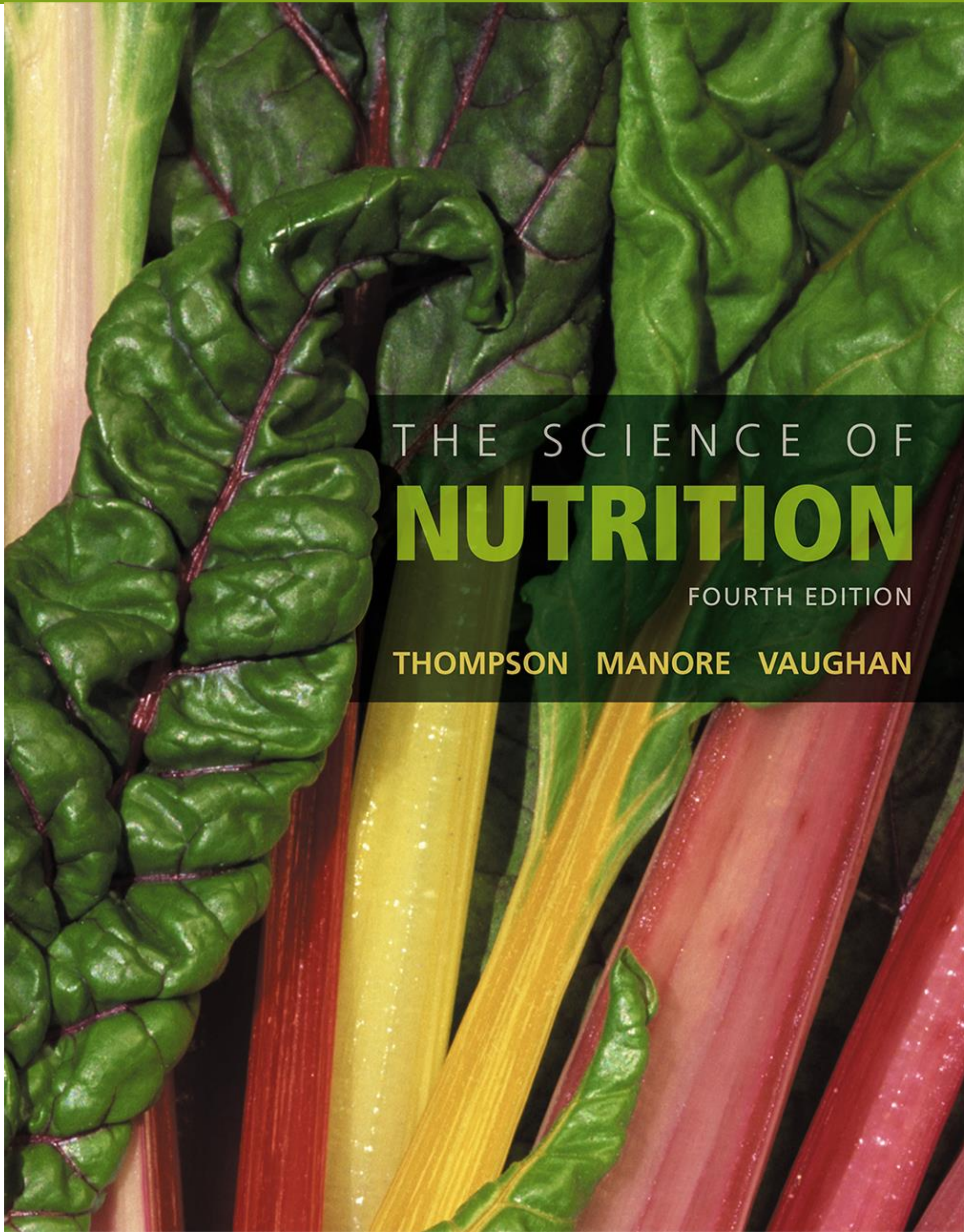
Chapter 7: Metabolism: From Food to Life

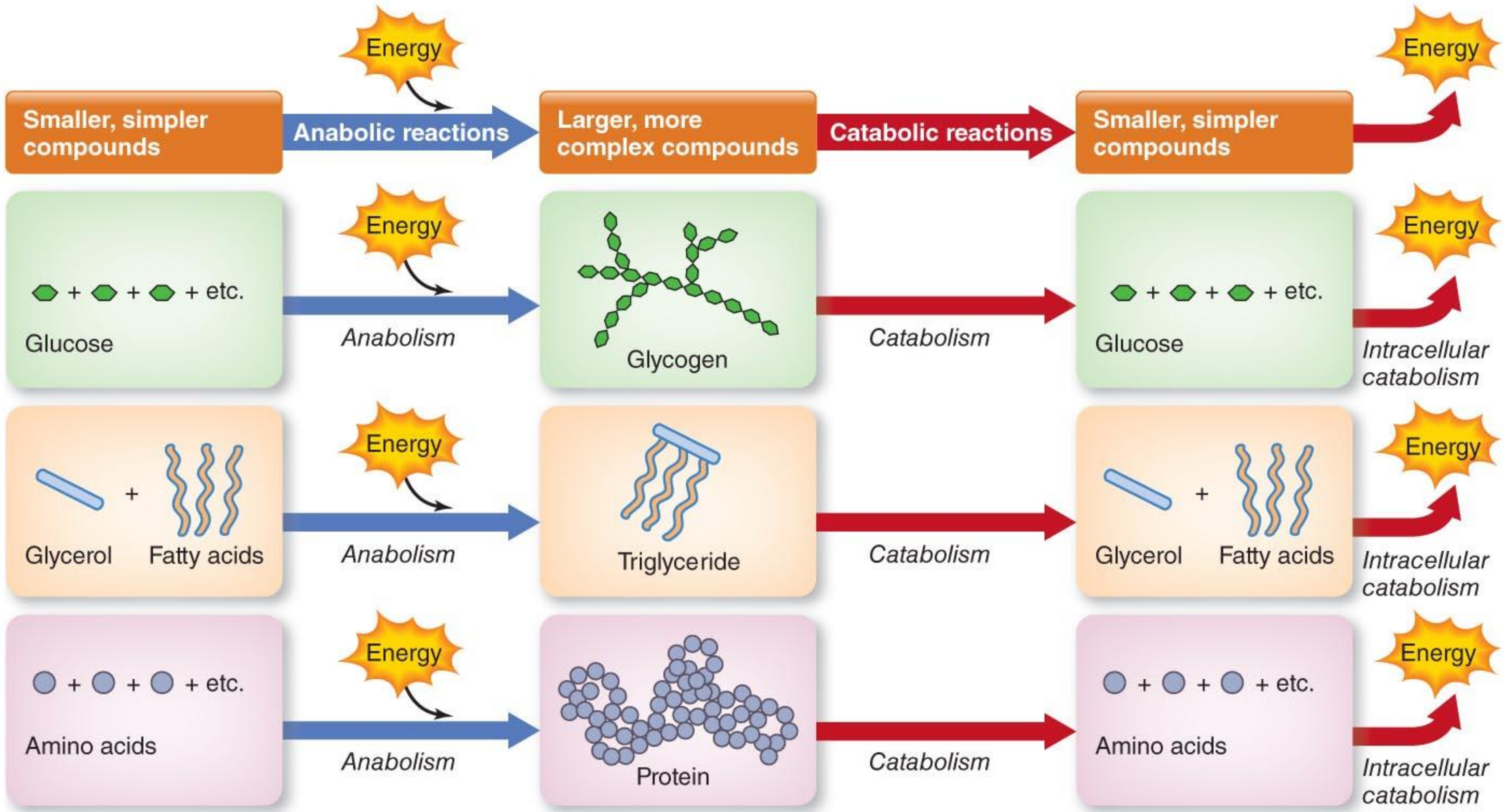


Metabolism

- **Metabolism** is the sum of all chemical and physical processes by which the body breaks down and builds up molecules
  - **Calorimeter** measures a food's caloric content
  - Chemical reactions in the body require or release energy

Anabolism

- **Anabolism** is the process of making larger, chemically complex molecules from smaller ones
  - Critical for growth, repair, maintenance, and synthesis of chemical products essential for human functioning
  - Requires energy

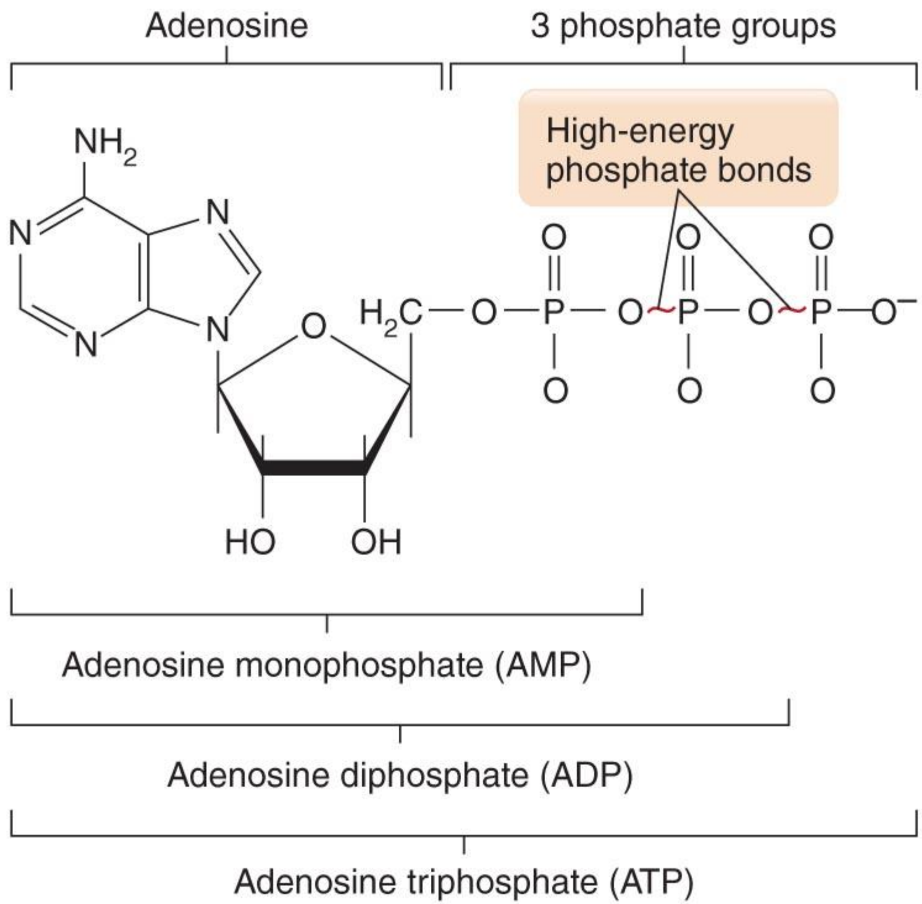

Energy
Smaller, simpler compounds
Anabolic reactions
Larger, more complex compounds
Catabolic reactions
Smaller, simpler compounds
Energy
Energy
+ + + etc.
Glucose
Anabolism
Glycogen
Catabolism
+ + + etc.
Glucose
Energy
Intracellular catabolism
Energy
+
Glycerol
Fatty acids
Anabolism
Triglyceride
Catabolism
+
Glycerol
Fatty acids
Energy
Intracellular catabolism
Energy
+ + + etc.
Amino acids
Anabolism
Protein
Catabolism
+ + + etc.
Amino acids
Energy
Intracellular catabolism

Catabolism

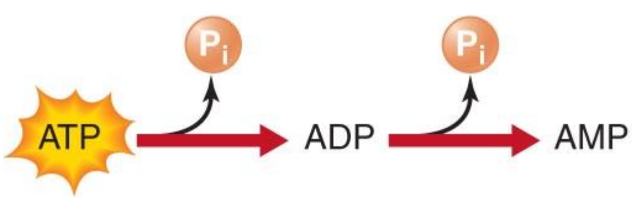
- **Catabolism**: breakdown of larger, complex molecules to smaller, more basic ones
  - Begins with digestion—chemical reactions break down proteins, lipids, carbohydrates
  - Old cells or tissues are broken down for repair or replacement
  - Releases energy

Adenosine Triphosphate (ATP)

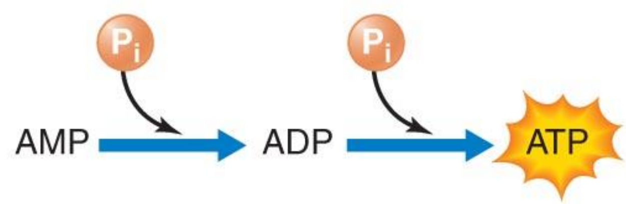
- ATP is an organic compound used by cells as a source of metabolic energy
  - Potential energy is stored in the *high-energy phosphate bonds*
  - When bonds are broken, energy is released
  - This energy is used to keep cells functioning
  - A small amount of ATP is stored in every cell for immediate use



