

Metabolism

- Today in class we will discuss:
 - The definitions of *metabolism*, *catabolism*, *anabolism* and *nutrient pool*
 - Their relationship
 - Carbohydrate metabolism
 - Glycolysis
 - Citric acid/tricarboxylic (TCA) cycle
 - Electron transport system (ETS)
 - Oxidative phosphorylation
 - Sources for glucose
 - Glycogenesis
 - Glycogenolysis
 - Gluconeogenesis

Energy

- Cells break down organic molecules to obtain energy
 - Used to generate ATP
- Most energy production takes place in mitochondria

Essential Materials

- Oxygen
- Water
- Nutrients
 - Organic substrates
 - Mineral ions
 - Vitamins

Sources of Essential Materials

- Oxygen
 - Absorbed at lungs
- Other substances
 - Absorbed at digestive tract

Materials Transport

- Cardiovascular system
 - Carries materials through body
- Materials diffuse
 - From bloodstream into cells

Metabolism

- Refers to all chemical reactions in an organism

Cellular Metabolism

- Includes all chemical reactions within cells
- Provides energy to:
 - Maintain homeostasis
 - Perform essential functions

Metabolic Turnover

- Cell recycling
- Periodic replacement of cell's organic components
- Involves:
 - Catabolism = breakdown of organic substrates
 - Releases energy used to form high-energy compounds (e.g., ATP)
 - Anabolism = synthesis of new organic molecules

Functions of Organic Compounds

- Perform structural maintenance and repairs
- Support growth
- Produce secretions
- Store nutrient reserves
 - Lipids in adipose tissue, bone marrow, liver
 - Glycogen in muscle and liver

Nutrient Pool

- Contains all organic building blocks cell needs to:
 - Provide energy
 - Create new cellular components
- Source of substrates (nutrients) for catabolism and anabolism, e.g.,
 - Glucose, fatty acids, amino acids

An Introduction to Cellular Metabolism

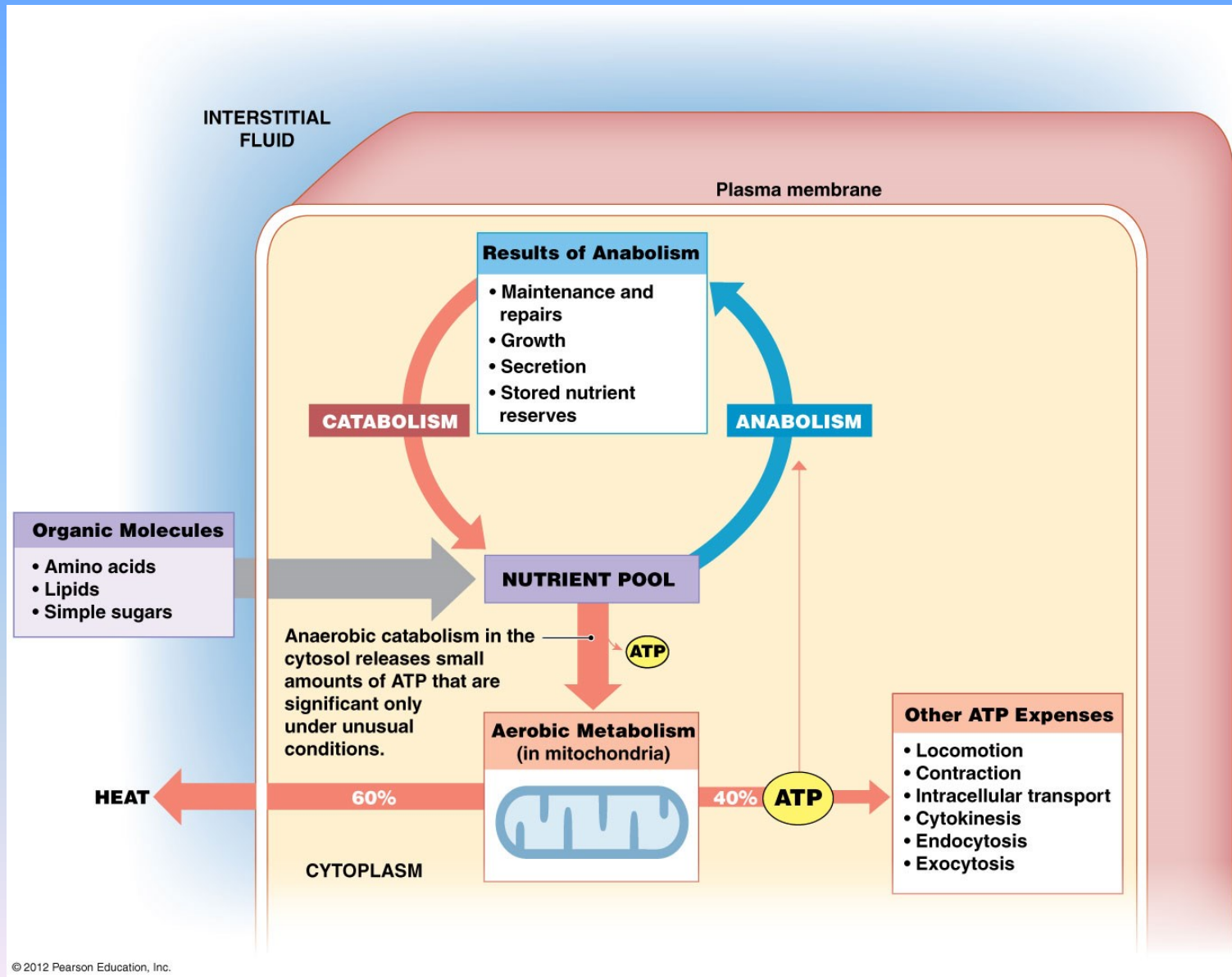
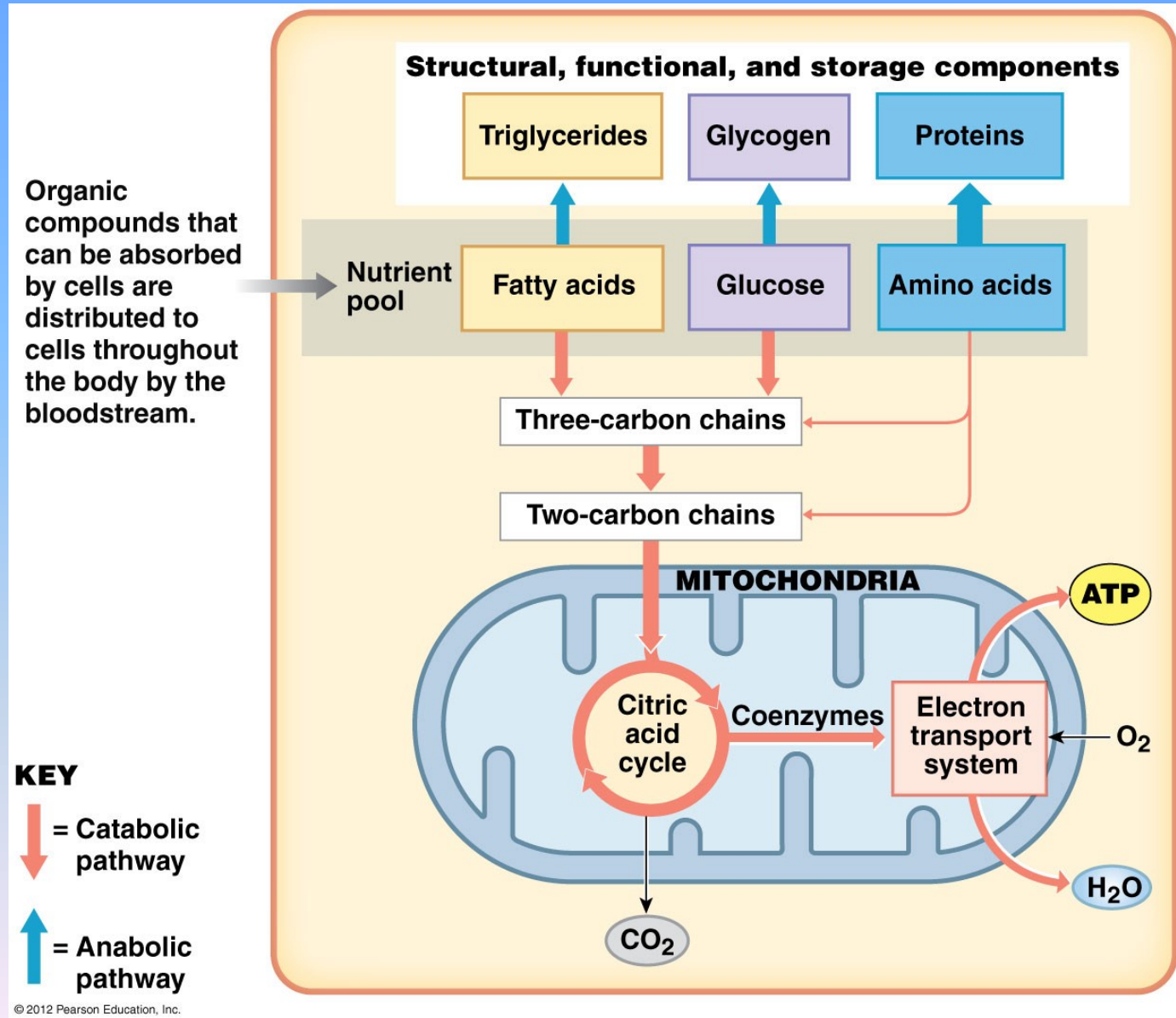


