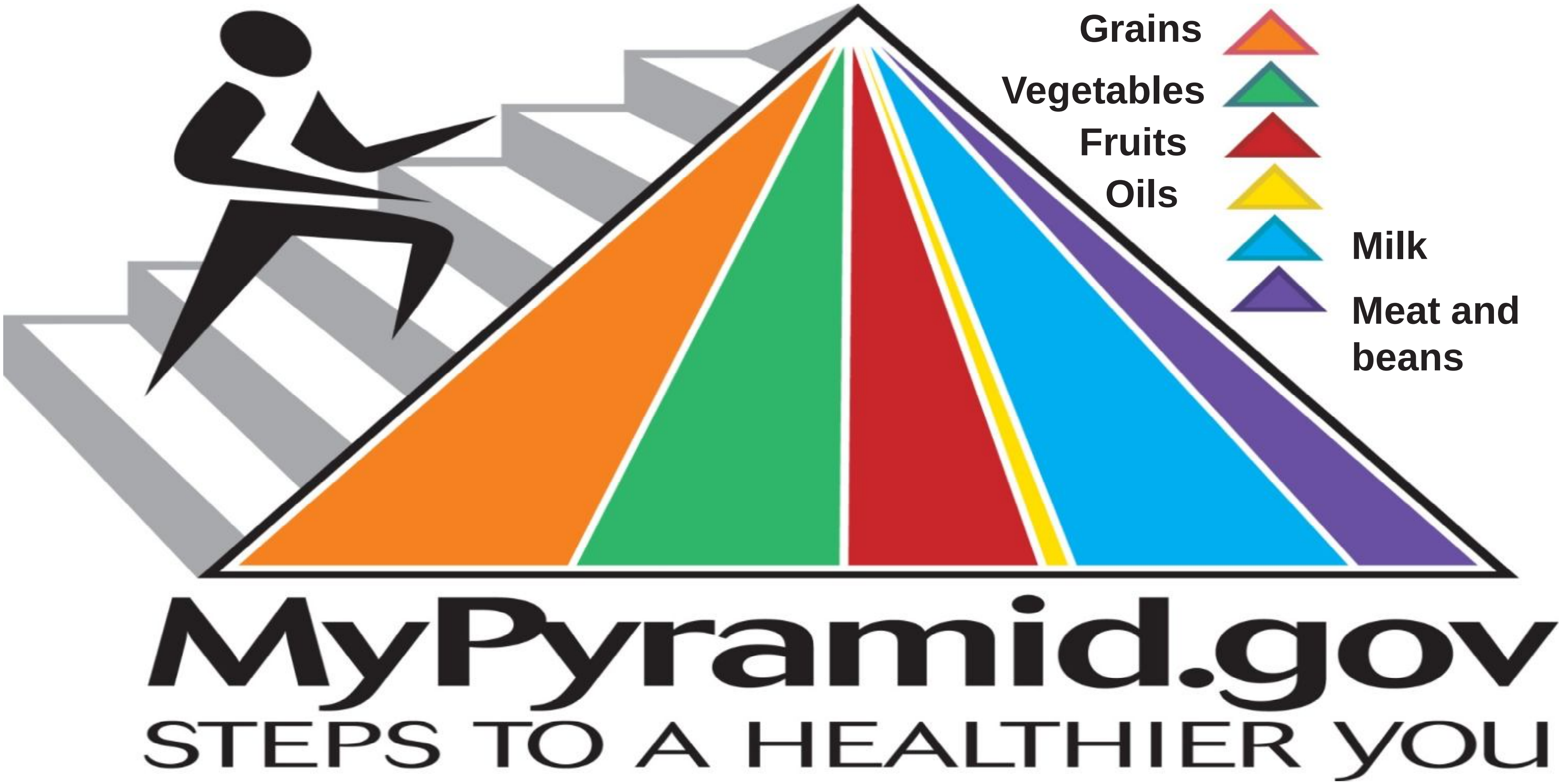
Do not salivate on your self

NUTRITION, METABOLISM,

D.HAMMOUDI.MD

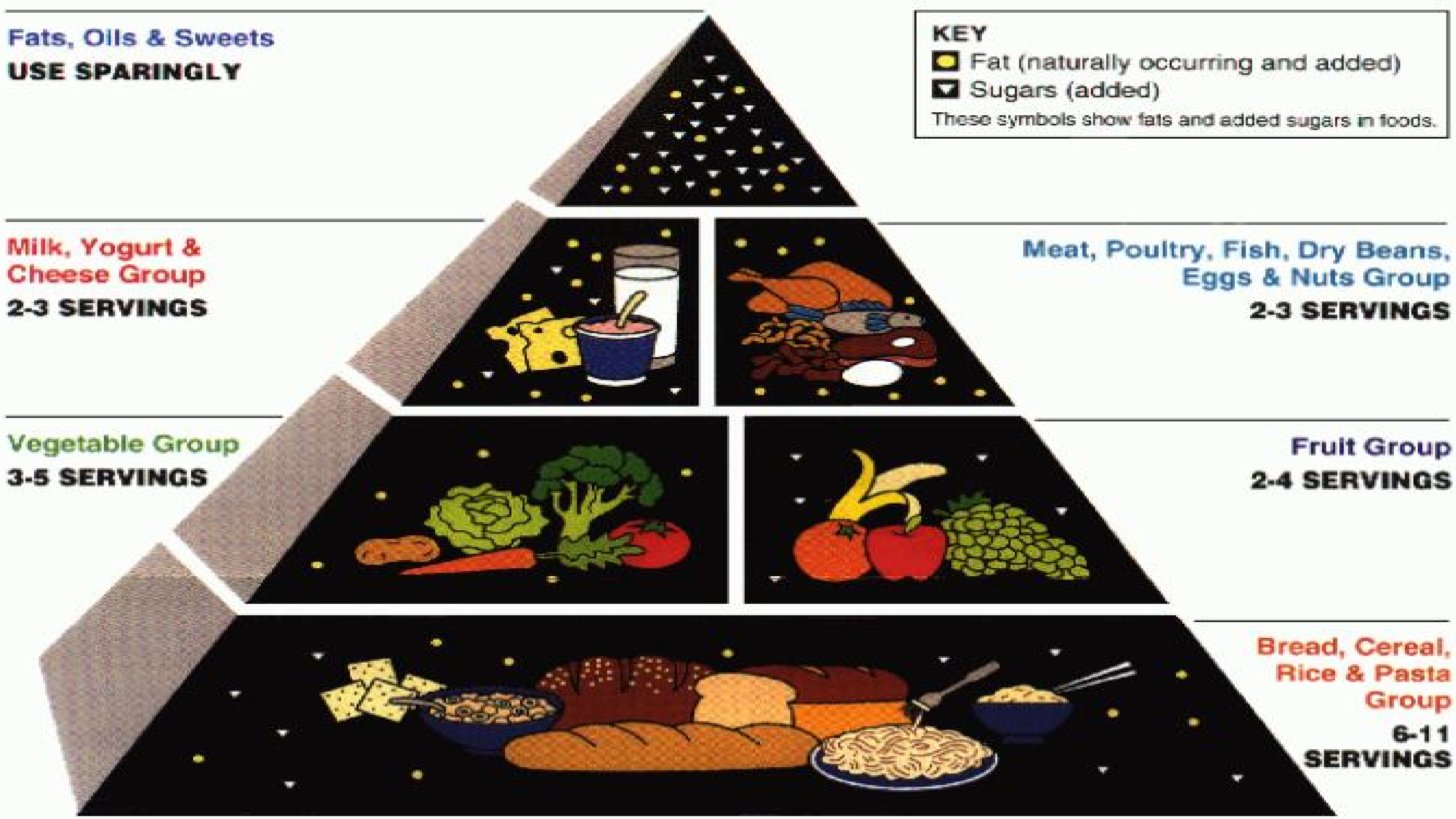
Nutrition

- Nutrient: a substance in food that promotes normal growth, maintenance, and repair
- Major nutrients
  - Carbohydrates, lipids, and proteins
- Other nutrients
  - Vitamins and minerals (and, technically speaking, water)



(a) USDA food guide pyramid

Figure 24.1a

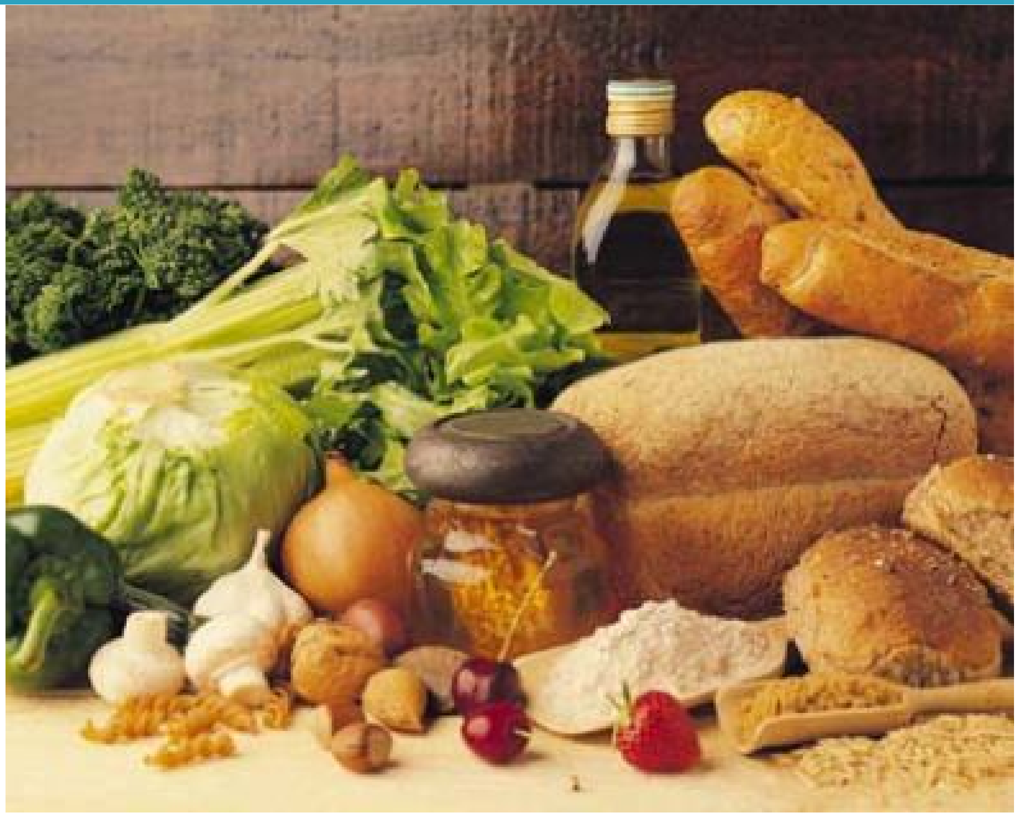


Fats, Oils & Sweets
USE SPARINGLY
KEY
Fat (naturally occurring and added)
Sugars (added)
These symbols show fats and added sugars in foods.
Milk, Yogurt & Cheese Group
2-3 SERVINGS
Meat, Poultry, Fish, Dry Beans, Eggs & Nuts Group
2-3 SERVINGS
Vegetable Group
3-5 SERVINGS
Fruit Group
2-4 SERVINGS
Bread, Cereal, Rice & Pasta Group
6-11 SERVINGS

Digestion

- Carbohydrate digestion starts in the mouth
- Protein digestion starts in the stomach
- Nucleic acids & fats start in the small intestine
- Everything completely digested and absorbed by the end of the small intestine

Carbohydrates



General characteristics

- the term carbohydrate is derived from the french: hydrate de carbone
- compounds composed of C, H, and O
- $(CH_2O)_n$ when n = 5 then $C_5H_{10}O_5$
- not all carbohydrates have this empirical formula: deoxysugars, aminosugars
- carbohydrates are the most abundant compounds found in nature (cellulose: 100 billion tons annually)

General characteristics

- Most carbohydrates are found naturally in bound form rather than as simple sugars
  - Polysaccharides (starch, cellulose, inulin, gums)
  - Glycoproteins and proteoglycans (hormones, blood group substances, antibodies)
  - Glycolipids (cerebrosides, gangliosides)
  - Glycosides
  - Mucopolysaccharides (hyaluronic acid)
  - Nucleic acids

Carbohydrates=4cal

- Dietary sources
  - Starch (complex carbohydrates) in grains and vegetables
  - Sugars in fruits, sugarcane, sugar beets, honey and milk
  - Insoluble fiber: cellulose in vegetables; provides roughage
  - Soluble fiber: pectin in apples and citrus fruits; reduces blood cholesterol levels

Carbohydrates

- Uses
  - Glucose is the fuel used by cells to make ATP
    - Neurons and RBCs rely almost entirely upon glucose
    - Excess glucose is converted to glycogen or fat and stored

Carbohydrates

- Dietary requirements
  - Minimum 100 g/day to maintain adequate blood glucose levels
  - Recommended minimum 130 g/day
  - Recommended intake: 45–65% of total calorie intake; mostly complex carbohydrates

Functions

- sources of energy
- intermediates in the biosynthesis of other basic biochemical entities (fats and proteins)
- associated with other entities such as glycosides, vitamins and antibiotics)
- form structural tissues in plants and in microorganisms (cellulose, lignin, murein)
- participate in biological transport, cell-cell recognition, activation of growth factors, modulation of the immune system

Sugar	Relative Sweetness	Type
Lactose	0.16	Disaccharide
Galactose	0.22	Monosaccharide
Maltose	0.32	Disaccharide
Xylose	0.40	Monosaccharide
Glucose	0.74	Monosaccharide
Sucrose	1.00	Disaccharide
Invert sugar	1.30	Mixture of glucose and fructose
Fructose	1.73	Monosaccharide

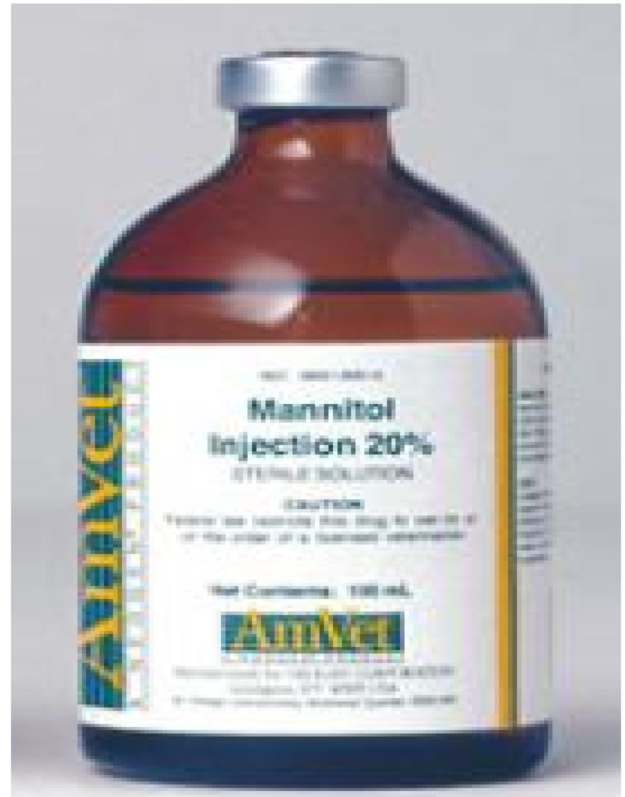
Classification of carbohydrates

- Monosaccharides (monoses or glycoses)
  - Trioses, tetroses, pentoses, hexoses
- Oligosaccharides
  - Di, tri, tetra, penta, up to 9 or 10
  - Most important are the disaccharides
- Polysaccharides or glycans
  - Homopolysaccharides
  - Heteropolysaccharides
  - Complex carbohydrates

Monosaccharides

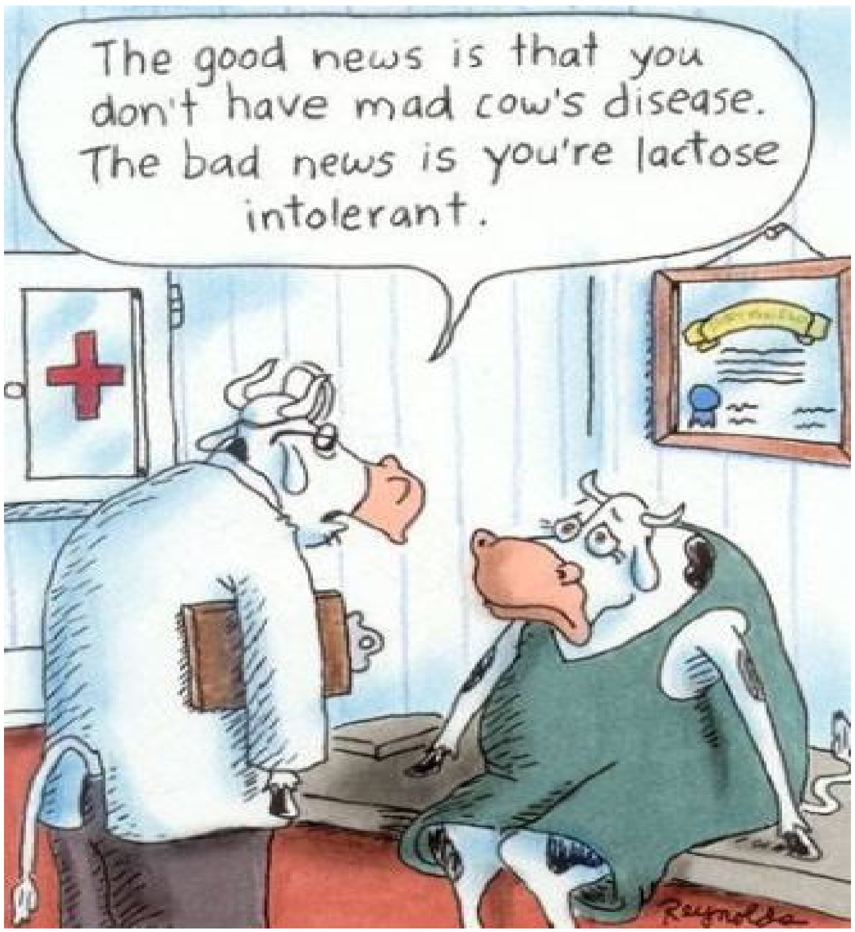
- also known as simple sugars
- classified by 1. the number of carbons and 2. whether aldoses or ketoses
- most (99%) are straight chain compounds
- D-glyceraldehyde is the simplest of the aldoses (aldotriose)
- all other sugars have the ending <u>ose</u> (glucose, galactose, ribose, lactose, etc…)