(a) Structure of ATP



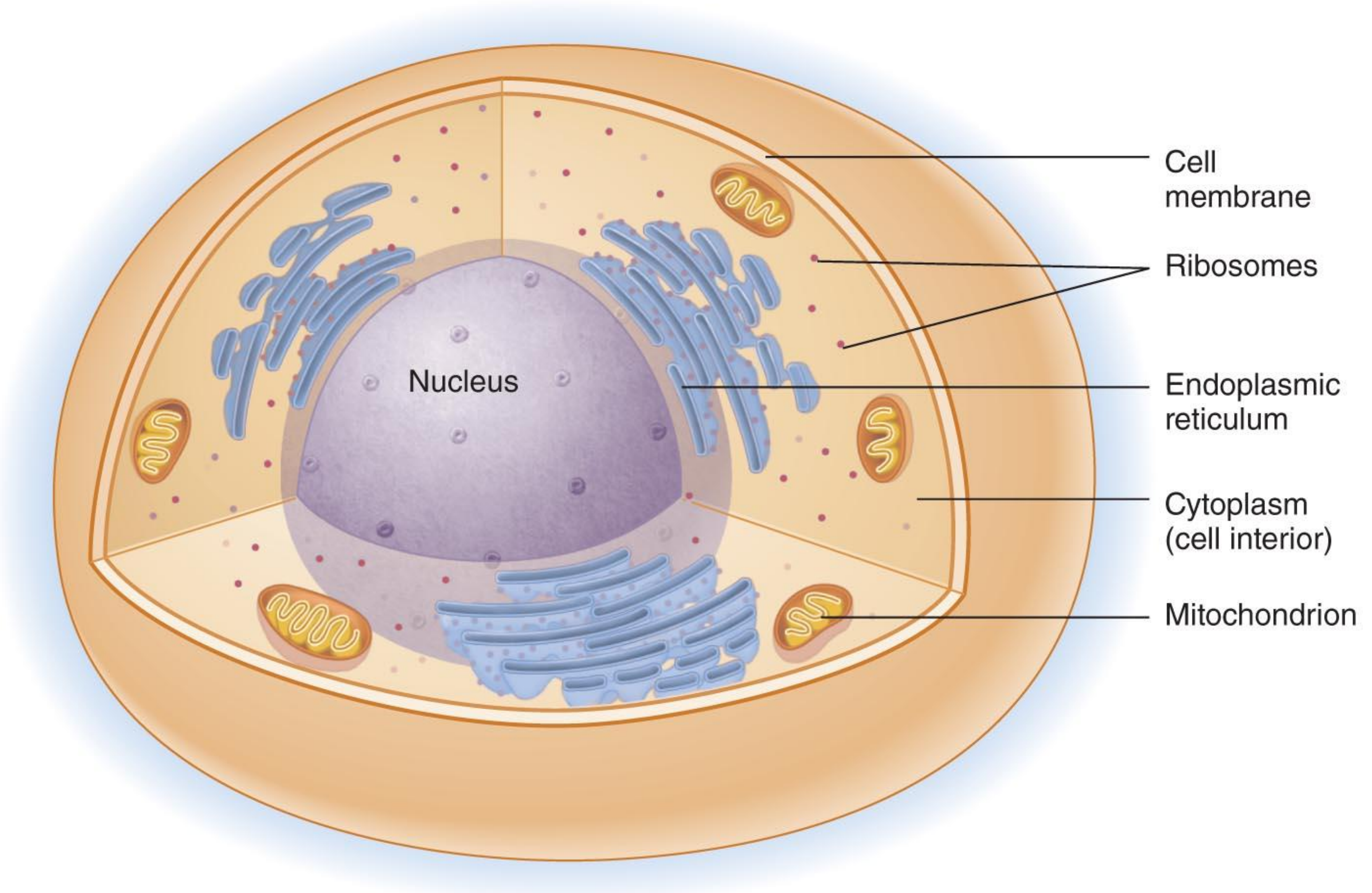
(b) Conversion of ATP to ADP and AMP



(c) Regeneration of ATP

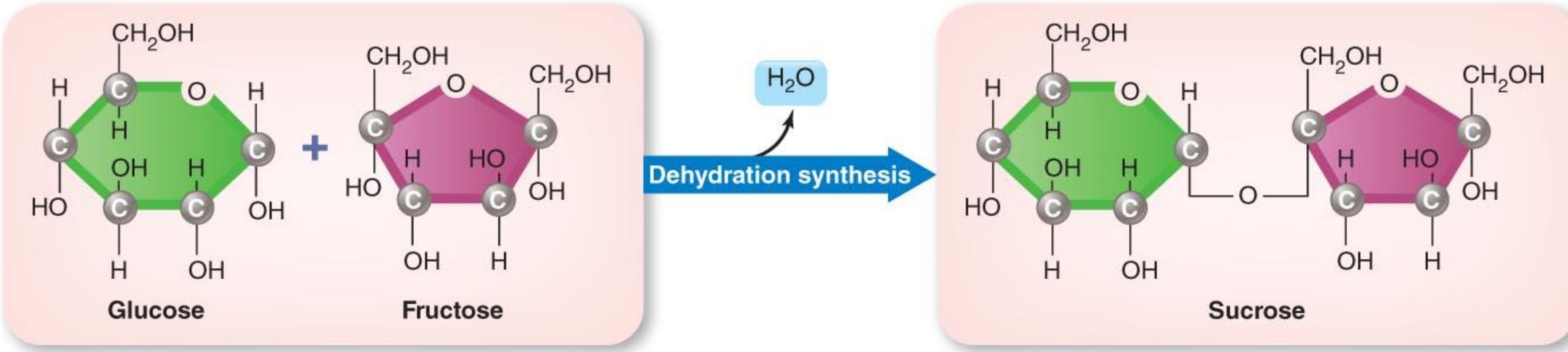
Metabolic Pathways

- *Metabolic pathways* are clusters of chemical reactions that occur sequentially to achieve a particular goal
  - Occur in a specific part of a cell
  - May be limited to specific organs or tissues
- *Mitochondria* are the primary site of chemical energy (ATP) production
- "Networking" of metabolic pathways

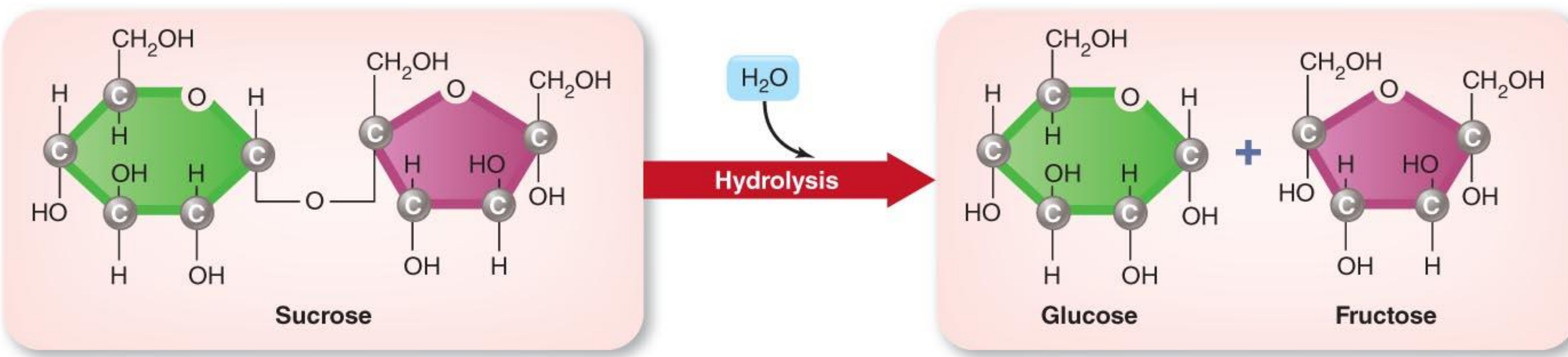

Nucleus
Cell membrane
Ribosomes
Endoplasmic reticulum
Cytoplasm (cell interior)
Mitochondrion

Dehydration Synthesis and Hydrolysis

- **Dehydration synthesis** (also called *condensation*) is an anabolic process
  - Simple units combine to form a larger, more complex molecule
  - Water is released as a by-product
- **Hydrolysis** is usually a catabolic process
  - A large molecule is broken apart with the addition of water



(a) Dehydration synthesis of glucose and fructose



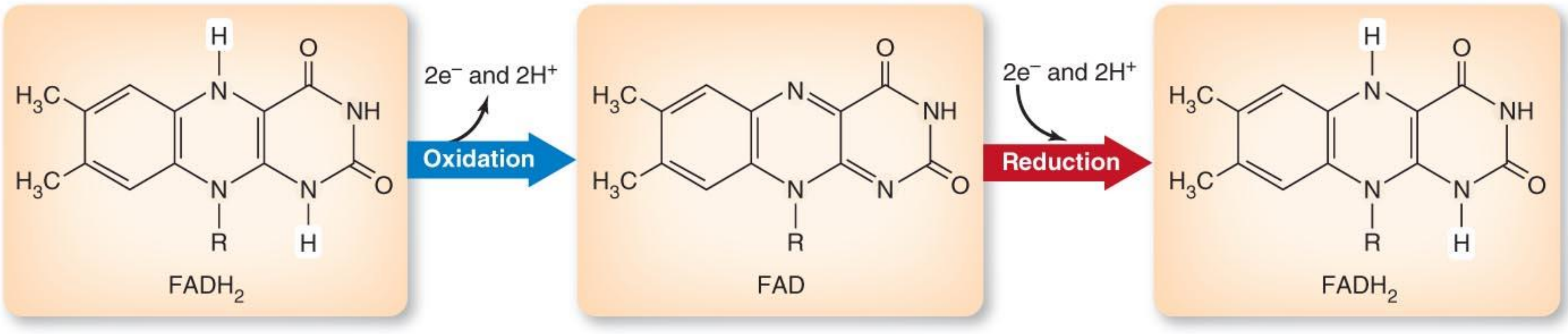
(b) Hydrolysis of sucrose

Phosphorylation

- **Phosphorylation**: addition of a phosphate group to a compound
- When the high-energy phosphate bonds in ATP are broken
  - Energy is released
  - Phosphate is transferred to other molecules
- When glucose is phosphorylated, it can be oxidized for energy or stored as glycogen

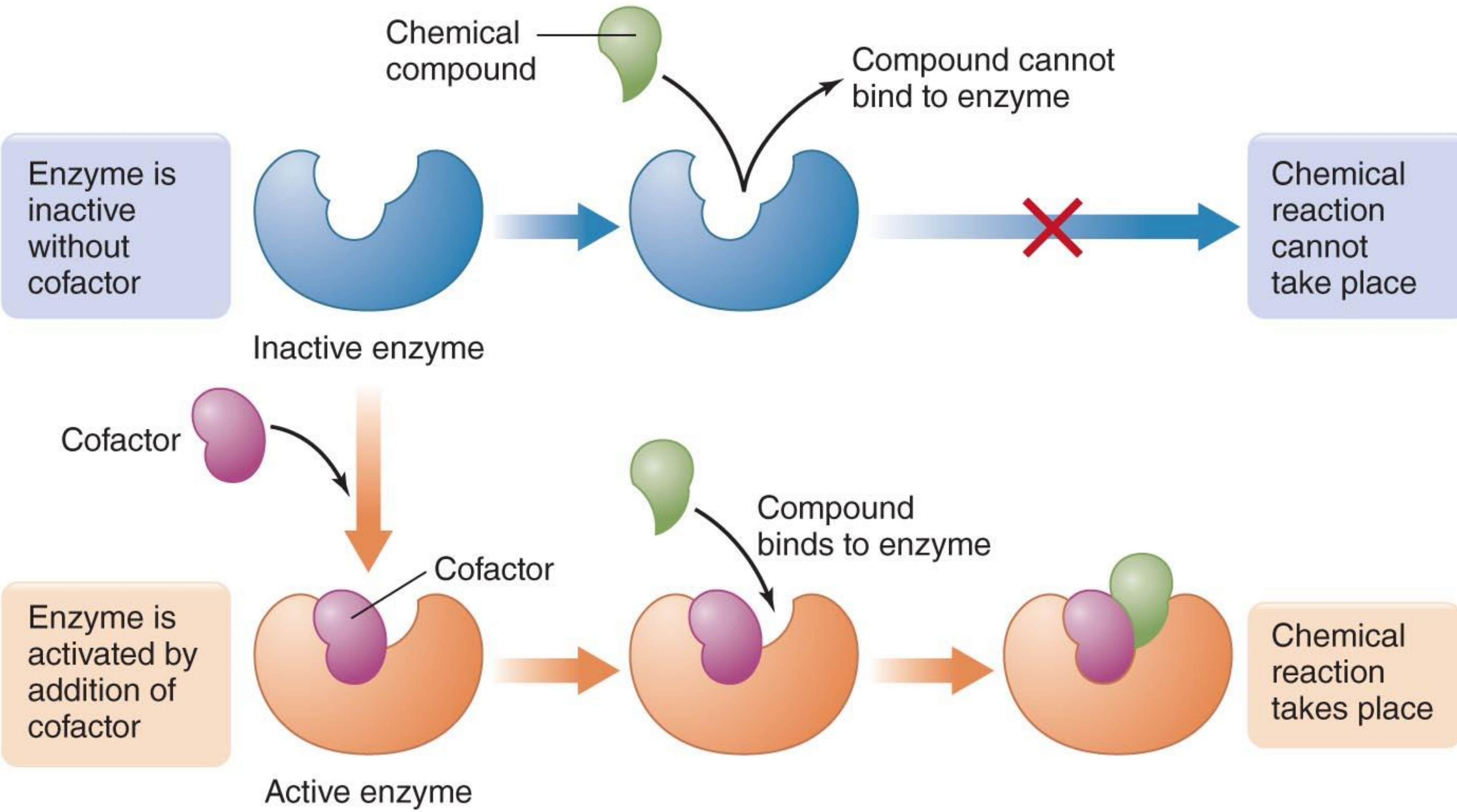
Oxidation–Reduction Reactions

- Molecules exchange electrons (hydrogen)
- Exchange reactions occur together
- Molecule donating an electron is *oxidized*
  - Its electron is removed by oxygen
- Molecule acquiring an electron is *reduced*
  - In gaining an electron, it becomes more negatively charged


H
O
H_3C
N
NH
H_3C
N
N
O
R
H
$FADH_2$
$2e^-$ and $2H^+$
Oxidation
O
H_3C
N
NH
H_3C
N
N
O
R
FAD
$2e^-$ and $2H^+$
Reduction
H
O
H_3C
N
NH
H_3C
N
N
O
R
H
$FADH_2$

Metabolic Enzymes

- Enzymes mediate chemical reactions
- **Coenzymes** are non-protein substances that enhance or are necessary for enzyme activity
  - FAD, $FADH_2$, and vitamins function as coenzymes
- **Cofactors** are typically minerals required for enzyme activity
  - Iron, magnesium, and zinc function as cofactors

