Chapter 4
Cellular Metabolism

Metabolic processes – all chemical reactions that occur in the body

Two types of metabolic reactions

Anabolism
- **larger molecules are made**
- **requires energy**

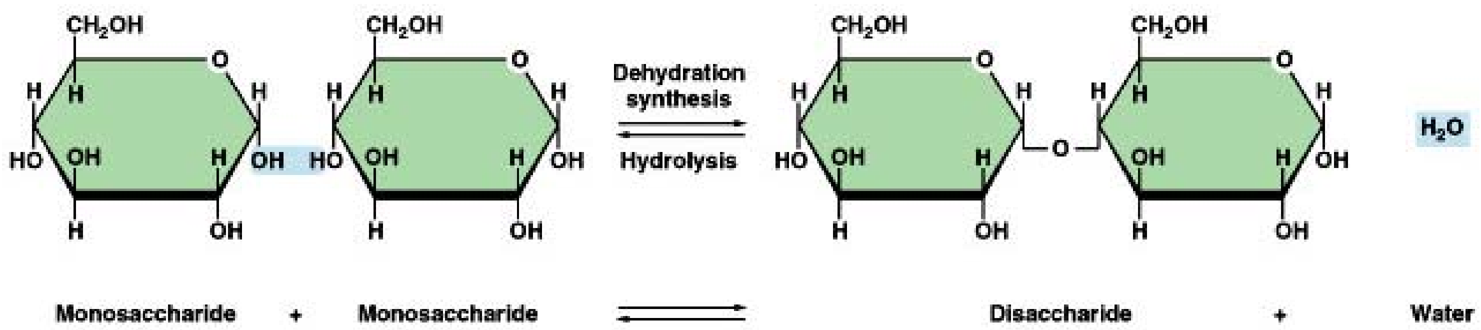
Catabolism
- **larger molecules are broken down**
- **releases energy**

Anabolism

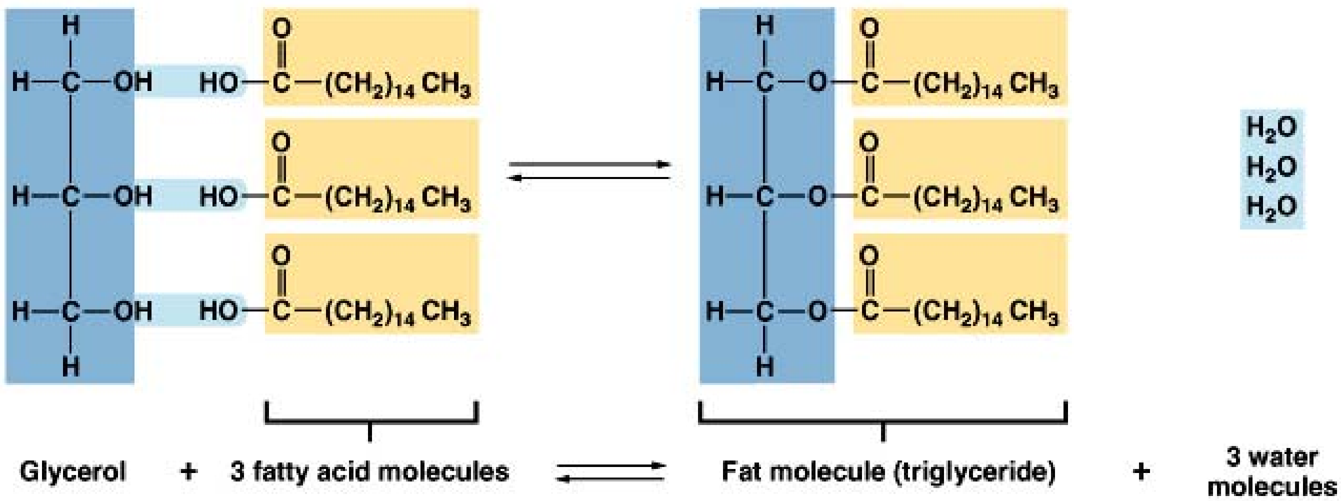
Anabolism provides the substances needed for cellular growth and repair

Dehydration synthesis

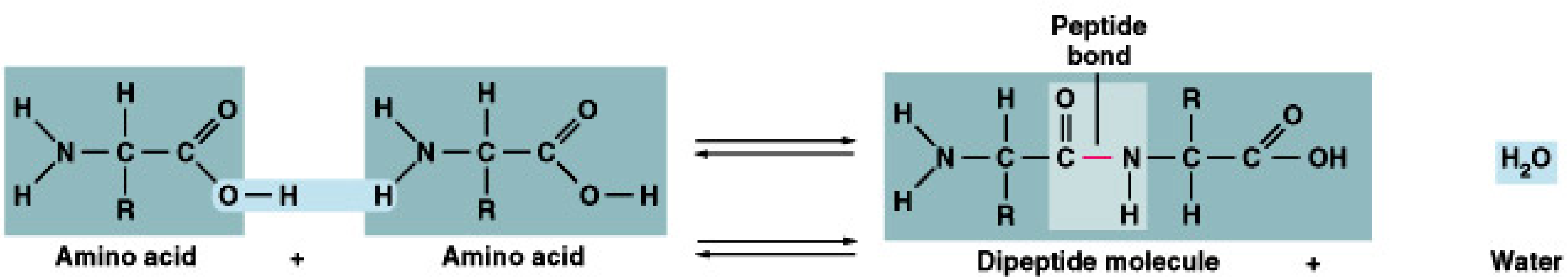
- **type of anabolic process**
- **used to make polysaccharides, triglycerides, and proteins**
- **produces water**



Anabolism



Glycerol
+
3 fatty acid molecules
Fat molecule (triglyceride)
+
3 water molecules



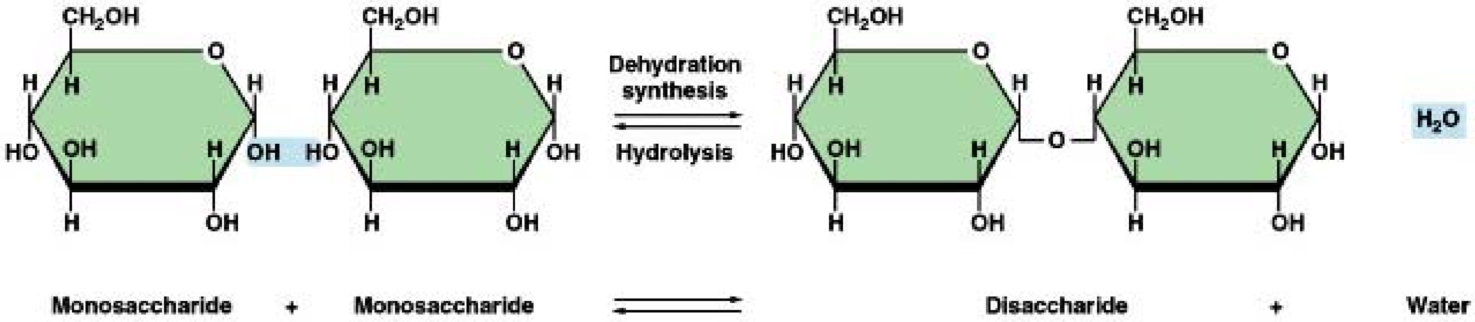
Peptide bond
Amino acid
+
Amino acid
Dipeptide molecule
+
Water

Catabolism

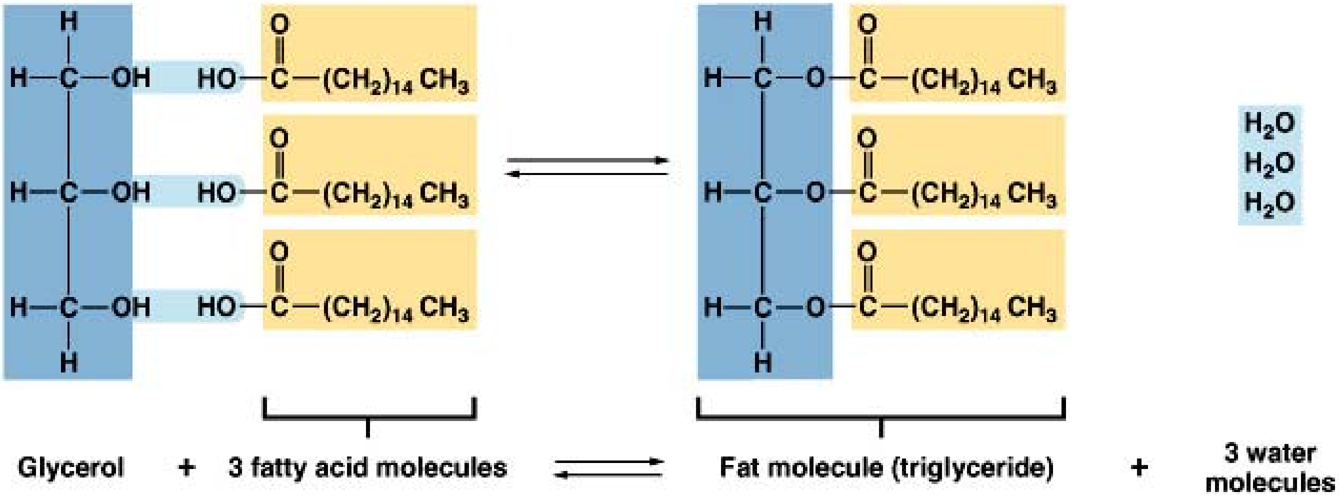
Catabolism breaks down larger molecules into smaller ones