Brite-Life
70% SORBITOL
SOLUTION USP


Mannitol
Injection 20%
STERILE SOLUTION
CAUTION
AmVet

Sugar cane

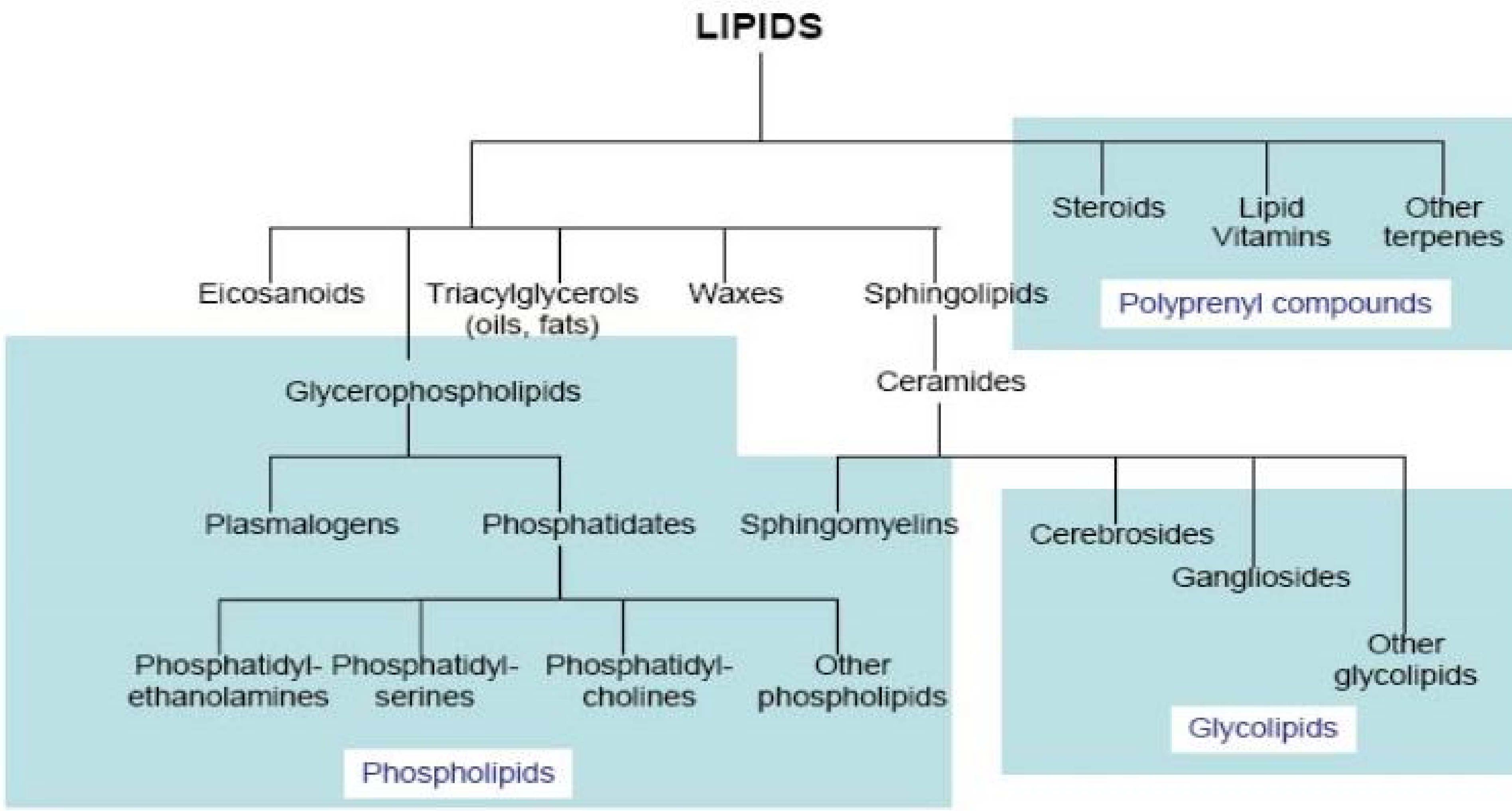
Sugar beet


The good news is that you don't have mad cow's disease. The bad news is you're lactose intolerant.
Reynolds


Lactaid
ORIGINAL
Strength
120 Caplets

Lipids


FREEZE!
HOMICIDE? BURGLARY?
WORSE. TRANS FAT.
RAISE YOUR HANDS AND STEP AWAY FROM THE CHICKEN.


LIPIDS
Eicosanoids
Triacylglycerols (oils, fats)
Waxes
Sphingolipids
Steroids
Lipid Vitamins
Other terpenes
Polyprenyl compounds
Glycerophospholipids
Ceramides
Plasmalogens
Phosphatidates
Sphingomyelins
Cerebrosides
Gangliosides
Other glycolipids
Phosphatidyl-ethanolamines
Phosphatidyl-serines
Phosphatidyl-cholines
Other phospholipids
Phospholipids
Glycolipids

Lipids=9cal

- Dietary sources
  - Triglycerides
    - Saturated fats in meat, dairy foods, and tropical oils
    - Unsaturated fats in seeds, nuts, olive oil, and most vegetable oils
  - Cholesterol in egg yolk, meats, organ meats, shellfish, and milk products

Lipids

- Essential fatty acids
  - Linoleic and linolenic acid, found in most vegetable oils
  - Must be ingested

Lipids

- Essential uses of lipids in the body
  - Help absorb fat-soluble vitamins
  - Major fuel of hepatocytes and skeletal muscle
  - Phospholipids are essential in myelin sheaths and all cell membranes

Lipids

- Functions of fatty deposits (adipose tissue)
  - Protective cushions around body organs
  - Insulating layer beneath the skin
  - Concentrated source of energy

Lipids

- Regulatory functions of prostaglandins
  - Smooth muscle contraction
  - Control of blood pressure
  - Inflammation
- Functions of cholesterol
  - Stabilizes membranes
  - Precursor of bile salts and steroid hormones

Lipids

- Dietary requirements suggested by the American Heart Association
  - Fats should represent 30% or less of total caloric intake
  - Saturated fats should be limited to 10% or less of total fat intake
  - Daily cholesterol intake should be no more than 300 mg

Lipid storage diseases

- also known as sphingolipidoses
- genetically acquired
- due to the deficiency or absence of a catabolic enzyme
- examples:
  - Tay Sachs disease
  - Gaucher's disease
  - Niemann-Pick disease
  - Fabry's disease

Proteins

Proteins

- Dietary sources
  - Eggs, milk, fish, and most meats contain complete proteins
  - Legumes, nuts, and cereals contain incomplete proteins (lack some essential amino acids)
  - Legumes and cereals together contain all essential amino acids

Proteins

- Uses
  - Structural materials: keratin, collagen, elastin, muscle proteins
  - Most functional molecules: enzymes, some hormones

Proteins

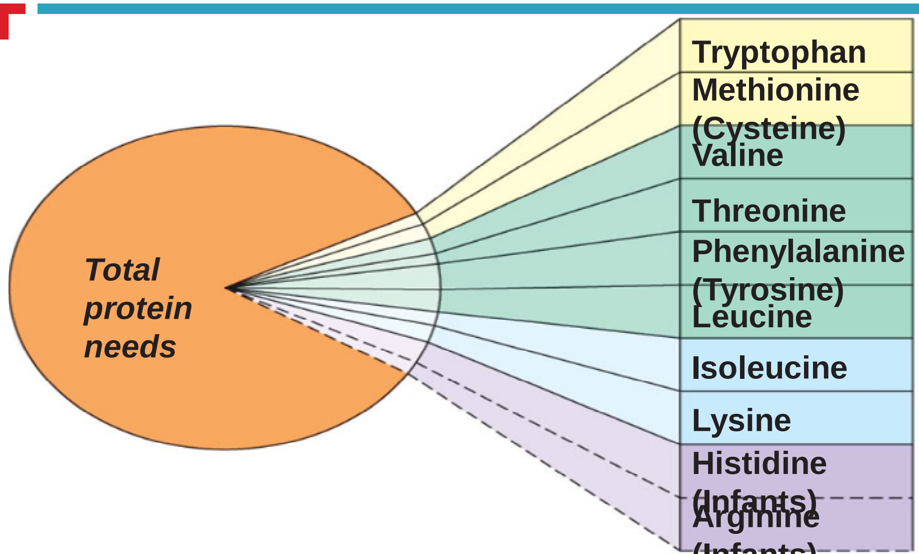
- Use of amino acids in the body
  1. All-or-none rule
     - All amino acids needed must be present for protein synthesis to occur
  2. Adequacy of caloric intake
     - Protein will be used as fuel if there is insufficient carbohydrate or fat available

Proteins

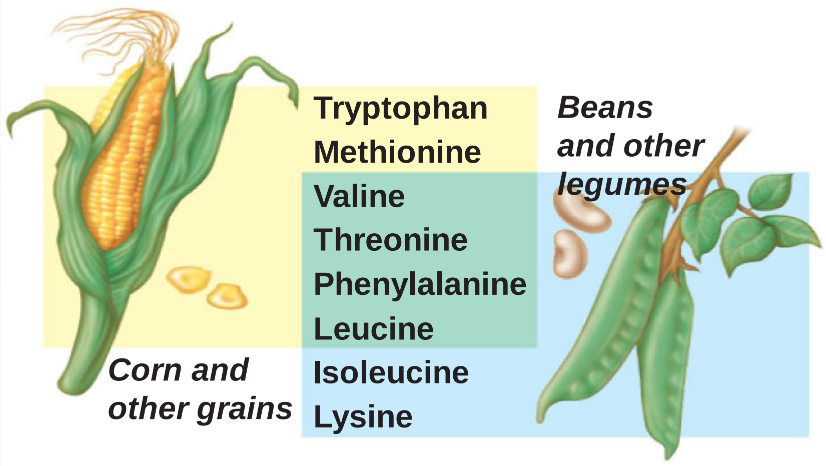
3. Nitrogen balance
   - State where the rate of protein synthesis equals the rate of breakdown and loss
   - Positive if synthesis exceeds breakdown (normal in children and tissue repair)
   - Negative if breakdown exceeds synthesis (e.g., stress, burns, infection, or injury)

Proteins

4. Hormonal controls
   - Anabolic hormones (GH, sex hormones) accelerate protein synthesis



(a) Essential amino acids



(b) Vegetarian diets providing the eight essential amino acids for humans

Figure 24.2

Proteins

- Dietary requirements
  - Rule of thumb: daily intake of 0.8 g per kg body weight

Vitamins

- Organic compounds
- Crucial in helping the body use nutrients
- Most function as coenzymes
- Vitamins D, some B, and K are synthesized in the body

Vitamins

- Two types, based on solubility
  1. Water-soluble vitamins
     - B complex and C are absorbed with water
     - B_{12} absorption requires intrinsic factor
     - Not stored in the body

Vitamins

2. Fat-soluble vitamins
   - A, D, E, and K are absorbed with lipid digestion products
   - Stored in the body, except for vitamin K
   - Vitamins A, C, and E act as antioxidants

Minerals

- Seven required in moderate amounts:
  - Calcium, phosphorus, potassium, sulfur, sodium, chloride, and magnesium
- Others required in trace amounts
- Work with nutrients to ensure proper body functioning
- Uptake and excretion must be balanced to prevent toxic overload

Minerals

- Examples
  - Calcium, phosphorus, and magnesium salts harden bone
  - Iron is essential for oxygen binding to hemoglobin
  - Iodine is necessary for thyroid hormone synthesis
  - Sodium and chloride are major electrolytes in the blood

Metabolism

- Metabolism: biochemical reactions inside cells involving nutrients
- Two types of reactions
  - Anabolism: synthesis of large molecules from small ones
  - Catabolism: hydrolysis of complex structures to simpler ones

Metabolism

- Cellular respiration: catabolism of food fuels and capture of energy to form ATP in cells
- Enzymes shift high-energy phosphate groups of ATP to other molecules (phosphorylation)
- Phosphorylated molecules are activated to perform cellular functions

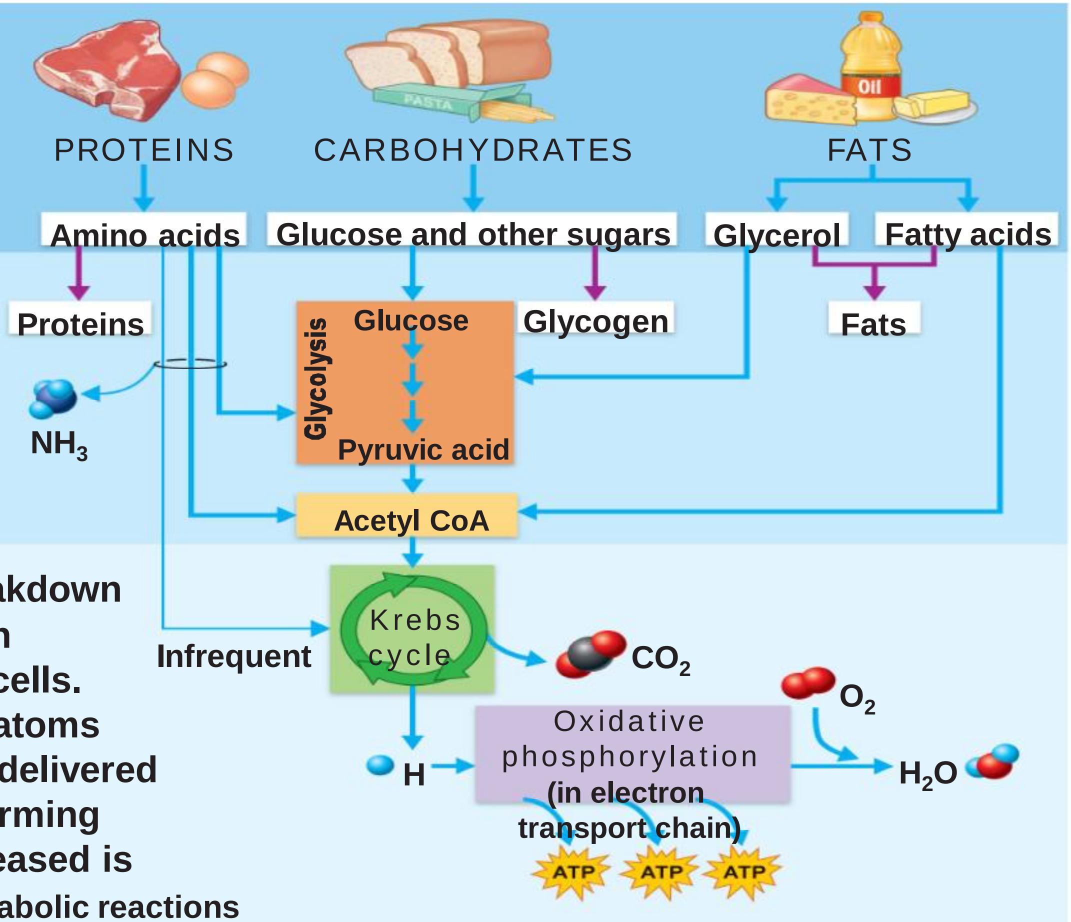
Stages of Metabolism

- Processing of nutrients
  1. Digestion, absorption and transport to tissues
  2. Cellular processing (in cytoplasm)
     - Synthesis of lipids, proteins, and glycogen, or
     - Catabolism (glycolysis) into intermediates
  3. Oxidative (mitochondrial) breakdown of intermediates into CO_2, water, and ATP

Stage 1 **Digestion in GI tract lumen to absorbable forms. Transport via blood to tissue cells.**

Stage 2 **Anabolism (incorporation into molecules) and catabolism of nutrients to form intermediates within tissue cells.**

Stage 3 **Oxidative breakdown of products of stage 2 in mitochondria of tissue cells. CO_2 is liberated, and H atoms removed are ultimately delivered to molecular oxygen, forming water. Some energy released is used to form ATP.**



Catabolic reactions

Anabolic reactions

Figure 24.3

Oxidation-Reduction (Redox) Reactions

- Oxidation; gain of oxygen or loss of hydrogen
- Oxidation-reduction (redox) reactions
  - Oxidized substances lose electrons and energy
  - Reduced substances gain electrons and energy

Oxidation-Reduction (Redox) Reactions

- Coenzymes act as hydrogen (or electron) acceptors
  - Nicotinamide adenine dinucleotide (NAD^+)
  - Flavin adenine dinucleotide (FAD)

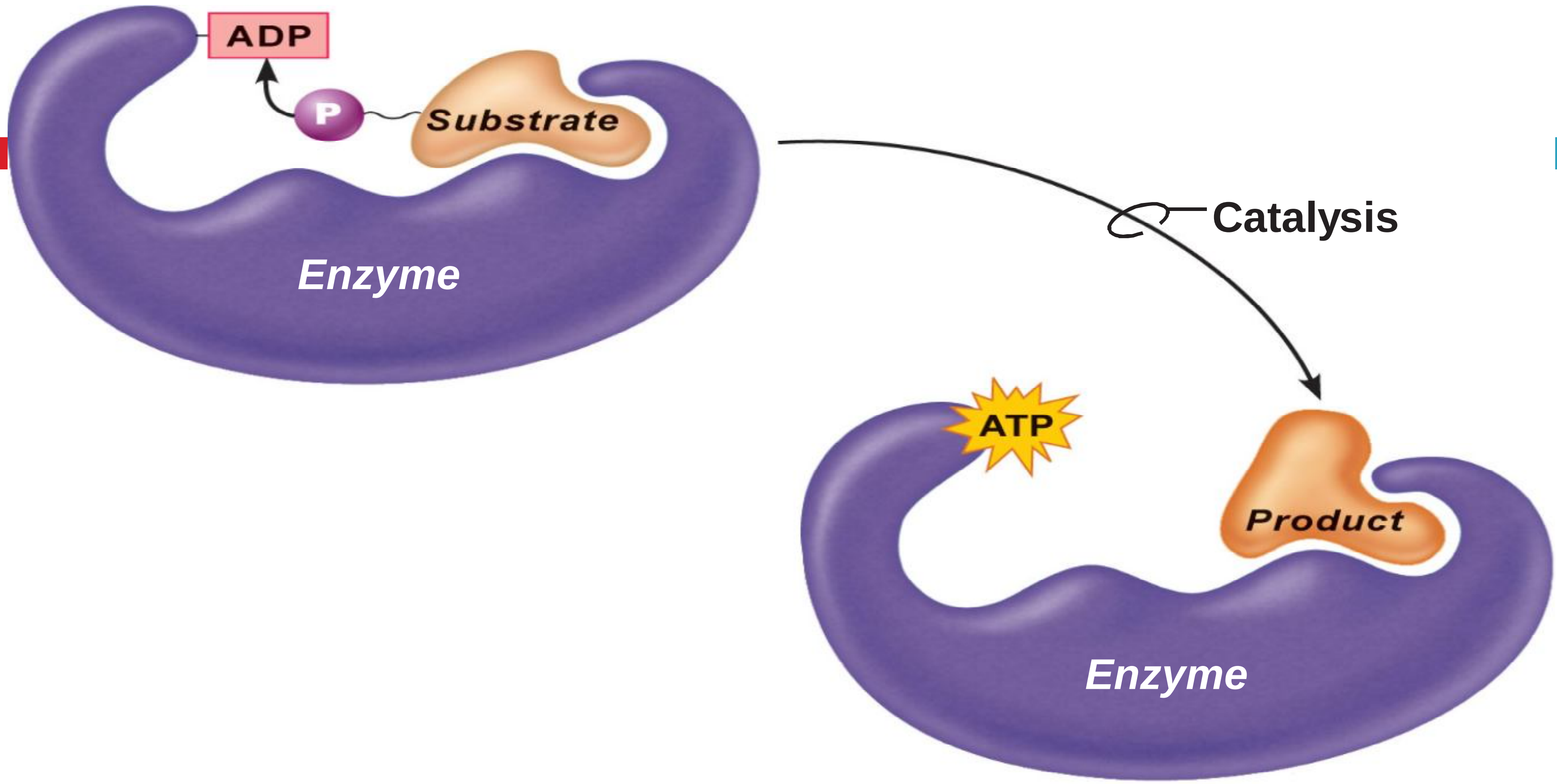
ATP Synthesis

- Two mechanisms

1. Substrate-level phosphorylation
2. Oxidative phosphorylation

Substrate-Level Phosphorylation

- High-energy phosphate groups directly transferred from phosphorylated substrates to ADP
- Occurs in glycolysis and the Krebs cycle