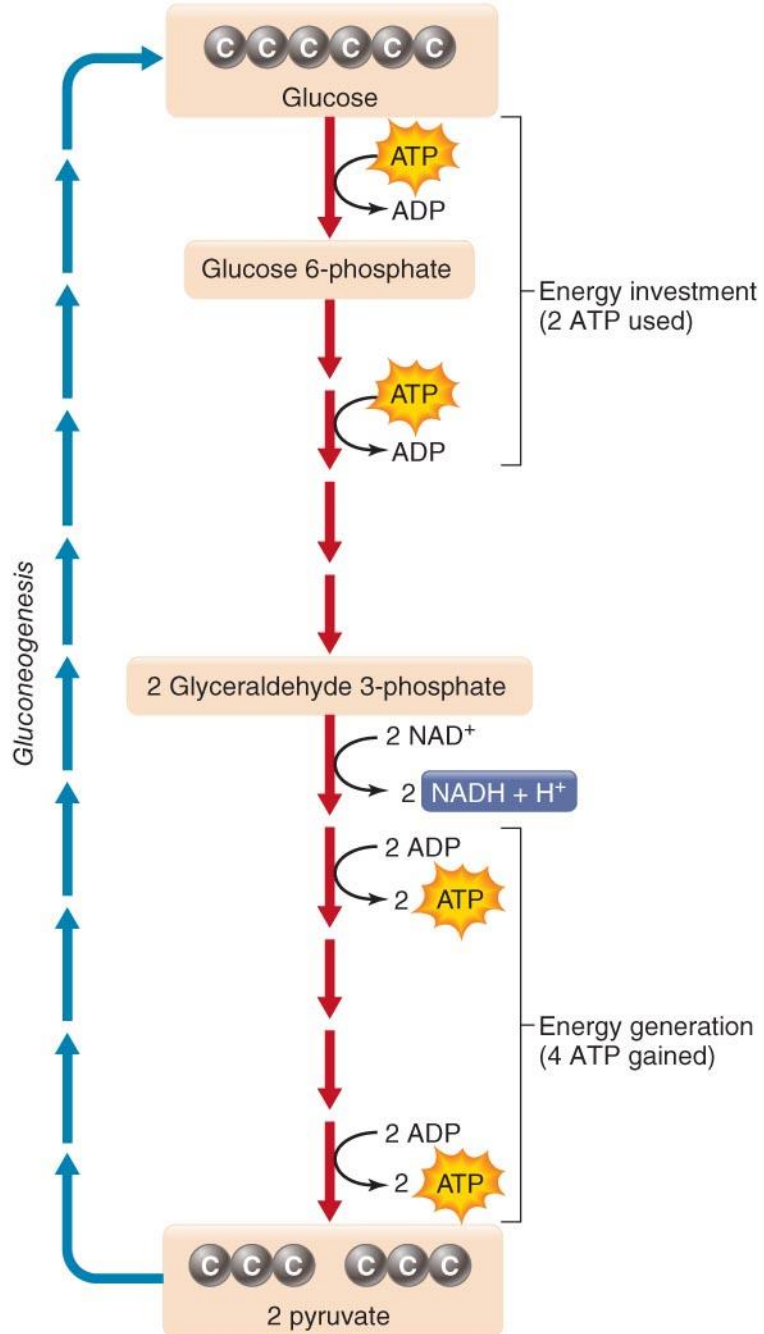

Chemical compound
Compound cannot bind to enzyme
Enzyme is inactive without cofactor
Chemical reaction cannot take place
Inactive enzyme
Cofactor
Compound binds to enzyme
Cofactor
Enzyme is activated by addition of cofactor
Chemical reaction takes place
Active enzyme

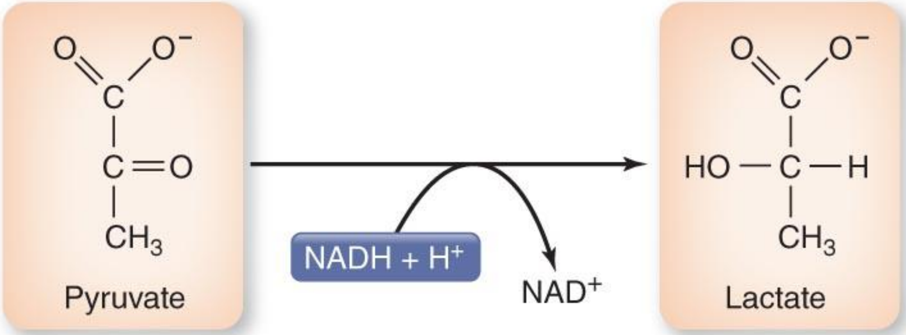
Energy from Carbohydrates

- When glucose is transported to the liver, it is:
  - Phosphorylated and metabolized for energy or stored as glycogen
  - Released into circulation for other cells to use as fuel or stored as glycogen (muscle tissue)
- If glucose exceeds energy needs, it can be converted to fatty acids and stored as triglycerides in adipose tissue
- Fructose and galactose are converted to glucose in the liver and follow the same process

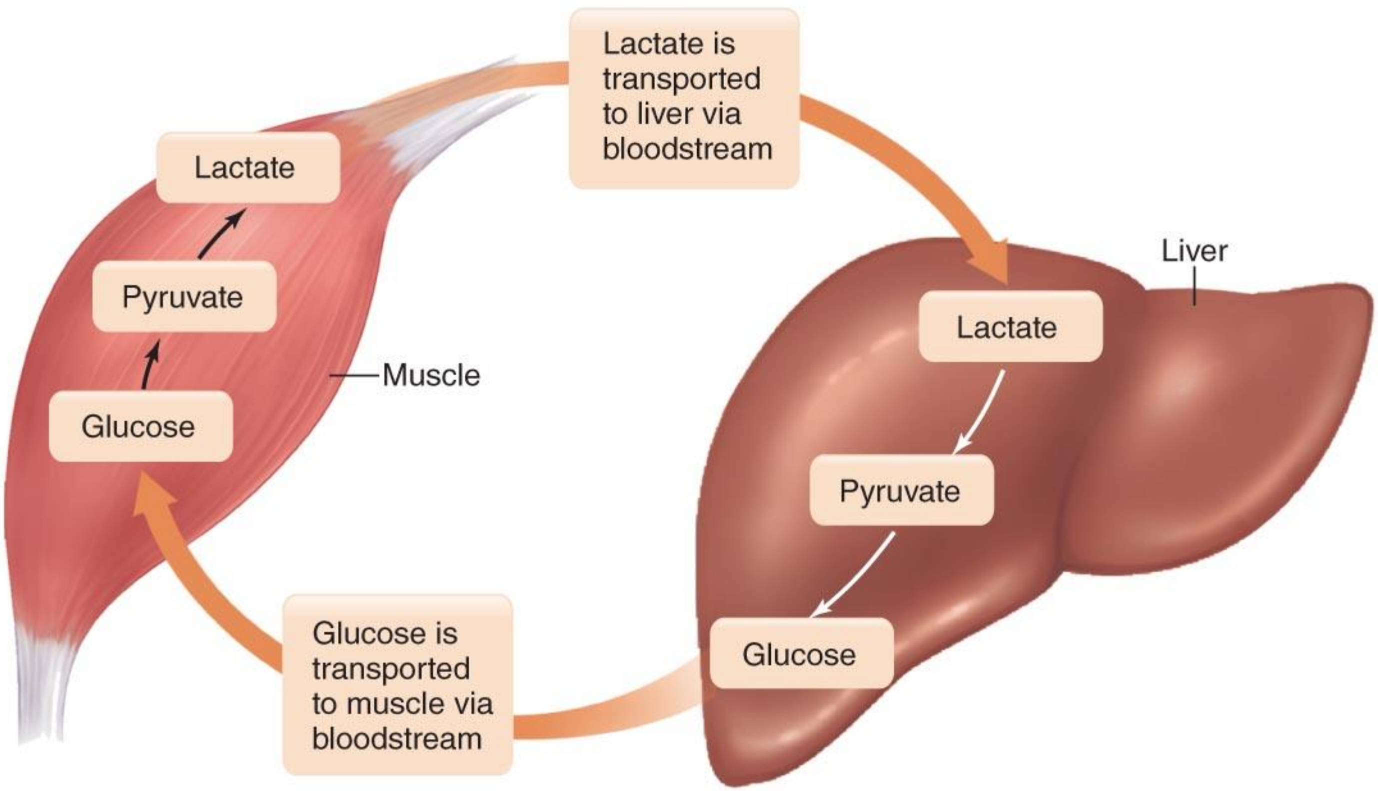
Glycolysis

- Occurs in the cytosol of cells
- Anaerobic reaction
- Final step is pyruvate production
- Net of 2 ATP to be used as energy for the cell

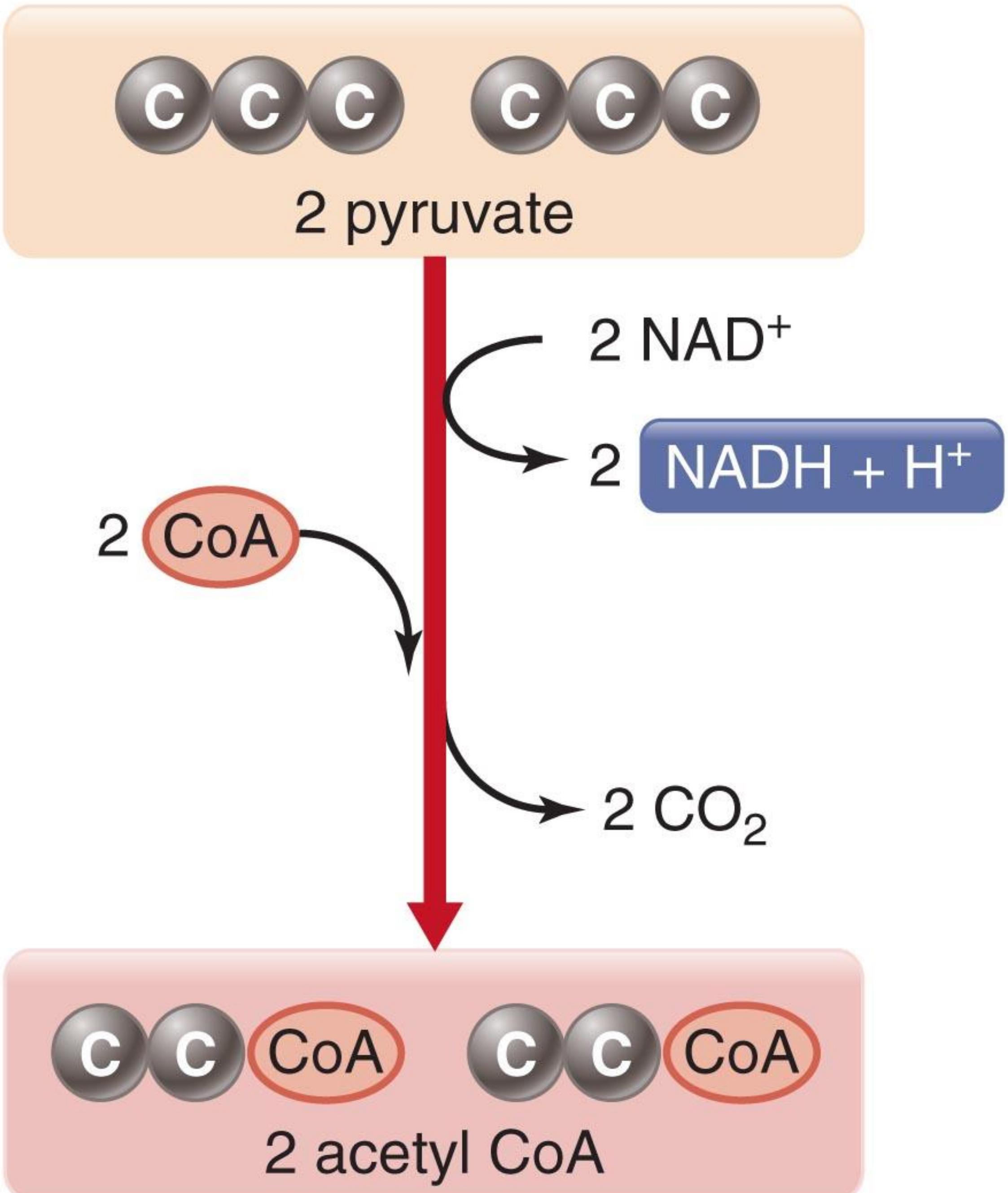

C C C C C C
Glucose
ATP
ADP
Glucose 6-phosphate
Energy investment
(2 ATP used)
ATP
ADP
2 Glyceraldehyde 3-phosphate
2 NAD+
2 NADH + H+
2 ADP
2 ATP
Energy generation
(4 ATP gained)
2 ADP
2 ATP
C C C C C C
2 pyruvate
Gluconeogenesis

