Do not salivate on your self

NUTRITION, METABOLISM,

D.HAMMOUDI.MD

- **Total Calories used = BMR + ACTIVITY + DIT + other factors. KCAL:**
- The energy content of foods is described in terms of kilocalories (kcal) or Joules (J).
- **One kilocalorie (kcal) is defined as the amount of heat required to raise the temperature of 1 kg water by 1 degree C while it is in the temperature range of 15 degrees C to 16 degrees C. 1 kcal = 4.128 kJ.**
- The term ``Calorie'' in common usage (capital ``C'') is 1 kcal.
- 1-9% of food energy is non-digestible.

- About 50% is lost as heat. 25-40% is converted to high energy phosphate band energy for use in basal metabolism (BMR) and physical activities.

Energy Intake, kcal/day ----- age	male	female
20	2900	1700
40	2550	1550
60	2100	1400

Basal metabolic rate, or **RMR** - **Resting Metabolic Rate, is the rate of energy utilization in the resting state is most closely related to lean body mass**.

Liver and brain, 4% of body mass, account for 40% of BMR. BMR is measured from O_2 consumption (CO_2 production) of a person awake, at rest, after an overnight fast.

Useful average for quick estimates:

Men: BMR = 1.0 kcal/(kg hr)

Women: BMR = 0.9 kcal/(kg hr)

BMR = 1.3 kcal/(kg hr) fat-free body weight (irrespective of sex and age) 1kg = 2.21 lbs. 100 lbs = 45.2 kg.

Nutritional Sources of Energy

Energy production is the consequence of the **oxidation of food by atmospheric O_2 to produce CO_2 and excreted nitrogen.**

CARBOHYDRATES - 4 KCAL/GRAM:

Metabolic energy produced from carbohydrate is about **4 kcal/gram.** The chief metabolic role of carbohydrates in the diet is for energy production. Carbohydrate in excess of that needed for energy is converted to glycogen and triglyceride for storage.

FATS - 9 KCAL/GRAM:

Metabolic energy derived from fat is **9 kcal/gram.** Triglycerides, or fats, can be directly utilized by many tissues of the body as an energy source and are an important part of membrane structure. Excess fat in the diet can be stored as triglyceride only.

PROTEINS - 4 KCAL/GRAM:

- The metabolic energy derived from protein is about **4 kcal/g.**
- Although protein contains more energy than carbohydrate, the metabolic energy derived from protein is the same because products of nitrogen metabolism are not completely oxidized.
- Dietary proteins are broken down to amino acids which are taken up by the cells for the synthesis of new proteins and other nitrogen containing compounds.
- Excess dietary protein is treated as a source of energy with glycogenic amino acids being converted to glucose and ketogenic amino acids being converted to fatty acids and keto acids.
- Although there is no separate class of ``storage'' protein, a certain percentage of muscle and structural protein is considered as expendable

NITROGEN BALANCE:

A comparison between the intake of nitrogen, mostly in the form of protein, and the excretion of nitrogen, mostly as undigested protein in the feces, and urea and ammonia in the urine.

UUN, 24 hour Urinary Urea Nitrogen:

Normal: <5g/day.

Usefulness: Determine level of catabolism (breakdown paths).

- Low UUN can be caused by low protein intake, active fluid retention, increasing BUN (blood urea nitrogen), and incomplete urine collection.

- High UUN can be caused by high protein intake, stress, corticosteroid therapy, active diuresis (increased secretion of urine), decreasing BUN, and >24-hr urine collection.

EPB, Estimated nitrogen (Protein) Balance:

EPB = protein intake - protein loss.

Protein loss = [24-hr UUN(g) + 4 (The 4 grams is an allowance for stool and nonurea nitrogen losses.)] X 6.25 (The 6.25 is for converting from urea to protein losses.)

There are exceptions to this formula for burn patients and others with large nonurinary nitrogen losses.

BUN, Blood Urea Nitrogen:

- Normal - 8-23mg/dl. Usefulness - measurement of protein intake;
- if serum creatinine is normal, use BUN for protein intake;
- if serum creatinine is high, use BUN/creatinine.
- **BUN/creatine < 8 suggests poor proteine intake.**
- A low value may also result from severe liver disease.
- A high value may occur despite low protein intake during renal failure, congestive heart failure, gastrointestinal hemorrhage, corticosteroid therapy, dehydration, and shock

Serum Creatinine:

Normal - 0.6 - 1.6 mg/dl.

Usefulness - a value less than 0.6 mg/dl indicates muscle wasting due to calorie deficiency.

A high value may be seen despite muscle wasting due to renal failure or severe dehydration (when creatinine simply cannot be excreted as it normally is in the urine).

Energy-releasing vitamins:

Thiamine, Riboflavin, Niacin, Pyridoxine, Pantothenic acid, Biotin: Because these vitamins

DERMATITIS

- inflamation of the skin

GLOSSITIS

- inflamation of the toung (swollen, red)

CHEILITIS

- (kil it'tis) inflamation of lips as in angular stomatitis

DIARRHEA

- inflamation of intestinal epithelium

Nerve cells use lots of energy, so symptoms also show up in nervous tissue:

PERIPHERAL NEUROPATHY

- tingling of nerves at extremities

DEPRESSION

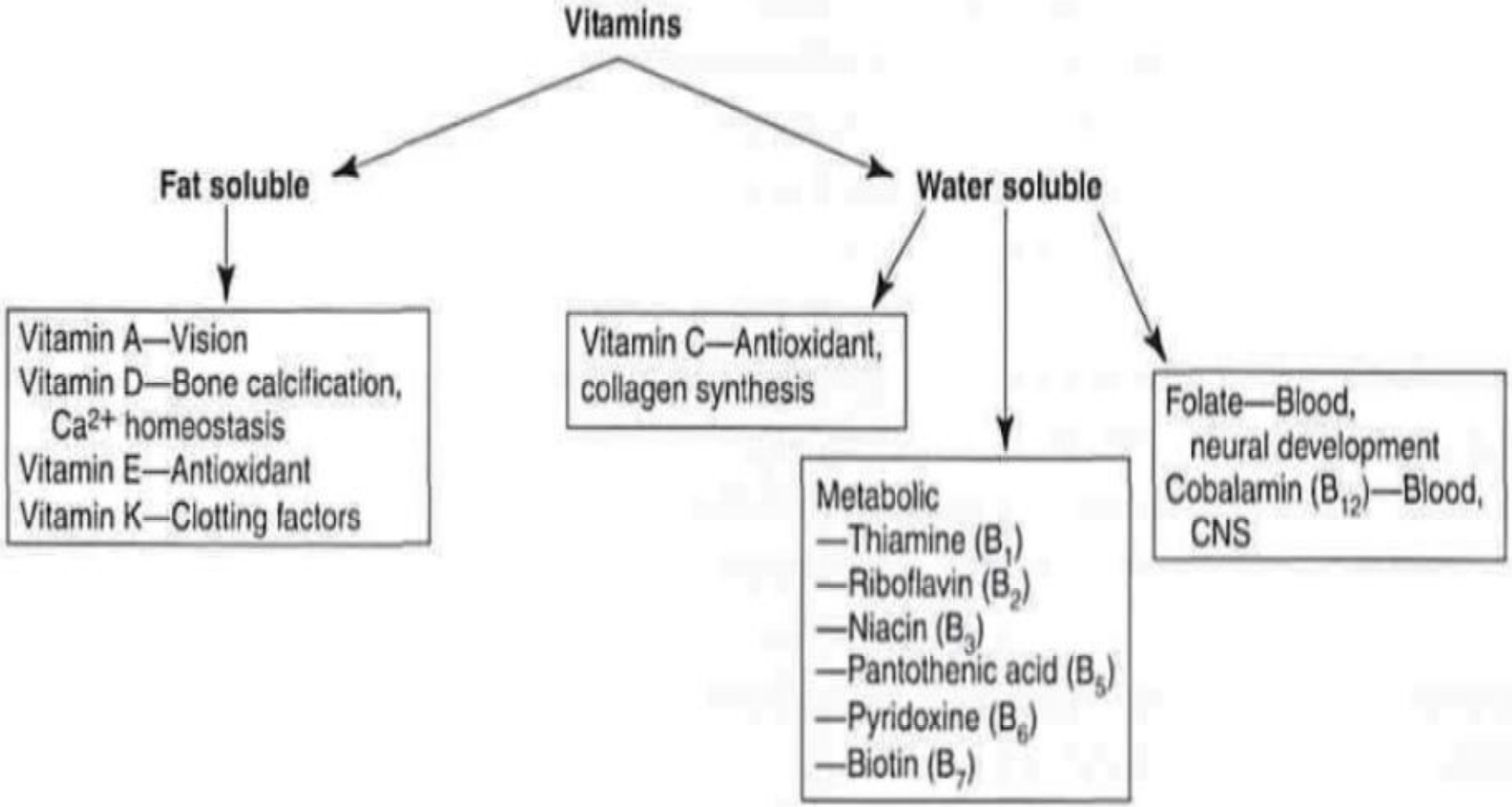
MENTAL CONFUSION

LACK OF MOTOR COORDINATION

MALAISE

- vague feeling of bodily discomfort

Vitamins


Vitamins
Fat soluble
Water soluble
Vitamin A—Vision
Vitamin D—Bone calcification, Ca^{2+} homeostasis
Vitamin E—Antioxidant
Vitamin K—Clotting factors
Vitamin C—Antioxidant, collagen synthesis
Metabolic
—Thiamine (B_1)
—Riboflavin (B_2)
—Niacin (B_3)
—Pantothenic acid (B_5)
—Pyridoxine (B_6)
—Biotin (B_7)
Folate—Blood, neural development
Cobalamin (B_{12})—Blood, CNS

