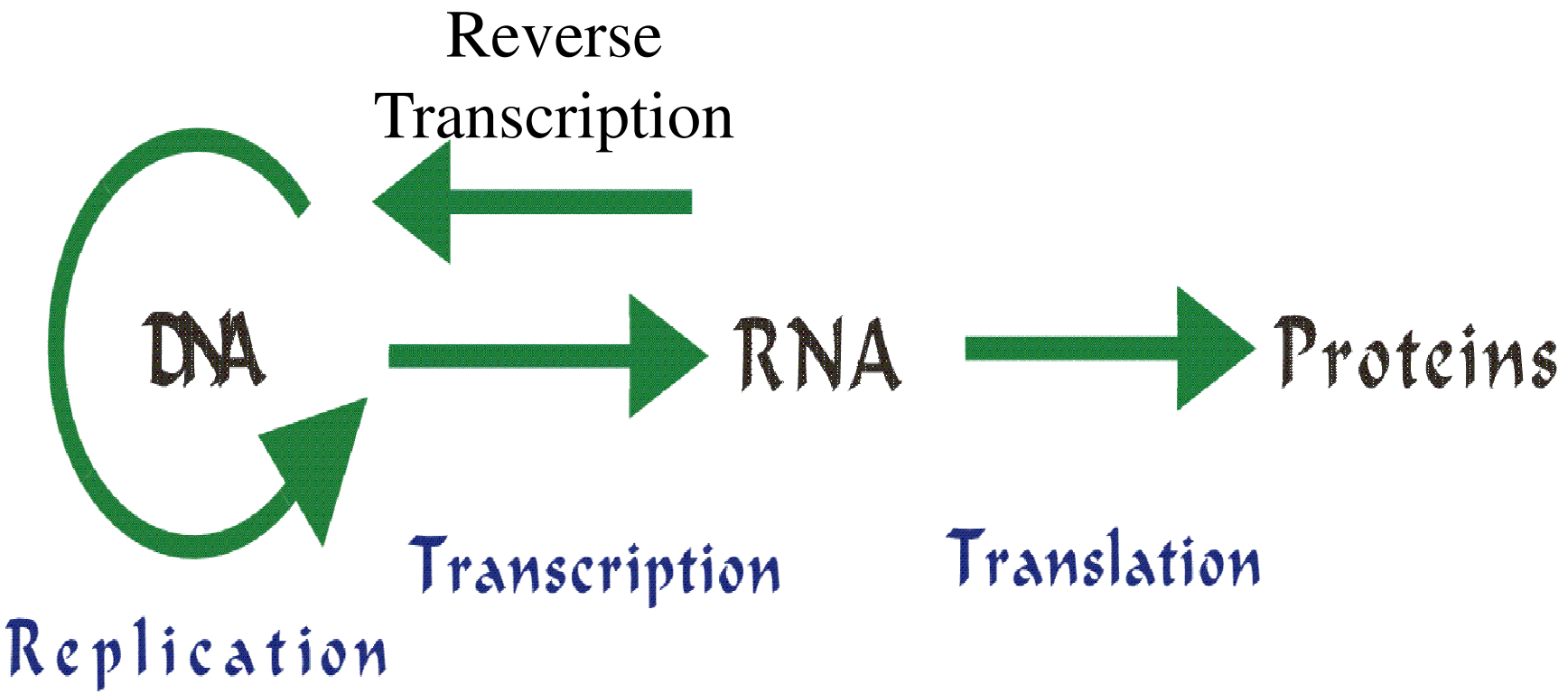
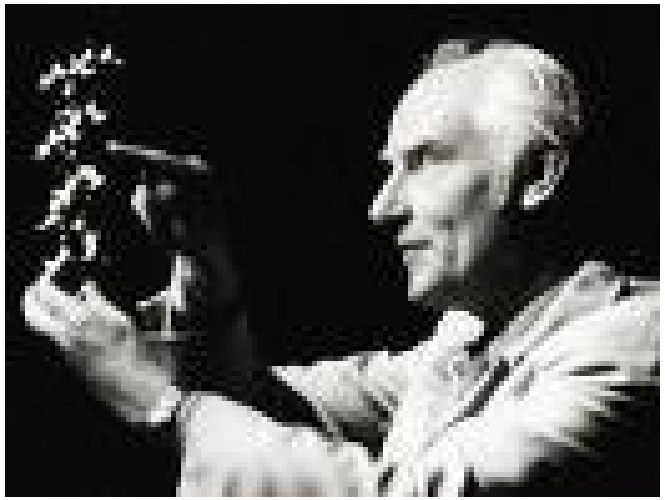
Central Dogma



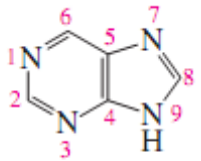
Central Dogma of Molecular Biology

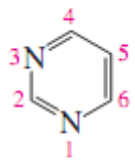
"The central dogma deals with the detailed residue-by-residue transfer of sequential information. It states that such information cannot be transferred back from protein to either protein or nucleic acid."



Francis Crick, 1958

Bases


purine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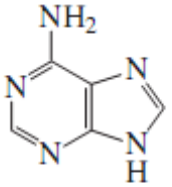
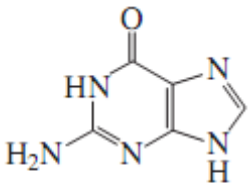

adenine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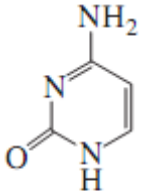
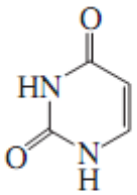
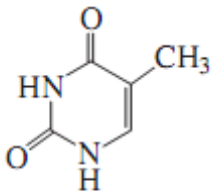
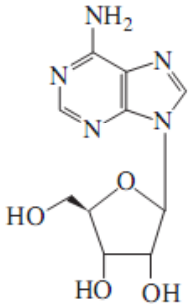
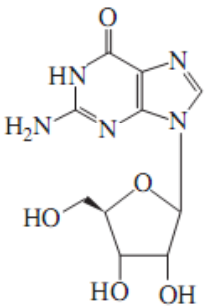