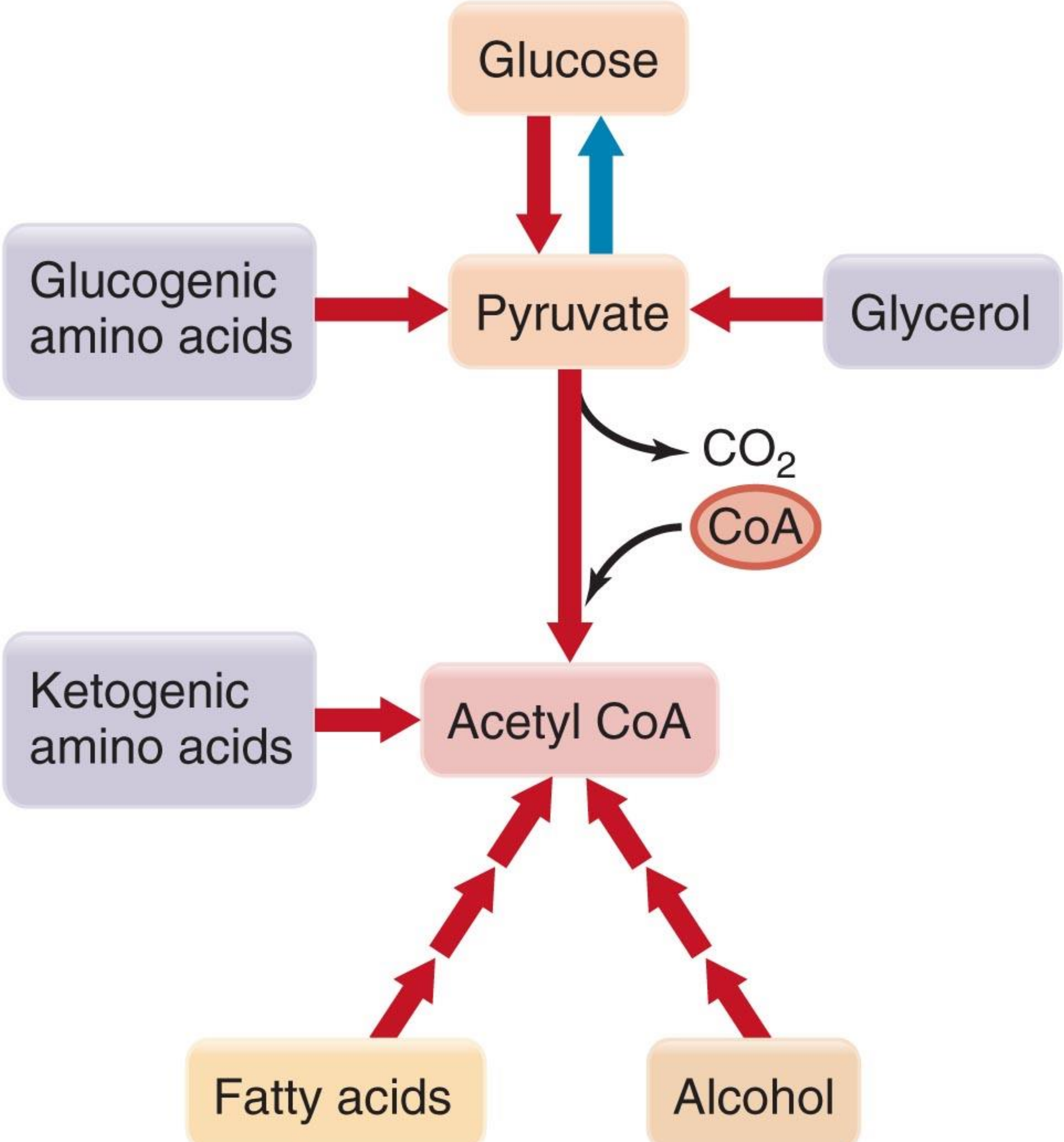


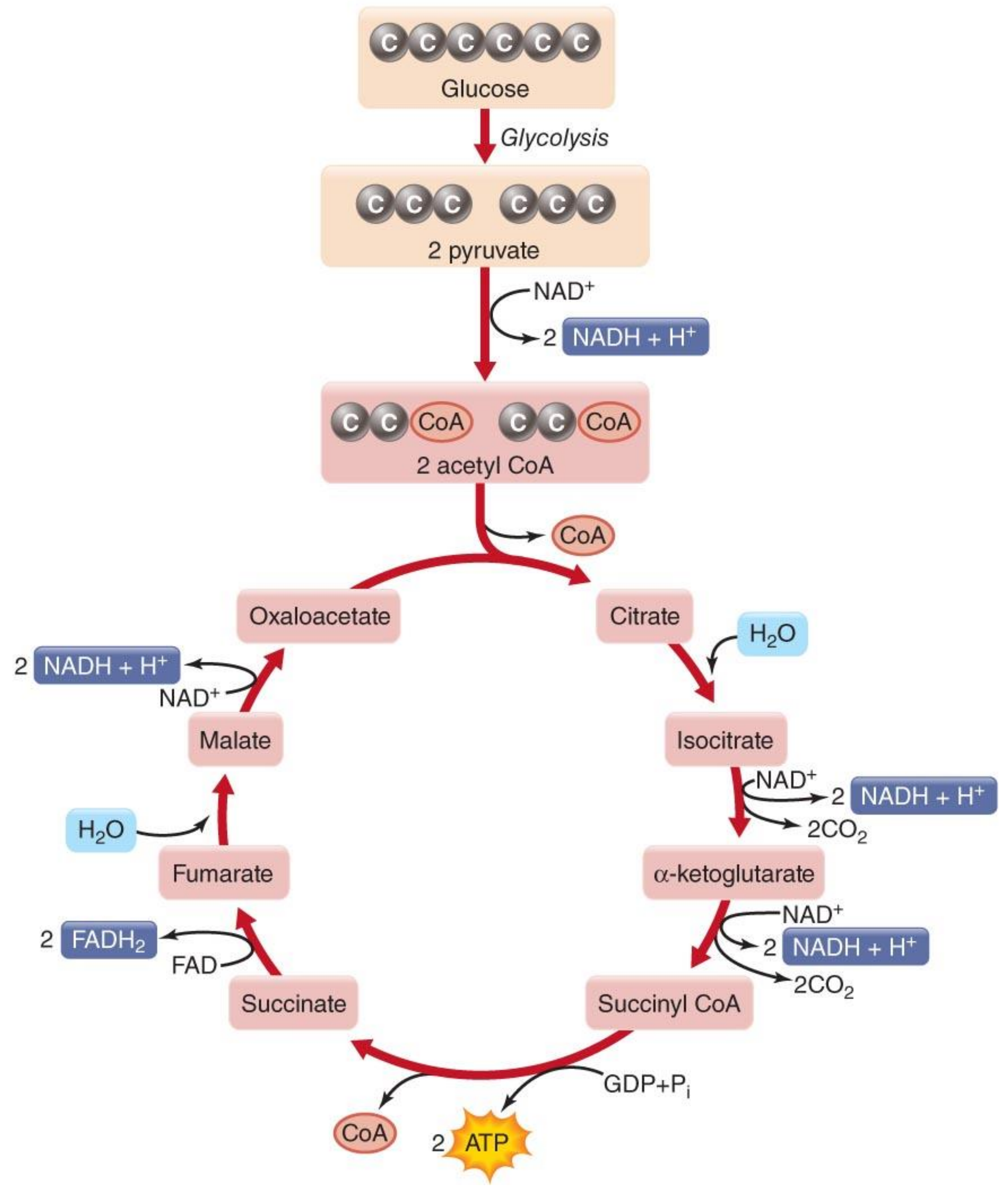
(a) Anaerobic conversion of pyruvate to lactate

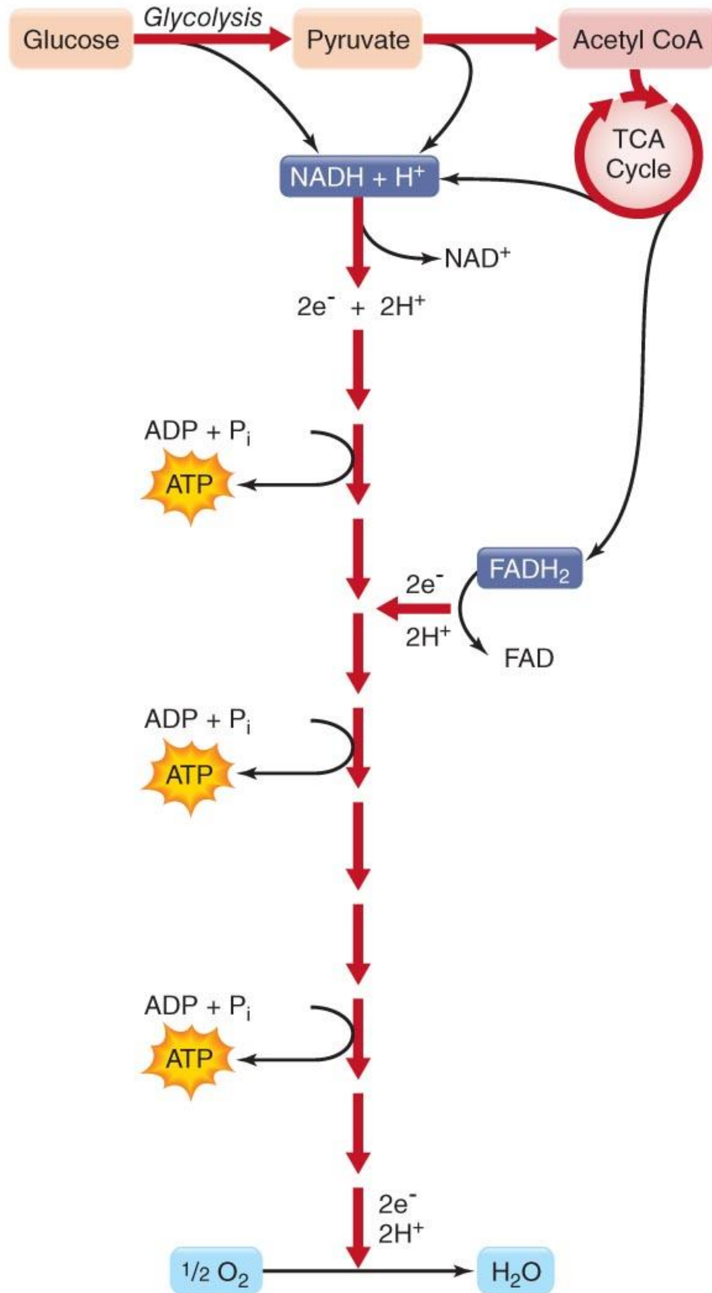


(b) Interconversion of lactate and glucose


C C C C C C
2 pyruvate
2 NAD+
2 NADH + H+
2 CoA
2 CO2
C C CoA C C CoA
2 acetyl CoA

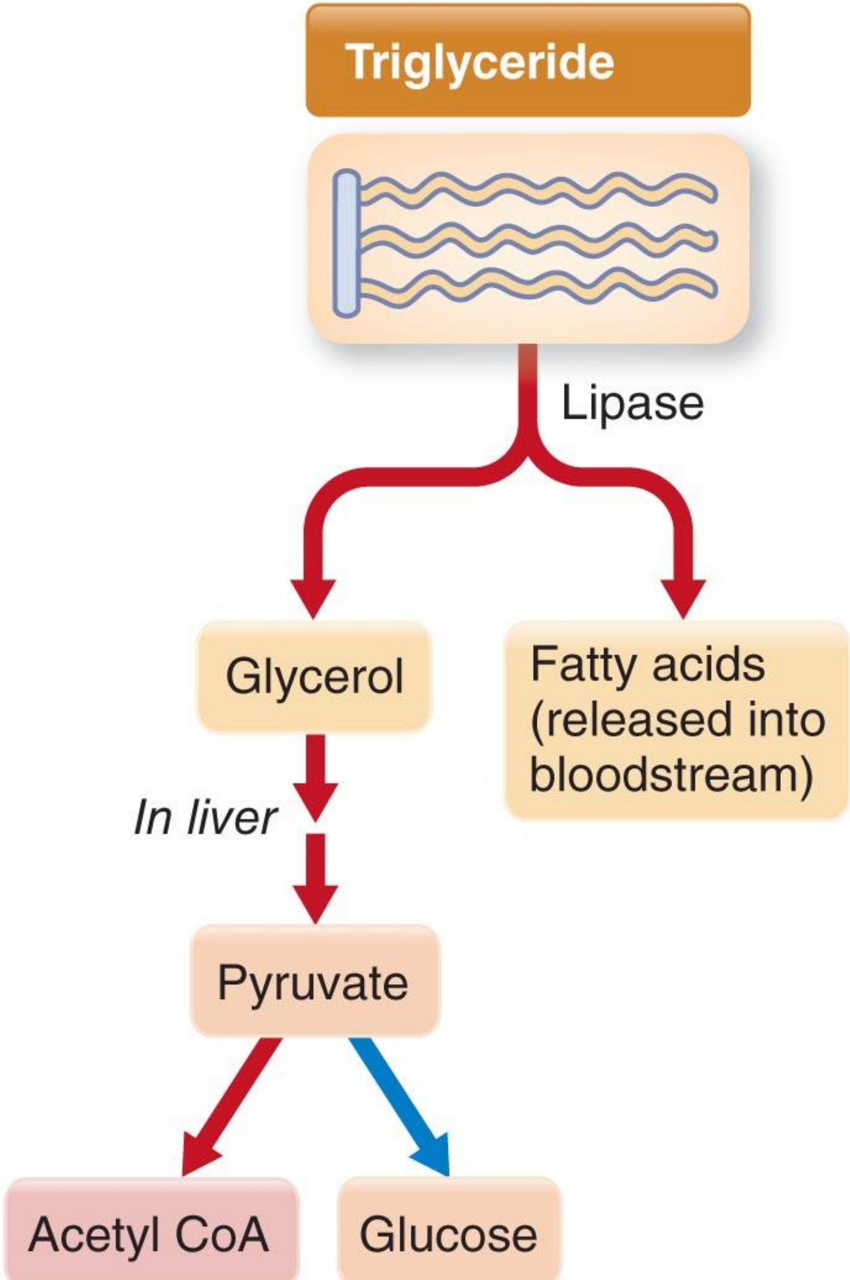

Glucose
Glucogenic amino acids
Pyruvate
Glycerol
CO_2
CoA
Ketogenic amino acids
Acetyl CoA
Fatty acids
Alcohol


C C C C C C
Glucose
Glycolysis
C C C C C C
2 pyruvate
NAD^+
2 $NADH + H^+$
C C CoA C C CoA
2 acetyl CoA
CoA
Oxaloacetate
Citrate
H_2O
Isocitrate
NAD^+
2 $NADH + H^+$
$2CO_2$
α-ketoglutarate
NAD^+
2 $NADH + H^+$
$2CO_2$
Succinyl CoA
GDP+P_i
2 ATP
CoA
Succinate
FAD
2 $FADH_2$
Fumarate
H_2O
Malate
NAD^+
2 $NADH + H^+$


Glucose
Glycolysis
Pyruvate
Acetyl CoA
TCA Cycle
NADH + H+
NAD+
2e- + 2H+
ADP + Pi
ATP
FADH2
2e-
2H+
FAD
ADP + Pi
ATP
ADP + Pi
ATP
2e-
2H+
1/2 O2
H2O