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

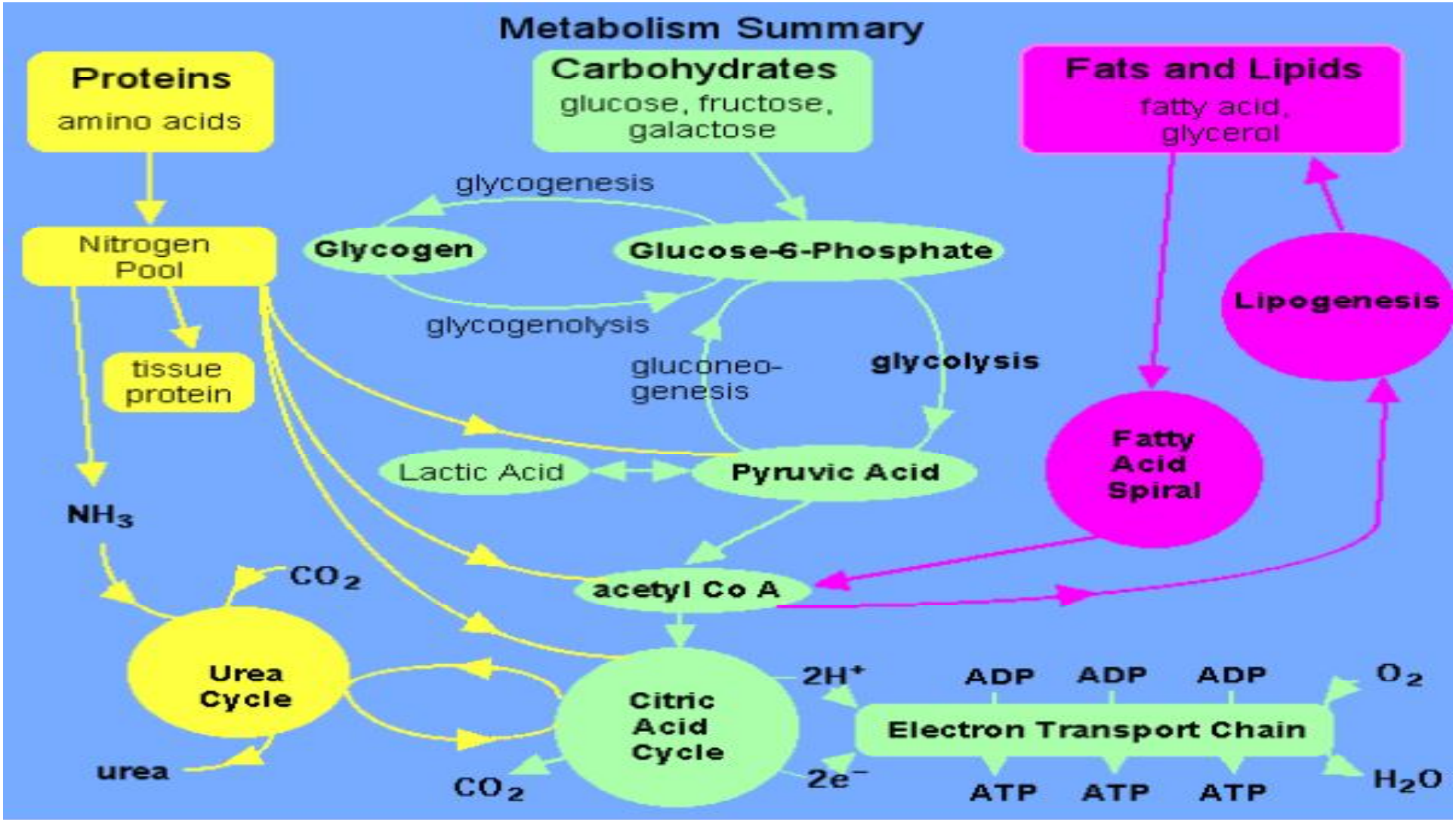
- Two types, based on solubility
  1. Water-soluble vitamins
     - B complex and C are absorbed with water
     - B_{12} absorption requires intrinsic factor
     - Not stored in the body

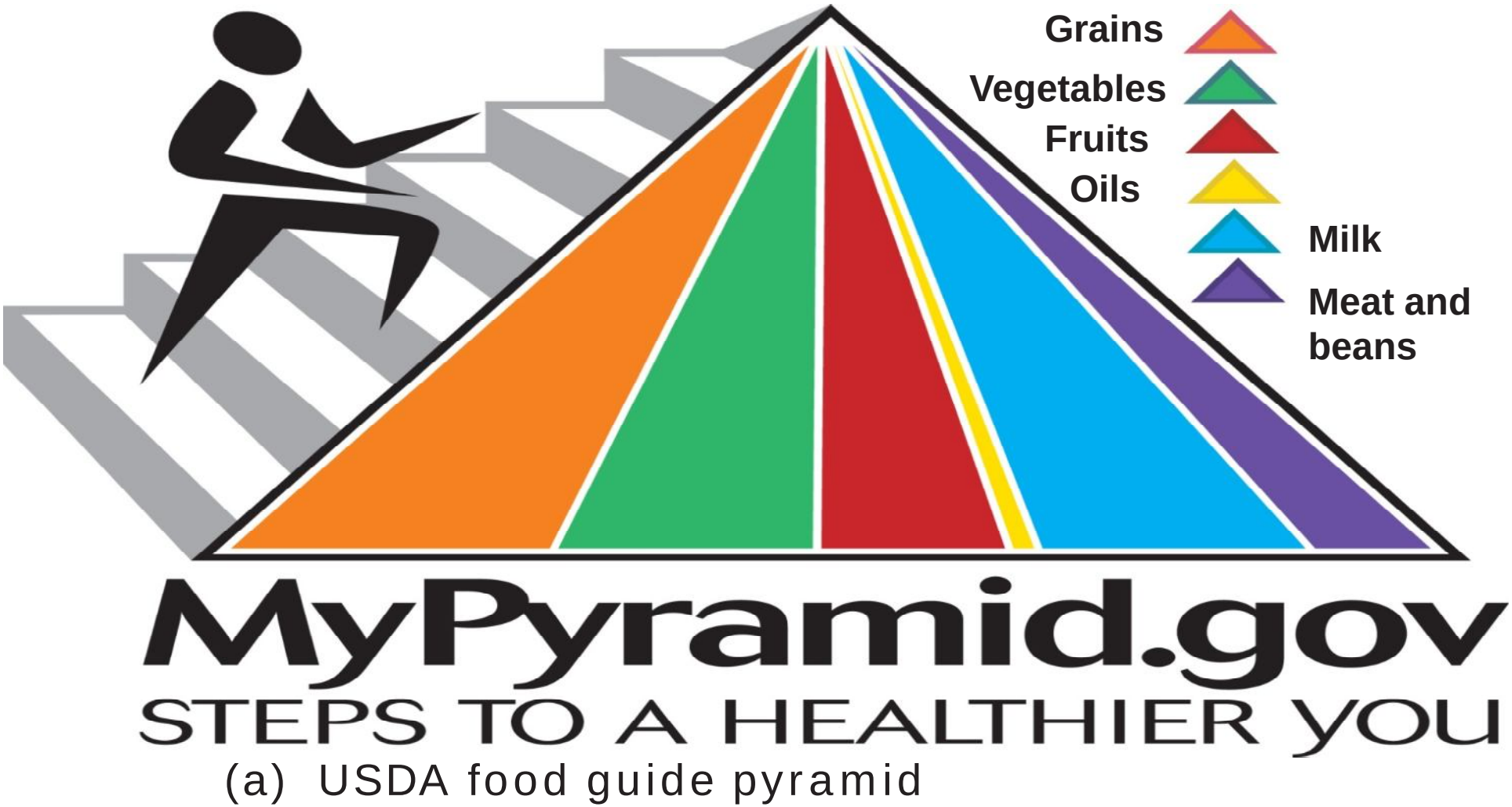
Vitamins

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

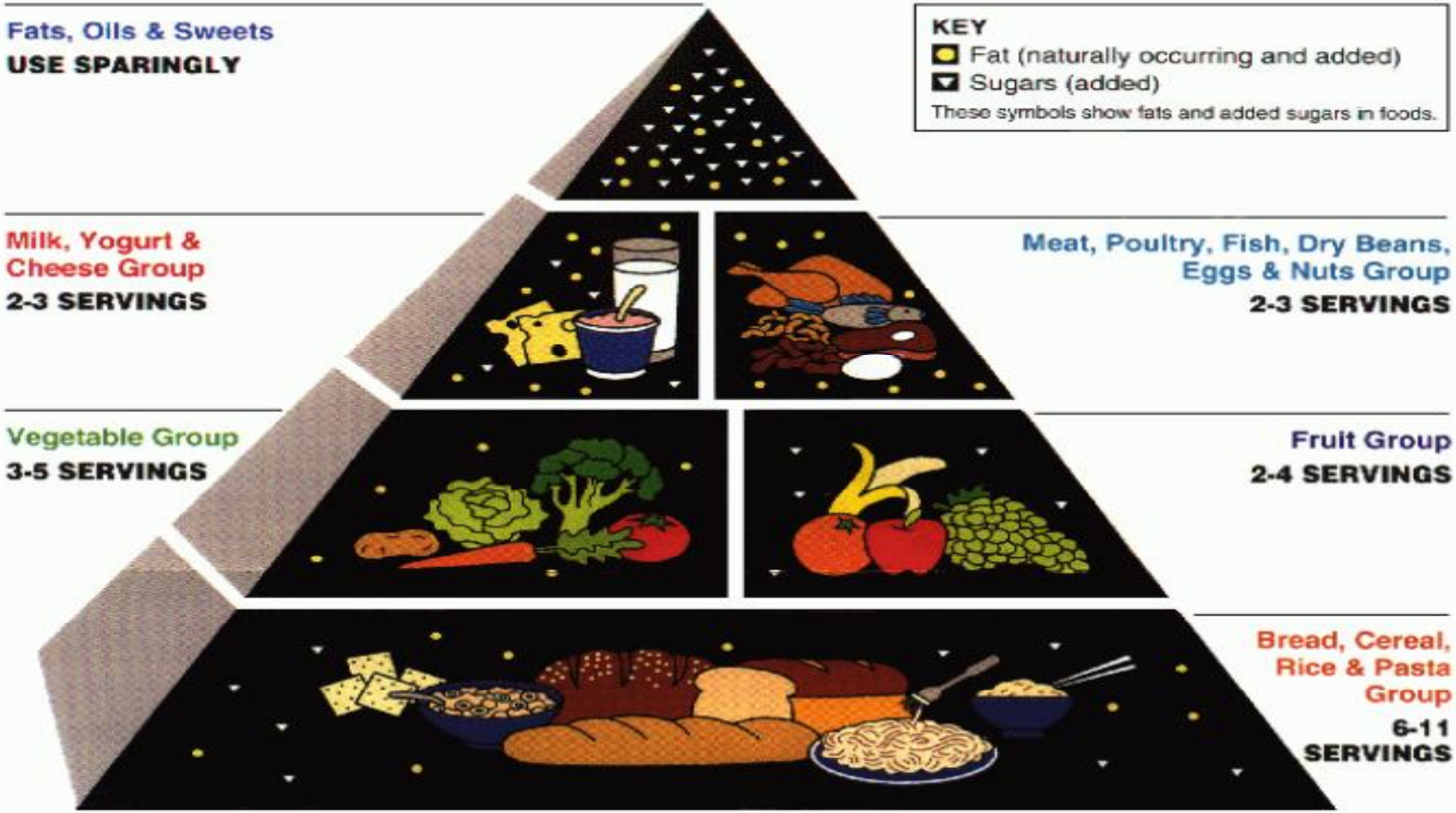
- Seven required in moderate amounts:
  - Calcium, phosphorus, potassium, sulfur, sodium, chloride, and magnesium
- Others required in trace amounts
- Work with nutrients to ensure proper body functioning
- Uptake and excretion must be balanced to prevent toxic overload


