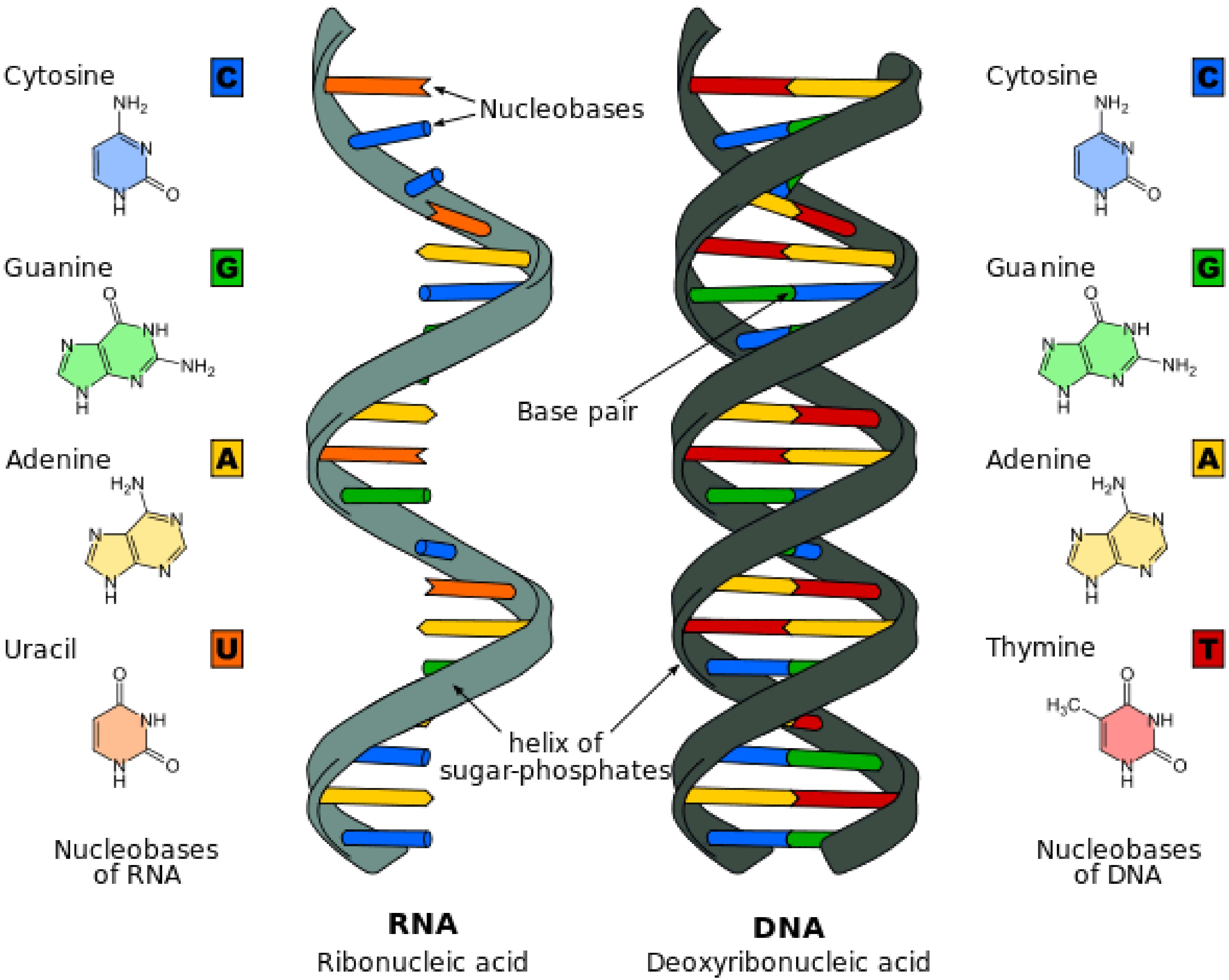
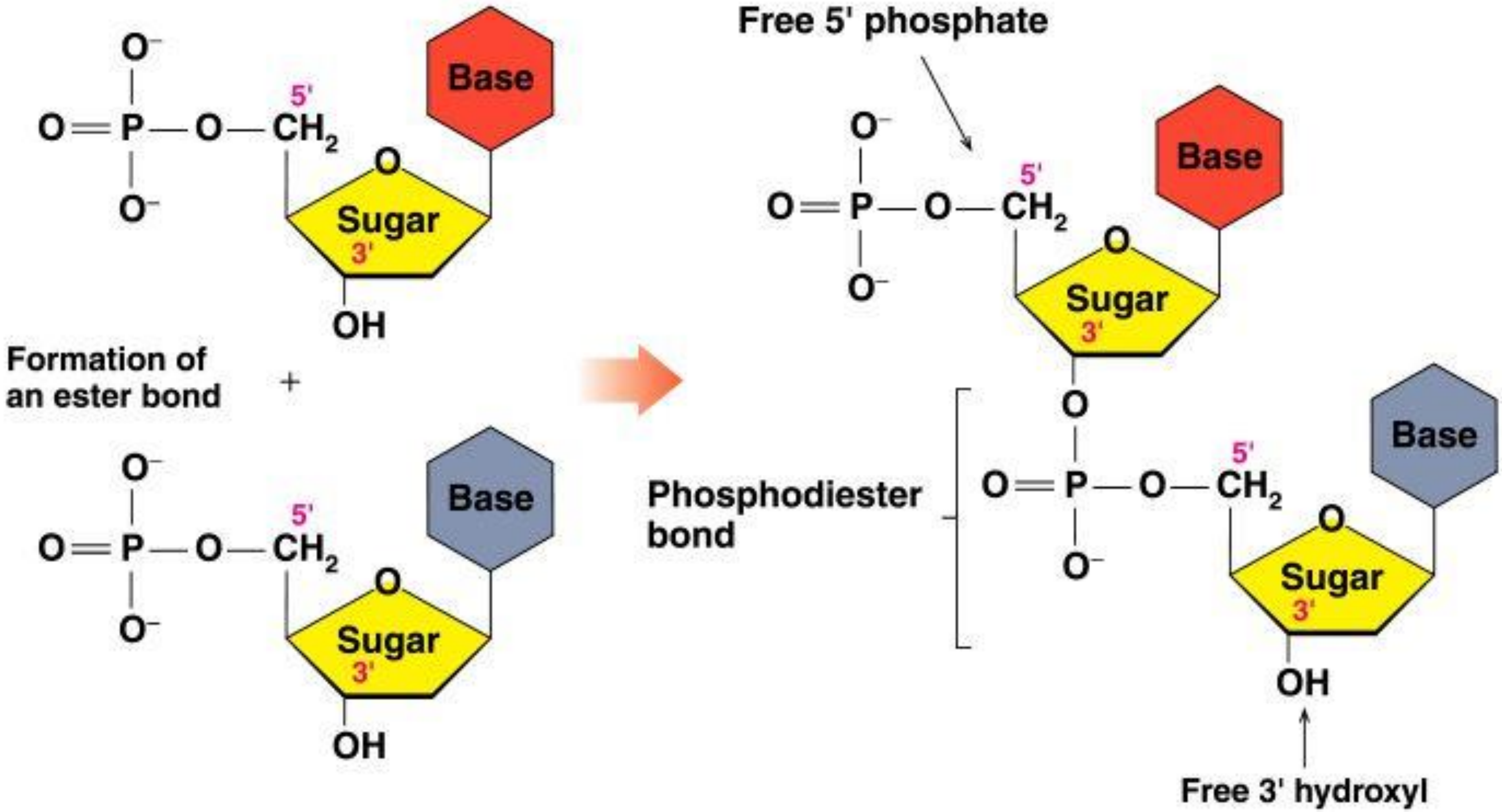
Bio-macromolecules: Molecules of Life

	Protein	Nucleic Acid	Lipid	Carbohydrates	Small molecules
Made of	Long chains of 20 kinds of amino acids	Long & short chains of nucleic acid bases form DNA, RNA, also ATP, GTP, ...	Phosphate or or other charged "head" with long hydro-carbon tail	Long & short chains of sugar molecules like glucose, fructose.	Various molecules such as hormones, vitamins, neurotransmitters, porphyrins
Functions	Most of the structure and function of living things; enzymes	Information storage (RNA, DNA), structure, enzymes, energy transfer	Energy storage Insulation Cushioning Membranes	Energy source Energy storage Structure	Mostly sending signals

Nucleic Acids

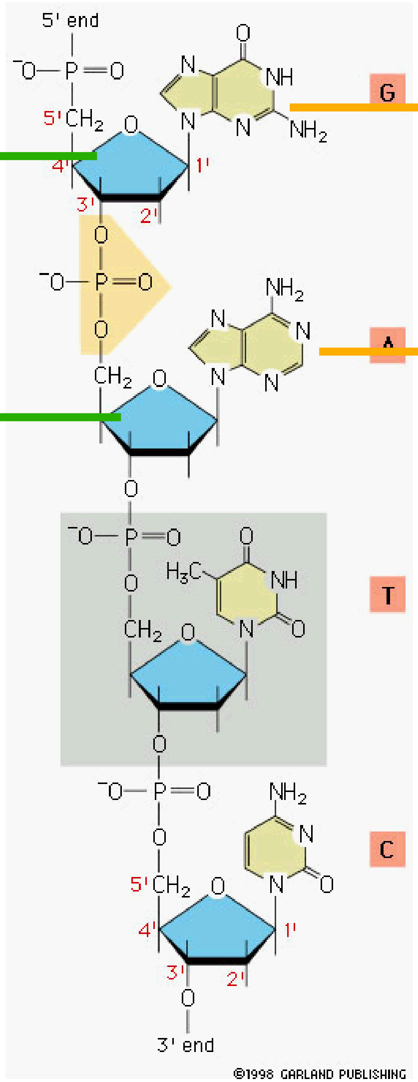


Nucleic Acid Structure Polymerization



Nucleic Acid Structure Polymerization

Sugar Phosphate “backbone”

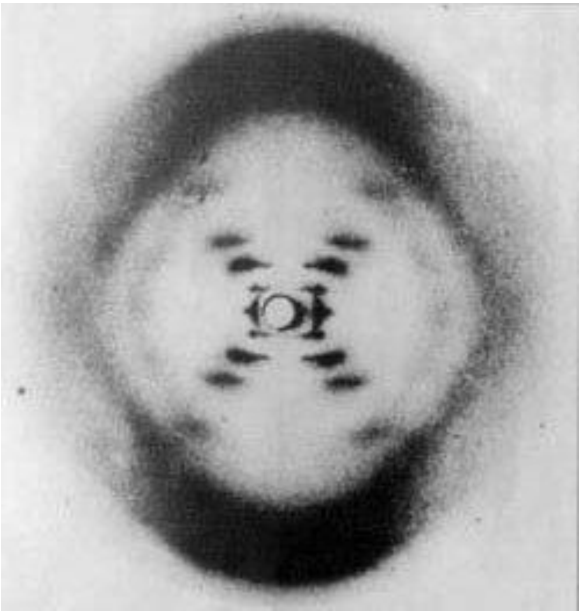


Nucleotide

PERIPHERY OF DNA
- SUGAR-PHOSPHATE CHAINS

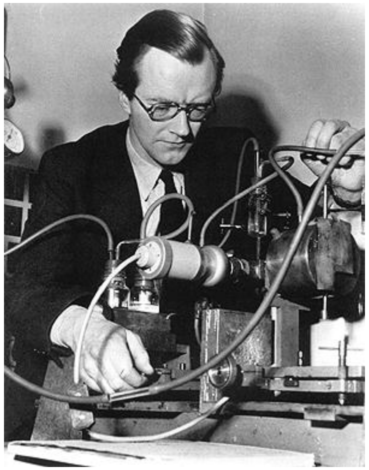
CORE OF DNA
- BASES ARE STACKED IN PARALLEL FASHION
- CHARGAFF’S RULES
  - A = T
  - G = C
- “COMPLEMENTARY” BASE-PAIRING

X-Ray Diffraction Pattern of DNA Fibers

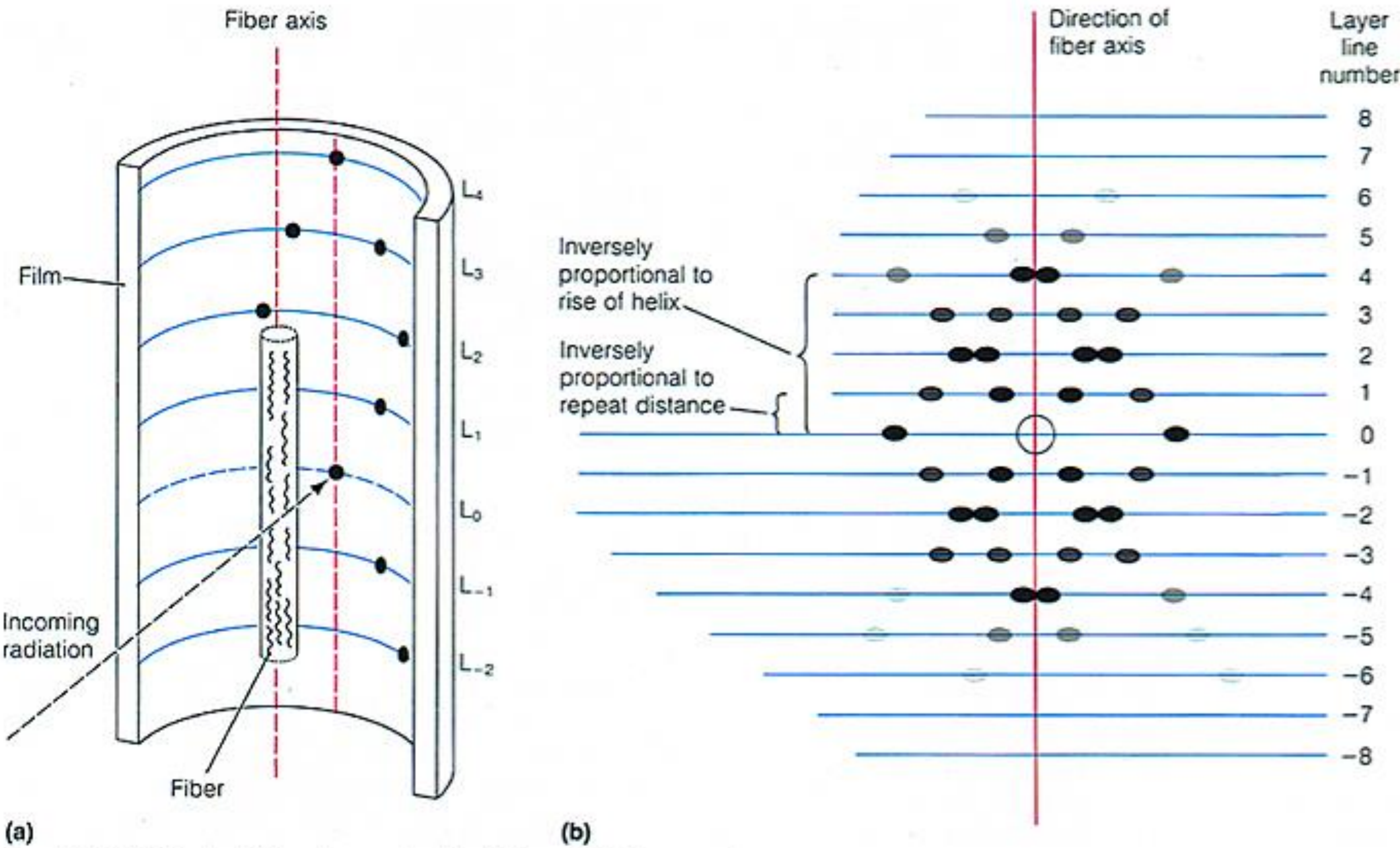


Franklin and Wilkins, 1953

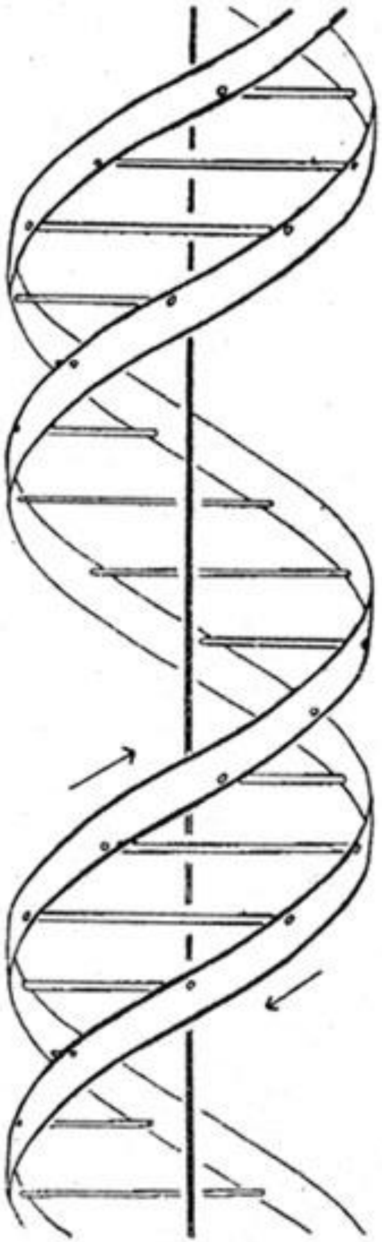
Rosalind Franklin



Maurice Wilkins



Fiber axis
Film
L_4
L_3
L_2
L_1
L_0
L_{-1}
L_{-2}
Incoming radiation
Fiber
(a)
Direction of fiber axis
Layer line number
8
7
6
5
4
3
2
1
0
−1
−2
−3
−4
−5
−6
−7
−8
Inversely proportional to rise of helix
Inversely proportional to repeat distance
(b)



April 25, 1953

MOLECULAR STRUCTURE OF NUCLEIC ACIDS

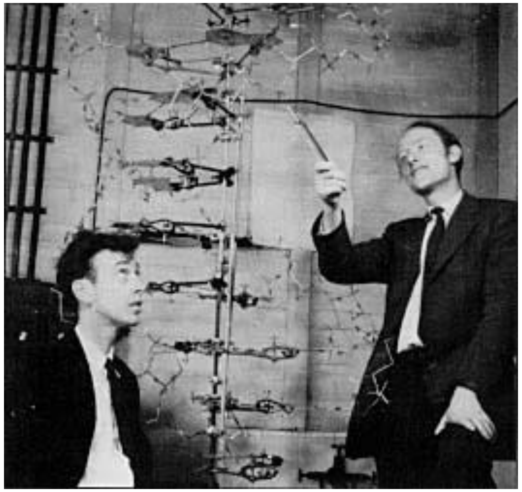
A Structure for Deoxyribose Nucleic Acid

We wish to suggest a structure for the salt of deoxyribose nucleic acid (D.N.A.). This structure has novel features which are of considerable biological interest.

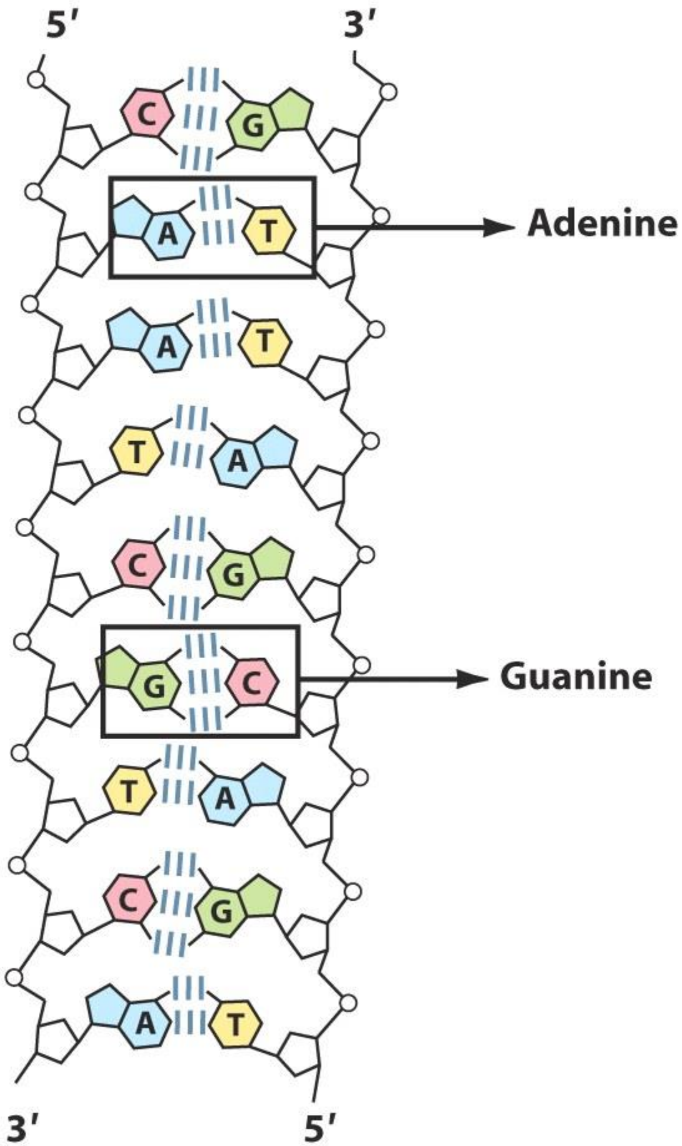
It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material.

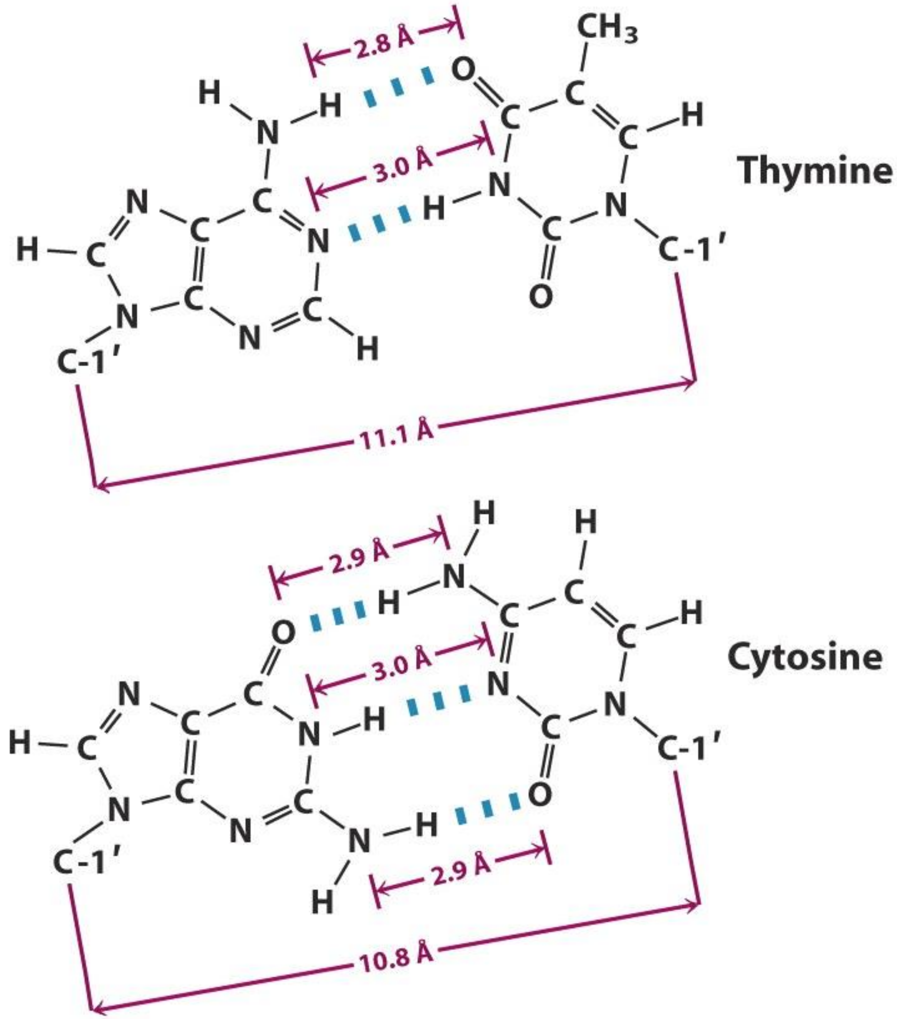
J. D. WATSON F. H. C. CRICK

Medical Research Council Unit for the Study of Molecular Structure of Biological Systems, Cavendish Laboratory, Cambridge.



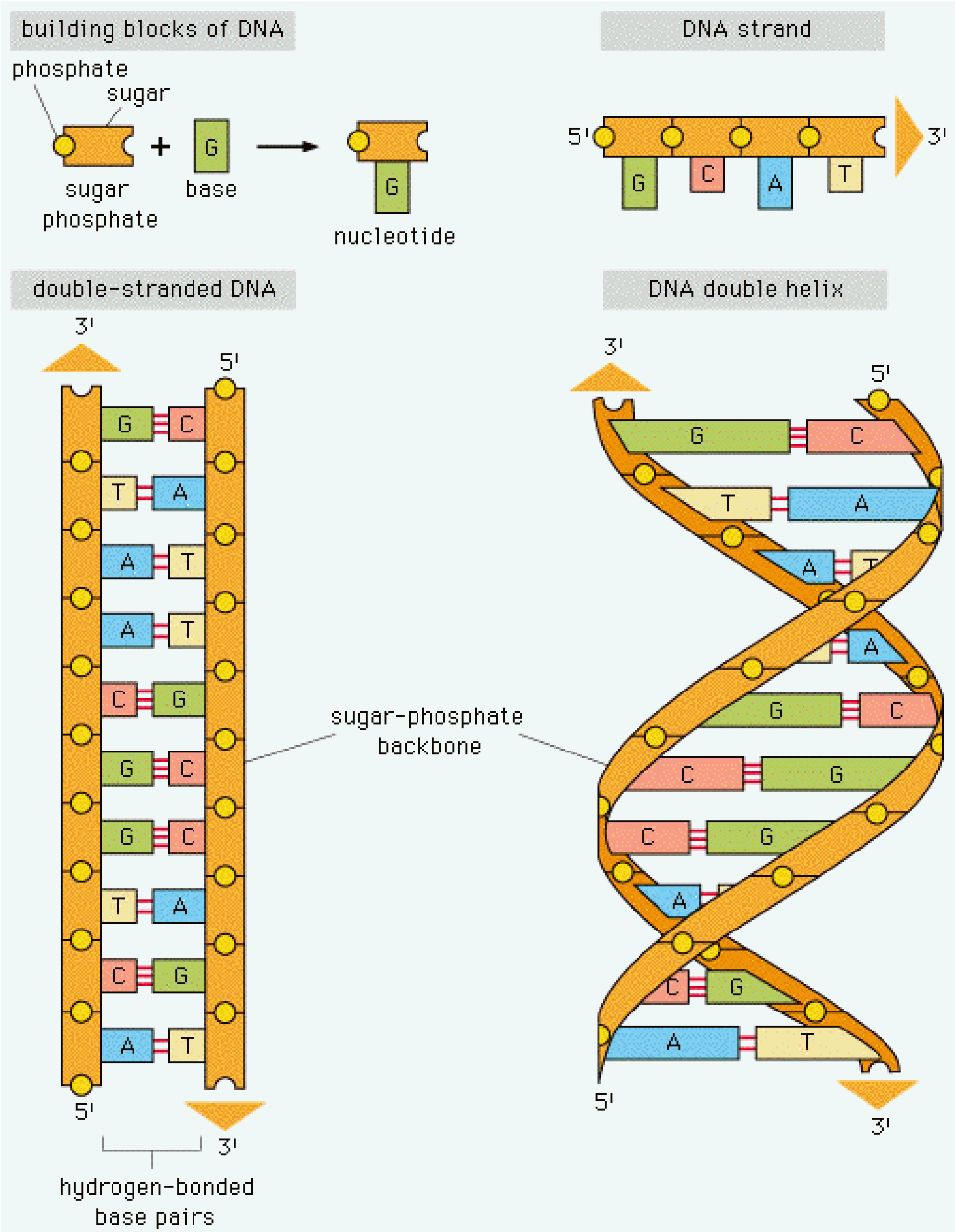
Elements of Structure in DNA Double Helix

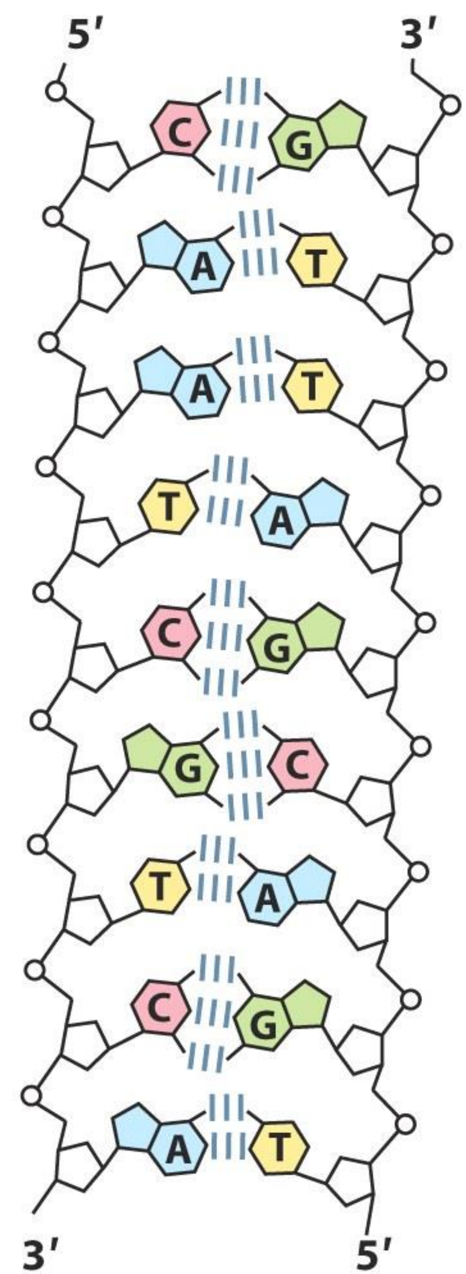




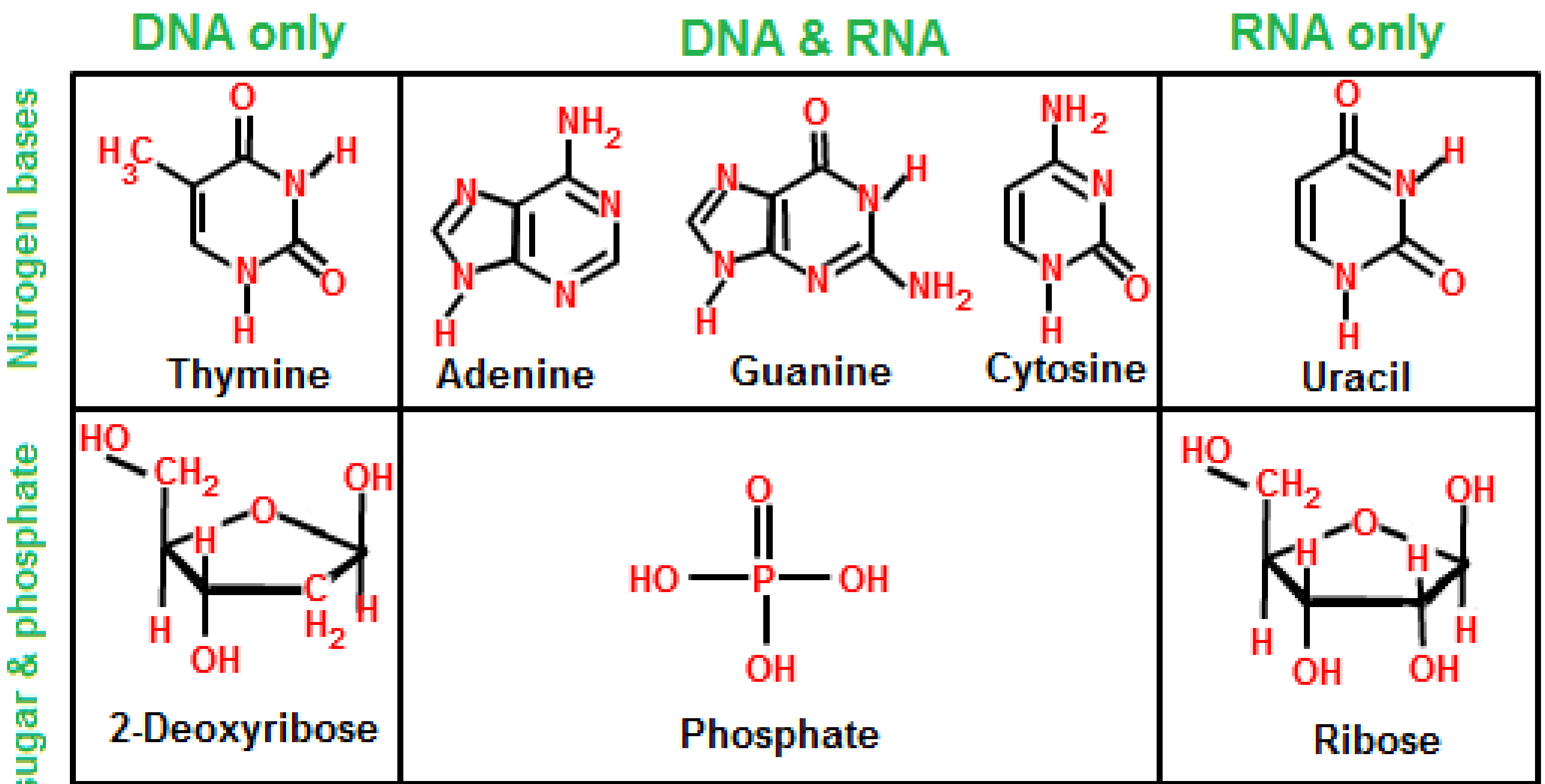
Watson-Crick Base Pairs

Elements of Structure in DNA Double Helix



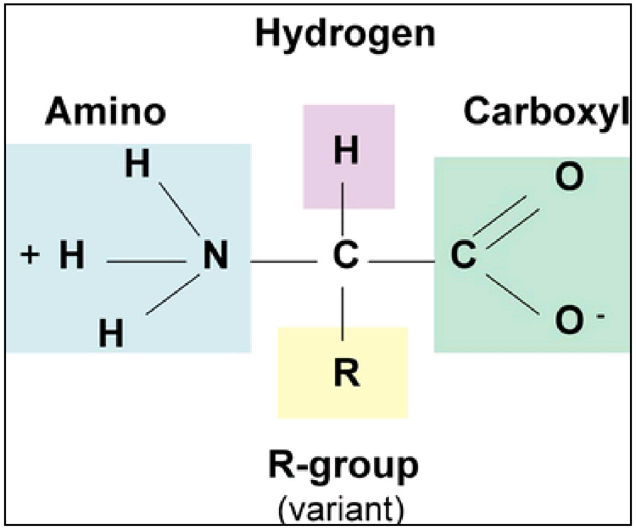


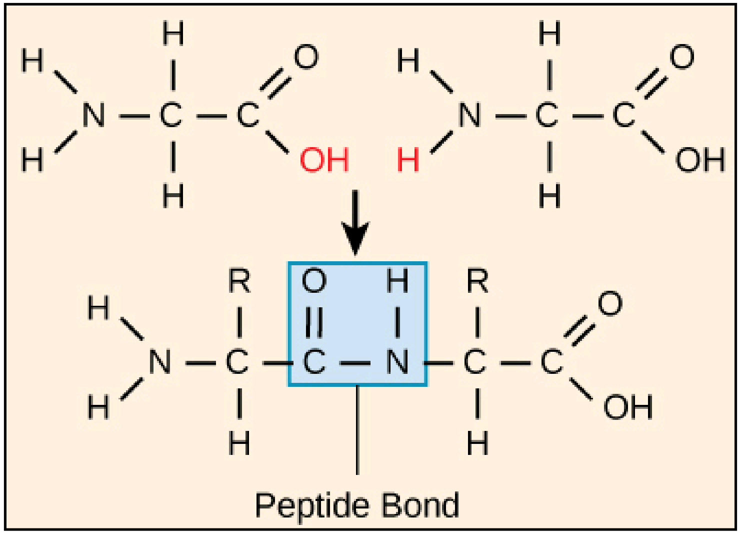
Components of Nucleic Acids

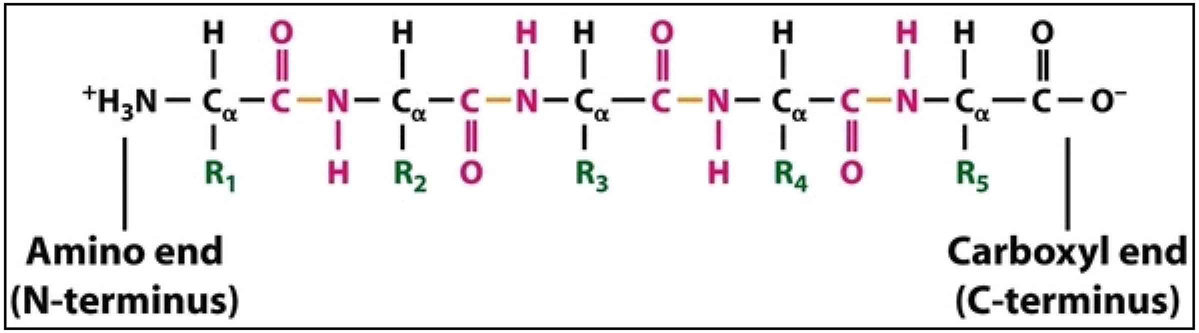


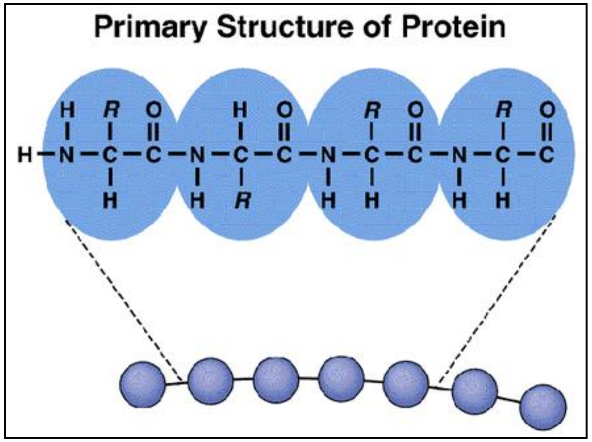
	DNA	RNA
Pentose sugar	Deoxyribose	Ribose
Base Composition	Adenine (A) Guanine (G) Cytosine (C) **Thymine (T)**	Adenine (A) Guanine (G) Cytosine (C) **Uracil (U)**
Number of strands	Double stranded (forms a double helix)	Single stranded

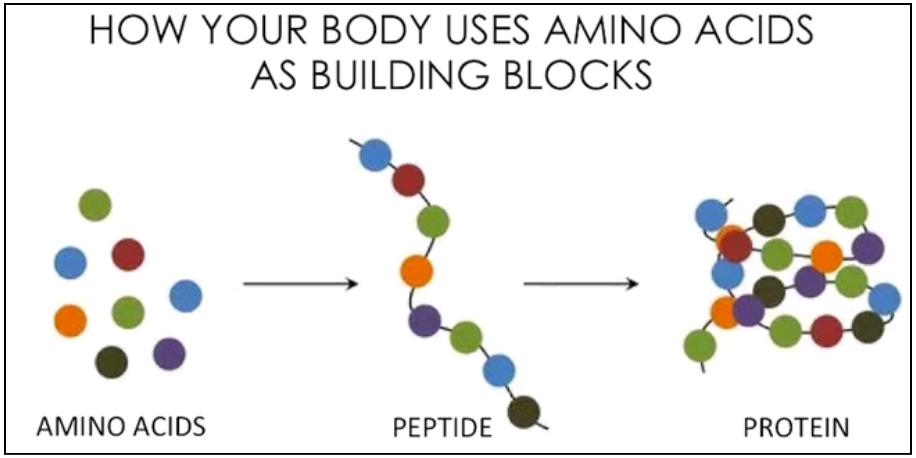
Proteins are made up of 20 amino acids linked by peptide bonds



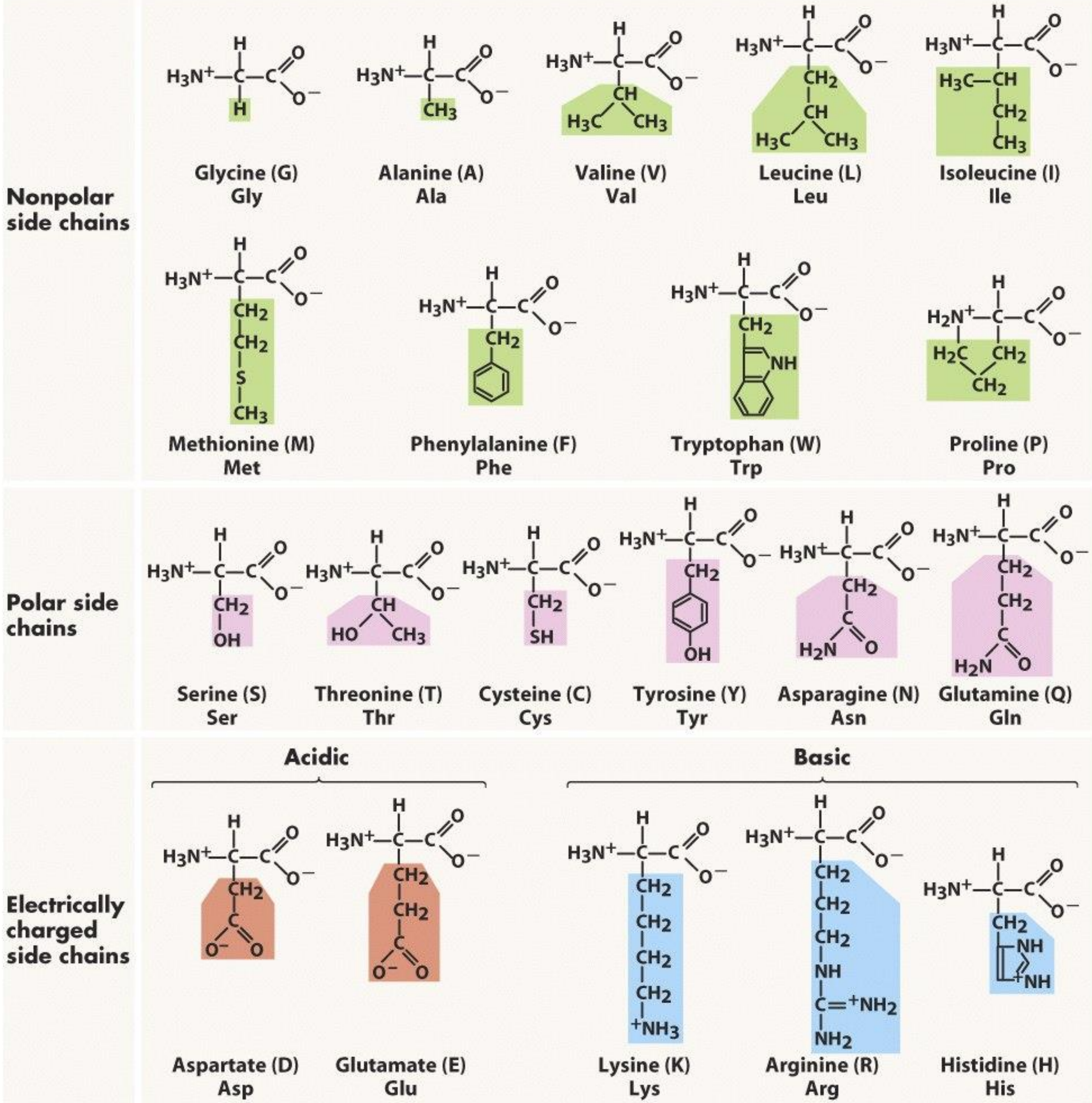




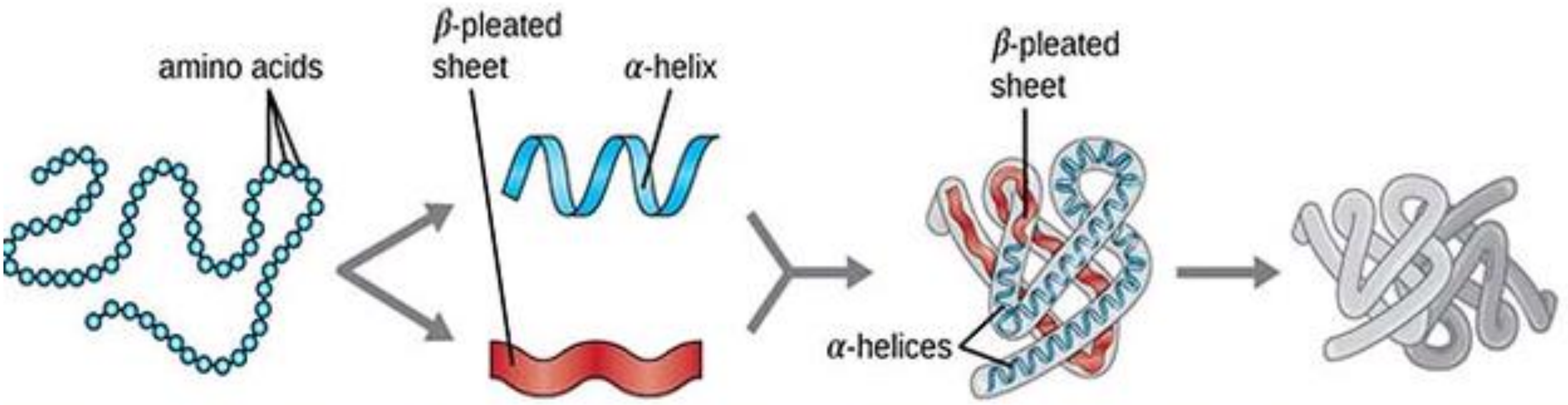




The structure of the R-group determines the chemical properties of the amino acid



Protein folding: Levels of protein structure



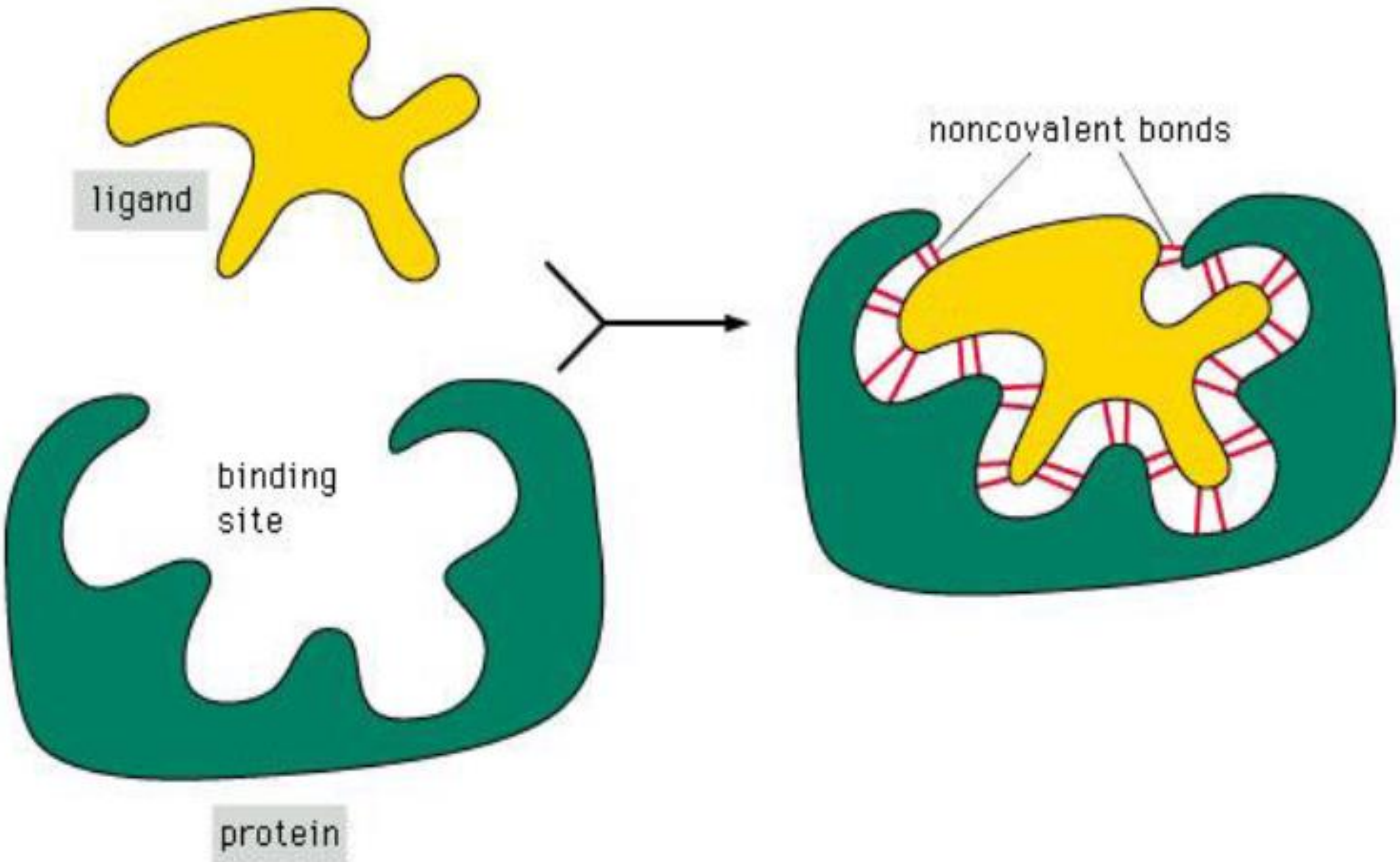
Primary Protein Structure
Sequence of a chain of amino acids

Secondary Protein Structure
Local folding of the polypeptide chain into helices or sheets

Tertiary Protein Structure
three-dimensional folding pattern of a protein due to side chain interactions

Quaternary Protein Structure
protein consisting of more than one amino acid chain

Ligand Binding



Proteins classified by Function

- **CATALYTIC:** enzymes
- **STORAGE:** ovalbumen (in eggs), casein (in milk), zein (in maize)
- **TRANSPORT:** haemoglobin
- **COMMUNICATION:** hormones (eg insulin) and neurotransmitters
- **CONTRACTILE:** actin, myosin, dynein (in microtubules)
- **PROTECTIVE:** Immunoglobulin, fibrinogen, blood clotting factors
- **TOXINS:** snake venom
- **STRUCTURAL:** cell membrane proteins, keratin (hair), collagen

Carbohydrates

- **Cells use carbohydrates for energy and structural materials**
- **Carbohydrates**
  - **Molecules that consist primarily of carbon, hydrogen, and oxygen atoms in a 1:2:1 ratio**

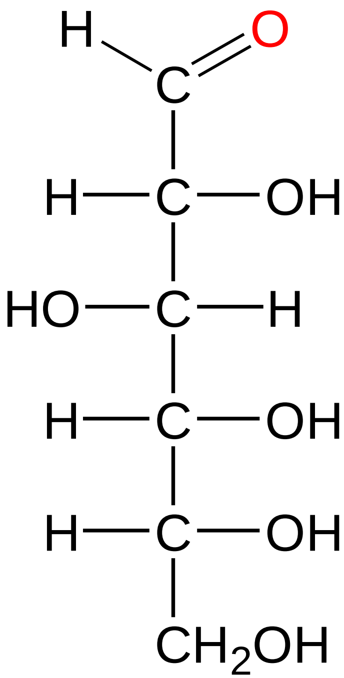
Carbohydrates (glycans) have the following basic composition:

$$(CH_2O)_n \quad \text{or} \quad \begin{array}{c} | \\ H - C - OH \\ | \end{array}$$

- **Monosaccharides - simple sugars with multiple OH groups. Based on number of carbons (3, 4, 5, 6), a monosaccharide is a triose, tetrose, pentose or hexose. 1:2:1 ratio of C:H:O- $C_6H_{12}O_6$**
- **Disaccharides - 2 monosaccharides covalently linked.**
- **Oligosaccharides - a few monosaccharides covalently linked.**
- **Polysaccharides - polymers consisting of chains of monosaccharide or disaccharide units.**

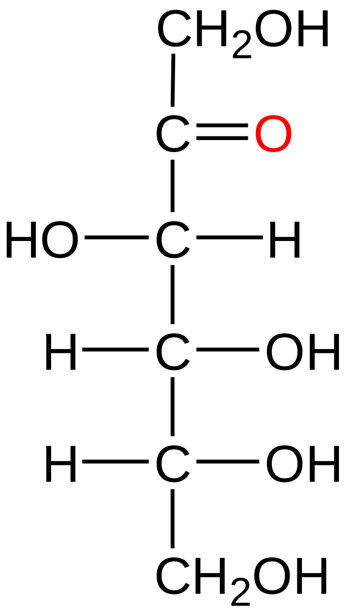
Monosaccharides

Aldoses (e.g., glucose) have an **aldehyde** group at one end.