(a) Substrate-level phosphorylation

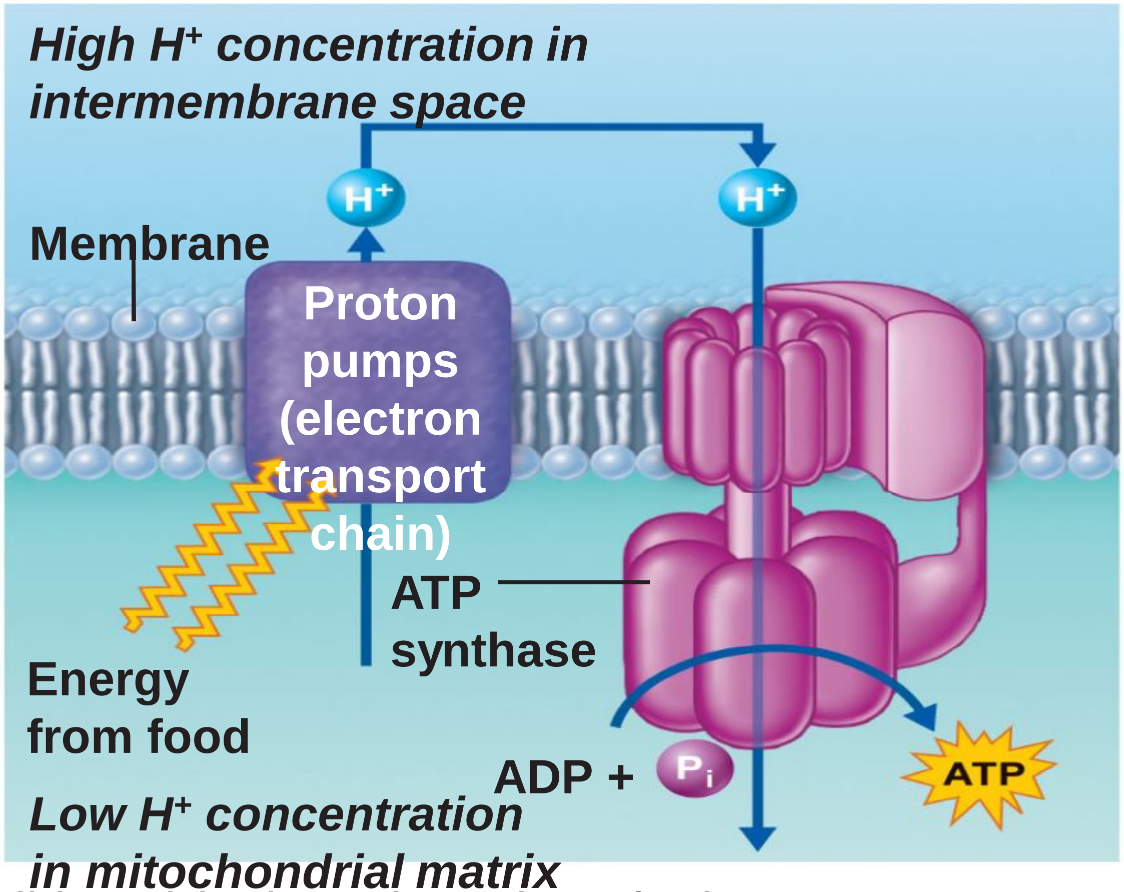
Figure 24.4a

Oxidative Phosphorylation

- Chemiosmotic process
  - Couples the movement of substances across a membrane to chemical reactions

Oxidative Phosphorylation

- In the mitochondria
  - Carried out by electron transport proteins
  - Nutrient energy is used to create H^+ gradient across mitochondrial membrane
  - H^+ flows through ATP synthase
  - Energy is captured and attaches phosphate groups to ADP



(b) Oxidative phosphorylation

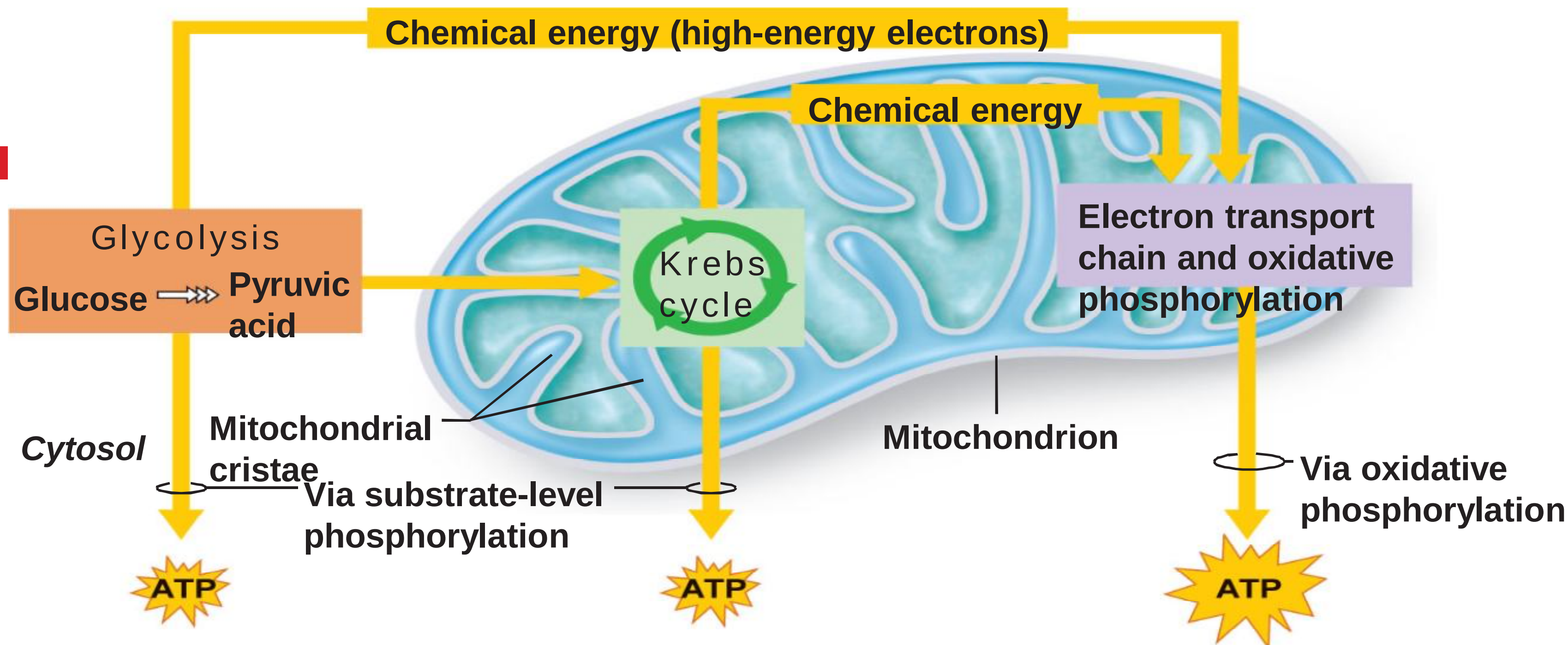
Figure 24.4b

Carbohydrate Metabolism

- Oxidation of glucose

  $C_6H_{12}O_6 + 6O_2 \rightarrow 6H_2O + 6CO_2 + 36\ ATP + heat$

- Glucose is catabolized in three pathways
  - Glycolysis
  - Krebs cycle
  - Electron transport chain and oxidative phosphorylation



① During glycolysis, each glucose molecule is broken down into two molecules of pyruvic acid in the cytosol.

② The pyruvic acid then enters the mitochondrial matrix, where the Krebs cycle decomposes it to CO_2. During glycolysis and the Krebs cycle, small amounts of ATP are formed by substrate-level phosphorylation.

③ Energy-rich electrons picked up by coenzymes are transferred to the electron transport chain, built into the cristae membrane. The electron transport chain carries out oxidative phosphorylation, which accounts for most of the ATP generated by cellular respiration.

Figure 24.5

Glycolysis

- 10-step pathway
- Anaerobic
- Occurs in the cytosol
- Glucose $\rightarrow$ 2 pyruvic acid molecules
- Three major phases
  1. Sugar activation
  2. Sugar cleavage
  3. Sugar oxidation and ATP formation

Phases of Glycolysis

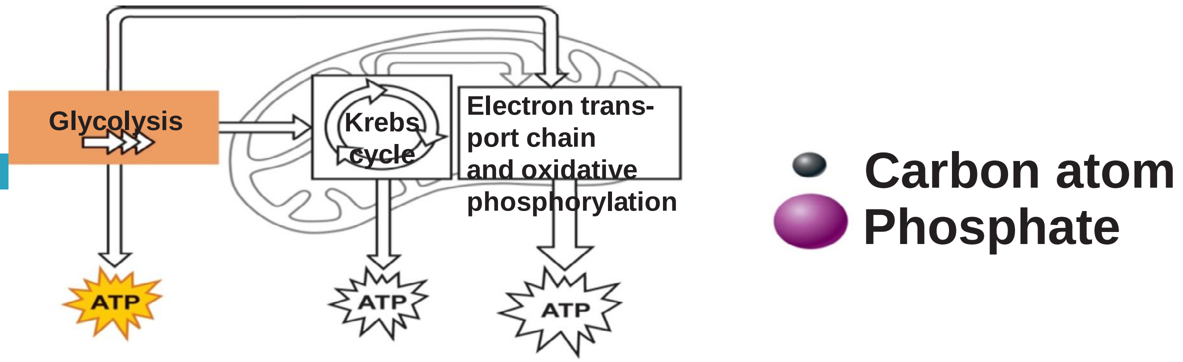
1. Sugar activation
   - Glucose is phosphorylated by 2 ATP to form fructose-1,6-bisphosphate

Phases of Glycolysis

2. Sugar cleavage
   - Fructose-1,6-bisphosphate is split into 3-carbon sugars
     - Dihydroxyacetone phosphate
     - Glyceraldehyde 3-phosphate

Phases of Glycolysis

3. Sugar oxidation and ATP formation
   - 3-carbon sugars are oxidized (reducing NAD^+)
   - Inorganic phosphate groups (P_i) are attached to each oxidized fragment
   - 4 ATP are formed by substrate-level phosphorylation



Phase 1
Sugar
Activation

Glucose is activated by phosphorylation and converted to fructose-1, 6-bisphosphate

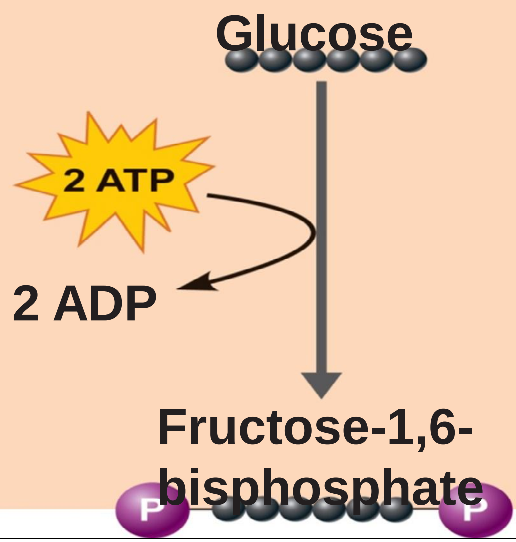
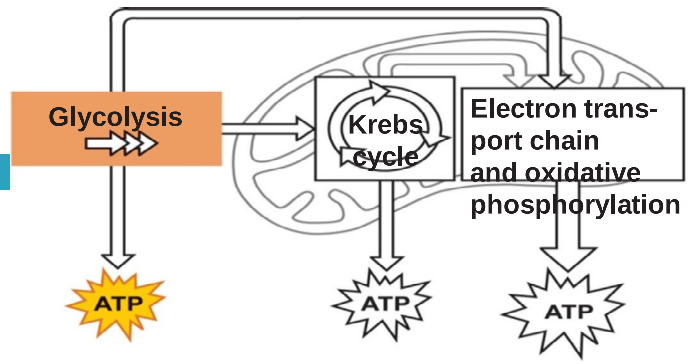


Figure 24.6 (1 of 3)



Carbon atom
Phosphate

Phase 2
Sugar
Cleavage

Fructose-1, 6-bisphosphate is cleaved into two 3-carbon fragments

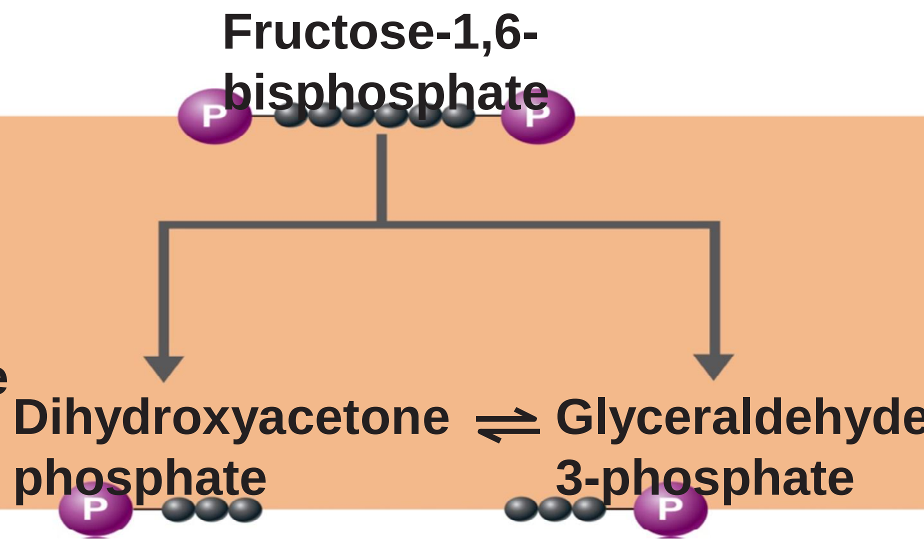


Figure 24.6 (2 of 3)

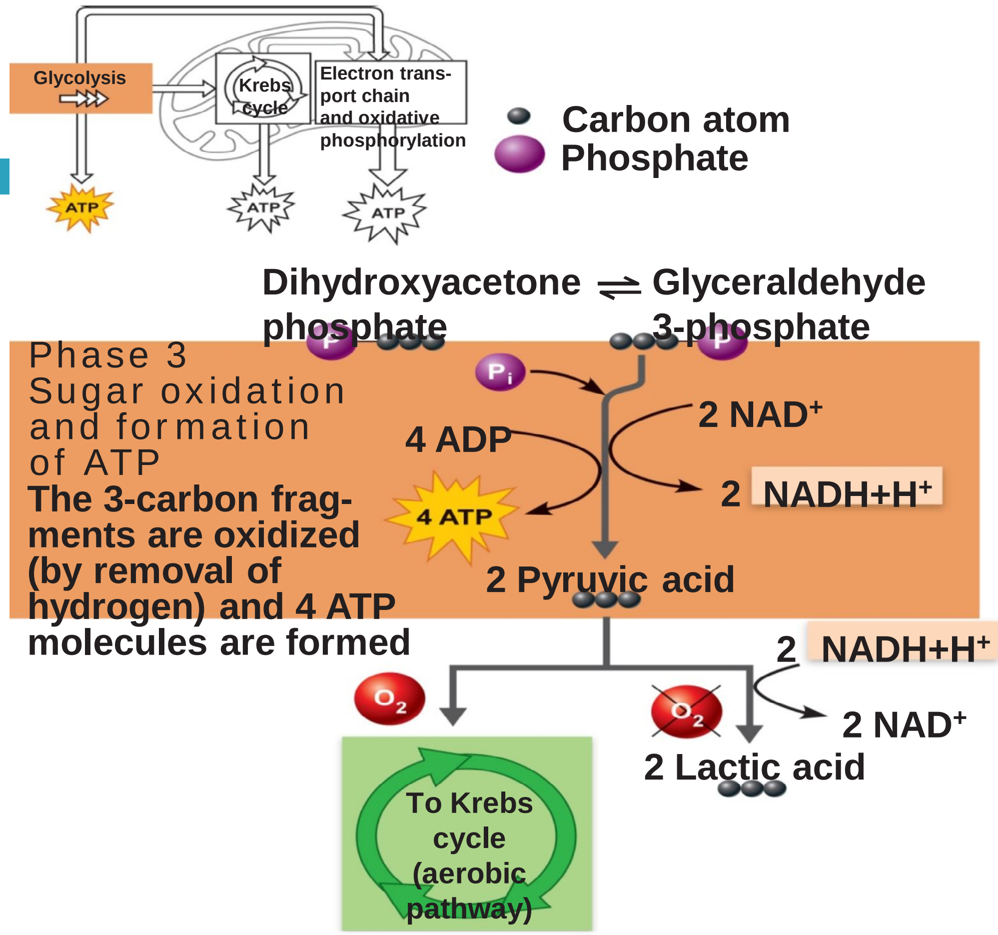


Figure 24.6 (3 of 3)

Glycolysis

- Final products of glycolysis
  - 2 pyruvic acid
    - Converted to lactic acid if O_2 not readily available
    - Enter aerobic pathways if O_2 is readily available
  - 2 NADH + H^+ (reduced NAD^+)
  - Net gain of 2 ATP

Krebs Cycle

- Occurs in mitochondrial matrix
- Fueled by pyruvic acid and fatty acids

Krebs Cycle

- Transitional phase
  - Each pyruvic acid is converted to acetyl CoA
    1. Decarboxylation: removal of 1 C to produce acetic acid and CO_2
    2. Oxidation: H^+ is removed from acetic acid and picked up by NAD^+
    3. Acetic acid + coenzyme A forms acetyl CoA