Figure 25-1

Nutrient Use in Cellular Metabolism



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Figure 25-2

Key Organic Compounds

- Glycogen
 - Most abundant storage carbohydrate
 - Branched chain of glucose molecules
- Triglycerides
 - Most abundant storage lipids
 - Primarily of fatty acids
- Proteins
 - Most abundant organic components in body
 - Perform many vital cellular functions

Preference for Energy Sources

- Carbohydrates (glycogen)
 - → short carbon chains, e.g., glucose
- Lipids (triglycerides)
 - → FAs + glycerol
- Proteins
 - → amino acids
 - Only used if other sources not available, e.g., in starvation

Summary of Digestion

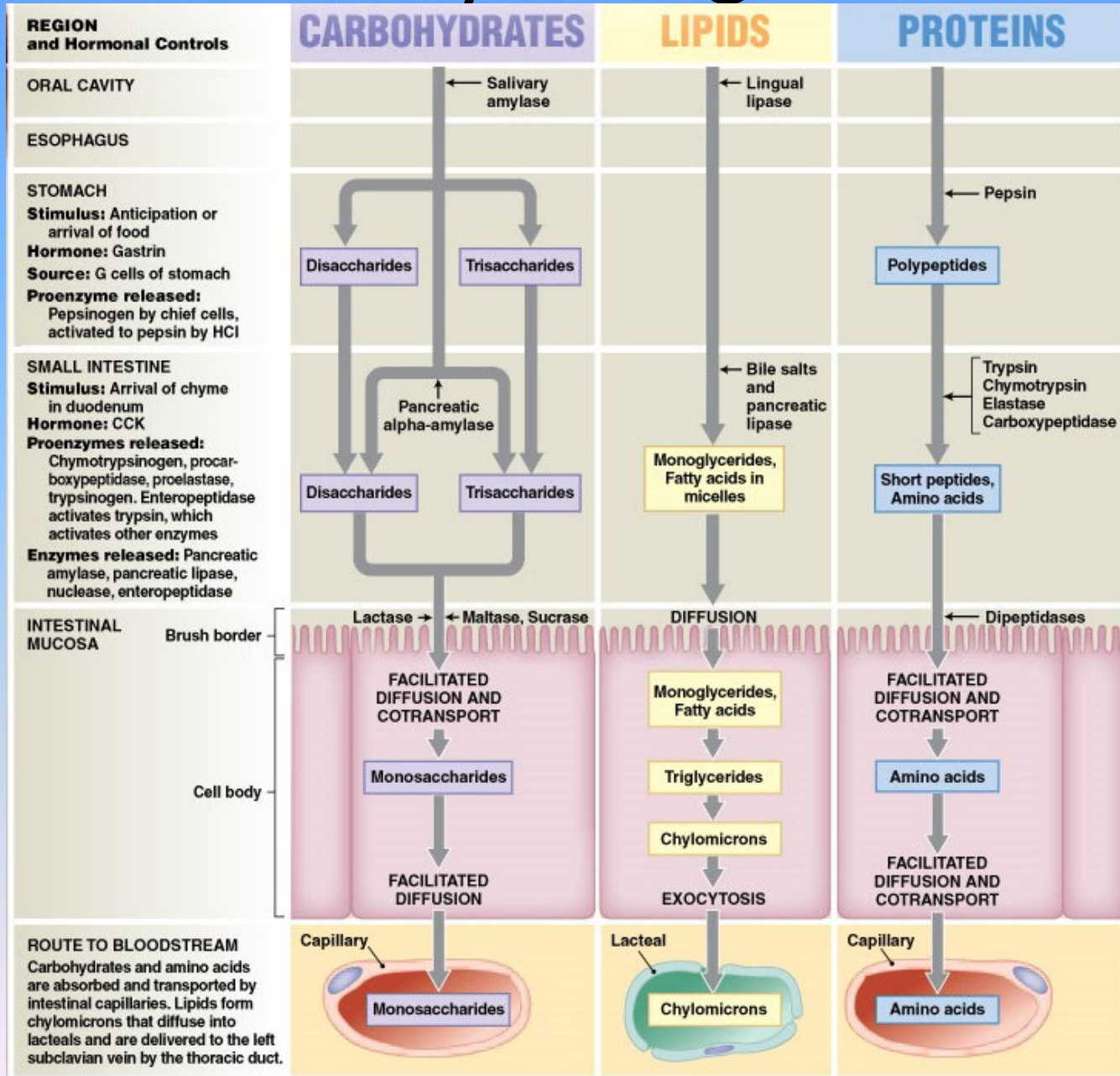


Figure 24-27

Carbohydrate Metabolism

- Generates ATP and other high-energy compounds by breaking down carbohydrates
→ glucose
 - glucose + oxygen → carbon dioxide + water

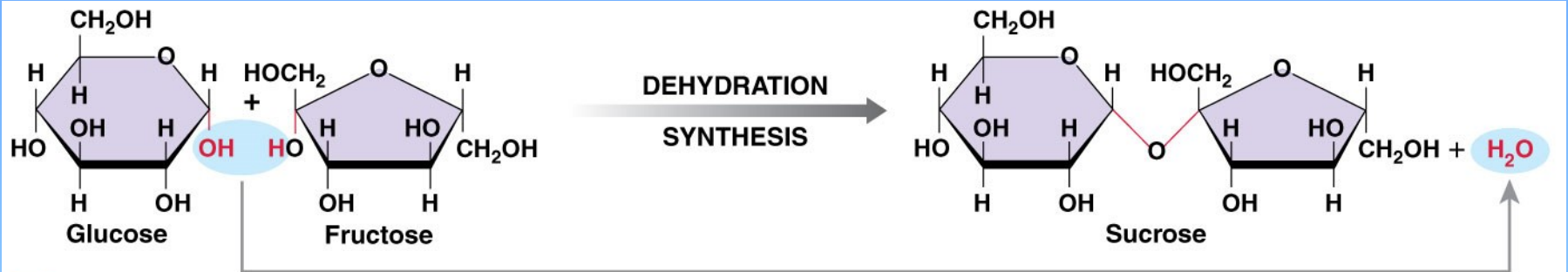
Step 1: Obtain Glucose

- From carbohydrate digestion
 - Polysaccharides (glycogen, starch)
 - Salivary and pancreatic amylases → glucose
 - Disaccharides, e.g., sucrose, maltose, lactose
 - Brush border enzymes
 - e.g., sucrase, maltase, lactase → glucose (from disaccharides)
 - Monosaccharides
 - Glucose
 - Fructose, galactose → glucose (in liver)