D-glucose

Ketoses (e.g., fructose) have a **keto** group, usually at C2.

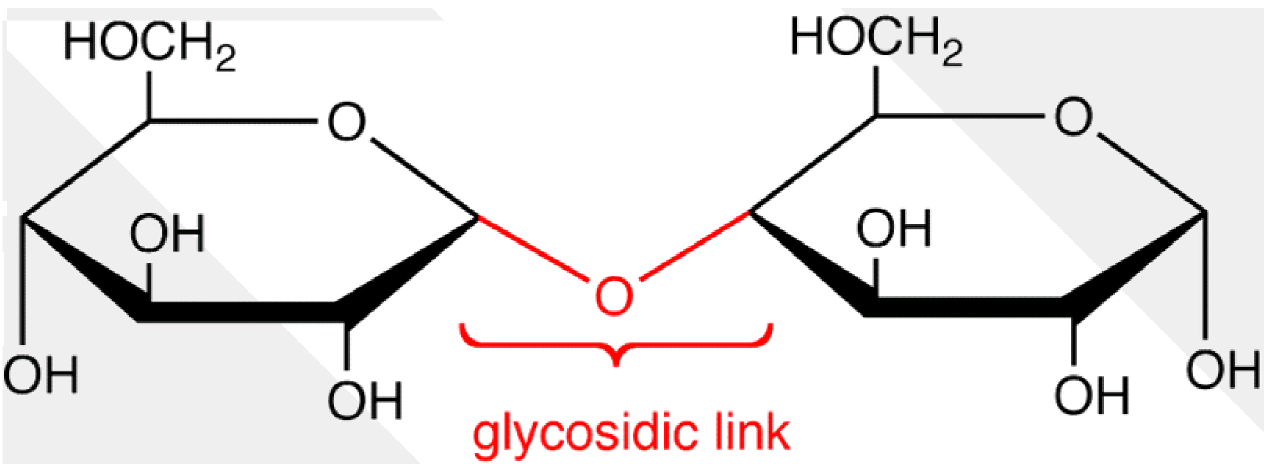


D-fructose

Most naturally occurring sugars are D isomers.

Disaccharides

- 2 monosaccharides linked together
- Key disaccharides you need to know:
  - Fructose + glucose → sucrose + H_2O
  - Glucose + galactose → lactose + H_2O
  - Glucose + glucose → maltose + H_2O



Glycosidic linkage:

The bond between monosaccharides

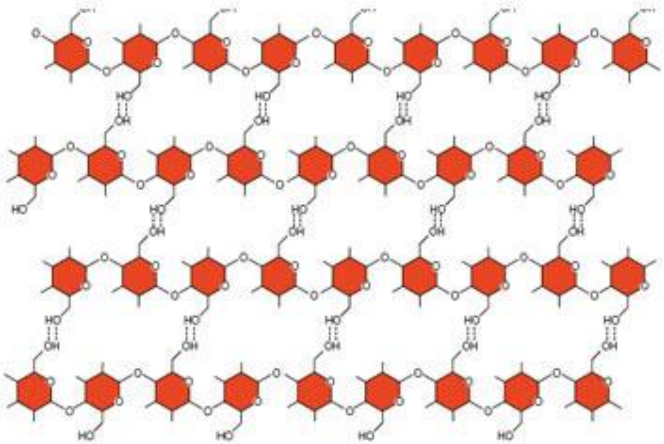
Complex Carbohydrates

Enzymes assemble complex carbohydrates (polysaccharides) from simple carbohydrate (sugar) subunits

Glucose monomers can bond in different patterns to form different complex carbohydrates

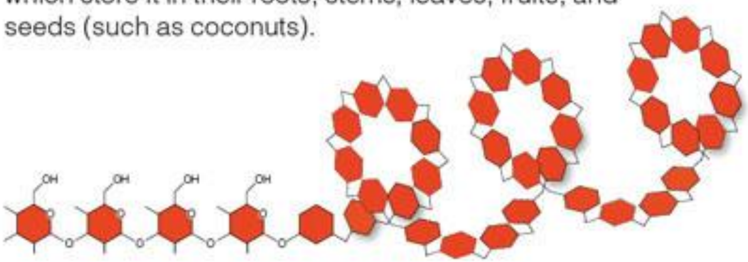
- **Cellulose (a structural component of plants)**
- **Starch (main energy reserve in plants)**
- **Glycogen (energy reserve in animals)**

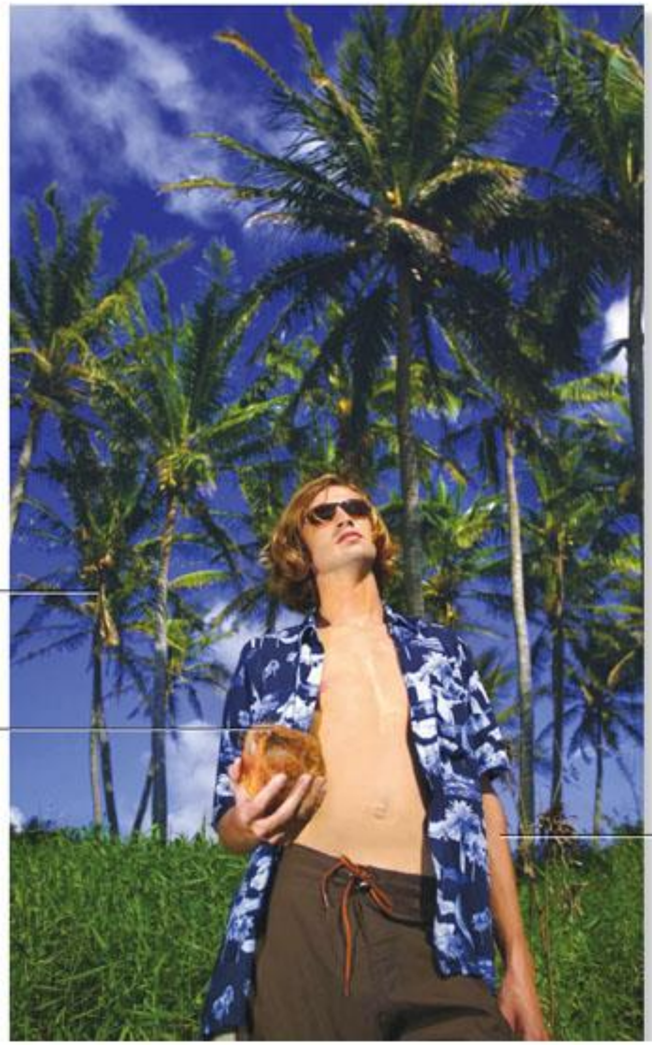
Some Complex Carbohydrates

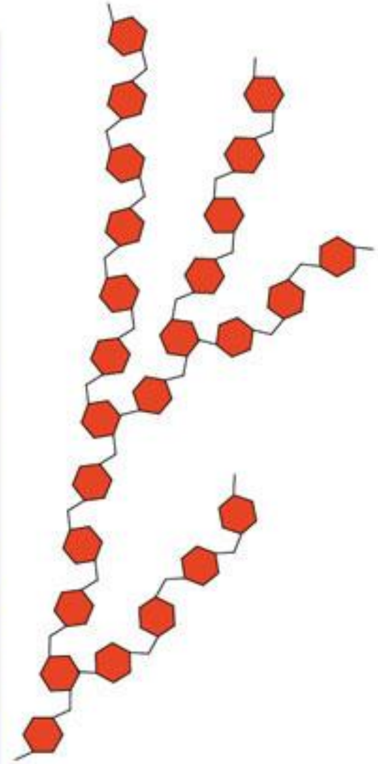


A Cellulose, a structural component of plants. Chains of glucose units stretch side by side and hydrogen-bond at many —OH groups. The hydrogen bonds stabilize the chains in tight bundles that form long fibers. Very few types of organisms can digest this tough, insoluble material.

B In starch, a series of glucose units form a chain that coils. Starch is the main energy reserve in plants, which store it in their roots, stems, leaves, fruits, and seeds (such as coconuts).







C Glycogen. In animals, this polysaccharide functions as an energy reservoir. It is especially abundant in the liver and muscles of active animals, including people.

Lipids

Lipids are a class of biological molecules defined by low solubility in water and high solubility in nonpolar solvents.

As molecules that are largely hydrocarbon in nature, lipids represent highly reduced forms of carbon and, upon oxidation in metabolism, yield large amounts of energy. Lipids are thus the molecules of choice for metabolic energy storage.

Classification

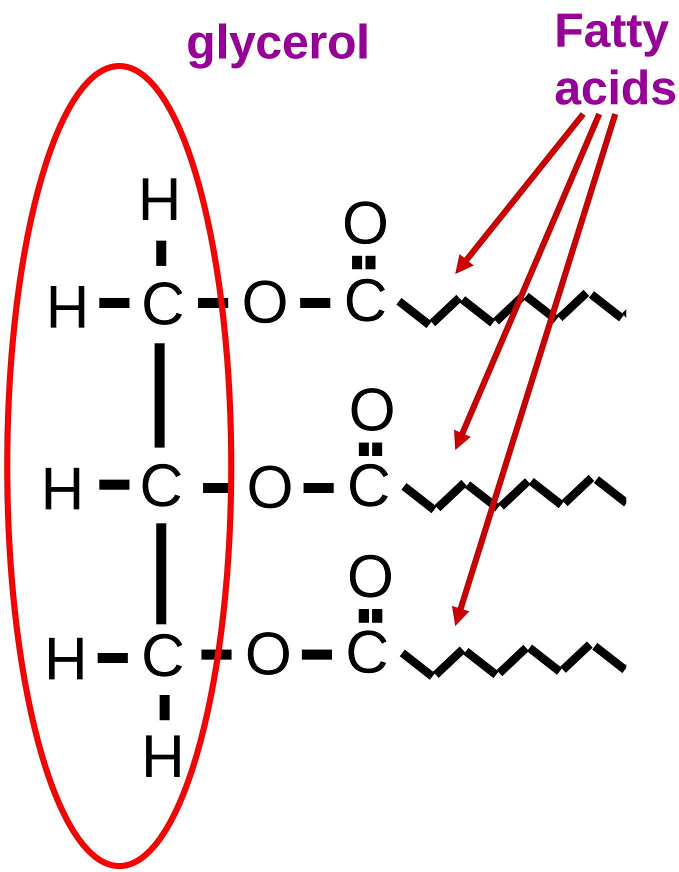
By structure:

1. **Simple: fats, oils, waxes, steroids.**
2. **Complex: phospholipids, spingolipids, glycolipids.**
3. **Derivatives: hormones, fat-solubility vitamins**

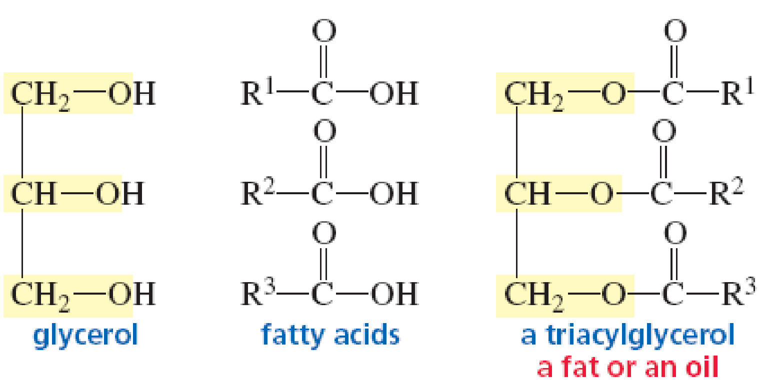
Biological functions

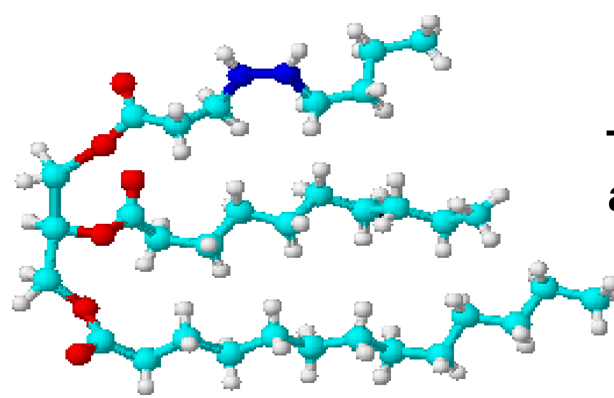
- The most important role of lipids is as a fuel. Thus fat is the most concentrated form in which potential energy can be stored.
- Since fat is a bad conductor of heat, it provides excellent insulation.
- Fat may also provide padding to protect the internal organs.
- Some compounds derived from lipids are important building blocks of biologically active materials.
- Lipoproteins are constituents of cell walls.
- One more important function of dietary lipids is that of supplying the so-called essential fatty acids

Oils and Fats



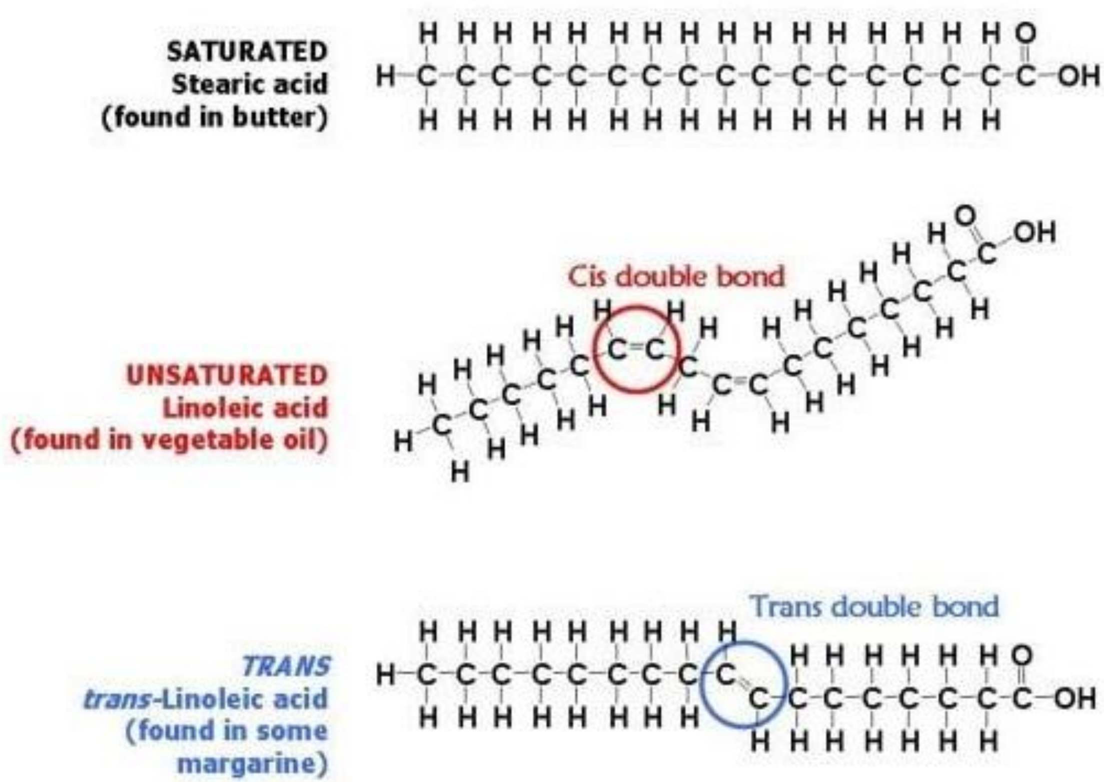
- **Fats, such as triglycerides, are the most abundant source of energy in vertebrates – stored in adipose tissue that insulates the body**
- **Fat**
  - **Lipid with one, two, or three fatty acid tails**
- **Triglyceride**
  - **Made up of 1 glycerol and 3 fatty acids**





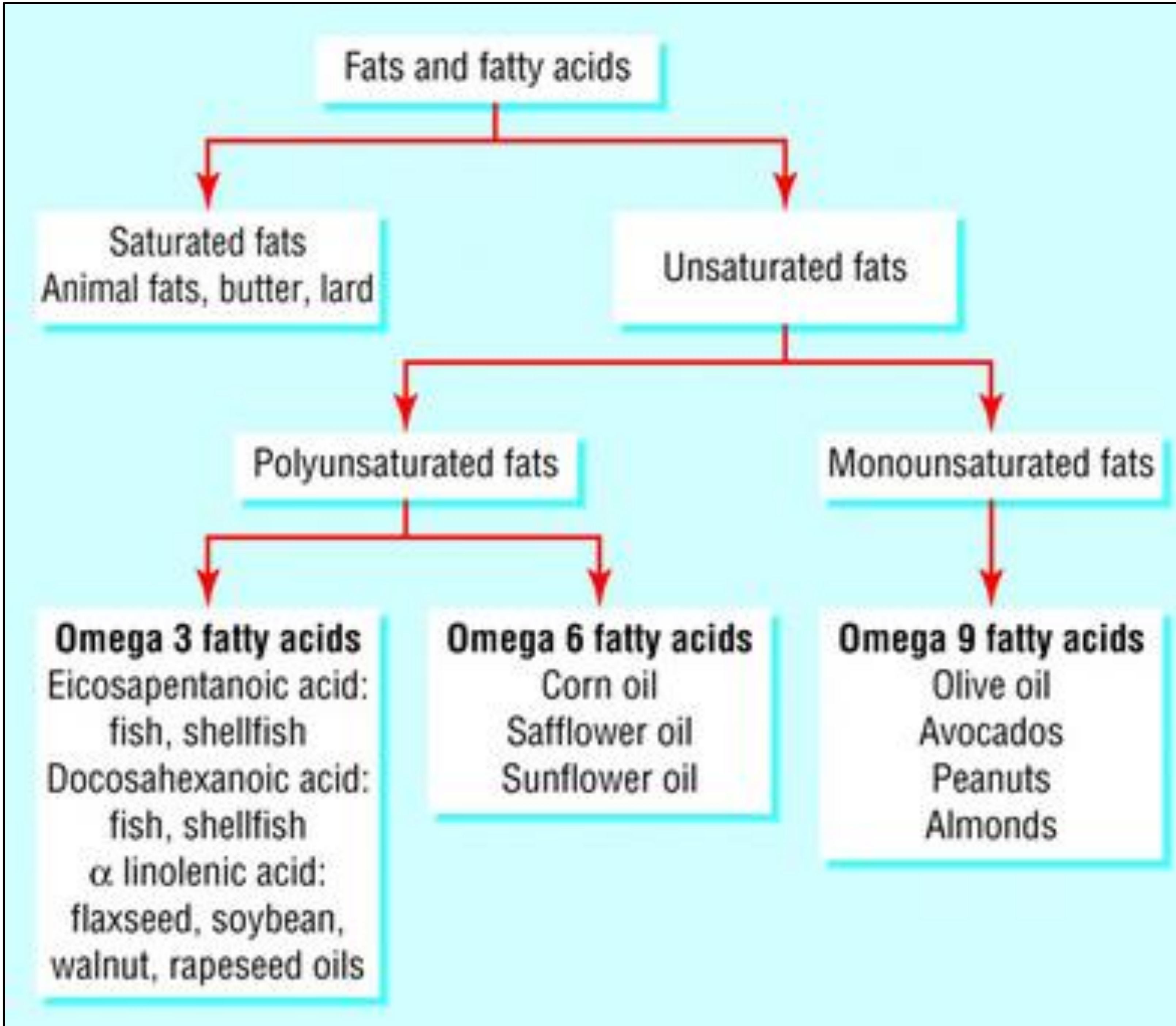
The Shape of a triglyceride is like the letter E

The Fats

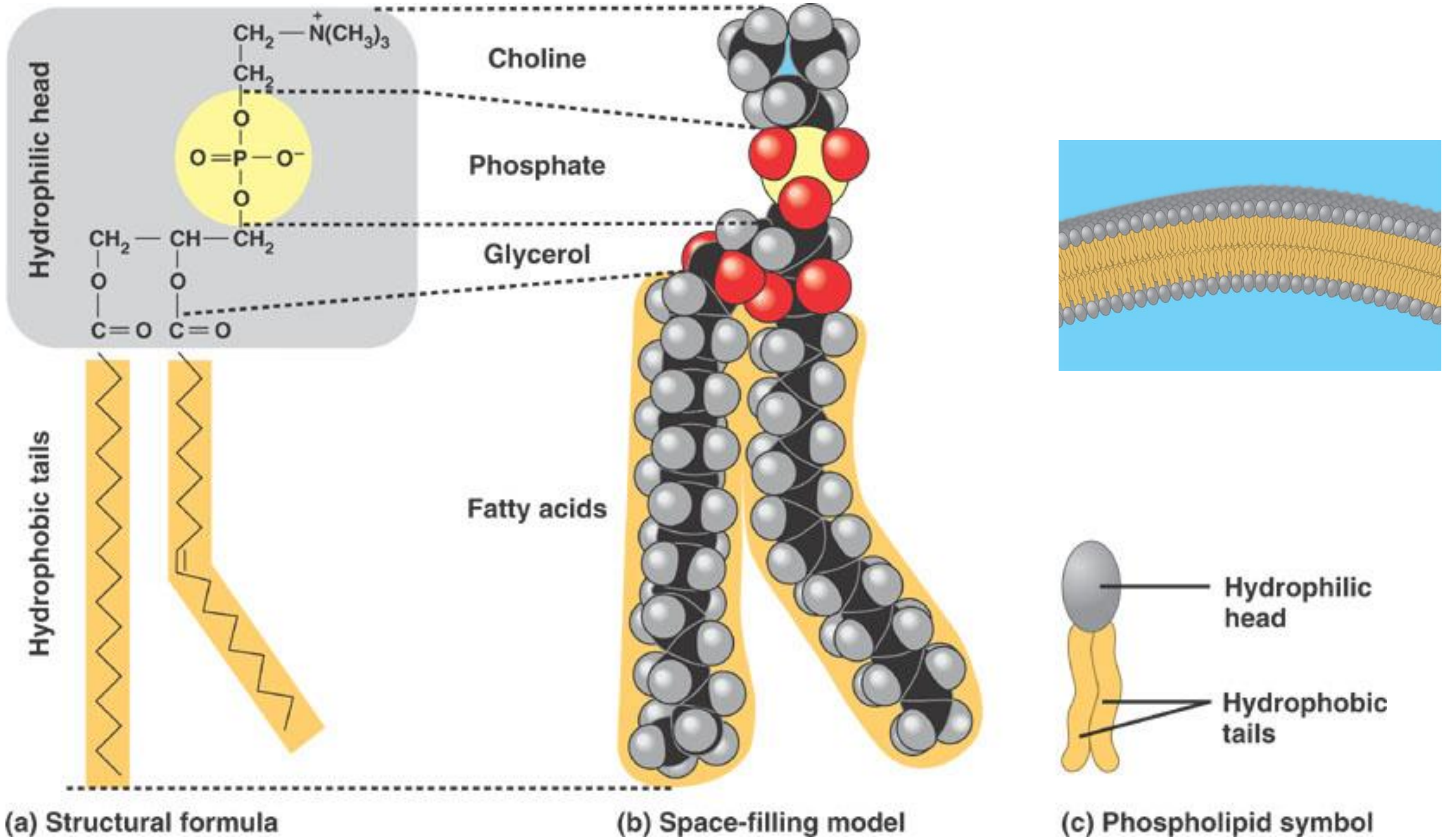


Type of Fatty Acid	Double Bonds	Diagram
Saturated	None	
Monounsaturated	One	
Polyunsaturated	Multiple (>1)	

- **Saturated fats pack more tightly than unsaturated fats, and tend to be more solid**
- **Saturated fat**
  - **Fatty acid with no double bonds in its carbon tail**
  - **Molecules are more straight**
  - **Fats: solid at room temperature**
- **Unsaturated fat**
  - **Lipid with one or more double bonds in a fatty acid tail**
  - **Causes “kinks” in molecule**
  - **Liquid at room temperature**

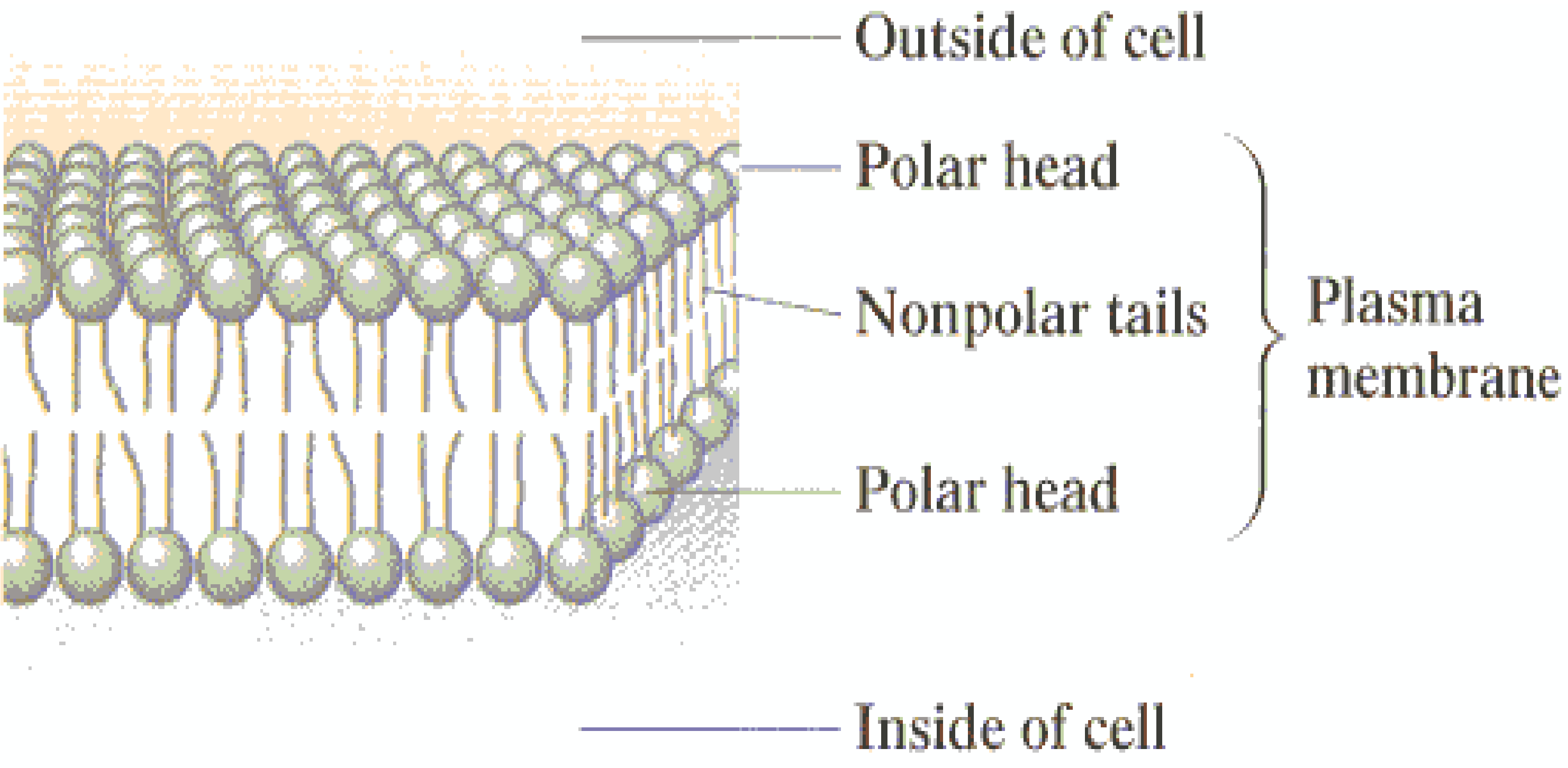

Fats and fatty acids
Saturated fats
Animal fats, butter, lard
Unsaturated fats
Polyunsaturated fats
Monounsaturated fats
Omega 3 fatty acids
Eicosapentanoic acid: fish, shellfish
Docosahexanoic acid: fish, shellfish
α linolenic acid: flaxseed, soybean, walnut, rapeseed oils
Omega 6 fatty acids
Corn oil
Safflower oil
Sunflower oil
Omega 9 fatty acids
Olive oil
Avocados
Peanuts
Almonds

Phospholipids: main structural component of cell membranes

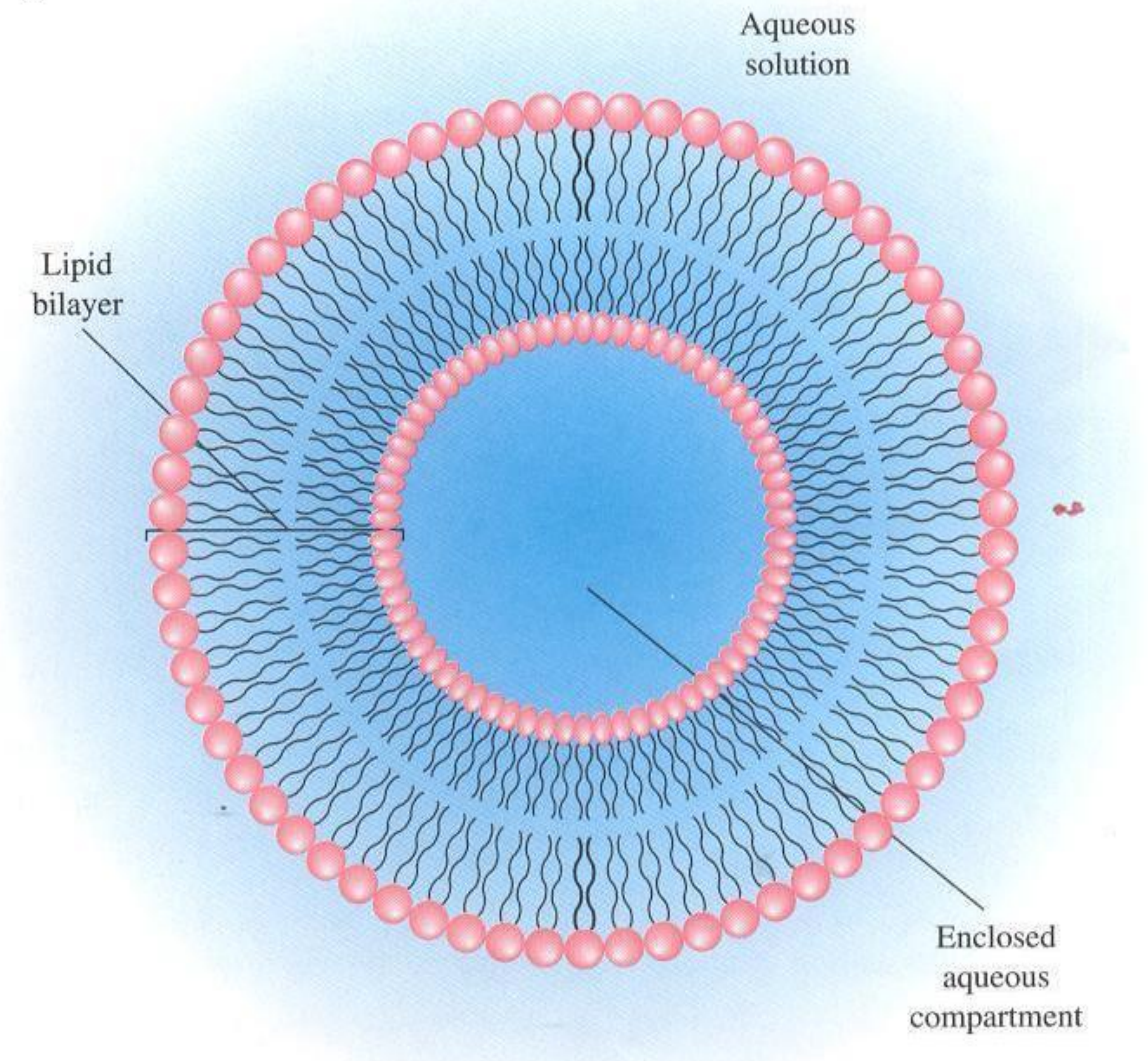


- Structurally and chemically similar to triglycerides
- One fatty acid is replaced with a phosphate group
- Phosphate group is hydrophilic
- Fatty acids are hydrophobic

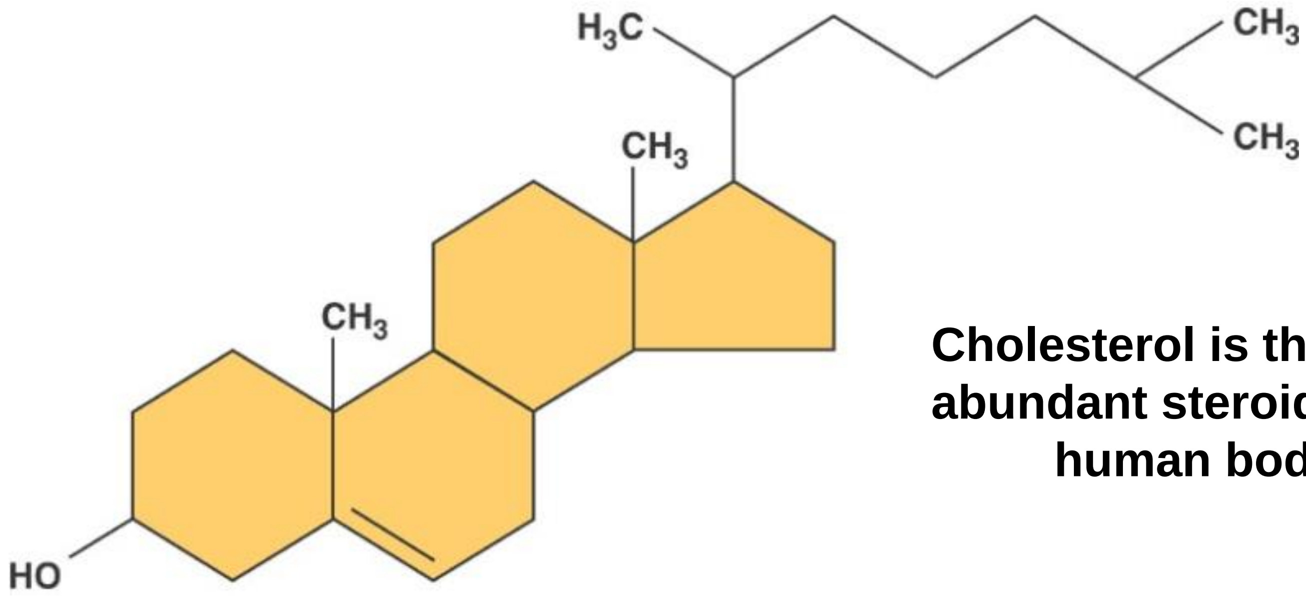
Lipid bilayer of plasma membrane



Liposome


Aqueous
solution
Lipid
bilayer
Enclosed
aqueous
compartment

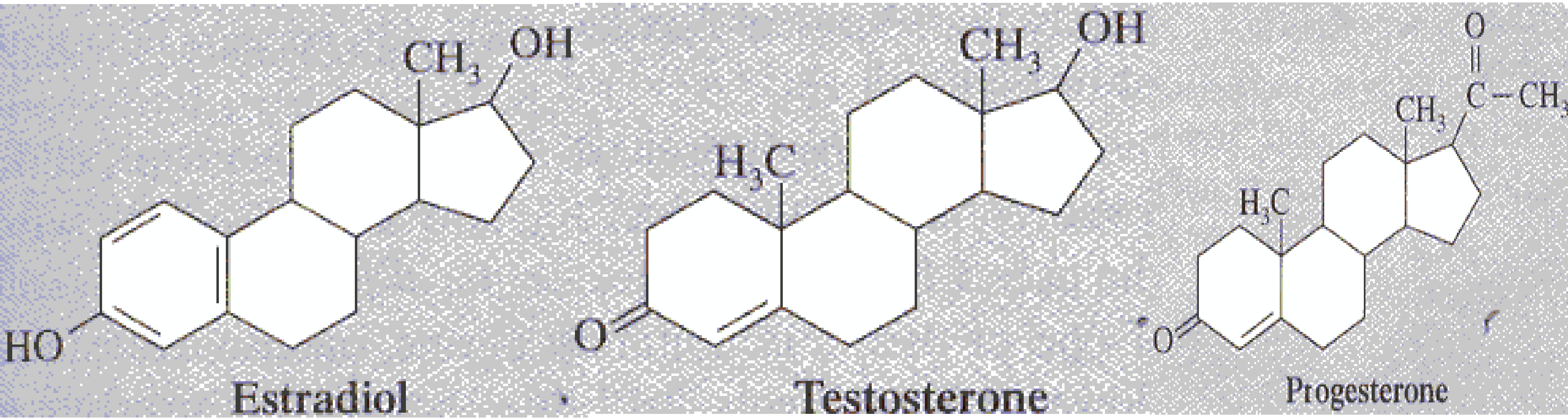
Steroids



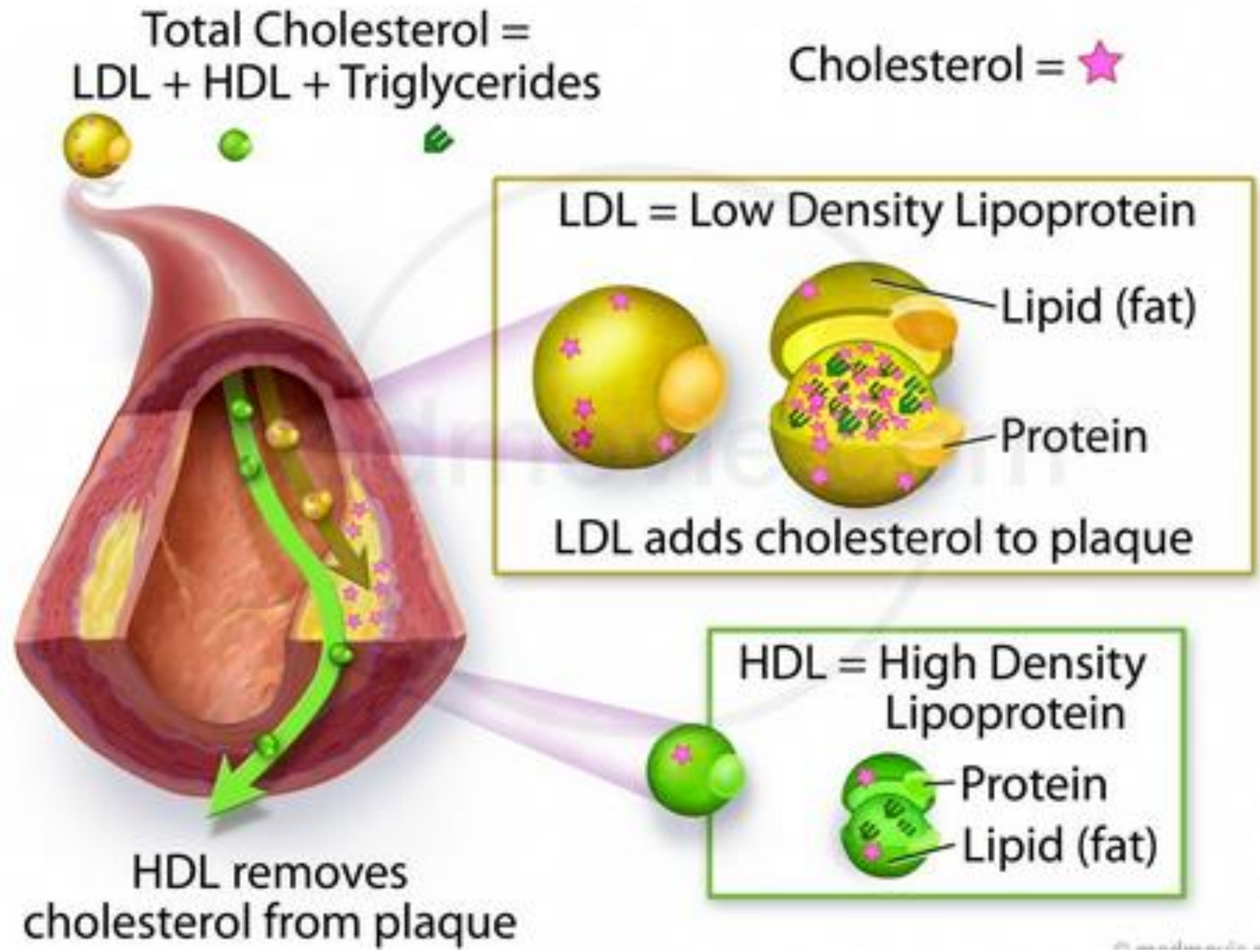
Cholesterol is the most abundant steroid in the human body