cytosine


uracil


thymine

nucleosides


adenosine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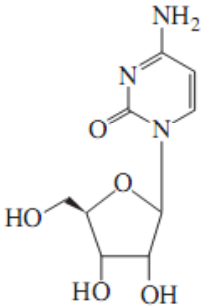
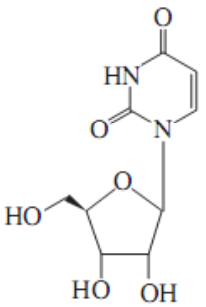
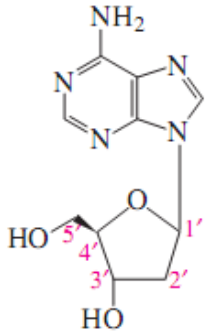
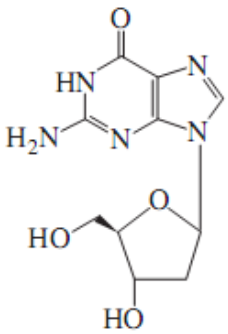

cytidine


uridine

Nucleosides


2′-deoxyadenosine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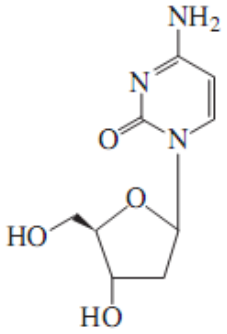
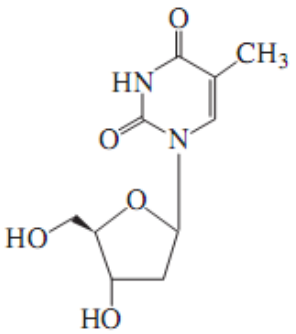
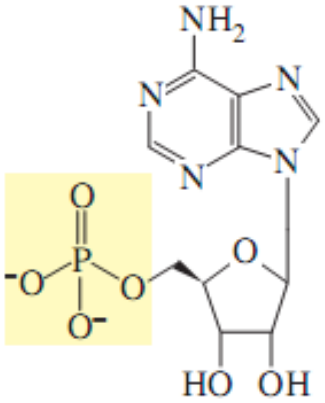
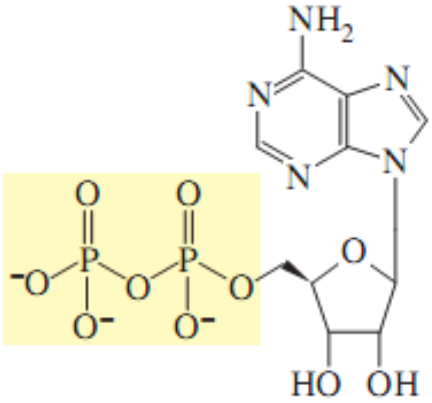