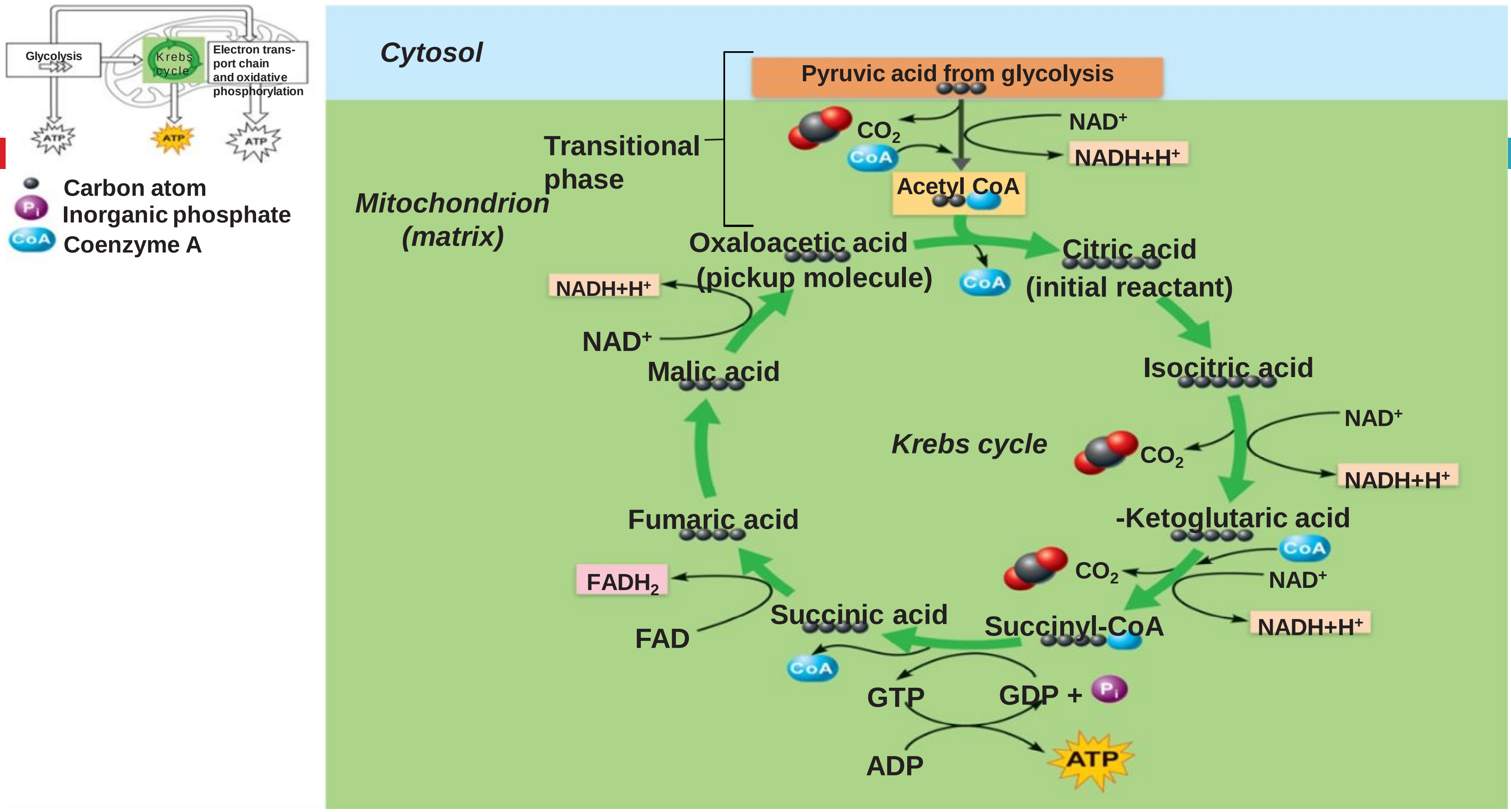
Krebs Cycle

- Coenzyme A shuttles acetic acid to an enzyme of the Krebs cycle
- Each acetic acid is decarboxylated and oxidized, generating:
  - 3 NADH + H^+
  - 1 $FADH_2$
  - 2 CO_2
  - 1 ATP

Krebs Cycle

- Does not directly use O_2
- Breakdown products of fats and proteins can also enter the cycle
- Cycle intermediates may be used as building materials for anabolic reactions

PLAY **Animation: Krebs Cycle**



Glycolysis
Krebs cycle
Electron transport chain and oxidative phosphorylation
ATP
ATP
ATP
Carbon atom
Inorganic phosphate
Coenzyme A
Cytosol
Mitochondrion (matrix)
Transitional phase
Pyruvic acid from glycolysis
CO_2
CoA
NAD^+
$NADH+H^+$
Acetyl CoA
Oxaloacetic acid (pickup molecule)
Citric acid (initial reactant)
CoA
$NADH+H^+$
NAD^+
Malic acid
Isocitric acid
NAD^+
Krebs cycle
CO_2
$NADH+H^+$
Fumaric acid
-Ketoglutaric acid
CoA
CO_2
NAD^+
$FADH_2$
FAD
Succinic acid
Succinyl-CoA
$NADH+H^+$
CoA
GTP
GDP +
ADP
ATP

Figure 24.7

Electron Transport Chain and Oxidative Phosphorylation

- The part of metabolism that directly uses oxygen
- Chain of proteins bound to metal atoms (cofactors) on inner mitochondrial membrane
- Substrates NADH + H^+ and $FADH_2$ deliver hydrogen atoms

Electron Transport Chain and Oxidative Phosphorylation

- Hydrogen atoms are split into H^+ and electrons
- Electrons are shuttled along the inner mitochondrial membrane, losing energy at each step
- Released energy is used to pump H^+ into the intermembrane space

Electron Transport Chain and Oxidative Phosphorylation

- Respiratory enzyme complexes I, III, and IV pump H^+ into the intermembrane space
- H^+ diffuses back to the matrix via ATP synthase
- ATP synthase uses released energy to make ATP

PLAY **Animation: Electron Transport**

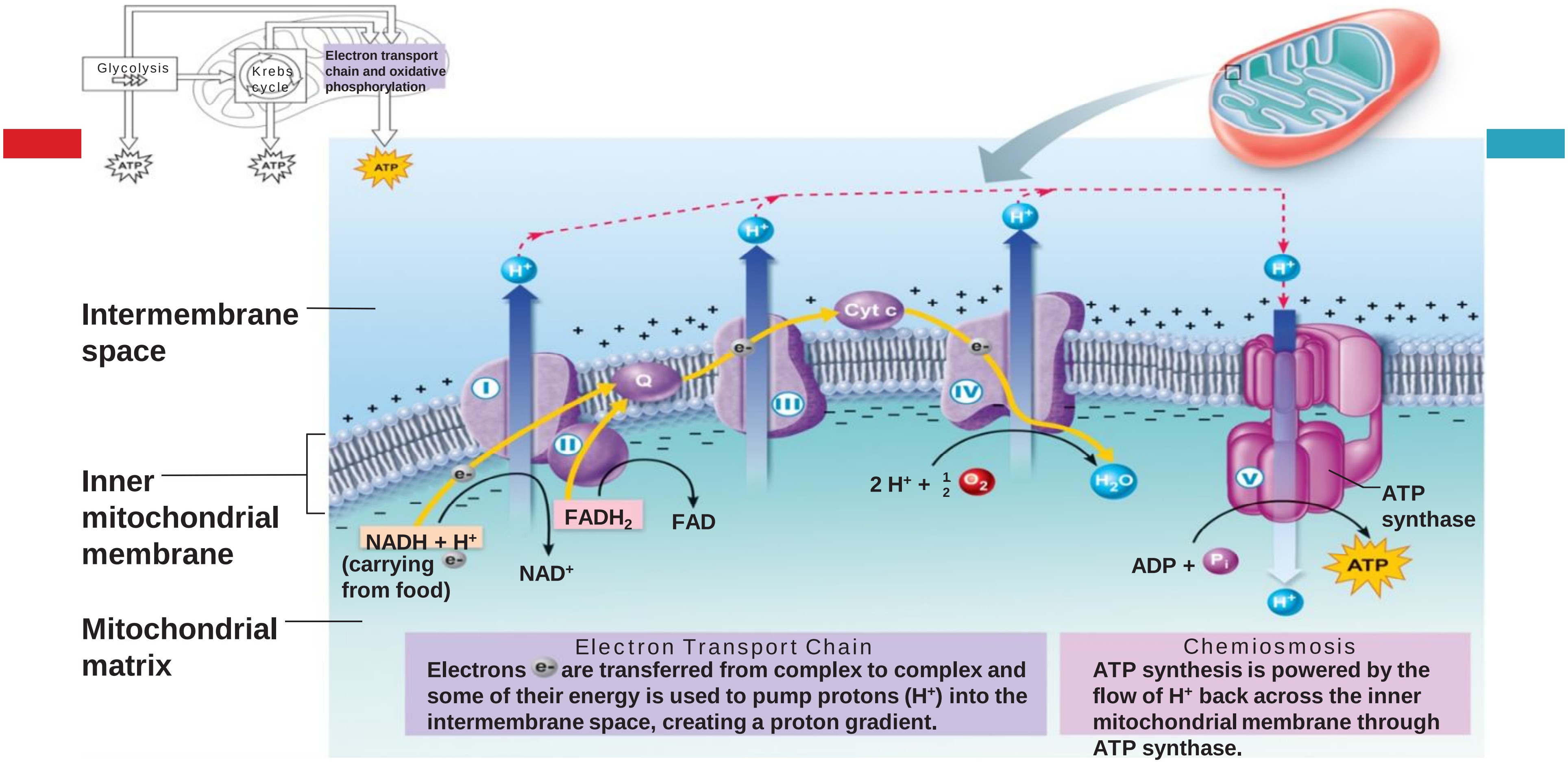
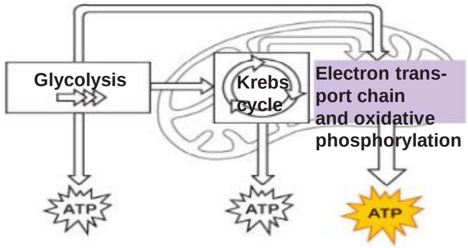

Glycolysis
Krebs cycle
Electron transport chain and oxidative phosphorylation
ATP
ATP
ATP
Intermembrane space
Inner mitochondrial membrane
Mitochondrial matrix
H+
H+
H+
H+
Cyt c
e-
e-
e-
Q
I
II
III
IV
V
NADH + H+ (carrying e- from food)
NAD+
FADH2
FAD
2 H+ + 1/2 O2
H2O
ATP synthase
ADP + Pi
ATP
H+
Electron Transport Chain
Electrons e- are transferred from complex to complex and some of their energy is used to pump protons (H+) into the intermembrane space, creating a proton gradient.
Chemiosmosis
ATP synthesis is powered by the flow of H+ back across the inner mitochondrial membrane through ATP synthase.

Figure 24.8

Electron Transport Chain and Oxidative Phosphorylation

- Electrons are delivered to O, forming O^-
- O^- attracts H^+ to form H_2O


Glycolysis
Krebs cycle
Electron transport chain and oxidative phosphorylation
ATP
ATP
ATP

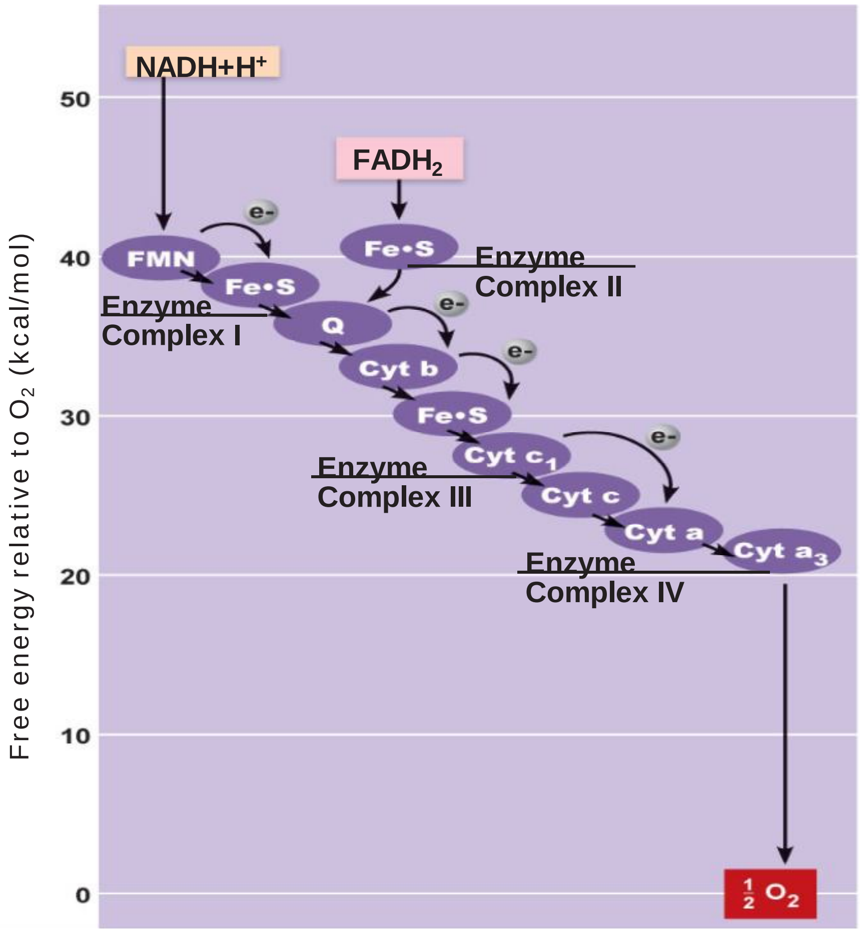

NADH+H+
FADH2
FMN
Fe•S
Fe•S
Q
Cyt b
Fe•S
Cyt c1
Cyt c
Cyt a
Cyt a3
e-
e-
e-
e-
Enzyme Complex I
Enzyme Complex II
Enzyme Complex III
Enzyme Complex IV
1/2 O2
Free energy relative to O2 (kcal/mol)
50
40
30
20
10
0

Figure 24.9

Electronic Energy Gradient

- Transfer of energy from NADH + H^+ and $FADH_2$ to oxygen releases large amounts of energy
- This energy is released in a stepwise manner through the electron transport chain

ATP Synthase

- Two major parts connected by a rod
  1. Rotor in the inner mitochondrial membrane
  2. Knob in the matrix
- Works like an ion pump in reverse

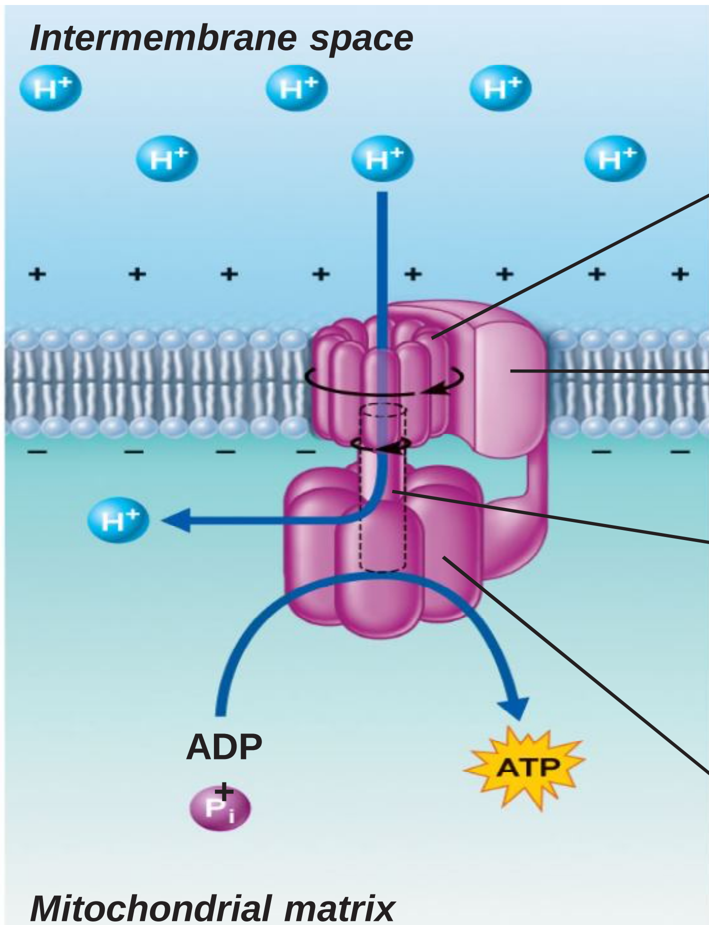

Intermembrane space
H+
ADP
+
Pi
ATP
Mitochondrial matrix
A rotor in the membrane spins clockwise when H+ flows through it down the H+ gradient.
A stator anchored in the membrane holds the knob stationary.
As the rotor spins, a rod connecting the cylindrical rotor and knob also spins.
The protruding, stationary knob contains three catalytic sites that join inorganic phosphate to ADP to make ATP when the rod is spinning.