Hydrolysis

- **a catabolic process**
- **used to decompose carbohydrates, lipids, and proteins**
- **water is used**
- **reverse of dehydration synthesis**



Catabolism



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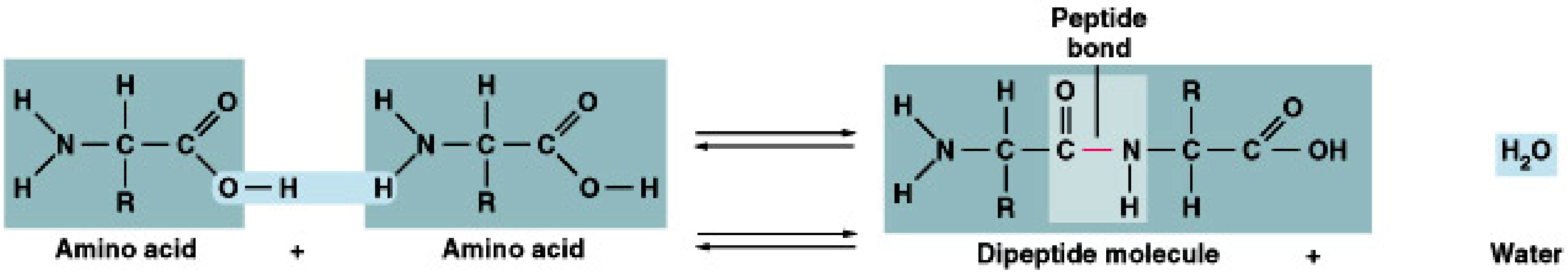
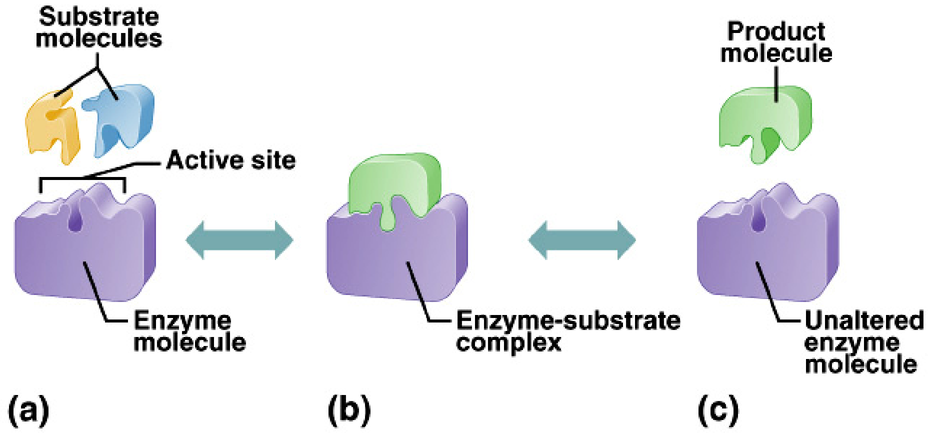


Peptide bond
Amino acid
+
Amino acid
Dipeptide molecule
+
Water

Control of Metabolic Reactions

Enzymes

- control rates of metabolic reactions
- lower activation energy needed to start reactions
- globular proteins with specific shapes
- not consumed in chemical reactions
- substrate specific
- shape of active site determines substrate



Control of Metabolic Reactions

Metabolic pathways

- **series of enzyme-controlled reactions leading to formation of a product**
- **each new substrate is the product of the previous reaction**

Enzyme names commonly

- **reflect the substrate**
- **have the suffix – ase**
- **sucrase, lactase, protease, lipase**

Tyrosinase and Melanin

Grey Squirrels:

Melanic and Albino Forms

tyrosinase - A copper-containing enzyme of plant and animal tissues that catalyzes the production of **melanin** and other pigments from tyrosine by oxidation, as in the blackening of a peeled or sliced potato exposed to air.

Control of Metabolic Reactions

Cofactors

- make some enzymes active
- ions or coenzymes

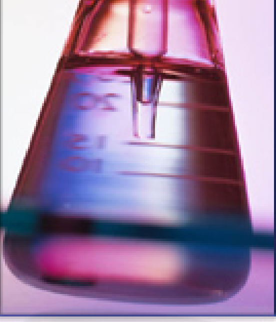
Coenzymes

- organic molecules that act as cofactors
- vitamins

Factors that alter enzymes

- temperature and heat
- radiation
- electricity
- chemicals
- changes in pH

Temperature Sensitive Tyrosinase – Siamese Cats & Himalayan Rabbits



Human Physiology: Energy Releasing Metabolic Reactions

Energy

- **ability to do work or change something**
- **heat, light, sound, electricity, mechanical energy, chemical energy**
- **changed from one form to another**
- **involved in all metabolic reactions**

Release of chemical energy

- **most metabolic processes depend on chemical energy**
- **oxidation of glucose generates chemical energy**
- **cellular respiration releases chemical energy from molecules and makes it available for cellular use**

Energy can be transformed from one form to another

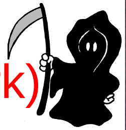
FREE ENERGY

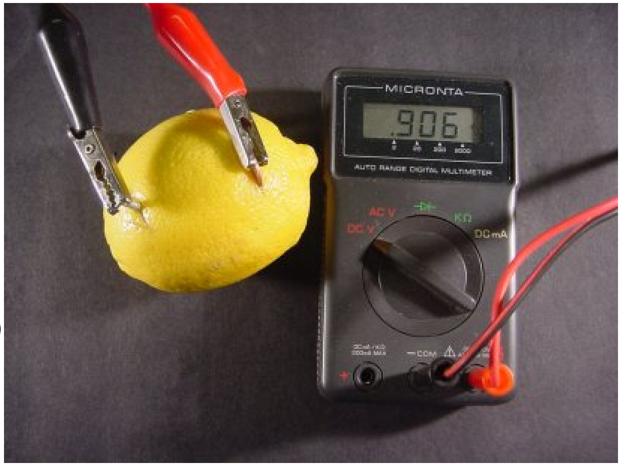
(available for work)

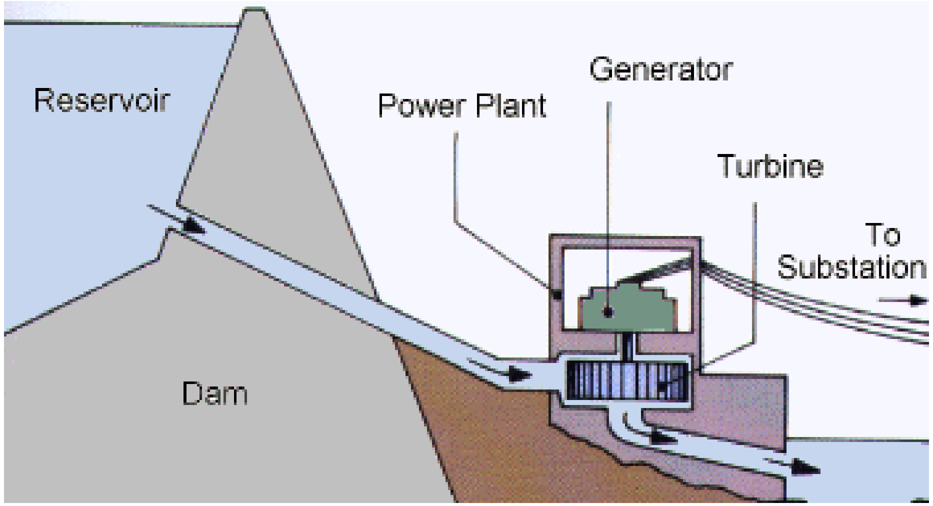
vs.

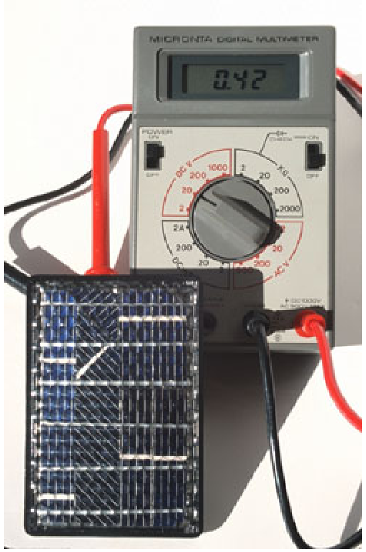
HEAT

(not available for work)





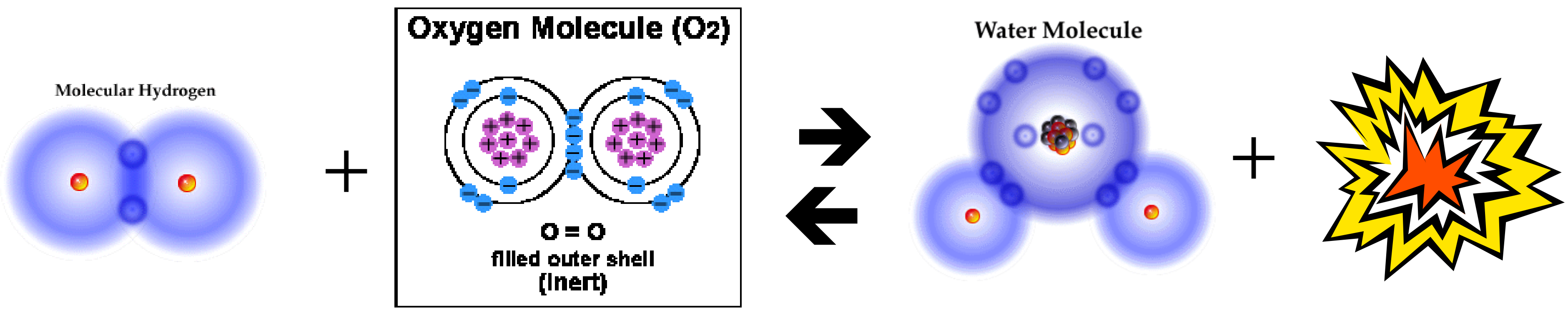




Regulation of energy-releasing (cellular respiration) and energy-acquiring chemical reactions in biological systems