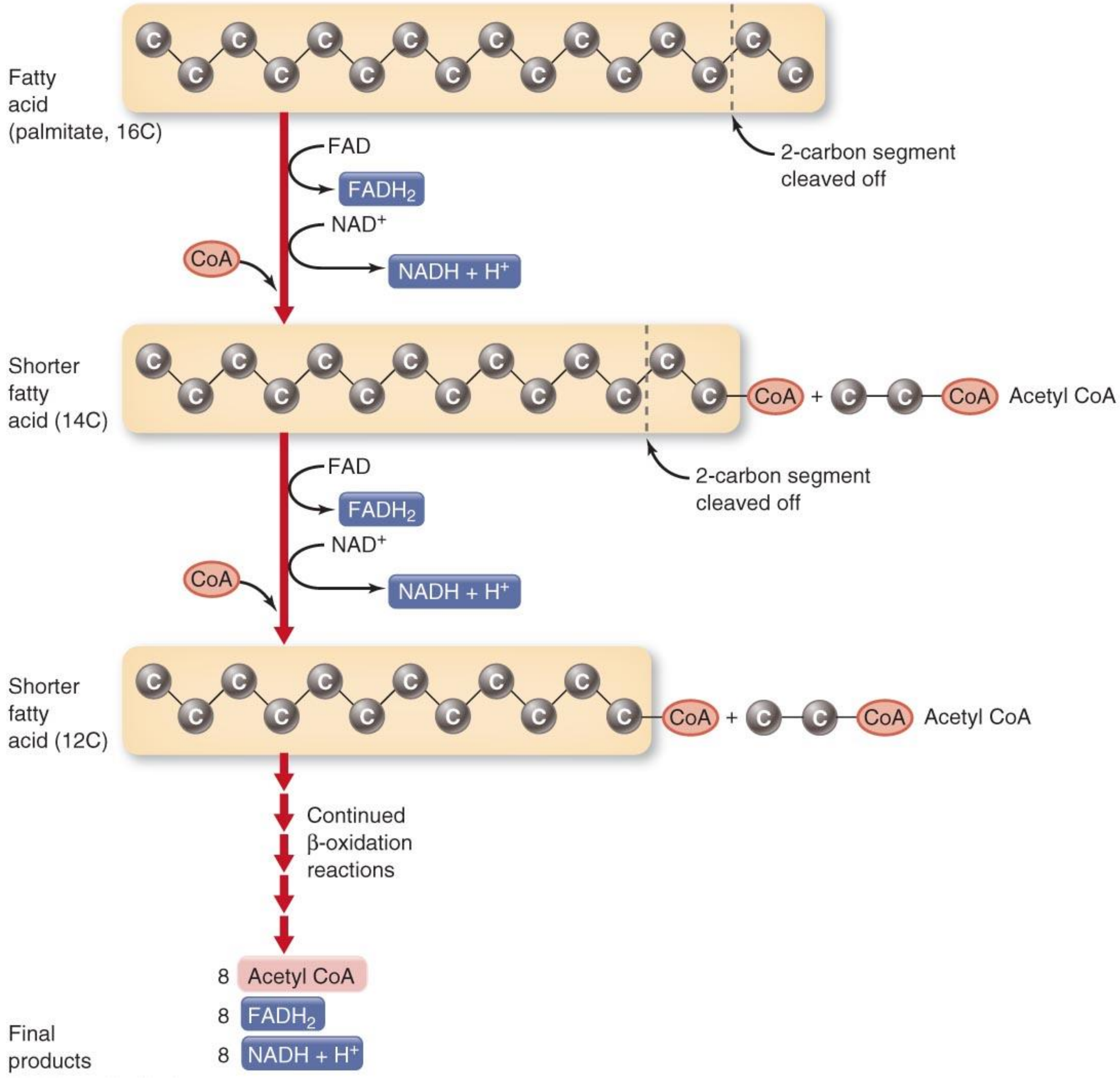
Energy from Fat

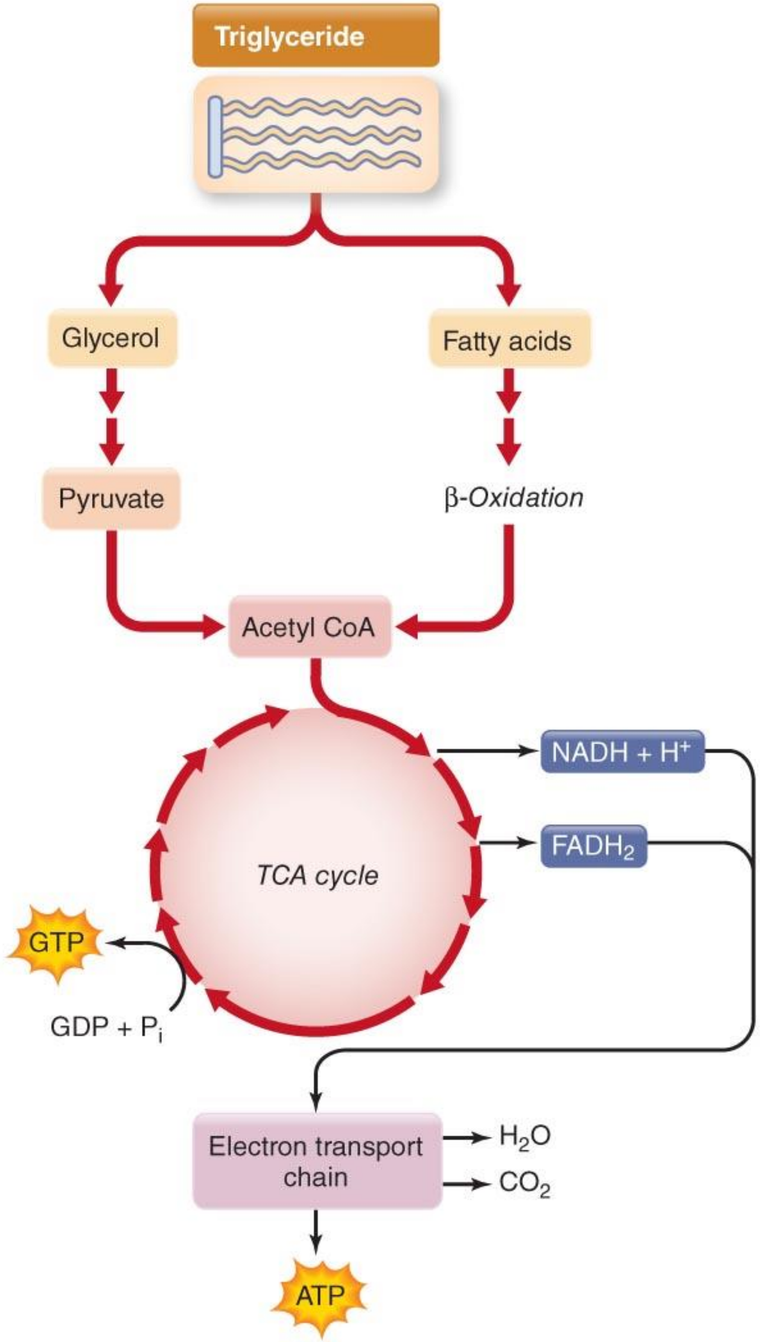
- **Lipolysis:** dietary and adipose triglycerides are broken down by lipases to yield glycerol and three free fatty acids
- Glycerol is converted to pyruvate, then to acetyl CoA for entry into the TCA cycle
- **β-oxidation (fatty acid oxidation):** metabolic reactions that oxidize free fatty acids, producing water, carbon dioxide and ATP


Triglyceride
Lipase
Glycerol
Fatty acids (released into bloodstream)
In liver
Pyruvate
Acetyl CoA
Glucose

β-oxidation of Fatty Acids

- Attached to albumin, fatty acids are transported to working cells in need of energy (muscle or liver cells)
- Fatty acids must be activated by *coenzyme* A before being shuttled across the mitochondrial membrane by *carnitine*
- Long-chain fatty acids are broken down into two-carbon segments to form *acetyl CoA*

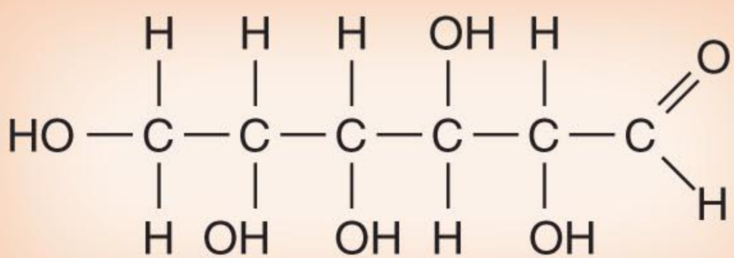

Fatty
acid
(palmitate, 16C)
2-carbon segment
cleaved off
FAD
FADH2
NAD+
CoA
NADH + H+
Shorter
fatty
acid (14C)
CoA
+
CoA
Acetyl CoA
2-carbon segment
cleaved off
FAD
FADH2
NAD+
CoA
NADH + H+
Shorter
fatty
acid (12C)
CoA
+
CoA
Acetyl CoA
Continued
β-oxidation
reactions
8 Acetyl CoA
8 FADH2
8 NADH + H+
Final
products


Triglyceride
Glycerol
Fatty acids
Pyruvate
β-Oxidation
Acetyl CoA
TCA cycle
NADH + H+
FADH2
GTP
GDP + Pi
Electron transport chain
H2O
CO2
ATP

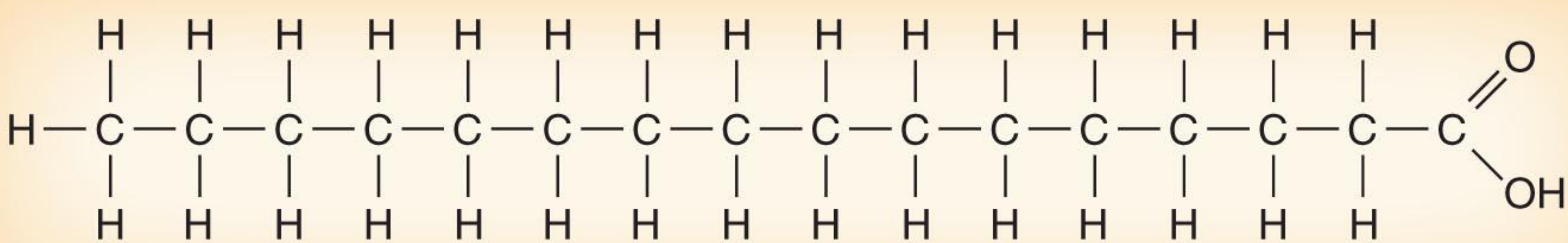
Fatty Acids Cannot Form Glucose

- There is no metabolic pathway to convert acetyl CoA into pyruvate
  - Cells cannot convert acetyl CoA to glucose
  - Impossible for fatty acids to feed into glucose production

Glucose



16-carbon fatty acid (palmitate)



Ketone Synthesis

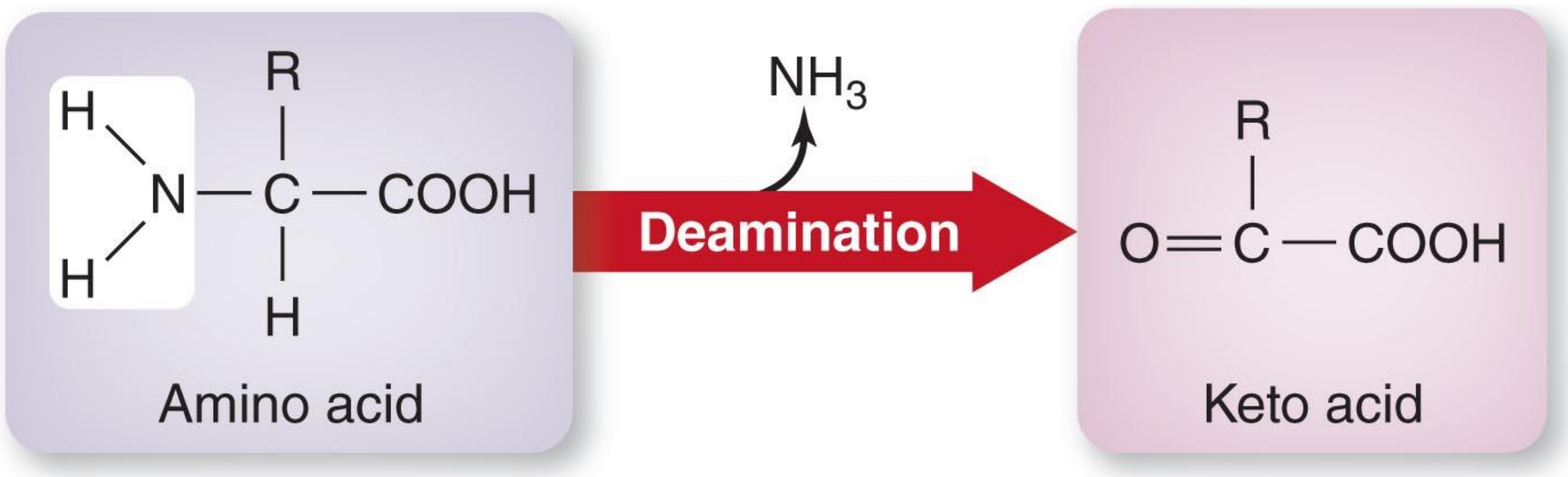
- *Ketones* are by-products of fat catabolism
- *Ketosis* occurs when ketones (acidic) inappropriately lower blood pH
- *Ketoacidosis* occurs when blood pH falls, further resulting in severe dehydration
- Production of energy from ketones is metabolically inefficient
- Ketone production is a back-up source of energy for carbohydrate-deprived cells

Energy from Protein

- The body preferentially uses fat and carbohydrate as fuel sources
- Protein is saved for metabolic functions that cannot be performed by other compounds
- Protein is used for fuel primarily when total energy or carbohydrate intake is low

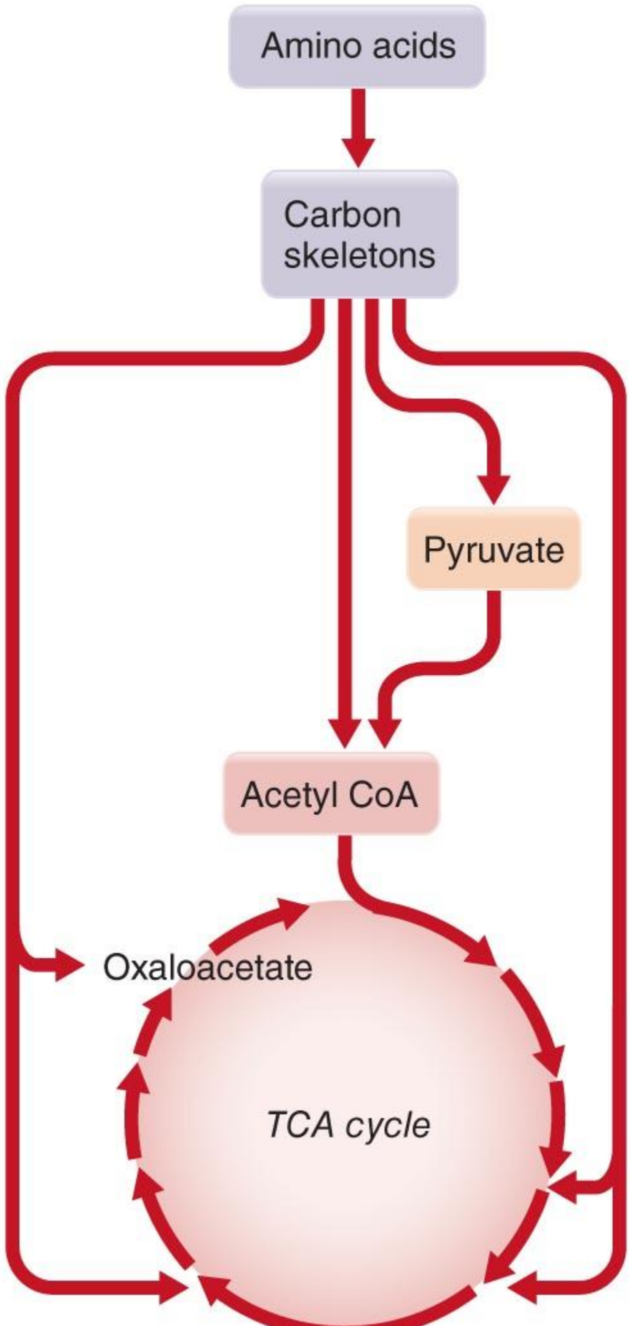
Energy from Protein (cont.)