2′-deoxycytidine


thymidine

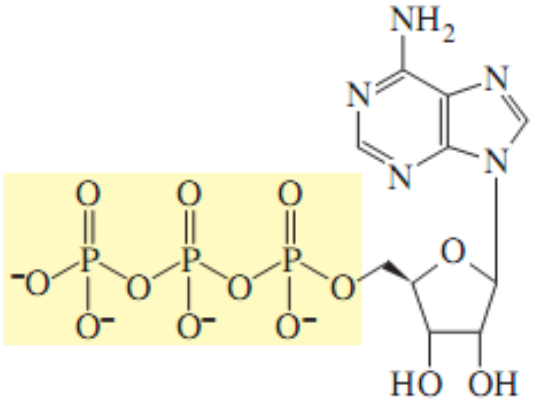
Nucleotides



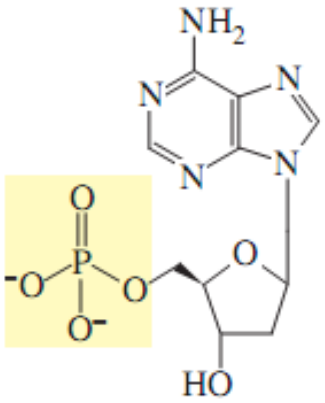
adenosine
5′-monophosphate
AMP



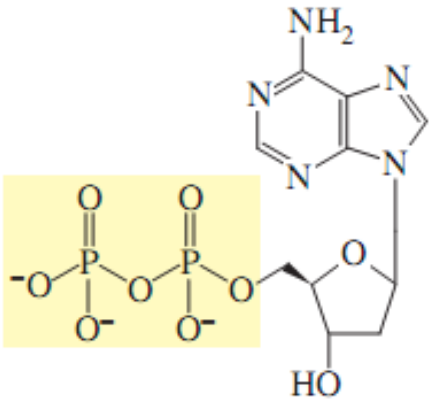
adenosine
5′-diphosphate
ADP



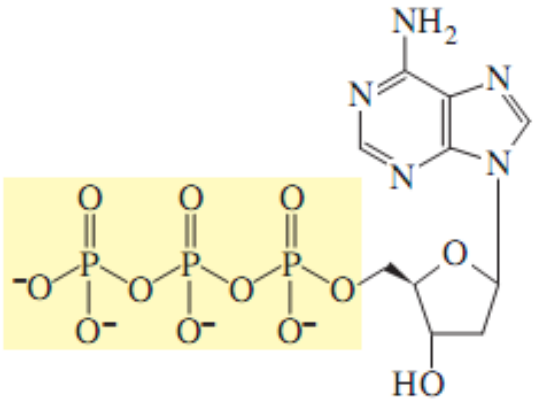
adenosine
5′-triphosphate
ATP



2′-deoxyadenosine
5′-monophosphate
dAMP

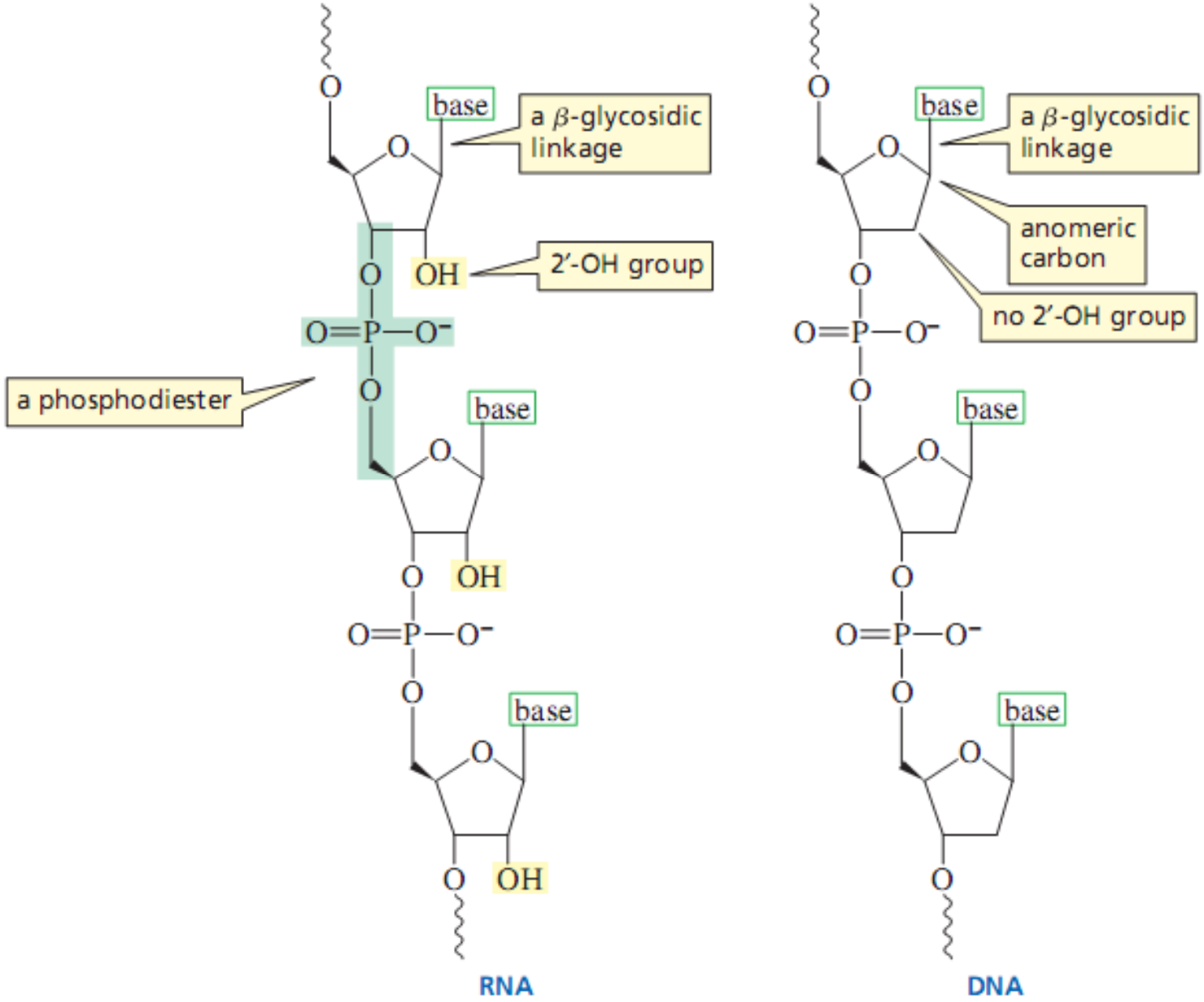


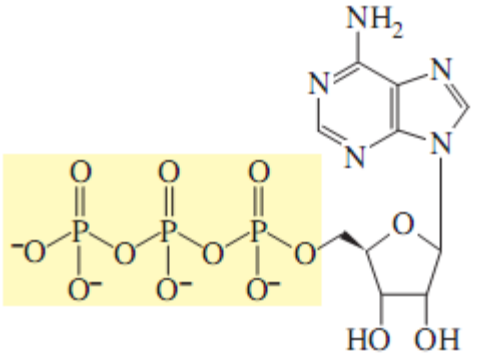
2′-deoxyadenosine
5′-diphosphate
dADP



2′-deoxyadenosine
5′-triphosphate
dATP

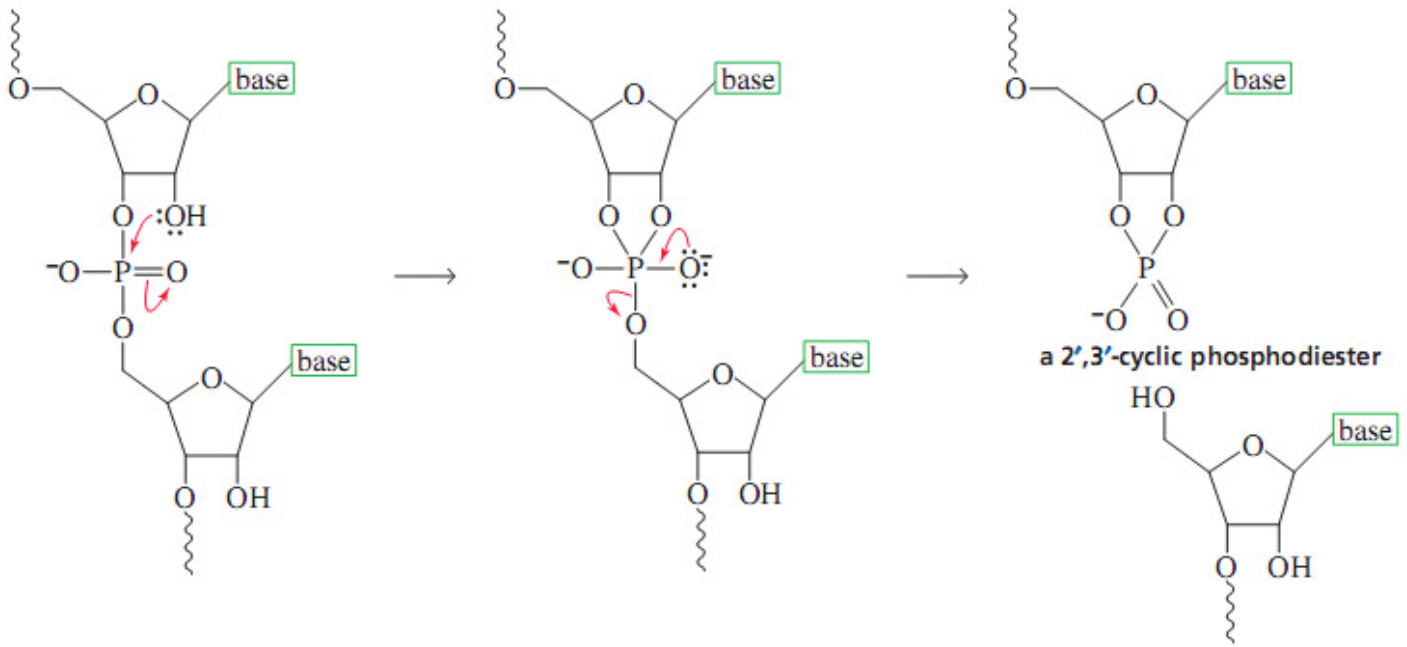
Nucleicacids





27.2 ATP: The Carrier of Chemical Energy

All cells require energy to ensure their survival and reproduction. They get the energy they need by converting nutrients into a chemically useful form of energy. The most important form of chemical energy is adenosine 5′-triphosphate (ATP). The importance of ATP to biological reactions is shown by its turnover rate in humans—each day, a person uses an amount of ATP equivalent to his or her body weight. ATP is known as the universal carrier of chemical energy because, as it is commonly stated, "the energy of hydrolysis of ATP converts endergonic reactions into exergonic reactions."



PROBLEM 11

The 2′,3′-cyclic phosphodiester, which is formed when RNA is hydrolyzed (Figure 27.8), reacts with water, forming a mixture of nucleotide 2′- and 3′-phosphates. Propose a mechanism for this reaction.

PROBLEM 12◆

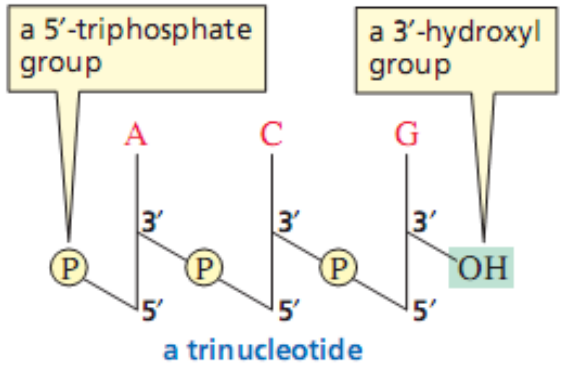
If one of the strands of DNA has the following sequence of bases running in the 5′ ⟶ 3′ direction,

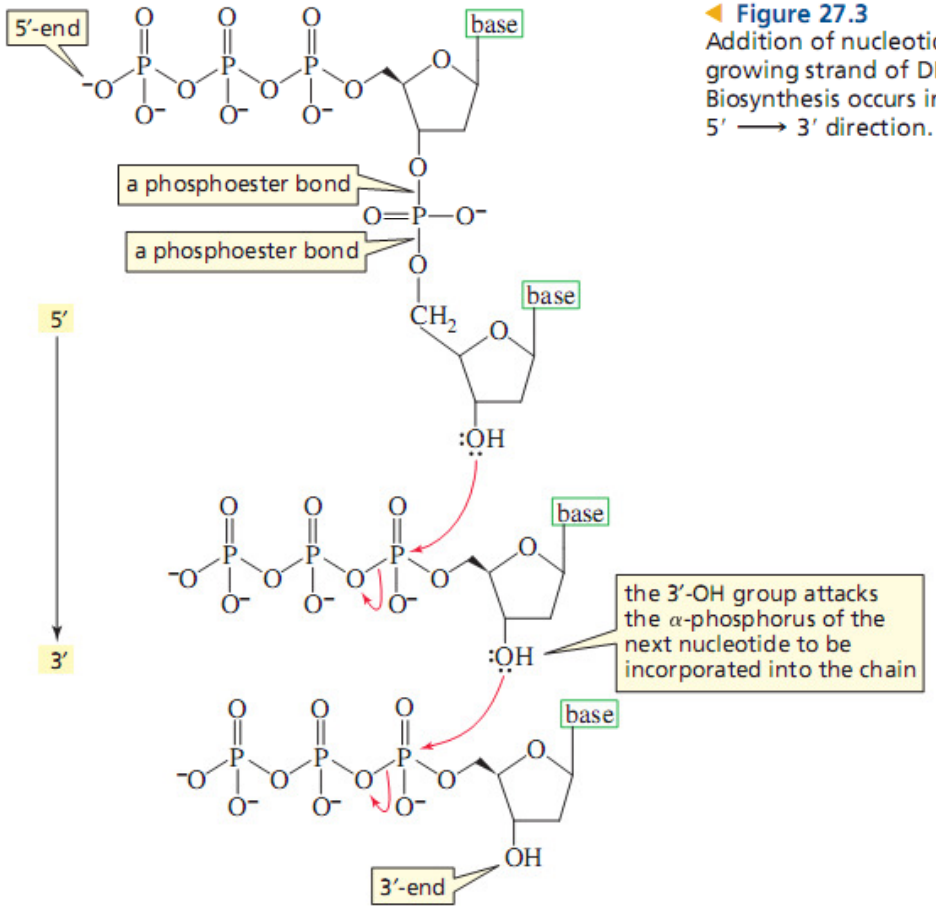
5′—G—G—A—C—A—A—T—C—T—G—C—3′

a. What is the sequence of bases in the complementary strand?