- Chemically-mediated by enzymes and co-factors
- Occur in a step-wise manner

$$2H_2 + O_2 \rightarrow 2H_2O + \text{energy}$$

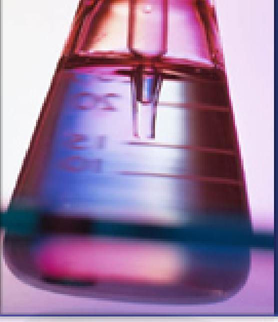


$$2H\text{-}H + O{=}O \rightarrow 2H_2O + \text{energy}$$

Modes of Energy Transformation: Rapid & Uncontrolled

- $2H_2 + O_2 \rightarrow 2H_2O$ + energy
- Release of energy can be uncontrolled and liberated mostly as heat!

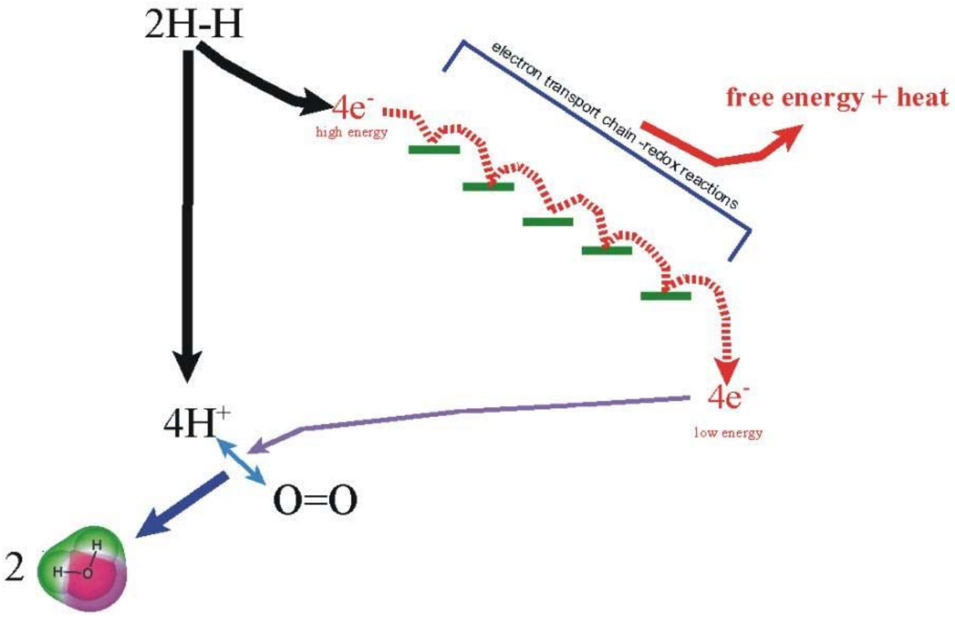
On May 6th, 1937 in Lakehurst, New Jersey. The German passenger Zeppelin Airship called the *Hindenburg*, was attempting a mooring when it exploded.



Modes of Energy Transformation: Released in controlled steps or stages

- $2H_2 + O_2 \rightarrow 2H_2O$ + energy
- Released in steps to salvage free energy and minimize heat production

The electrons from the hydrogen bond go through a series of oxidation & reduction reactions. During each step some energy is harvested, while the remainder is released as heat.



Cellular Respiration

Occurs in three series of reactions

1. **Glycolysis**
2. **Citric acid cycle**
3. **Electron transport chain**

Produces

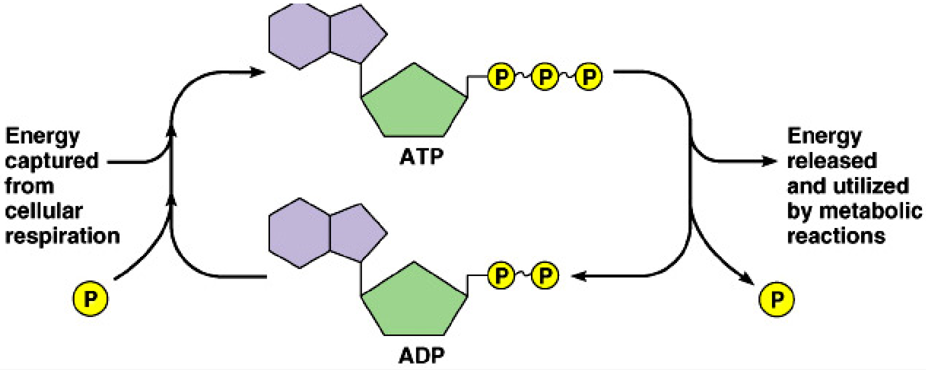
- **carbon dioxide**
- **water**
- **ATP (chemical energy)**
- **heat**

Includes

- **anaerobic reactions (without O_2) - produce little ATP**
- **aerobic reactions (requires O_2) - produce most ATP**

ATP Molecules

- each ATP molecule has three parts:
  - an adenine molecule
  - a ribose molecule
  - three phosphate molecules in a chain
- third phosphate attached by high-energy bond
- when the bond is broken, energy is transferred
- when the bond is broken, ATP becomes ADP
- ADP becomes ATP through phosphorylation
- phosphorylation requires energy released from cellular respiration



Glycolysis (sugar-breaking)

- **series of ten reactions**
- **breaks down glucose into 2 pyruvic acids**
- **occurs in cytosol**
- **anaerobic phase of cellular respiration**
- **yields two ATP molecules per glucose**

Summarized by three main events

1. **phosphorylation**
2. **splitting**
3. **production of NADH and ATP**

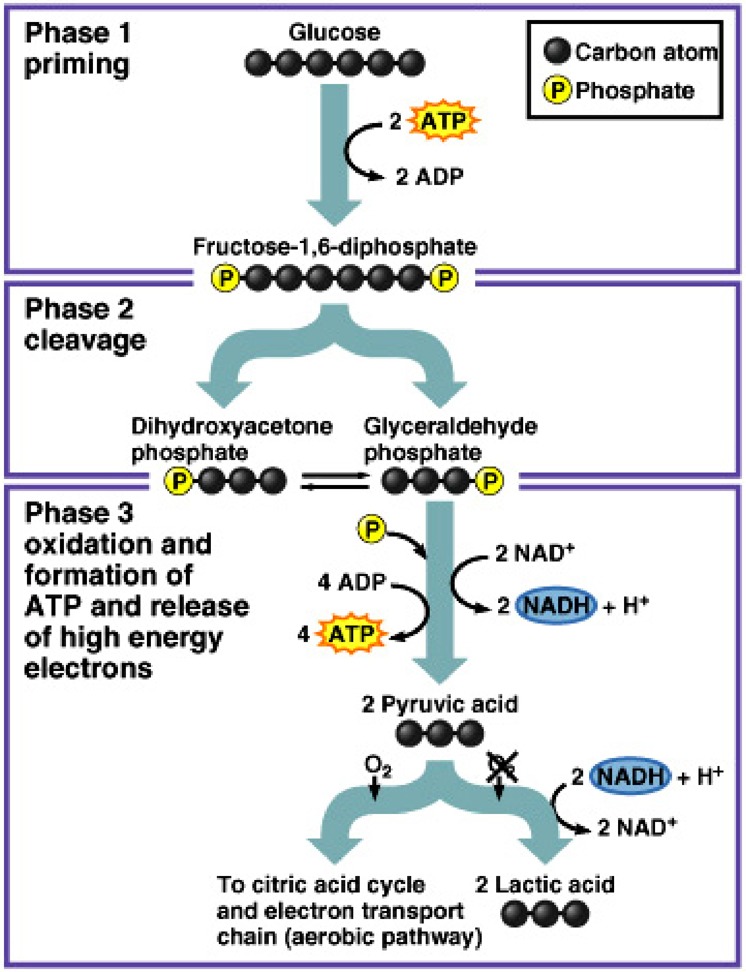
Glycolysis

Event 1 - Phosphorylation

- two phosphates added to glucose
- requires ATP

Event 2 – Splitting (cleavage)