- **Proteolysis**: dietary proteins are digested into amino acids or small peptides
- Amino acids are transported to the liver
  - Made into proteins
  - Released into the blood for uptake by other cells for building and repair functions
- Excess dietary protein
  - Used for energy or stored as triglycerides

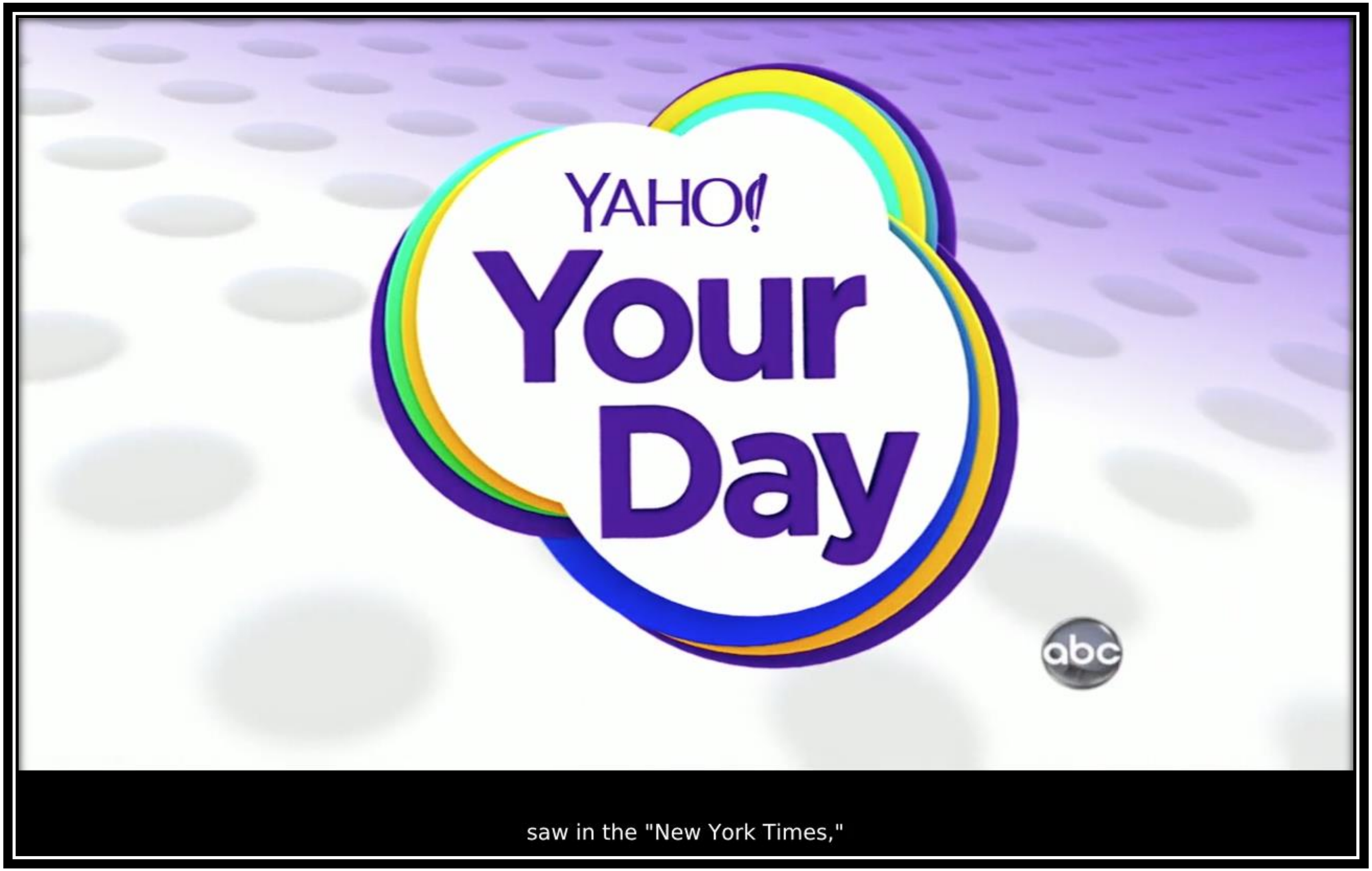

R
H
N
C
COOH
H
H
Amino acid
NH_3
Deamination
R
O
C
COOH
Keto acid

Energy from Protein (cont.)

- During *starvation*, the body turns to its own tissues for energy
- *Deamination*: amine group is removed from amino acid; end products are carbon skeleton and ammonia
- Ammonia is used as nitrogen source for synthesis of nonessential amino acids
  - High levels are toxic
  - Liver converts ammonia to less toxic urea

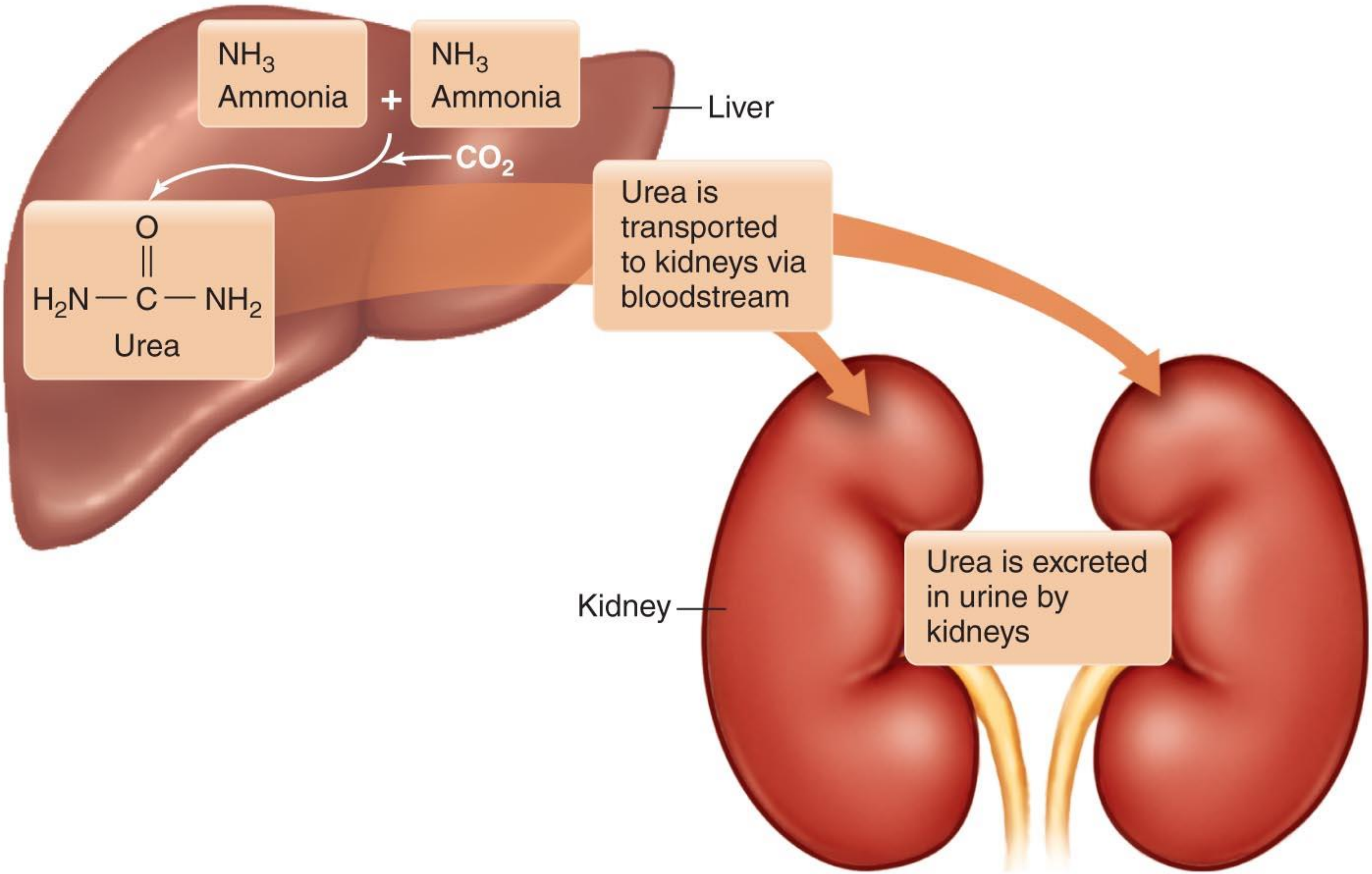

Amino acids
Carbon skeletons
Pyruvate
Acetyl CoA
Oxaloacetate
TCA cycle

ABC News Video: Could Chocolate Milk be the Perfect Post-Workout Drink?



Alcohol Oxidation

- Alcohol is oxidized primarily in the liver by enzymes:
  - Alcohol dehydrogenase (ADH)
  - Aldehyde dehydrogenase (ALDH)
  - Microsomal ethanol oxidizing system (MEOS)


NH_3
Ammonia
+
NH_3
Ammonia
Liver
CO_2
O
H_2N — C — NH_2
Urea
Urea is transported to kidneys via bloodstream
Urea is excreted in urine by kidneys
Kidney

Alcohol Oxidation (cont.)

- *First-pass metabolism:* small amount of alcohol is oxidized in the stomach, before being absorbed into the bloodstream
- Gastric **alcohol dehydrogenase (ADH)** activity
  - Reduces alcohol absorption
  - Genetic differences in amount of activity

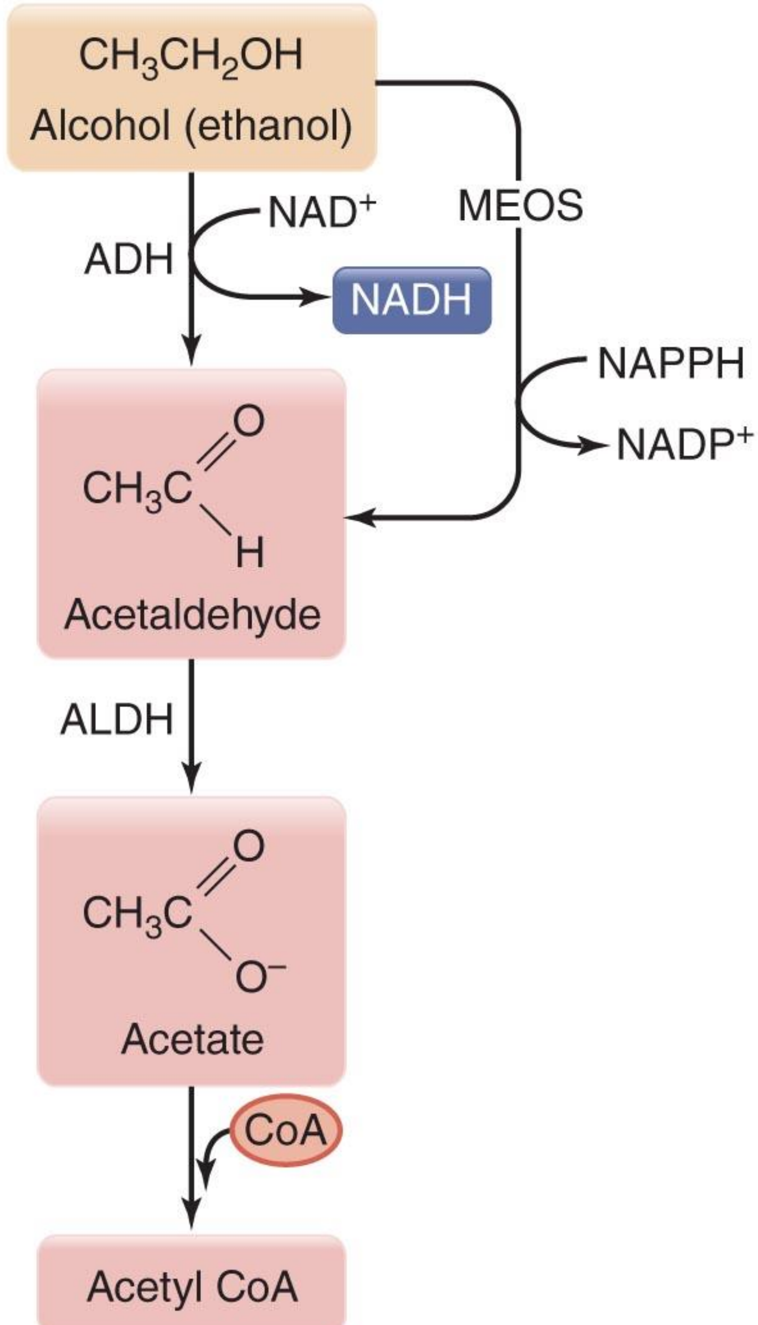

CH_3CH_2OH
Alcohol (ethanol)
ADH
NAD^+
NADH
MEOS
NAPPH
$NADP^+$
CH_3C
O
H
Acetaldehyde
ALDH
CH_3C
O
O^-
Acetate
CoA
Acetyl CoA