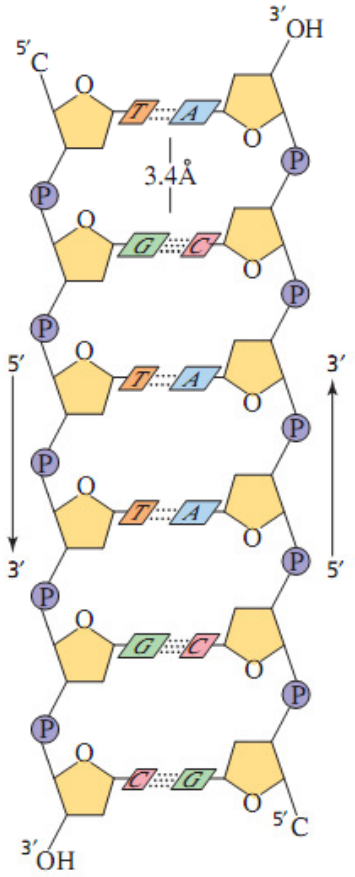
b. What base is closest to the 5′-end in the complementary strand?

The Nucleic Acids



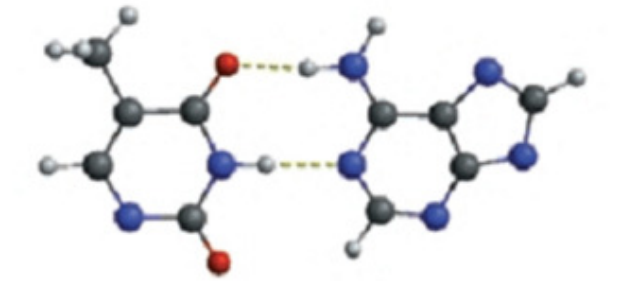


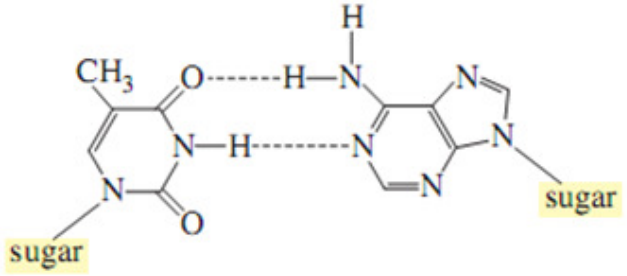
◀ **Figure 27.3**
Addition of nucleotides to a growing strand of DNA. Biosynthesis occurs in the 5′ ⟶ 3′ direction.