Figure 24.11

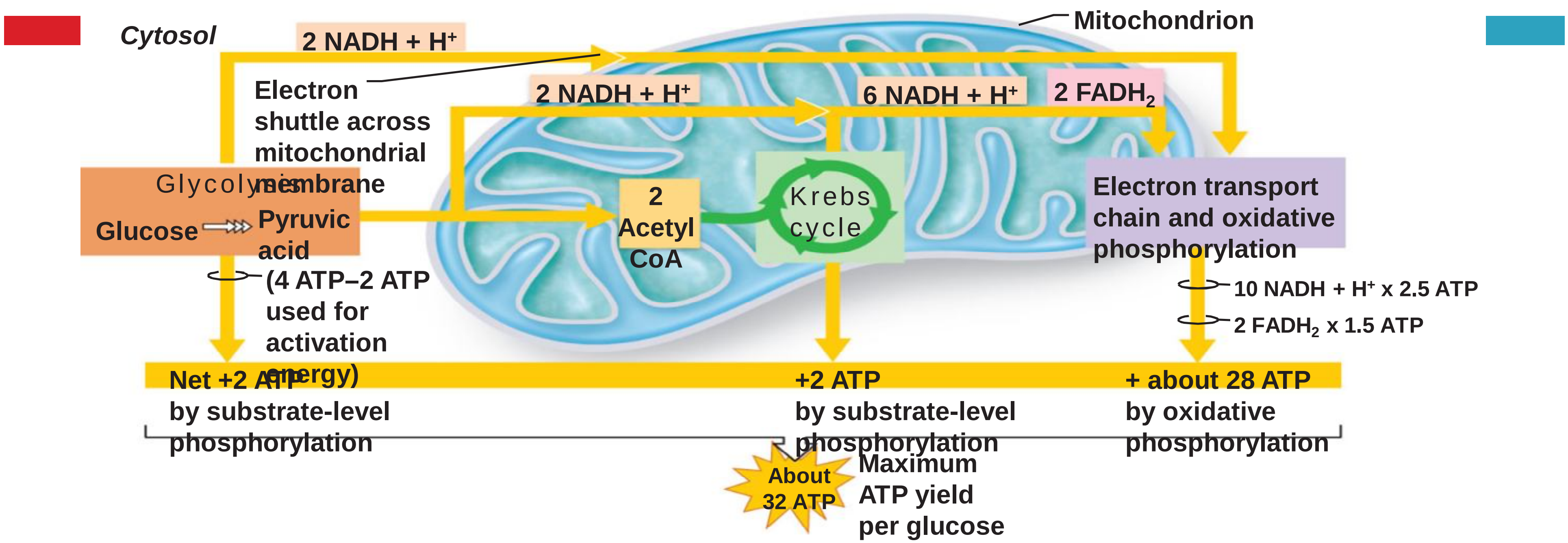

Cytosol
Mitochondrion
2 NADH + H+
Electron shuttle across mitochondrial membrane
2 NADH + H+
6 NADH + H+
2 FADH2
Glycolysis
Glucose
Pyruvic acid
2 Acetyl CoA
Krebs cycle
Electron transport chain and oxidative phosphorylation
(4 ATP–2 ATP used for activation energy)
10 NADH + H+ x 2.5 ATP
2 FADH2 x 1.5 ATP
Net +2 ATP by substrate-level phosphorylation
+2 ATP by substrate-level phosphorylation
+ about 28 ATP by oxidative phosphorylation
About 32 ATP
Maximum ATP yield per glucose

Figure 24.12

Glycogenesis and Glycogenolysis

- Glycogenesis
  - Glycogen formation when glucose supplies exceed need for ATP synthesis
  - Mostly in liver and skeletal muscle
- Glycogenolysis
  - Glycogen beakdown in response to low blood glucose

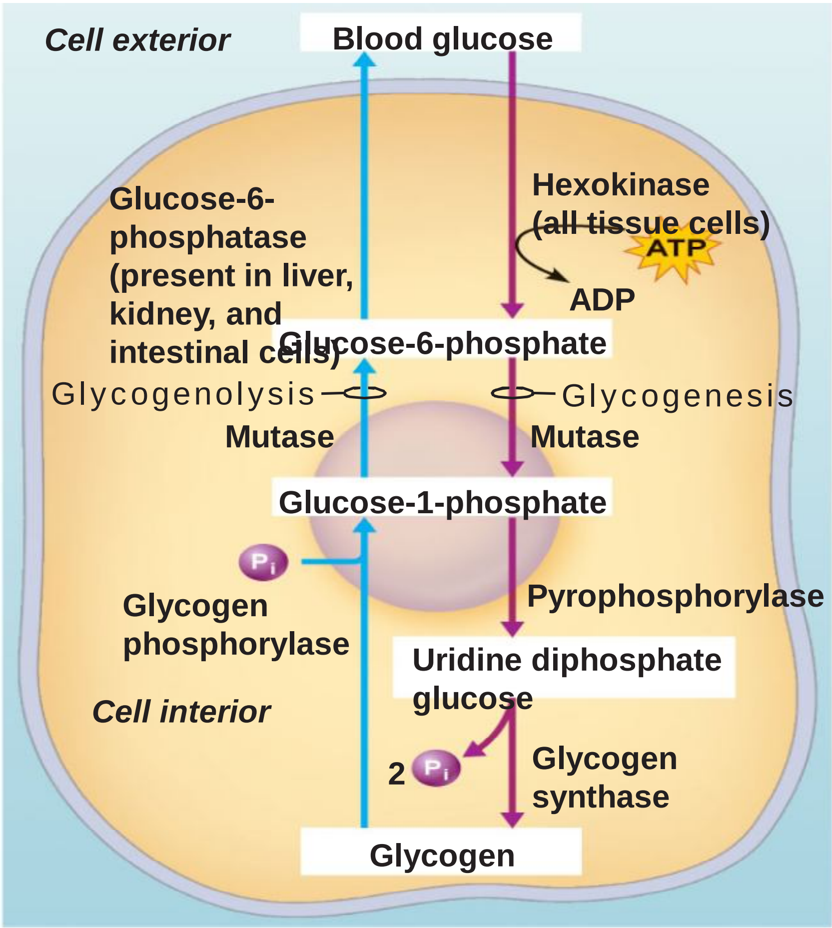

Cell exterior
Blood glucose
Glucose-6-
phosphatase
(present in liver,
kidney, and
intestinal cells)
Hexokinase
(all tissue cells)
ATP
ADP
Glucose-6-phosphate
Glycogenolysis
Glycogenesis
Mutase
Mutase
Glucose-1-phosphate
Pi
Glycogen
phosphorylase
Pyrophosphorylase
Uridine diphosphate
glucose
Cell interior
2 Pi
Glycogen
synthase
Glycogen

Figure 24.13

Gluconeogenesis

- Glucose formation from noncarbohydrate (glycerol and amino acid) molecules
- Mainly in the liver
- Protects against damaging effects of hypoglycemia

Lipid Metabolism

- Fat catabolism yields 9 kcal per gram (vs 4 kcal per gram of carbohydrate or protein)
- Most products of fat digestion are transported as chylomicrons and are hydrolyzed by endothelial enzymes into fatty acids and glycerol

Lipid Metabolism

- Only triglycerides are routinely oxidized for energy
- The two building blocks are oxidized separately
  - Glycerol pathway
  - Fatty acid pathway

Lipid Metabolism

- Glycerol is converted to glyceraldehyde phosphate
  - Enters the Krebs cycle
  - Equivalent to $^1/_2$ glucose

Lipid Metabolism

- Fatty acids undergo beta oxidation, which produces
  - Two-carbon acetic acid fragments, which enter the Krebs cycle
  - Reduced coenzymes, which enter the electron transport chain

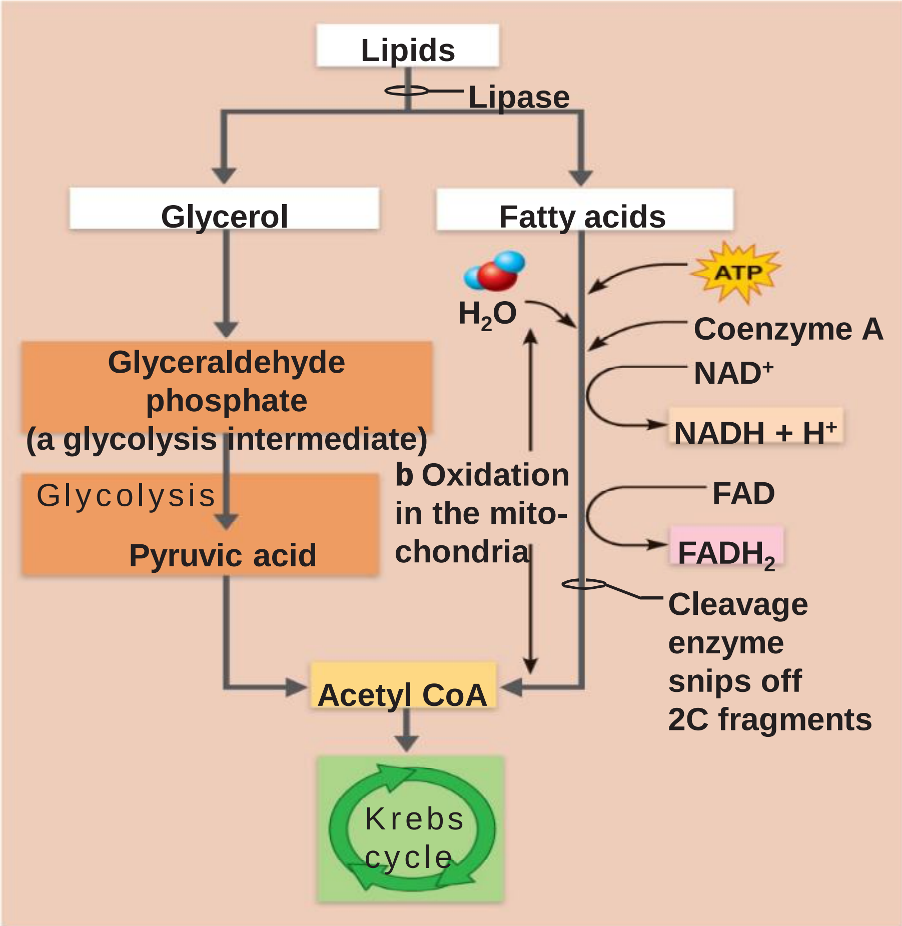

Lipids
Lipase
Glycerol
Fatty acids
ATP
H_2O
Coenzyme A
NAD^+
$NADH + H^+$
FAD
$FADH_2$
Glyceraldehyde phosphate (a glycolysis intermediate)
Glycolysis
Pyruvic acid
b Oxidation in the mito-chondria
Cleavage enzyme snips off 2C fragments
Acetyl CoA
Krebs cycle

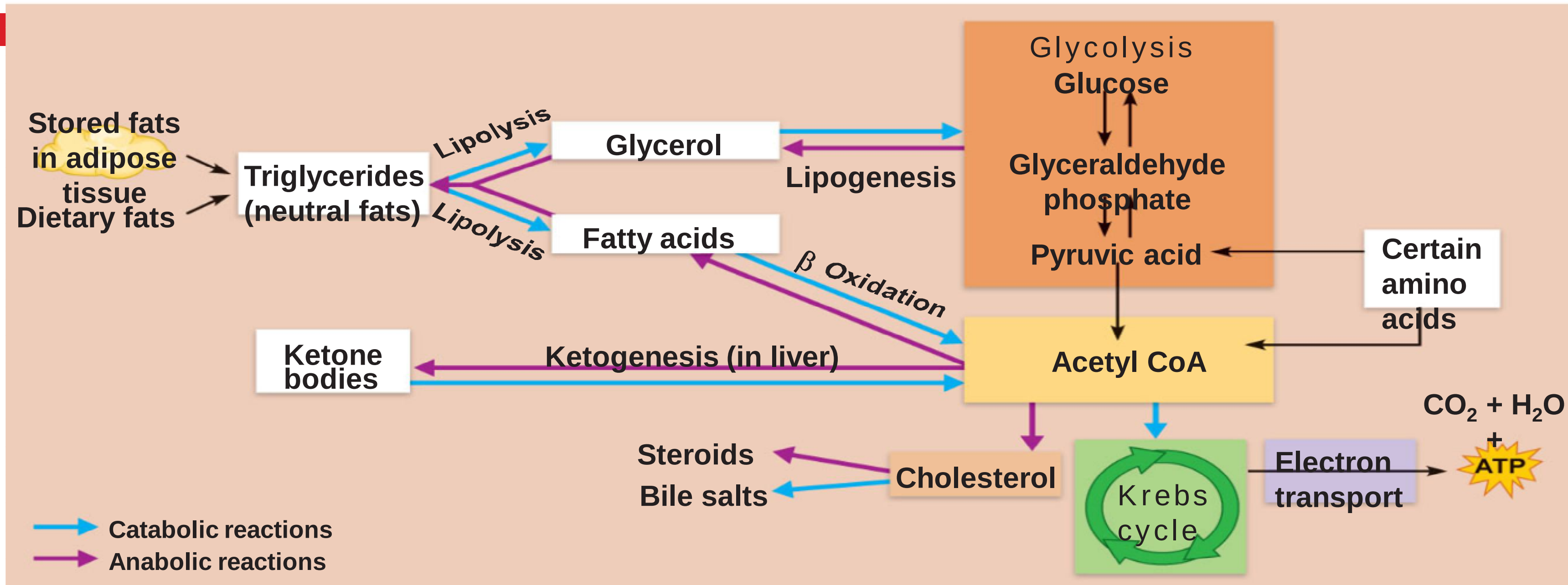
Figure 24.14

Lipogenesis

- Triglyceride synthesis occurs when cellular ATP and glucose levels are high
- Glucose is easily converted into fat because acetyl CoA is
  - An intermediate in glucose catabolism
  - A starting point for fatty acid synthesis

Lipolysis

- The reverse of lipogenesis
- Oxaloacetic acid is necessary for complete oxidation of fat
  - Without it, acetyl CoA is converted by ketogenesis in the liver into ketone bodies (ketones)



Glycolysis
Glucose
Glyceraldehyde phosphate
Pyruvic acid
Stored fats in adipose tissue
Dietary fats
Triglycerides (neutral fats)
Lipolysis
Lipolysis
Glycerol
Fatty acids
Lipogenesis
β Oxidation
Certain amino acids
Ketone bodies
Ketogenesis (in liver)
Acetyl CoA
$CO_2 + H_2O$ +
ATP
Steroids
Bile salts
Cholesterol
Krebs cycle
Electron transport
Catabolic reactions
Anabolic reactions

Figure 24.15

Synthesis of Structural Materials

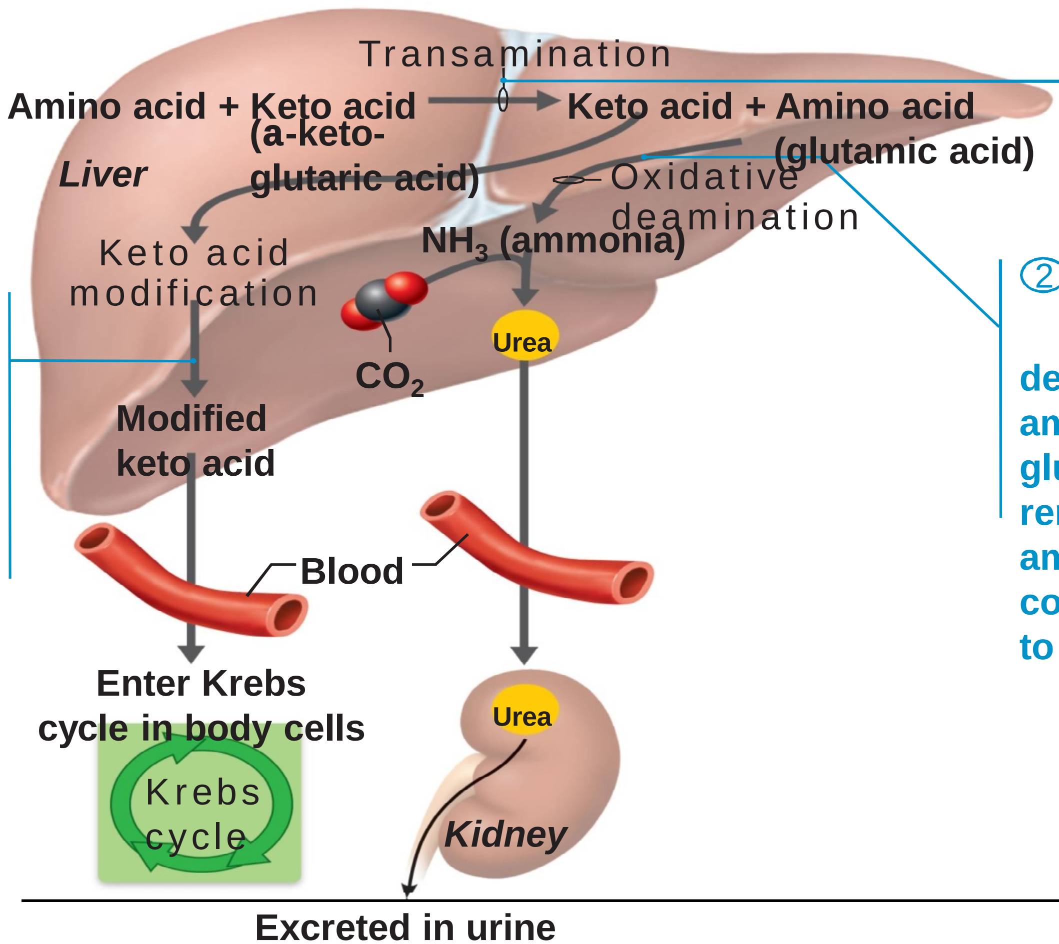
- Phospholipids for cell membranes and myelin
- Cholesterol for cell membranes and steroid hormone synthesis
- In the liver
  - Synthesis of transport lipoproteins for cholesterol and fats
  - Synthesis of cholesterol from acetyl CoA
  - Use of cholesterol to form bile salts

Protein Metabolism

- When dietary protein is in excess, amino acids are
  - Oxidized for energy
  - Converted into fat for storage

Oxidation of Amino Acids

- First deaminated; then converted into
  - Pyruvic acid
  - A keto acid intermediate of the Krebs cycle
- Events include transamination, oxidative deamination, and keto acid modification



1 During transamination a amine group is switched from an amino acid to a keto acid.

2 In oxidative deamination, the amine group of glutamic acid is removed as ammonia and combined with CO^2 to form urea.

3 During keto acid modification the keto acids formed during transamination are altered so they can easily enter the Krebs cycle pathways.