Metabolism Summary
Proteins
amino acids
Carbohydrates
glucose, fructose, galactose
Fats and Lipids
fatty acid, glycerol
glycogenesis
Nitrogen Pool
Glycogen
Glucose-6-Phosphate
Lipogenesis
glycogenolysis
tissue protein
gluconeo-genesis
glycolysis
Fatty Acid Spiral
Lactic Acid
Pyruvic Acid
NH3
CO2
acetyl Co A
Urea Cycle
Citric Acid Cycle
2H+
ADP ADP ADP
O2
Electron Transport Chain
urea
CO2
2e−
ATP ATP ATP
H2O



(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

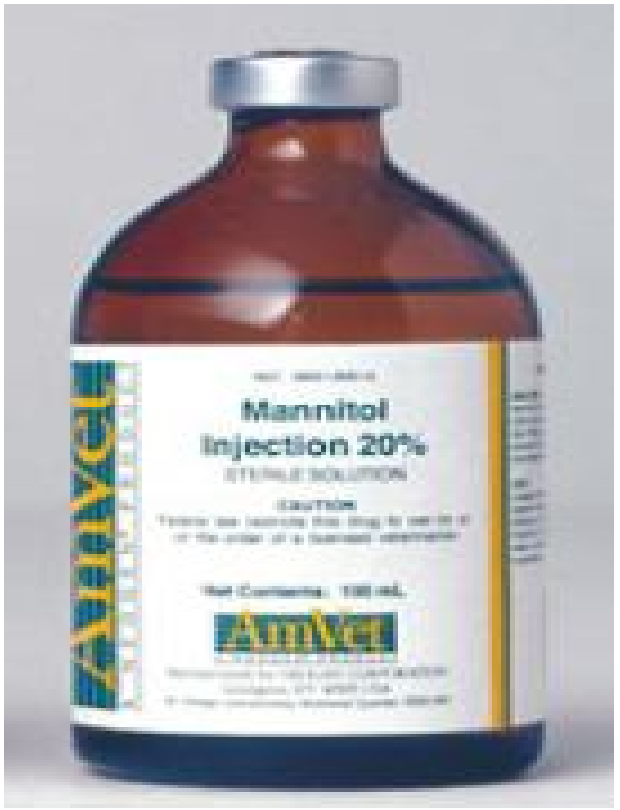
Digestion

- 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

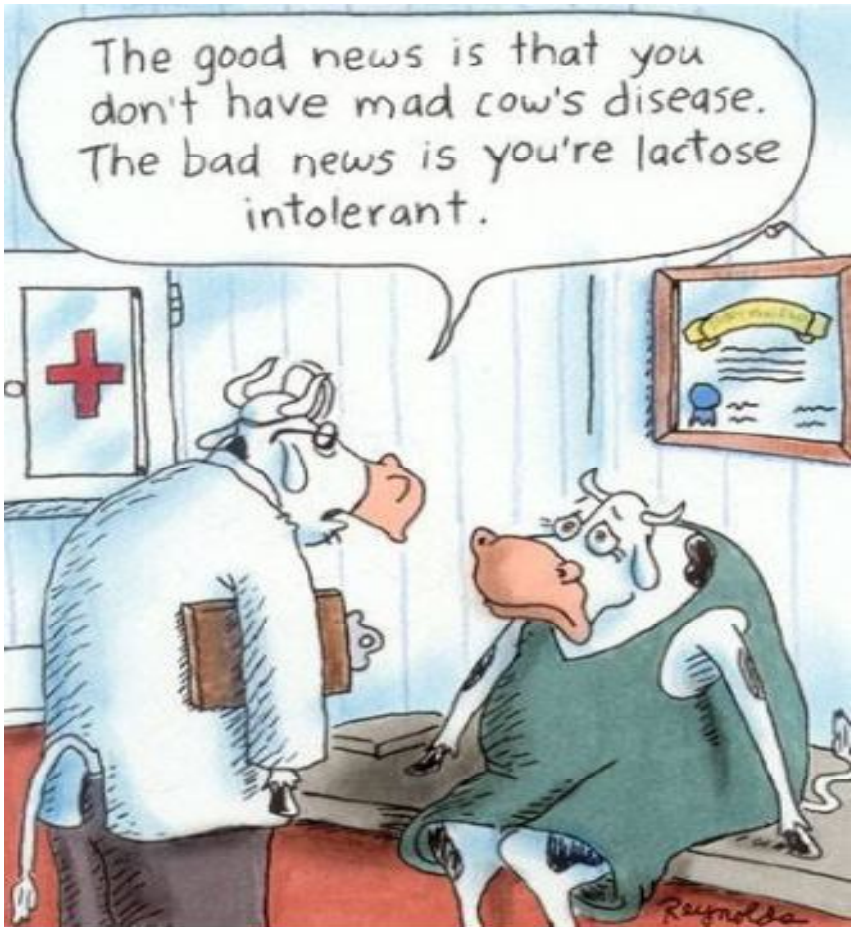
- Dietary requirements
  - Minimum 100 g/day to maintain adequate blood glucose levels
  - Recommended minimum 130 g/day
  - Recommended intake: 45–65% of total calorie intake; mostly complex carbohydrates