- Chemically and structurally different from other lipid categories (no fatty acid tails)
- Classified as a lipid because of their nonpolar/hydrophobic nature
- Three of the rings are six-membered, while the fourth is five-membered.
- Chemical messengers (hormones)
- Structural components in cell membranes

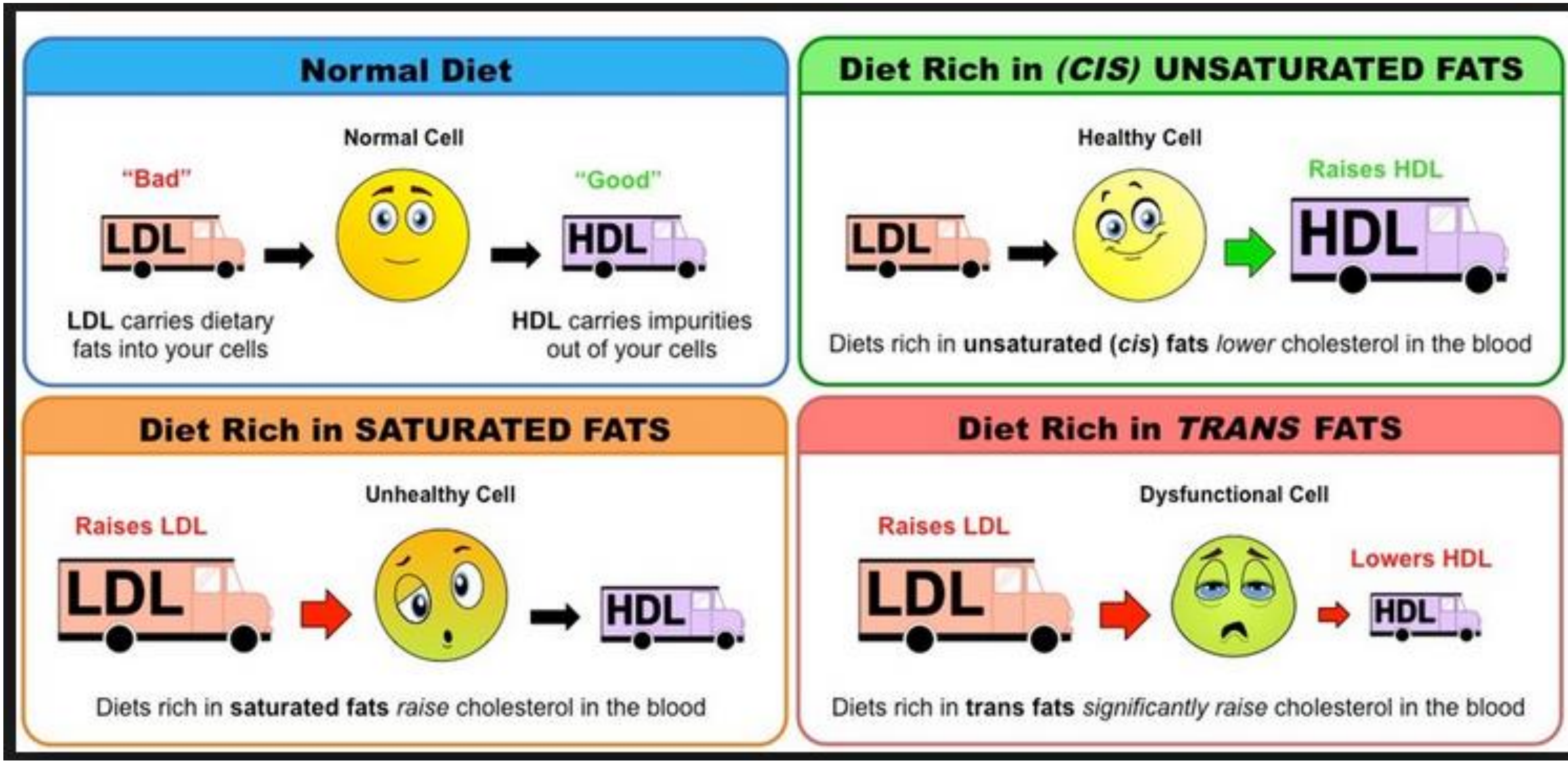
Steroids Hormones

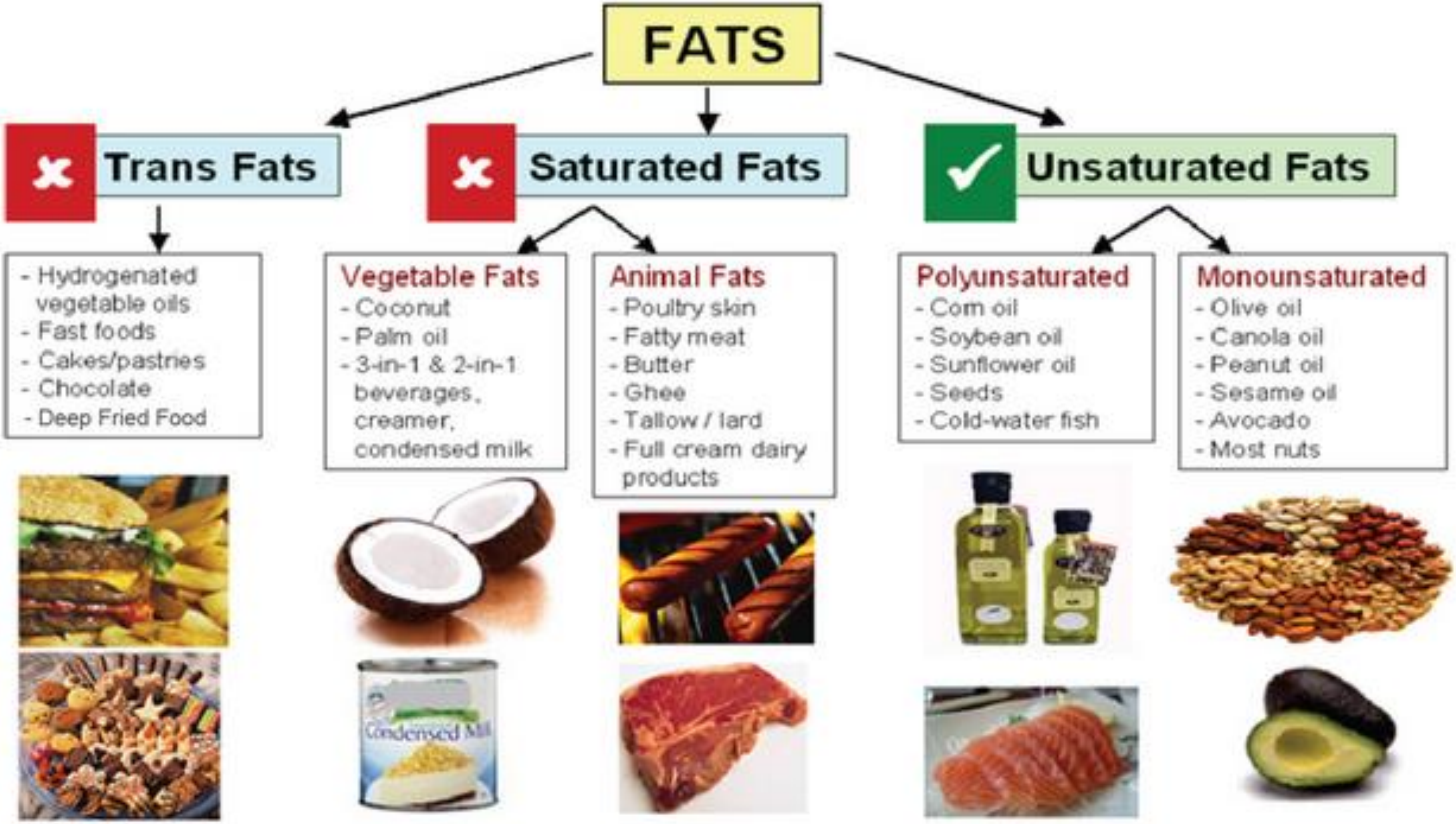


Hormones are chemical messengers produced by ductless glands.

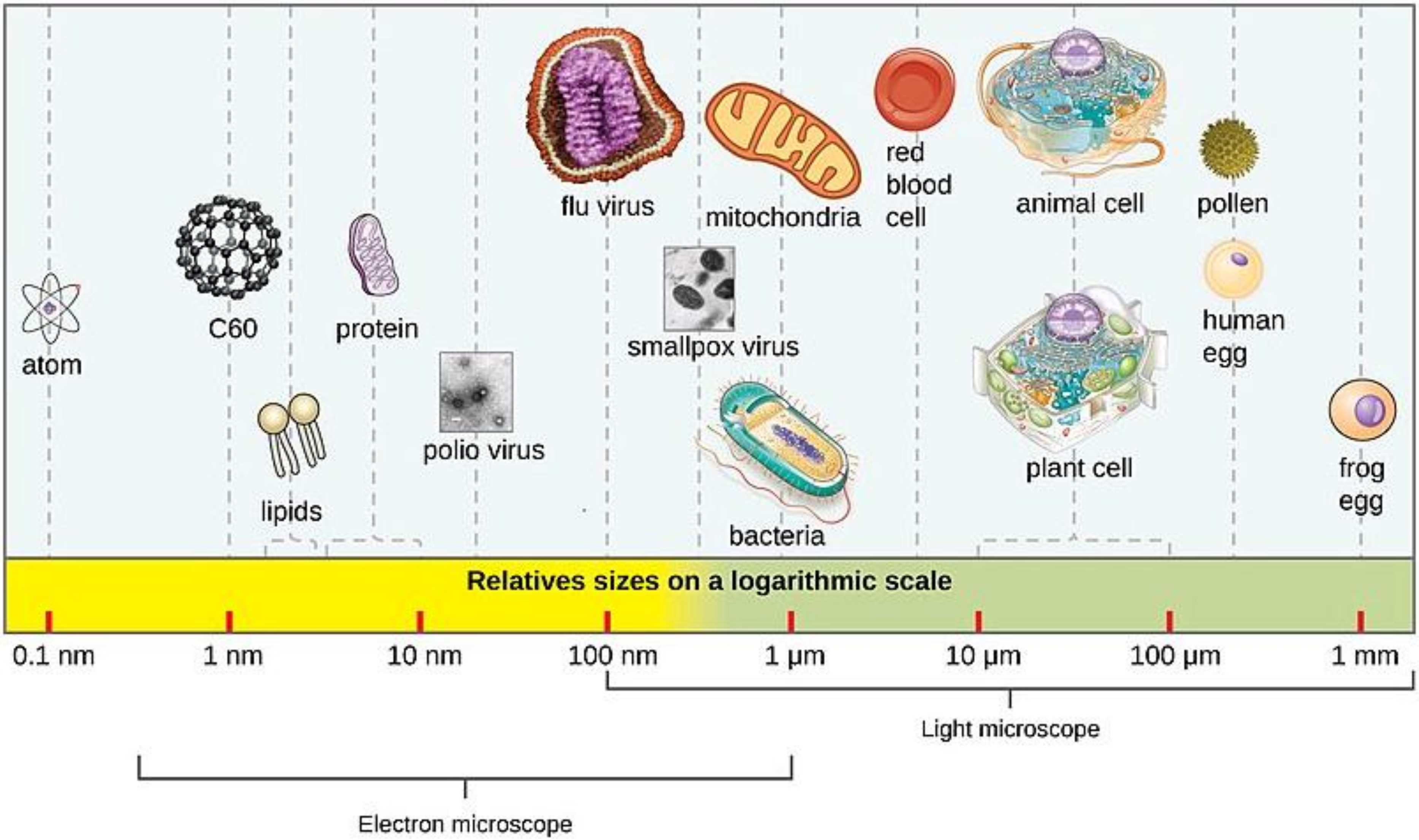


Total Cholesterol =
LDL + HDL + Triglycerides
Cholesterol =
LDL = Low Density Lipoprotein
Lipid (fat)
Protein
LDL adds cholesterol to plaque
HDL = High Density
Lipoprotein
Protein
Lipid (fat)
HDL removes
cholesterol from plaque


Normal Diet
Normal Cell
"Bad"
LDL
"Good"
HDL
LDL carries dietary fats into your cells
HDL carries impurities out of your cells
Diet Rich in (CIS) UNSATURATED FATS
Healthy Cell
Raises HDL
LDL
HDL
Diets rich in unsaturated (cis) fats lower cholesterol in the blood
Diet Rich in SATURATED FATS
Unhealthy Cell
Raises LDL
LDL
HDL
Diets rich in saturated fats raise cholesterol in the blood
Diet Rich in TRANS FATS
Dysfunctional Cell
Raises LDL
Lowers HDL
LDL
HDL
Diets rich in trans fats significantly raise cholesterol in the blood

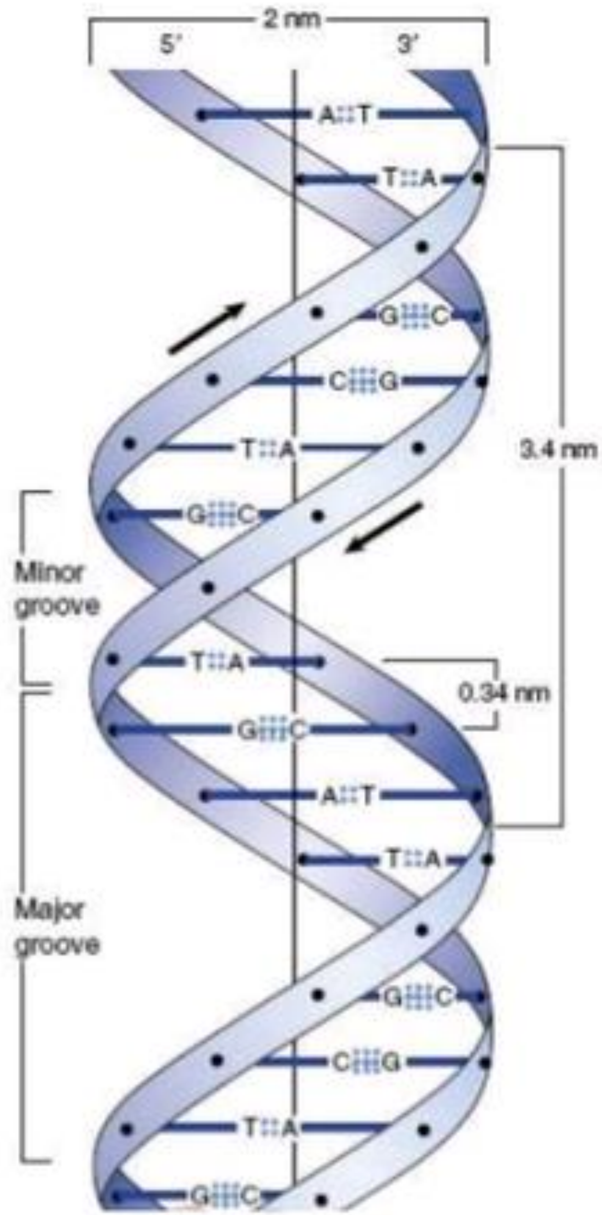

FATS
Trans Fats
Saturated Fats
Unsaturated Fats
- Hydrogenated vegetable oils
- Fast foods
- Cakes/pastries
- Chocolate
- Deep Fried Food
Vegetable Fats
- Coconut
- Palm oil
- 3-in-1 & 2-in-1 beverages, creamer, condensed milk
Animal Fats
- Poultry skin
- Fatty meat
- Butter
- Ghee
- Tallow / lard
- Full cream dairy products
Polyunsaturated
- Corn oil
- Soybean oil
- Sunflower oil
- Seeds
- Cold-water fish
Monounsaturated
- Olive oil
- Canola oil
- Peanut oil
- Sesame oil
- Avocado
- Most nuts
Condensed Milk

DNA, Genes, Chromosomes and Chromosomal Aberration


atom
C60
lipids
protein
polio virus
flu virus
smallpox virus
mitochondria
bacteria
red blood cell
animal cell
plant cell
pollen
human egg
frog egg
Relatives sizes on a logarithmic scale
0.1 nm
1 nm
10 nm
100 nm
1 µm
10 µm
100 µm
1 mm
Light microscope
Electron microscope

The double-helical structure of DNA

- Right-handed helix;
- The diameter of the double helix: 2 nm
- The distance between two base pairs: 0.34 nm;
- Each turn of the helix involves 10 bases pairs, 3.4 nm.



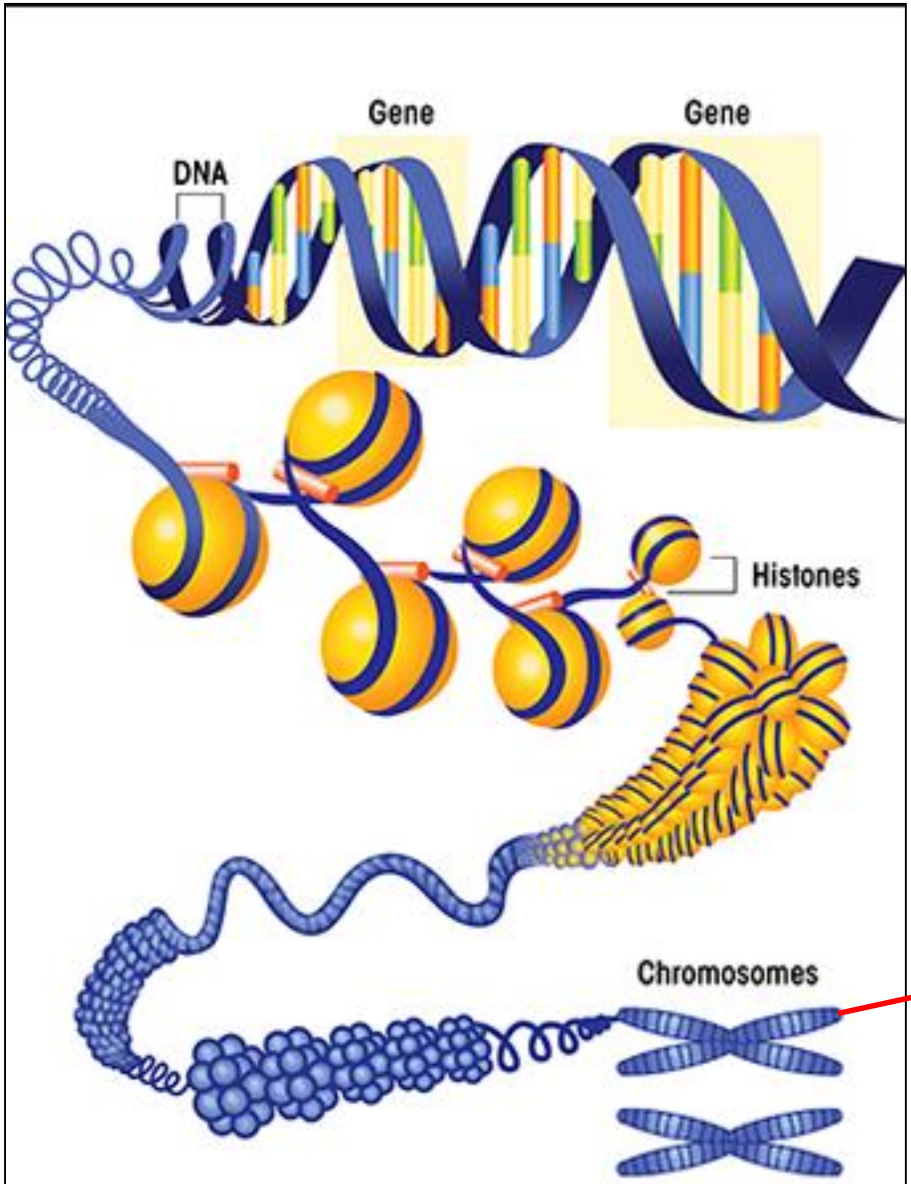
Each of us has enough DNA to reach from here to the sun and back, more than 300 times.

The haploid human genome contains approximately 3 billion base pairs of DNA packaged into 23 chromosomes. Of course, most cells in the body (except for female ova and male sperm) are diploid, with 23 pairs of chromosomes. That makes a total of 6 billion base pairs of DNA per cell. Because each base pair is around 0.34 nanometers long (a nanometer is one-billionth of a meter), each diploid cell therefore contains about 2 meters of DNA $[(0.34 \times 10^{-9}) \times (6 \times 10^{9})]$.

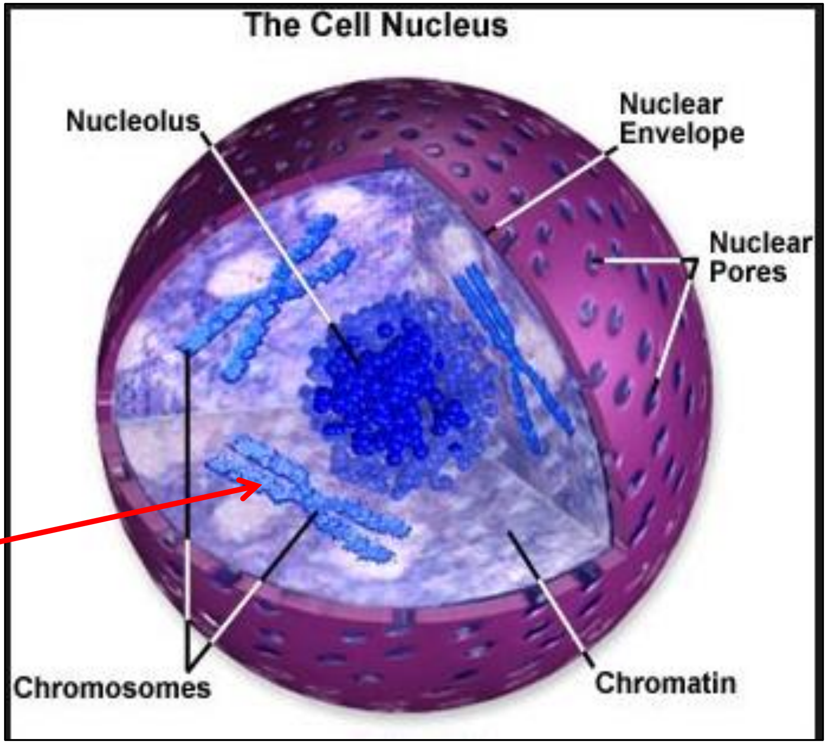
It is estimated that the human body contains about 50 trillion cells—which works out to 100 trillion meters of DNA per human. Now, consider the fact that the Sun is 150 billion meters from Earth. This means that each of us has enough DNA to go from here to the Sun and back more than 300 times, or around Earth's equator 2.5 million times!

How is this possible?

How is all of that DNA packaged so tightly into chromosomes and squeezed into a tiny nucleus?

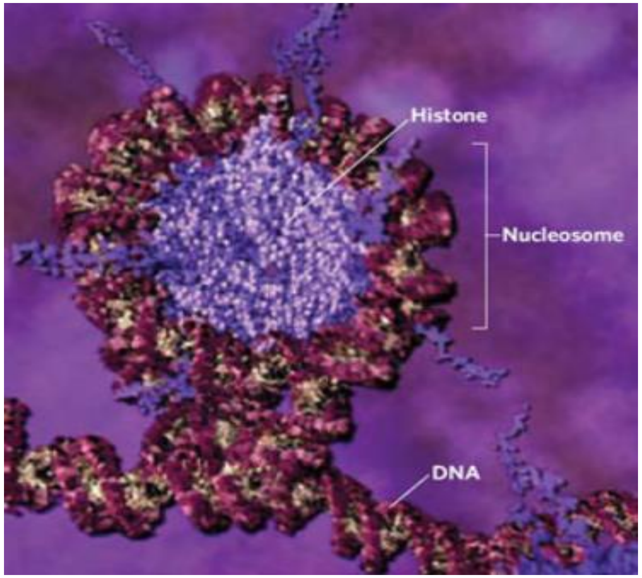


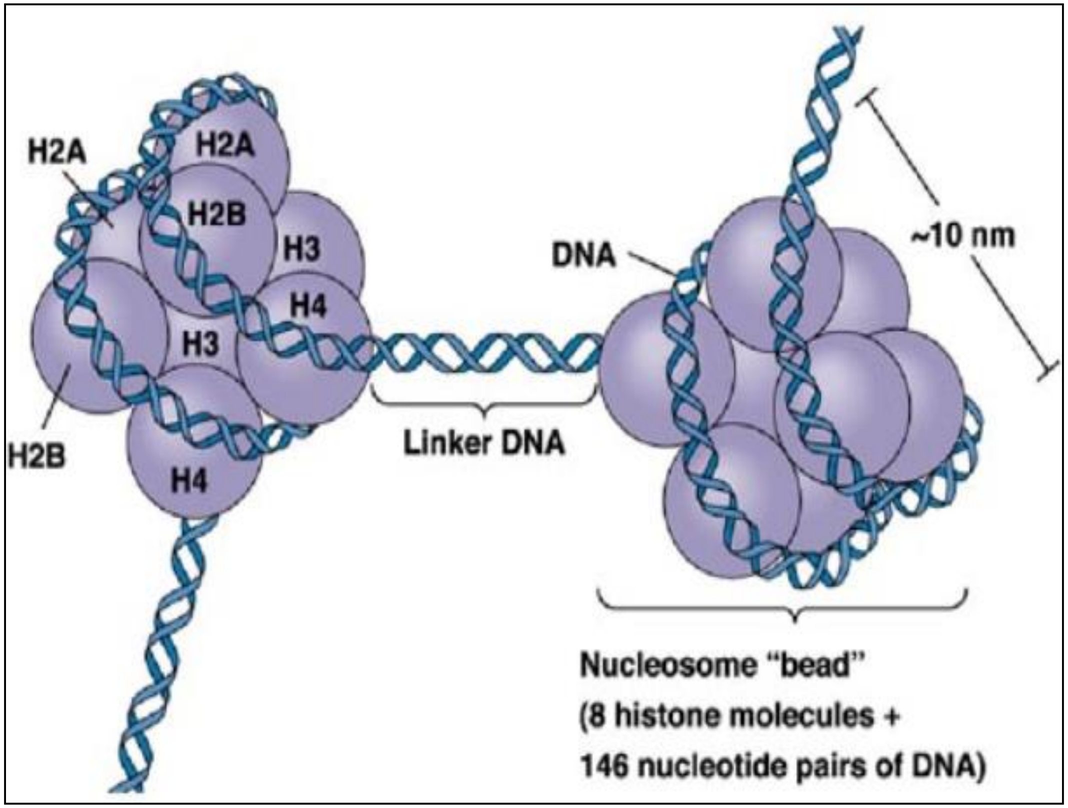
Human cells have 23 pairs of chromosomes. Each one is made up of a DNA molecule that is made up of a series of nucleotides arranged in 2 strands that spiral to form a double helix.



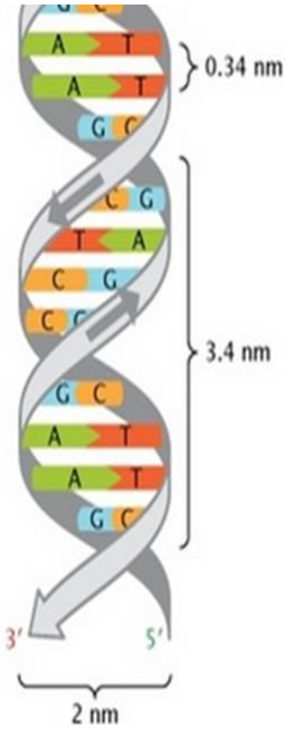
Chromosomal DNA is packaged inside microscopic nuclei with the help of Histones

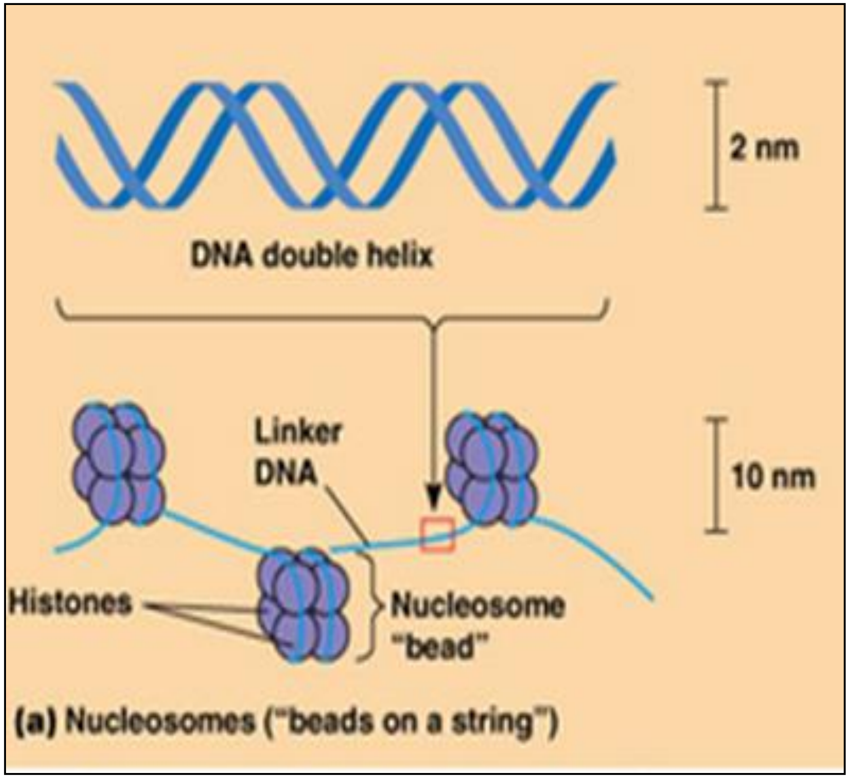
Histones are positively-charged proteins that strongly adhere to negatively-charged DNA and form complexes called nucleosomes.

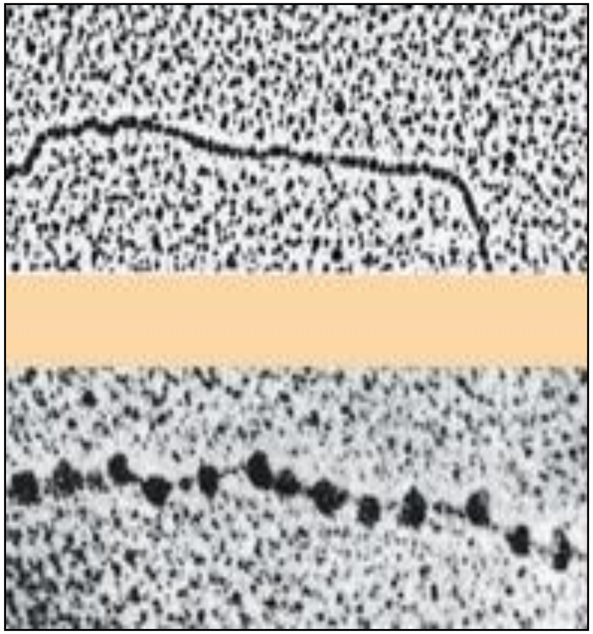




DNA Double helix to The Nucleosome



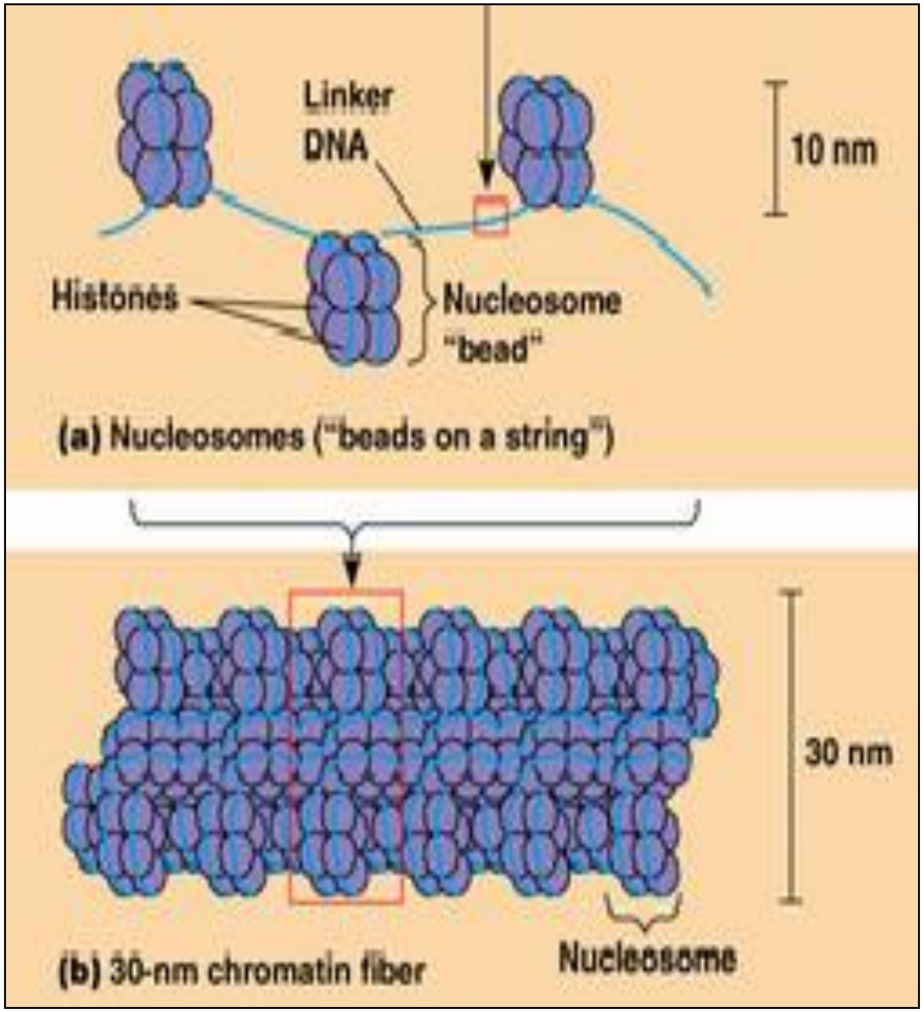


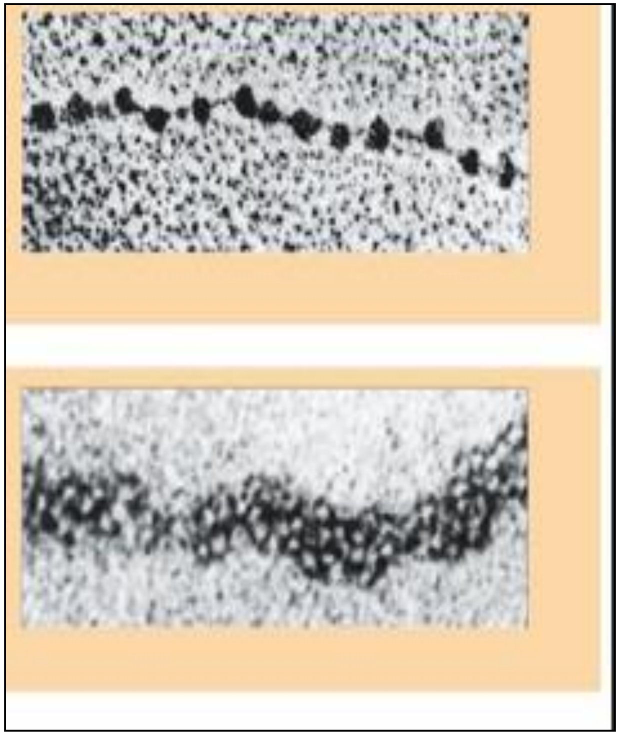


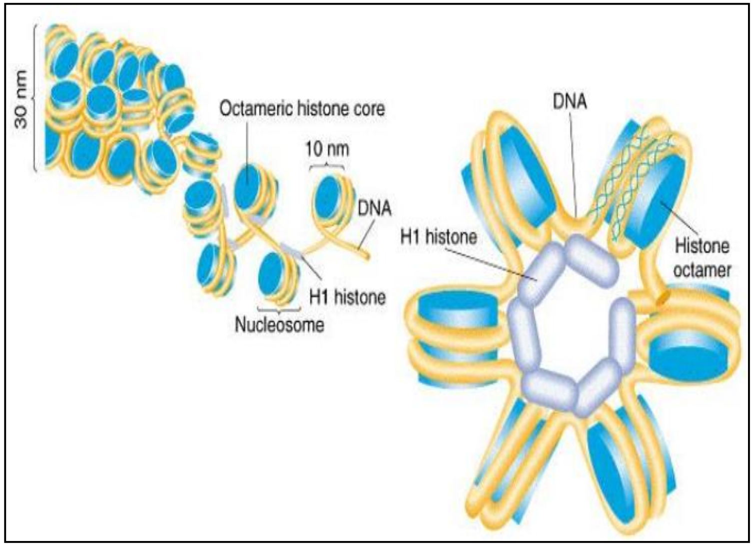
Schematic diagram of chromatin: the beads on a string

Electron micrograph of chromatin: the beads on a string

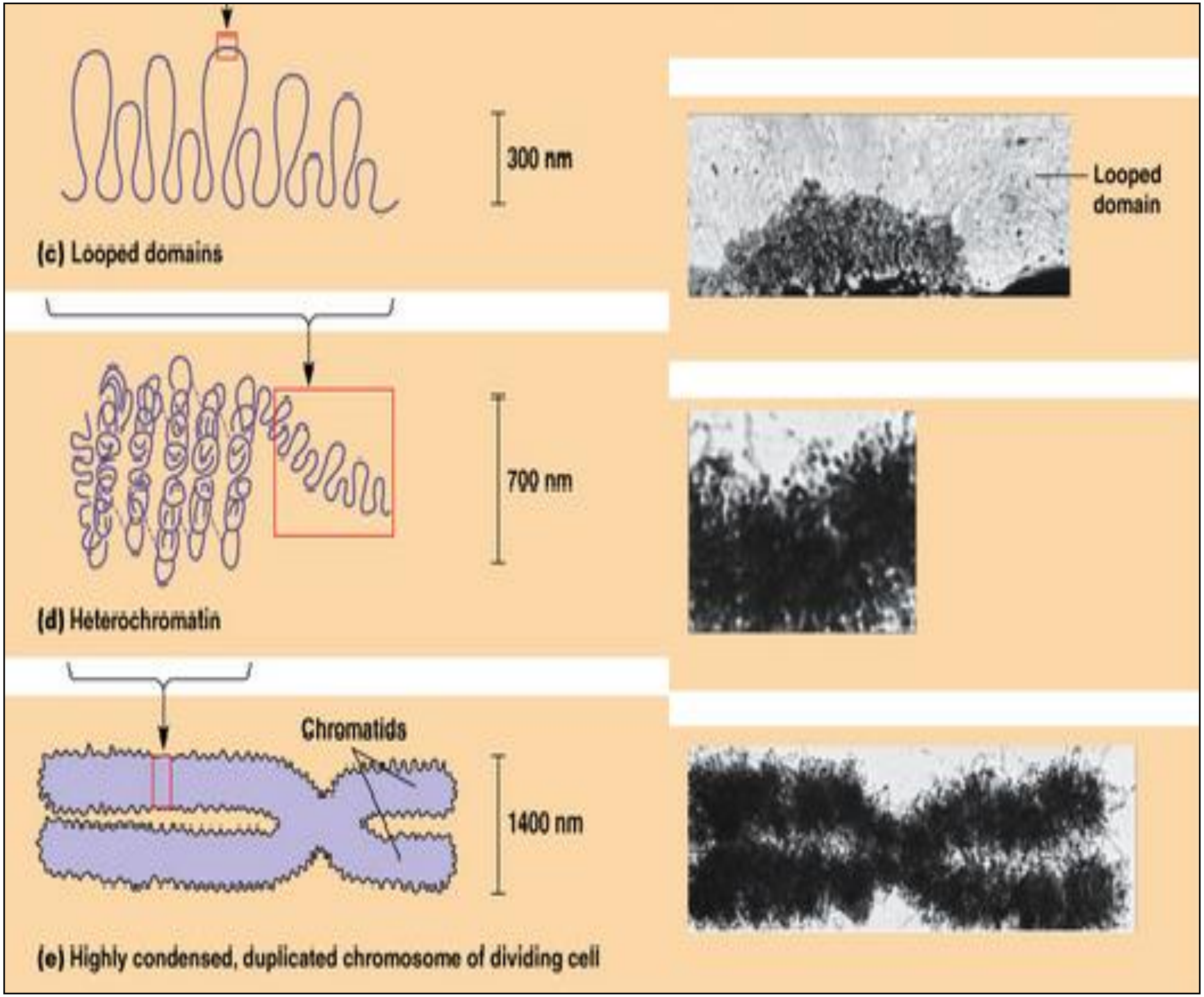
Nucleosomes fold up to form a 30-nanometer chromatin fiber







30-nanometer chromatin fiber forms loops averaging 300 nanometers in length. The 300 nm fibers are compressed and folded to wide fiber, which is tightly coiled into the chromatid of a chromosome.

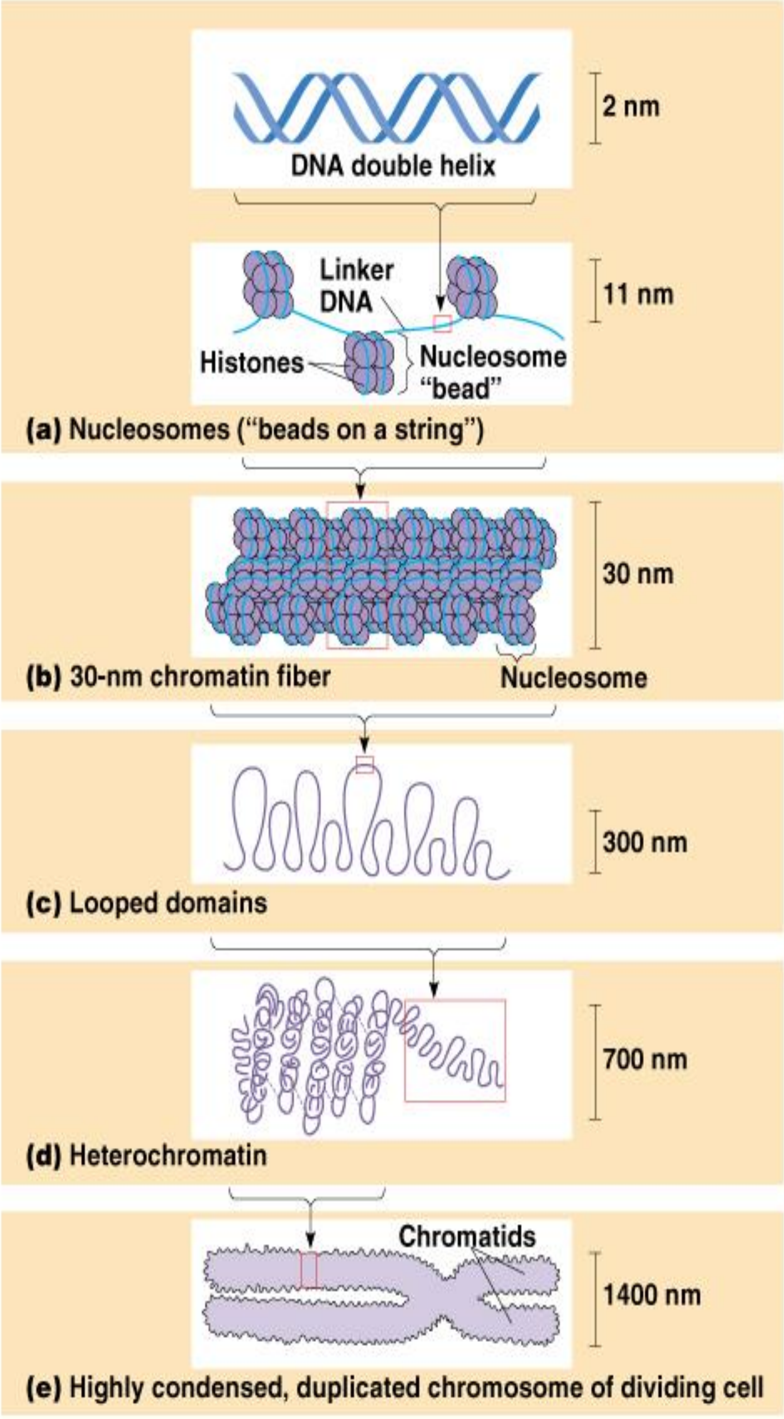


Summary

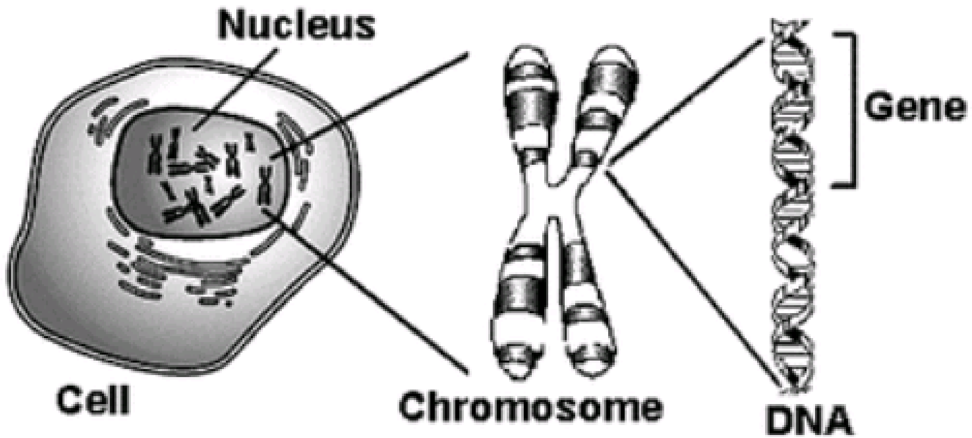
DNA molecules are packaged in the cell as structures called <u>chromosomes</u>.

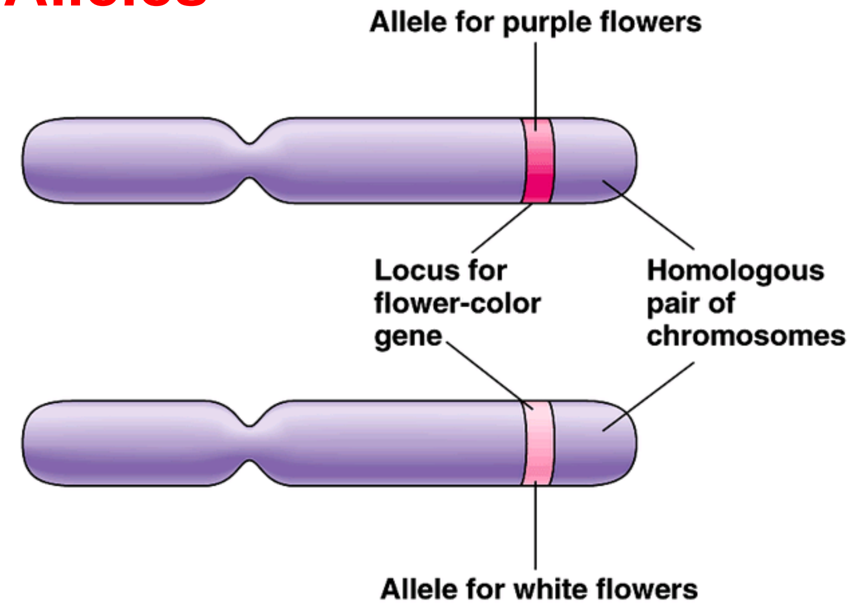
Bacteria have a single chromosome. Eukaryotes have multiple chromosomes. Humans have 46 chromosomes.