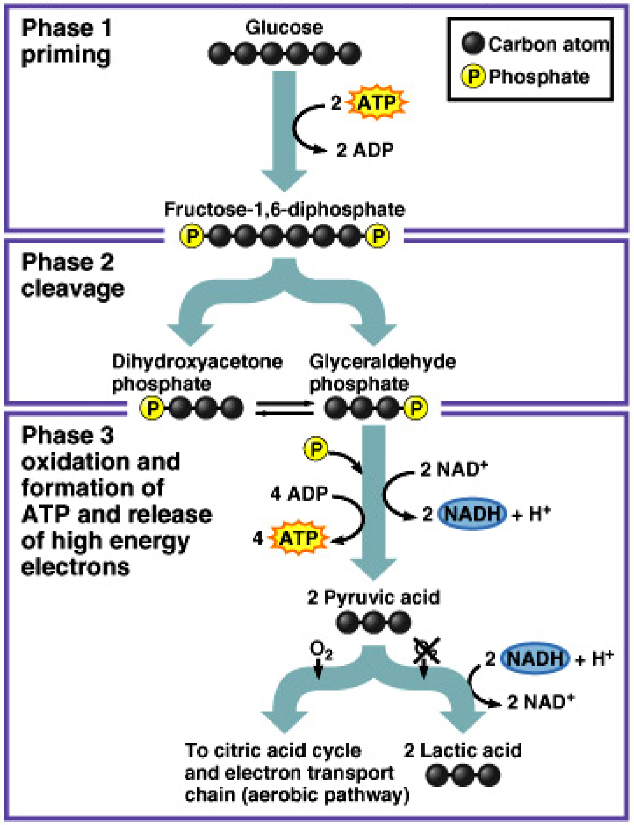
- 6-carbon glucose split into two 3-carbon molecules



Glycolysis

Event 3 – Production of NADH and ATP

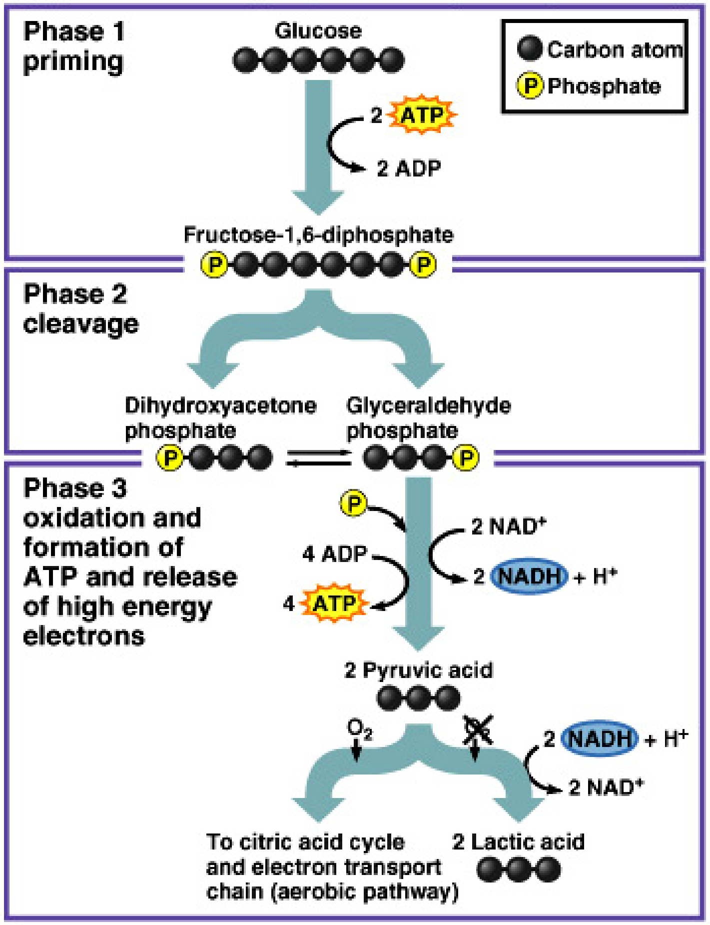
- hydrogen atoms are released
- hydrogen atoms bind to NAD^+ to produce NADH
- NADH delivers hydrogen atoms to electron transport chain if oxygen is available
- ADP is phosphorylated to become ATP
- two molecules of pyruvic acid are produced



Anaerobic Reactions (Absence of Oxygen)

If oxygen is not available -

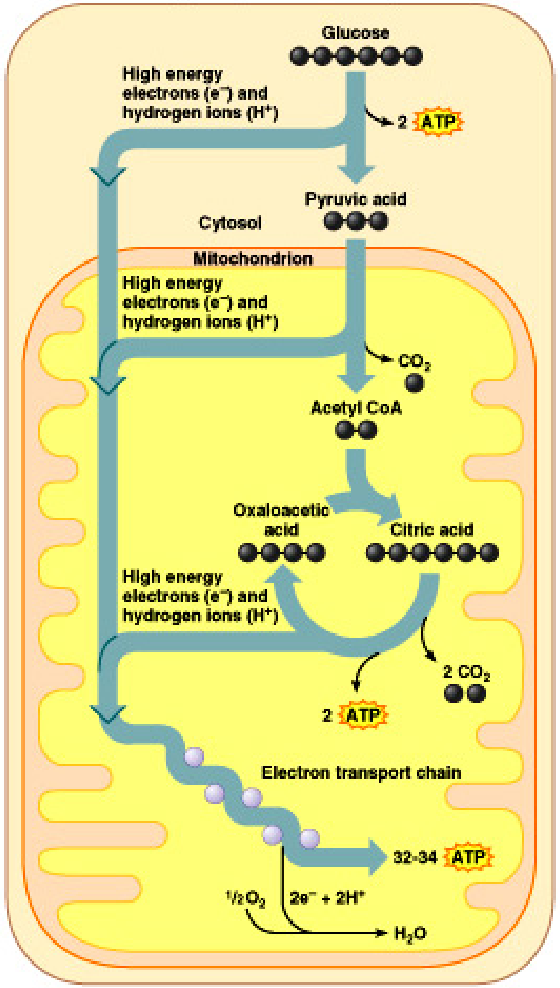
- **electron transport chain cannot accept NADH**
- **pyruvic acid is converted to lactic acid**
- **glycolysis is inhibited**
- **ATP production declines**



Aerobic Reactions (Presence of Oxygen)

If oxygen is available –

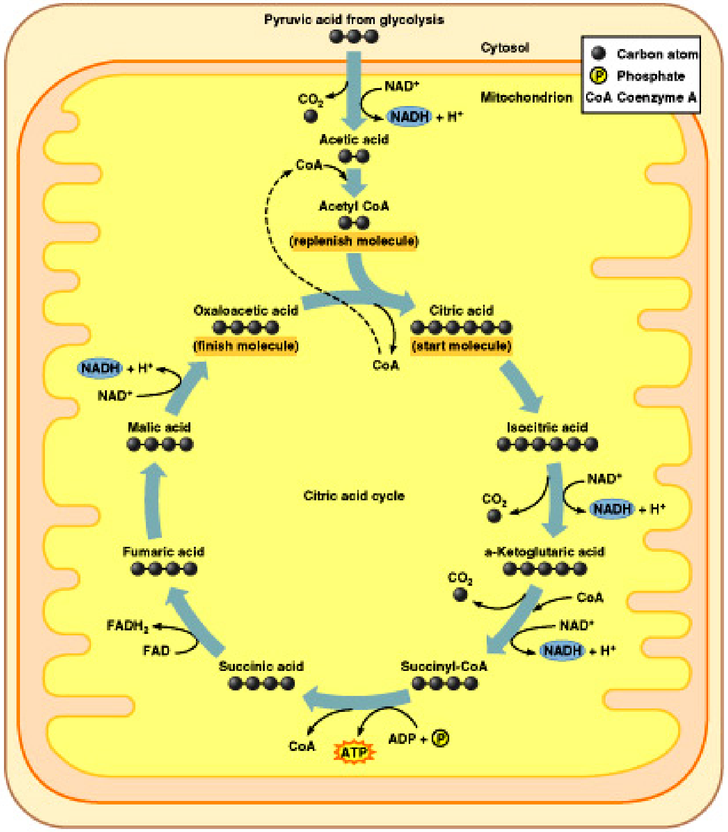
- **pyruvic acid is used to produce acetyl CoA**
- **citric acid cycle begins**
- **electron transport chain functions**
- **carbon dioxide and water are formed**
- **36 molecules of ATP produced per glucose molecule**



Citric Acid Cycle

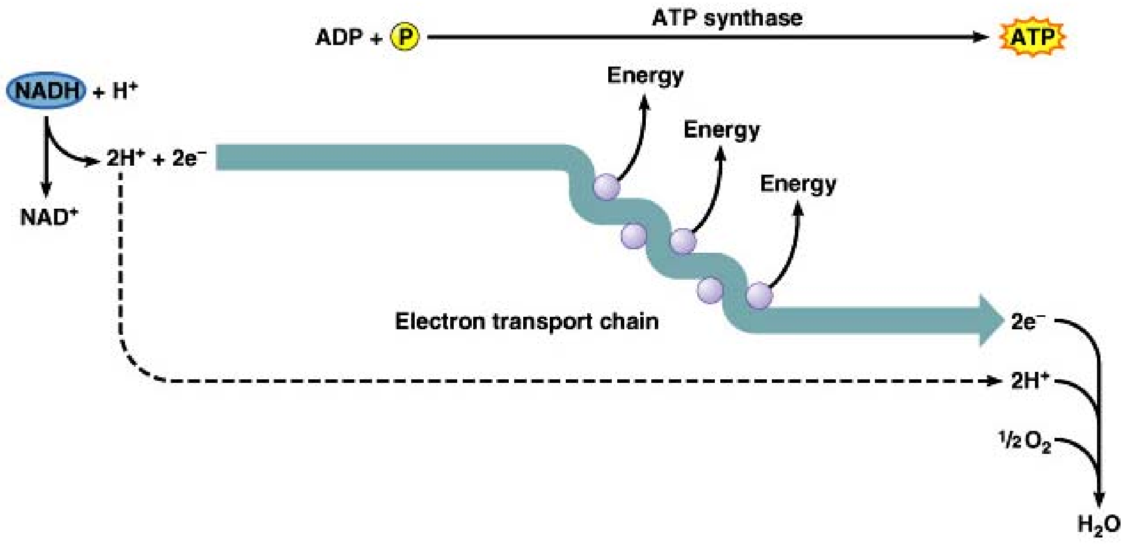
• begins when acetyl CoA combines with oxaloacetic acid to produce citric acid
• citric acid is changed into oxaloacetic acid through a series of reactions
• cycle repeats as long as pyruvic acid and oxygen are available

• for each citric acid molecule:
  • one ATP is produced
  • eight hydrogen atoms are transferred to NAD^+ and FAD
  • two CO_2 produced



Electron Transport Chain

- NADH and FADH2 carry electrons to the ETC
- ETC series of electron carriers located in cristae of mitochondria
- energy from electrons transferred to ATP synthase
- ATP synthase catalyzes the phosphorylation of ADP to ATP
- water is formed



Summary of Cellular Respiration

Glycolysis

1 The 6-carbon sugar glucose is broken down into two 3-carbon pyruvic acid molecules with a net gain of 2 ATP and the release of high energy electrons.