Brite-Life
70% SORBITOL
SOLUTION USP


Mannitol
Injection 20%
AMYCEL

Sugar cane

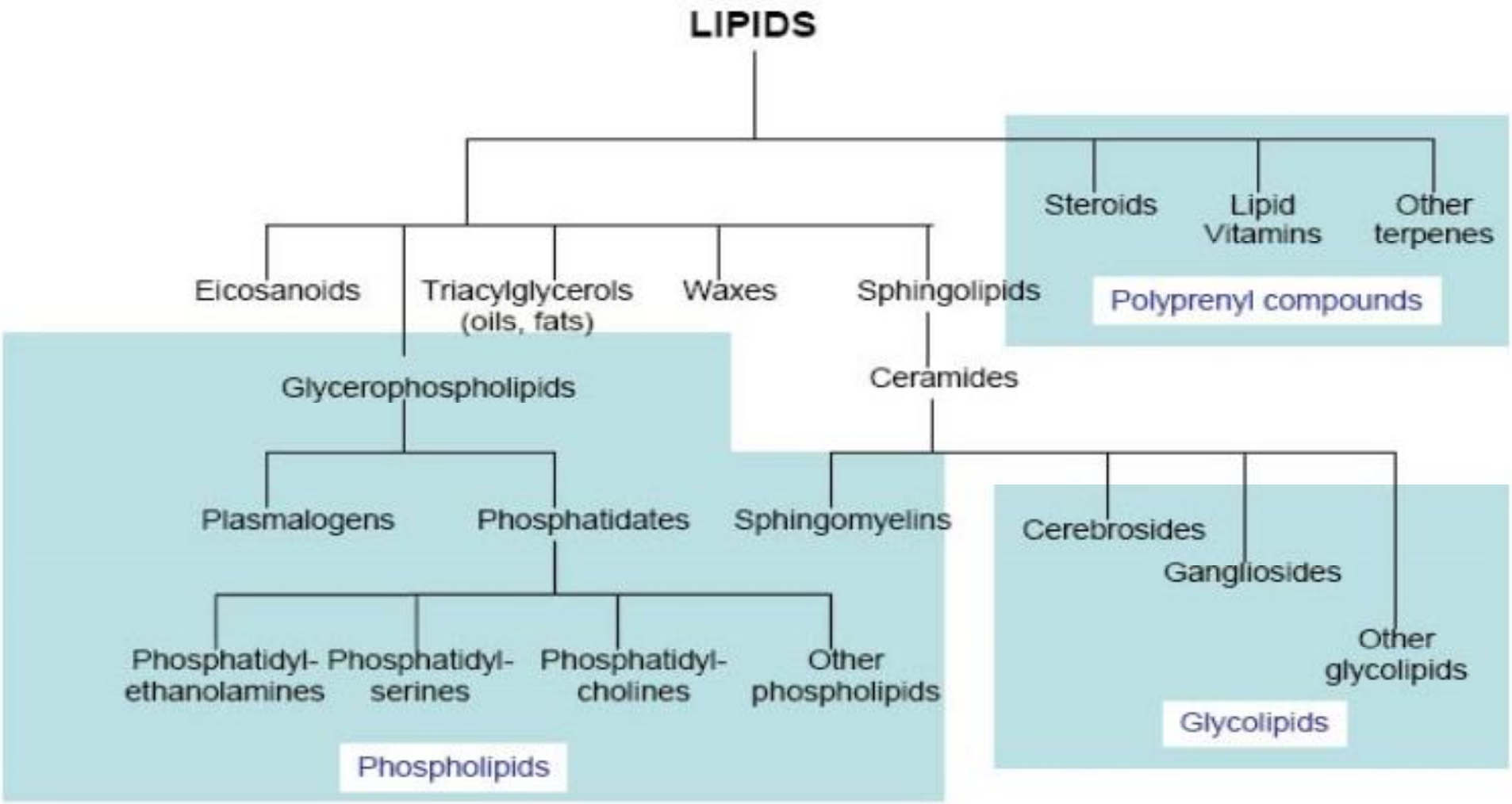
Sugar beet


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


Lactaid
ORIGINAL
Strength
120 Caplets

Lipids


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


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

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

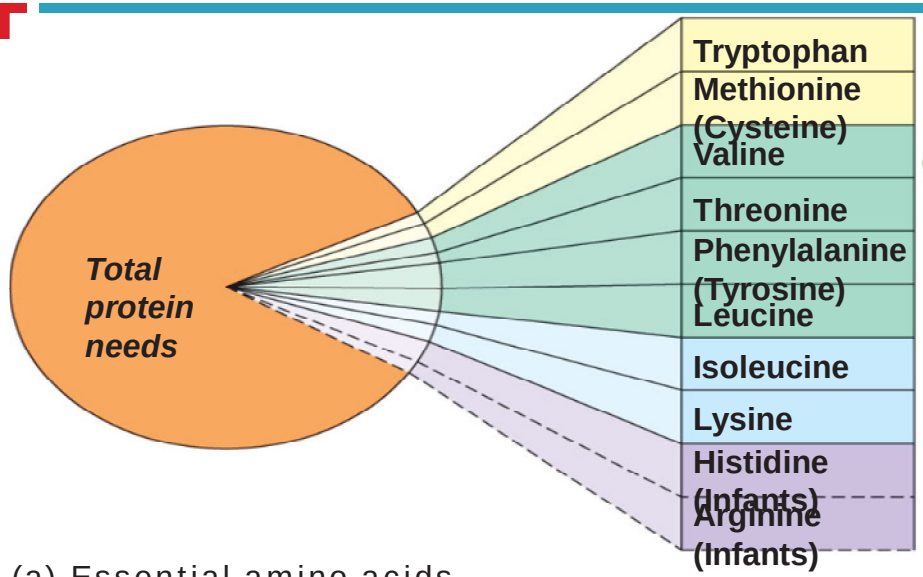
- also known as sphingolipidoses
- genetically acquired
- due to the deficiency or absence of a catabolic enzyme
- examples:
  - Tay Sachs disease
  - Gaucher's disease
  - Niemann-Pick disease
  - Fabry's disease

Proteins

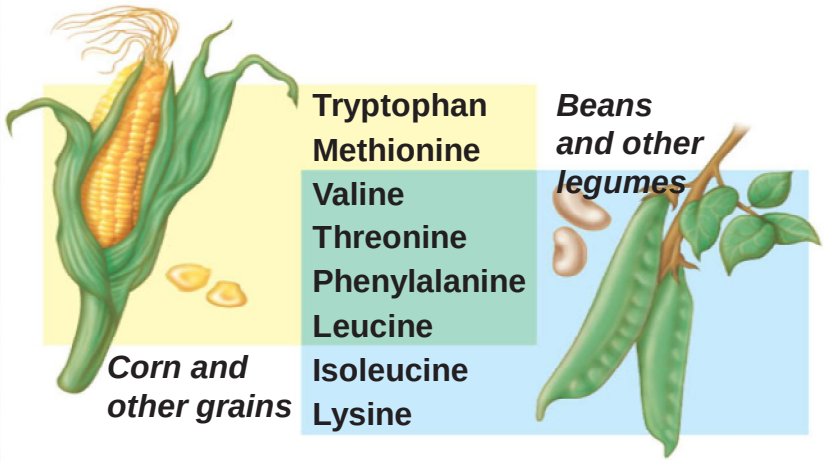
3. Nitrogen balance
   - State where the rate of protein synthesis equals the rate of breakdown and loss
   - Positive if synthesis exceeds breakdown (normal in children and tissue repair)
   - Negative if breakdown exceeds synthesis (e.g., stress, burns, infection, or injury)

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
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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

Metabolism

- 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

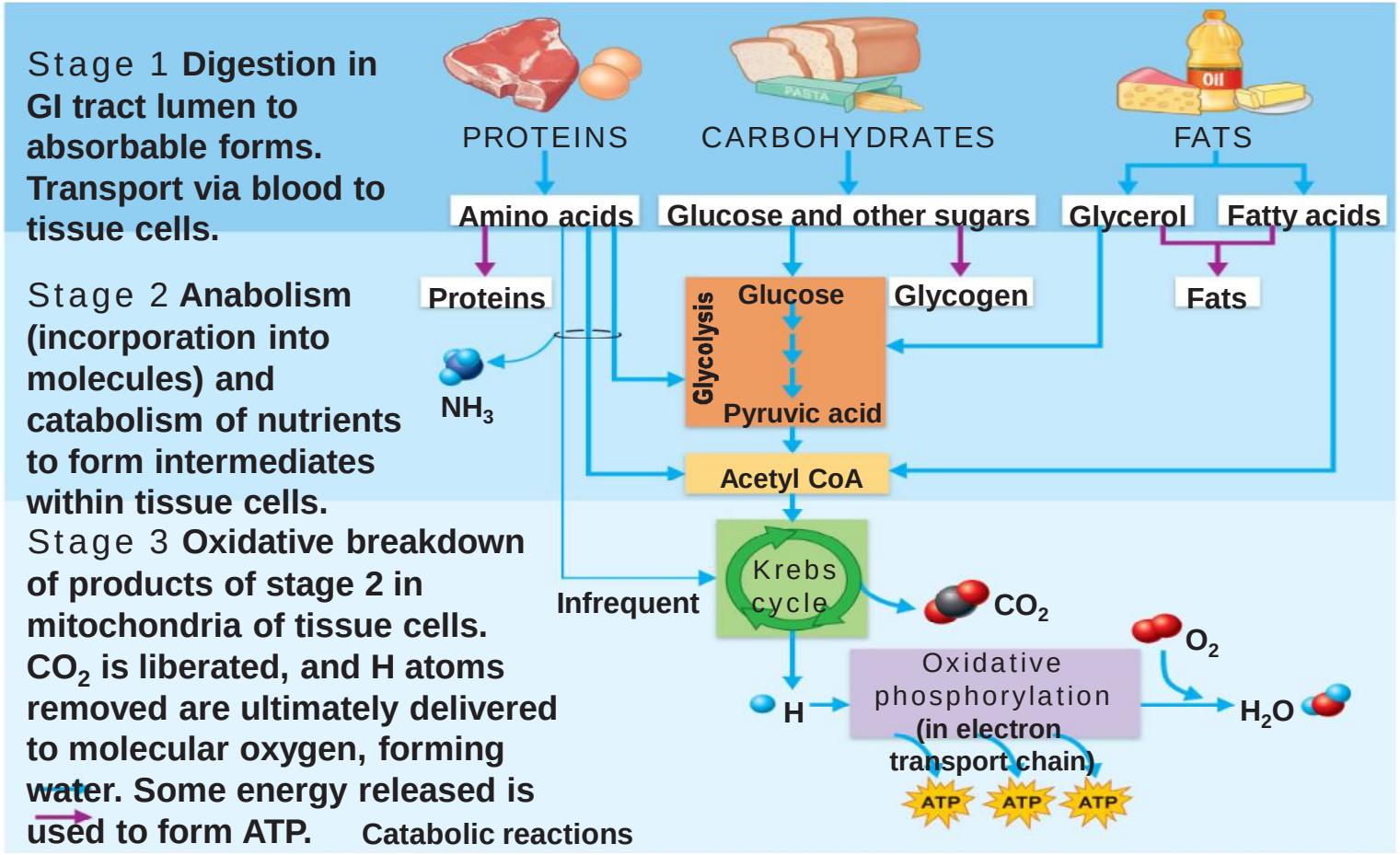

Stage 1 Digestion in GI tract lumen to absorbable forms. Transport via blood to tissue cells.
Stage 2 Anabolism (incorporation into molecules) and catabolism of nutrients to form intermediates within tissue cells.
Stage 3 Oxidative breakdown of products of stage 2 in mitochondria of tissue cells. CO_2 is liberated, and H atoms removed are ultimately delivered to molecular oxygen, forming water. Some energy released is used to form ATP.
PROTEINS
CARBOHYDRATES
FATS
Amino acids
Glucose and other sugars
Glycerol
Fatty acids
Proteins
Glucose
Glycogen
Fats
Glycolysis
NH_3
Pyruvic acid
Acetyl CoA
Infrequent
Krebs cycle
CO_2
O_2
H
Oxidative phosphorylation (in electron transport chain)
H_2O
ATP
ATP
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

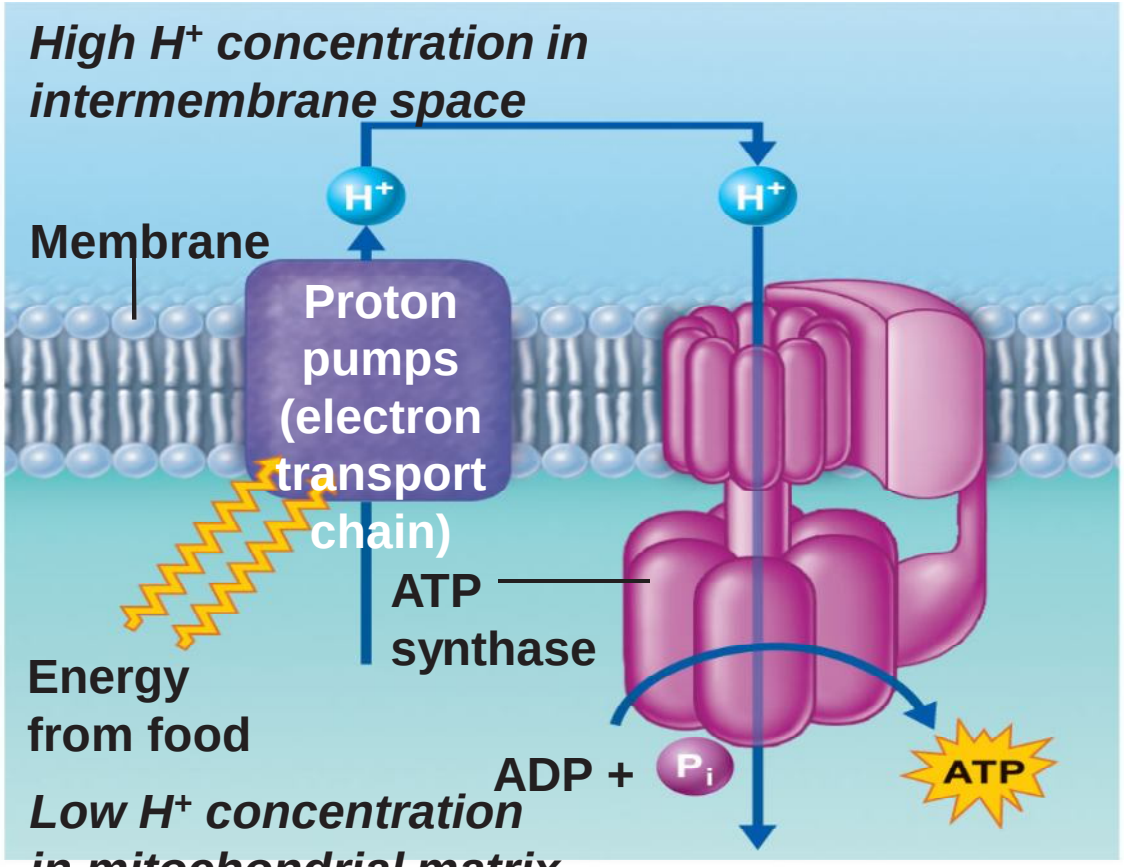
- Two mechanisms
  1. Substrate-level phosphorylation
  2. Oxidative phosphorylation