Figure 24.16

Protein Synthesis

- Is hormonally controlled
- Requires a complete set of amino acids
  - Essential amino acids must be provided in the diet

Catabolic-Anabolic Steady State

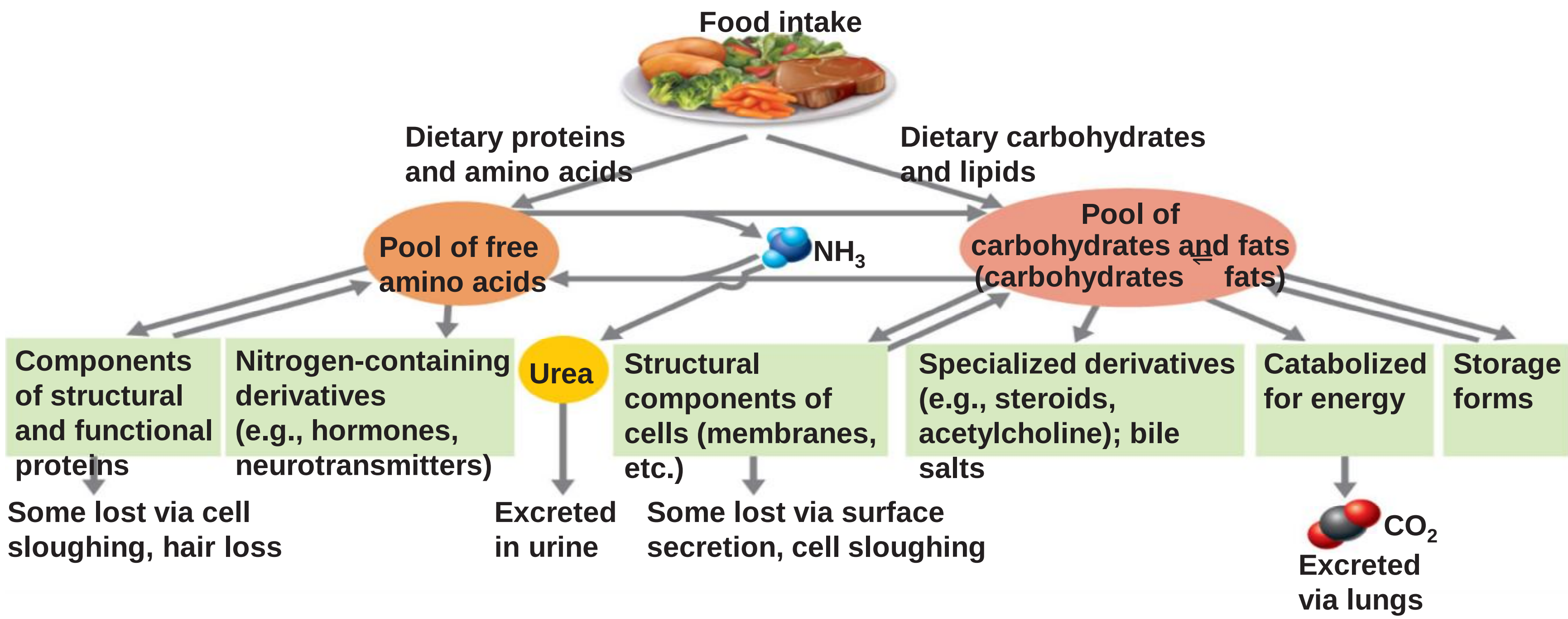
- A dynamic state in which
  - Organic molecules (except DNA) are continuously broken down and rebuilt
  - Organs have different fuel preferences

Nutrient Pools

- Three interconvertible pools
  - Amino acids
  - Carbohydrates
  - Fats

Amino Acid Pool

- Body's total supply of free amino acids
- Source for
  - Resynthesizing body proteins
  - Forming amino acid derivatives
  - Gluconeogenesis



Food intake
Dietary proteins and amino acids
Dietary carbohydrates and lipids
Pool of free amino acids
NH3
Pool of carbohydrates and fats (carbohydrates ⇌ fats)
Components of structural and functional proteins
Nitrogen-containing derivatives (e.g., hormones, neurotransmitters)
Urea
Structural components of cells (membranes, etc.)
Specialized derivatives (e.g., steroids, acetylcholine); bile salts
Catabolized for energy
Storage forms
Some lost via cell sloughing, hair loss
Excreted in urine
Some lost via surface secretion, cell sloughing
CO2
Excreted via lungs

Figure 24.17

Carbohydrate and Fat Pools

- Easily interconverted through key intermediates
- Differ from the amino acid pool in that:
  - Fats and carbohydrates are oxidized directly to produce energy
  - Excess carbohydrate and fat can be stored

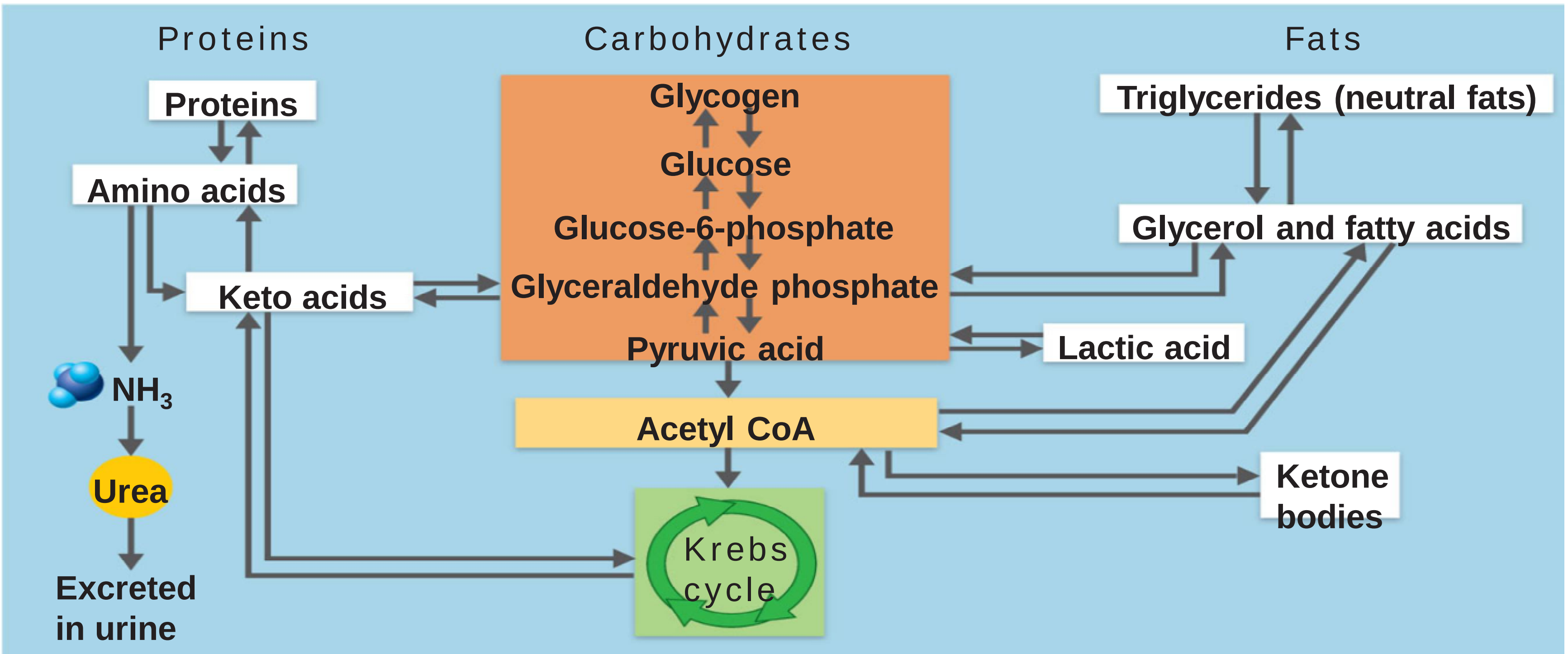

Proteins
Carbohydrates
Fats
Proteins
Amino acids
Keto acids
NH_3
Urea
Excreted in urine
Glycogen
Glucose
Glucose-6-phosphate
Glyceraldehyde phosphate
Pyruvic acid
Acetyl CoA
Krebs cycle
Triglycerides (neutral fats)
Glycerol and fatty acids
Lactic acid
Ketone bodies

Figure 24.18

Absorptive and Postabsorptive States

- Absorptive (fed) state
  - During and shortly after eating
  - Absorption of nutrients is occurring
- Postabsorptive (fasting) state
  - When the GI tract is empty
  - Energy sources are supplied by breakdown of reserves

Absorptive State

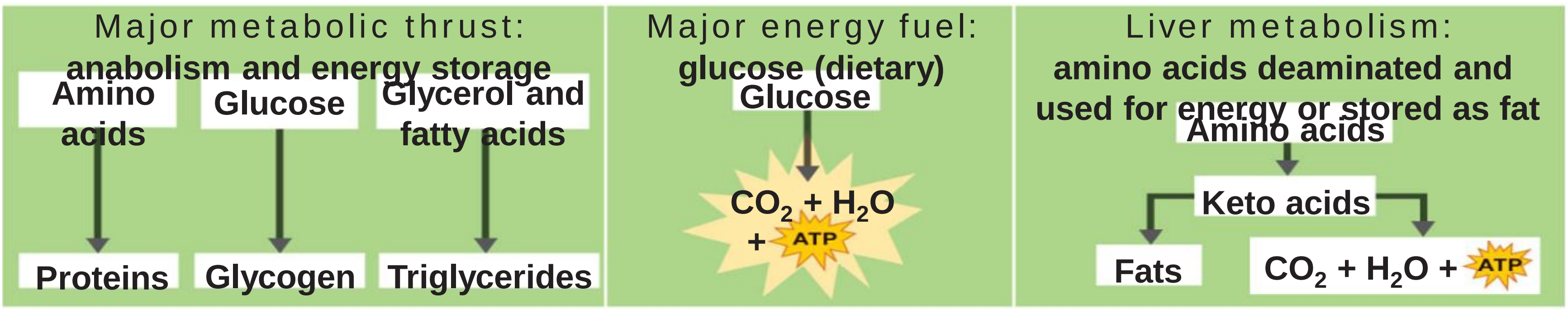
- Anabolism exceeds catabolism
- Carbohydrates
  - Glucose is the major energy fuel
  - Glucose is converted to glycogen or fat

Absorptive State

- Fats
  - Lipoprotein lipase hydrolyzes lipids of chylomicrons in muscle and fat tissues
  - Most glycerol and fatty acids are converted to triglycerides for storage
  - Triglycerides are used by adipose tissue, liver, and skeletal and cardiac muscle as a primary energy source

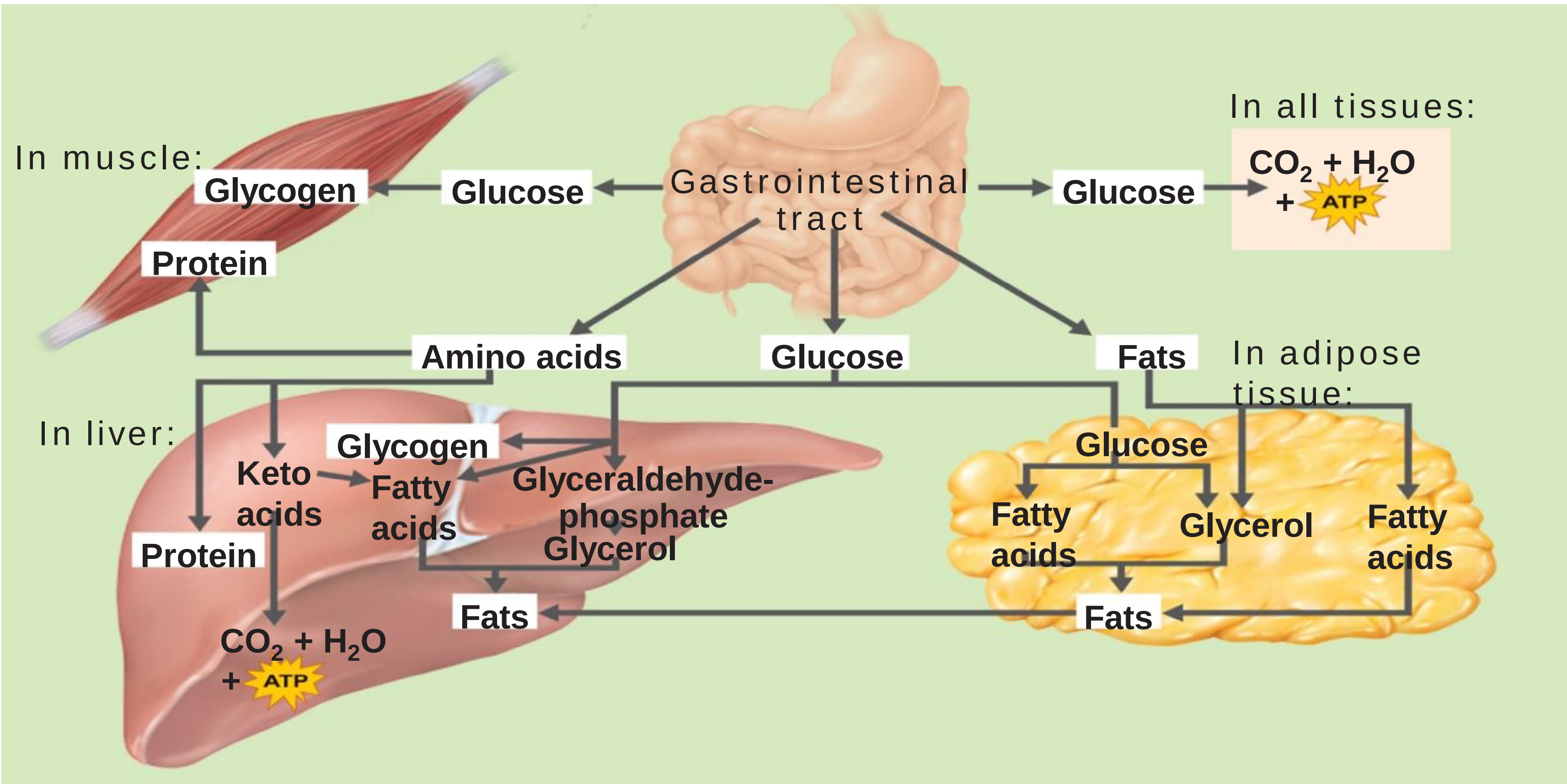
Absorptive State

- Proteins
  - Excess amino acids are deaminated and used for ATP synthesis or stored as fat in the liver
  - Most amino acids are used in protein synthesis



(a) Major events of the absorptive state

Figure 24.19a



(b) Principal pathways of the absorptive state

Figure 24.19b

Absorptive State: Hormonal Control

- Insulin secretion is stimulated by
  - Elevated blood levels of glucose and amino acids
  - GIP and parasympathetic stimulation

Insulin Effects on Metabolism

- Insulin, a hypoglycemic hormone, enhances
  - Facilitated diffusion of glucose into muscle and adipose cells
  - Glucose oxidation
  - Glycogen and triglyceride formation
  - Active transport of amino acids into tissue cells
  - Protein synthesis

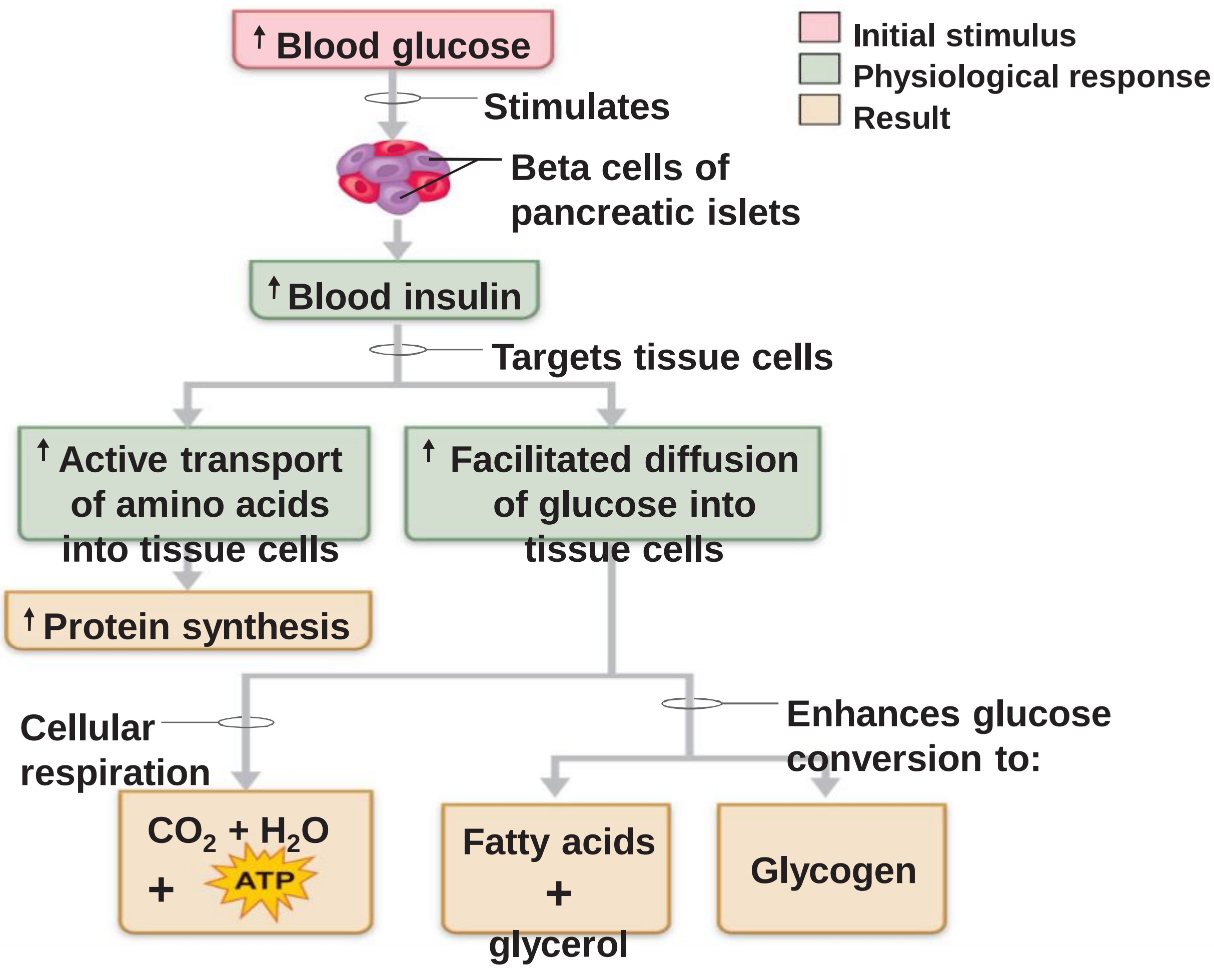

↑ Blood glucose
Initial stimulus
Physiological response
Result
Stimulates
Beta cells of
pancreatic islets
↑ Blood insulin
Targets tissue cells
↑ Active transport
of amino acids
into tissue cells
↑ Facilitated diffusion
of glucose into
tissue cells
↑ Protein synthesis
Cellular
respiration
Enhances glucose
conversion to:
$CO_2 + H_2O$
+ ATP
Fatty acids
+
glycerol
Glycogen

Figure 24.20

Postabsorptive State

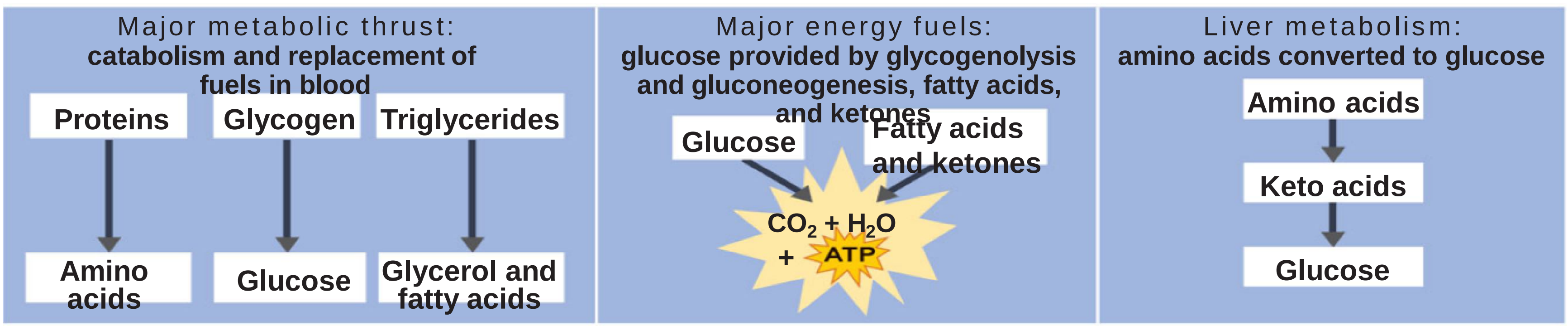
- Catabolism of fat, glycogen, and proteins exceeds anabolism
- Goal is to maintain blood glucose between meals
  - Makes glucose available to the blood
  - Promotes use of fats for energy (glucose sparing)

Sources of Blood Glucose

1. Glycogenolysis in the liver
2. Glycogenolysis in skeletal muscle
3. Lipolysis in adipose tissues and the liver
   - Glycerol is used for gluconeogenesis in the liver

