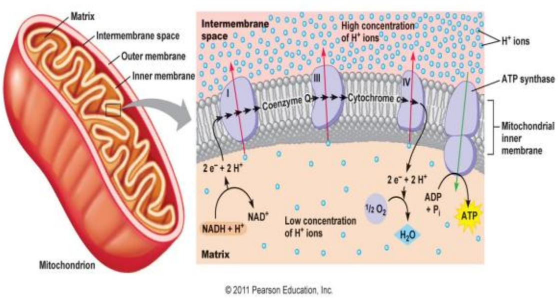
Electron Transport Chain

Figure 3.19

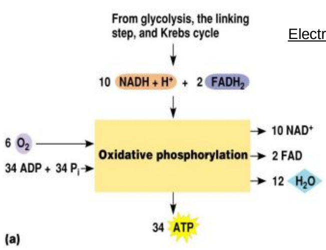
Mechanisms of ATP Synthesis

- Substrate-level phosphorylation
  - X-P + ADP → X + ATP
  - Glycolysis
  - Krebs cycle
- Oxidative phosphorylation
  - Transport H atoms or electrons along the electron transport chain and to capture energy by chemiosmotic coupling
  - ADP + P_i → ATP

Chemiosmotic Coupling



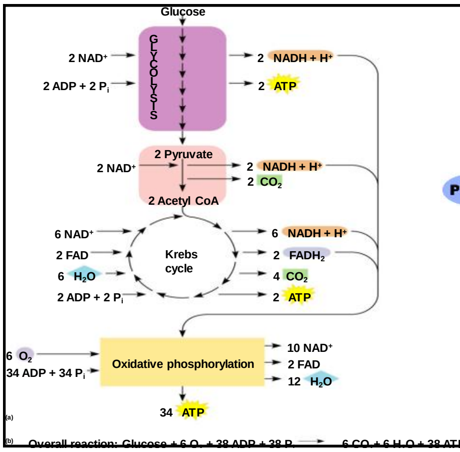
Summary of Oxidative Phosphorylation



Electron Donor	# of ATP per ½ O2
NADH	2.5-3
FADH2	1.5-2

(b) Overall reaction: 10 NADH + 10 H^+ + 2 $FADH_2$ + 34 ADP + 34 P_i + 6 O_2 → 10 NAD^+ + 2 FAD + 12 H_2O + 34 ATP

Figure 3.21



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Summary of Glucose Catabolism

Figure 3.22

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Incomplete Glucose Oxidation

- Anaerobic respiration or fermentation
- Red blood cells do not have mitochondria
- Low oxygen availability in other cells
  - Electron transport in chain backs up
  - Krebs cycle stops
- Glycolysis can continue only if NADH is oxidized to form NAD^+

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Conversion of Pyruvate to Lactate

- Conversion of pyruvate to lactate when oxygen supply is low
- Function: Regenerate NAD^+

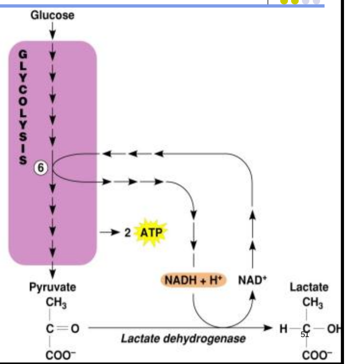

Figure 3.22

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Summary of Glucose Catabolism for Energy

- Aerobic conditions
  - Glucose + $6O_2$ + 38ADP + $38P_i$ → $6CO_2$ + $6H_2O$ + 38ATP
- Anaerobic conditions
  - Glucose + 2ADP + $2P_i$ → 2 Lactic Acid + 2ATP

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IV. Energy Storage and Use: Metabolism of Carbohydrates, Fats and Proteins

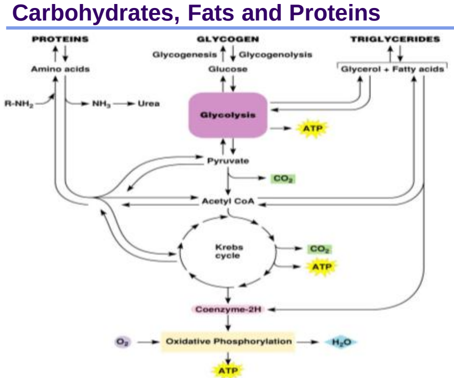

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Figure 3.24

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Table 5.1 Common Terms for Some Metabolic Processes in the Body

Term	Process
Glycolysis	Conversion of glucose into two molecules of pyruvic acid
Glycogenesis	The production of glycogen, mostly in skeletal muscles and the liver
Glycogenolysis	Hydrolysis (breakdown) of glycogen; yields glucose-6-phosphate for glycolysis, or (in the liver only) free glucose that can be secreted into the blood
Gluconeogenesis	The production of glucose from noncarbohydrate molecules, including lactic acid and amino acids, primarily in the liver
Lipogenesis	The formation of triglycerides (fat), primarily in adipose tissue
Lipolysis	Hydrolysis (breakdown) of triglycerides, primarily in adipose tissue
Ketogenesis	The formation of ketone bodies, which are four-carbon-long organic acids, from fatty acids; occurs in the liver

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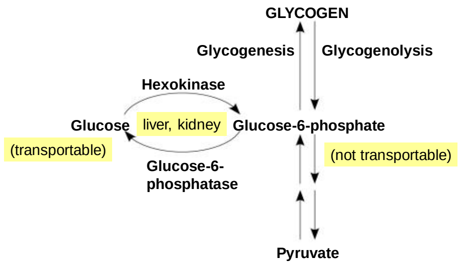
Glycogen Metabolism



Liver (and kidney) glycogen stores provide glucose for other cells (via blood). Other tissue cannot.

Figure 3.25

Gluconeogenesis

Synthesis of new glucose

- Substrates
  - Glycerol
  - Lactate
  - Amino acids
- Occurs in liver, small extent in kidneys

Fat Metabolism

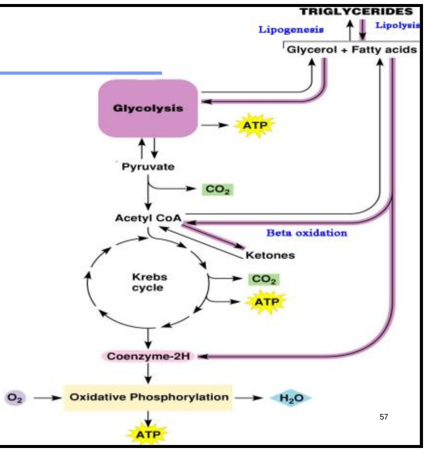


Figure 3.27

Protein Metabolism

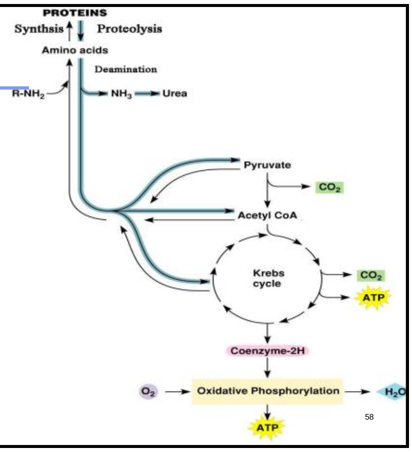


Figure 3.28

Hereditary Metabolic Disorder

http://www.merckmanuals.com/home/sec23/ch282/ch282a.html