Substrate-Level Phosphorylation

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

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

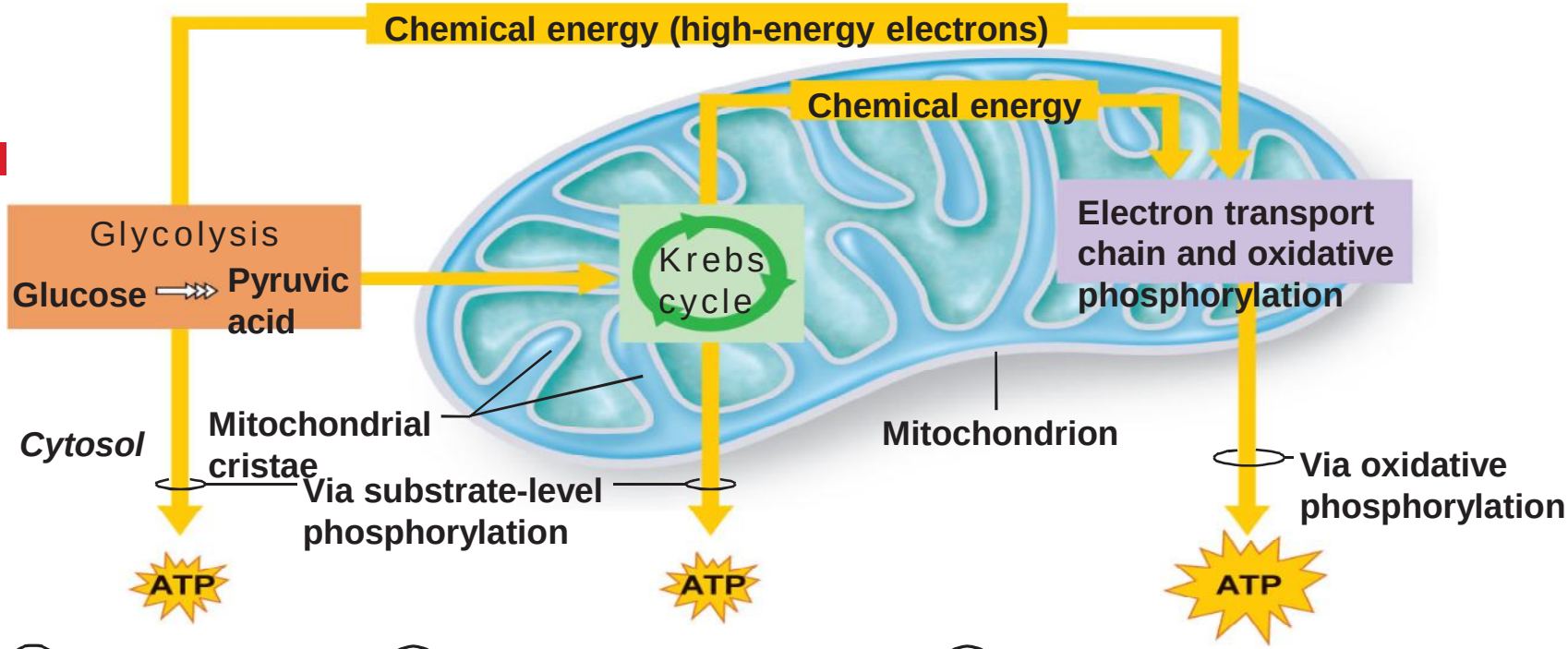
Figure 24.4b

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.

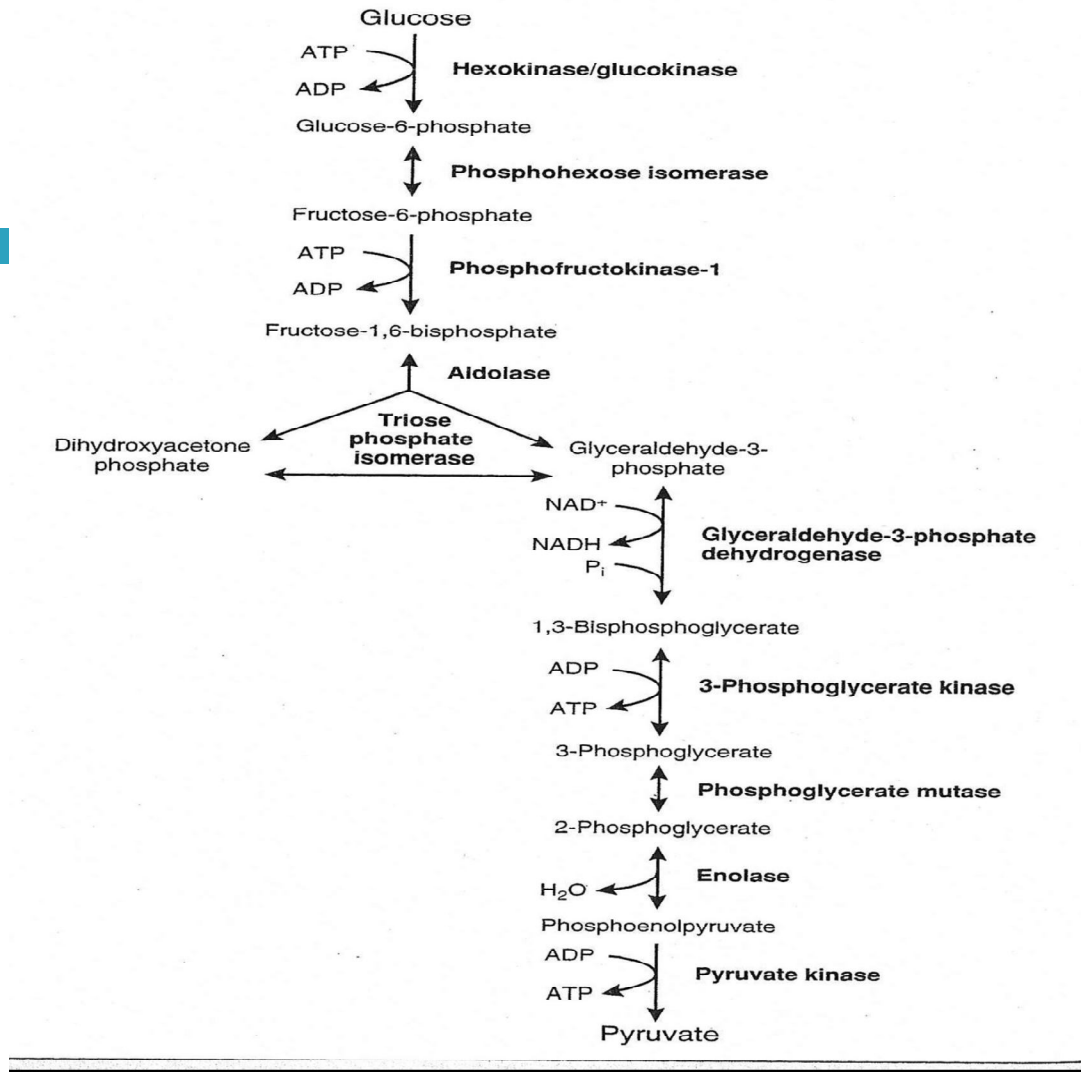
③ Energy-rich electrons picked up by coenzymes are transferred to the electron transport chain, built into the cristae membrane. The electron transport chain carries out oxidative phosphorylation, which accounts for most of the ATP generated by cellular respiration.