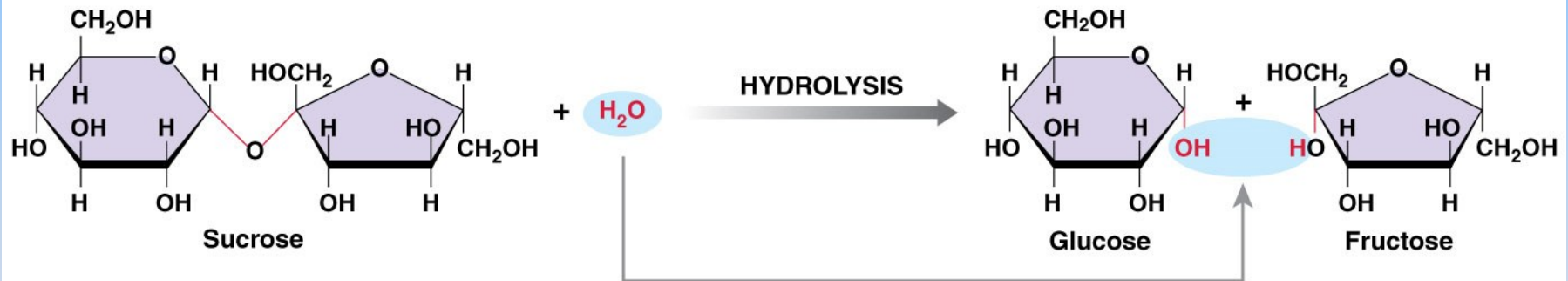
Disaccharide Digestion

Disaccharide ($C_{12}H_{22}O_{11}$)	Enzyme (Brush Border)	Monosaccharide ($C_6H_{12}O_6$)
Sucrose	Sucrase	Glucose + Fructose
Lactose	Lactase	Glucose + Galactose
Maltose	Maltase	2 molecules of Glucose

Formation and Breakdown of Complex Sugars



a Formation of the disaccharide sucrose through dehydration synthesis. During dehydration synthesis, two molecules are joined by the removal of a water molecule.



b Breakdown of sucrose into simple sugars by hydrolysis. Hydrolysis reverses the steps of dehydration synthesis; a complex molecule is broken down by the addition of a water molecule.

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Step 1: Obtain Glucose

- From glycogenolysis
 - Catabolic conversion of glycogen into glucose
- From gluconeogenesis
 - Synthesis of glucose from lipid or protein

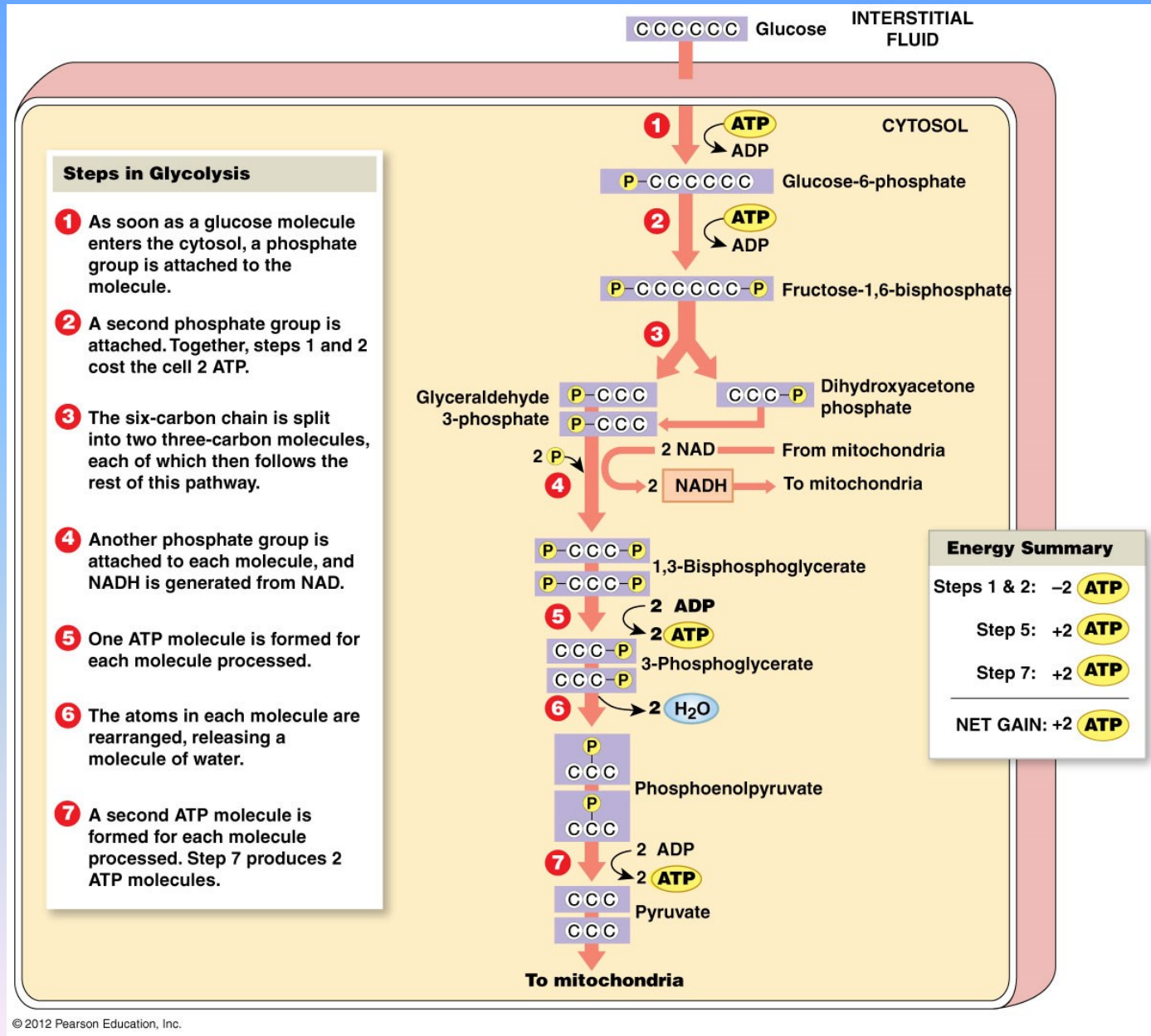
Step 2: Use Glucose to Generate ATP

- Involves 2 pathways
 - Glycolysis
 - Anaerobic catabolism of glucose (C6) to pyruvic acid (C3)
 - Cellular respiration
 - Aerobic catabolism of pyruvic acid

Glycolysis

- Anaerobic metabolism
 - Does not require O₂
- Breaks down glucose (6C) in cytosol
 - Into 2 pyruvic acid (3C) molecules used by the mitochondria
- Energy yield
 - Net gain = 2 ATP/1 glucose molecule
- Only source of ATP for energy for RBCs (lack mitochondria)
- Used by muscle fibers during periods of active contraction (when O₂ used up)

Glycolysis



Cellular Respiration

- Aerobic metabolism
 - Requires O₂
- Occurs in mitochondria
 - Consumes O₂
 - Produces ATP
- Involves:
 - Tricarboxylic acid (TCA) cycle
 - aka citric acid cycle, Krebs's cycle
 - Oxidative phosphorylation
 - Electron transport system (ETS)
 - aka respiratory chain