All of an organism's chromosomes make up the <u>genome</u>.



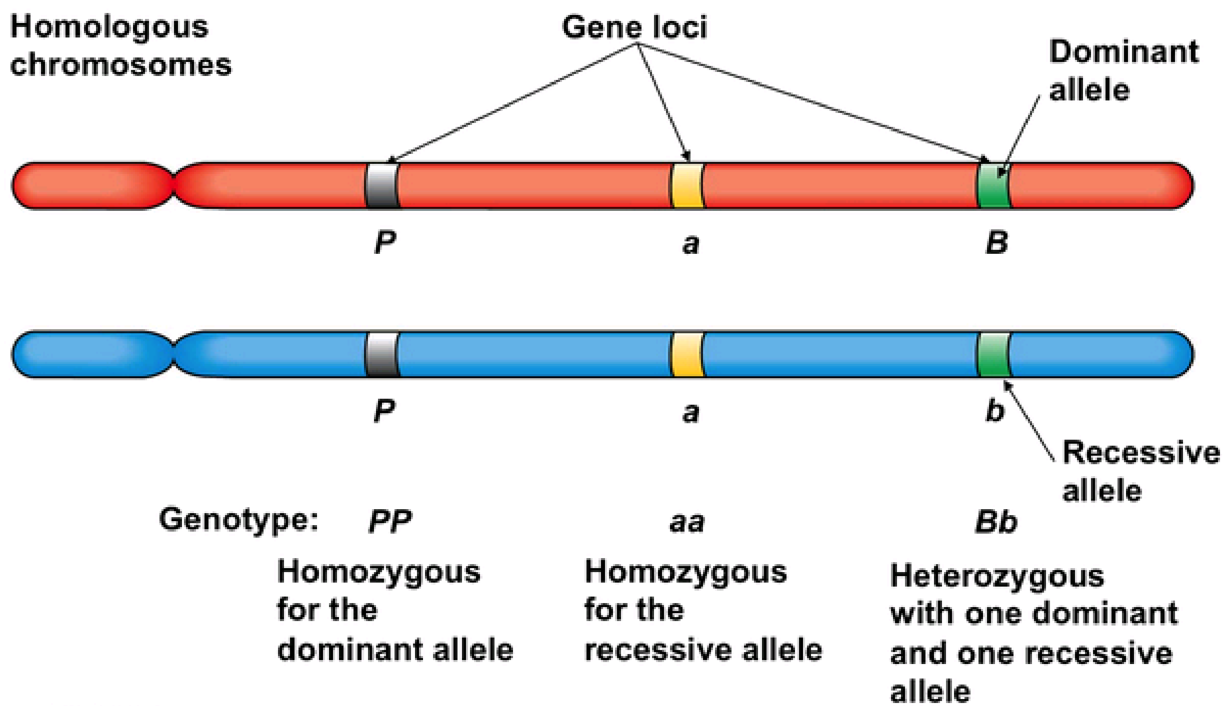
Genes and Alleles



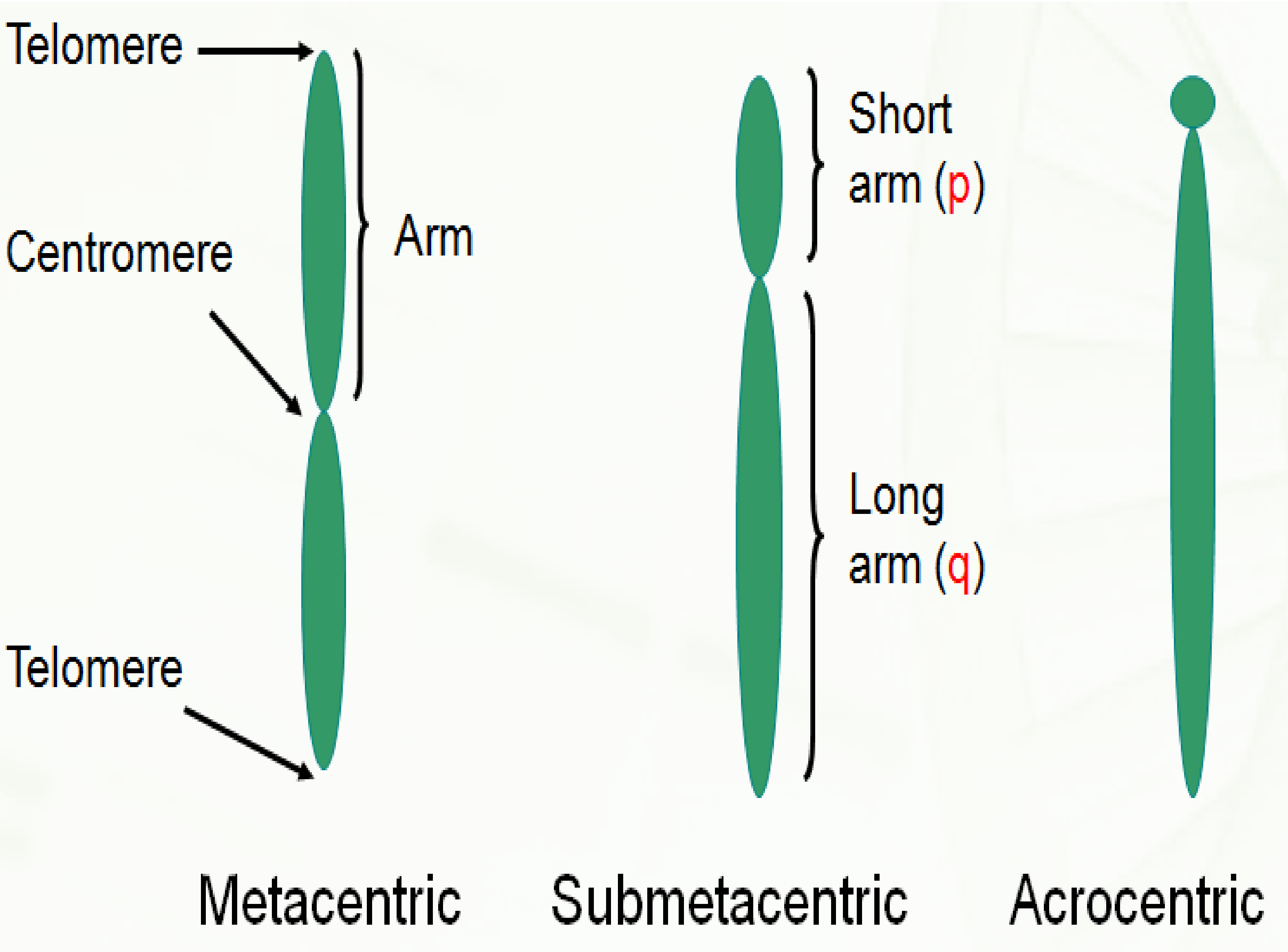


gene – segment of DNA containing instructions for a trait

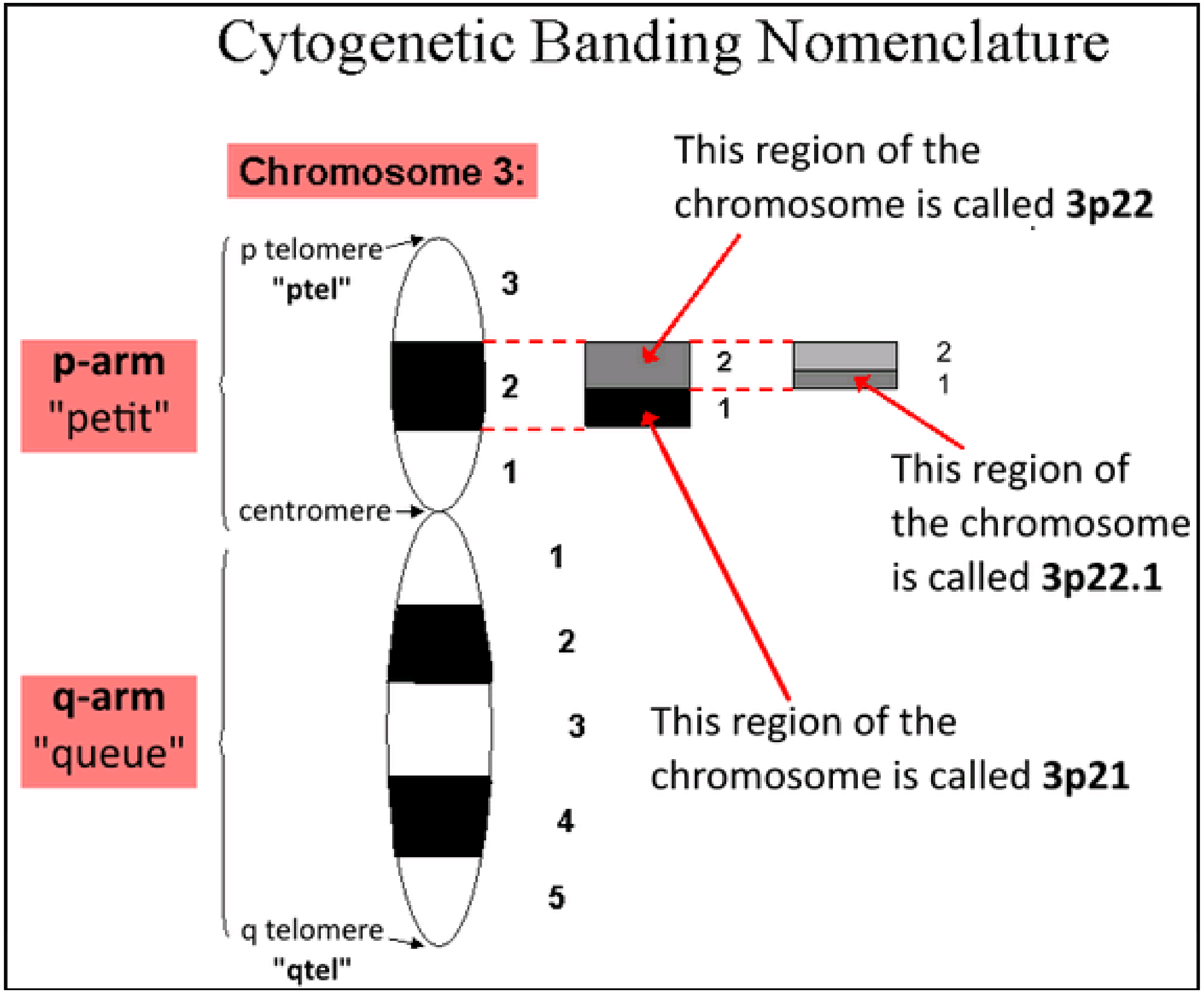
allele – one version of a gene that governs a characteristic (such as fur color)



Chromosome Morphology

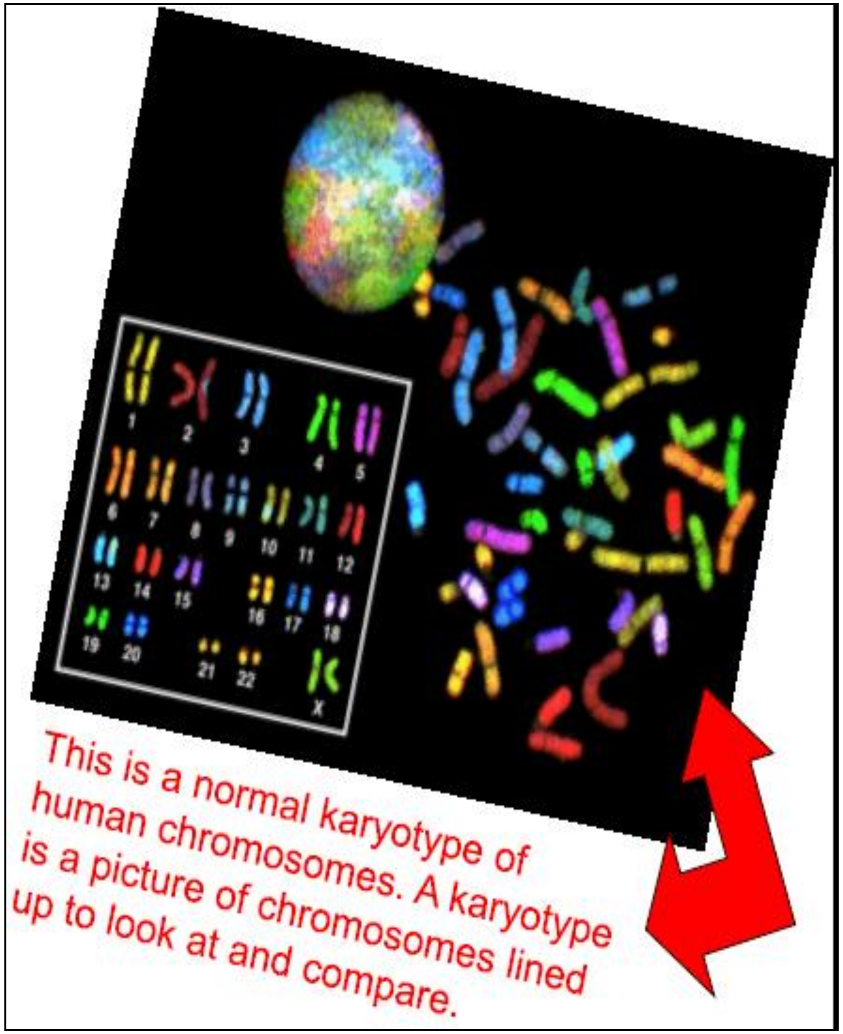


Defining Chromosomal Location

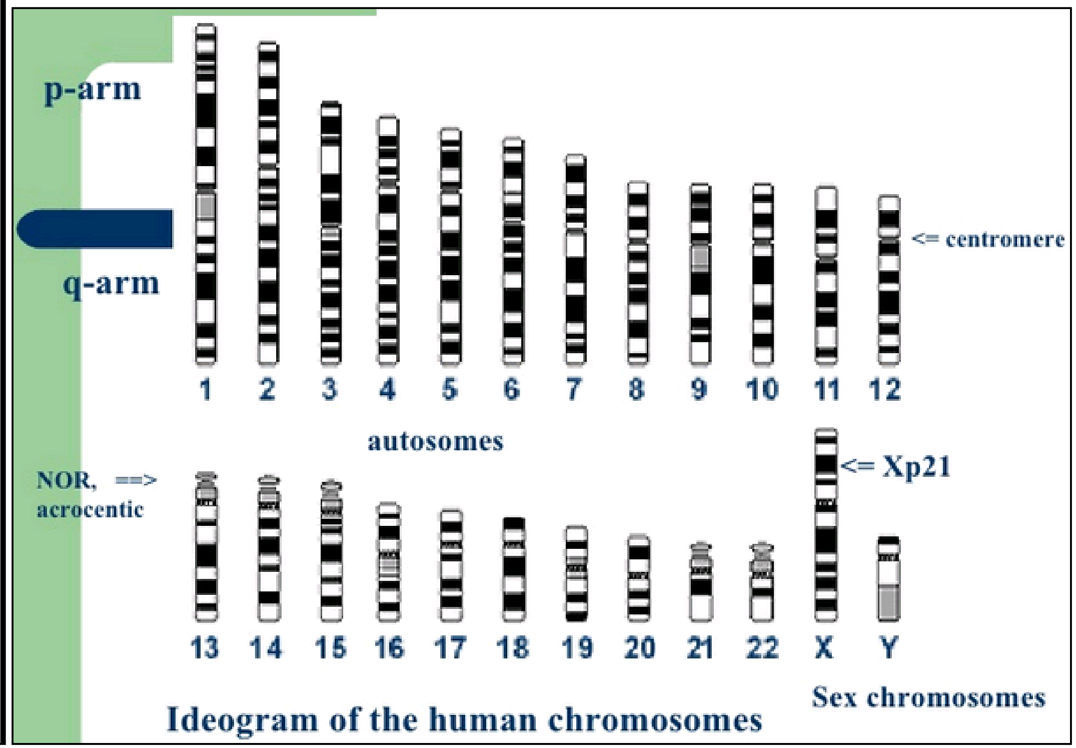


The bands are visible under a MICROSCOPE when chromosome is suitably stained. Each of the bands is numbered, beginning with 1 for the band nearest the centromere. Sub-bands and sub-sub-bands are visible at higher resolution.

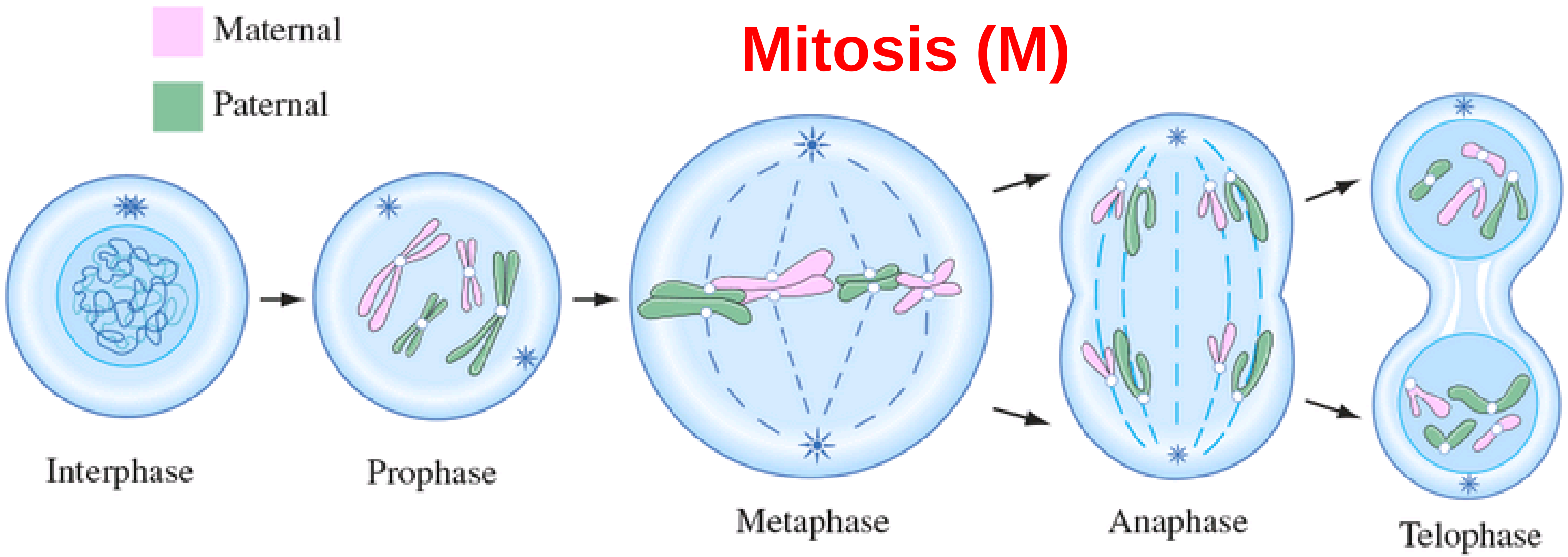
Human Genome: karyotype and idiogram

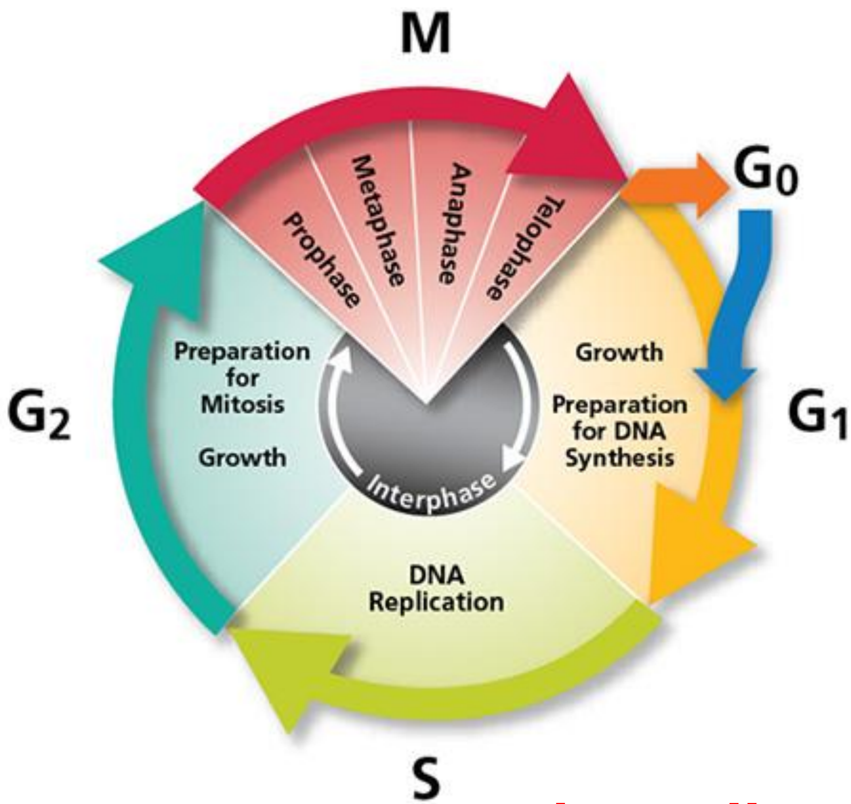


A diagrammatic representation of chromosome morphology characteristic of a species or a population is known as Idiogram



Mitosis (M)





The Cell Cycle

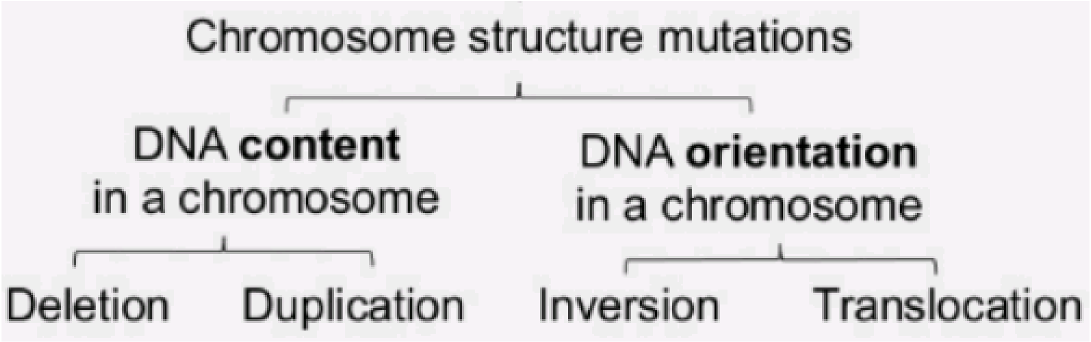
Chromosomal Mutations

- Any change in the **structure** or **number** of chromosomes

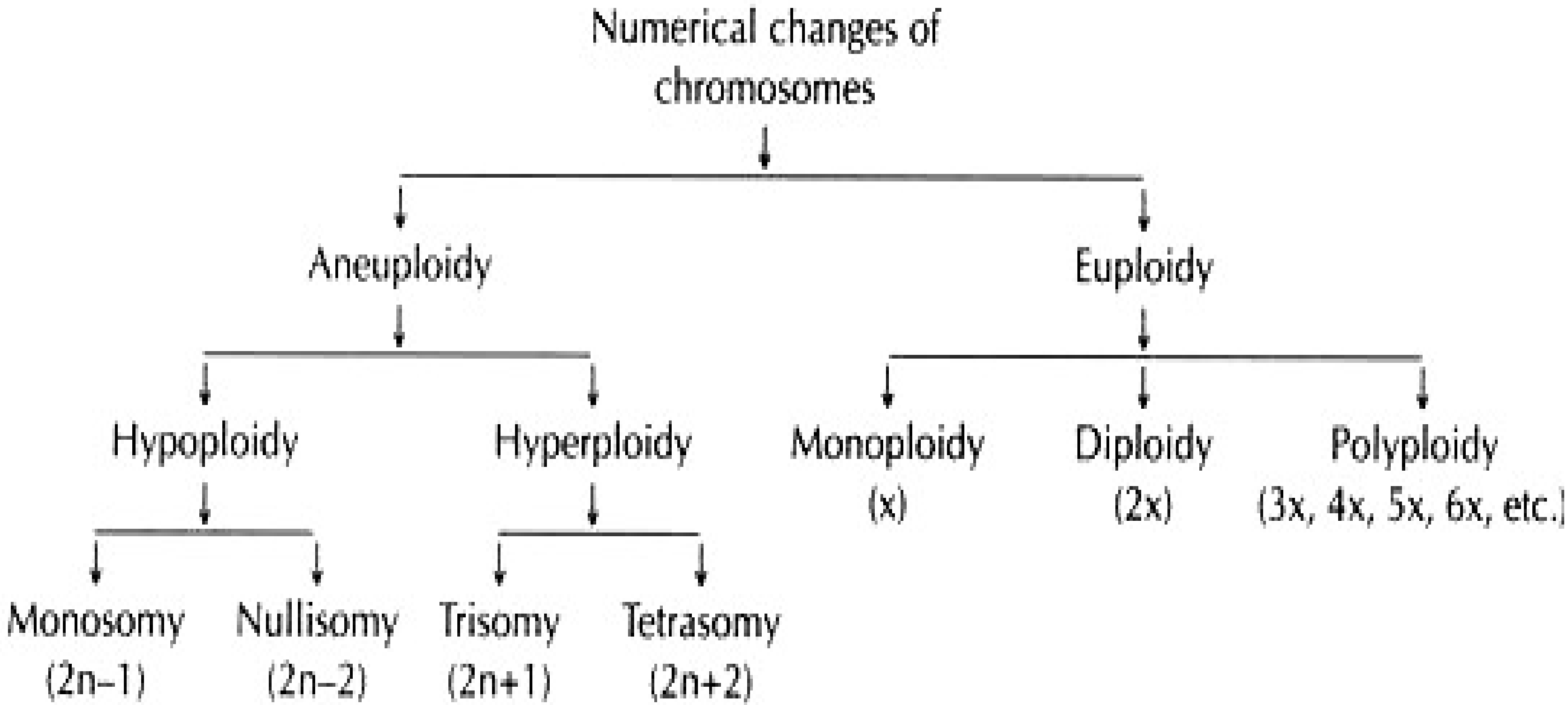
- Large scale: Affect *many* genes

Chromosomal Mutation

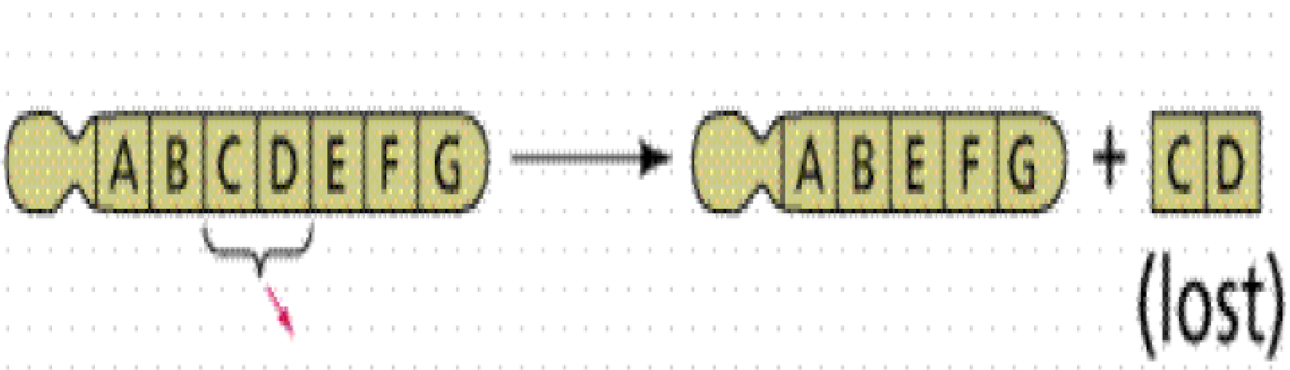
1. Chromosomal Mutation due to change in structure



2. Chromosomal Mutation due to change in number



Chromosomal Deletion



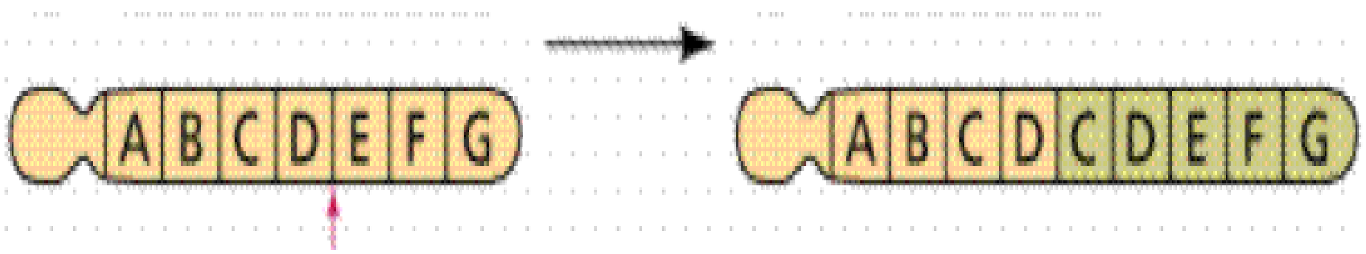
One or more genes are removed

Causes:

Wolf-Hirschhorn syndrome (severe mental retardation)

cri du chat syndrome (mewing sounds, mental retardation)

Chromosomal Duplication



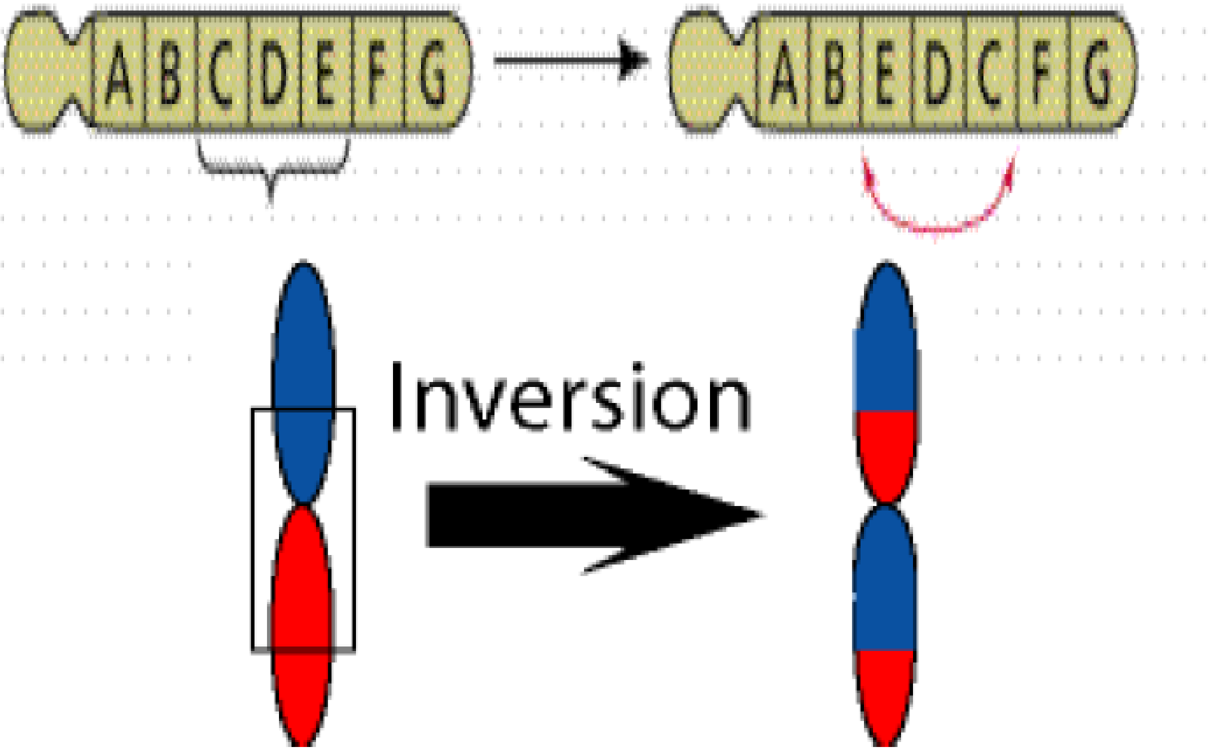
A segment of genes is copied twice and added to the chromosome

Causes:

Charcot–Marie–Tooth disease

(high arched foot, claw feet, confined to a wheelchair)

Chromosomal Inversion



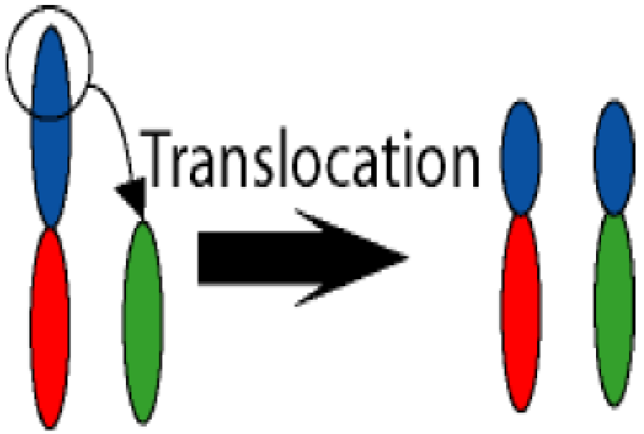
a segment of genes flip end-to-end on the chromosome

Causes:

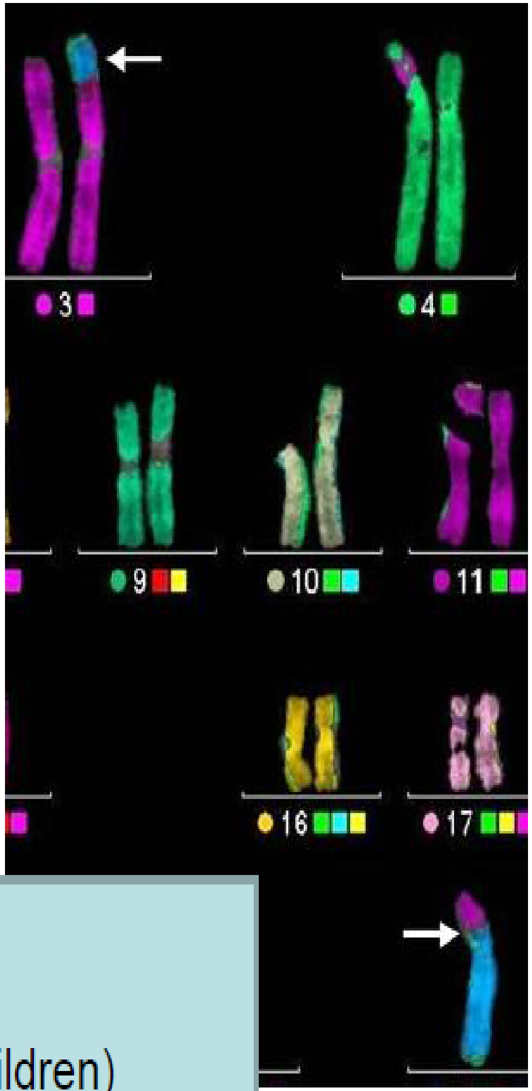
Four-Ring Syndrome

(cleft pallate, club feet, testes don't descend)

Chromosomal Translocation



Material is swapped with another chromosome



Causes:

Burkitt's Lymphoma

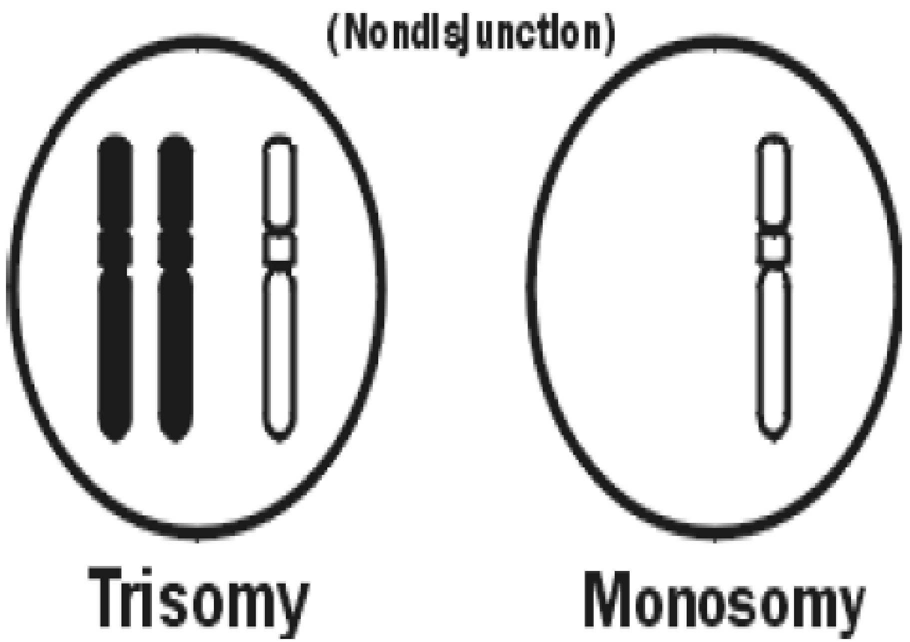
(cancer of the lymph nodes, in children)

- Chromosome numbers can vary in two main ways
  - Euploidy
    - Variation in the number of complete sets of chromosome
  - Aneuploidy
    - Variation in the number of particular chromosomes within a set

- Euploid variations occur occasionally in animals and frequently in plants
- Aneuploid variations, on the other hand, are regarded as abnormal conditions

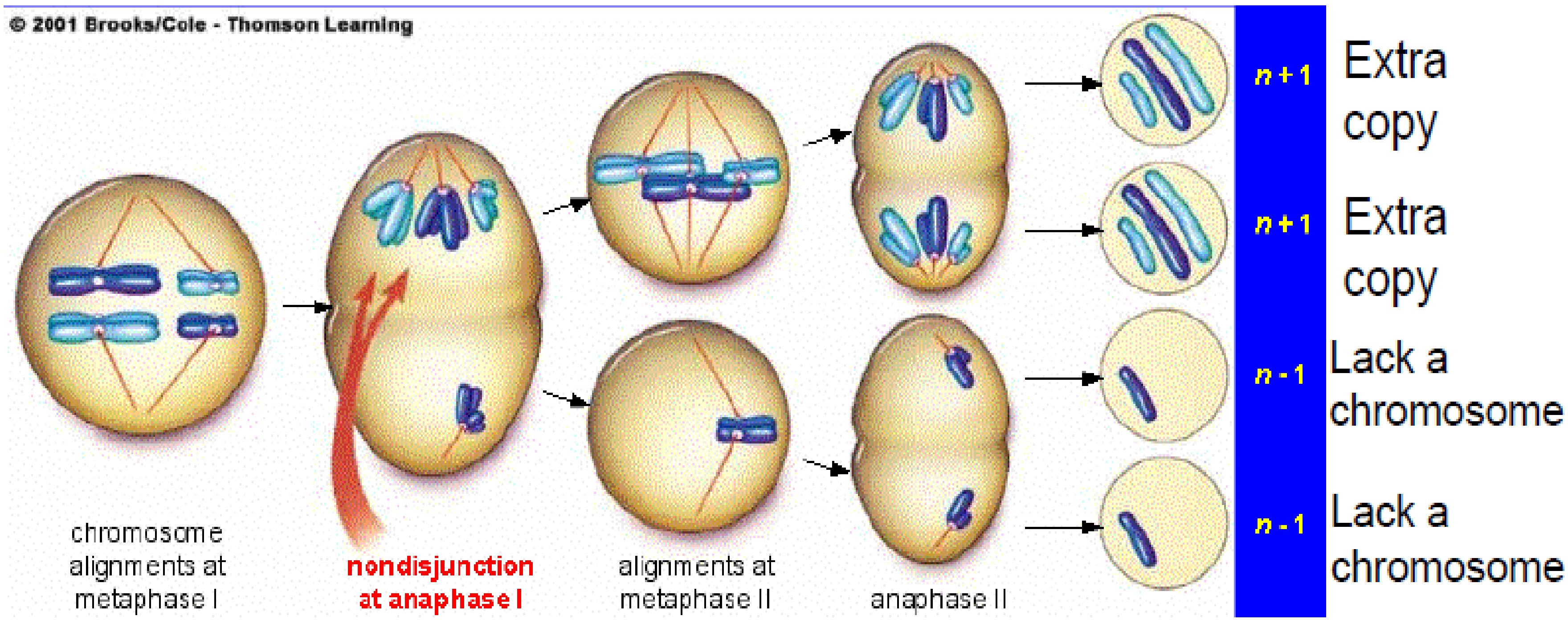
Nondisjunction

- Produces gametes (and therefore a baby) with one missing chromosome **or** one extra chromosome



Nondisjunction: Chromosomes FAIL TO SEPARATE during meiosis

These abnormal gametes are formed when a spindle fibre fails and one of the pair of homologous chromosomes fail to become separated



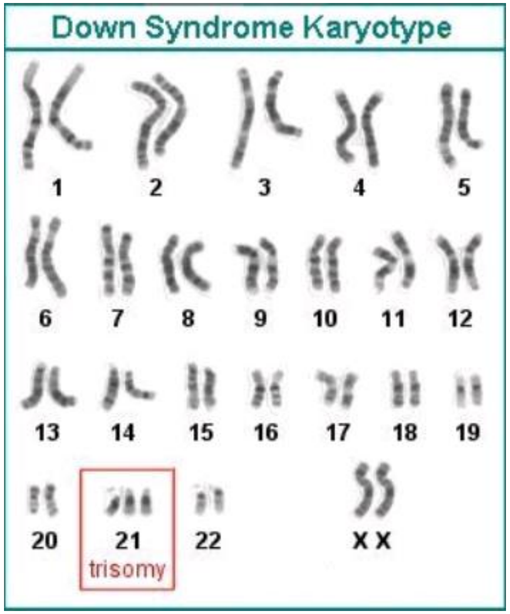
Chromosomal Mutations

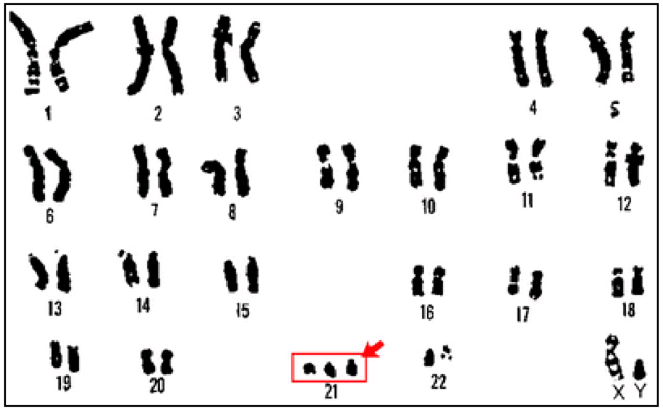
- Most chromosomal mutations are *lethal*
- *If* the fetus survives: Tend to cause wide-spread abnormalities
- *Example:* Down Syndrome

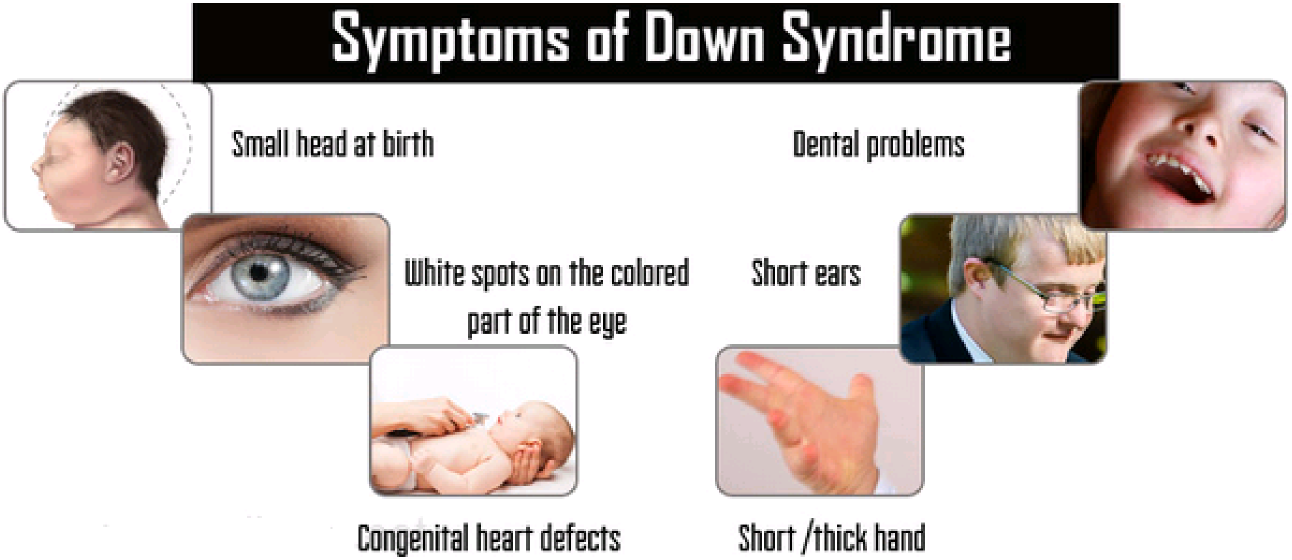
Down Syndrome

Cause: Nondisjunction of chromosome 21

=> Instead of two copies there are THREE copies of chromosome 21 = TRISOMY 21





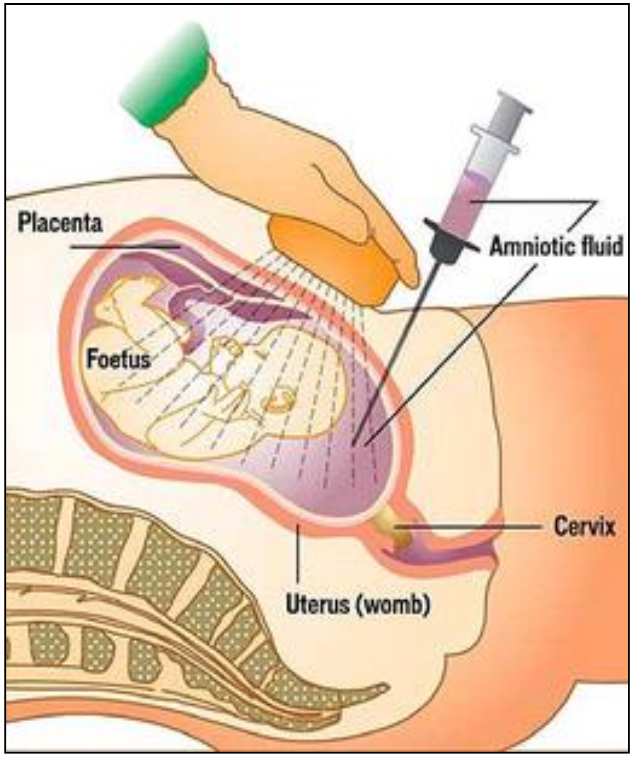


Affected individual is characterized by mental retardation and distinctive physical features

Down Syndrome affects 1 in every 800 babies

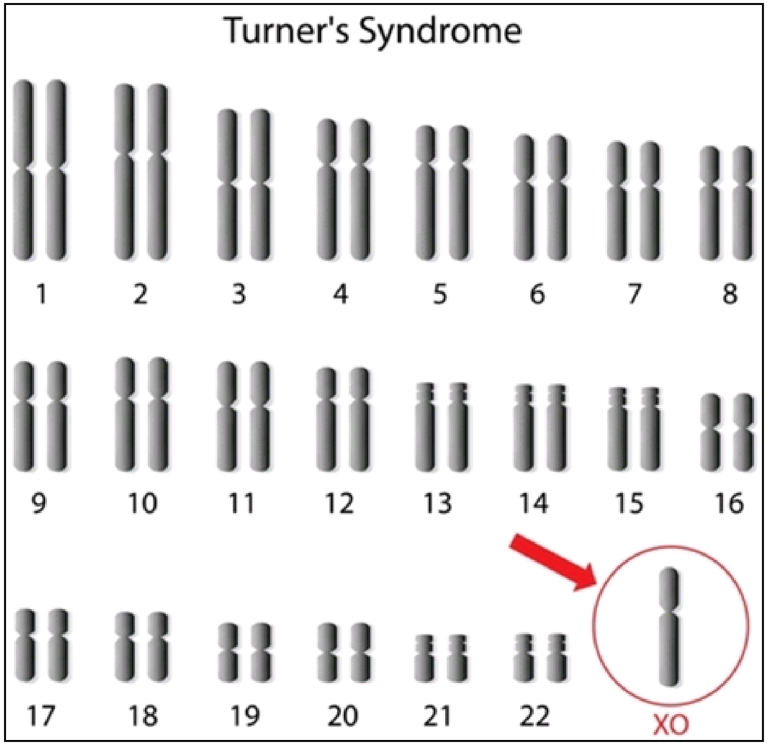
An abnormal egg (n=24) + normal sperm (n=23)
=> Abnormal zygote (n=47)

Egg mother cells of older (≥35) woman (80% due to maternal age tend to be more prone to non-disjunction at meiosis)



Amniocentesis is used to detect possible abnormalities in unborn children.