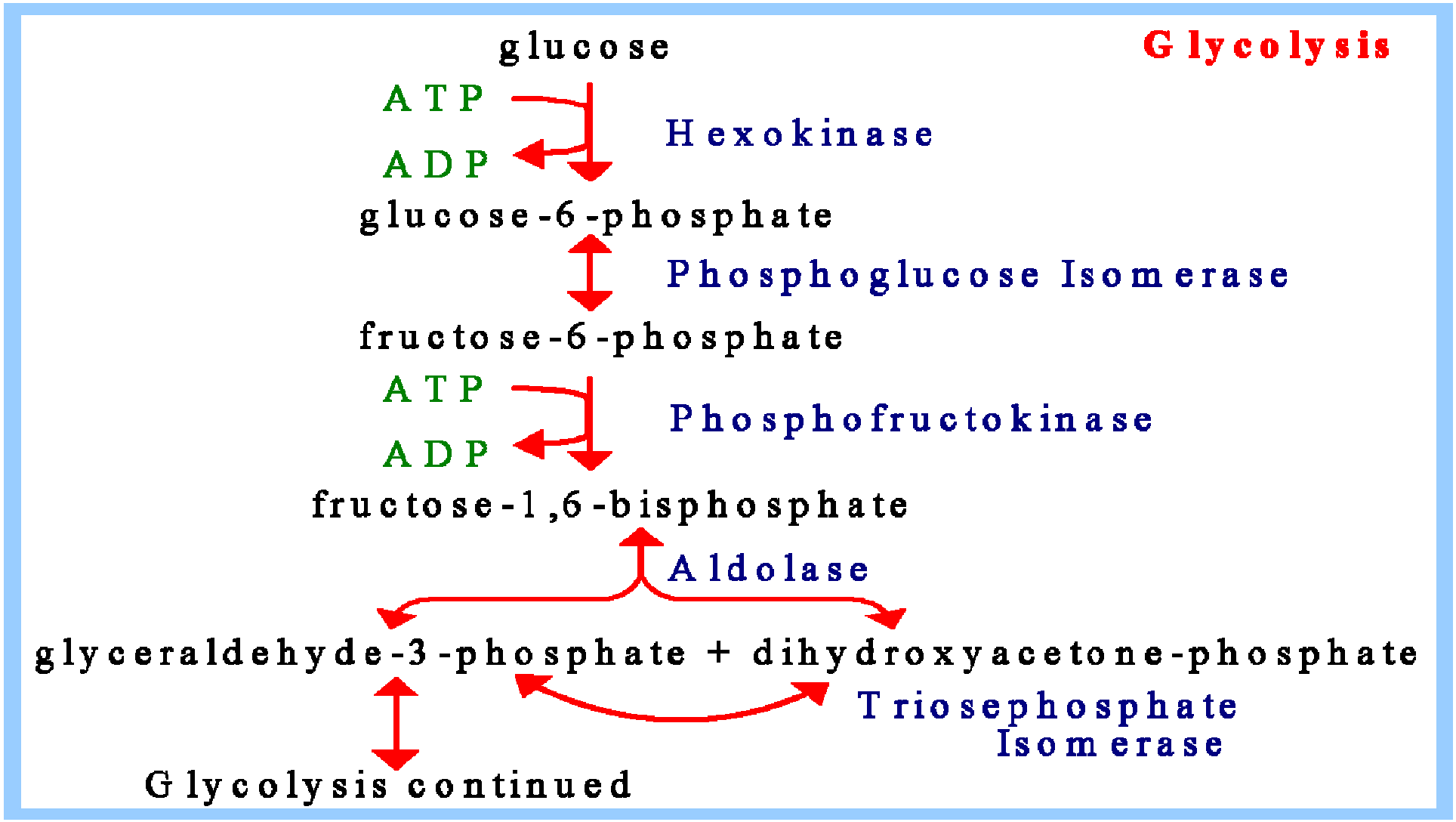
Figure 24.5

Glycolysis:

Embden-Myerhof Pathway

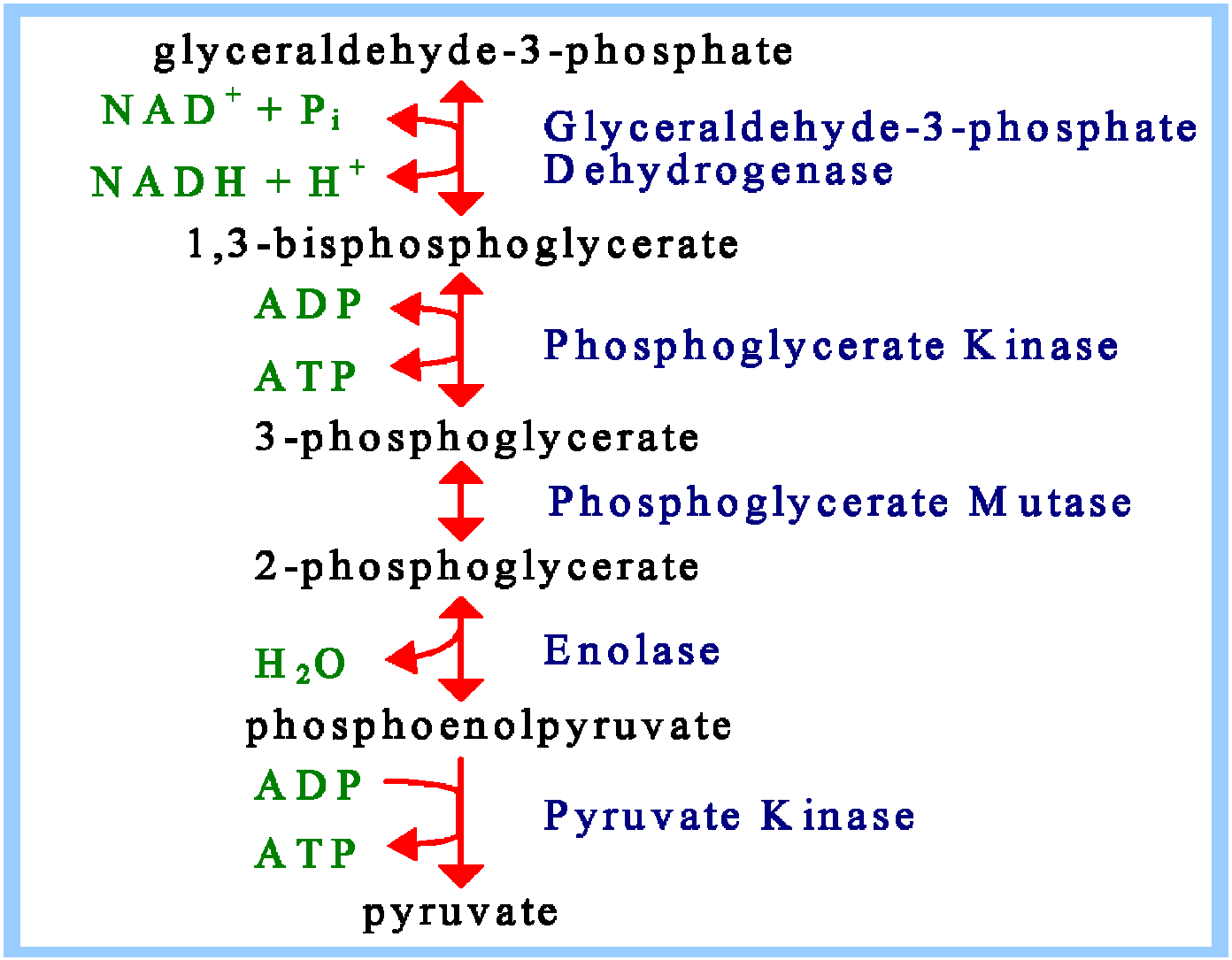
- Oxidation of glucose
- Products:
  - 2 Pyruvate
  - 2 ATP
  - 2 NADH
- Cytosolic




Glycolysis
glucose
ATP
ADP
Hexokinase
glucose-6-phosphate
Phosphoglucose Isomerase
fructose-6-phosphate
ATP
ADP
Phosphofructokinase
fructose-1,6-bisphosphate
Aldolase
glyceraldehyde-3-phosphate + dihydroxyacetone-phosphate
Triosephosphate Isomerase
Glycolysis continued

Glycolysis continued.

Recall that there are 2 GAP per glucose.



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

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

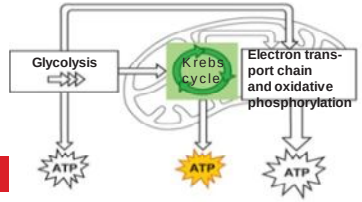
Krebs Cycle

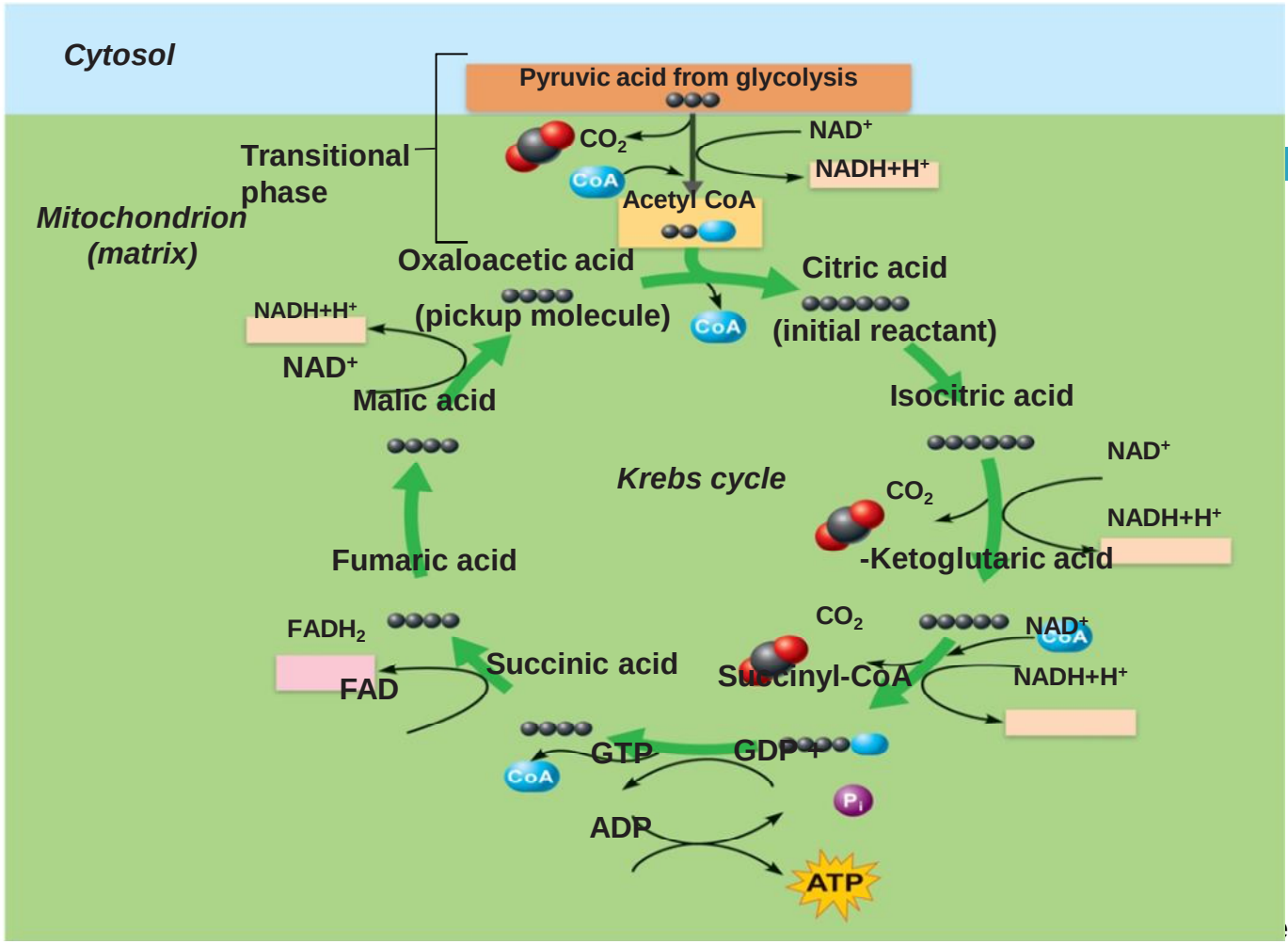
- Coenzyme A shuttles acetic acid to an enzyme of the Krebs cycle
- Each acetic acid is decarboxylated and oxidized, generating:
  - 3 $NADH + H^+$
  - 1 $FADH_2$
  - 2 CO_2
  - 1 ATP