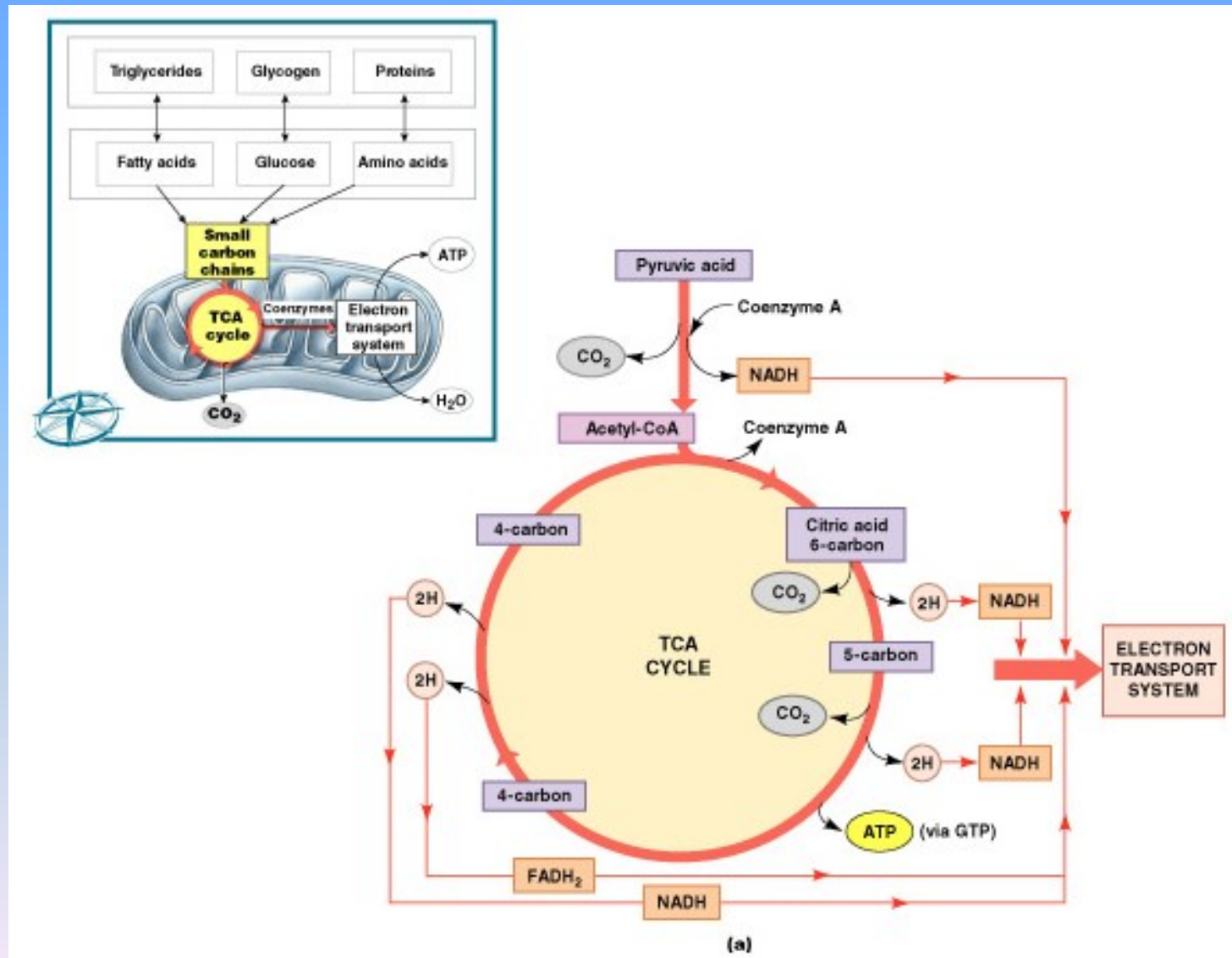
Catabolism of Pyruvic Acid

- If O₂ supplies adequate mitochondria absorb pyruvic acid molecules
- (In glycolysis, 1 glucose molecule) → 2 Pyruvic acids (3C) →
 - 2 Acetyl-CoAs (2C) + 2 CO₂

TCA Cycle

- Occurs in mitochondrial matrix
- Acetyl-CoA (2C) + 4C \rightarrow 6C \rightarrow 5C \rightarrow 4C
- C atoms removed and combined with O₂ \rightarrow CO₂
- H atoms removed by coenzymes (FAD, NAD)

TCA Cycle



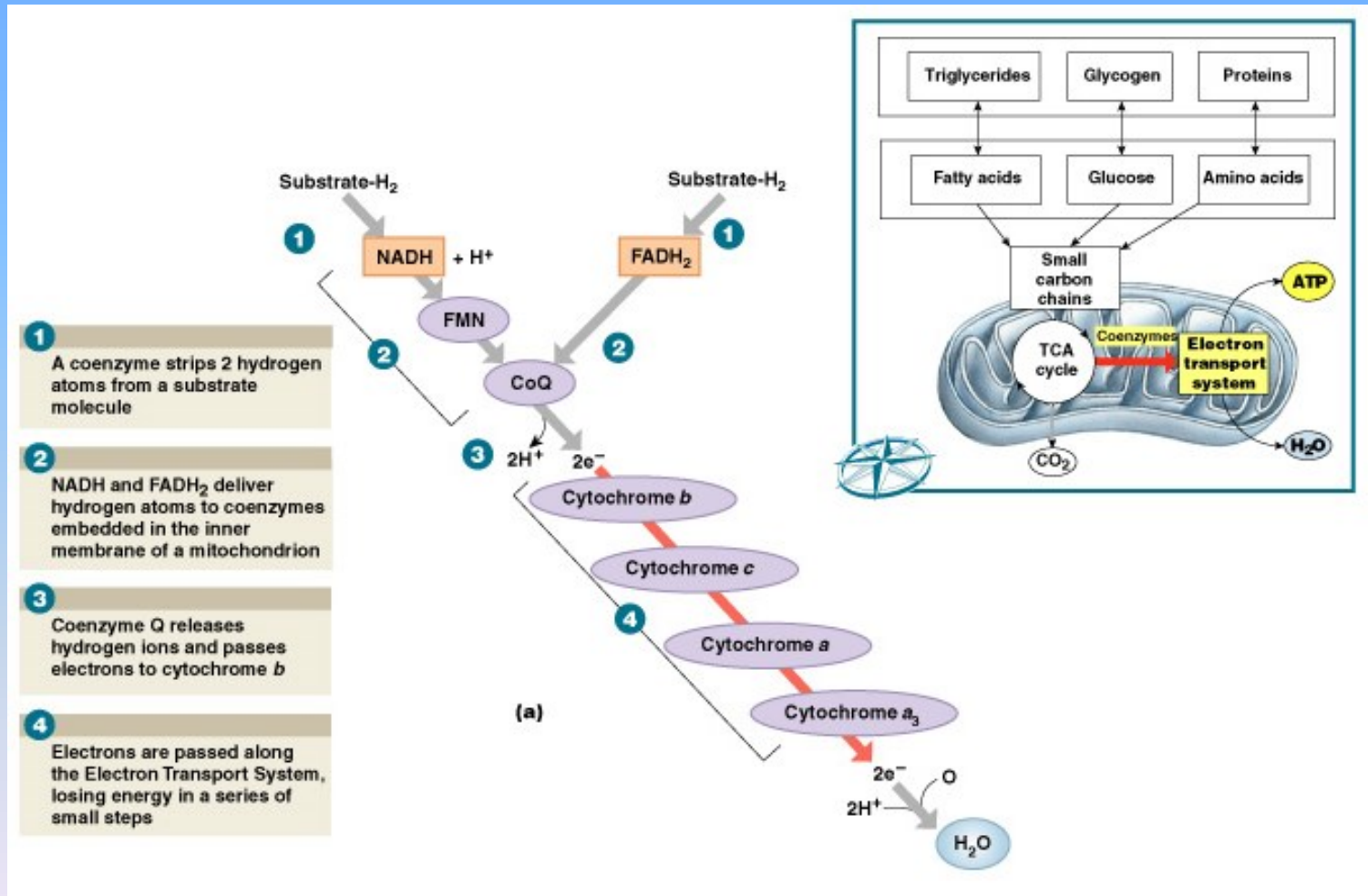
Oxidative Phosphorylation

- Most important mechanism for generating ATP (90% used by body)
- Occurs in mitochondria
- Requires:
 - O₂
 - Coenzymes (FAD, NAD)
 - Electrons (from H atom)
- Results in:
 - $2 \text{ H}_2 + \text{ O}_2 \rightarrow 2 \text{ H}_2\text{O}$

Electron Transport System (ETS)