Turner’s Syndrome- Female Only

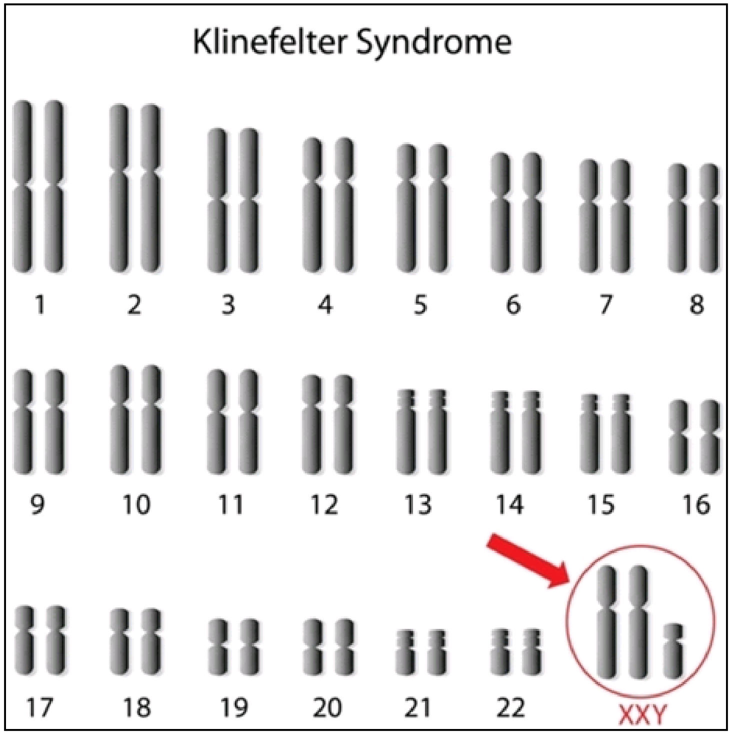


If a gamete which possesses no sex chromosomes meets and fuses with a normal X gamete, the zygote formed has the following chromosome complement - **2n = 44 + XO**

- The reason behind the absence of an X chromosome may be because of an error in the father's sperm or in the mother's egg. This results in every cell having only one X chromosome.
- In certain cases, an error occurs in cell division during initial stages of foetal development. This results in some cells having two copies of the X chromosome. Other cells contain only one copy of the X chromosome.
- Individuals are always female and short in stature
- Their ovaries do not develop so they are infertile and fail to develop secondary sexual characteristics e.g. breast development and menstruation.
- Happens 1:2500 live births

Webbed neck, unusual fingers, short stature, low neckline are all features of the condition. Heart, hearing and visual problems can also occur

Klinefelter's Syndrome- Male Only (47, XXY)

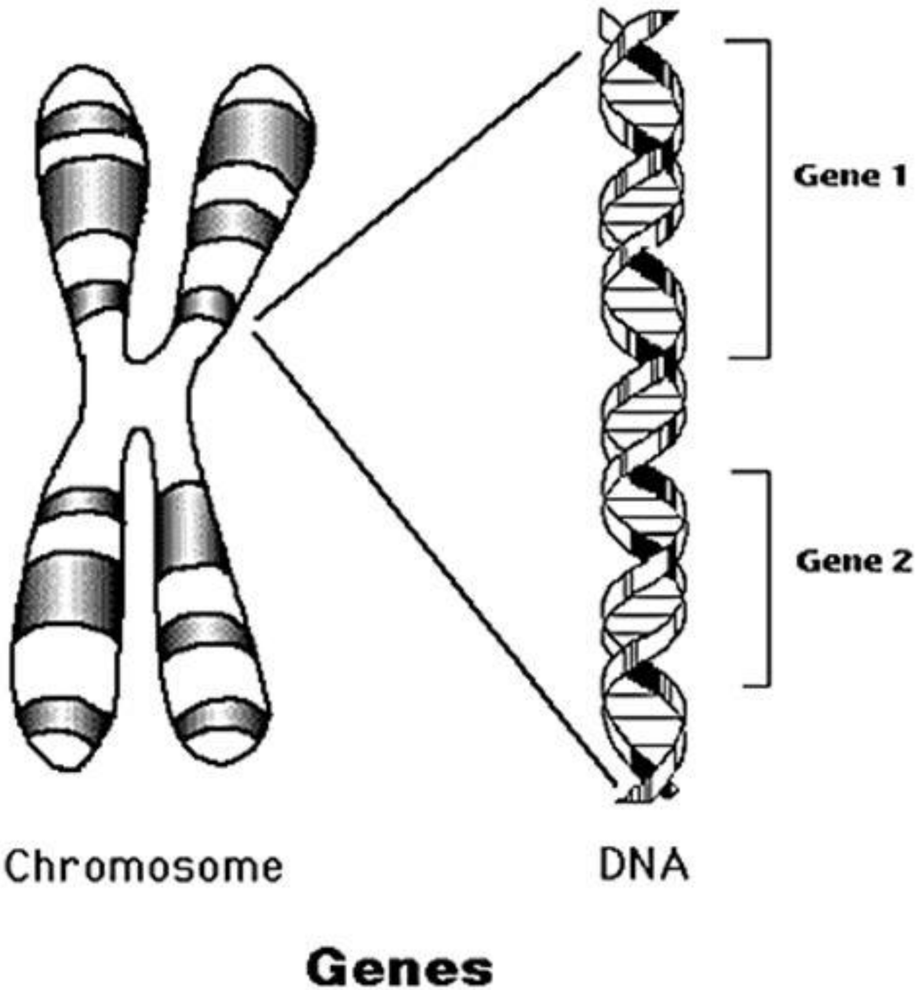


- Happens when:
  - An XX egg is fertilised by a normal Y sperm
  - OR an normal X egg is fertilised by an XY sperm
- **Resulting with chromosome complement 2n = 44 + XXY**
- Individuals are always male and possess male sex organs
- However they are infertile since their testes only develop to half the normal size and fail to produce sperm
- Testes produce low levels of testosterone so facial hair, deepening of voice are only weakly expressed. Some sufferers develop small breasts.
- Occurs in 1:1000 live male births

KEY POINT

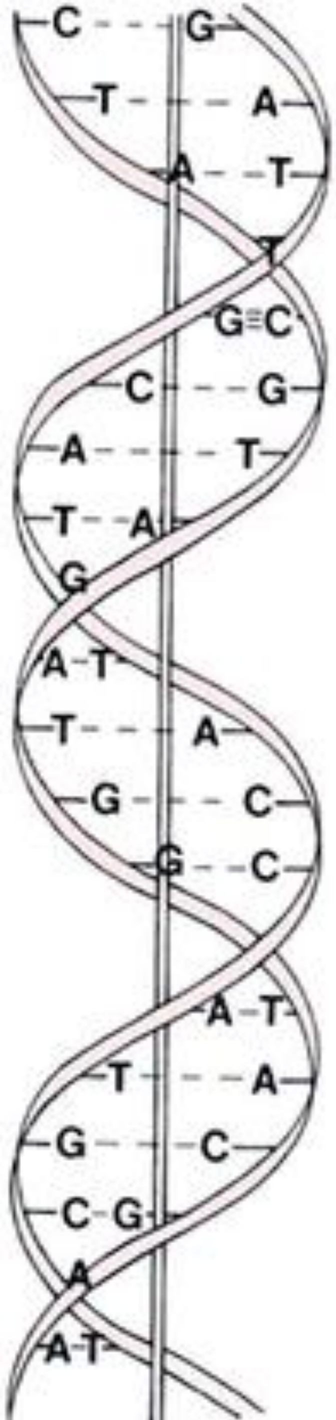
Too much or too little DNA is bad!

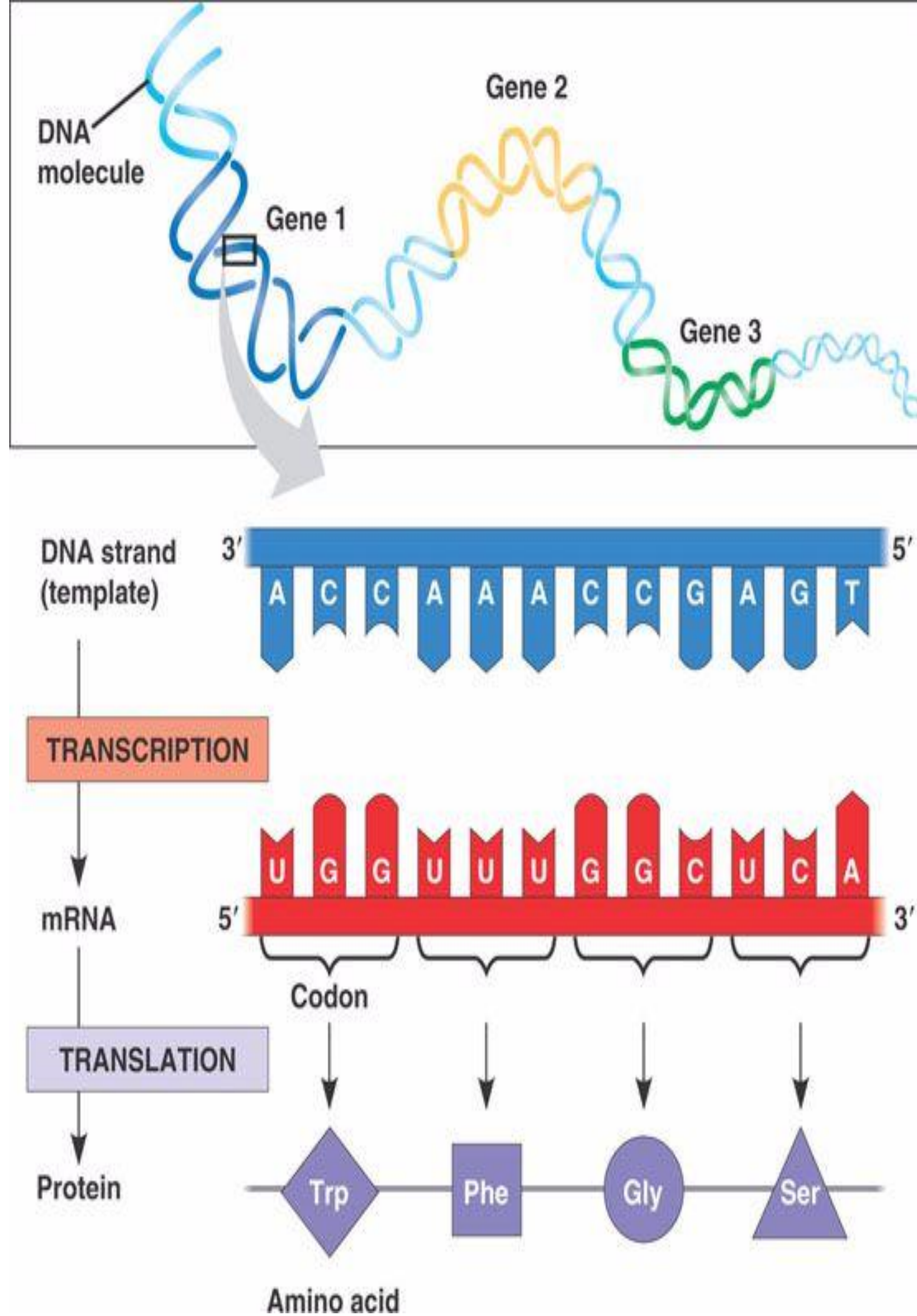
Types of mutations



Chromosomal mutation: affecting whole or a part of a chromosome

Gene mutation: changes to the bases in the DNA of one gene


C G
T A
A T
T
G C
C G
A T
T A
G
A T
T A
G C
G C
A T
T A
G C
C G
A
A T


DNA molecule
Gene 1
Gene 2
Gene 3
DNA strand (template)
3′
5′
A C C A A A C C G A G T
TRANSCRIPTION
U G G U U U G G C U C A
mRNA
5′
3′
Codon
TRANSLATION
Protein
Trp
Phe
Gly
Ser
Amino acid

A single chromosome contains thousands of genes, each encoding a protein.

TABLE 24–2 DNA, Gene, and Chromosome Content in Some Genomes

	Total DNA (bp)	Number of chromosomes*	Approximate number of genes
Escherichia coli K12 (bacterium)	4,639,675	1	4,435
Saccharomyces cerevisiae (yeast)	12,080,000	16†	5,860
Caenorhabditis elegans (nematode)	90,269,800	12‡	23,000
Arabidopsis thaliana (plant)	119,186,200	10	33,000
Drosophila melanogaster (fruit fly)	120,367,260	18	20,000
Oryza sativa (rice)	480,000,000	24	57,000
Mus musculus (mouse)	2,634,266,500	40	27,000
Homo sapiens (human)	3,070,128,600	46	29,000

GENETIC CODE TABLE:
Most genetic code tables designate the codons for amino acids as mRNA sequences

Second letter

First letter	U	C	A	G	Third letter
U	UUU Phe	UCU Ser	UAU Tyr	UGU Cys	U
U	UUC Phe	UCC Ser	UAC Tyr	UGC Cys	C
U	UUA Leu	UCA Ser	UAA STOP	UGA STOP	A
U	UUG Leu	UCG Ser	UAG STOP	UGG Trp	G
C	CUU Leu	CCU Pro	CAU His	CGU Arg	U
C	CUC Leu	CCC Pro	CAC His	CGC Arg	C
C	CUA Leu	CCA Pro	CAA Gln	CGA Arg	A
C	CUG Leu	CCG Pro	CAG Gln	CGG Arg	G
A	AUU Ile	ACU Thr	AAU Asn	AGU Ser	U
A	AUC Ile	ACC Thr	AAC Asn	AGC Ser	C
A	AUA Ile	ACA Thr	AAA Lys	AGA Arg	A
A	AUG Met	ACG Thr	AAG Lys	AGG Arg	G
G	GUU Val	GCU Ala	GAU Asp	GGT Gly	U
G	GUC Val	GCC Ala	GAC Asp	GGC Gly	C
G	GUA Val	GCA Ala	GAA Glu	GGA Gly	A
G	GUG Val	GCG Ala	GAG Glu	GGG Gly	G

Key:

Ala = Alanine (**A**)
Arg = Arginine (**R**)
Asn = Asparagine (**N**)
Asp = Aspartate (**D**)
Cys = Cysteine (**C**)
Gln = Glutamine (**Q**)
Glu = Glutamate (**E**)
Gly = Glycine (**G**)
His = Histidine (**H**)
Ile = Isoleucine (**I**)
Leu = Leucine (**L**)
Lys = Lysine (**K**)
Met = Methionine (**M**)
Phe = Phenylalanine (**F**)
Pro = Proline (**P**)
Ser = Serine (**S**)
Thr = Threonine (**T**)
Trp = Tryptophan (**W**)
Tyr = Tyrosine (**Y**)
Val = Valine (**V**)

Type of code	Number of permutations
Singlet	$4^1 = 4$
Doublet	$4^2 = 16$
Triplet	$4^3 = 64$
Quadruplet	$4^4 = 256$
Pentuplet	$4^5 = 1024$

Only the triplet code really looks feasible

THE GENETIC CODE

- Each codon consists of three bases (triplet). There are 64 codons. They are all written in the 5' to 3' direction.
- 61 codons code for amino acids. The other three (UAA, UGA, UAG) are stop codons (or nonsense codons) that terminate translation.
- There is one start codon (initiation codon), AUG, coding for methionine. Protein synthesis begins with methionine (Met) in eukaryotes, and formylmethionine (fmet) in prokaryotes.
- The code is unambiguous. Each codon specifies no more than one amino acid.
- The code is degenerate. More than one codon can specify a single amino acid.
- All amino acids, except Met and tryptophan (Trp), have more than one codon.
- For those amino acids having more than one codon, the first two bases in the codon are usually the same. The base in the third position often varies.
- The code is almost universal (the same in all organisms). Some minor exceptions to this occur in mitochondria and some organisms.
- The code is commaless (contiguous). There are no spacers or "commas" between codons on an mRNA.

Gene Mutations

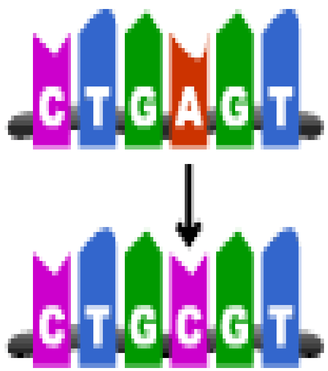
- ***Small scale:*** one gene is affected

- Any change to the DNA sequence of a gene:

  Nucleotides/Bases may be **added**, **missing**, or **changed**

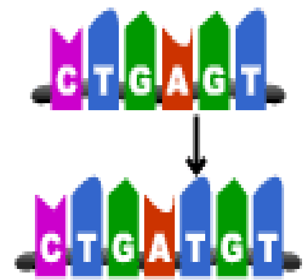
Gene Mutations: 2 Types

Point Mutation

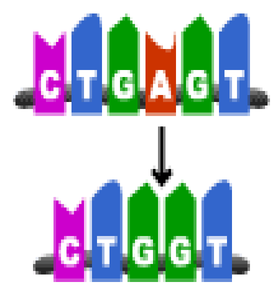


Point mutation

Frameshift Mutation



Insertion



Deletion

Point Mutation

- One base (A, T, C, or G) is **substituted for another**

Base pair substitutions- two types

a) **Transitions**
   - Convert a purine-pyrimidine to the other purine-pyrimidine.
   - 4 types of transitions; A $\leftrightarrow$ G and T $\leftrightarrow$ C

b) **Transversions**
   - Convert a purine-pyrimidine to a pyrimidine-purine.
   - 8 types of transversions; A $\leftrightarrow$ T, G $\leftrightarrow$ C, A $\leftrightarrow$ C, and G $\leftrightarrow$ T

- Case: ***Sickle-cell anemia***

- 3 Possible Consequences:
  - **nonsense mutations:** code for a stop, which can translate the protein
  - **missense mutations:** code for a different amino acid
  - **silent mutations:** code for the same amino acid

Frameshift Mutation

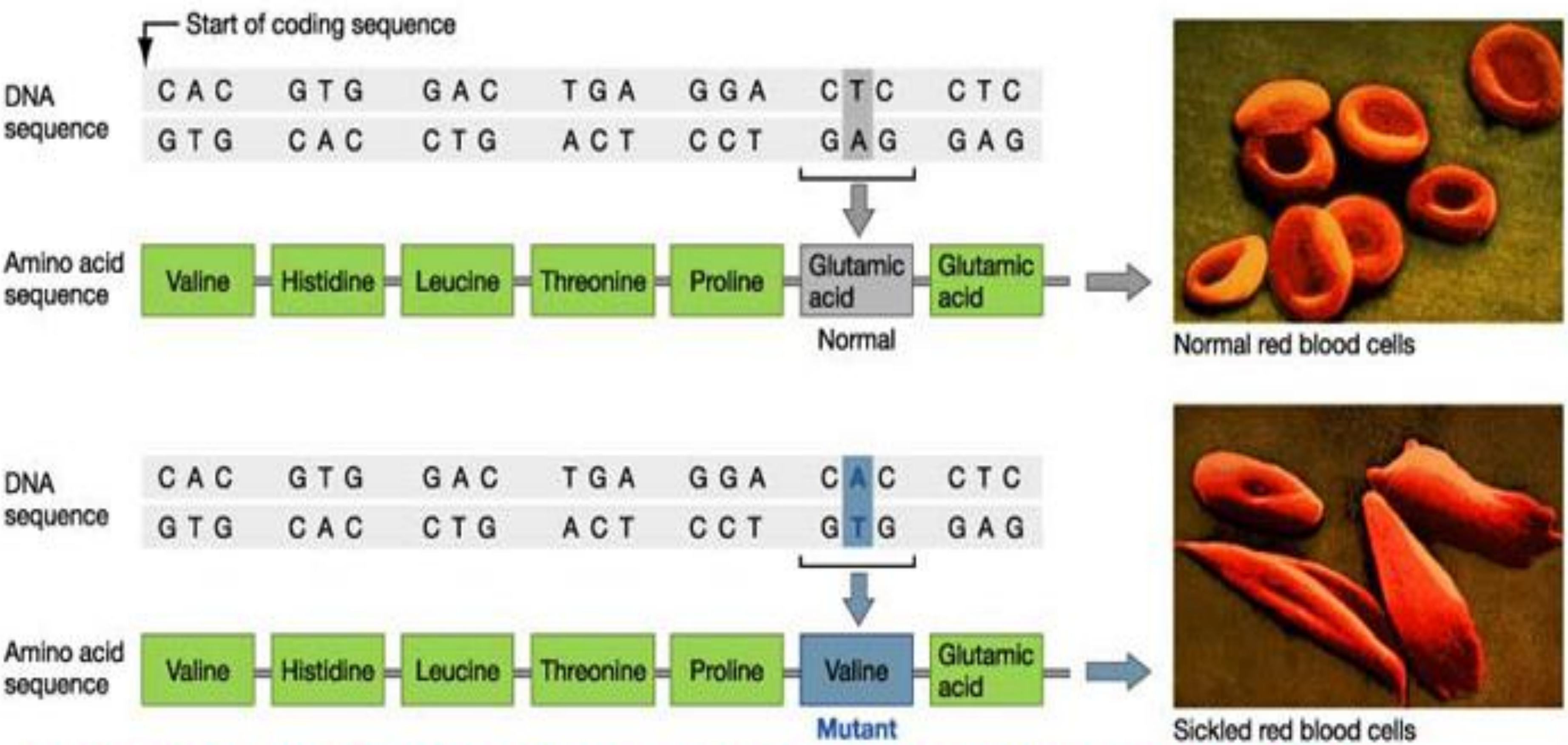
- One or more bases (A, T, C, or G) are added or deleted
- **Case: *Cystic Fibrosis***
- Caused by: Base pair deletions and insertions
  - **Insertion**: adding a base
  - **Deletion**: removing a base

Gene Mutations

- **KEY IDEA:** A mutated ***gene*** will make a mutated ***protein***

- **Mutant proteins are trouble!**
  - They do not ***go*** where they are supposed to go
  - They do not ***do*** what they are supposed to d

sickle-cell anemia



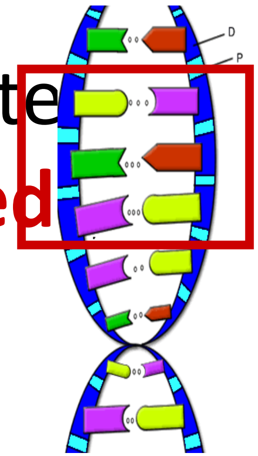
The change in amino acid sequence causes hemoglobin molecules to crystallize when oxygen levels in the blood are low. As a result, red blood cells sickle and get stuck in small blood vessels.

Example: Cystic Fibrosis (CF)

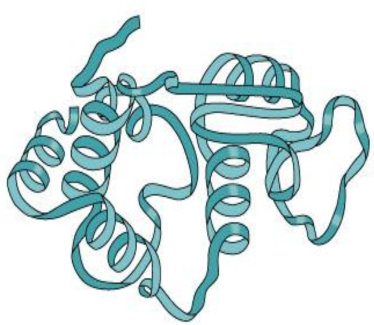
- ***What is it?***
  - **Autosomal, recessive disorder**
- ***Who gets it?***
  - **Anyone; most common in Caucasians**
- ***Prevalence***
  - **1 in ~3,000 Americans has CF**
  - **1 in 23 white Americans carries the mutant allele!**
- ***Symptoms***
  - **Thick mucus in the lungs and digestive track**
  - **Constant lung infections and impaired digestion**

Cause of Cystic Fibrosis (CF)

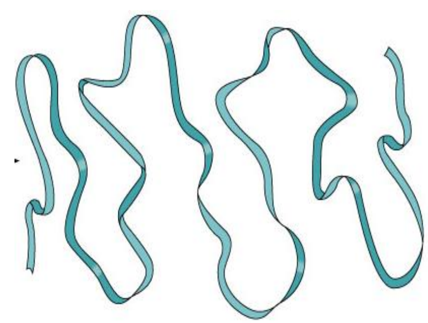
- The “CFTR” gene is mutate
  - 3 base pairs are **deleted**



- Mutant protein is missing an amino acid and cannot fold correctly



vs



KEY POINT

Mutation of a gene = Mutant protein

Dysfunctional proteins cause the symptoms of the disorder

Process of Mutations: Mutagenesis

a) **Spontaneous: mainly during DNA Replication**

- **1 in 10^9 (a billion) replicated base pairs or 1 in 10^6 (a million) replicated genes. Mistakes occur during DNA Replication just before cell division. This is natural error rate of DNA polymerase.**
- **Many spontaneous errors are repaired.**

b) **Induced mutations: Caused by MUTAGENS**

- **Mutagens increase mistakes 10^{-5} (100 thousand) or 10^{-3} (a thousand) per replicated gene**

- **Physical mutagen: Ex: radiation from UV rays, X-rays or extreme heat**
- **Chemical mutagen: molecules that misplace base pairs or disrupt the helical shape of DNA.**

Physical Mutagen: X-rays and Gamma Rays Cause Breaks in DNA

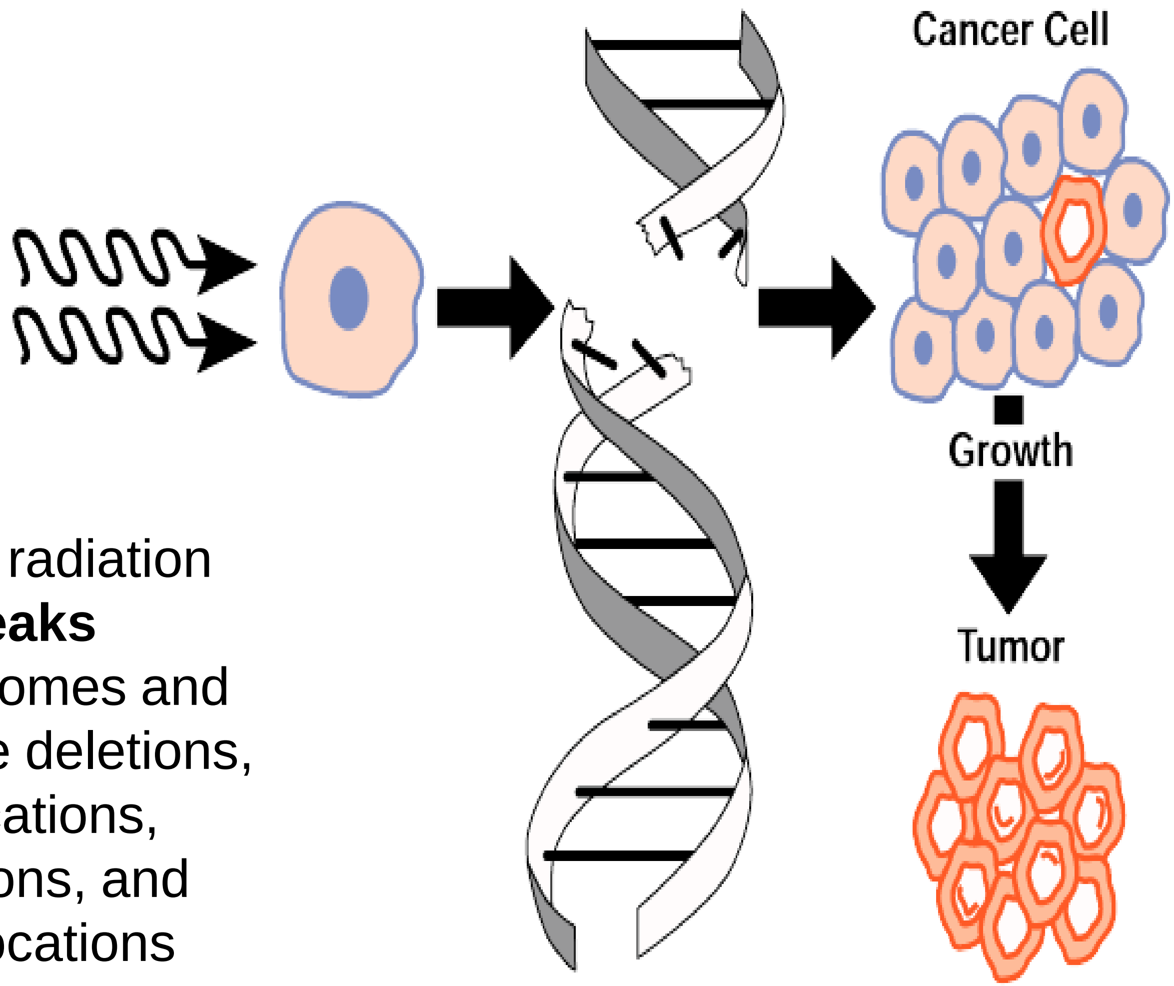
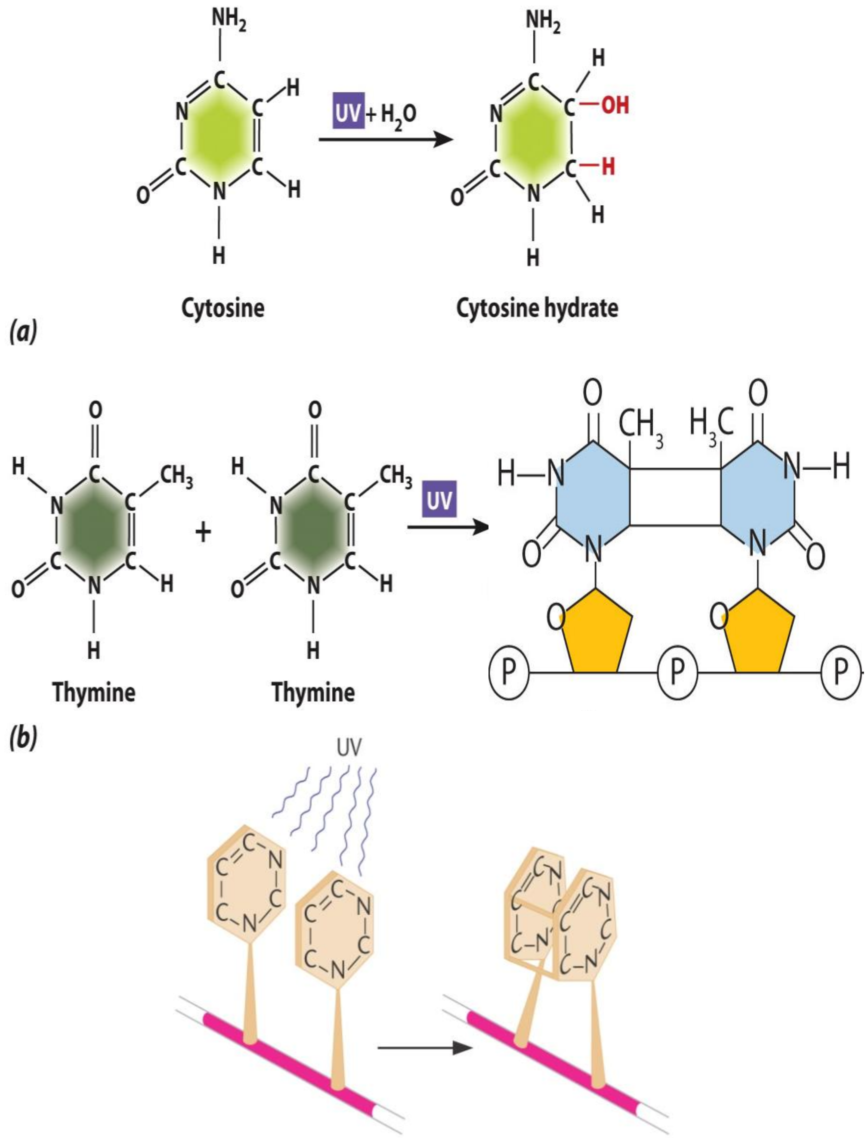


Figure 1. Development of cancer from mutation produced by ionizing radiation.

Ionizing radiation **breaks** chromosomes and can cause deletions, duplications, inversions, and translocations

Physical Mutagen: Mutagenesis by Ultraviolet Irradiation



Dimer formed between adjacent thymidine residues along a DNA strand

- Hydrolysis of cytosine to a hydrate may cause **mis-pairing** during replication
- Cross-linking of adjacent thymine forms **thymidine dimers**, which block DNA replication and activate DNA repair mechanisms.

Chemical Mutagens

Alkylating agents

$Cl—CH_2—CH_2—S—CH_2—CH_2—Cl$

Di-(2-chloroethyl) sulfide

(Mustard gas)

$CH_3—CH_2—O—SO_2—CH_3$

Ethyl methane sulfonate

(EMS)

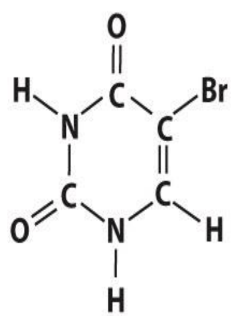
$CH_3—CH_2—O—SO_2—CH_2—CH_3$

Ethyl ethane sulfonate

(EES)

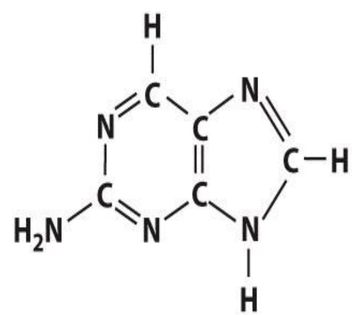
(a)

Base analogs



5-Bromouracil

(5-BU)

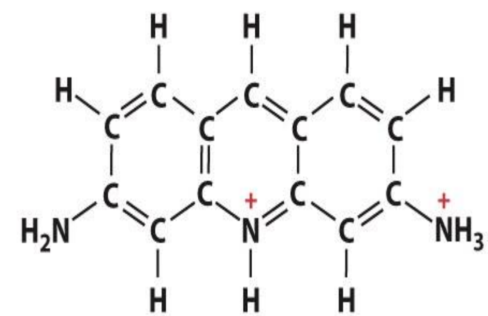


2-Aminopurine

(2-AP)

(b)

Acridines



2,8-Diamino acridine

(Proflavin)

(c)

Deaminating agent

HNO_2

Nitrous acid

(d)

Hydroxylating agent

NH_2OH

Hydroxylamine

(e)

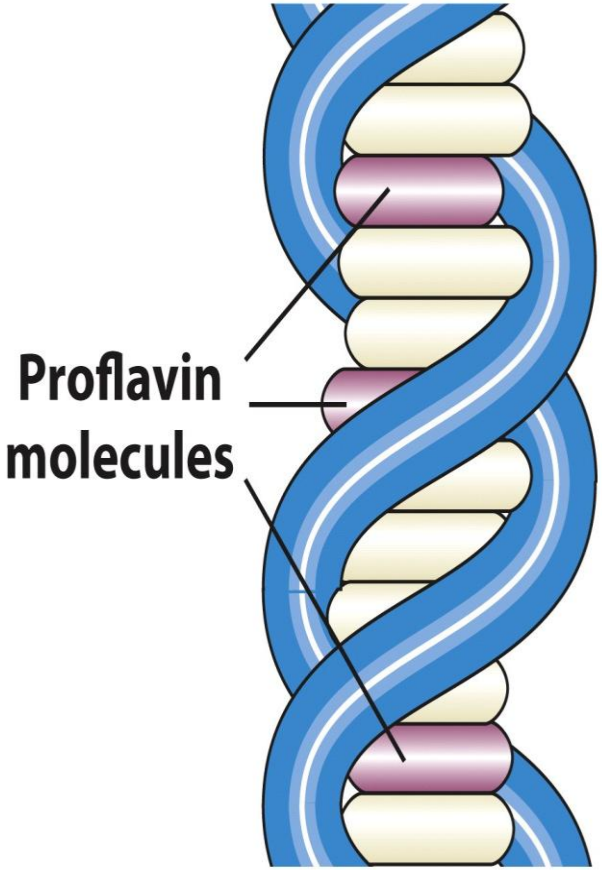
Intercalation of an Acridine Dye Causes Frameshift Mutations

--(+) charges molecules

--Incorporated into DNA

--DNA is more rigid

--Change conformation (non-bending)



What means GMO?

Genetically Modified Organisms

- Recombinant DNA technology goes beyond traditional cross breeding techniques, **making possible an exchange of traits from different species, even among plants, animals and bacteria.**

- GMO are a result of technology that has altered the DNA of living organisms (animals, plants or bacteria)

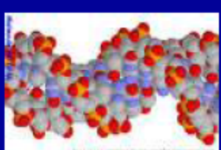
- Other terms that mean the same thing:
  - Genetically engineered
  - Transgenic
  - Recombinant DNA (rDNA) technology

Genetic engineered
Transgenic
Recombinant DNA

Biotechnology, defined broadly, is the engineering of organisms for useful purposes.

Often, biotechnology involves the creation of hybrid genes and their introduction into organisms in which some or all of the gene is not normally present.

Recombinant DNA Technology



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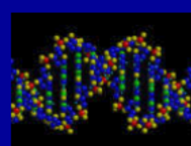


How to Mess with DNA

for Fun and Profit

What the heck is Recombinant DNA?

Recombinant DNA is what you get when you combine DNA from two different sources.

For example:

Mouse + Human DNA

Human + Bacterial DNA

Viral + Bacterial DNA

Human + (other) Human DNA

Why Make Recombinant DNA?

Recombinant DNA Technology May Allow Us To:

- *Cure or treat disease*
- *Genetically modify our foods to increase flavor, yield, nutritional value or shelf-life*
- *Better understand human genetics*
- *Clone cells or organs*

Molecular Biology's Best Friends: *Bacteria*

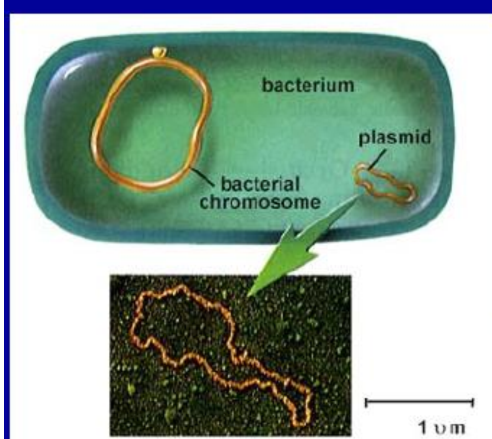
Why use bacteria?

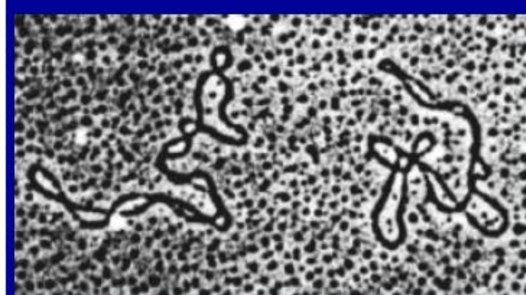
- They're relatively ***simple*** organisms.
- They reproduce ***very quickly*** and ***asexually*** (this means that the "daughter" cells will contain the exact same DNA as the "parent" cell).
- It's pretty easy to get DNA back into the bacteria after you've changed it.
- We can mess around with their DNA and kill a lot of them during our experiments and nobody gets mad. ;-)

Few vocabulary →

Plasmids

Small, circular pieces of "extra" DNA found in bacteria.





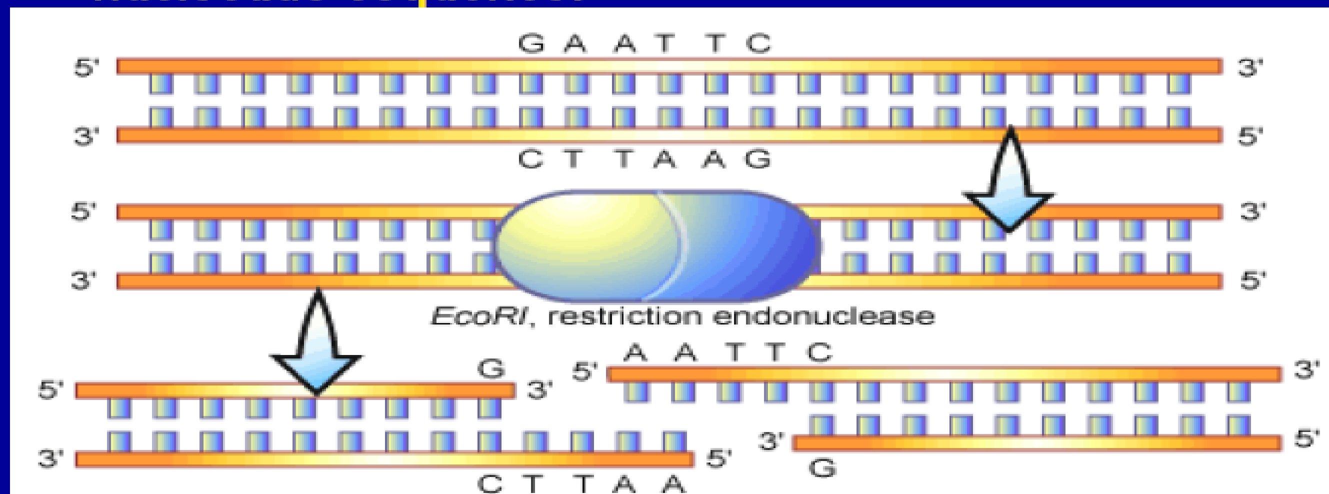
Plasmids often carry antibiotic resistance.

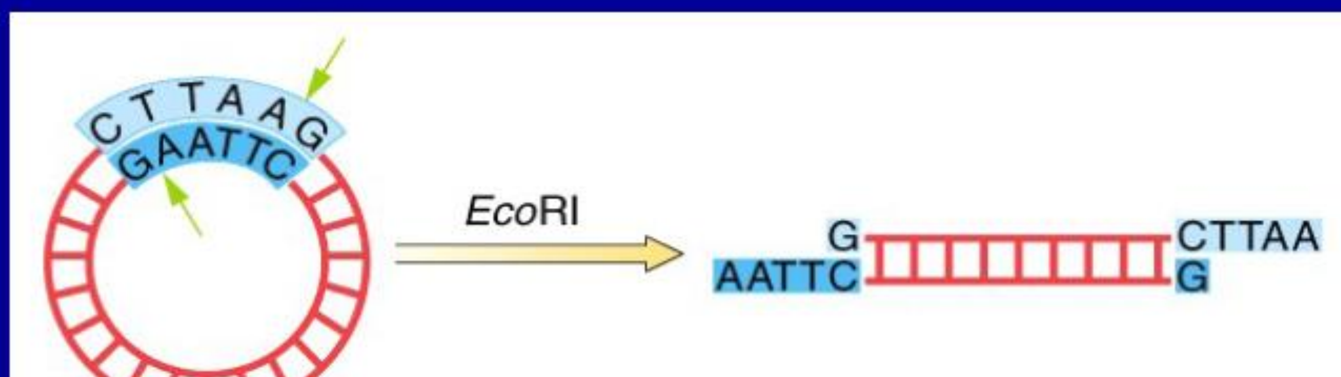
Restriction Enzymes: Molecular Scissors

- Any piece of DNA cut with a certain restriction enzyme will “stick” to any other piece cut with that same RE, even if they come from different sources.

A restriction enzyme (RE) is a specialized protein that cuts DNA in a *very specific* place.