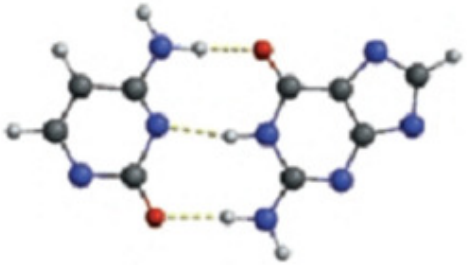
▲ **Figure 27.4**

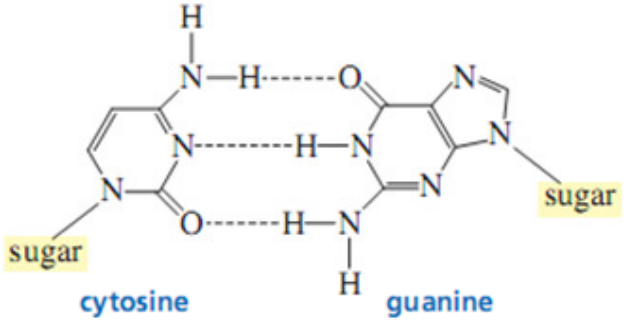
Base Pairing



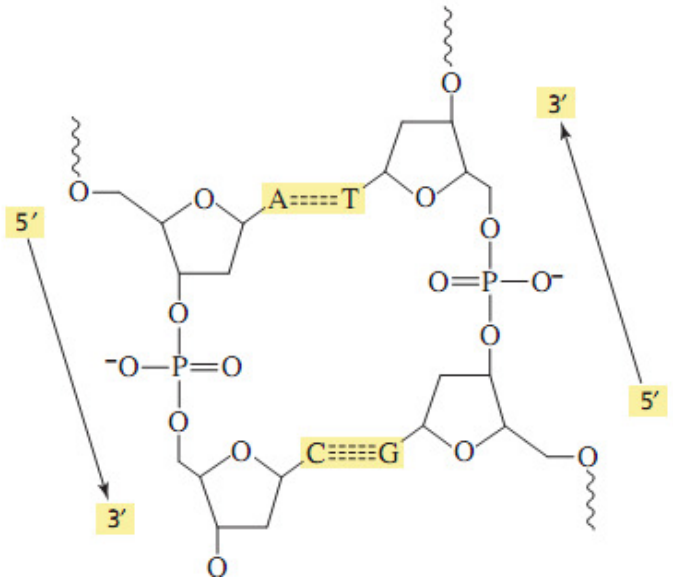


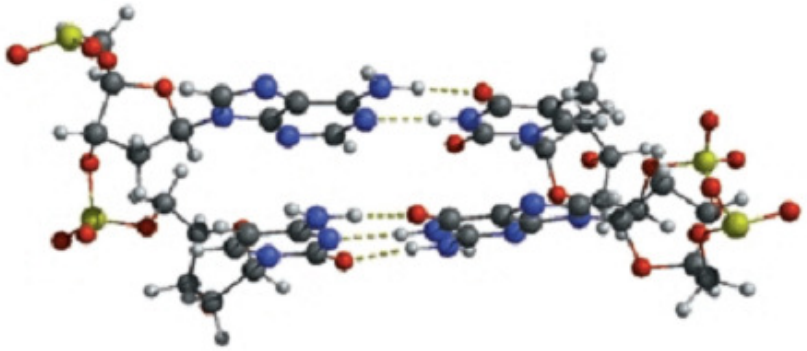