- Key series of reactions in oxidative phosphorylation
- Involves sequence of cytochromes (protein + pigment) in inner mitochondrial membrane
- Coenzymes (NAD, FAD) deliver H atoms to inner mitochondrial membrane
- H atom \rightarrow H⁺ + e⁻ (electron)
- Electrons
 - Enter ETS and pass along cytochromes

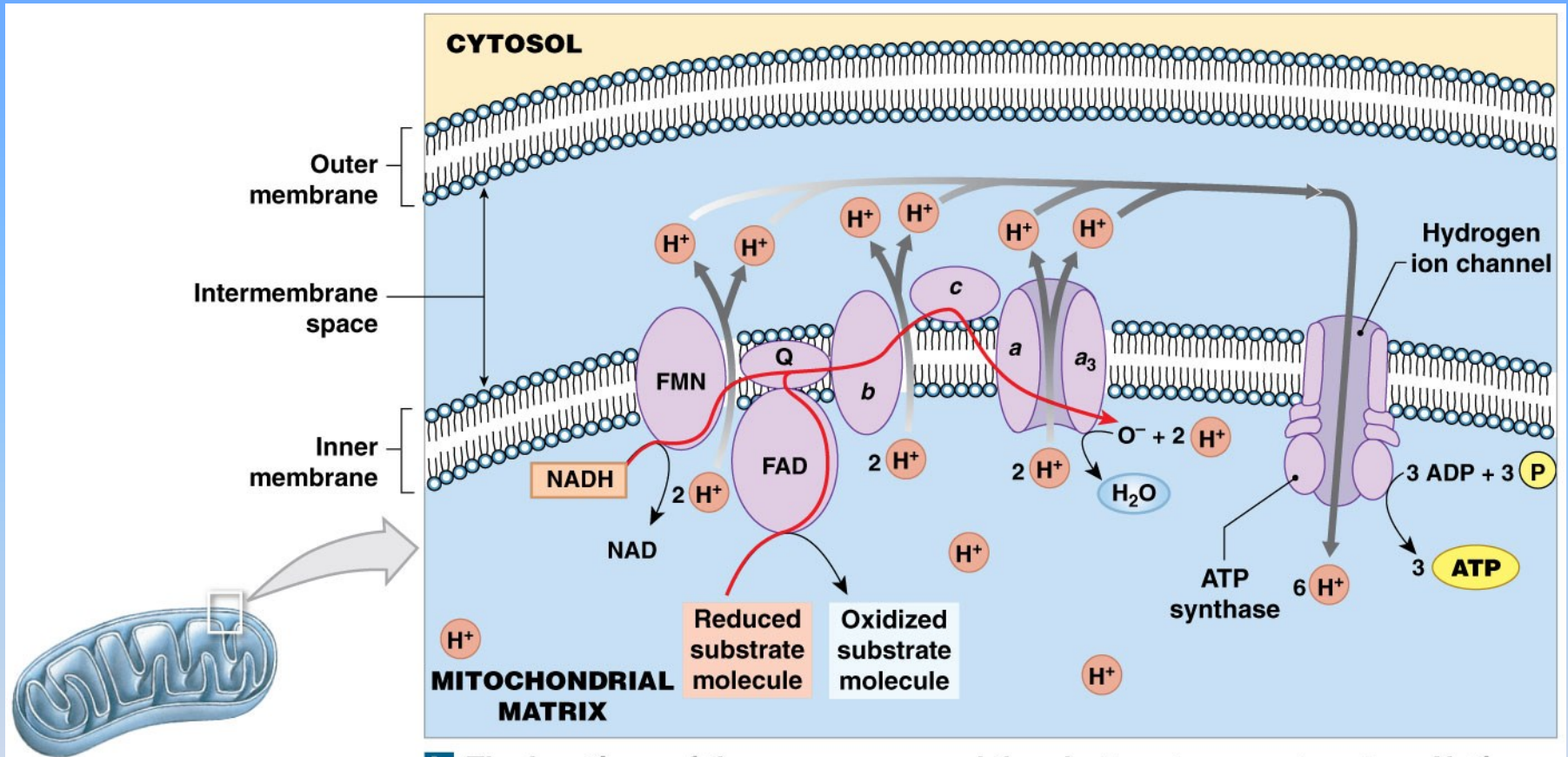
Oxidative Phosphorylation



Oxidative Phosphorylation

- Electrons
 - Transfer energy
- H⁺
 - Pumped into intermembrane space
 - Re-enters matrix → energy to generate ATP
- At end of ETS, $e^- + O^- + H^+ \rightarrow H_2O$
- Energy yield = 36 ATP/glucose
 - 2 from glycolysis
 - 34 from oxidative phosphorylation

Oxidative Phosphorylation



b The locations of the coenzymes and the electron transport system. Notice the sites where hydrogen ions are pumped into the intermembrane space, providing the concentration gradient essential to the generation of ATP. The red line indicates the path taken by the electrons.

Summary: Energy Yield of Aerobic Metabolism = 36 ATP

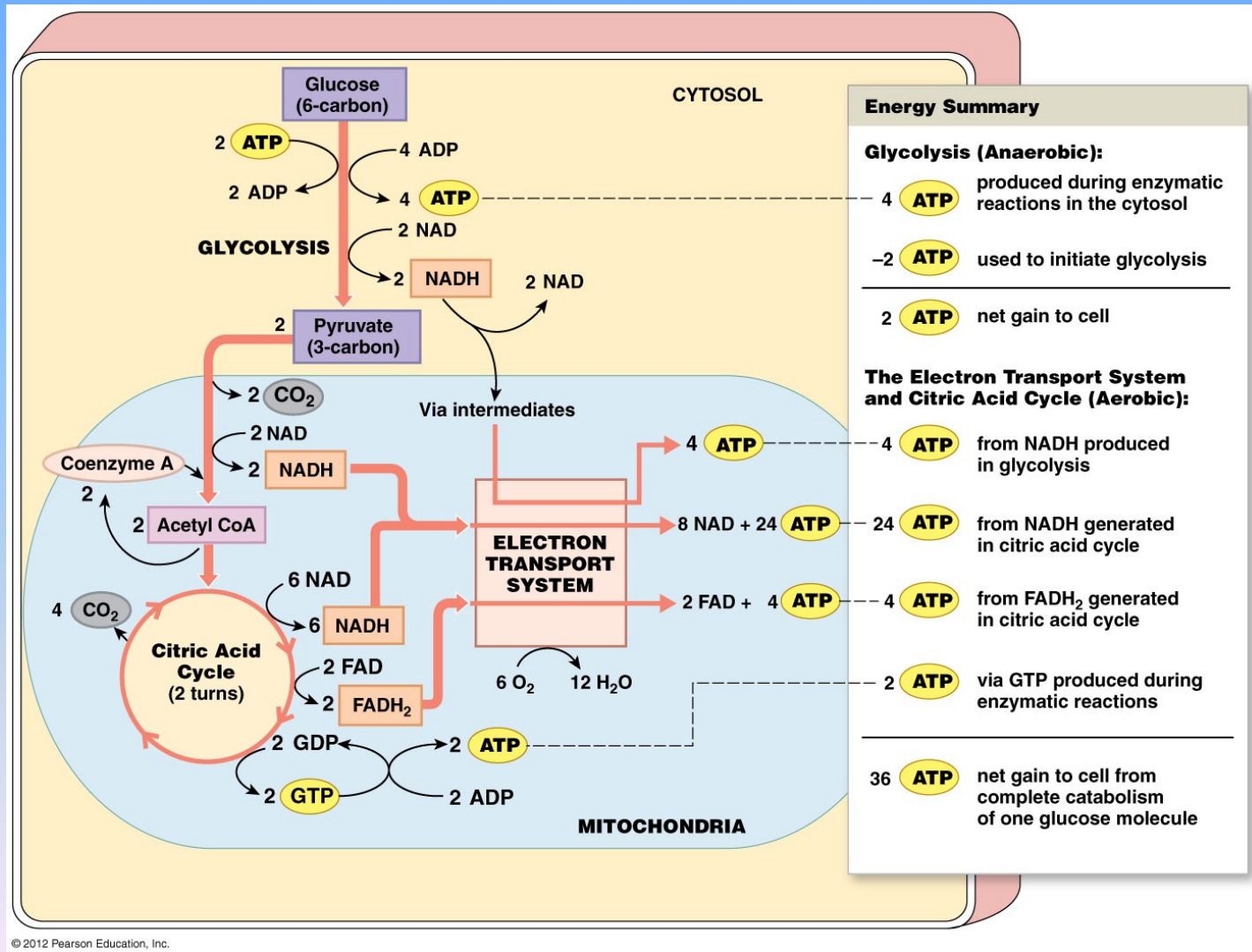


Figure 25-6

Summary: Cellular Respiration

- Begins with glucose
- TCA \rightarrow CO₂ of respiration
- Oxidative phosphorylation
 - Uses O₂ of respiration
 - Combines H + O \rightarrow H₂O