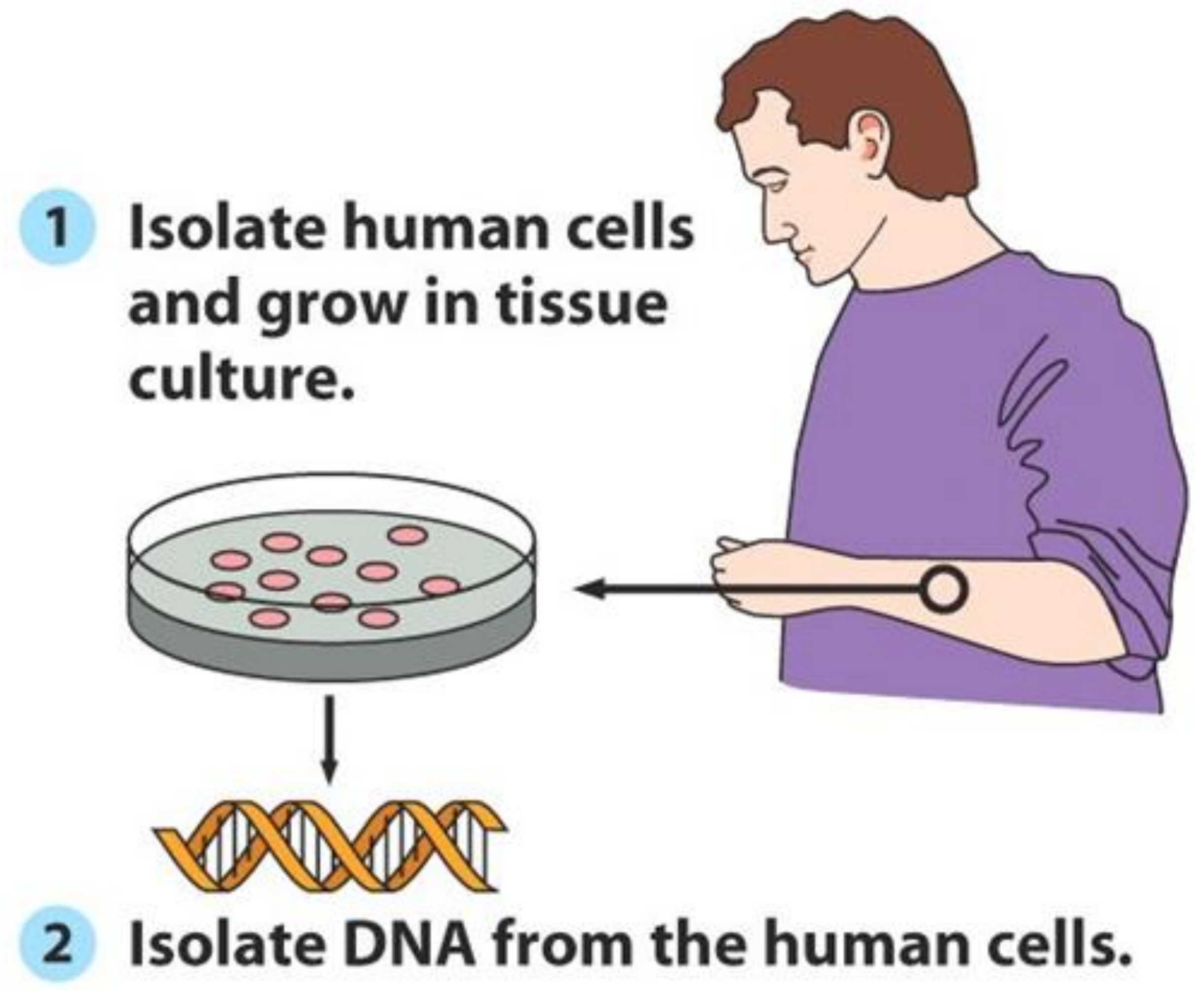
- **Different REs cut at different places along the nucleotide sequence.**

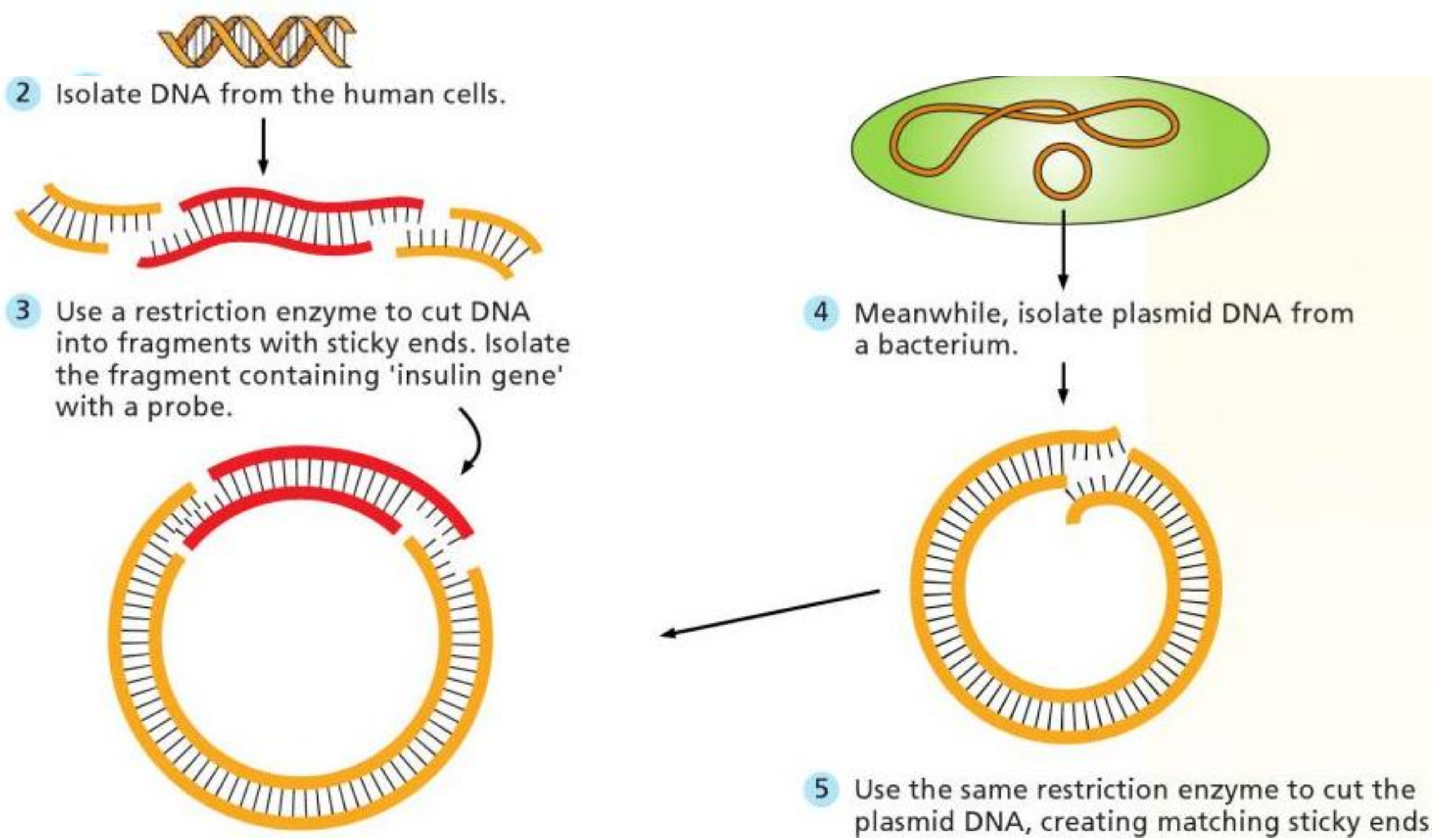




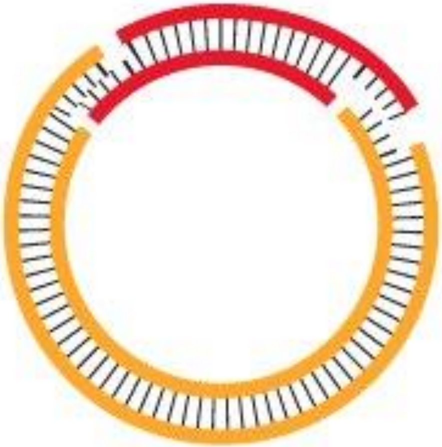
Bacterial species/strain	Enzyme name	Recognition sequences and cleavage sites
Bacillus amyloliquefaciens H	*Bam* H1	GGATCC CCTAGG
Escherichia coli Ry13	*Eco* R1	GAATTC CTTAAG
Providencia stuartii 164	*Pst* 1	CTGCAG GACGTC
Serratia marcescens SB	*Sma* H1	CCCGGG GGGCCC
Rhodopseudomonas sphaeroides	*Rsa* 1	GTAC CATG

CASE STUDY: Human Insulin (Humulin) Production by Bacteria





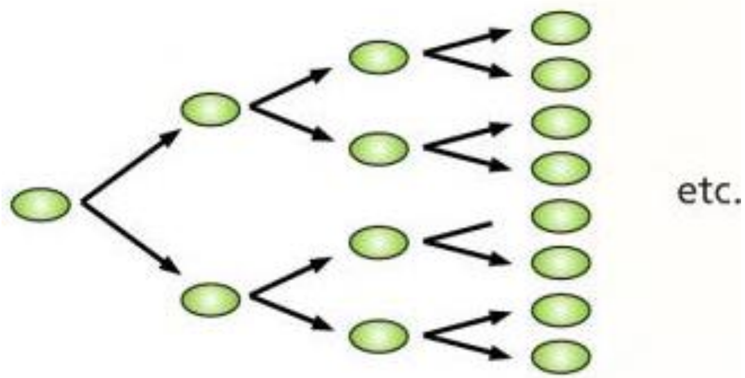
6) join the plasmid and human fragment



Mix the recombinant plasmid with bacteria.

7 Allow new bacteria to incorporate the recombinant plasmid into the bacterial cell, then screen bacteria to find the ones that have incorporated the human gene for insulin.

One cell with the recombinant plasmid



8 Grow trillions of new insulin-producing bacteria.

The final steps are to collect the bacteria, break open the cells, and purify the insulin protein expressed from the recombinant human insulin gene.

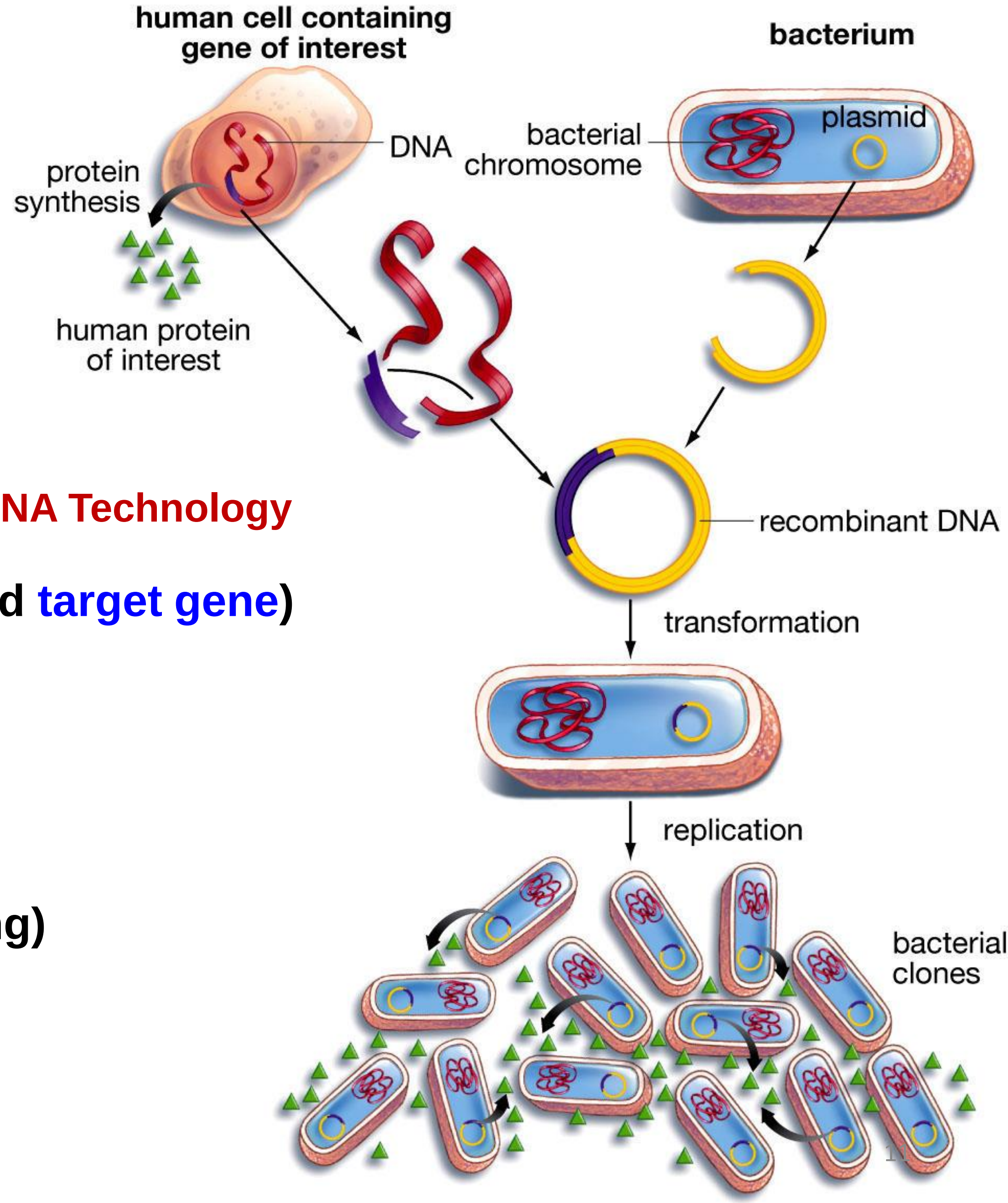
Now your E. coli will use its new DNA to make human insulin!

Because they reproduce so quickly, you'll soon have thousands, millions, or ***billions*** of human insulin making machines.

By filtering out the bacteria after they've made insulin, you've got clean human insulin that can be packaged and given to diabetic patients.

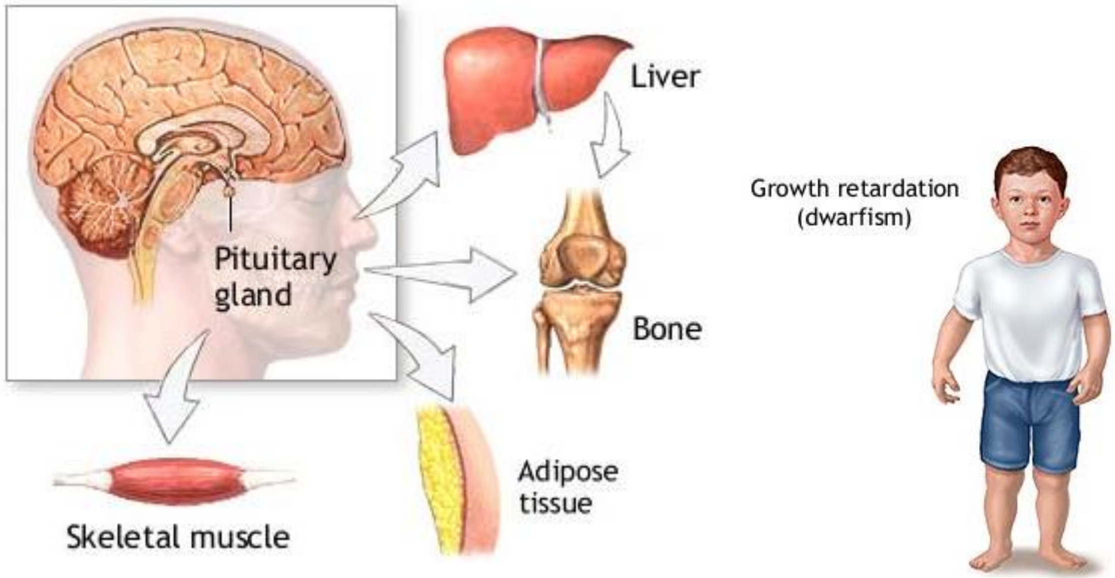
YAY!

Overview: Route to the Production by Bacteria of Human Insulin



Six steps of Recombinant DNA Technology

1. Isolating (vector and target gene)
2. Cutting (Cleavage)
3. Joining (Ligation)
4. Transforming
5. Cloning
6. Selecting (Screening)



- **Insulin**
  - **Hormone required to properly process sugars and fats**
  - **Treat diabetes**
  - **Now easily produced by bacteria**

- **Growth hormone deficiency**
  - **Faulty pituitary and regulation**
  - **Had to rely on cadaver source**
  - **Now easily produced by bacteria**

SOME PROTEIN PRODUCTS OF RECOMBINANT DNA TECHNOLOGY

Product	Made In	Use
Human insulin	*E. coli*	Treatment for diabetes
Human growth hormone (GH)	*E. coli*	Treatment for growth defects
Epidermal growth factor (EGF)	*E. coli*	Treatment for burns, ulcers
Interleukin-2 (IL-2)	*E. coli*	Possible treatment for cancer
Bovine growth hormone (BGH)	*E. coli*	Improving weight gain in cattle
Cellulase	*E. coli*	Breaking down cellulose for animal feeds
Taxol	*E. coli*	Treatment for ovarian cancer
Interferons (alpha and gamma)	*S. cerevisiae; E. coli*	Possible treatment for cancer and viral infections
Hepatitis B vaccine	*S. cerevisiae*	Prevention of viral hepatitis
Erythropoietin (EPO)	Mammalian cells	Treatment for anemia
Factor VIII	Mammalian cells	Treatment for hemophilia
Tissue plasminogen activator (TPA)	Mammalian cells	Treatment for heart attacks

Use recombinant cells to mass produce proteins

- **Bacteria**
- **Yeast**
- **Mammalian**

GMO: What is it?

US Crops	Main food for US
– Corn*	Cornstarch, corn syrup, corn oil
– Soy*	Soymilk, tofu, soy lecithin
– Canola	Canola oil
– Sugar beets	Sugar
– Cotton	Cottonseed oil, tampons
– Squash	Zucchini, crooked neck
– HI Papaya	Papaya from Hawaii

* Main ingredient of US raised cows, pigs & chickens

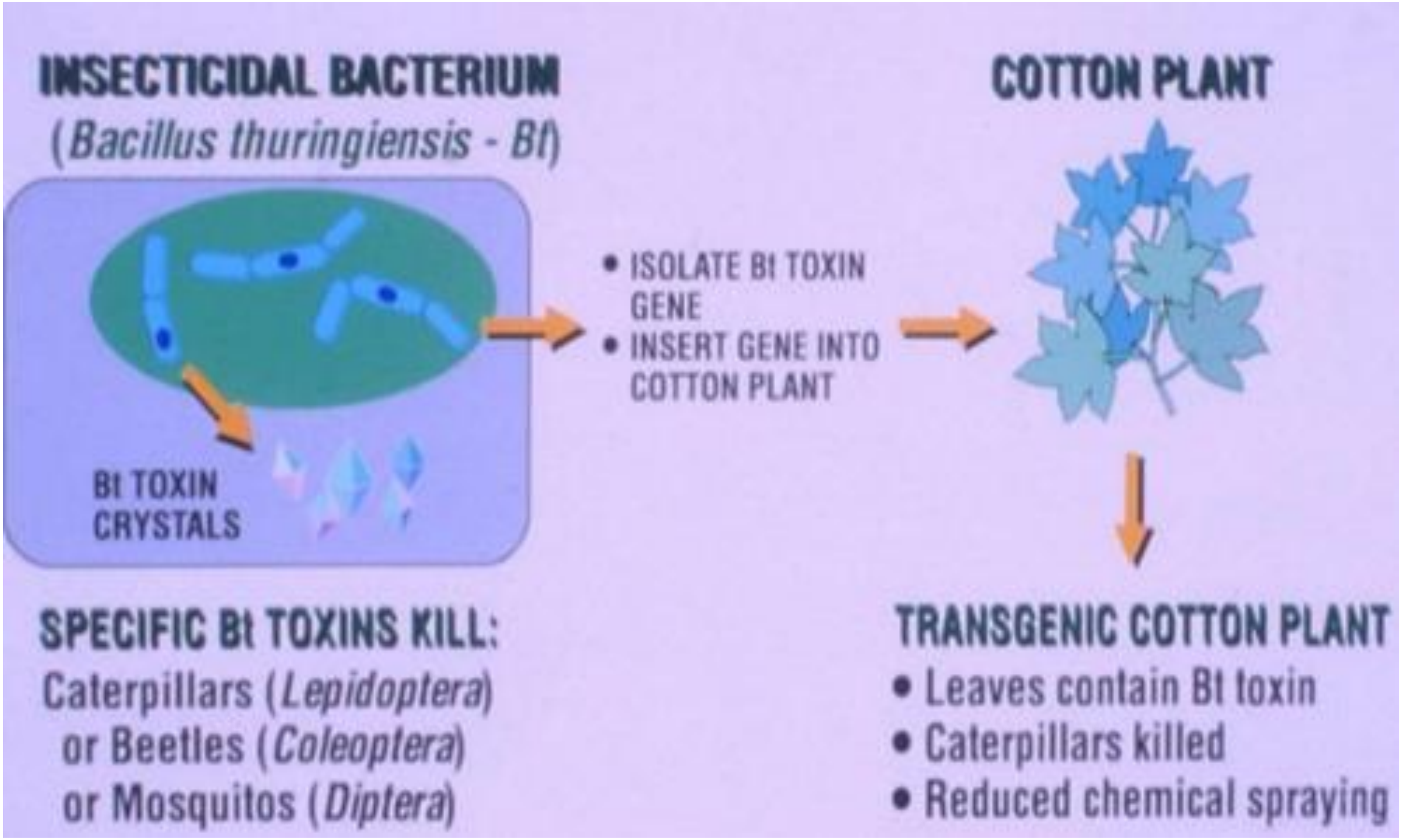
80% of what you buy in the grocery store contains GMOs

Table 19.4

Genetically Modified Crops

Altered Plant	Effect
Rice with beta carotene and extra iron	Added nutritional value
Canola with high-laurate oil	Can be grown domestically; less costly than importing palm and coconut oils
Delayed ripening tomato	Extended shelf life
Herbicide-resistant cotton	Herbicide kills weeds without harming crop
Minipeppers	Improved flavor, fewer seeds
Bananas resistant to fungal infection	Extended shelf life
Delayed-ripening bananas and pineapples	Extended shelf life
Elongated sweet pepper	Improved flavor, easier to slice
Altered cotton fiber	"Plasticized" fabric
Altered paper pulp trees	Paper component (lignin) easier to process
High-starch potatoes	Absorb less oil when fried
Pest-resistant corn	Can resist European corn borer
Seedless minimelons	Single serving size
Sweet peas and peppers	Retain sweetness longer
Sugarcane with corn gene	Resists bacterial and fungal toxins

Bt Toxin: Genetically Engineered Insecticidal Cotton



<u>Microbial Bio-pesticide</u> :Genetically Modified Cotton

Genetically Modified Cotton (contains a bacterial gene for pest resistance)

Standard Cotton

Advantages and Disadvantages of GMOs

Advantages	Disadvantages
Higher yield of crops due to less crops damaged by insects and disease	GMO foods don't taste as natural as non GMO foods
Less pesticides need to be purchased and used, causing more economically productive farmers and less pollution	Some organisms (such as butterflies and bees) are harmed by pesticides in GMO foods
Food production increased, causing decreasing starvation in LDCs	Labeling GMO foods causes additional expenses in processing and labeling
Added nutritional value in food due to incorporating additional vitamins into crops	Possible cross pollination of GMO foods with non GMO foods result in the inability to track GMOs
Smell of GMO foods are often enhanced	Insects can possibly evolve to be resistant to insect resistant GMO crops
GMO foods do not need as fertile land as natural foods in order to grow	Cross pollination of GMO crops with weeds could result in "super weeds"
Less additives are needed to keep GMO foods fresh	New allergies could develop to GMO foods
GMO crops are less likely to get sicknesses	Possible health complications could arise due to unknown long term affects of GMO foods
GMO crops that freeze less in the winter can be produced	GMO crops sometimes fail like normal crops (genetically modified cotton has failed in India)

Molecular Archaeology: DNA Analysis

Photograph of Iceman: Discovered in 1991, and approximately 5000 years old

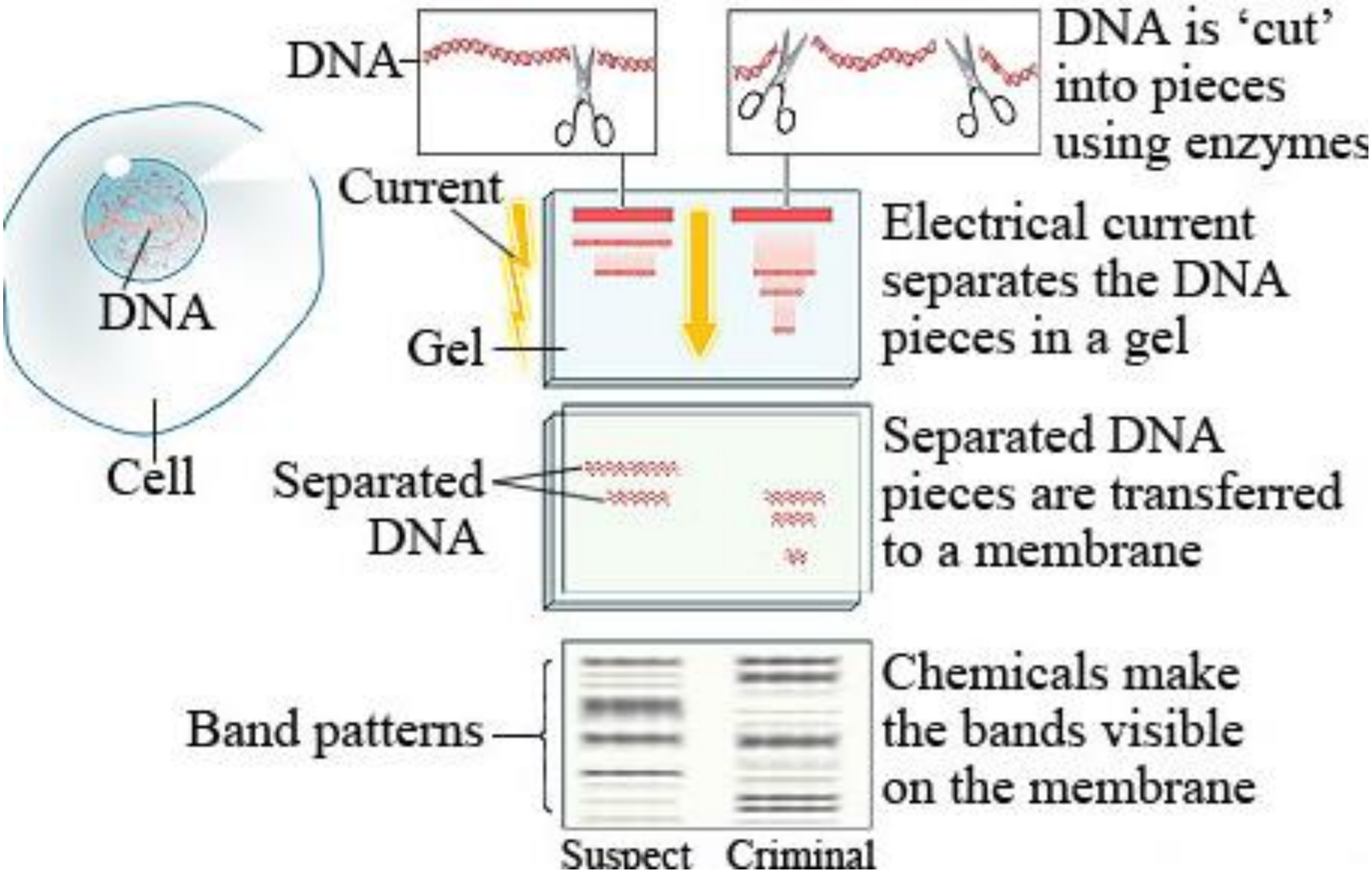
It is the oldest human sample to undergo such an analysis.
Analysis of his mitochondrial DNA indicated he came from the Italian Alps region.

DNA Analysis

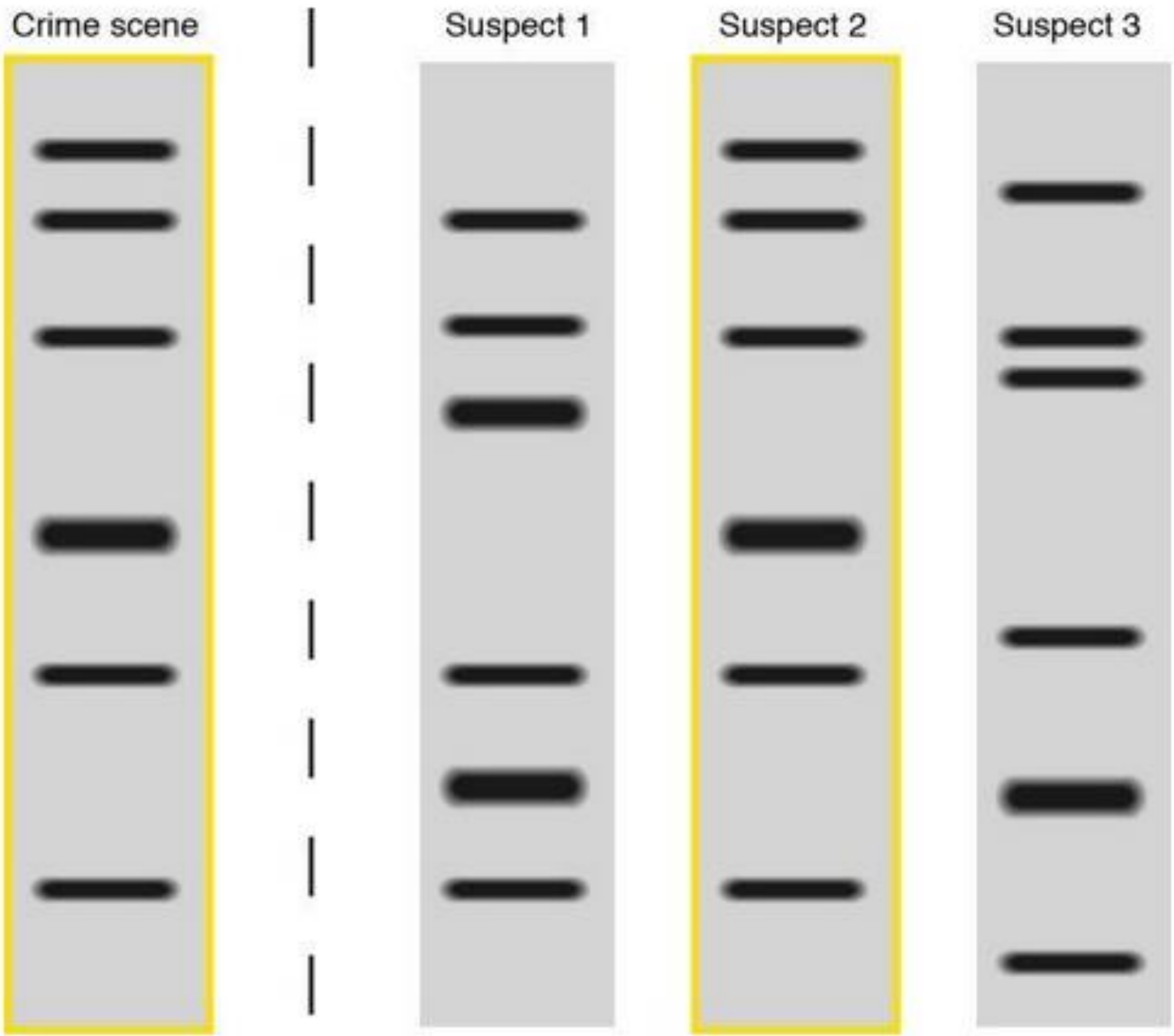
DNA Fingerprinting or DNA Typing

- Method to identify the DNA of an individual
- DNA is unique to a person, no two individuals have identical DNA except identical twins or clones
- All the cells of a person has same DNA
- A specimen for DNA fingerprinting can be any type of cell
  - Blood, saliva, sperm, muscle, teeth, bones or any DNA bearing cell

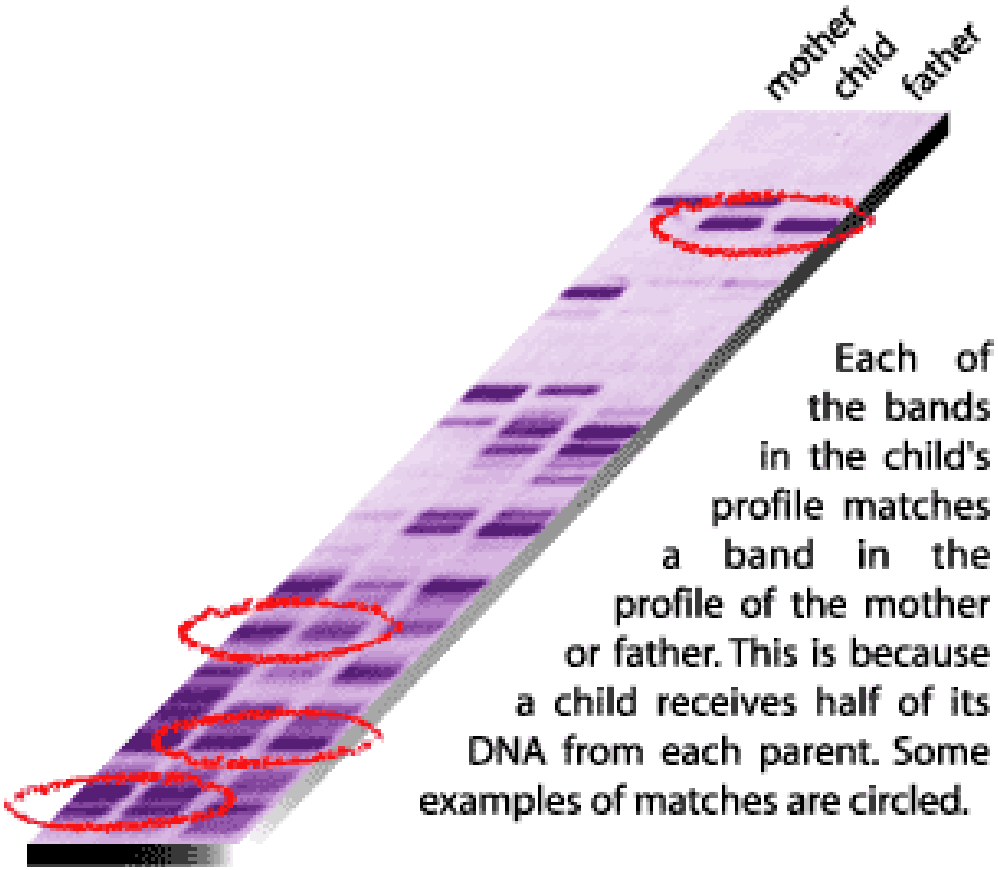
Process of Making a DNA fingerprint



How DNA fingerprinting can point to a criminal



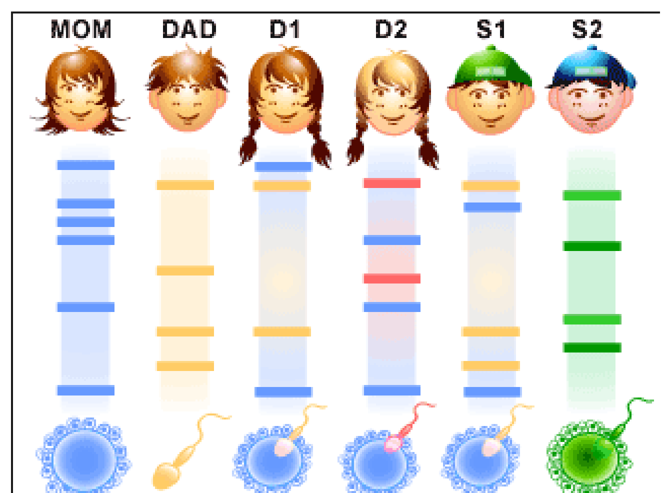
How DNA fingerprinting can identify a child’s parents



Case Study: A family consists of a mom and dad, two daughters and two sons.

OBSERVATION:

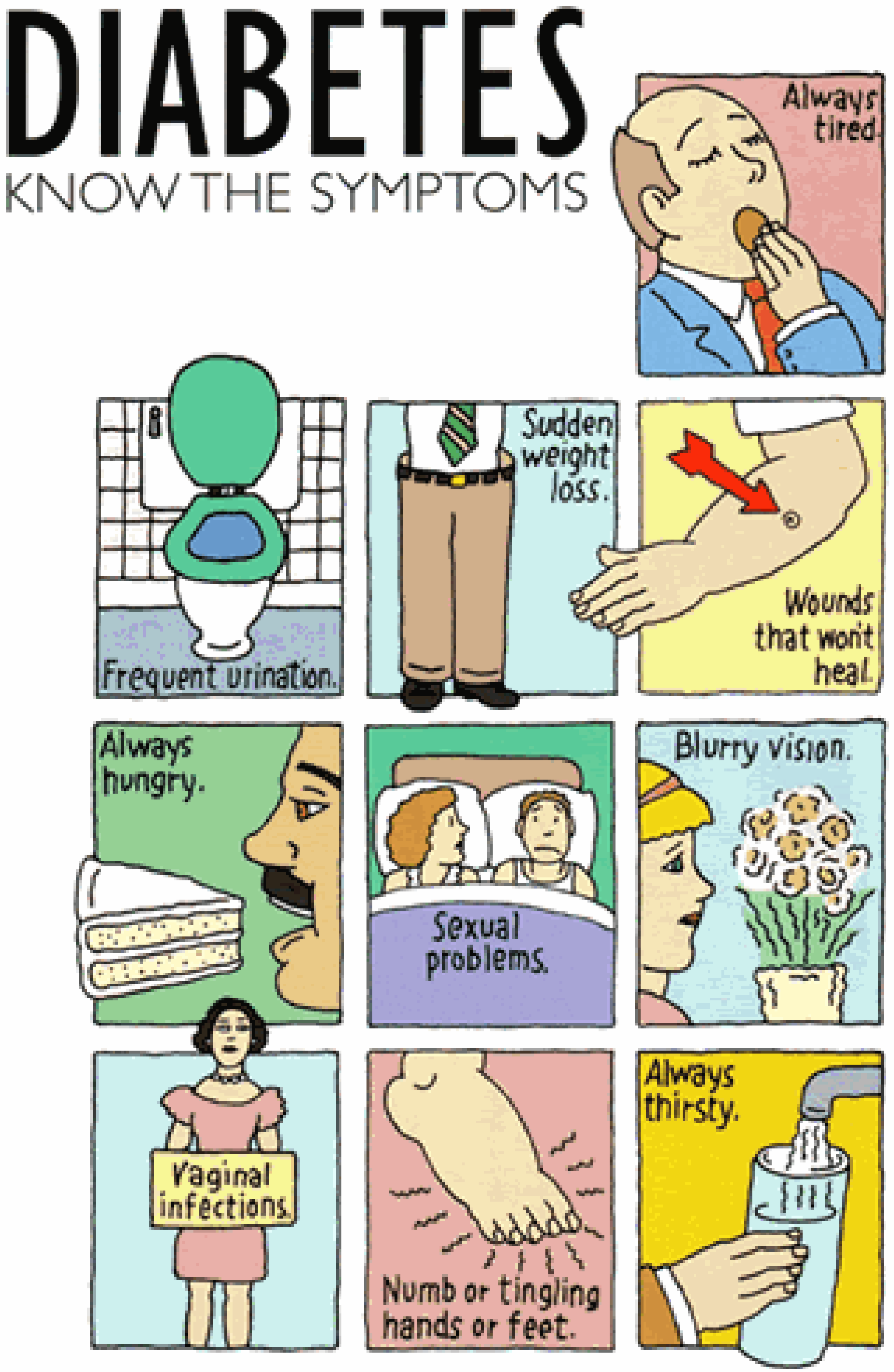
Both daughter 1 and son 1 share RFLPs with both the mom and dad while daughter 2 has RFLPs of the mom but not the dad, and son 2 does not have RFLPs from either parent.



CONCLUSION:

Daughter 2 :child from the mother’s previous marriage

Son 2: Adopted.



Diabetes mellitus	Diabetes insipidus
It results from hyposecretion of insulin.	It results from hyposecretion of ADH.
Excretion of urine with sugar.	Excretion of large amounts of dilute urine.
Excessive eating.	Dehydration.

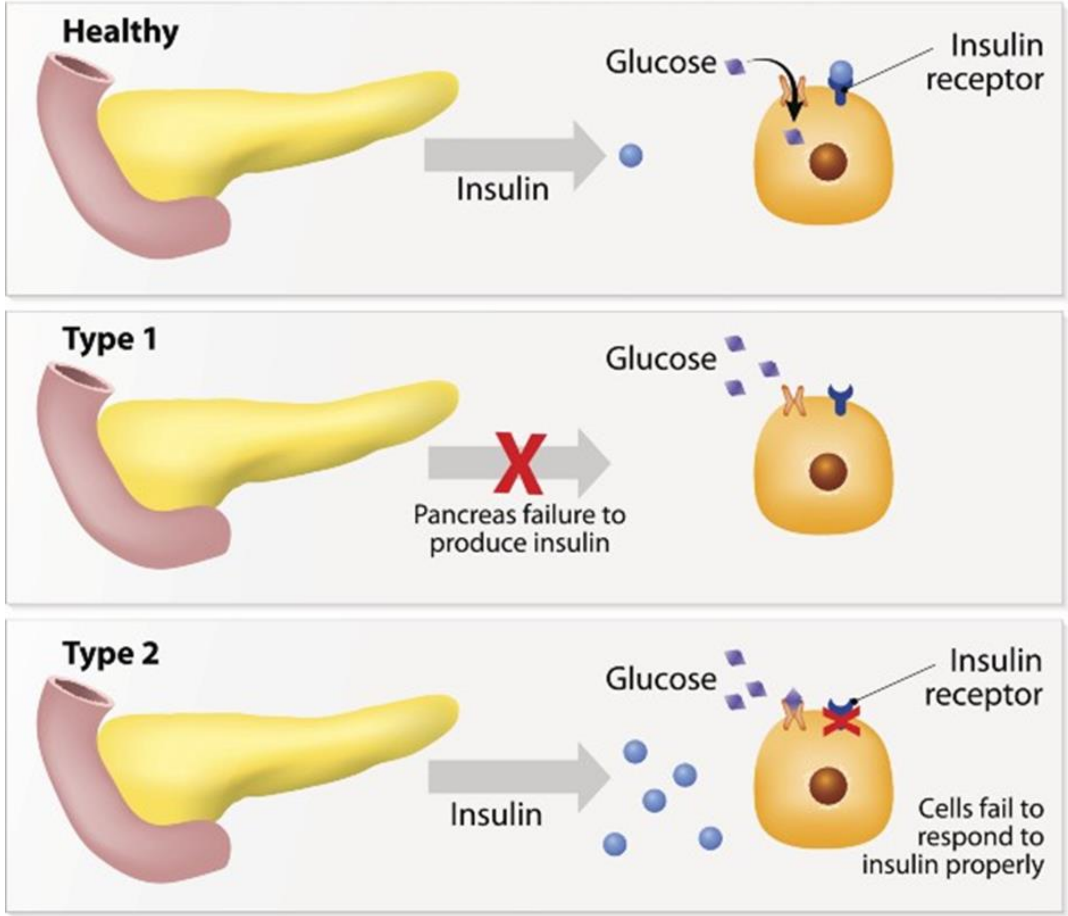
DIFFERENCE BETWEEN DIABETES MELLITUS AND DIABETES INSIPIDUS

Diabetes insipidus should not be confused with diabetes mellitus (DM), which results from insulin deficiency or resistance leading to high blood glucose, also called blood sugar.

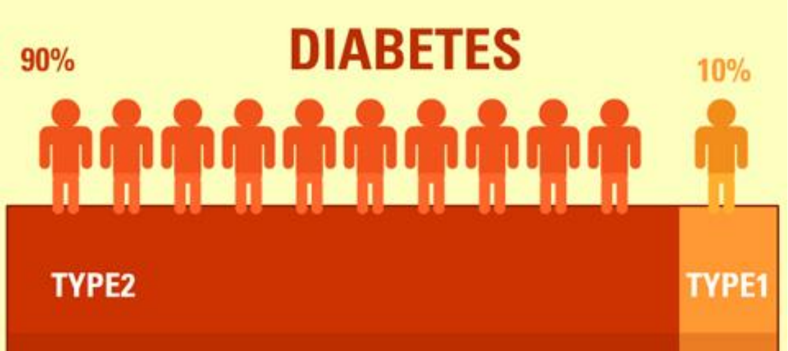
Diabetes insipidus and diabetes mellitus are unrelated, although they can have similar signs and symptoms, like excessive thirst and excessive urination.

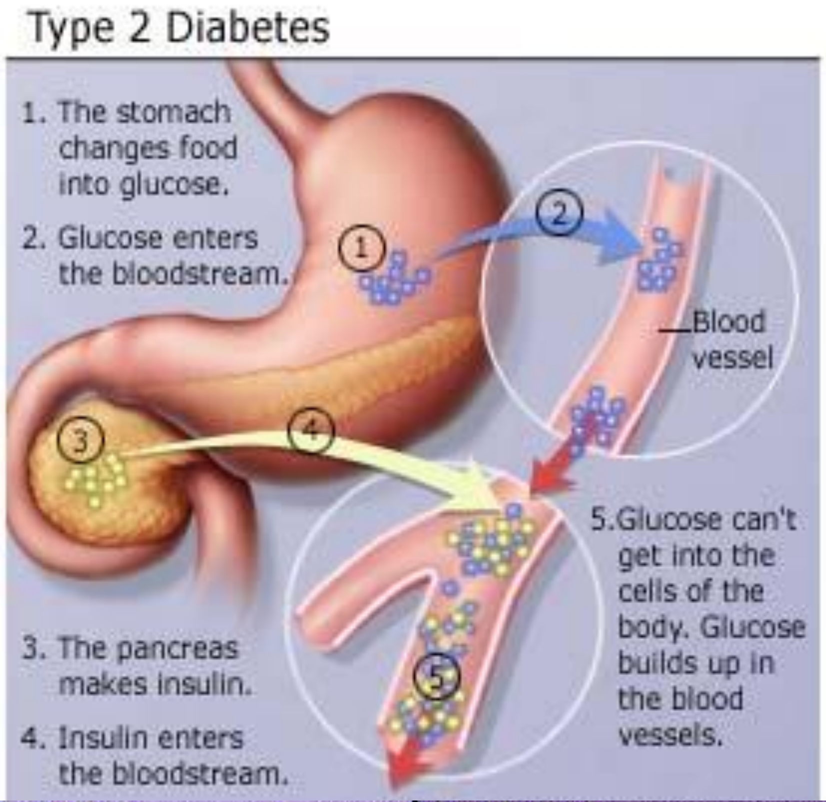
Diabetes mellitus is far more common than diabetes insipidus and receives more news coverage. Diabetes mellitus has two main forms, type 1 diabetes and type 2 diabetes. Diabetes insipidus is a different form of illness altogether.