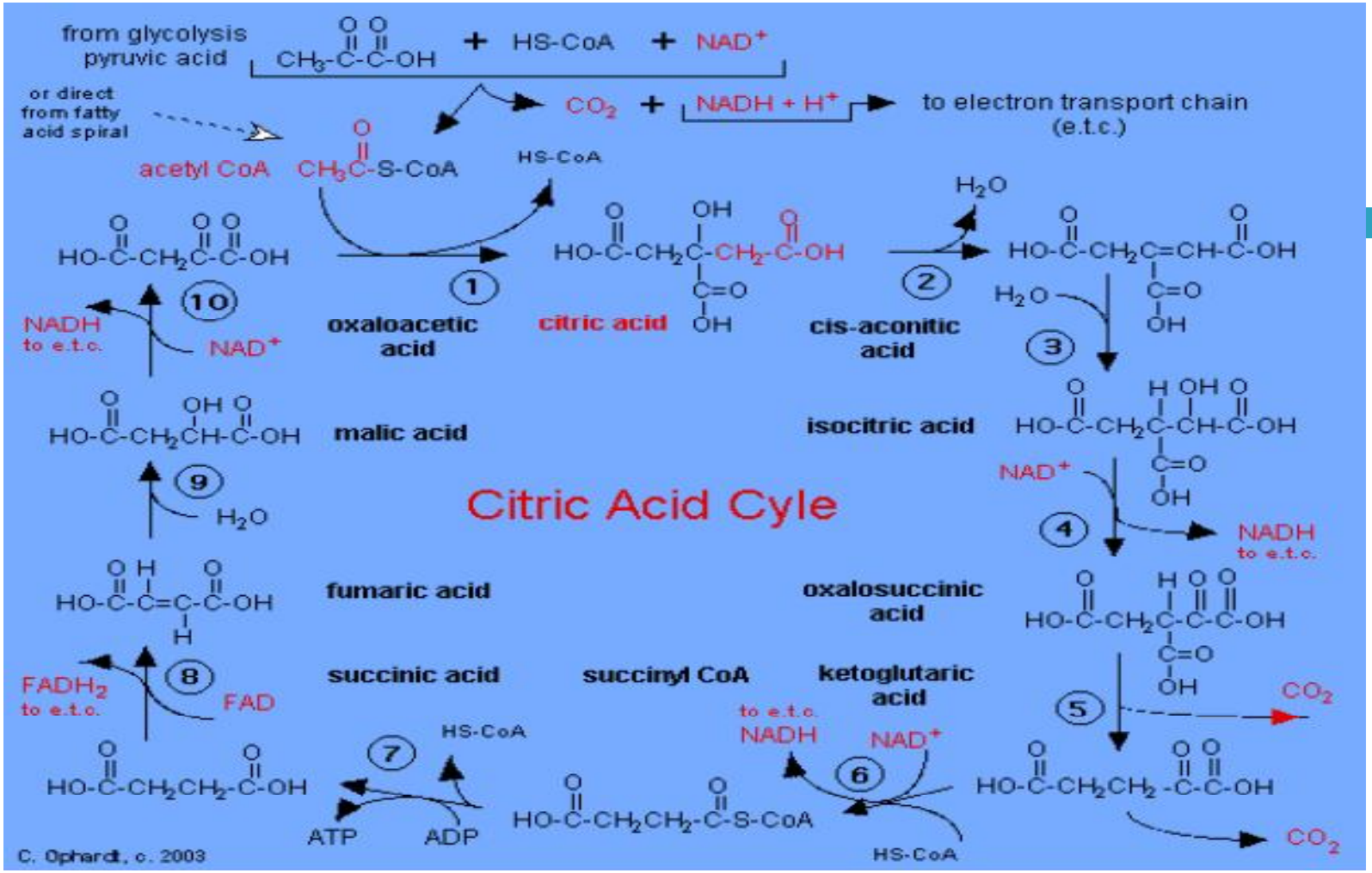
Krebs Cycle

- 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

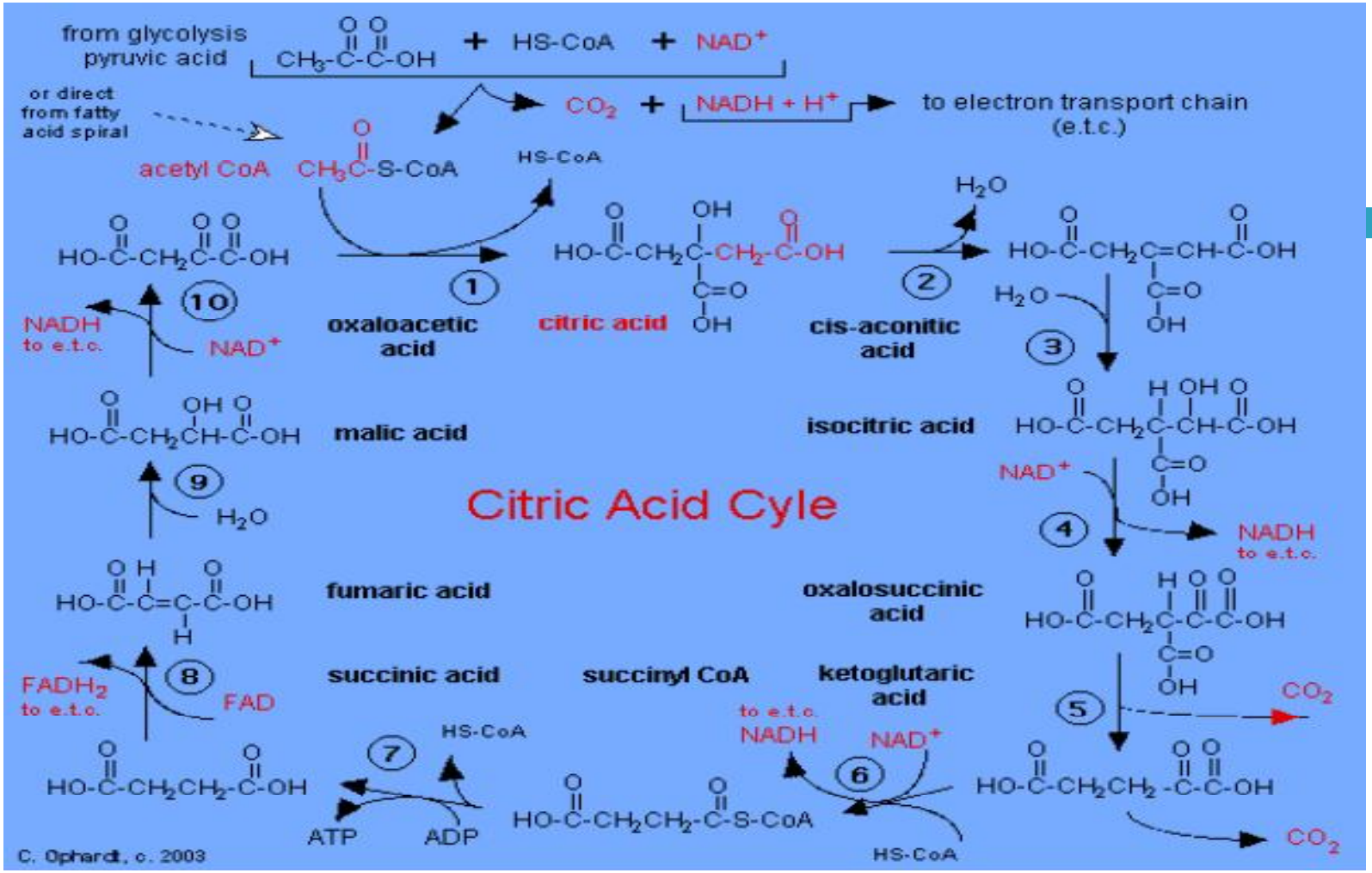
PLAY **Animation: Krebs Cycle**


Glycolysis
Krebs cycle
Electron transport chain and oxidative phosphorylation
ATP
ATP
ATP
Carbon atom
Inorganic phosphate
Coenzyme A


Cytosol
Pyruvic acid from glycolysis
Transitional phase
CO2
NAD+
NADH+H+
CoA
Acetyl CoA
Mitochondrion (matrix)
Oxaloacetic acid
(pickup molecule)
Citric acid
(initial reactant)
NADH+H+
NAD+
Malic acid
Isocitric acid
Krebs cycle
NAD+
CO2
NADH+H+
-Ketoglutaric acid
Fumaric acid
FADH2
FAD
Succinic acid
CO2
NAD+
Succinyl-CoA
NADH+H+
GTP
GDP
ADP
ATP