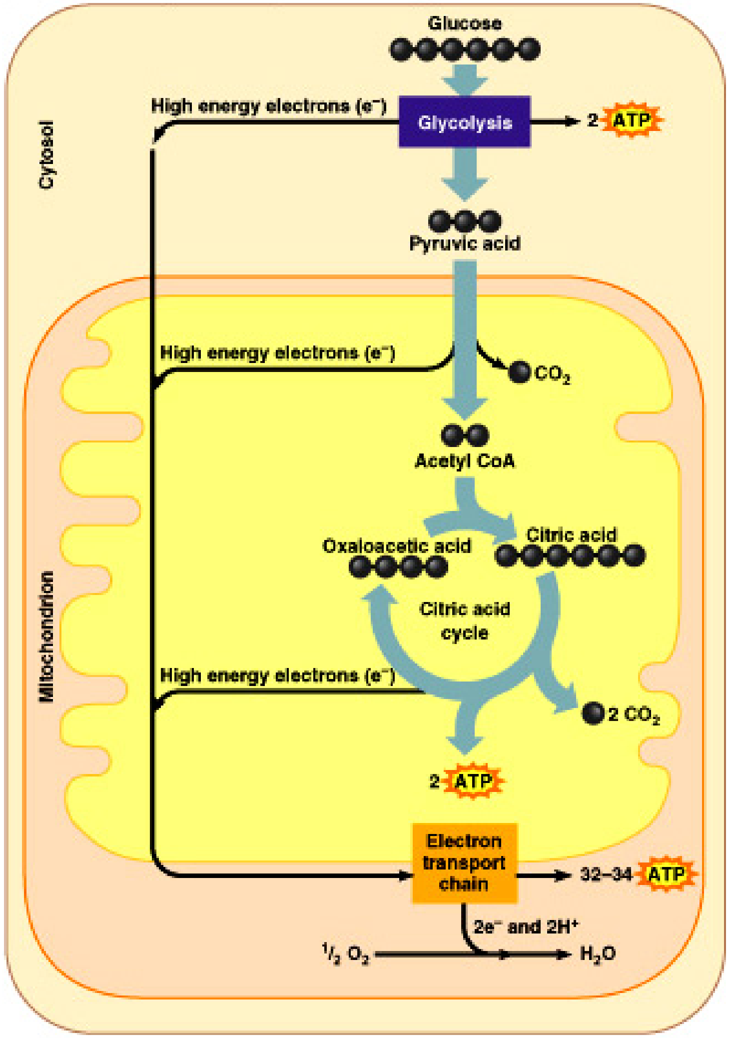
Citric Acid Cycle

2 The 3-carbon pyruvic acids generated by glycolysis enter the mitochondria. Each loses a carbon (generating CO_2) and is combined with a coenzyme to form a 2-carbon acetyl coenzyme A (acetyl CoA). More high energy electrons are released.

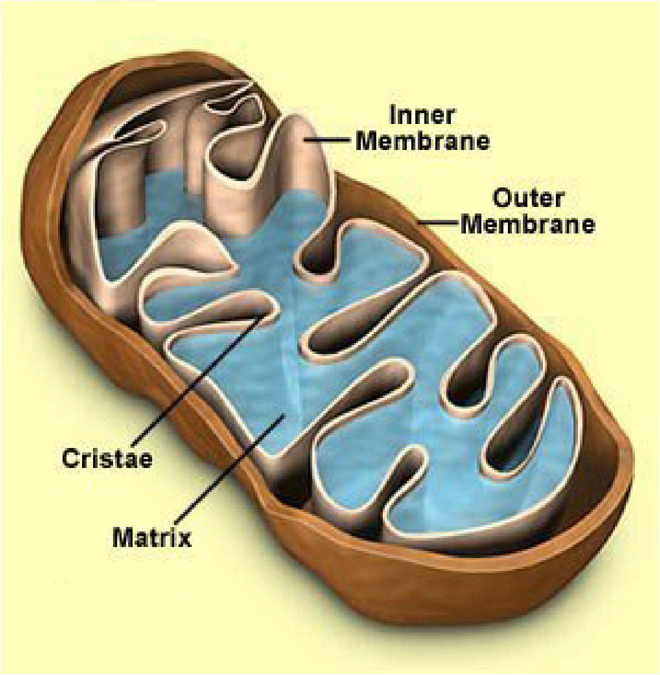
3 Each acetyl CoA combines with a 4-carbon oxaloacetic acid to form the 6-carbon citric acid, for which the cycle is named. For each citric acid a series of reactions removes 2 carbons (generating 2 CO_2's), synthesizes 1 ATP and releases more high energy electrons. The figure shows 2 ATP, resulting directly from 2 turns of the cycle per glucose molecule that enters glycolysis.

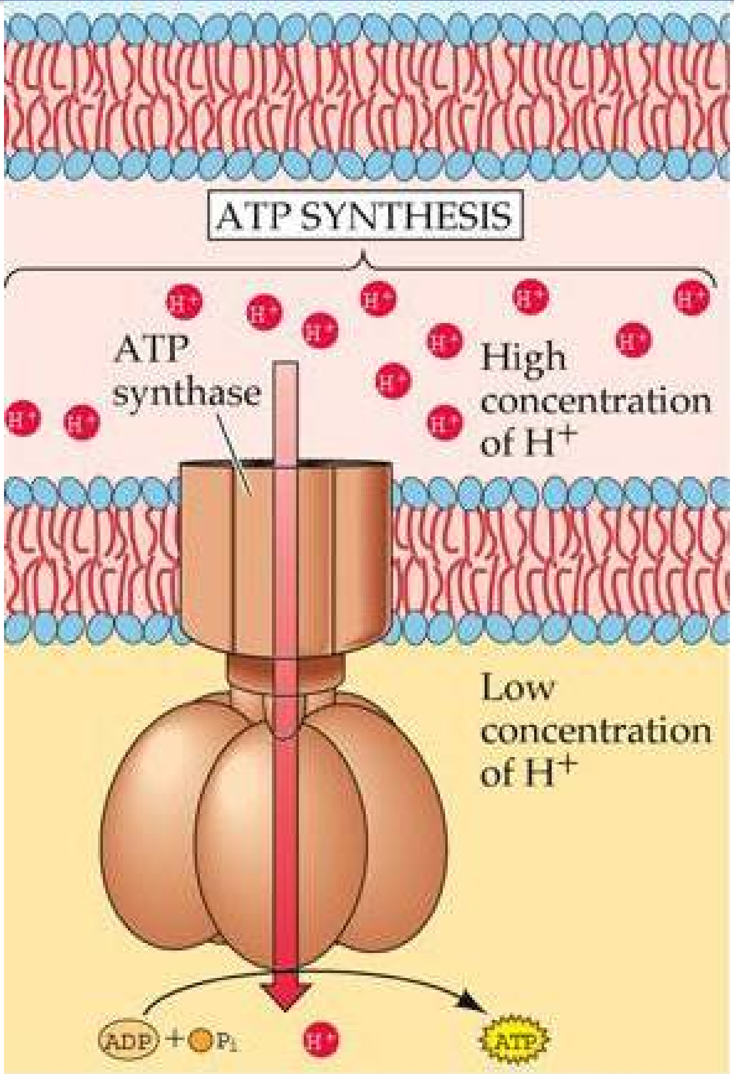
Electron Transport Chain

4 The high energy electrons still contain most of the chemical energy of the original glucose molecule. Special carrier molecules bring the high energy electrons to a series of enzymes that convert much of the remaining energy to more ATP molecules. The other products are heat and water. The requirement of oxygen in this last step is why the overall process is called aerobic respiration.