Summary: Carbohydrate Metabolism

- Involves:
 - Catabolism
 - Anabolism
- Independently regulated
- Requires different sets of enzymes

Glycogen Metabolism

- Anabolism = glycogenesis
 - = Formation of glycogen from glucose
 - Occurs slowly
 - Glycogen stored in cytoplasmic granules
- Catabolism = glycogenolysis
 - = Breakdown of glycogen to form glucose
 - Occurs very quickly

Carbohydrate Catabolism and Anabolism

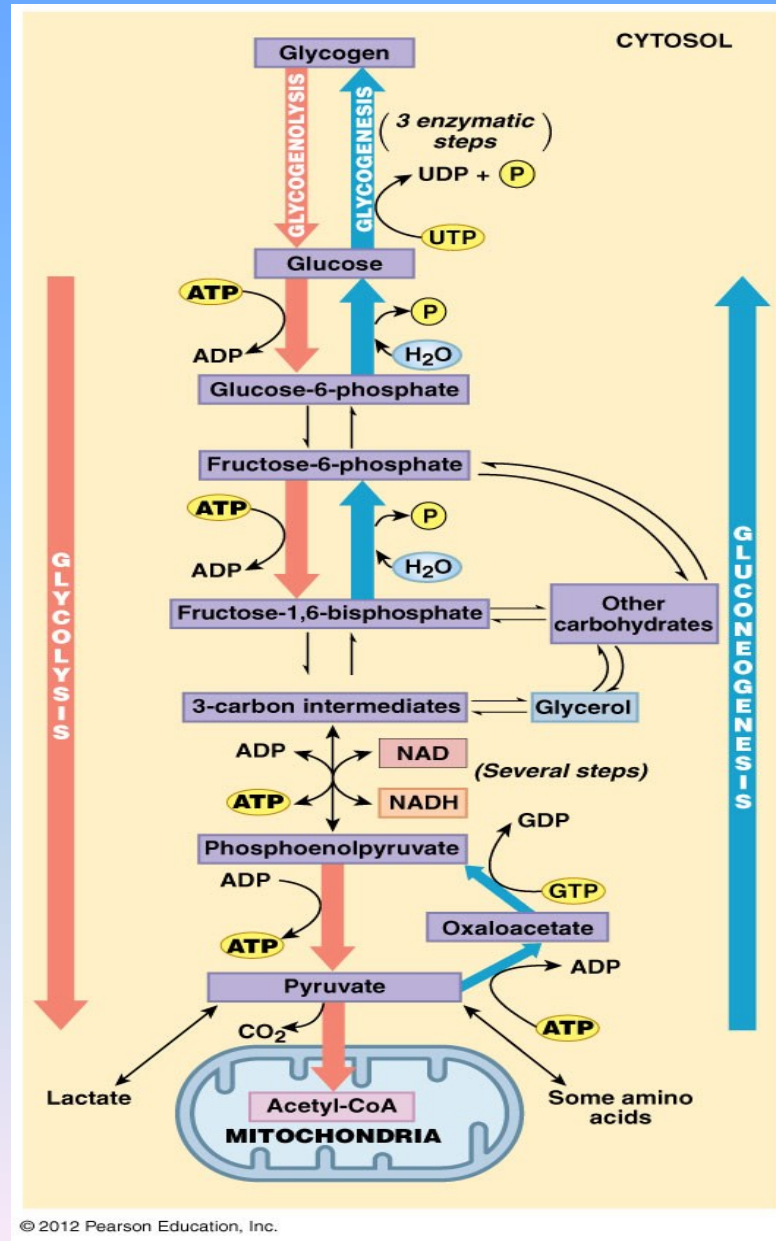


Figure 25-7

Gluconeogenesis

- = Synthesis of glucose from non-carbohydrate precursors:
 - Lactic acid
 - Glycerol
 - Amino acids
- Glucose stored as glycogen in liver and skeletal muscle

Lipids

- Largest energy reserve in adults (especially when glucose limited
 - Basis for Atkins diet
- Produce large amounts of ATP
 - FA release 1.5X energy of glucose but takes longer
- Excess CHOs converted into lipids
- Stored as adipose tissue
- Triglycerides = most abundant lipid in body

Lipid Catabolism

- Also called lipolysis
- Breaks lipids down into pieces that can be:
 - Utilized for energy
 - Converted to pyruvic acid or acetyl-CoA and enter TCA cycle
 - Stored
- Occurs in mitochondria

Triglyceride Catabolism

- Hydrolysis splits TG into glycerol + 3 FA
- Glycerol → pyruvic acid → TCA cycle
- FA → acetyl-CoA (via beta oxidation) → TCA cycle

Lipid Anabolism

- Also called lipogenesis
- Glycerol + FA(s) \rightarrow mono-/di-/tri-glycerides
- Can use almost any organic substrate to synthesize lipids
 - Because lipids, amino acids, and carbohydrates can be converted to acetyl-CoA

Free Fatty Acids (FFAs)

- Are lipids
- Important energy source:
 - When glucose supplies limited
 - During periods of starvation
- Liver cells, cardiac muscle cells, skeletal muscle fibers, etc.:
 - Metabolize free fatty acids
- In blood, are generally bound to albumin (most abundant plasma protein)

Lipoproteins

- Lipid-protein complexes
- Form in which most lipids circulate in bloodstream
- Distribution and formation controlled by liver
- Classified according to size and proportions of lipid (glycerides, cholesterol) vs. protein
 - Chylomicrons
 - LDLs
 - HDLs

Lipoproteins

- Chylomicrons
 - Largest lipoproteins
 - Produced in intestinal tract and enter lacteals → thoracic duct → systemic circulation
 - Carry absorbed lipids from intestinal tract to bloodstream
(vs. other lipoproteins that carry lipids between tissues)

Lipoproteins

- LDLs (low-density lipoproteins)
 - “Bad” cholesterol
 - Deliver cholesterol to peripheral tissues for:
 - Membranes, hormones, storage
 - Excess cholesterol → plaques = atherosclerosis
 - Primary cause of coronary artery disease (CAD)
 - May → myocardial infarction (heart attack)

Lipoproteins

- HDLs (high-density lipoproteins)
 - “Good” cholesterol
 - Transport excess cholesterol from peripheral tissues back to liver for storage or excretion in bile
 - Do not cause circulatory problems