thymine adenine





cytosine guanine





ATGAGCCATGTAGCCTAATCGGC

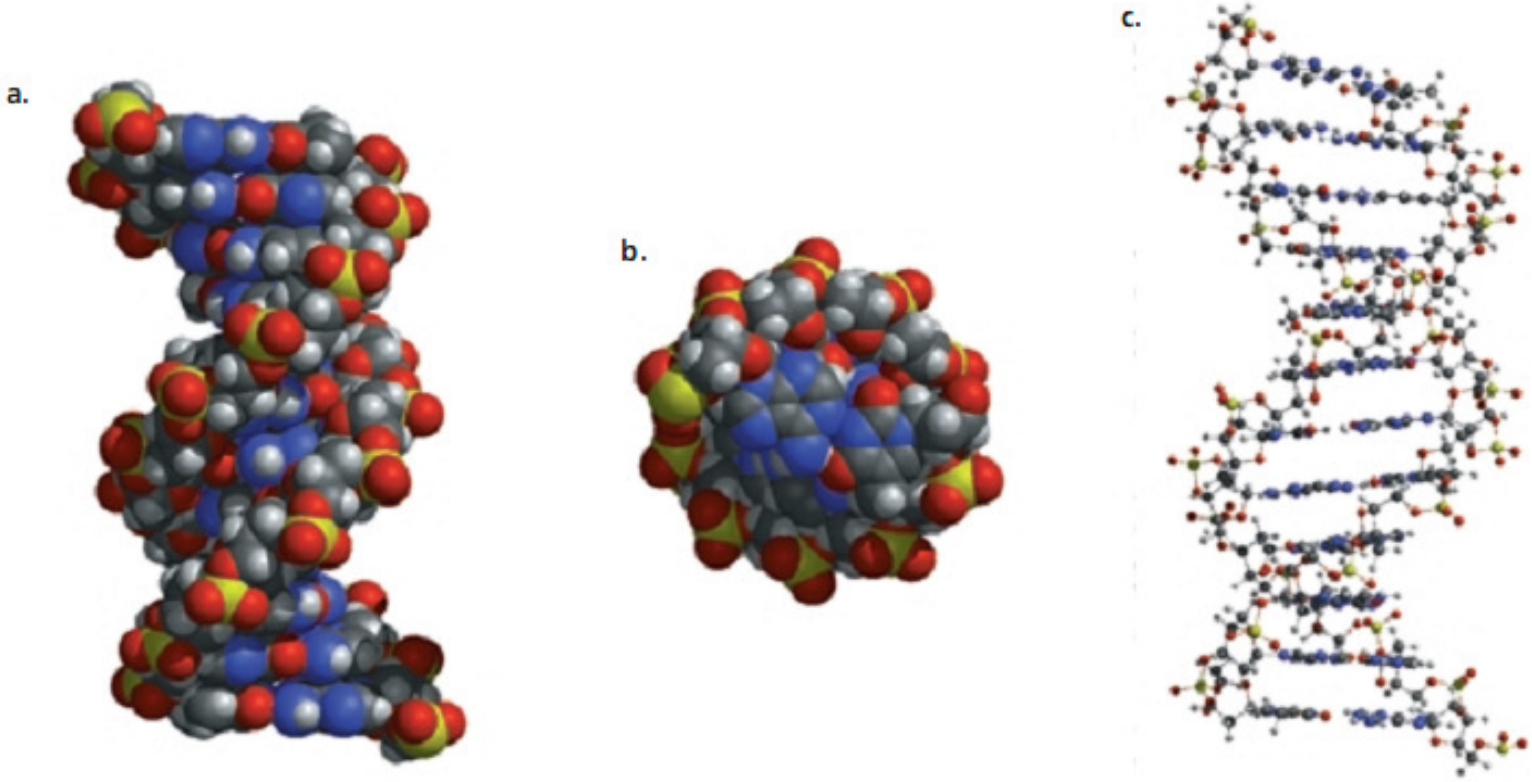
5′-end

3′-end

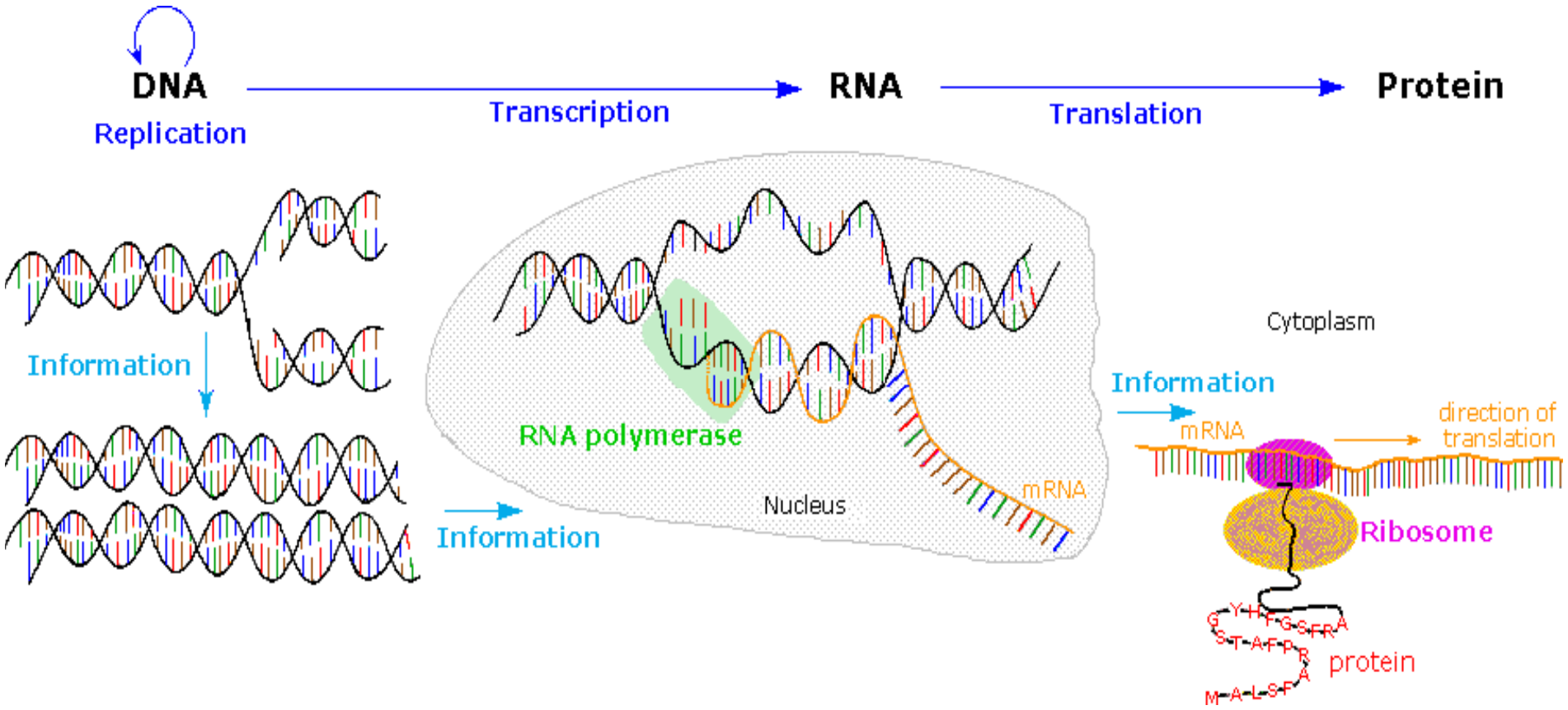
a.

b.

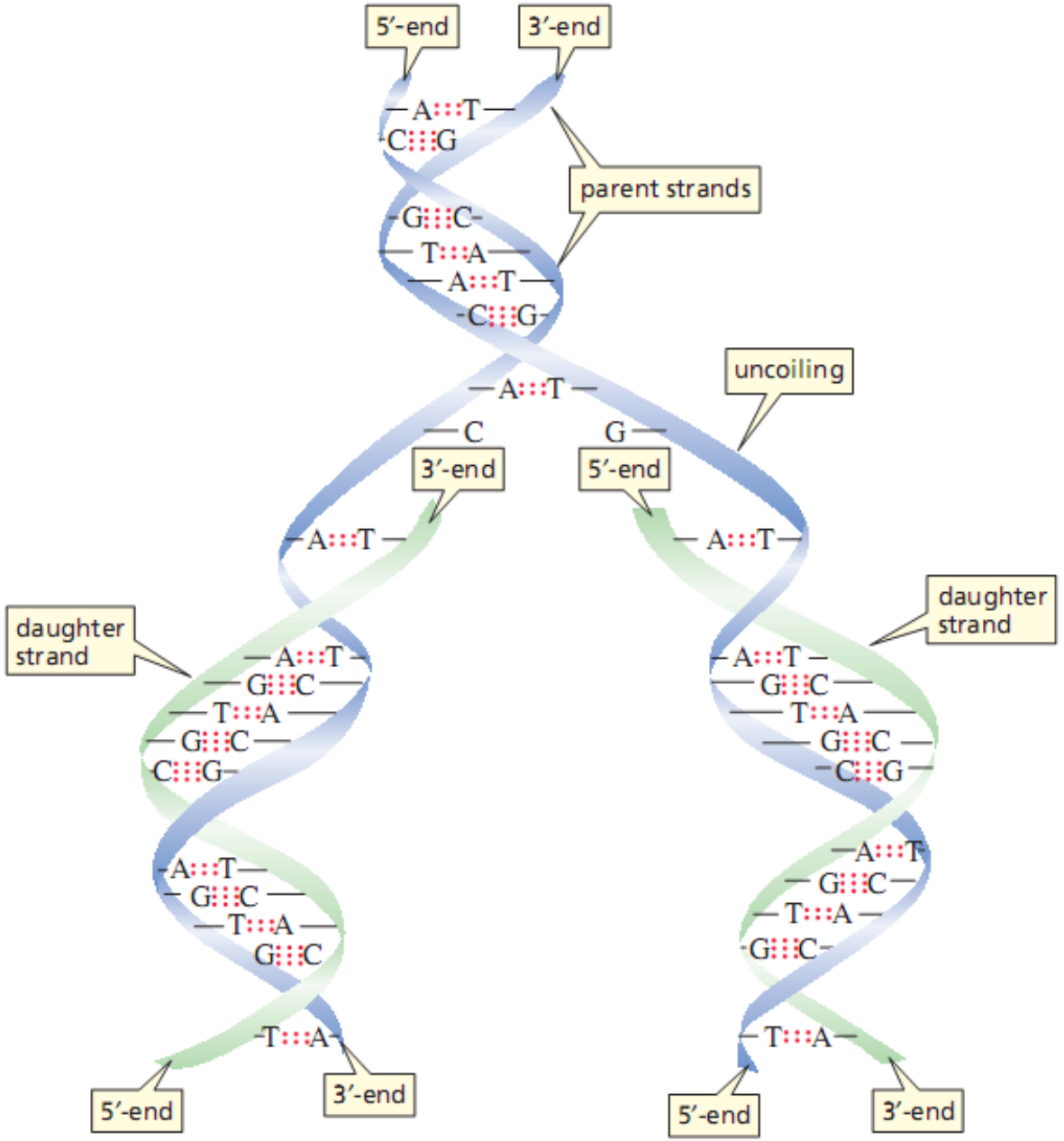
c.