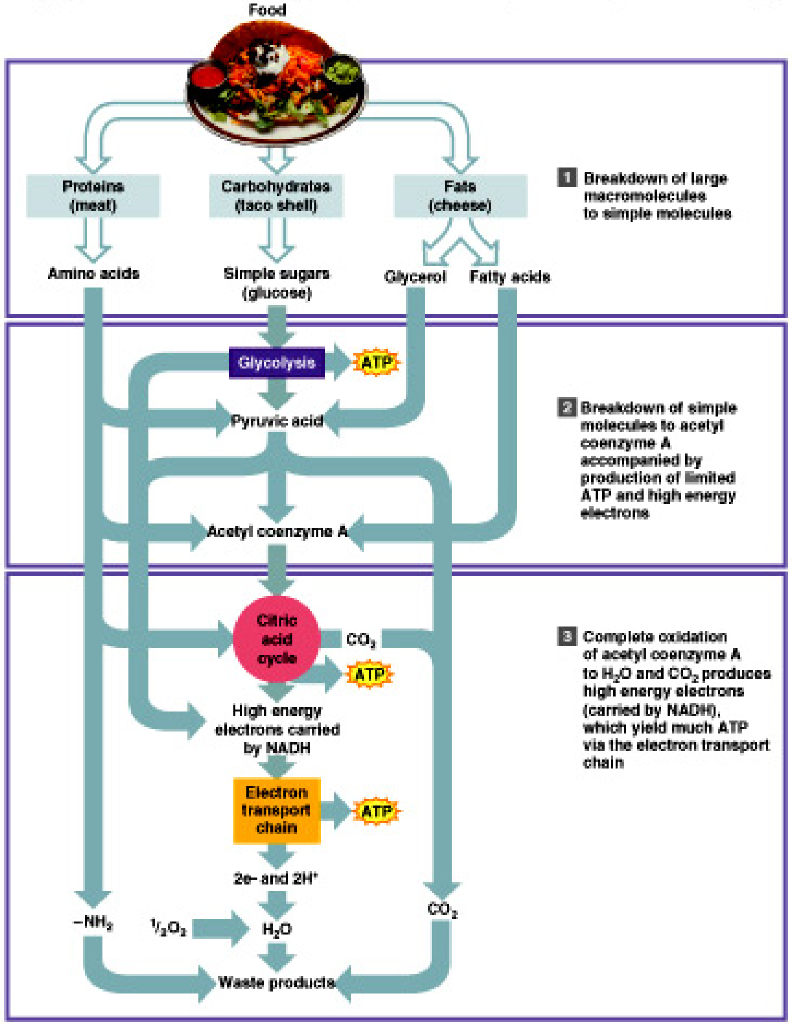


Chemiosmosis formation of Adenosine Triphosphate





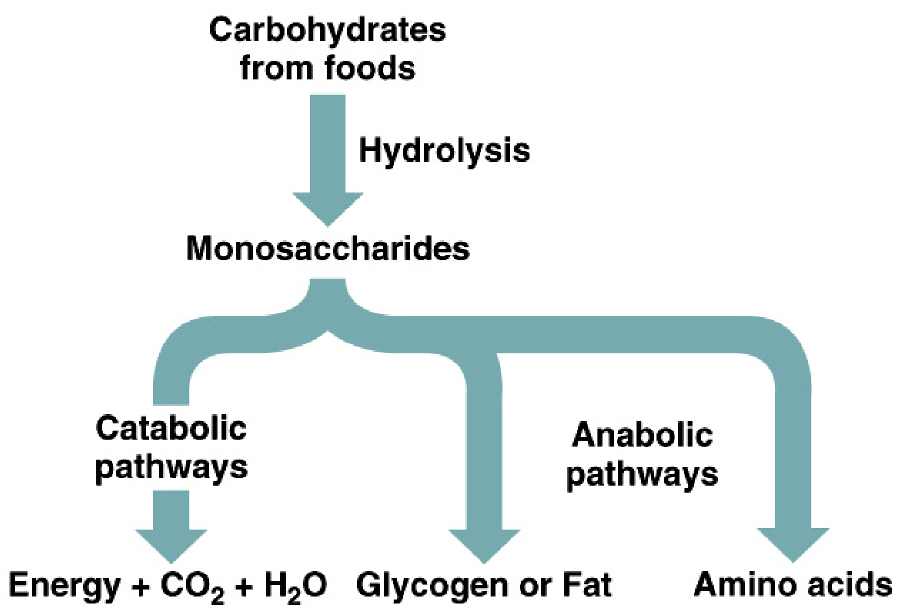
Summary of Catabolism of Proteins, Carbohydrates, and Fats



Carbohydrate Storage

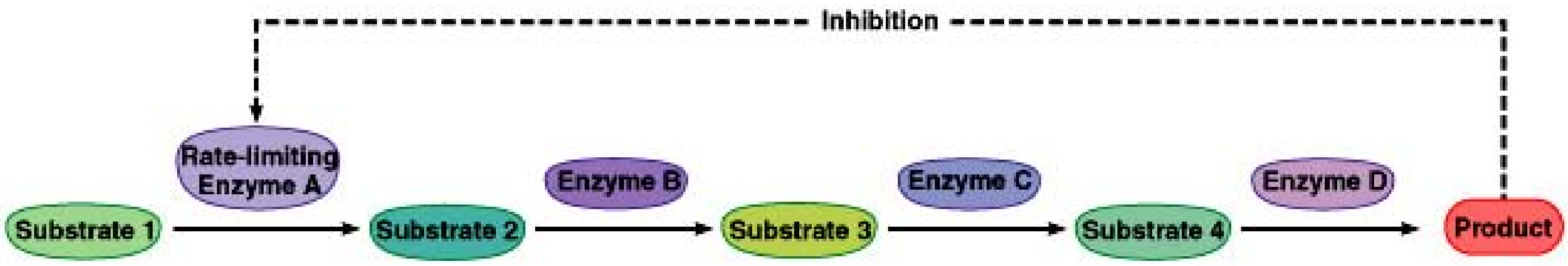
Excess glucose stored as

- **glycogen (primarily by liver and muscle cells)**
- **fat**
- **converted to amino acids**



Regulation of Metabolic Pathways

- limited number of regulatory enzymes
- negative feedback



Nucleic Acids and Protein Synthesis

Genetic information – instructs cells how to construct proteins; stored in DNA

Gene – segment of DNA that codes for one protein

Genome – complete set of genes

Genetic Code – method used to translate a sequence of nucleotides of DNA into a sequence of amino acids

Genotype: genetic makeup of an individual

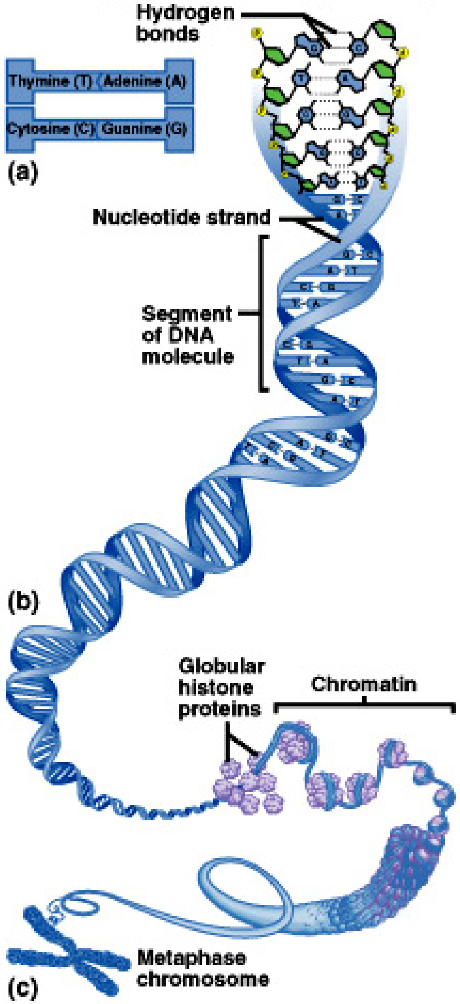
Phenotype: physical manifestation of a trait (the genotype + influence of the environment)

TABLE 4.1 A Comparison of DNA and RNA Molecules

	DNA	RNA
Main location	Part of chromosomes, in nucleus	Cytoplasm
5-carbon sugar	Deoxyribose	Ribose
Basic molecular structure	Double-stranded	Single-stranded
Organic bases included	Cytosine, guanine, adenine, thymine	Cytosine, guanine, adenine, uracil
Major functions	Contains genetic code for protein synthesis, replicates prior to mitosis	Messenger RNA carries transcribed DNA information to cytoplasm and acts as template for synthesis of protein molecules; transfer RNA carries amino acids to messenger RNA; ribosomal RNA provides structure and enzyme activity for ribosomes