Lipid Transport and Utilization

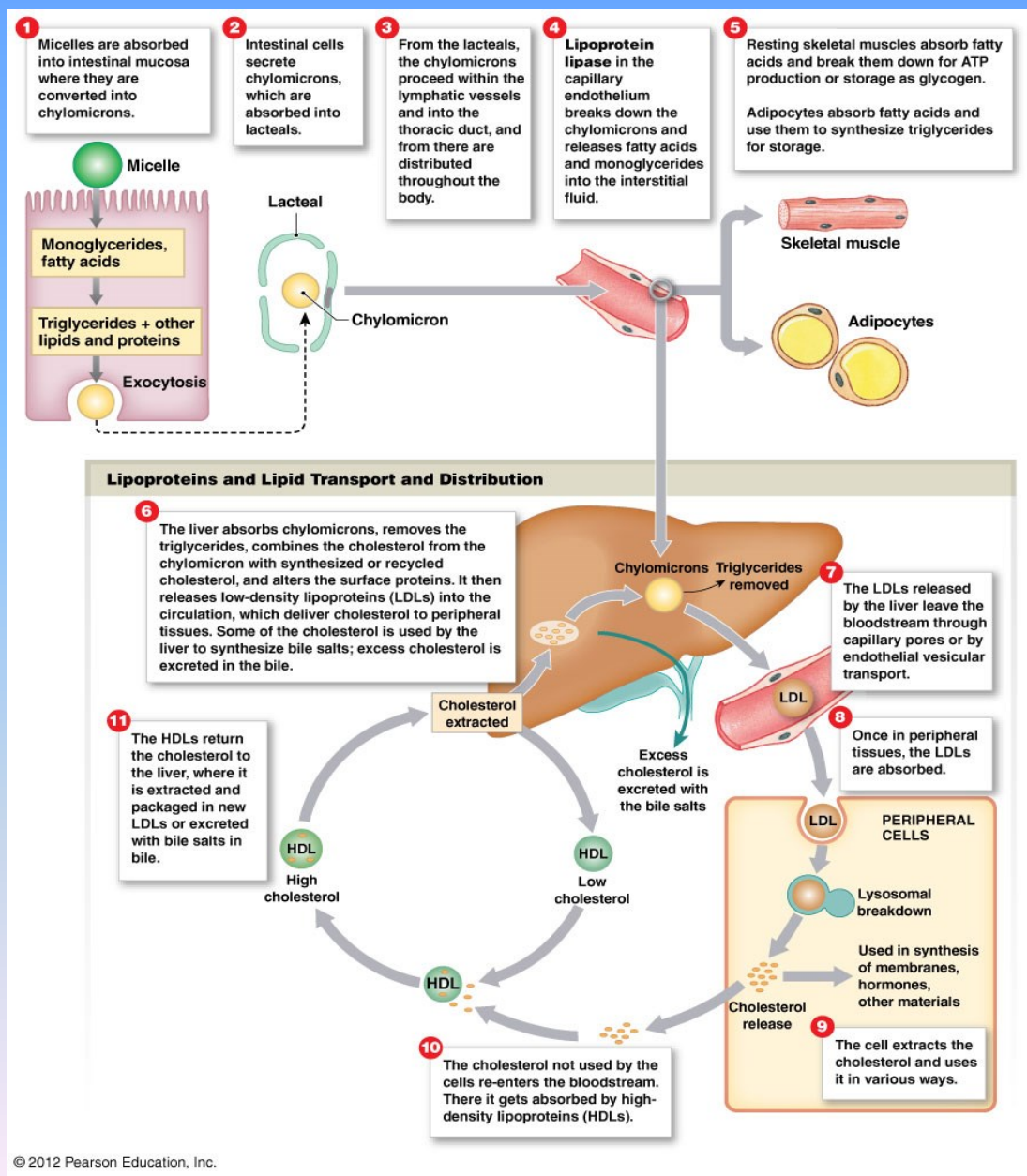


Figure 25-9

Proteins

- Body synthesizes 100,000 to 140,000 proteins:
 - Each with different form, function, and structure
- All proteins are built from the 20 amino acids

Protein Metabolism

- Cellular proteins continuously recycled in cytosol
 - Peptide bonds broken → amino acids (AAs)
 - Free AAs used in new proteins

Protein Metabolism

- If other energy sources (CHO, lipid) inadequate, AAs can enter TCA cycle → ATP but:
 - More difficult to break apart
 - Produce toxic by-product, ammonia (NH_3) which is converted into urea in liver
 - Body needs protein for structural and functional cell components

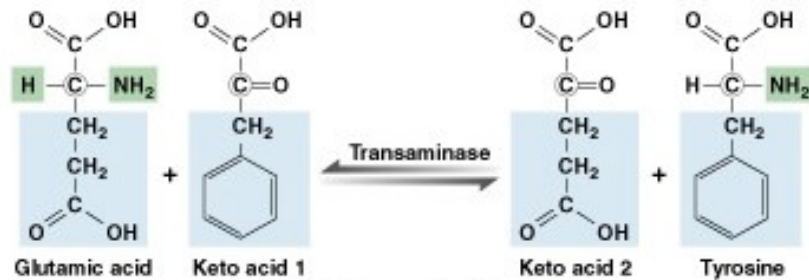
Deamination

- Prepares amino acid for breakdown in TCA cycle
- Removes amino group and hydrogen atom and generates NH_4 (ammonium ion)

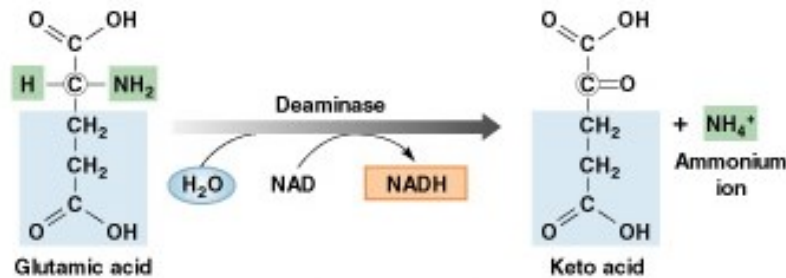
Ammonium ions

- Highly toxic, even in low concentrations
- Liver cells (primary sites of deamination) have enzymes that use ammonium ions to synthesize urea (water-soluble compound excreted in urine)