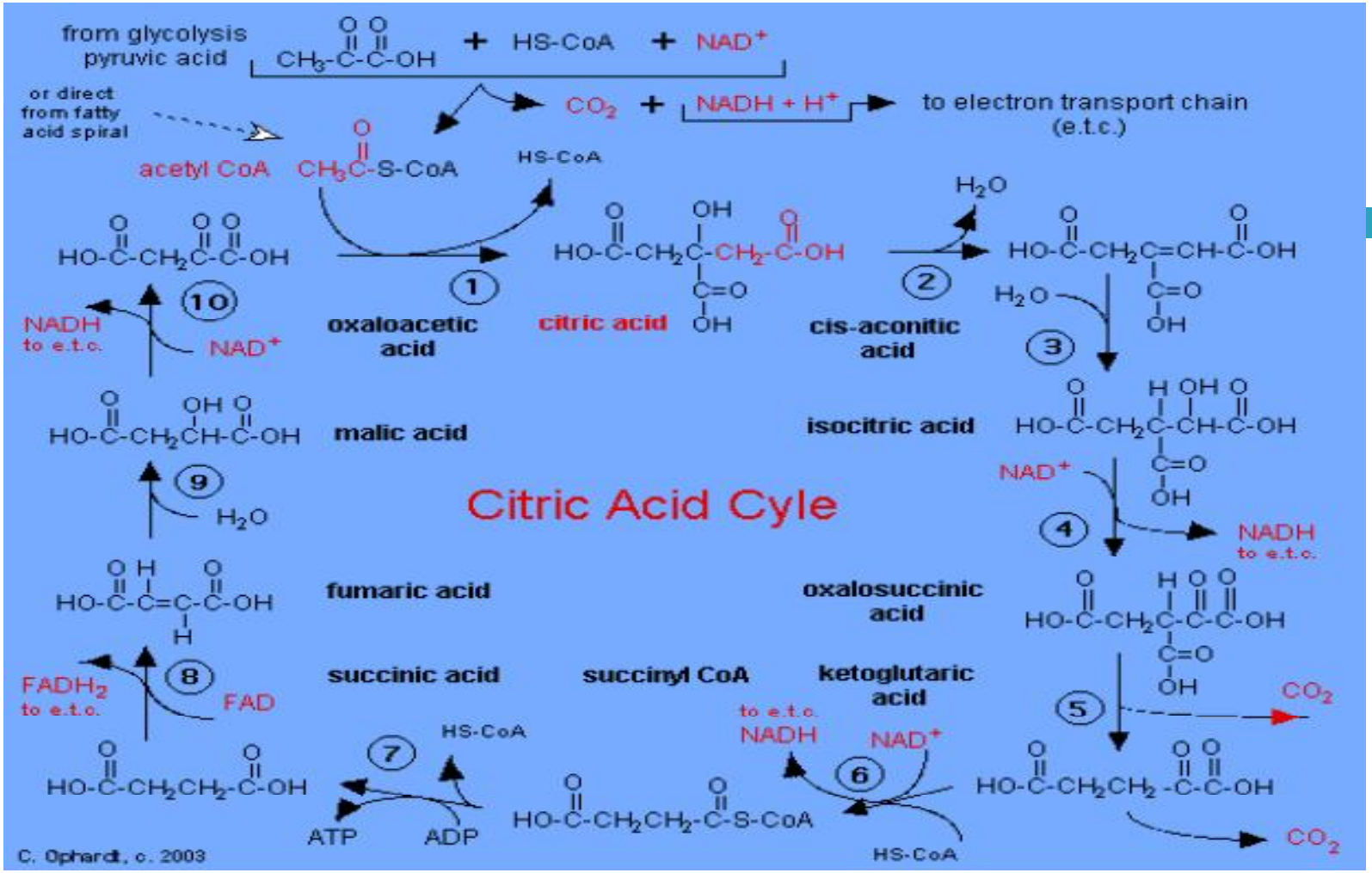


1. Synthesis of citric acid
2. Dehydra-tion
3. Hydration



4. Oxidation NAD^+ to electron transport

5. Decar-boxy-lation Remove CO_2

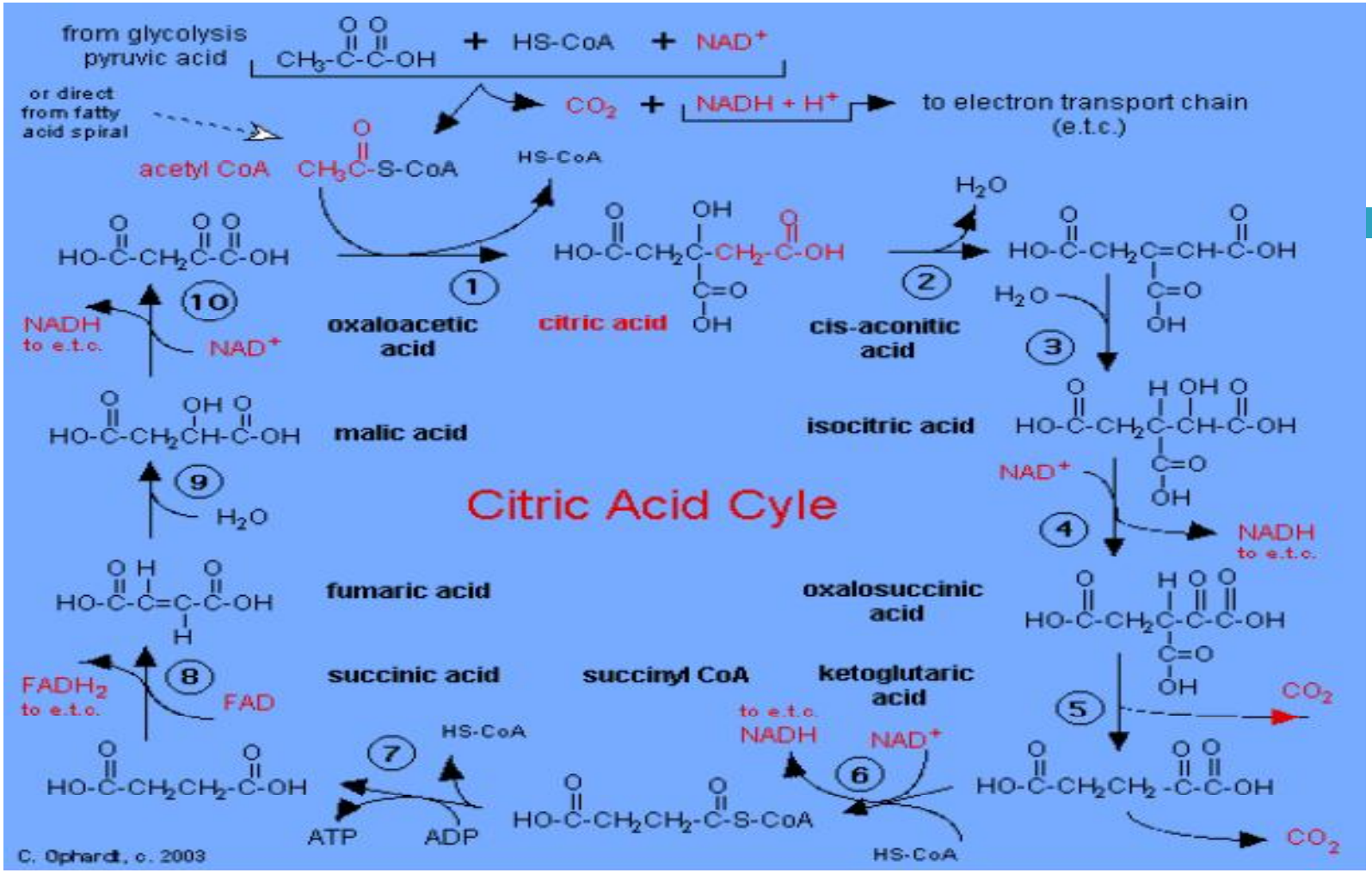


6. Oxidation

NAD^+ to electron transport

Decar-boxy-lation

Thiol synthesis



7. Hydrol-ysis

Make ATP

8. Oxidation

9. Hydration

10. Oxidation

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

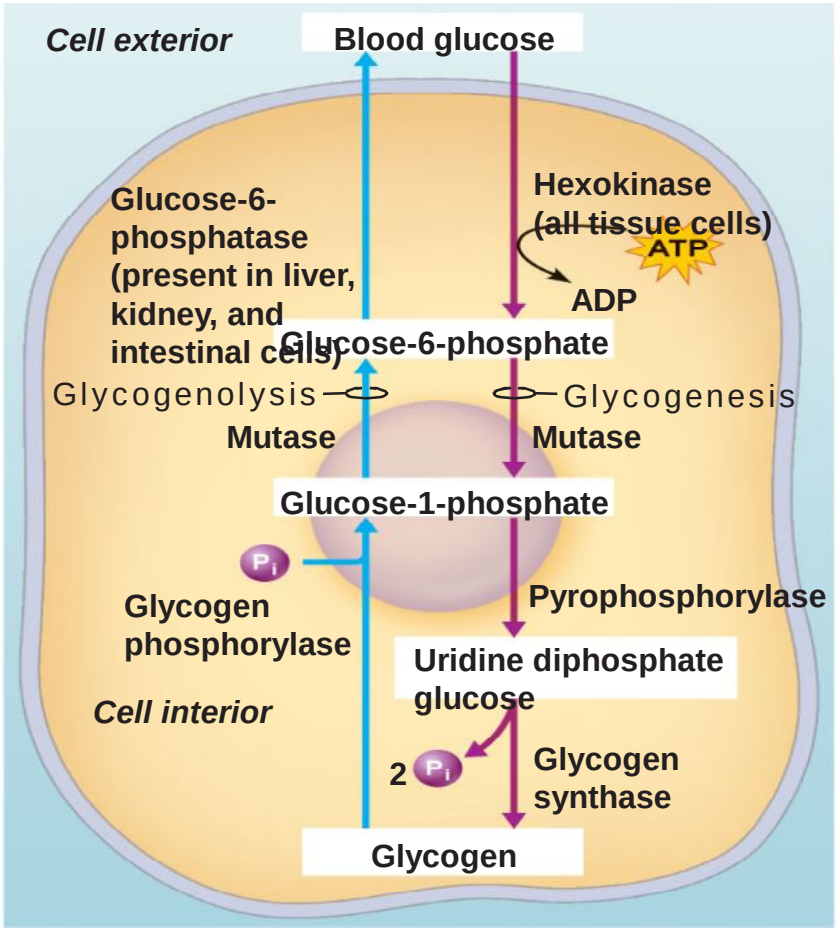

Cell exterior
Blood glucose
Glucose-6-phosphatase (present in liver, kidney, and intestinal cells)
Hexokinase (all tissue cells)
ATP
ADP
Glucose-6-phosphate
Glycogenolysis
Glycogenesis
Mutase
Mutase
Glucose-1-phosphate
Pi
Glycogen phosphorylase
Pyrophosphorylase
Uridine diphosphate glucose
Cell interior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