Structure of DNA

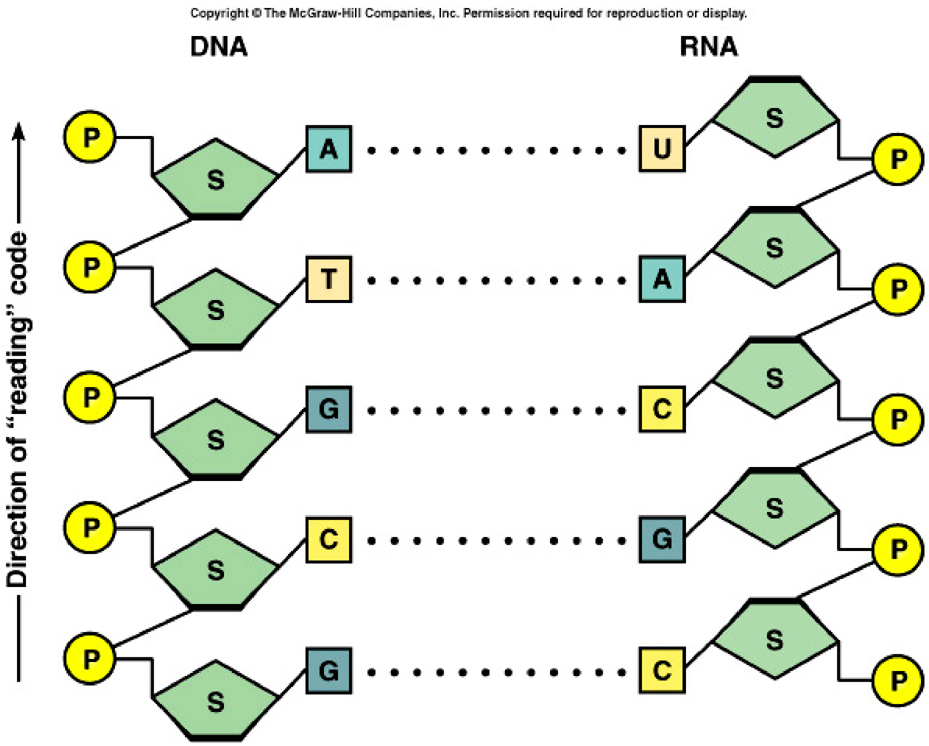
- two polynucleotide chains
- hydrogen bonds hold nitrogenous bases together
- bases pair specifically (A-T and C-G)
- forms a helix
- DNA wrapped about histones forms chromosomes



RNA Molecules

Messenger RNA (mRNA) -

- **delivers genetic information from nucleus to the cytoplasm**
- **single polynucleotide chain**
- **formed beside a strand of DNA**
- **RNA nucleotides are complementary to DNA nucleotides (exception – no thymine in RNA; replaced with uracil)**
- **making of mRNA is transcription**



From DNA to Protein

- DNA replicates DNA
  - Regions of DNA form basis of genes
  - When the information stored in a gene is expressed this becomes a protein.
- DNA transcribes itself into a RNA (leaves the nucleus)
- RNA interacts with other RNAs and translates itself into a sequence of amino acids (a polypeptide chain or protein).

RNA Molecules

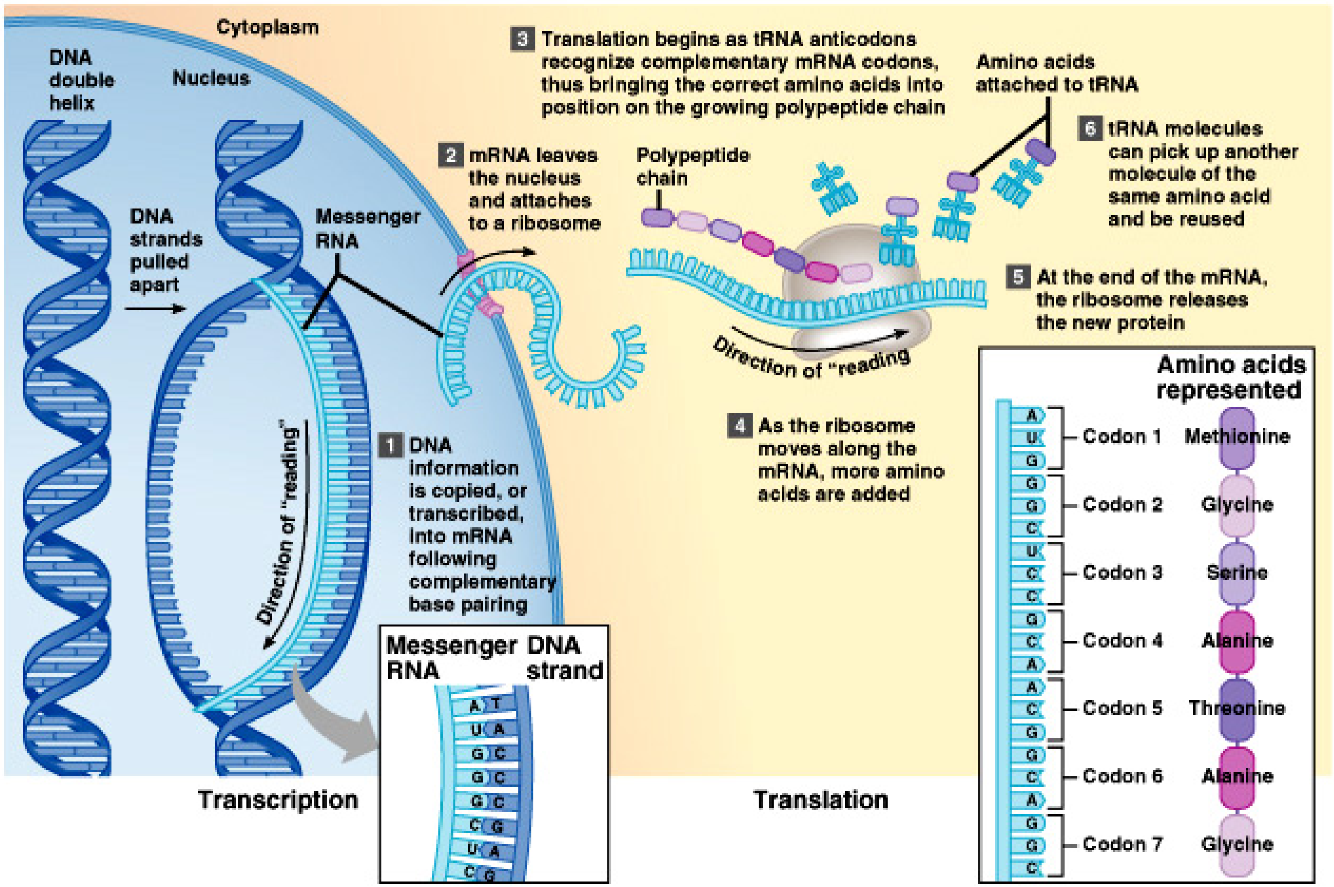
Transfer RNA (tRNA) -

- **carries amino acids to mRNA**
- **carries anticodon to mRNA**
- **translates a codon of mRNA into an amino acid**

Ribosomal RNA (rRNA) –

- **provides structure and enzyme activity for ribosomes**

Protein Synthesis



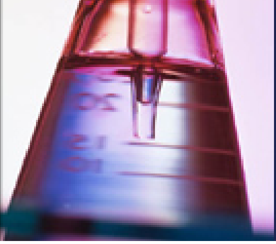


TABLE 4.2 Codons (mRNA Three Base Sequences)

First Letter	Second Letter: U		Second Letter: C		Second Letter: A		Second Letter: G		Third Letter
U	UUU	phenylalanine (phe)	UCU	serine (ser)	UAU	tyrosine (tyr)	UGU	cysteine (cys)	U
	UUC		UCC		UAC		UGC		C
	UUA	leucine (leu)	UCA		UAA	STOP	UGA	STOP	A
	UUG		UCG		UAG	STOP	UGG	tryptophan (trp)	G
C	CUU	leucine (leu)	CCU	proline (pro)	CAU	histidine (his)	CGU	arginine (arg)	U
	CUC		CCC		CAC		CGC		C
	CUA		CCA		CAA	glutamine (gln)	CGA		A
	CUG		CCG		CAG		CGG		G
A	AUU	isoleucine (ilu)	ACU	threonine (thr)	AAU	asparagine (asn)	AGU	serine (ser)	U
	AUC		ACC		AAC		AGC		C
	AUA		ACA		AAA	lysine (lys)	AGA	arginine (arg)	A
	AUG	START methionine (met)	ACG		AAG		AGG		G
G	GUU	valine (val)	GCU	alanine (ala)	GAU	aspartic acid (asp)	GGU	glycine (gly)	U
	GUC		GCC		GAC		GGC		C
	GUA		GCA		GAA	glutamic acid (glu)	GGA		A
	GUG		GCG		GAG		GGG		G

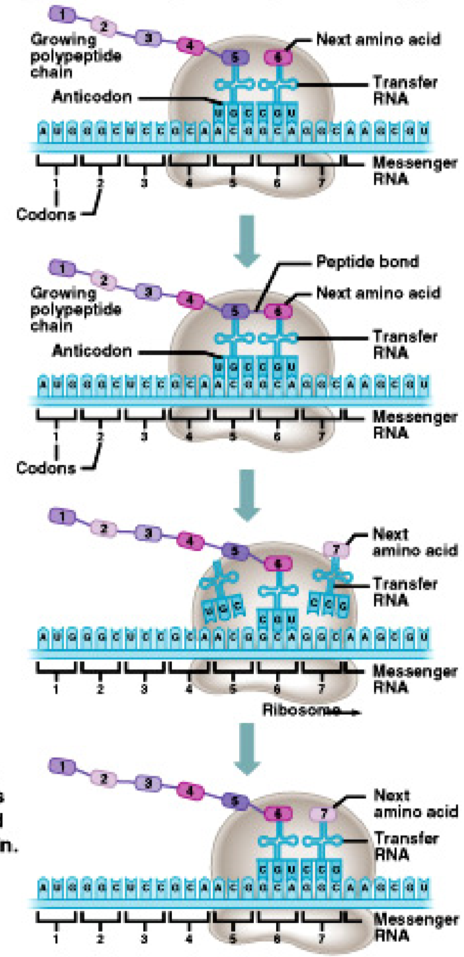
Protein Synthesis

1 The transfer RNA molecule for the last amino acid added holds the growing polypeptide chain and is attached to its complementary codon on mRNA.