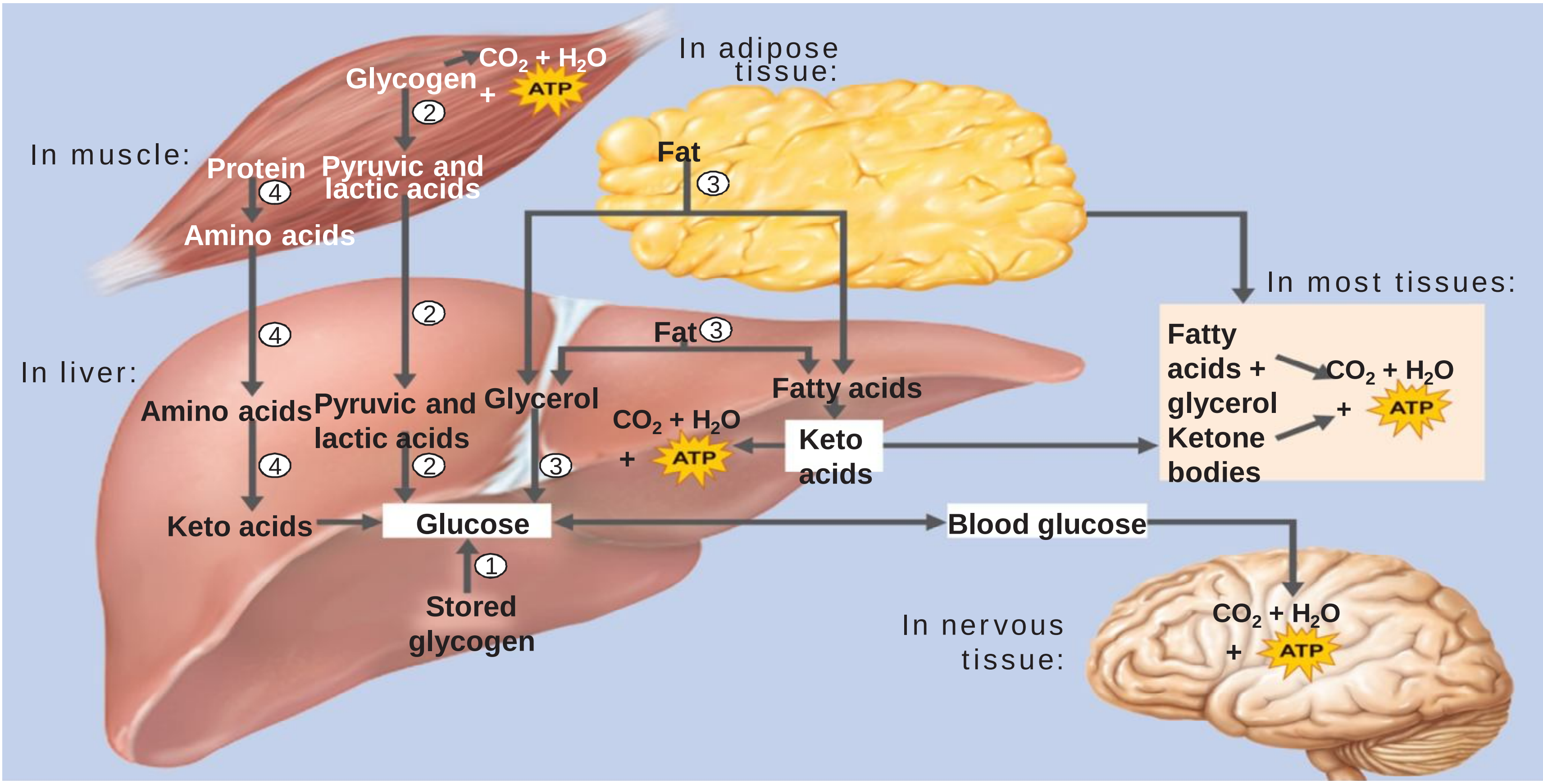
Sources of Blood Glucose

4. Catabolism of cellular protein during prolonged fasting
   - Amino acids are deaminated and used for gluconeogenesis in the liver and (later) in the kidneys



(a) Major events of the postabsorptive state

Figure 24.21a



(b) Principal pathways of the postabsorptive state

Figure 24.21b

Postabsorptive State: Hormonal Controls

- Glucagon release is stimulated by
  - Declining blood glucose
  - Rising amino acid levels

Effects of Glucagon

- Glucagon, a hyperglycemic hormone, promotes
  - Glycogenolysis and gluconeogenesis in the liver
  - Lipolysis in adipose tissue
  - Modulation of glucose effects after a high-protein, low-carbohydrate meal

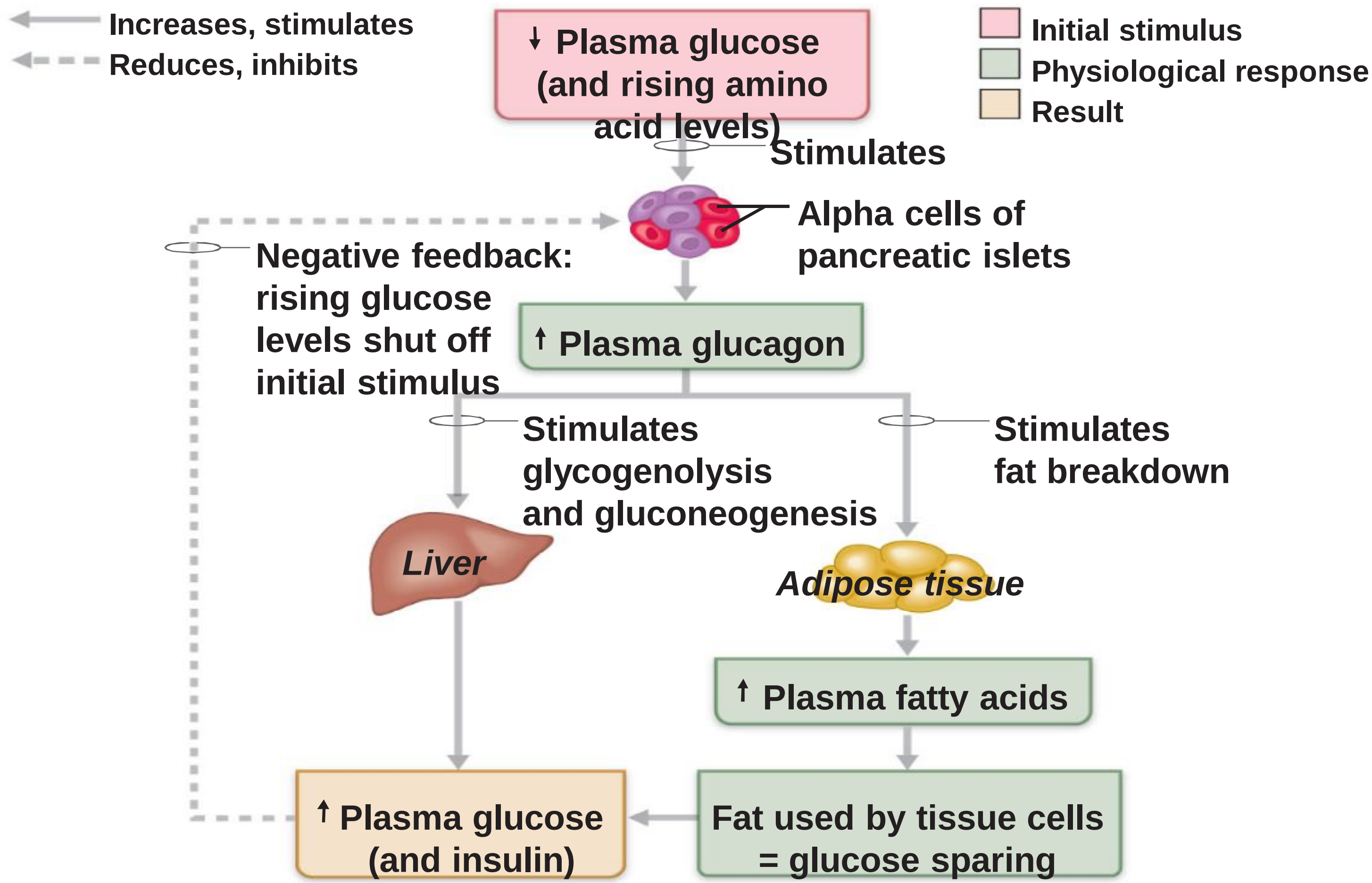

Increases, stimulates
Reduces, inhibits
↓ Plasma glucose (and rising amino acid levels)
Initial stimulus
Physiological response
Result
Stimulates
Alpha cells of pancreatic islets
Negative feedback: rising glucose levels shut off initial stimulus
↑ Plasma glucagon
Stimulates glycogenolysis and gluconeogenesis
Stimulates fat breakdown
Liver
Adipose tissue
↑ Plasma fatty acids
↑ Plasma glucose (and insulin)
Fat used by tissue cells = glucose sparing

Figure 24.22

Postabsorptive State: Neural Controls

- In response to low plasma glucose, or during fight-or-flight or exercise, the sympathetic nervous system and epinephrine from the adrenal medulla promote
  - Fat mobilization
  - Glycogenolysis

Metabolic Role of the Liver

- Hepatocytes
  - Process nearly every class of nutrient
  - Play a major role in regulating plasma cholesterol levels
  - Store vitamins and minerals
  - Metabolize alcohol, drugs, hormones, and bilirubin

Cholesterol

- Structural basis of bile salts, steroid hormones, and vitamin D
- Major component of plasma membranes
- Makes up part of the hedgehog signaling molecule that directs embryonic development
- Transported in lipoprotein complexes containing triglycerides, phospholipids, cholesterol, and protein

Lipoproteins

- Types of lipoproteins
  - HDLs (high-density lipoproteins)
    - The highest protein content
  - LDLs (low-density lipoproteins)
    - Cholesterol-rich
  - VLDLs (very low density lipoproteins)
    - Mostly triglycerides
  - Chylomicrons

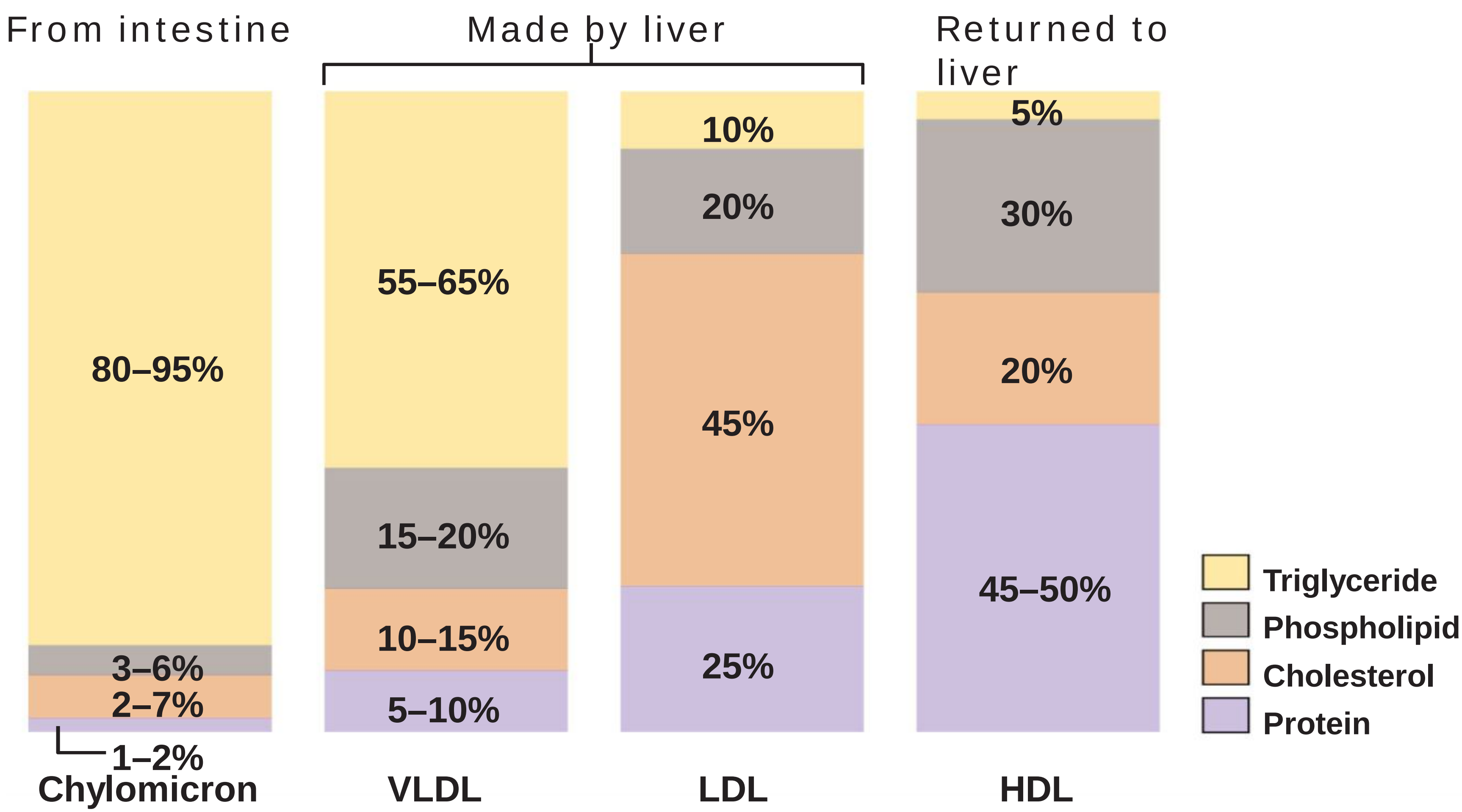

From intestine
Made by liver
Returned to liver
80–95%
3–6%
2–7%
1–2%
Chylomicron
55–65%
15–20%
10–15%
5–10%
VLDL
10%
20%
45%
25%
LDL
5%
30%
20%
45–50%
HDL
Triglyceride
Phospholipid
Cholesterol
Protein

Figure 24.23

Lipoproteins

- VLDLs
  - Transport triglycerides to peripheral tissues (mostly adipose)
- LDLs
  - Transport cholesterol to peripheral tissues for membranes, storage, or hormone synthesis
- HDLs
  - Transport excess cholesterol from peripheral tissues to the liver to be broken down and secreted into bile
  - Also provide cholesterol to steroid-producing organs

Lipoproteins

- High levels of HDL are thought to protect against heart attack
- High levels of LDL, especially lipoprotein (a) increase the risk of heart attack

Plasma Cholesterol Levels

- The liver produces cholesterol
  - At a basal level regardless of dietary cholesterol intake
  - In response to saturated fatty acids

Plasma Cholesterol Levels

- Saturated fatty acids
  - Stimulate liver synthesis of cholesterol
  - Inhibit cholesterol excretion from the body
- Unsaturated fatty acids
  - Enhance excretion of cholesterol

Plasma Cholesterol Levels

- Trans fats
  - Increase LDLs and reduce HDLs

Plasma Cholesterol Levels

- Unsaturated omega-3 fatty acids (found in cold-water fish)
  - Lower the proportions of saturated fats and cholesterol
  - Have antiarrhythmic effects on the heart
  - Help prevent spontaneous clotting
  - Lower blood pressure

Non-Dietary Factors Affecting Cholesterol

- Stress, cigarette smoking, and coffee lower HDL levels
- Aerobic exercise and estrogen increase HDL levels and decrease LDL levels
- Body shape
  - "Apple": Fat carried on the upper body is correlated with high cholesterol and LDL levels
  - "Pear": Fat carried on the hips and thighs is correlated with lower cholesterol and LDL levels

Energy Balance

- Bond energy released from food must equal the total energy output
- Energy intake = the energy liberated during food oxidation
- Energy output
  - Immediately lost as heat (~60%)
  - Used to do work (driven by ATP)
  - Stored as fat or glycogen

Energy Balance

- Heat energy
  - Cannot be used to do work
  - Warms the tissues and blood
  - Helps maintain the homeostatic body temperature
  - Allows metabolic reactions to occur efficiently

Obesity

- Body mass index (BMI) = wt (lb) $\times$ 705 / ht (inches)^2
- Considered overweight if BMI is 25 to 30
- Considered obese if BMI is greater than 30
  - Higher incidence of atherosclerosis, diabetes mellitus, hypertension, heart disease, and osteoarthritis

Regulation of Food Intake

- Two distinct sets of hypothalamic neurons
  1. LHA neurons promote hunger when stimulated by neuropeptides (e.g., NPY)
  2. VMN neurons cause satiety through release of CRH when stimulated by appetite-suppressing peptides (e.g., POMC and CART peptides)

Regulation of Food Intake

- Factors that affect brain thermoreceptors and chemoreceptors
  - Neural signals from the digestive tract
  - Bloodborne signals related to body energy stores
  - Hormones
  - To a lesser extent, body temperature and psychological factors

Short-Term Regulation of Food Intake

- Neural signals
  - High protein content of meal increases and prolongs afferent vagal signals
  - Distension sends signals along the vagus nerve that suppress the hunger center

Short-Term Regulation of Food Intake

- Nutrient signals
  - Increased nutrient levels in the blood depress eating
    - Blood glucose
    - Amino acids
    - Fatty acids

Short-Term Regulation of Food Intake

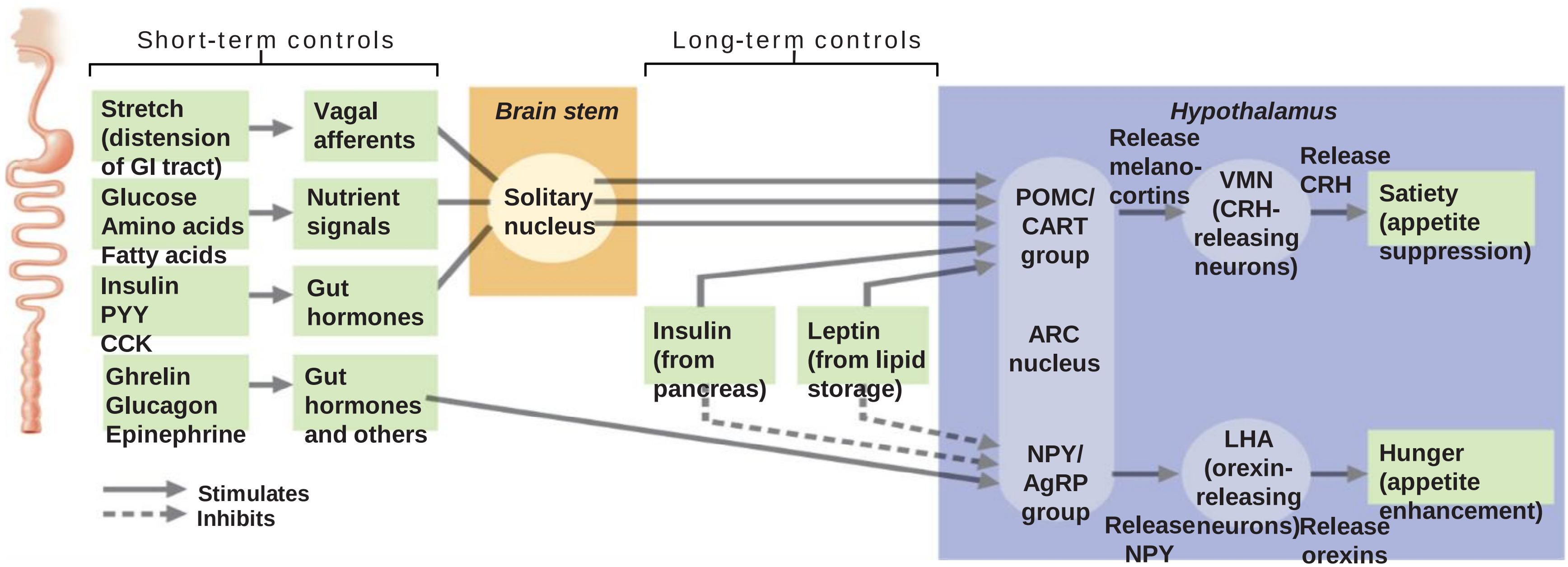
- Hormones
  - Gut hormones (e.g., insulin and CCK) depress hunger
  - Glucagon and epinephrine stimulate hunger
  - Ghrelin (Ghr) from the stomach stimulates appetite just before a meal