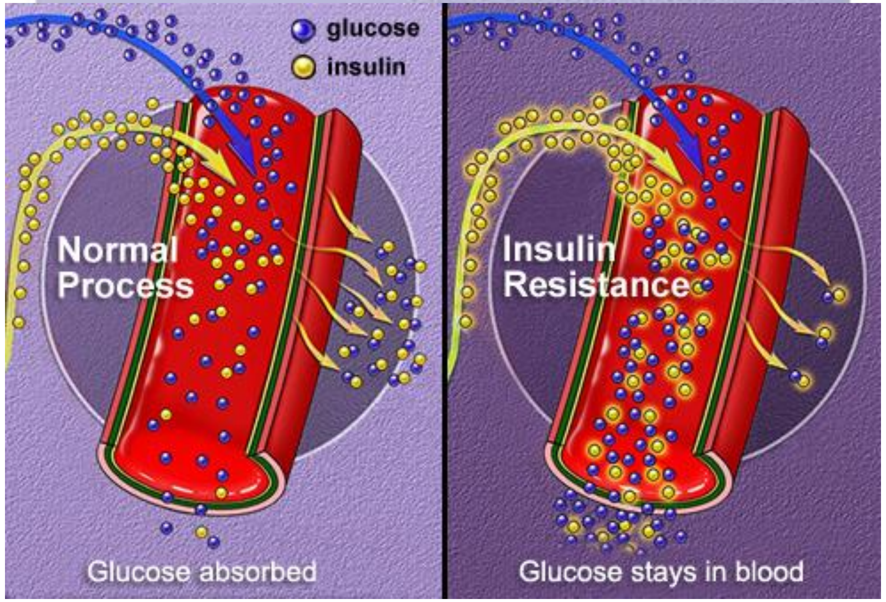
DIABETES MELLITUS

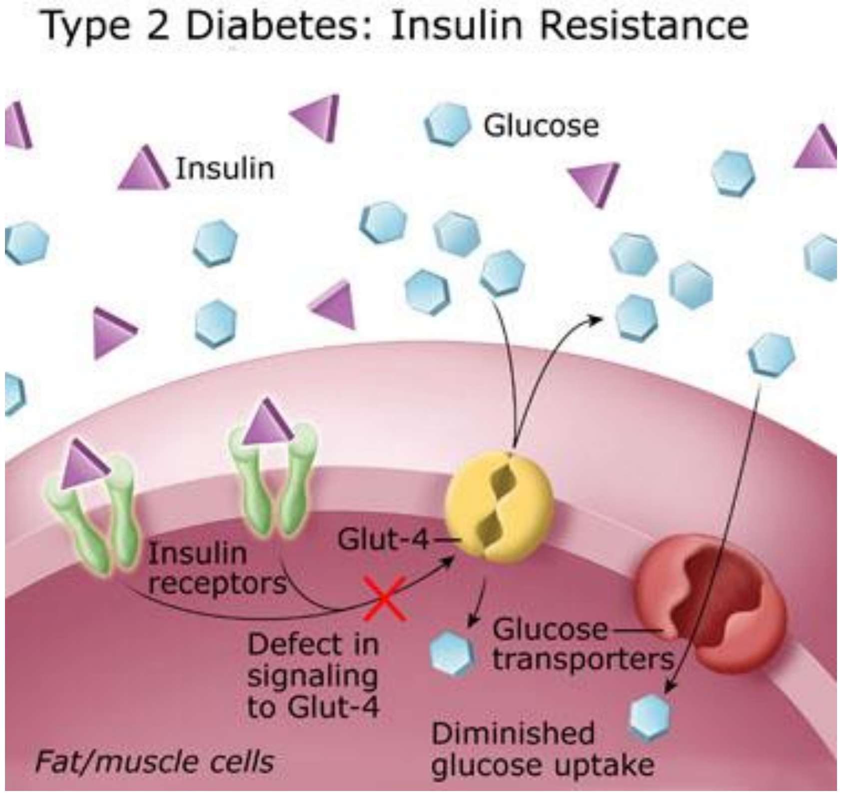


Type 1	Type 2
Usually young	Usually older
Short history- acute onset	Insidious onset
Not overweight	Often overweight
Insulin deficiency	Insulin resistance
Rare	Common
Requires insulin from diagnosis	Diet and lifestyle change can reverse it Then add oral medications May require insulin
Often random	Strong family history

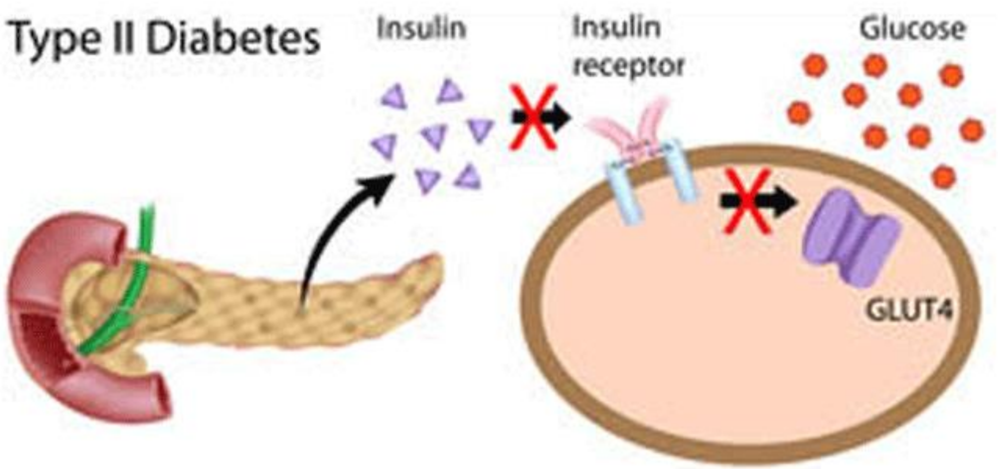


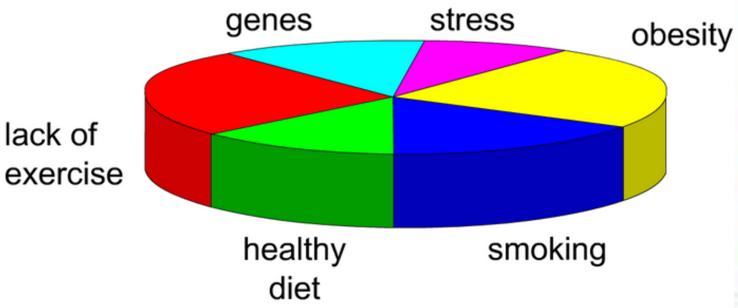




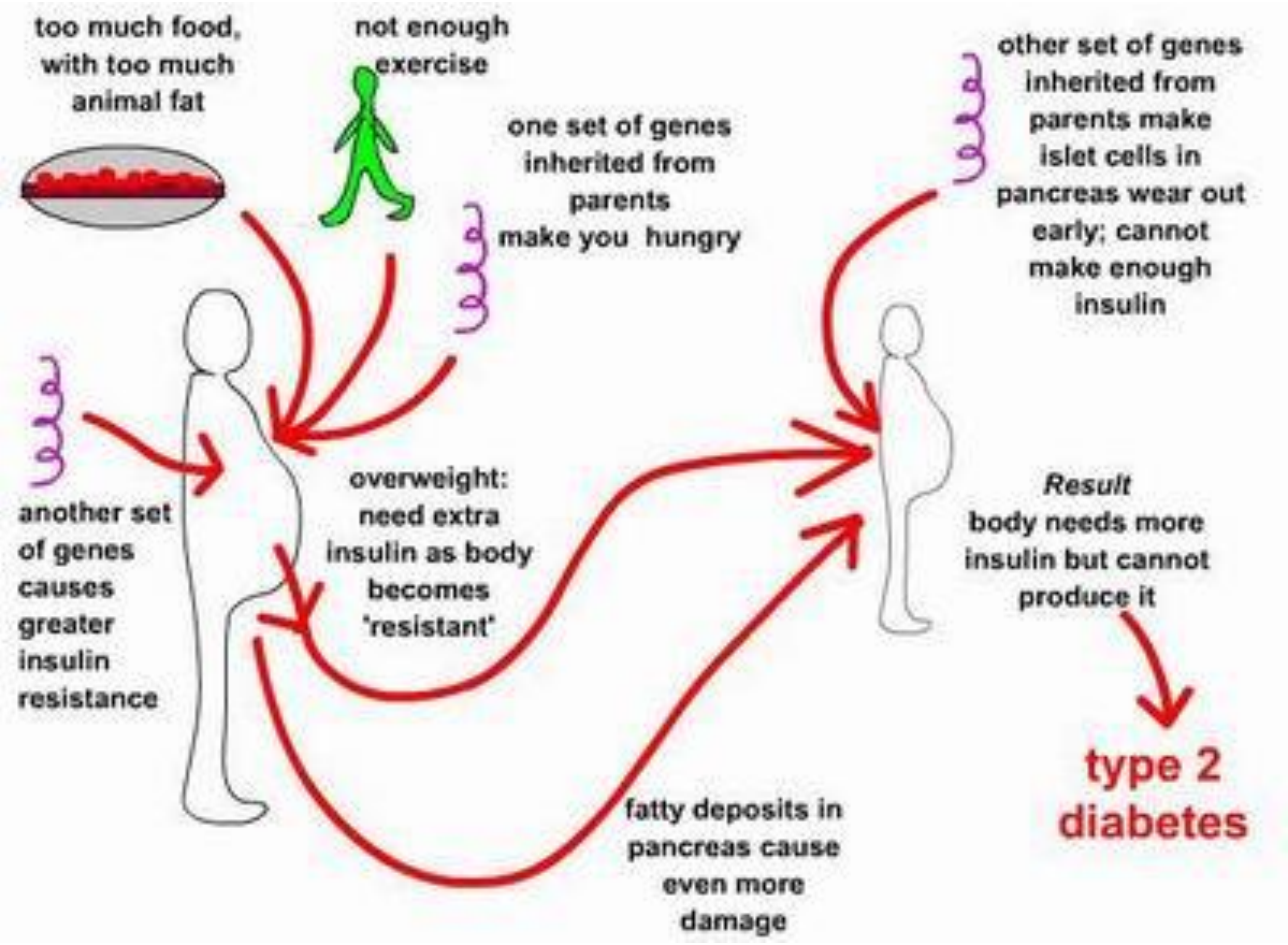


Pancreas and Type II Diabetes





factors contributing to type 2 diabetes

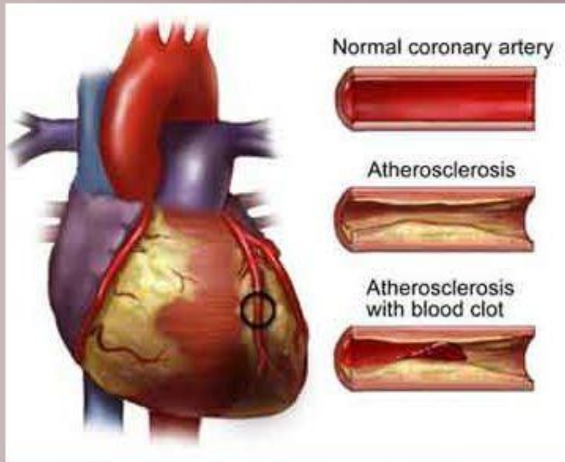


Types Of Cardiovascular Disease

- Atherosclerosis ----(Plaque)
- Coronary heart disease (CHD) ---Myocardial infarction (MI) or heart attack
- Chest pain (angina pectoris)
  - Ischemia (an inadequate blood and oxygen supply to the heart muscles.)
- Irregular heartbeat (arrhythmia)
  - » Tachycardia = more than 100 beats/min
  - » Bradycardia = less than 60 beats/min
- Congestive heart failure (CHF)
  - heart muscle is unable to keep blood circulating normally
- Congenital heart disease (problem in the structure of the heart that is present at birth)
- Stroke--- Myocardial infarction (MI)
- **Embolism**: blockage of blood vessels

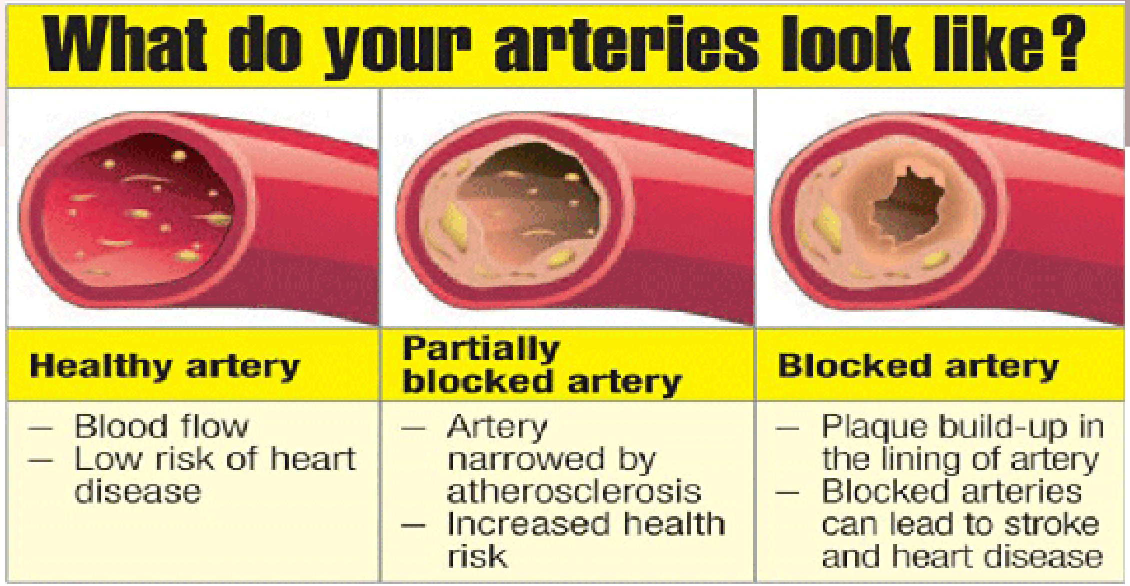
Coronary Heart Disease

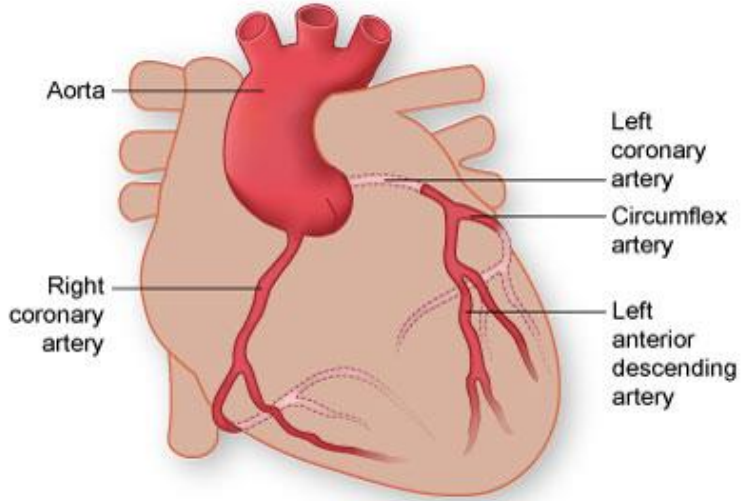
- Slow build up of plaque (lipids, cholesterol)
= **ATHEROSCLEROSIS**
- Arteries become harder, less flexible
- Less space for blood
- Coronary arteries supply O_2 to heart cells
- Thrombosis = clot = heart attack = heart cells die

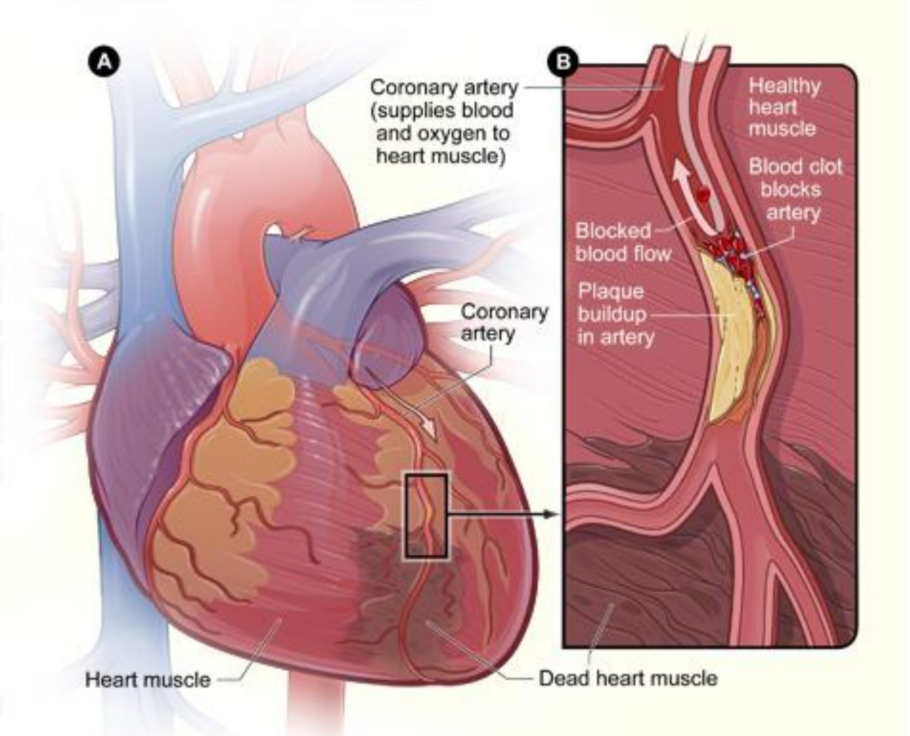


- Factors affecting <u>coronary heart disease</u> (CHD):

    Age, race, heredity, gender, cholesterol levels, blood pressure, obesity, diabetes, smoking, sedentary lifestyle, stress

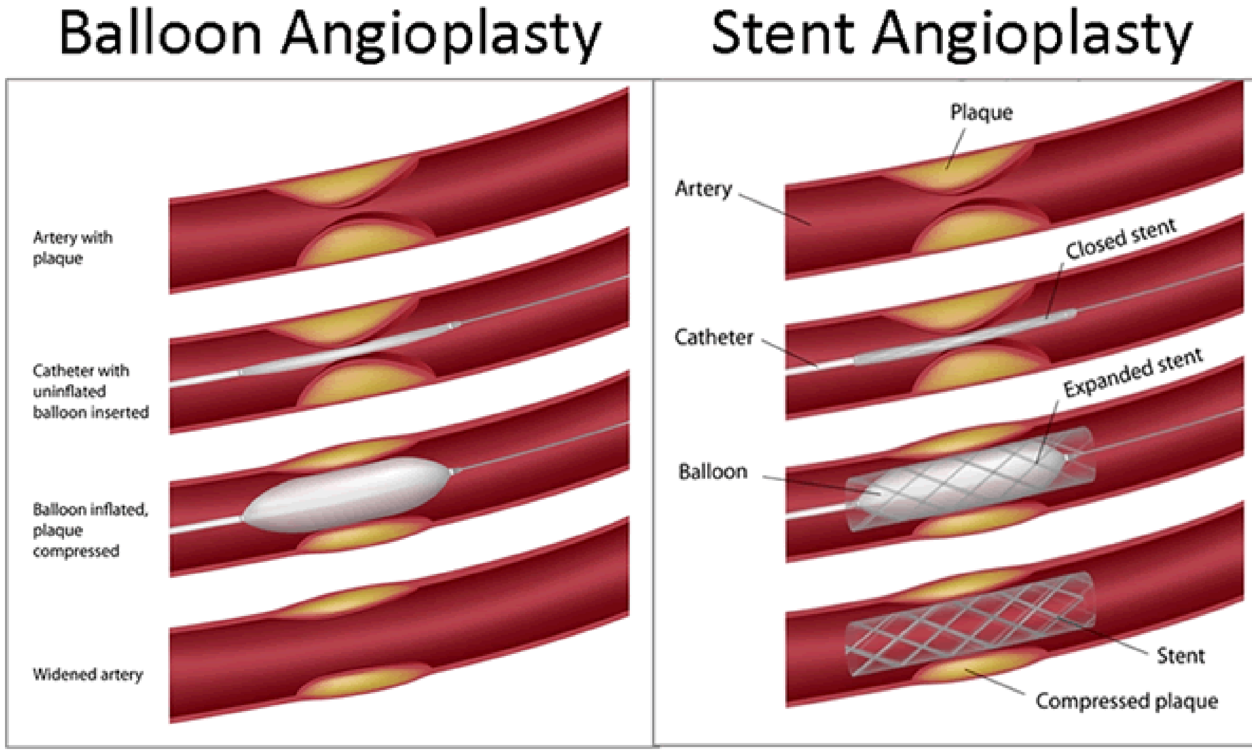


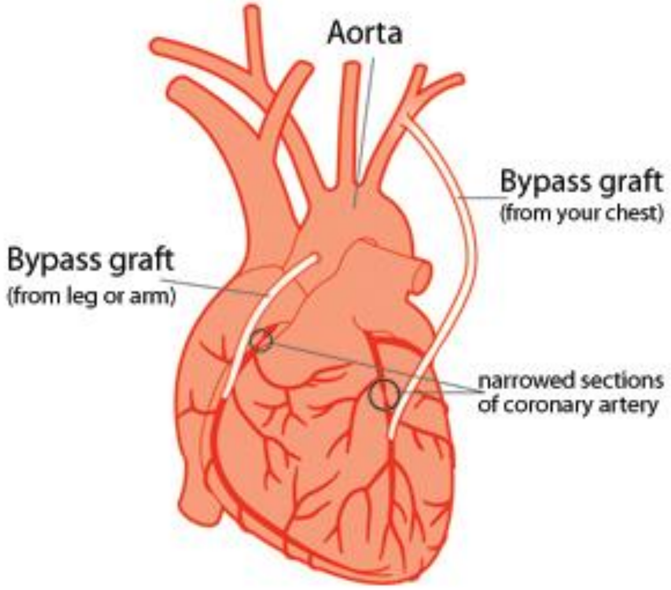




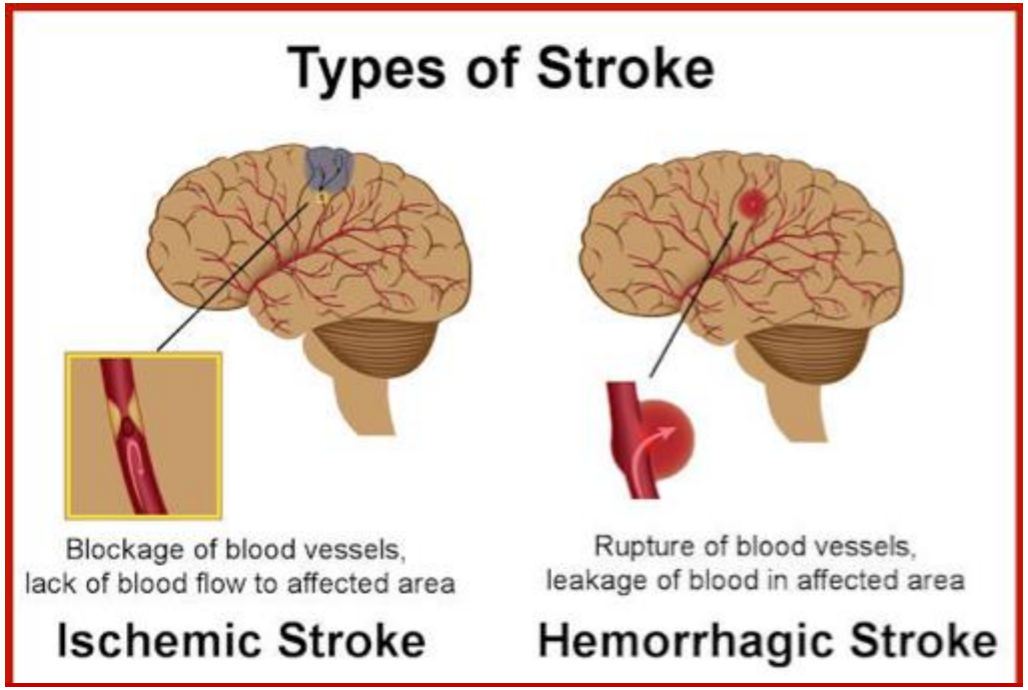
TREATMENT

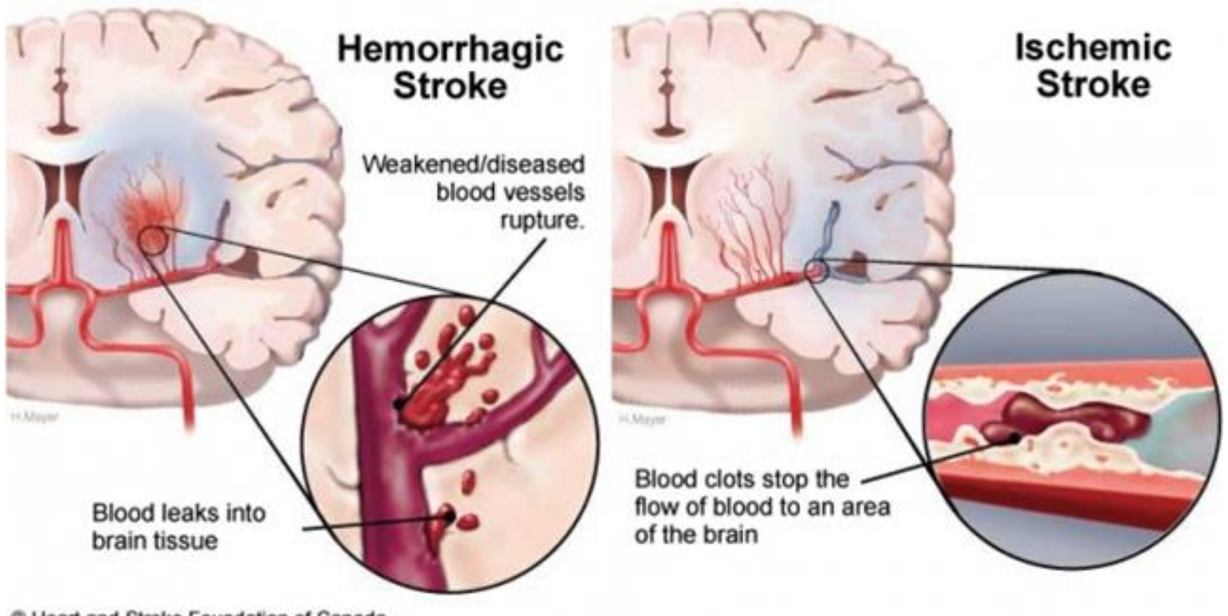
- Treatment of cardiovascular disease depends on the specific form of the disease in each patient, but effective treatment always includes preventive lifestyle changes discussed above.
- Medications, such as blood pressure reducing medications, aspirin and the statin cholesterol-lowering drugs may be helpful.
- In some circumstances, surgery or angioplasty may be warranted to reopen, repair, or replace damaged blood vessels.





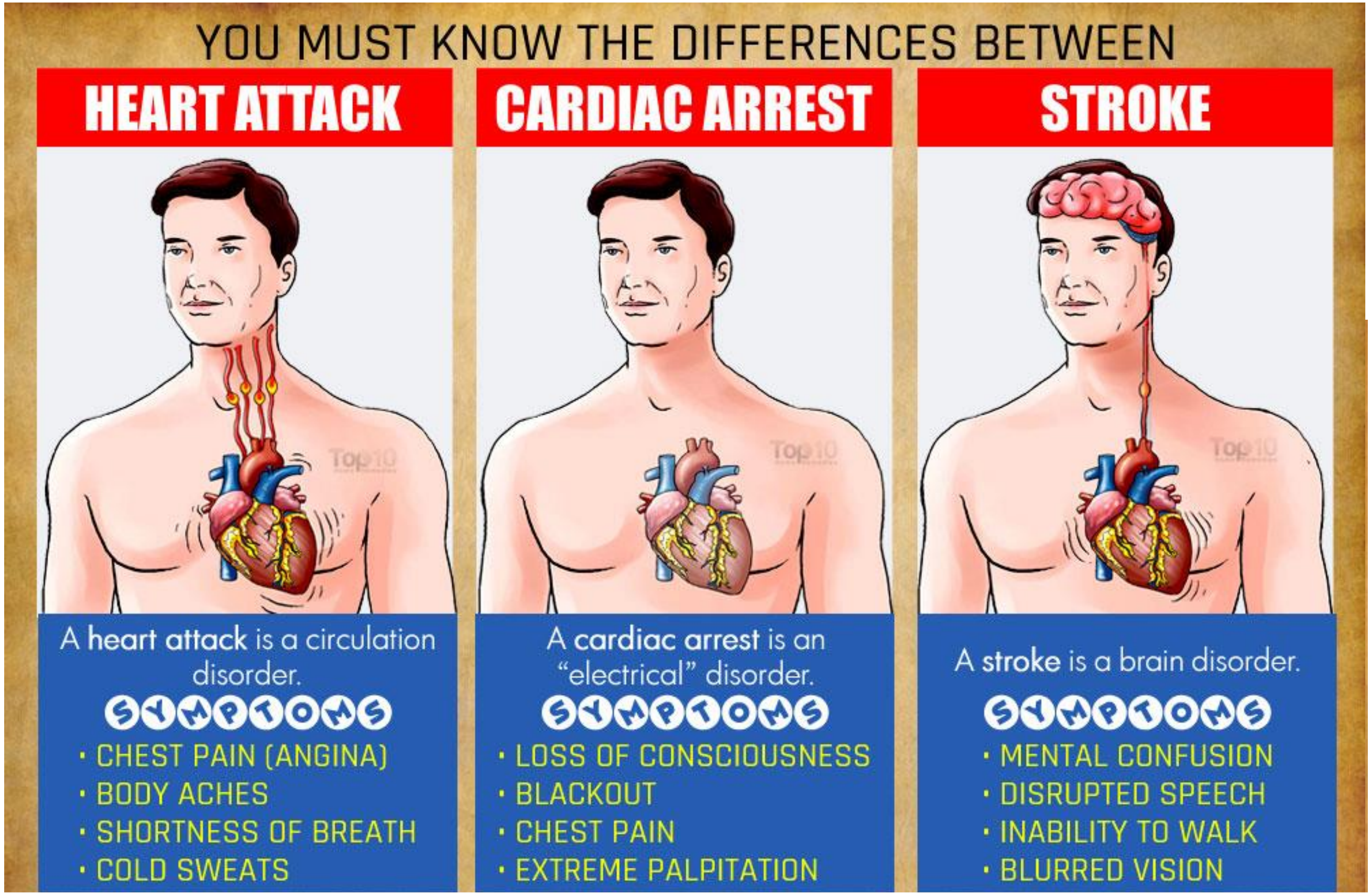
Coronary Bypass Surgery





What is Stroke?

- A **stroke** happens when a blood vessel that carries oxygen to the brain gets blocked or bursts. When that happens, blood can't deliver oxygen to part of the brain and that part of the brain starts to die.
- Without the right medical attention, a stroke can cause major damage to the brain. People who have a stroke may have problems speaking, seeing or moving normally for a short time or for the rest of their lives. The person can even die from a stroke.
- Older adults are more likely to have a stroke than younger people, but people can have a stroke at any age. Other factors that increase risk of stroke include high blood pressure, cigarette smoking, diabetes, other types of cardiovascular disease, and high blood cholesterol.



Heart Attack occurs when blood supply to the heart is **severely reduced or cut off**. Lack of oxygen can **damage the heart** and it will begin to die.

Cardiac Arrest occurs when the heart suddenly **stops beating**, **preventing blood and oxygen** from getting to **vital organs**.

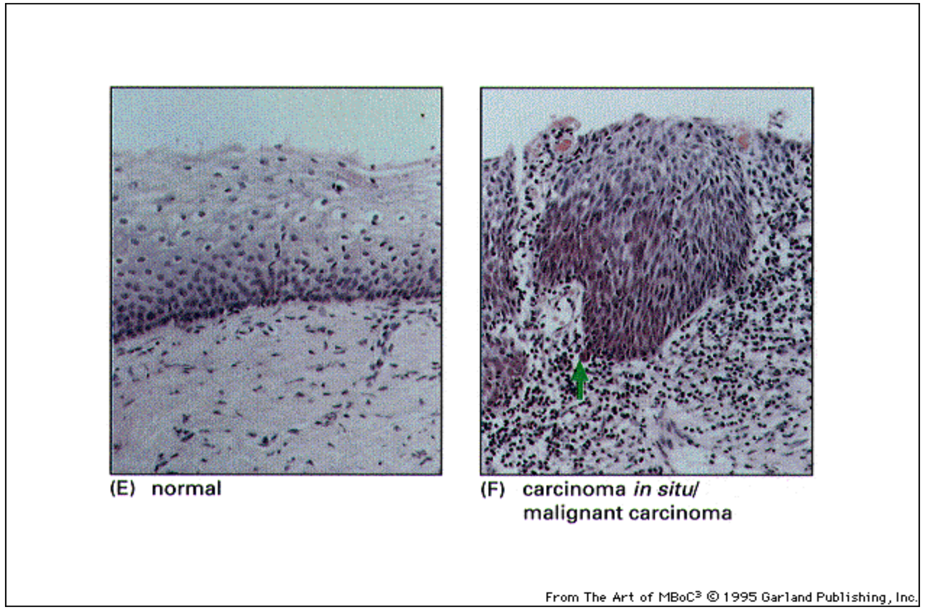
Stroke happens when the **blood flow to the brain is interrupted** or severely limtied cutting off oxygen and nutrients from brain tissue. **Brain cells start dying minutes after a stroke.**

Remember, you can stop heart disease before it starts. Start small and keep it simple. Make one change today and then you're ready to make another!

Life's Simple 7

1. Avoid smoking and using tobacco products
2. Be physically active every day
3. Eat a heart-healthy diet
4. Keep a healthy weight
5. Keep your blood pressure healthy
6. Keep your total cholesterol healthy
7. Keep your blood sugar healthy

What is cancer?



- Caner is defined as the continuous uncontrolled growth of cells.
- A tumor is a any abnormal proliferation of cells.
- **Benign tumors** stays confined to its original location
- **Malignant tumors** are capable of invading surrounding tissue or invading the entire body
- Tumors can arise from any cell type in the body

Abnormal cell growth (**neoplasia**)

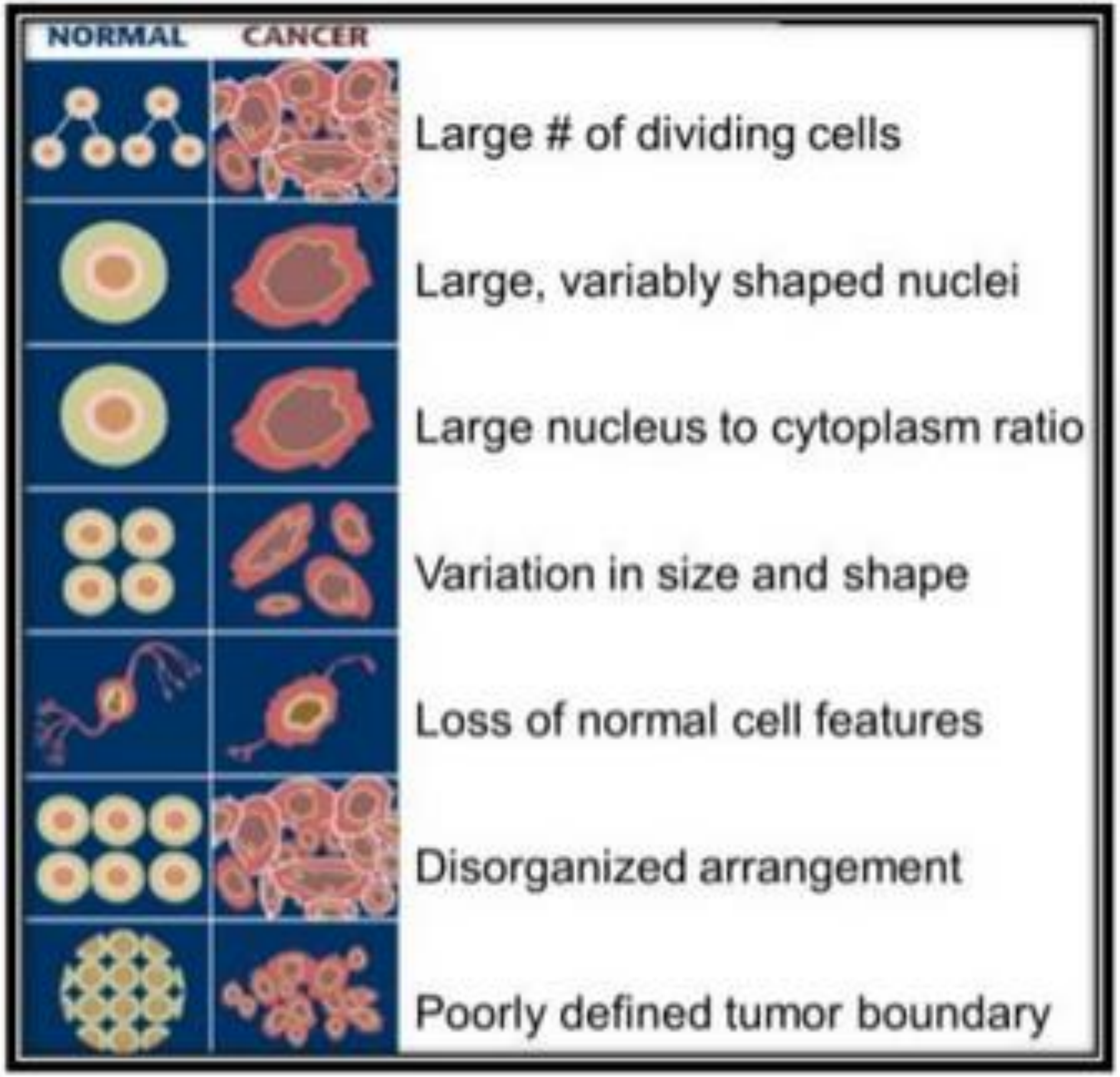
Benign: slow growth, non-invasive, no metastasis

Malignant: rapid growth, **invasive**, potential for metastasis

Is cancer a heritable disease?

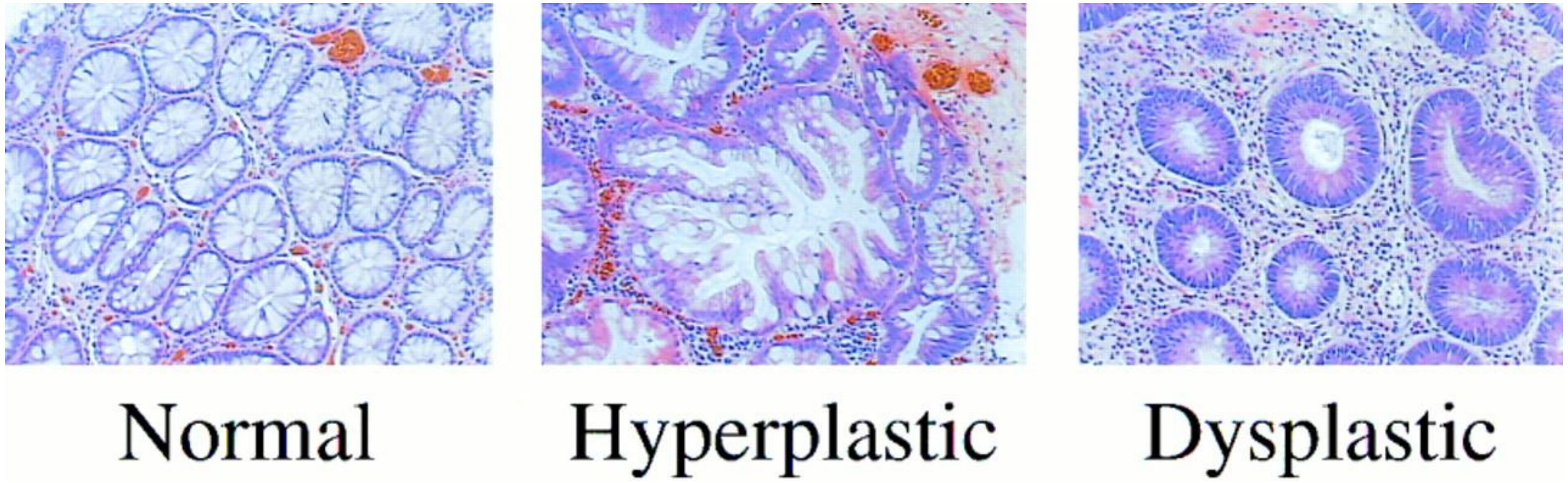
There are heritable cancer syndromes. The majority of cancers, however, are not familial. Cancer is a genetic disease, but the majority of mutations that lead to cancer are **somatic**

Normal Cells vs. Cancer Cells



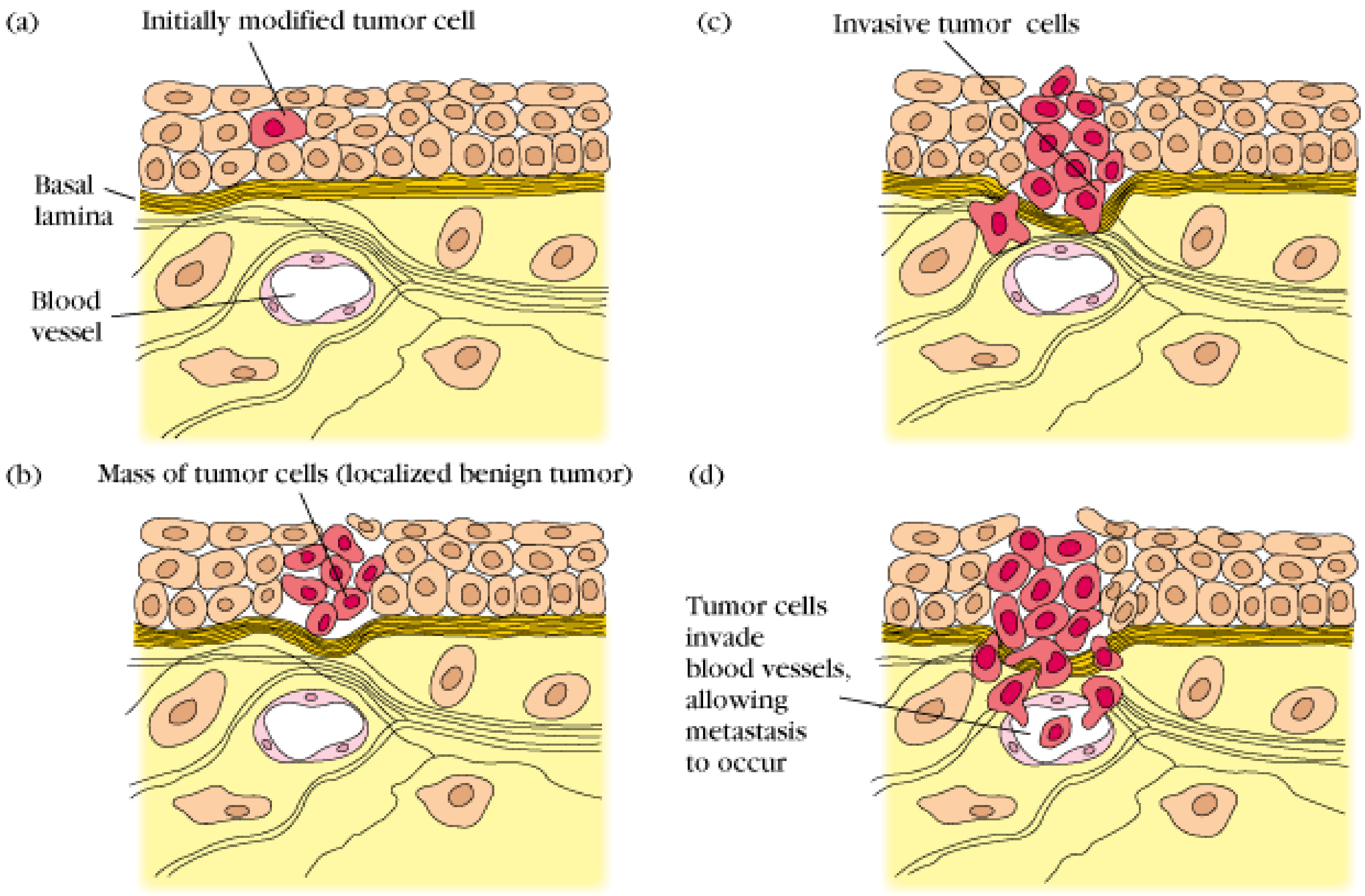
The Vocabulary

- **Hyperplasia** – increased number of cells
- **Hypertrophy** – increased size of cells
- **Dysplasia** – disorderly proliferation
- **Neoplasia** – abnormal new growth
- **Anaplasia** – lack of differentiation
- **Tumor** – originally meant any swelling, but now equated with neoplasia
- **Metastasis** –growth at a distant site



Most malignant cells become metastatic

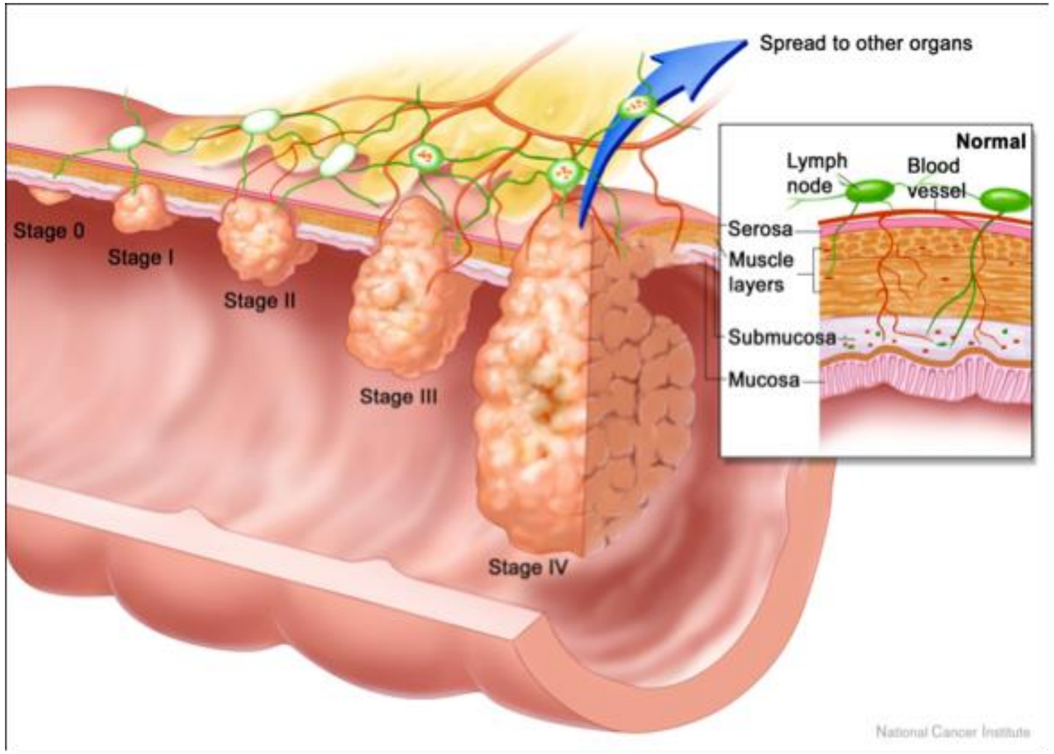
Invade surrounding tissue and establishment of secondary areas of growth: **Metastasis**



Predictors of Behavior

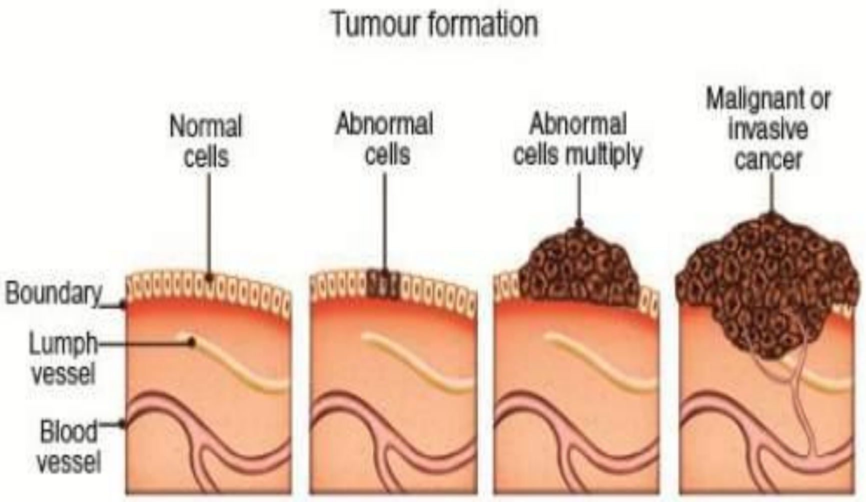
- **Grade – How bad do the cells look?**
- The pathologist gives the cancer a grade based on how different they look from normal cells (differentiation), how quickly they are growing and dividing, and how likely they are to spread. (How aggressive is the cancer?)
- **Stage – Where has the cancer spread?**
  - **Tumor (Size of Tumor)**
  - **Nodes (degree of spread to regional lymph nodes)**
  - **Metastasis (if cancer has spread to other body parts)**

Staging is a way of describing or classifying a cancer based on the extent of cancer in the body. The stage is often based on the size of the tumour, whether the cancer has spread (metastasized) from where it started to other parts of the body and where it has spread.