TABLE 7.1 Extraction of Energy from Carbohydrate, Triglycerides, Protein, and Alcohol

Nutrient	Yields Energy as ATP?	Oxidative End Products?	Feeds into Glucose Production?	Feeds into Nonessential Amino Acid Production?	Feeds into Fatty Acid Production and Storage as Triglycerides?
Carbohydrate (glucose)	Yes	CO_2, H_2O	Yes	Yes, if source of nitrogen is available	Yes, although process is inefficient
Triglycerides: fatty acids	Yes	CO_2, H_2O	No	No	Yes
Triglycerides: glycerol	Yes	CO_2, H_2O	Yes, if carbohydrate is unavailable to cells	Yes, if source of nitrogen is available	Yes
Protein (amino acids)	Yes	CO_2, H_2O, N as urea	Yes, if carbohydrate is unavailable to cells	Yes	Yes
Alcohol	Yes	CO_2, H_2O	No	No	Yes

Alcohol Absorption

- Most is absorbed into the blood and transported to be oxidized by the liver
- Liver typically oxidizes alcohol at a constant rate (about 1 drink per hour)
- This rate varies with the individual's genetic profile, state of health, body size, use of medication, and nutritional status
- Excess alcohol goes back into the blood

ALCOHOL IMPAIRMENT CHART

FEMALE

Approximate blood alcohol concentration

Drinks	90	100	120	140	160	180	200	220	240	
	Body Weight in Pounds									
0	.00	.00	.00	.00	.00	.00	.00	.00	.00	ONLY SAFE DRIVING LIMIT
1	.05	.05	.04	.03	.03	.03	.02	.02	.02	Impairment Begins
2	.10	.09	.08	.07	.06	.05	.05	.04	.04	Driving Skills Affected / Possible Criminal Penalties
3	.15	.14	.11	.10	.09	.08	.07	.06	.06	
4	.20	.18	.15	.13	.11	.10	.09	.08	.08	Legally Intoxicated / Criminal Penalties
5	.25	.23	.19	.16	.14	.13	.11	.10	.09	
6	.30	.27	.23	.19	.17	.15	.14	.12	.11	
7	.35	.32	.27	.23	.20	.18	.16	.14	.13	
8	.40	.36	.30	.26	.23	.20	.18	.17	.15	
9	.45	.41	.34	.29	.26	.23	.20	.19	.17	
10	.51	.45	.38	.32	.28	.25	.23	.21†	.19	

MALE

Approximate blood alcohol concentration

Drinks	100	120	140	160	180	200	220	240	
	Body Weight in Pounds								
0	.00	.00	.00	.00	.00	.00	.00	.00	ONLY SAFE DRIVING LIMIT
1	.04	.03	.03	.02	.02	.02	.02	.02	Impairment Begins
2	.08	.06	.05	.05	.04	.04	.03	.03	Driving Skills Affected / Possible Criminal Penalties
3	.11	.09	.08	.07	.06	.06	.05	.05	
4	.15	.12	.11	.09	.08	.08	.07	.06	
5	.19	.16	.13	.12	.11	.09	.09	.08	Legally Intoxicated / Criminal Penalties
6	.23	.19	.16	.14	.13	.11	.10	.09	
7	.26	.22	.19	.16	.15	.13	.12	.11	
8	.30	.25	.21	.19	.17	.15	.14	.13	
9	.34	.28	.24	.21	.19	.17	.15	.14	
10	.38	.31	.27	.23	.21	.19	.17	.16	

Your body can get rid of one drink per hour. Each 1.5 oz of 80 proof liquor, 12 oz of beer or 5 oz of table wine = 1 drink.

Stored Energy

- Stored energy can be used during times of sleep, fasting, or exercise
- Extra energy is stored as
  - Carbohydrate in *limited* amounts as liver and muscle glycogen
  - Fat (triglycerides) in *unlimited* amounts
- The body has no mechanism for storing amino acids or nitrogen

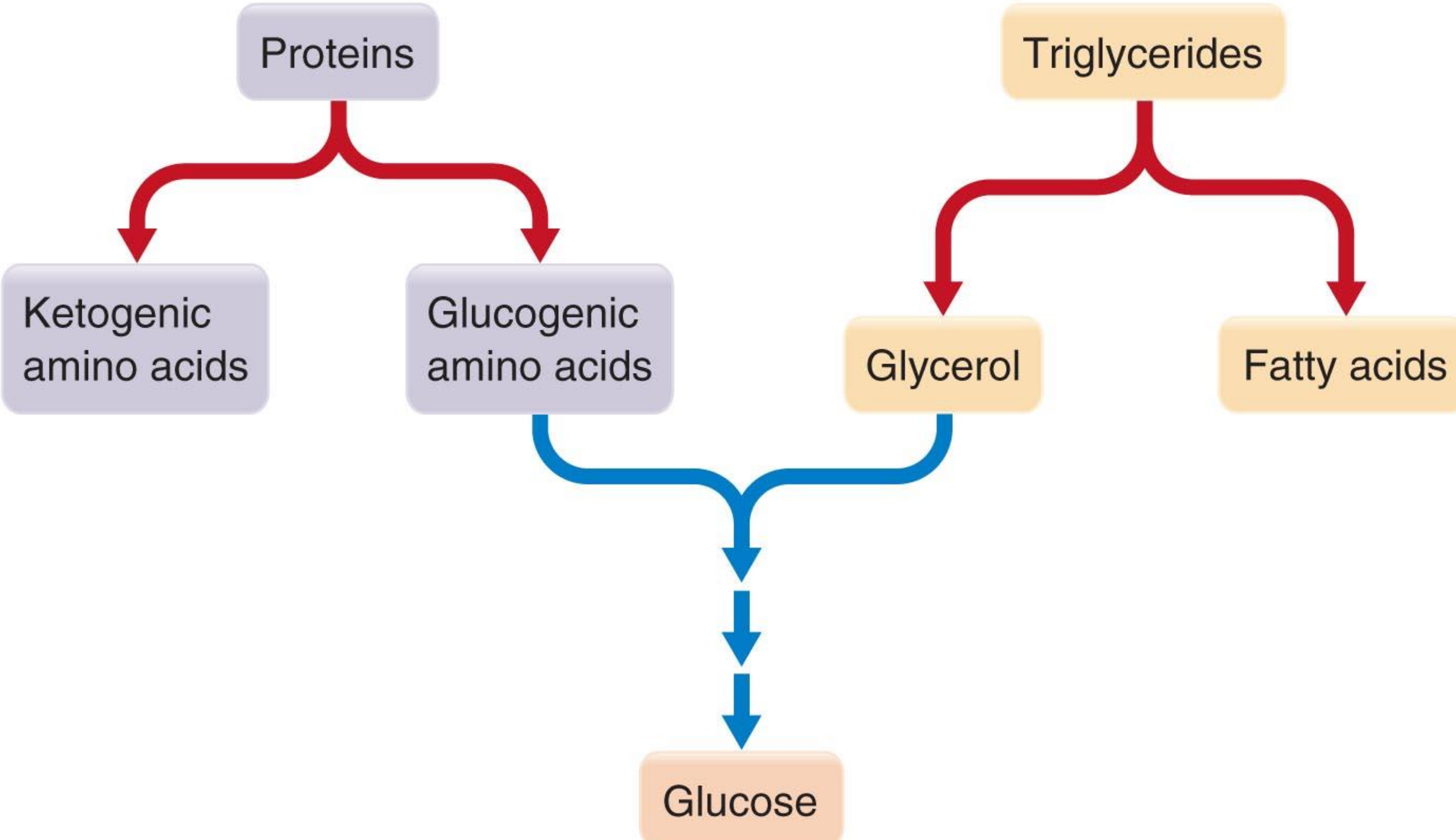
TABLE 7.2 Body Energy Reserves of a Well-Nourished 70-kg* Male

	Triglycerides	Glycogen	Protein
Weight	15 kg	0.2 kg	6 kg
Kilocalories	135,000	800	24,000

*70 kg equals about 154 lb.

Synthesizing Macronutrients

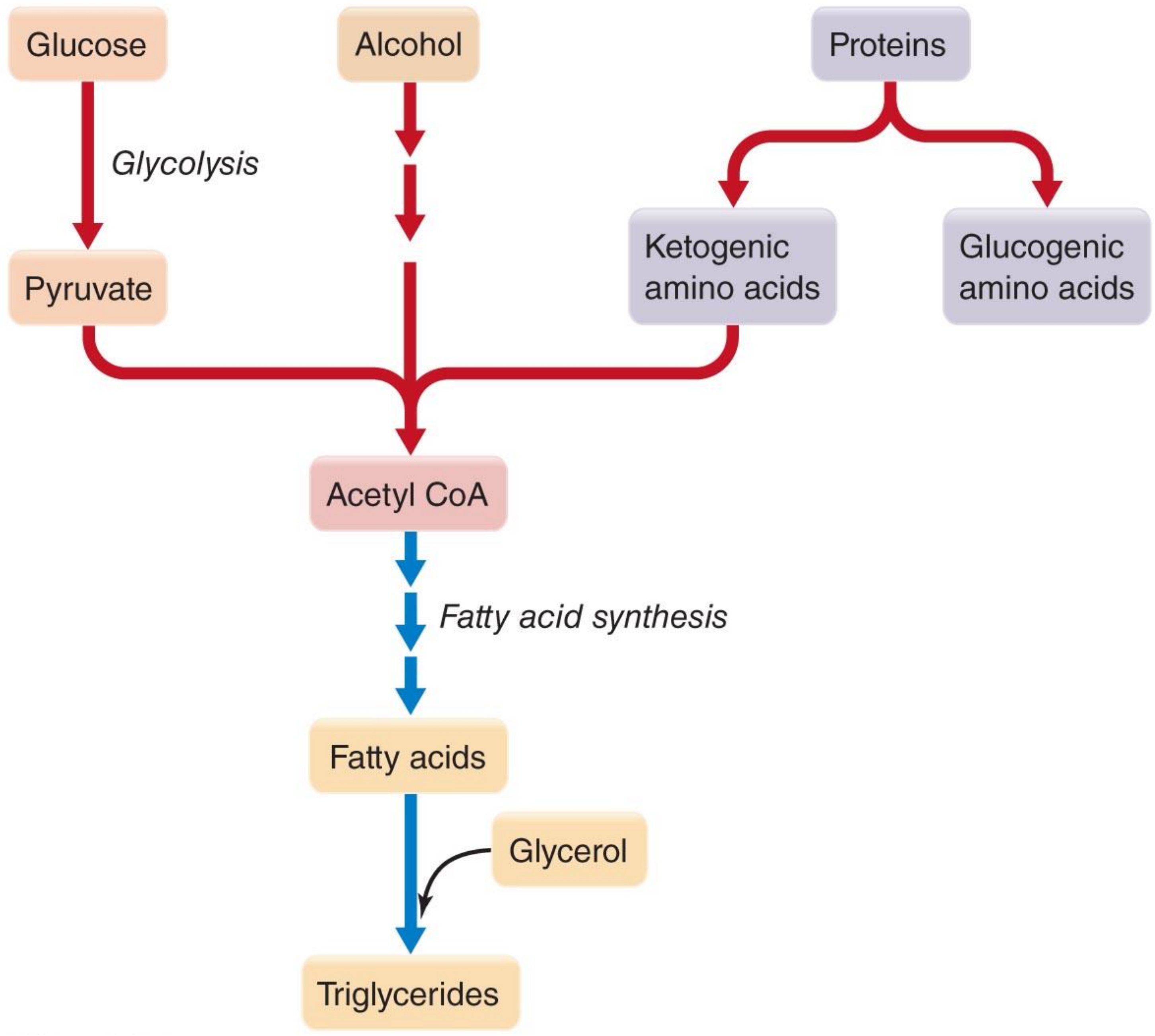
- **Gluconeogenesis**: making new glucose from noncarbohydrate precursors
  - Primarily from glucogenic amino acids
  - Small amount from glycerol (triglyceride)
  - Maintains blood glucose during sleep, fasting, trauma, and exercise
- *Protein catabolism* for glucose production can draw on vital tissue proteins (skeletal and heart muscles and organ proteins)



Proteins
Triglycerides
Ketogenic amino acids
Glucogenic amino acids
Glycerol
Fatty acids
Glucose