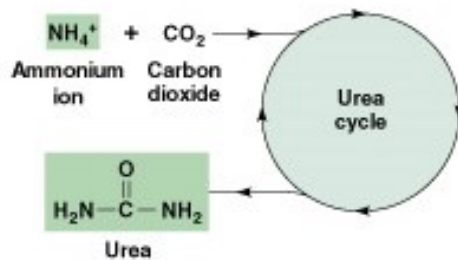
Amino Acid Catabolism



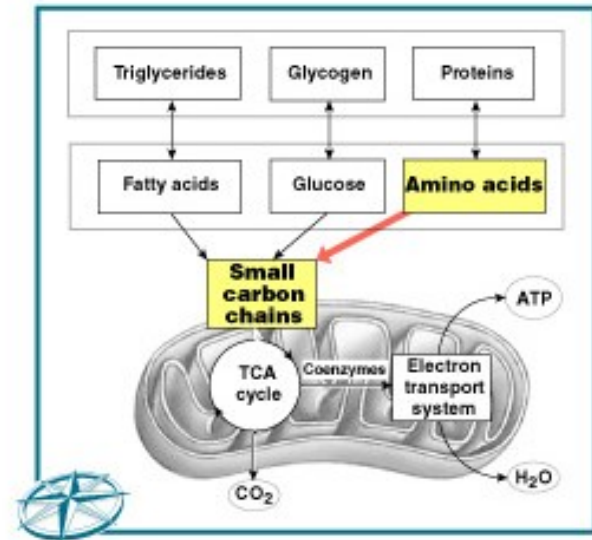
(a) Transamination



(b) Deamination



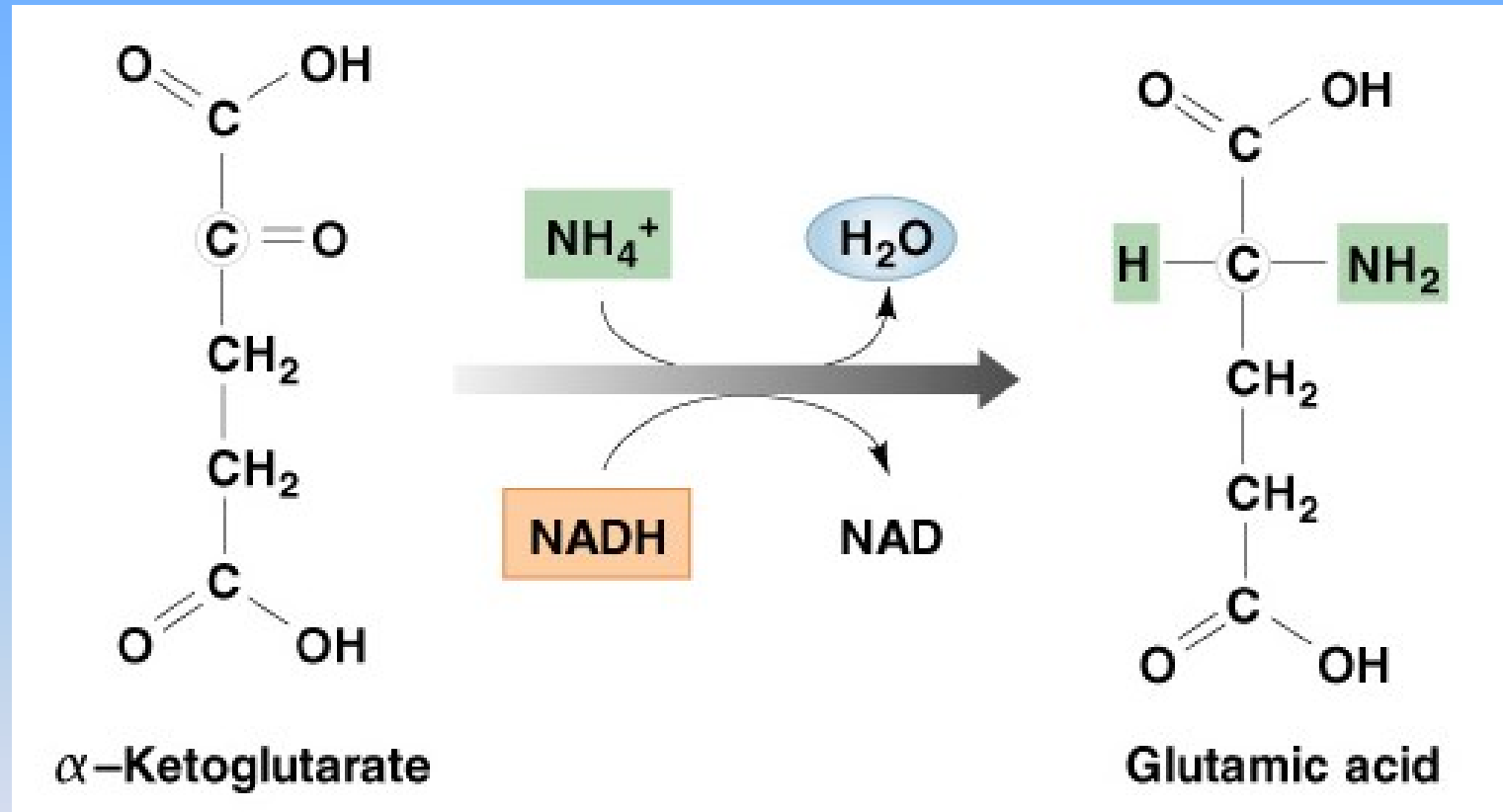
(c) Urea cycle



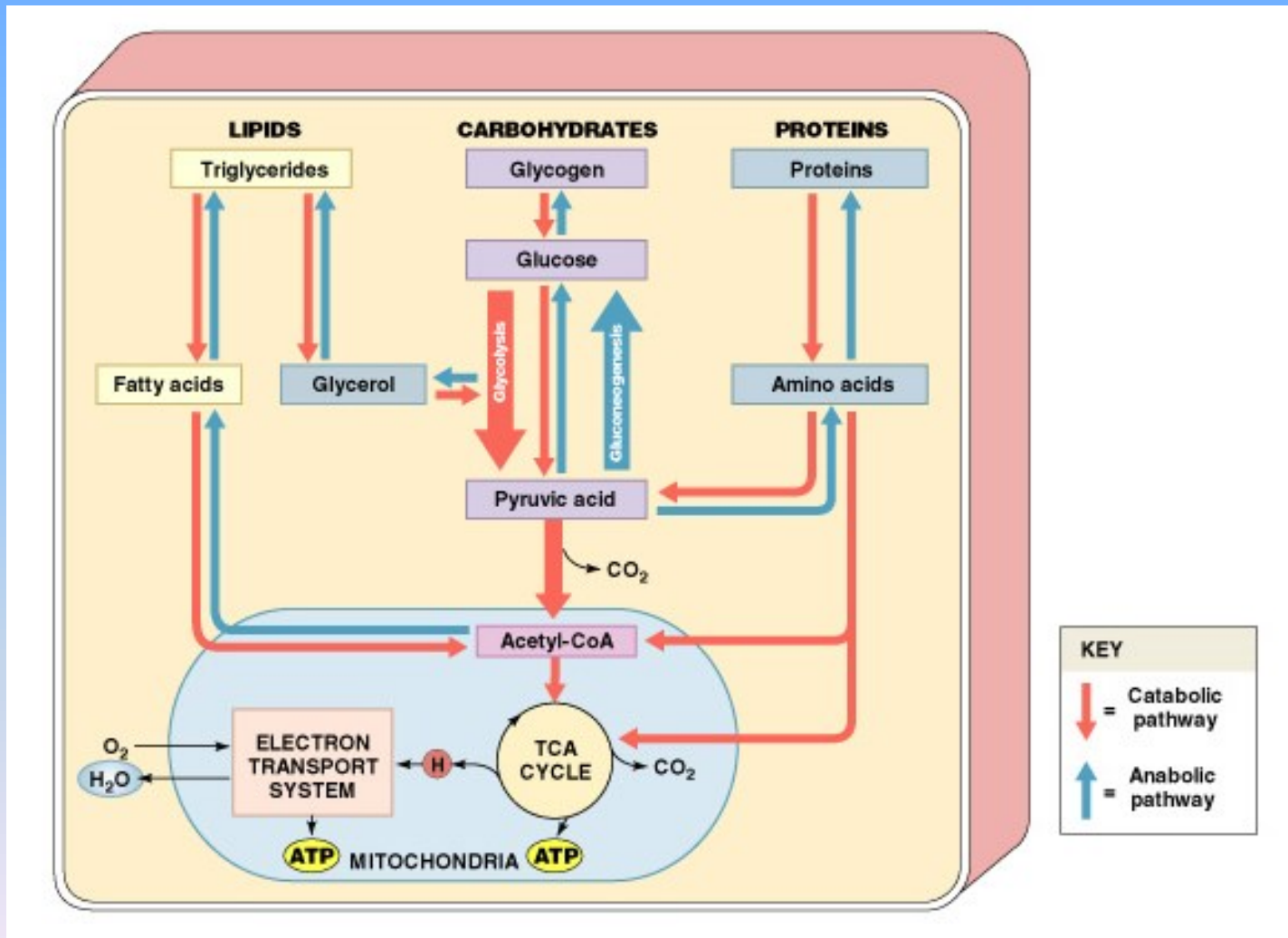
Amino Acid Anabolism

- 12/22 AAs readily synthesized by body = nonessential AAs
- Other 10 = essential AAs
 - Must be acquired through diet

Amination



Summary: Pathways of Catabolism and Anabolism



Ketone Bodies

- During fasting or in absence of glucose (e.g., diabetes)
 - Lipid and amino acid catabolism → acetyl-CoA
- Increased acetyl-CoA causes ketone bodies to form, e.g., acetone

Ketosis

- High concentration of ketone bodies in body fluids
- Lowers plasma pH
- May cause dangerous drop in blood pH (ketoacidosis)
 - pH < 7.05
 - May cause coma, cardiac arrhythmias, death

Energy Yield from Nutrients

- When nutrients (organic molecules) are catabolized they $\rightarrow \text{CO}_2 + \text{H}_2\text{O} + \text{ATP}$
- Energy released measured in calorimeter
- Expressed in Calories (C)/gram
- Calorie = amt of heat required to raise temperature of 1 kg of water 1 degree C

Energy Yield from Nutrients

- Lipids → 9.5 C/g
 - Greater because many C and H atoms already bound to oxygen
- CHO → 4.2 C/g
- Protein → 4.3 C/g
- Calorie count of foods reflects mixture of fats, CHO, proteins