Tumor size

TUMOR (T)	DESCRIPTION
TX	Primary tumor cannot be evaluated
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor < 2cm
T2	Tumor 2-5cm
T3	Tumor > 5cm



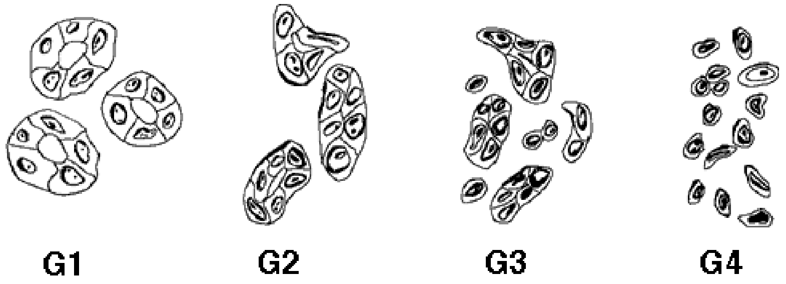
Lymph Node Status

LYMPH NOTE STATUS (N)	DESCRIPTION
NX	Regional lymph nodes cannot be evaluated
N0	No regional lymph node involvement
N1	3 Lymph nodes + Axillary
N2	10 Lymph nodes+

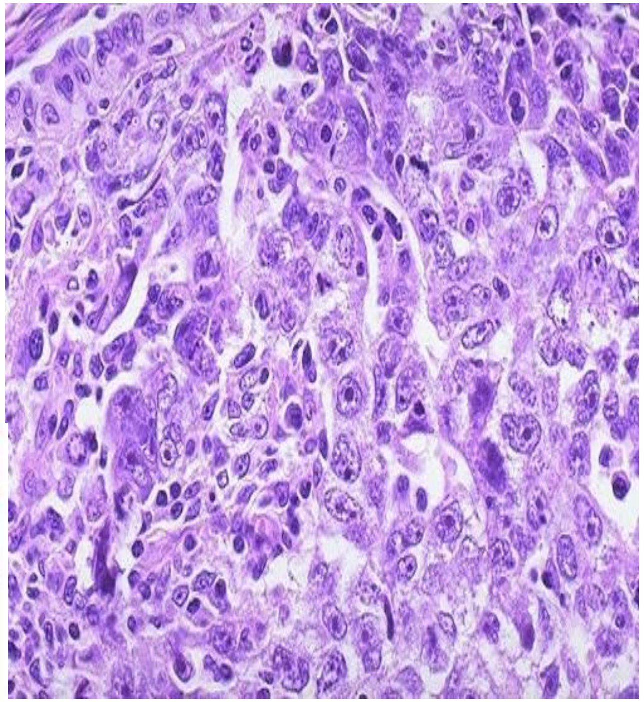
Distant Metastasis (+/-)

METASTASIS	DESCRIPTION
MX	Distant metastasis cannot be evaluated
M0	No distant metastasis
M1	Distant metastasis is present

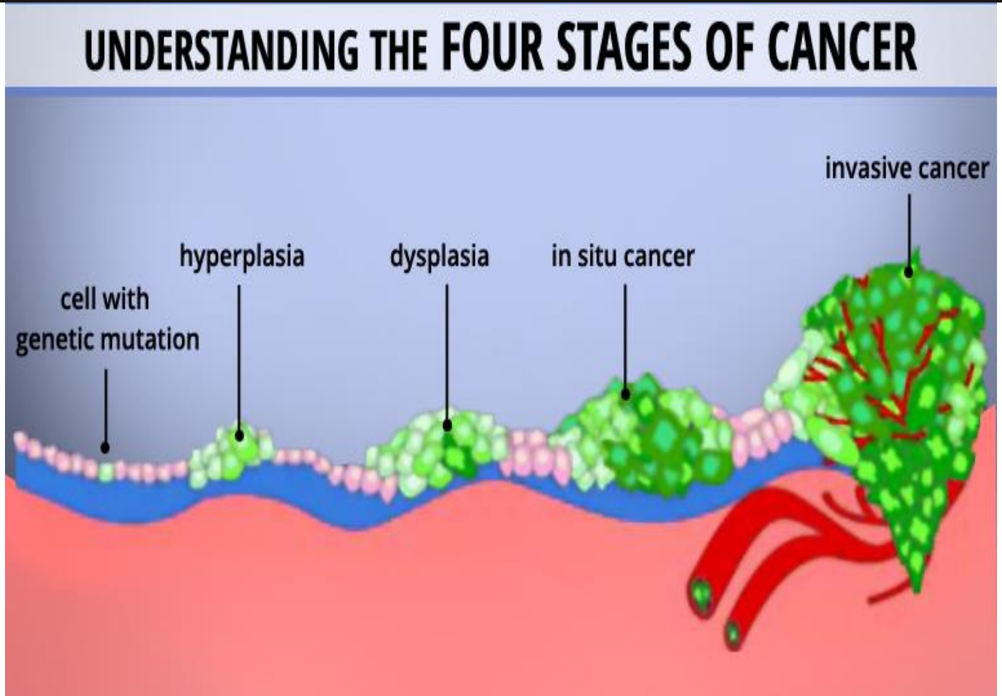
Grading Cancer



GRADES	DESCRIPTION
GX	Grade cannot be assessed
G1	Well differentiated (Low grade)
G2	Moderately differentiated (Intermediate grade)
G3	Poorly differentiated (High grade)
G4	Undifferentiated (High grade- ANAPLASIA)



TNM Classification (American Joint Commission on Cancer)				Dukes' Classification
Stages	T	N	M	Stages
Stage 0	Tis	N0	M0	
Stage I	T1	N0	M0	A
	T2	N0	M0	B1
Stage II	T3	N0	M0	B2
	T4	N0	M0	B2
Stage III	T1, T2	N1 or N2	M0	C1
	T3, T4	N1 or N2	M0	C2
Stage IV	Any T	Any N	M1	D



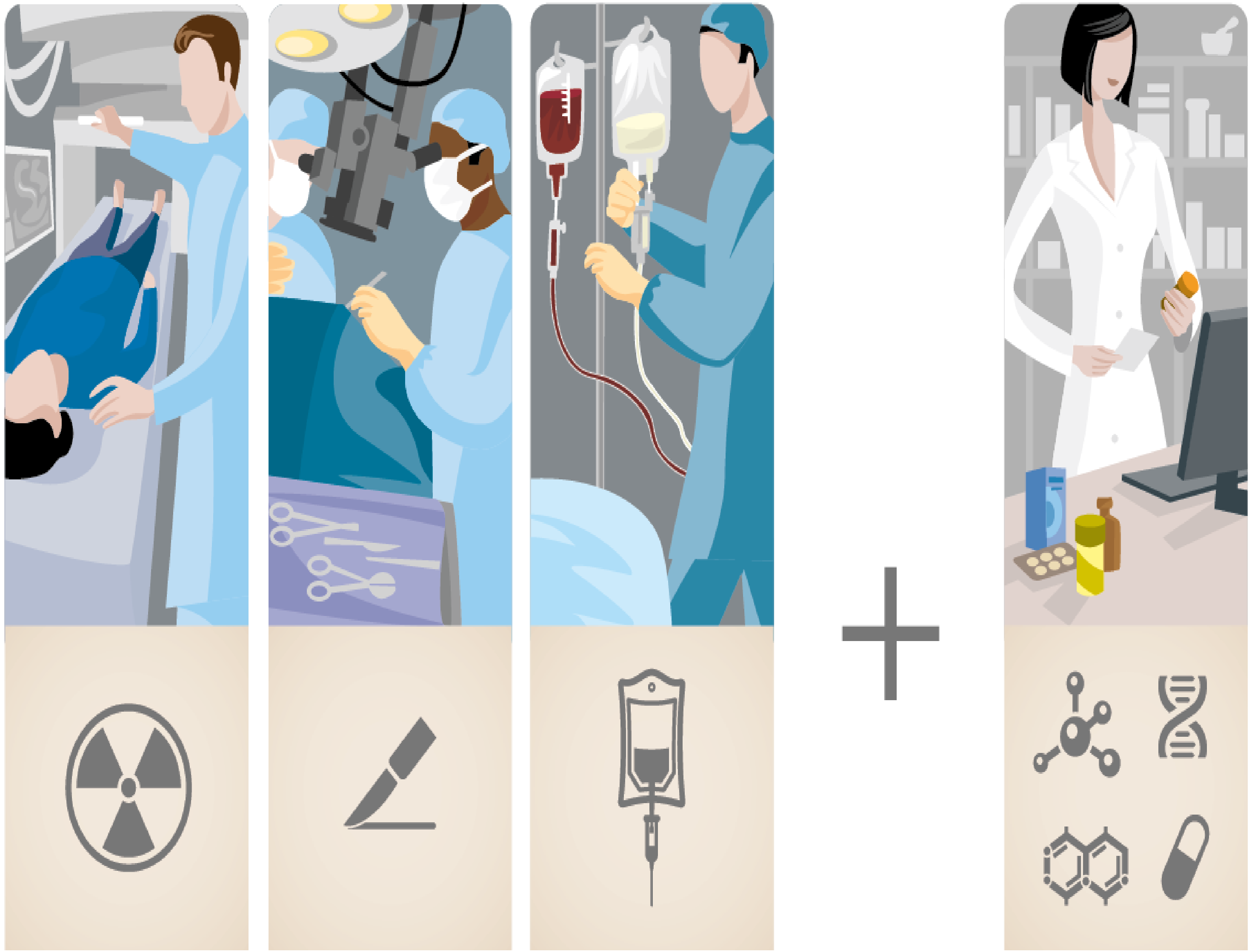
What causes the mutations that lead to cancer?

- **Chemical Exposure**
  - Tobacco smoke
  - Environmental (PCBs)
  - Occupational (coal tar, asbestos, aniline dye)
  - Diet (aflatoxin)
- **Radiation (UV, ionizing)**
- **Infection**
  - Viruses (EBV, hepatitis B, papilloma)
  - Bacteria (Helicobacter)
- **Inherited familial cancer syndromes**

What do these agents have in common?

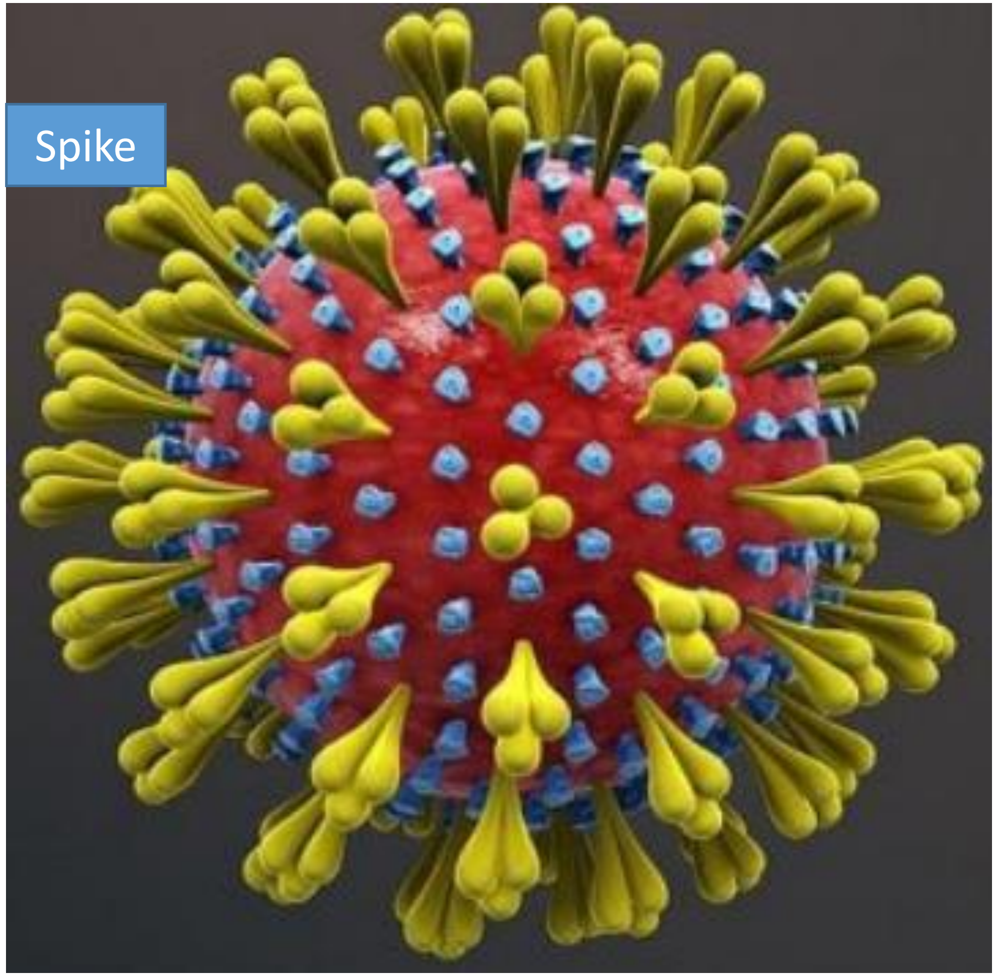
Viruses: insertional mutagenesis
Chemicals: DNA adducts
UV and ionizing radiation: single and double strand DNA breaks

Traditional cancer treatment



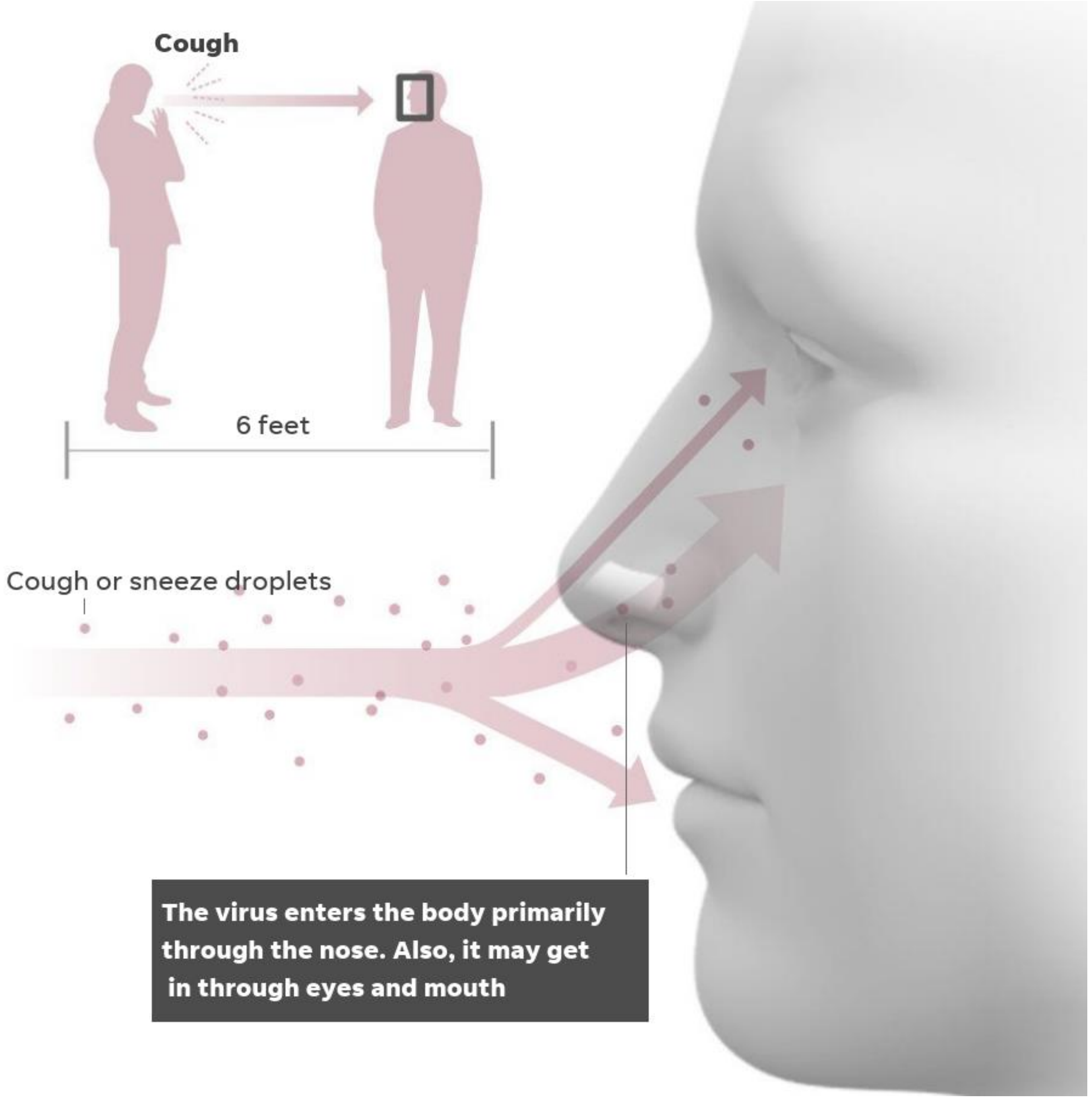
RADIATION SURGERY CHEMOTHERAPY + TARGETED DRUG THERAPIES

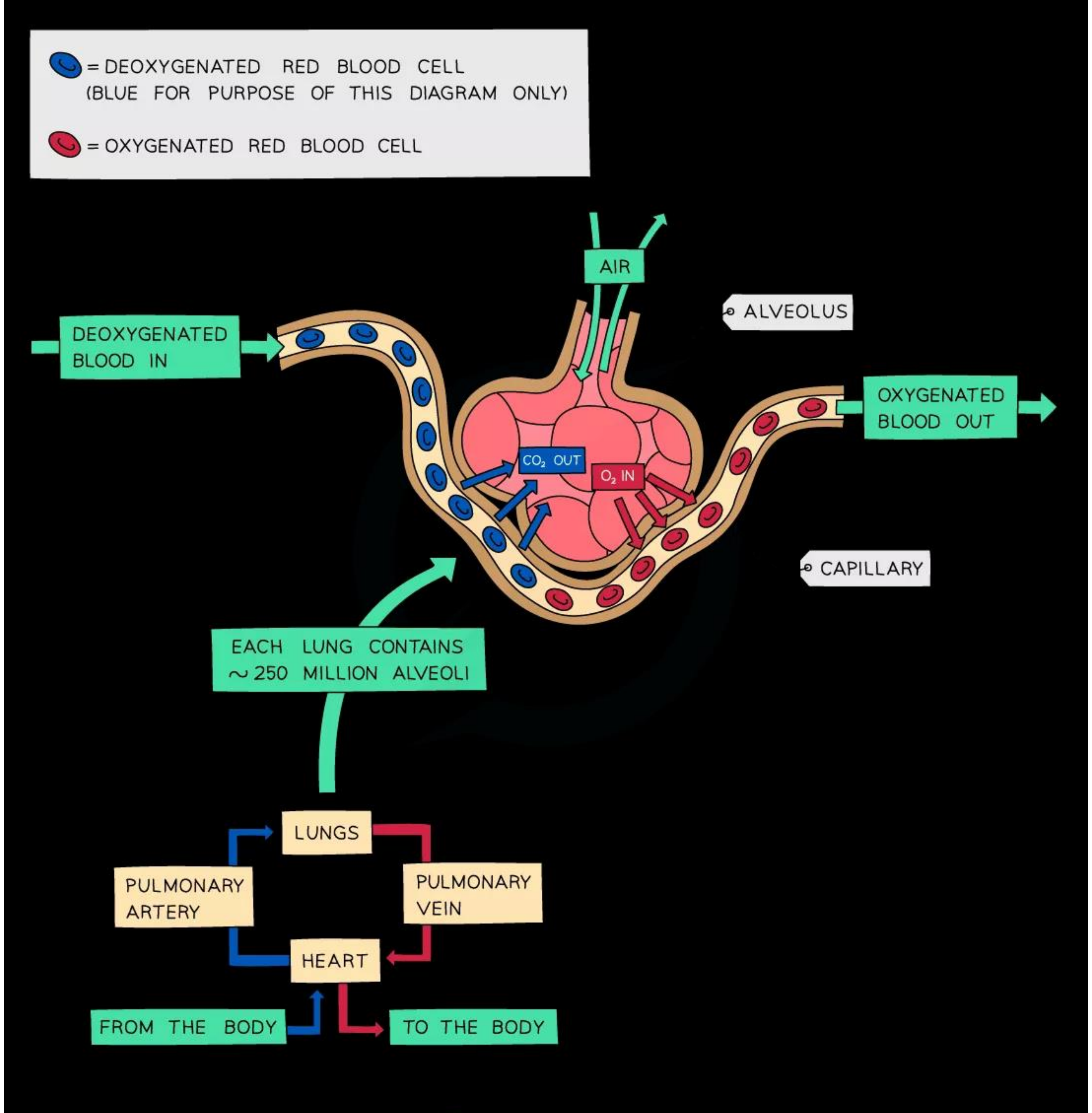
Corona virus disease-2019 (COVID-19)

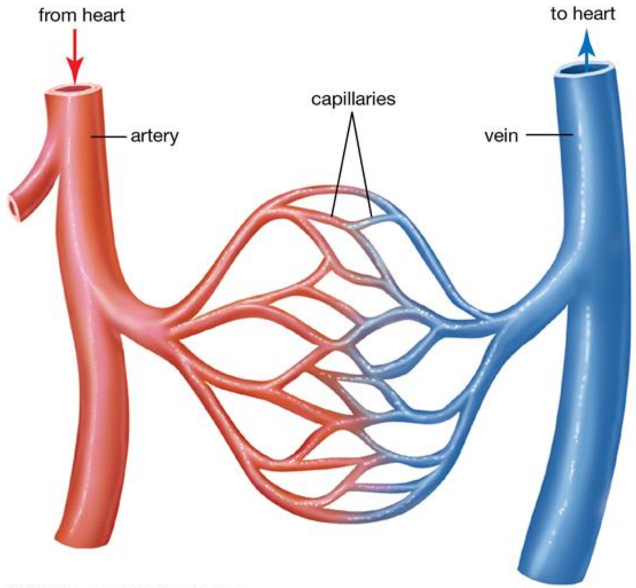


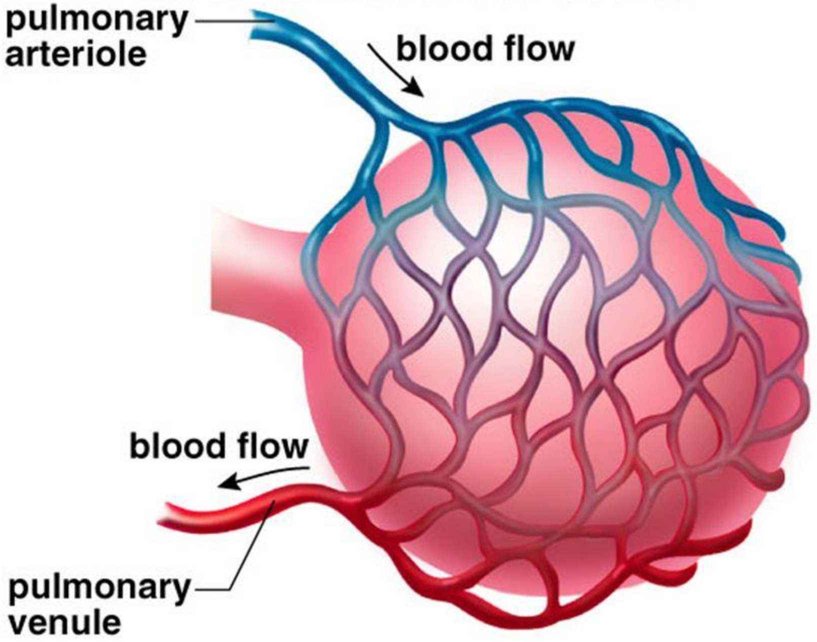
Coronavirus

Name: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)

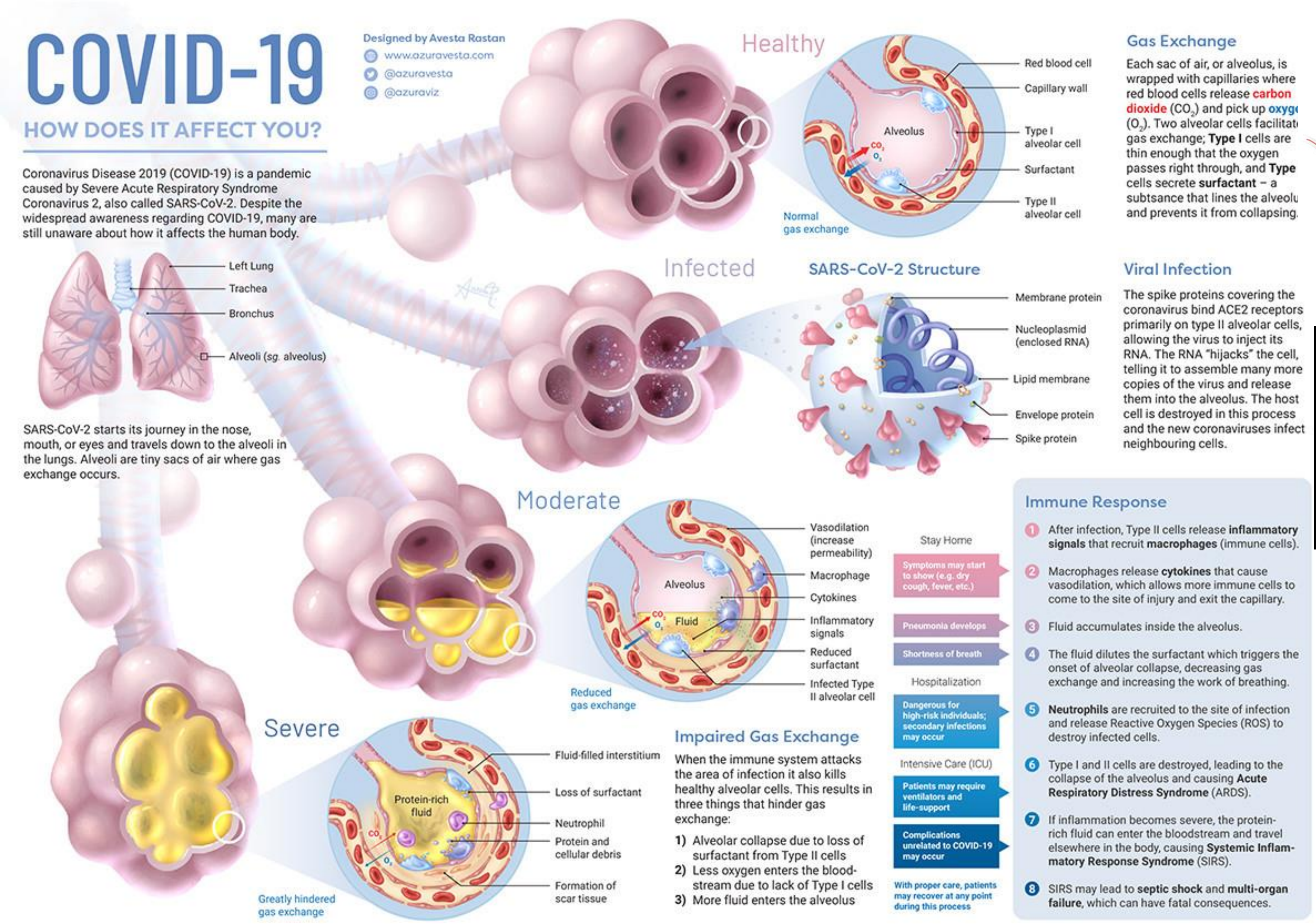


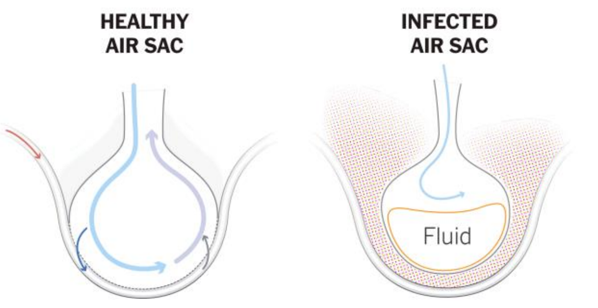


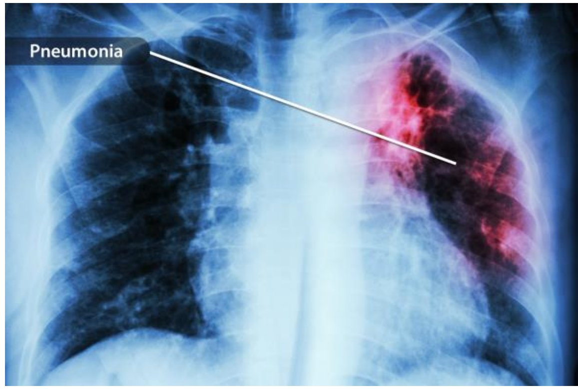




Capillary network of one alveolus

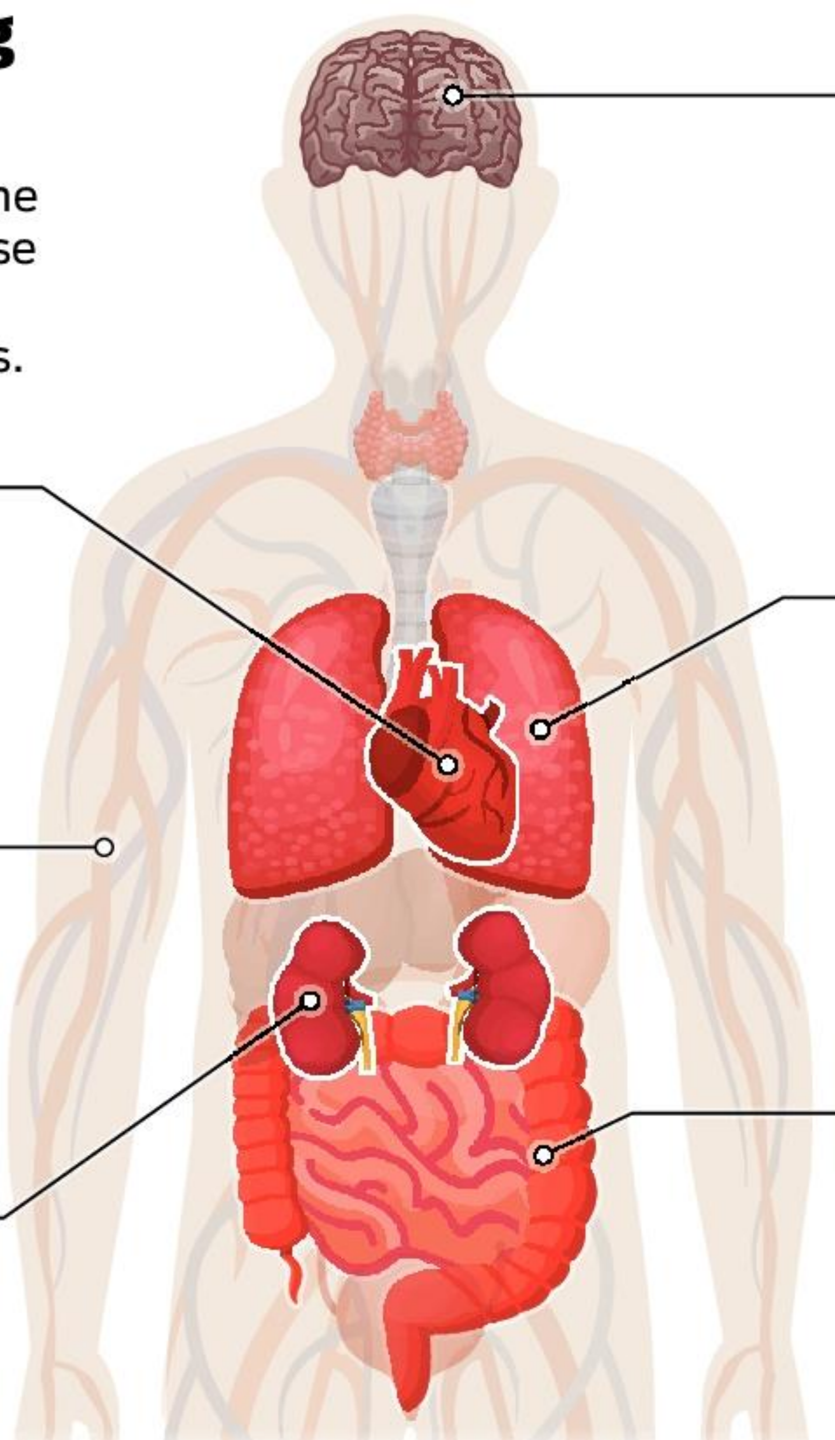

COVID-19
HOW DOES IT AFFECT YOU?
Designed by Avesta Rastan
www.azuravesta.com
@azuravesta
@azuraviz
Coronavirus Disease 2019 (COVID-19) is a pandemic caused by Severe Acute Respiratory Syndrome Coronavirus 2, also called SARS-CoV-2. Despite the widespread awareness regarding COVID-19, many are still unaware about how it affects the human body.
Left Lung
Trachea
Bronchus
Alveoli (sg. alveolus)
SARS-CoV-2 starts its journey in the nose, mouth, or eyes and travels down to the alveoli in the lungs. Alveoli are tiny sacs of air where gas exchange occurs.
Healthy
Red blood cell
Capillary wall
Alveolus
CO_2
O_2
Type I alveolar cell
Surfactant
Type II alveolar cell
Normal gas exchange
Gas Exchange
Each sac of air, or alveolus, is wrapped with capillaries where red blood cells release carbon dioxide (CO_2) and pick up oxyg (O_2). Two alveolar cells facilitat gas exchange; Type I cells are thin enough that the oxygen passes right through, and Type cells secrete surfactant – a subtsance that lines the alveolu and prevents it from collapsing.
Infected
SARS-CoV-2 Structure
Membrane protein
Nucleoplasmid (enclosed RNA)
Lipid membrane
Envelope protein
Spike protein
Viral Infection
The spike proteins covering the coronavirus bind ACE2 receptors primarily on type II alveolar cells, allowing the virus to inject its RNA. The RNA "hijacks" the cell, telling it to assemble many more copies of the virus and release them into the alveolus. The host cell is destroyed in this process and the new coronaviruses infect neighbouring cells.
Moderate
Vasodilation (increase permeability)
Macrophage
Alveolus
Cytokines
CO_2
O_2
Fluid
Inflammatory signals
Reduced surfactant
Infected Type II alveolar cell
Reduced gas exchange
Severe
Fluid-filled interstitium
Protein-rich fluid
Loss of surfactant
Neutrophil
CO_2
O_2
Protein and cellular debris
Formation of scar tissue
Greatly hindered gas exchange
Impaired Gas Exchange
When the immune system attacks the area of infection it also kills healthy alveolar cells. This results in three things that hinder gas exchange:
1) Alveolar collapse due to loss of surfactant from Type II cells
2) Less oxygen enters the bloodstream due to lack of Type I cells
3) More fluid enters the alveolus
Stay Home
Symptoms may start to show (e.g. dry cough, fever, etc.)
Pneumonia develops
Shortness of breath
Hospitalization
Dangerous for high-risk individuals; secondary infections may occur
Intensive Care (ICU)
Patients may require ventilators and life-support
Complications unrelated to COVID-19 may occur
With proper care, patients may recover at any point during this process
Immune Response
1 After infection, Type II cells release inflammatory signals that recruit macrophages (immune cells).
2 Macrophages release cytokines that cause vasodilation, which allows more immune cells to come to the site of injury and exit the capillary.
3 Fluid accumulates inside the alveolus.
4 The fluid dilutes the surfactant which triggers the onset of alveolar collapse, decreasing gas exchange and increasing the work of breathing.
5 Neutrophils are recruited to the site of infection and release Reactive Oxygen Species (ROS) to destroy infected cells.
6 Type I and II cells are destroyed, leading to the collapse of the alveolus and causing Acute Respiratory Distress Syndrome (ARDS).
7 If inflammation becomes severe, the protein-rich fluid can enter the bloodstream and travel elsewhere in the body, causing Systemic Inflammatory Response Syndrome (SIRS).
8 SIRS may lead to septic shock and multi-organ failure, which can have fatal consequences.


HEALTHY AIR SAC
INFECTED AIR SAC
Fluid


Pneumonia

COVID-19's damaging effects on the body

Growing evidence suggests that the coronavirus, mostly known to cause respiratory illness, can also affect many of the body's primary organs.



Brain

People with COVID-19 have had strokes and seizures. Some have reported confusion or delirium. Not directly involving the brain but a central nervous issue: Many patients have reported losing their sense of smell.

Heart

Doctors have reported inflammation to the heart and damage to the muscle. Some patients have died from severe heart attacks.

Lungs

The virus can cause pneumonia, in which the lungs become inflamed and fill with fluid. Patients may require ventilation. As the infection progresses, the virus can cause serious lung damage, which can be fatal.

Blood vessels

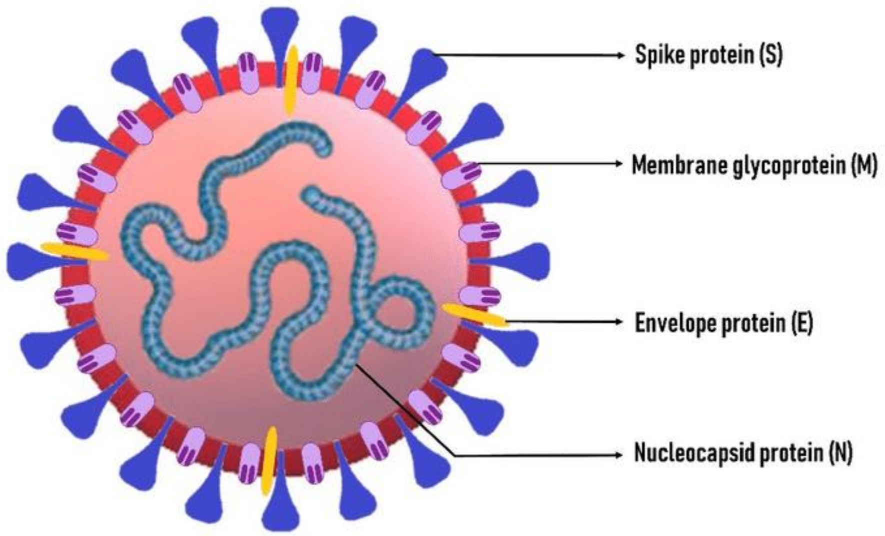
Blood clotting in major arteries and veins has been reported. Clots can break off and damage multiple organs by stopping blood flow.

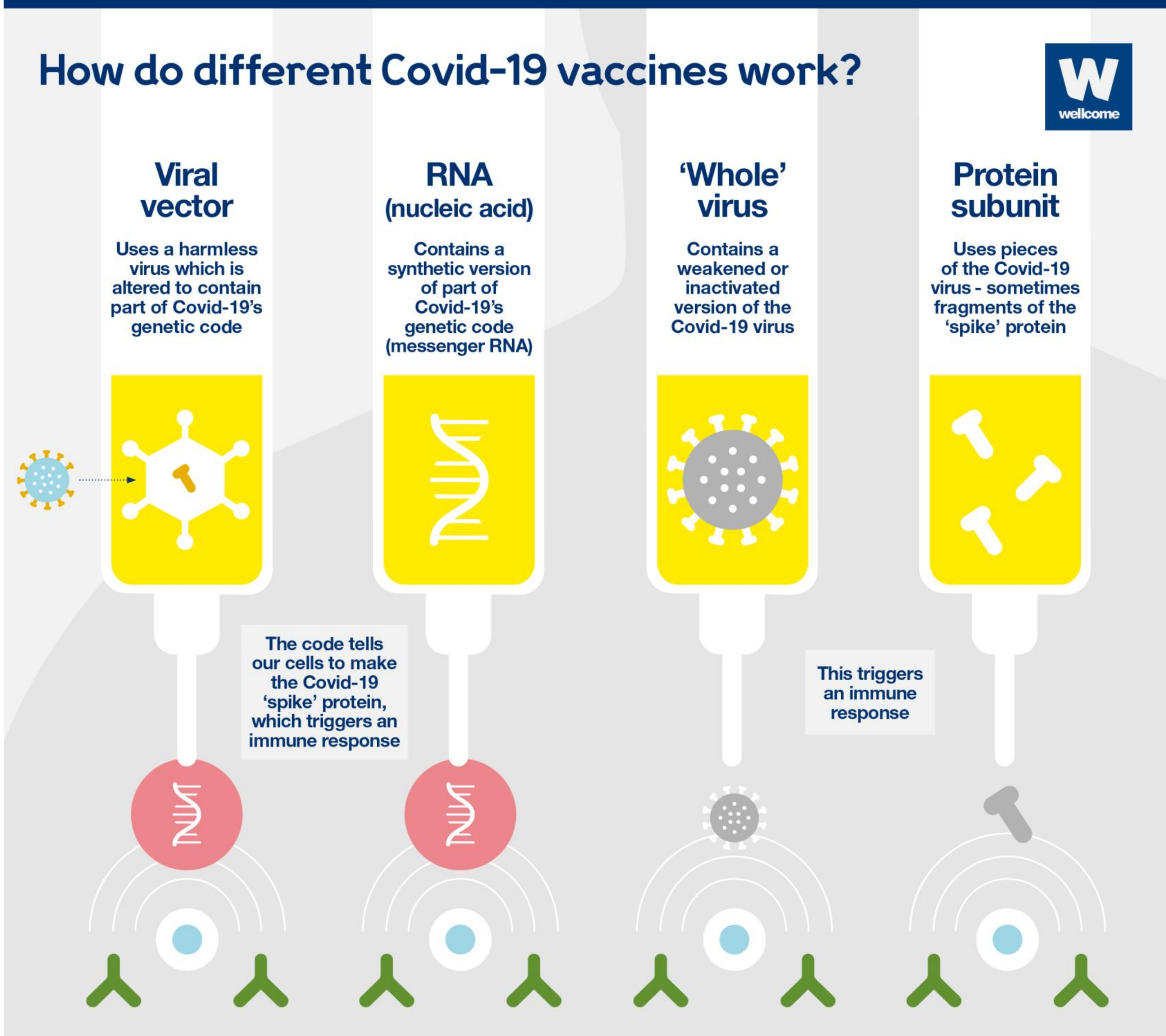
Kidneys

Many COVID-19 patients suffer serious kidney damage and require dialysis.

Intestines

Roughly 20% of patients report diarrhea as an early symptom. The virus has been found in the lower intestinal tract of some patients.


Spike protein (S)
Membrane glycoprotein (M)
Envelope protein (E)
Nucleocapsid protein (N)


How do different Covid-19 vaccines work?
wellcome
Viral vector
Uses a harmless virus which is altered to contain part of Covid-19's genetic code
RNA (nucleic acid)
Contains a synthetic version of part of Covid-19's genetic code (messenger RNA)
'Whole' virus
Contains a weakened or inactivated version of the Covid-19 virus
Protein subunit
Uses pieces of the Covid-19 virus - sometimes fragments of the 'spike' protein
The code tells our cells to make the Covid-19 'spike' protein, which triggers an immune response
This triggers an immune response

COVID VACCINES: PEER COMPARISON

VACCINE	SPUTNIK V	COVISHIELD	COVAXIN
DEVELOPED BY	RDIF	ASTRAZENECA	BHARAT BIOTECH
INDIAN MANUFACTURER	DRL, MANKIND, HETERO	SERUM INSTITUTE OF INDIA	BHARAT BIOTECH
TECHNOLOGY	USES TWO MODIFIED HUMAN ADENOVIRUS VECTOR	USES CHIMPANZEE ADENOVIRUS VECTOR	INACTIVATED VACCINE USING THE VIRUS STRAIN