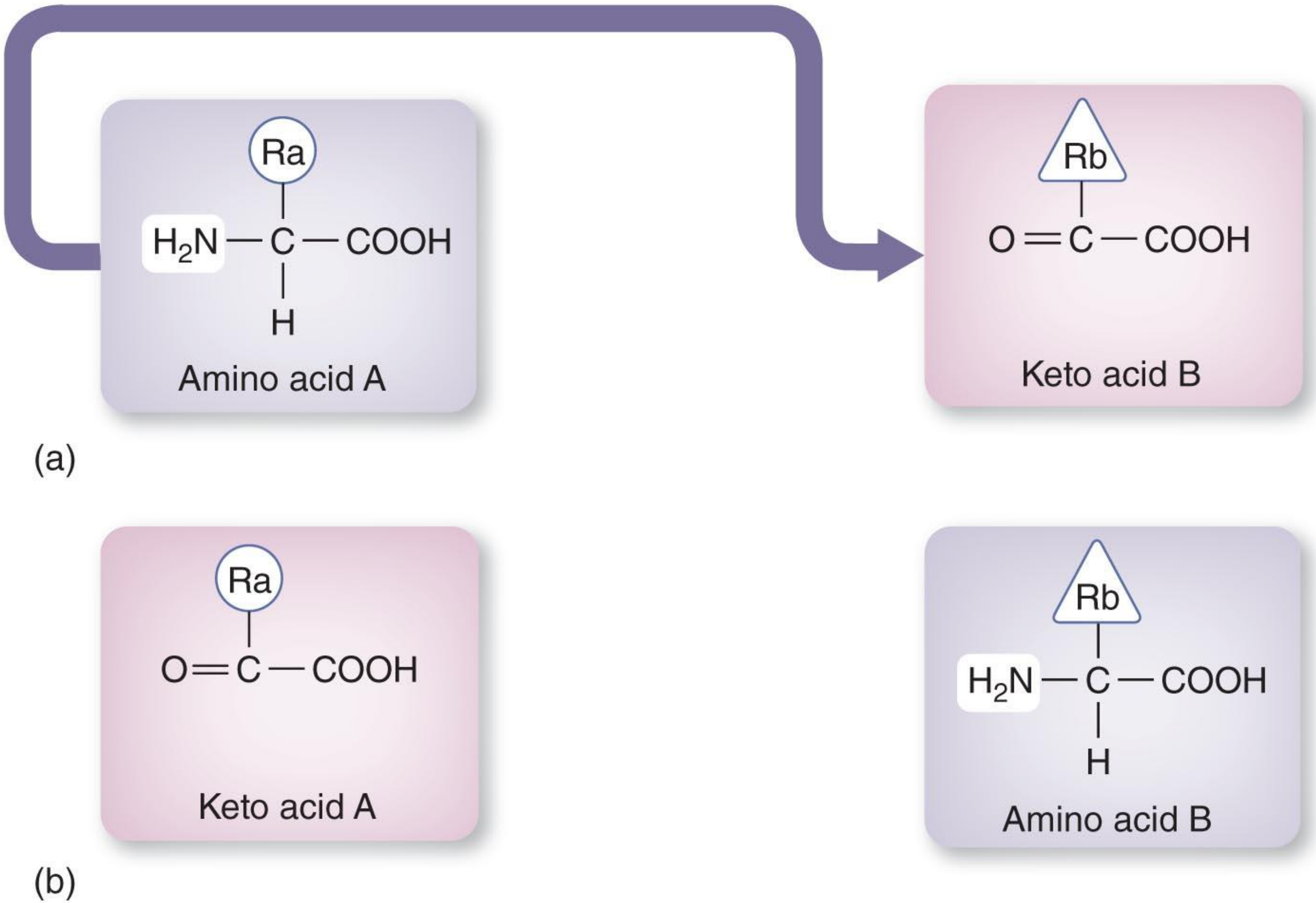
Synthesizing Macronutrients (cont.)

- **Lipogenesis (de novo synthesis):** production of fat from nonfat substances such as carbohydrates, ketogenic amino acids, and alcohol
  - When consuming excess calories, acetyl CoA units form fatty acid chains
  - Fatty acids combine with glycerol to form triglycerides
  - Mostly occurs in liver cells


Glucose
Alcohol
Proteins
Glycolysis
Pyruvate
Ketogenic amino acids
Glucogenic amino acids
Acetyl CoA
Fatty acid synthesis
Fatty acids
Glycerol
Triglycerides

Synthesizing Macronutrients

- Amino acid synthesis
  - The body makes the carbon skeleton of nonessential amino acids (NEAA)
  - Amine group comes from *transamination*
  - Synthesis of NEAA occurs only when the body has enough energy and nitrogen
  - Since essential amino acids cannot be synthesized, they must be consumed


Ra
H_2N—C—COOH
H
Amino acid A
Rb
O═C—COOH
Keto acid B
(a)
Ra
O═C—COOH
Keto acid A
Rb
H_2N—C—COOH
H
Amino acid B
(b)

Hormones Regulate Metabolism

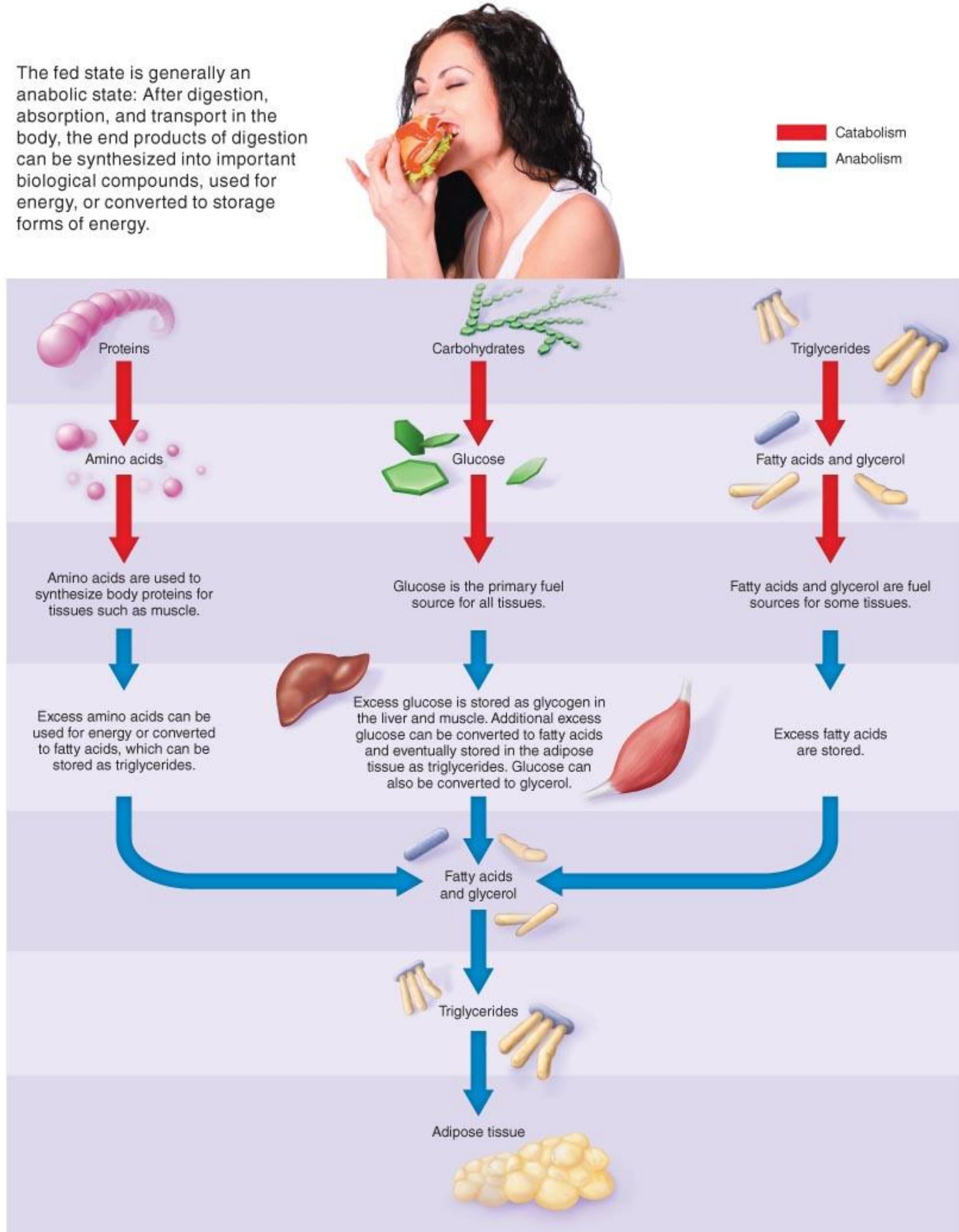
- Insulin is the primary *anabolic* hormone
  - Increases in the blood after a meal
  - Activates storage enzymes
  - Signals cellular uptake of glucose, fatty acids, and amino acids
- Glucagon, epinephrine, and cortisol are *catabolic* hormones
  - Trigger the breakdown of stored triglycerides, glycogen, and body protein for energy

TABLE 7.3 Hormonal Regulation of Metabolism

Metabolic State	Hormone	Site of Secretion	Role in Carbohydrate Metabolism	Role in Lipid Metabolism	Role in Protein Metabolism	Overall Metabolic Effect
Fed	Insulin	Pancreatic beta cells	Increases cell uptake of glucose Increases glycogen synthesis	Increases synthesis and storage of triglycerides	Increases cell uptake of amino acids and protein synthesis	Anabolic
Fasted	Glucagon	Pancreatic alpha cells	Increases glycogen degradation Increases gluconeogenesis	Increases lipolysis	Increases degradation of proteins	Catabolic
Exercise	Epinephrine	Adrenal medulla	Increases glycogen degradation	Increases lipolysis	No significant effect	Catabolic
Stress	Cortisol	Adrenal cortex	Decreases cell uptake of glucose Increases gluconeogenesis	Increases lipolysis	Decreases cell uptake of amino acids Increases degradation of proteins	Catabolic

Metabolic Responses to Feeding

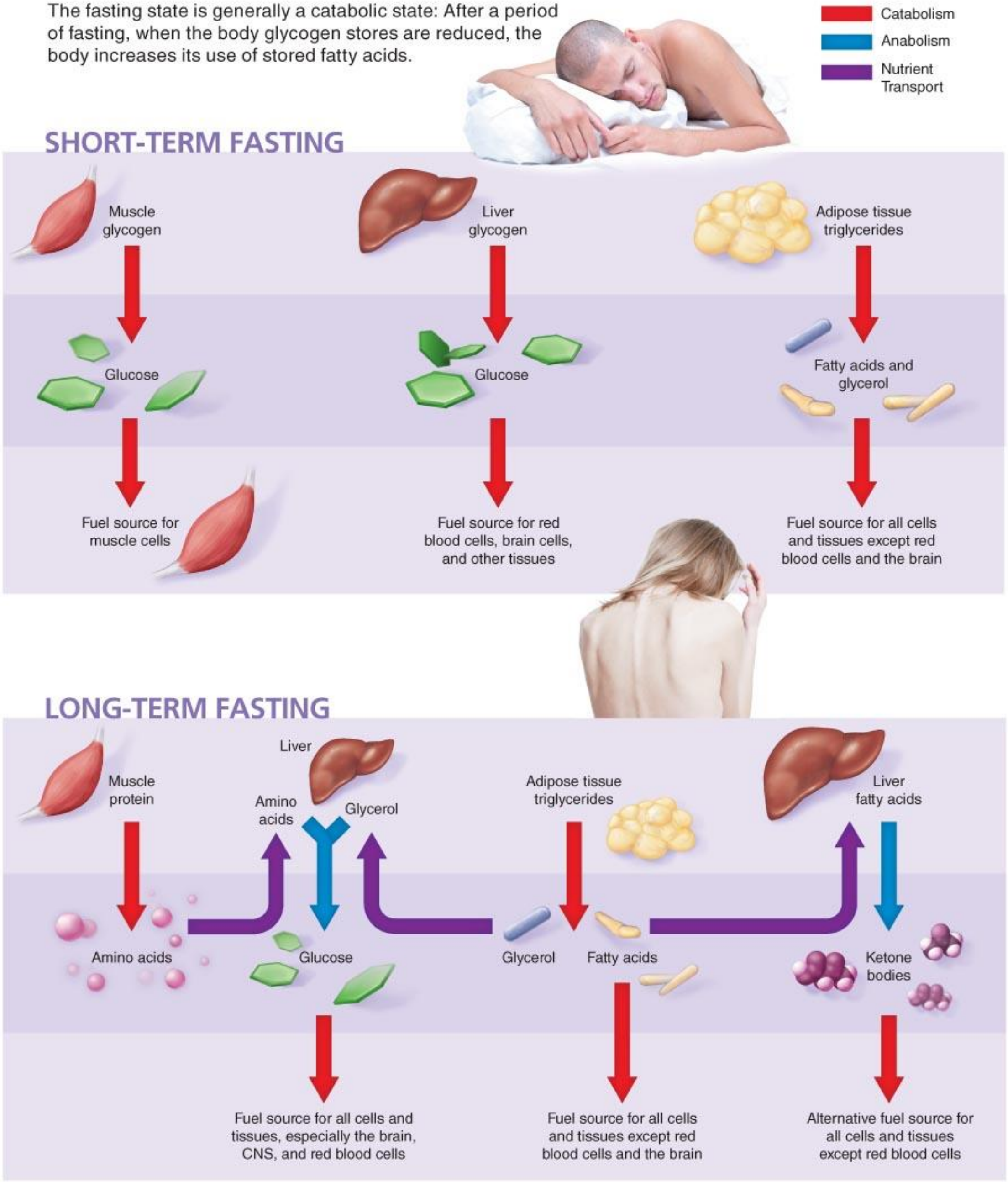
- *Anabolic state*: bloodstream is enriched with glucose, fatty acids, and amino acids
  - Glucose is stored as glycogen
  - When glycogen stores are saturated, remaining glucose is stored as triglycerides
  - Fatty acids are stored as triglycerides mostly in adipose tissues
  - Amino acids are deaminated and carbon skeletons are converted to fatty acids for storage as triglycerides


The fed state is generally an anabolic state: After digestion, absorption, and transport in the body, the end products of digestion can be synthesized into important biological compounds, used for energy, or converted to storage forms of energy.
Catabolism
Anabolism
Proteins
Carbohydrates
Triglycerides
Amino acids
Glucose
Fatty acids and glycerol
Amino acids are used to synthesize body proteins for tissues such as muscle.
Glucose is the primary fuel source for all tissues.
Fatty acids and glycerol are fuel sources for some tissues.
Excess amino acids can be used for energy or converted to fatty acids, which can be stored as triglycerides.
Excess glucose is stored as glycogen in the liver and muscle. Additional excess glucose can be converted to fatty acids and eventually stored in the adipose tissue as triglycerides. Glucose can also be converted to glycerol.
Excess fatty acids are stored.
Fatty acids and glycerol
Triglycerides
Adipose tissue

Metabolic Responses to Short-Term Fasting

- Liver glycogen is broken down, releasing glucose into the blood
- Most cells can switch to using fatty acids as fuel to conserve glucose for brain and other cells that rely on glucose as fuel
- Ketones form as acetyl CoA units are blocked from entering TCA cycle
- Glucose synthesis from glucogenic amino acids and glycerol

The fasting state is generally a catabolic state: After a period of fasting, when the body glycogen stores are reduced, the body increases its use of stored fatty acids.



Metabolic Responses to Starvation

- The body shifts to survival mode
- Blood glucose is maintained to support brain and red blood cells
- Decline in activity, body temperature, and resting metabolic rate
- Fatty acids become the primary fuel
- Brain cells start to use ketone bodies
- Muscle (skeletal, cardiac) and organ proteins supplies glucose

LONG-TERM FASTING