Long-Term Regulation of Food Intake

- Leptin
  - Hormone secreted by fat cells in response to increased body fat mass
  - Indicator of total energy stores in fat tissue
  - Protects against weight loss in times of nutritional deprivation

Long-Term Regulation of Food Intake

- Leptin
  - Acts on the ARC neurons in the hypothalamus
  - Suppresses the secretion of NPY, a potent appetite stimulant
  - Stimulates the expression of appetite suppressants (e.g., CART peptides)



Short-term controls
Long-term controls
Stretch (distension of GI tract)
Vagal afferents
Glucose Amino acids Fatty acids
Nutrient signals
Insulin PYY CCK
Gut hormones
Ghrelin Glucagon Epinephrine
Gut hormones and others
Brain stem
Solitary nucleus
Insulin (from pancreas)
Leptin (from lipid storage)
Hypothalamus
POMC/ CART group
Release melano-cortins
VMN (CRH-releasing neurons)
Release CRH
Satiety (appetite suppression)
ARC nucleus
NPY/ AgRP group
Release NPY
LHA (orexin-releasing neurons)
Release orexins
Hunger (appetite enhancement)
Stimulates
Inhibits

Figure 24.24

Long-Term Regulation of Food Intake

- Additional factors
  - Temperature
  - Stress
  - Psychological factors
  - Adenovirus infections
  - Sleep deprivation

Metabolic Rate

- Total heat produced by chemical reactions and mechanical work of the body
- Measured directly with a calorimeter or indirectly with a respirometer

Metabolic Rate

- Basal metabolic rate (BMR)
  - Reflects the energy the body needs to perform its most essential activities

Factors that Influence BMR

- As the ratio of body surface area to volume increases, BMR increases
- Decreases with age
- Increases with temperature or stress
- Males have a disproportionately higher BMR
- Thyroxine increases oxygen consumption, cellular respiration, and BMR

Metabolic Rate

- Total metabolic rate (TMR)
  - Rate of kilocalorie consumption to fuel all ongoing activities
  - Increases with skeletal muscle activity and food ingestion

Regulation of Body Temperature

- Body temperature reflects the balance between heat production and heat loss
- At rest, the liver, heart, brain, kidneys, and endocrine organs generate most heat
- During exercise, heat production from skeletal muscles increases dramatically

Regulation of Body Temperature

- Normal body temperature = 37°C ± 5°C (98.6°F)
- Optimal enzyme activity occurs at this temperature
- Increased temperature denatures proteins and depresses neurons

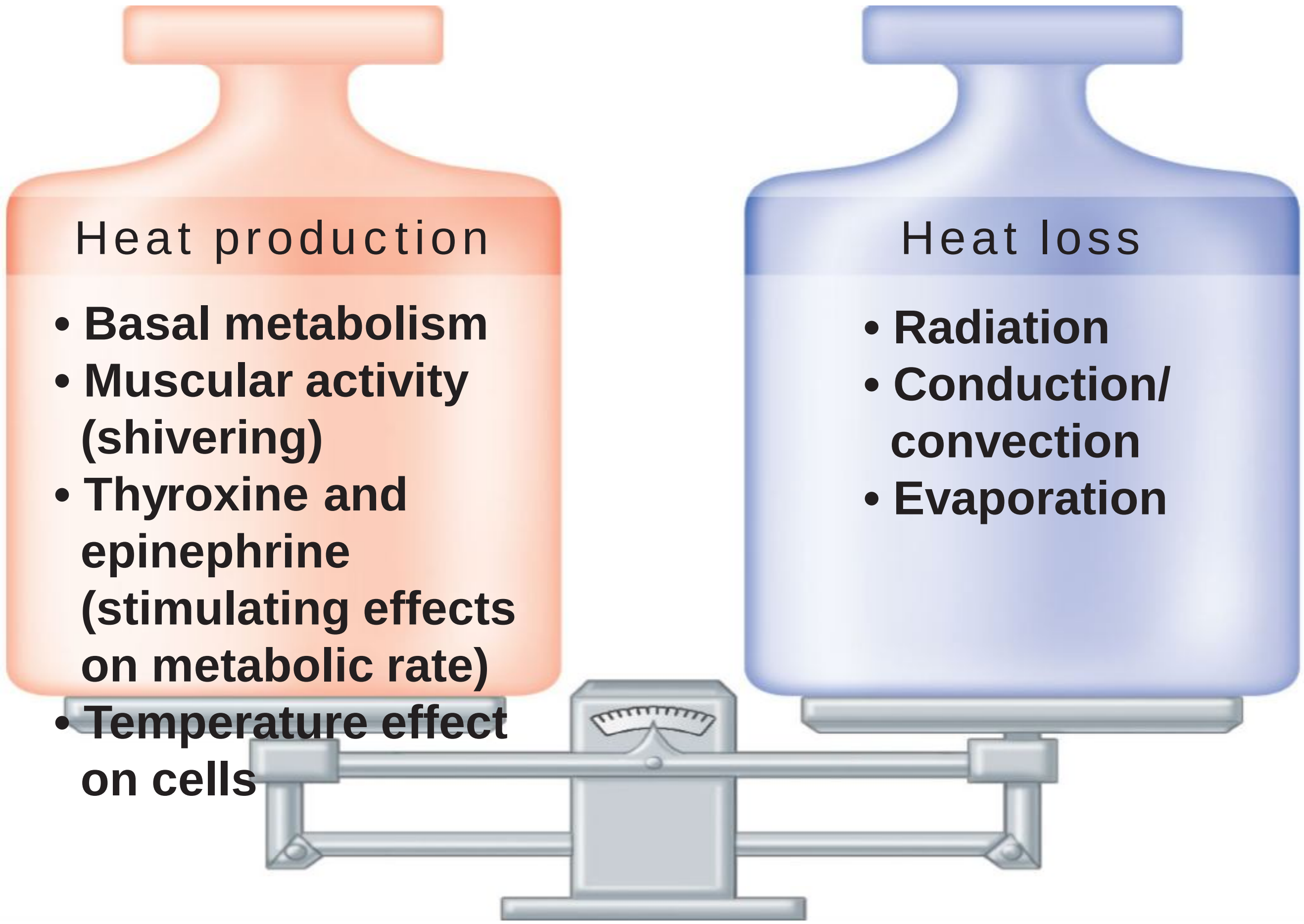

Heat production
• Basal metabolism
• Muscular activity (shivering)
• Thyroxine and epinephrine (stimulating effects on metabolic rate)
• Temperature effect on cells
Heat loss
• Radiation
• Conduction/ convection
• Evaporation

Figure 24.25

Core and Shell Temperature

- Organs in the core have the highest temperature
- Blood is the major agent of heat exchange between the core and the shell
- Core temperature is regulated
- Core temperature remains relatively constant, while shell temperature fluctuates substantially (20°C–40°C)

Mechanisms of Heat Exchange

- Four mechanisms
  1. Radiation is the loss of heat in the form of infrared rays
  2. Conduction is the transfer of heat by direct contact
  3. Convection is the transfer of heat to the surrounding air
  4. Evaporation is the heat loss due to the evaporation of water from body surfaces

Figure 24.26

Mechanisms of Heat Exchange

- Insensible heat loss accompanies insensible water loss from lungs, oral mucosa, and skin
- Evaporative heat loss becomes sensible (active) when body temperature rises and sweating increases water vaporization

Role of the Hypothalamus

- Preoptic region of the hypothalamus contains the two thermoregulatory centers
  - Heat-loss center
  - Heat-promoting center

Role of the Hypothalamus

- The hypothalamus receives afferent input from
  - Peripheral thermoreceptors in the skin
  - Central thermoreceptors (some in the hypothalamus)
- Initiates appropriate heat-loss and heat-promoting activities

Heat-Promoting Mechanisms

- Constriction of cutaneous blood vessels
- Shivering
- Increased metabolic rate via epinephrine and norepinephrine
- Enhanced thyroxine release

Heat-Promoting Mechanisms

- Voluntary measures include
  - Putting on more clothing
  - Drinking hot fluids
  - Changing posture or increasing physical activity

Heat-Loss Mechanisms

- Dilation of cutaneous blood vessels
- Enhanced sweating
- Voluntary measures include
  - Reducing activity and seeking a cooler environment
  - Wearing light-colored and loose-fitting clothing

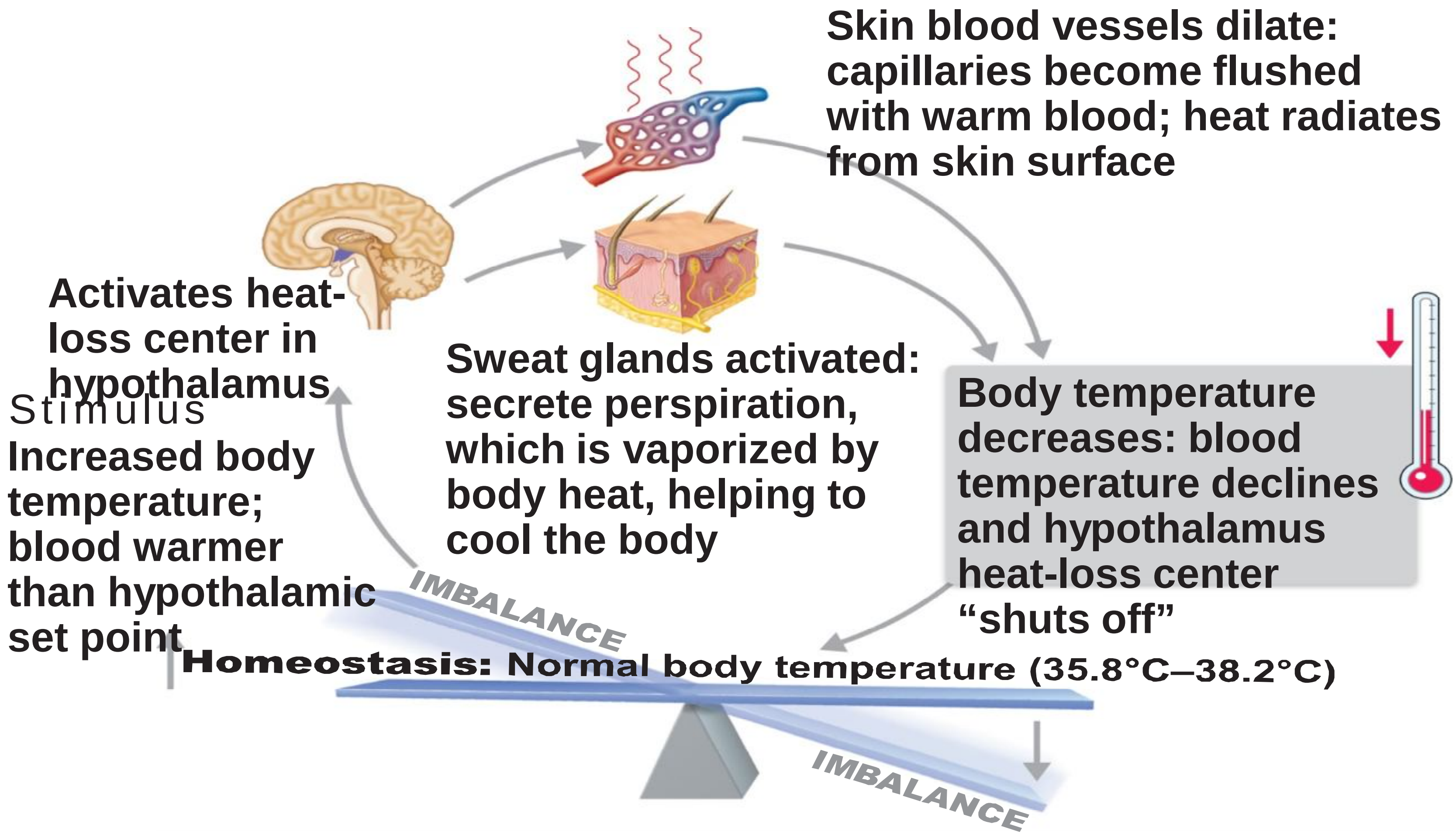


Figure 24.27, step 1

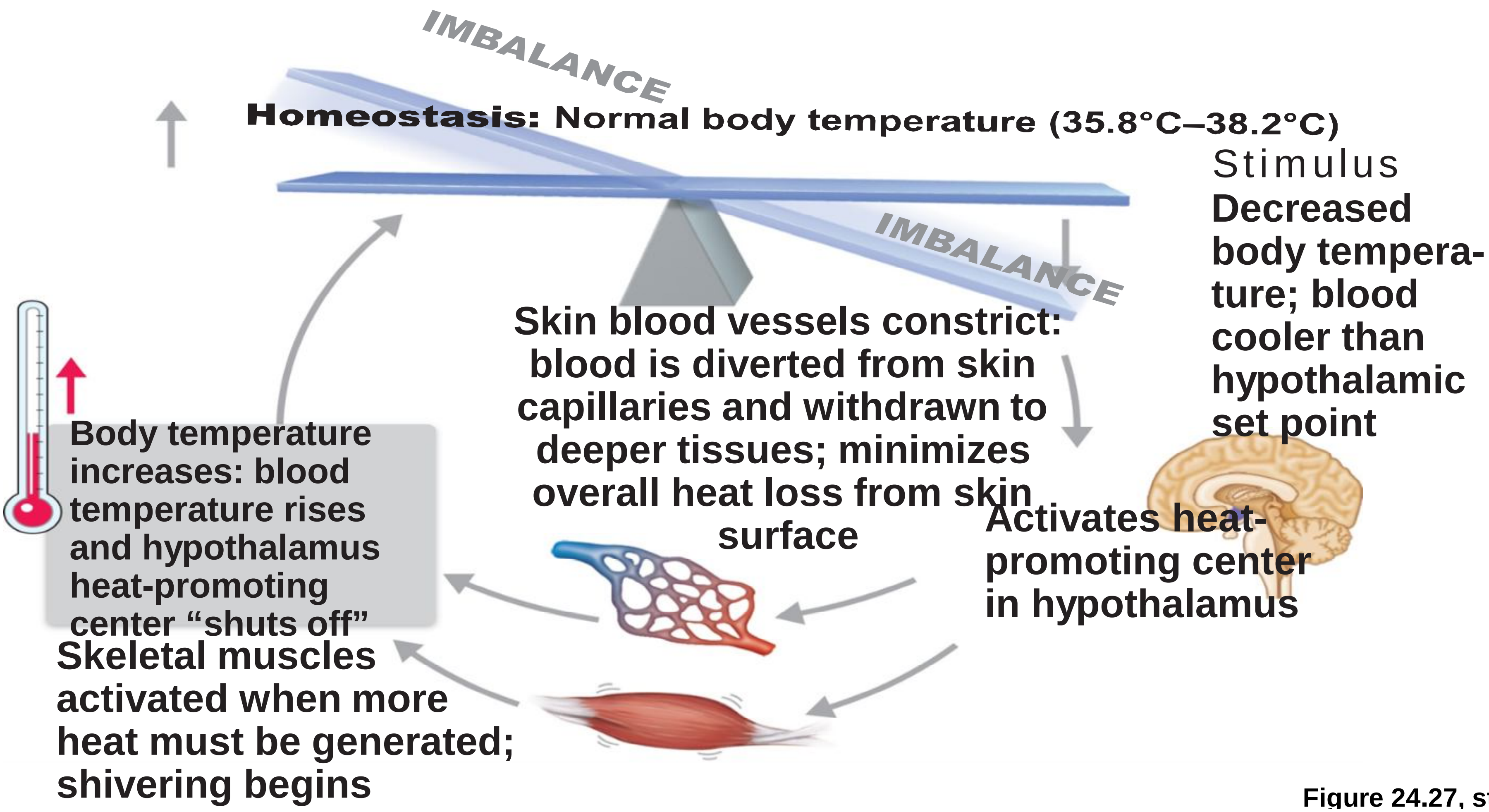


Figure 24.27, step 2

Homeostatic Imbalance

- Hyperthermia
  - Elevated body temperature depresses the hypothalamus
  - Positive-feedback mechanism (heat stroke) begins at core temperature of 41°C
  - Can be fatal if not corrected

Homeostatic Imbalance

- Heat exhaustion
  - Heat-associated collapse after vigorous exercise
  - Due to dehydration and low blood pressure
  - Heat-loss mechanisms are still functional
  - May progress to heat stroke

Homeostatic Imbalance

- Hypothermia
  - Low body temperature where vital signs decrease
  - Shivering stops at core temperature of 30 - 32°C
  - Can progress to coma a death by cardiac arrest at ~ 21°C

Fever

- Controlled hyperthermia
- Due to infection (also cancer, allergies, or CNS injuries)
- Macrophages release interleukins ("pyrogens") that cause the release of prostaglandins from the hypothalamus

Fever

- Prostaglandins reset the hypothalamic thermostat higher
- Natural body defenses or antibiotics reverse the disease process; cryogens (e.g., vasopressin) reset the thermostat to a lower (normal) level

Developmental Aspects

- Lack of proteins in utero and in the first three years → mental deficits and learning disorders
- Insulin-dependent diabetes mellitus and genetic disorders → metabolic problems in children
- Non-insulin–dependent diabetes mellitus may occur in middle and old age, especially in obese people
- Metabolic rate declines throughout the life span

Developmental Aspects

- Many medications for age-related problems influence nutrition:
  - Diuretics for heart failure and hypertension increase the risk of hypokalemia
  - Some antibiotics interfere with digestion and absorption
  - Mineral oil (laxative) decrease absorption of fat-soluble vitamins
  - Excessive alcohol consumption may lead to malabsorption, vitamin and mineral deficiencies, deranged metabolism, damage to liver and pancreas

Developmental Aspects

- Nonenzymatic binding of glucose to proteins increases with age, leading to lens clouding and general tissue stiffening