2 A second tRNA binds complementarily to the next codon, and in doing so brings the next amino acid into position on the ribosome. A peptide bond forms, linking the new amino acid to the growing polypeptide chain.

3 The tRNA molecule that brought the last amino acid to the ribosome is released to the cytoplasm, and will be used again. The ribosome moves to a new position at the next codon on mRNA.

4 A new tRNA complementary to the next codon on mRNA brings the next amino acid to be added to the growing polypeptide chain.



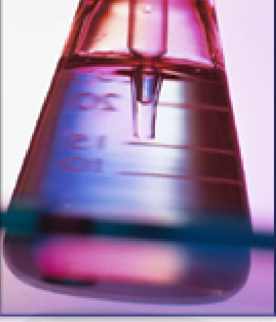


TABLE 4.3 Protein Synthesis

Transcription (Within the Nucleus)

1. RNA polymerase binds to the base sequence of a gene.
2. This enzyme unwinds a portion of the DNA molecule, exposing part of the gene.
3. RNA polymerase moves along one strand of the exposed gene and catalyzes synthesis of an mRNA molecule, whose nucleotides are complementary to those of the strand of the gene.
4. When RNA polymerase reaches the end of the gene, the newly formed mRNA molecule is released.
5. The DNA molecule rewinds and closes the double helix.
6. The mRNA molecule passes through a pore in the nuclear envelope and enters the cytoplasm.

Translation (Within the Cytoplasm)

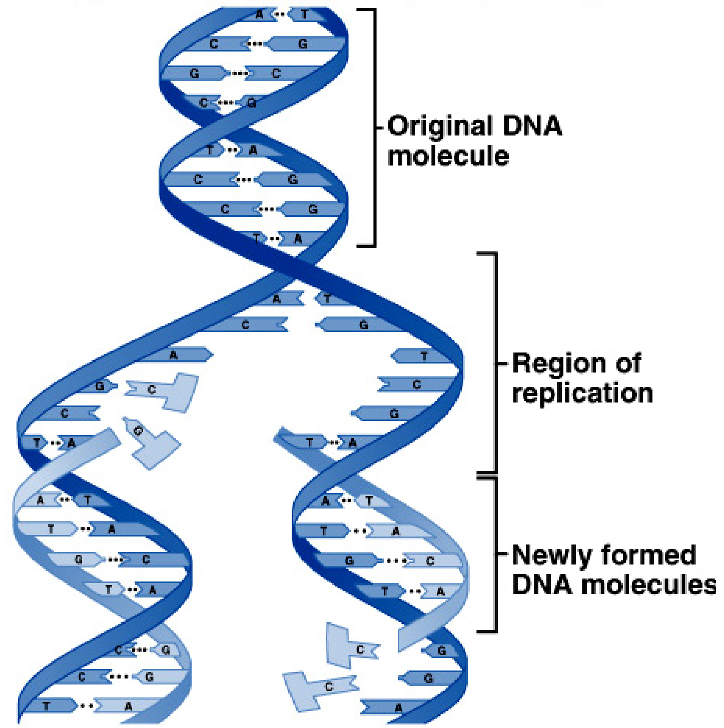
1. A ribosome binds to the mRNA molecule near the codon at the beginning of the messenger strand.
2. A tRNA molecule that has the complementary anticodon brings its amino acid to the ribosome.
3. A second tRNA brings the next amino acid to the ribosome.
4. A peptide bond forms between the two amino acids, and the first tRNA is released.
5. This process is repeated for each codon in the mRNA sequence as the ribosome moves along its length, forming a chain of amino acids.
6. As the chain of amino acids grows, it folds, with the help of chaperone proteins, into the unique conformation of a functional protein molecule.
7. The completed protein molecule (polypeptide) is released. The mRNA molecule, ribosome, and tRNA molecules are recycled.

Metabolic Poisons

- Examples of Toxins that Disrupt Cellular Respiration ultimately preventing production of ATP
  - Rotenone and cyanide are electron transport inhibitors
  - 2,4 Dinitrophenol is disrupts the electrochemical gradient of protons in the mitochondria
- Examples of Toxins that Disrupt Protein Synthesis
  - Alpha amanitin – produced by certain mushrooms (e.g. *Amanita virosa*, *A. phalloides*, *Galerina autumnalis*) interferes with RNA polymerase (transcription).
  - Ricin from castor beans **inhibits protein synthesis** by specifically and irreversibly inactivating **eukaryotic ribosomes**.
    - In 1978, Georgi Markov, a Bulgarian writer and journalist who was living in London, died after he was attacked by a man with an umbrella. The umbrella had been rigged to inject a poison ricin pellet under Markov's skin.

DNA Replication

• hydrogen bonds break between bases
• double strands unwind and pull apart
• new nucleotides pair with exposed bases
• controlled by DNA polymerase



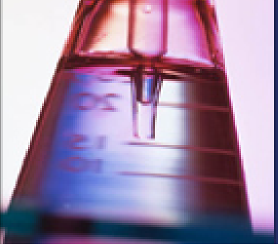


TABLE 4A PCR Applications

PCR Has Been Used to Amplify:
Genetic material from HIV in a human blood sample when infection has been so recent that antibodies are not yet detectable.
A bit of DNA in a preserved quagga (a relative of the zebra) and a marsupial wolf, which are recently extinct animals.
DNA in sperm cells found in the body of a rape victim so that specific sequences could be compared to those of a crime suspect.
Genes from microorganisms that cannot be grown or maintained in culture for study.
Mitochondrial DNA from various modern human populations. Comparisons of mitochondrial DNA sequences indicate that *Homo sapiens* originated in Africa, supporting fossil evidence.
DNA from the brain of a 7,000-year-old human mummy, which indicated that native Americans were not the only people to dwell in North America long ago.
DNA sequences unique to moose in hamburger meat, proving that illegal moose poaching had occurred.
DNA sequences in maggots in a decomposing human corpse, enabling forensic scientists to determine the time of death.
DNA in deteriorated road kills and carcasses washed ashore, to identify locally threatened species.
DNA in products illegally made from endangered species, such as powdered rhinoceros horn, sold as an aphrodisiac.
DNA sequences in animals that are unique to the bacteria that cause Lyme disease, providing clues to how the disease is transmitted.
DNA from genetically altered microbes that are released in field tests, to follow their dispersion.
DNA from a cell of an eight-celled human preembryo, to diagnose cystic fibrosis.
Y chromosome-specific DNA from a human egg fertilized in the laboratory to determine the sex.
A papilloma virus DNA sequence present in, and possibly causing, an eye cancer.
DNA from remains of journalist Daniel Pearl, who was beheaded in Pakistan.

Mutations

Mutations – change in genetic information

Result when

- extra bases are added or deleted
- bases are changed

May or may not change the protein

Repair enzymes correct mutations

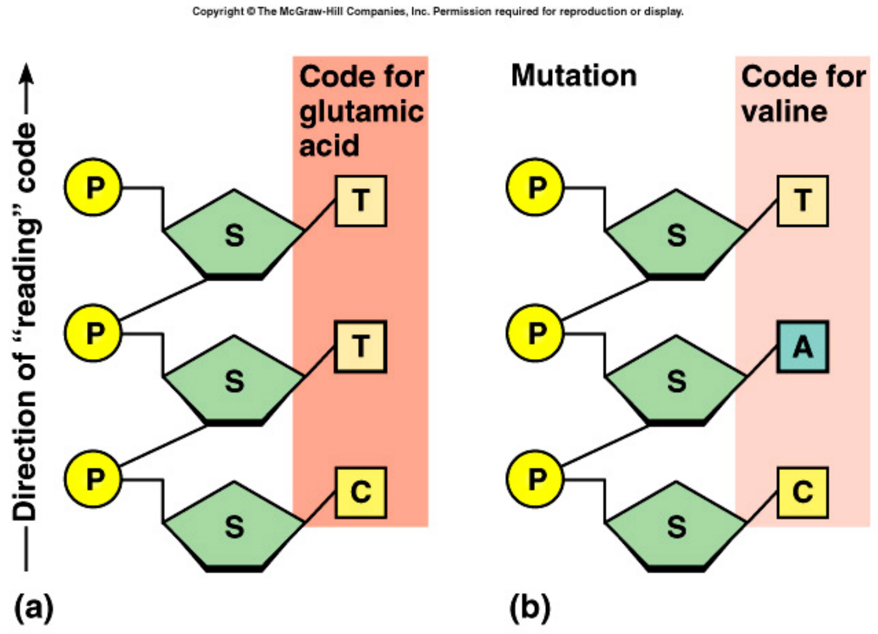


TABLE 4.4 Commonly Encountered Mutagens

Mutagen	Source
Aflatoxin B	Fungi growing on peanuts and other foods
2-amino 5-nitrophenol 2,4-diaminoanisole 2,5-diaminoanisole 2,4-diaminotoluene p-phenylenediamine	Hair dye components
Caffeine	Cola, tea, coffee
Furylfuramide	Food additive
Nitrosamines	Pesticides, herbicides, cigarette smoke
Proflavine	Antiseptic in veterinary medicine
Sodium nitrite	Smoked meats
Tris (2,3-dibromopropyl phosphate)	Flame retardant in children's sleepwear

Clinical Application

Phenylketonuria
PKU

- **enzyme that breaks down the amino acid phenylalanine is missing**
- **build up of phenylalanine causes mental retardation**
- **treated by diets very low in phenylalanine**