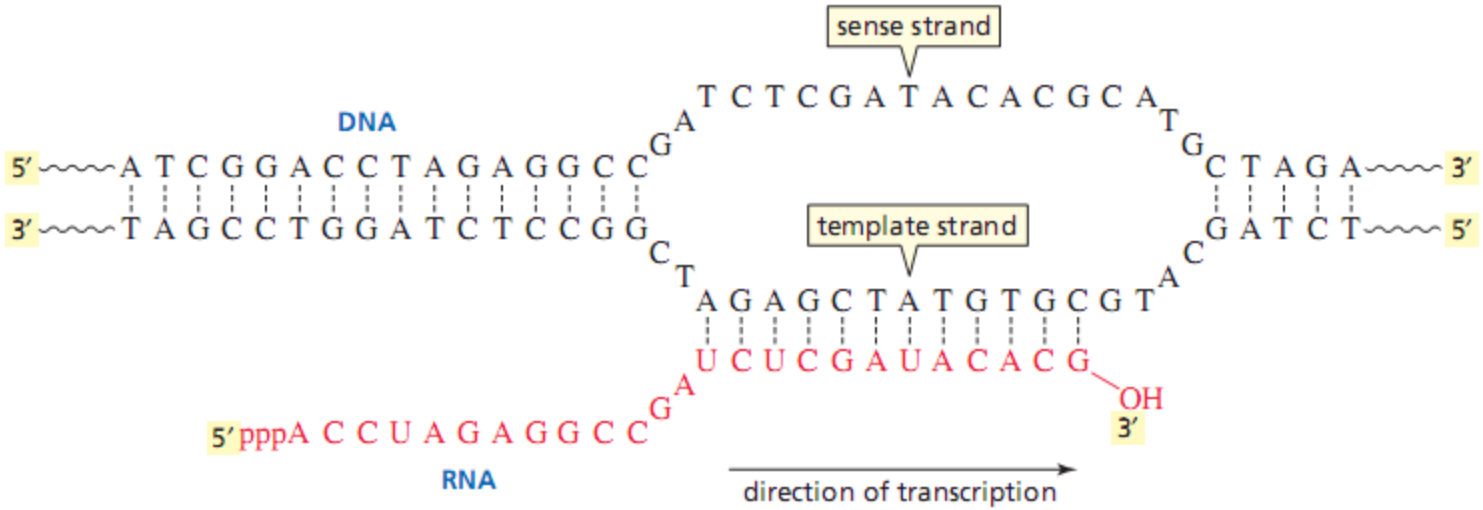
▲ **Figure 27.7**
(a) The DNA double helix. (b) View looking down the long axis of the helix. (c) The bases are planar and parallel on the inside of the helix.


DNA
Replication
Transcription
RNA
Translation
Protein
Information
Information
RNA polymerase
mRNA
Nucleus
Cytoplasm
Information
mRNA
direction of translation
Ribosome
protein

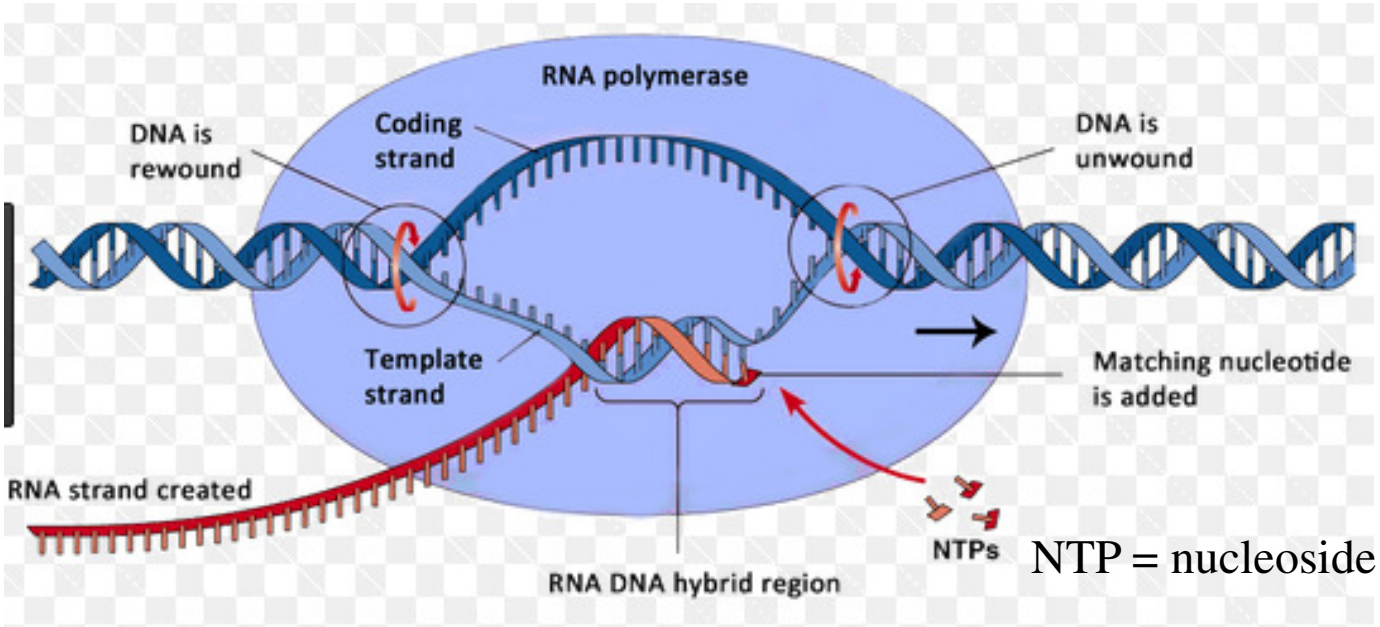
Biosynthesis of DNA: Replication



Biosynthesis of RNA: Transcription

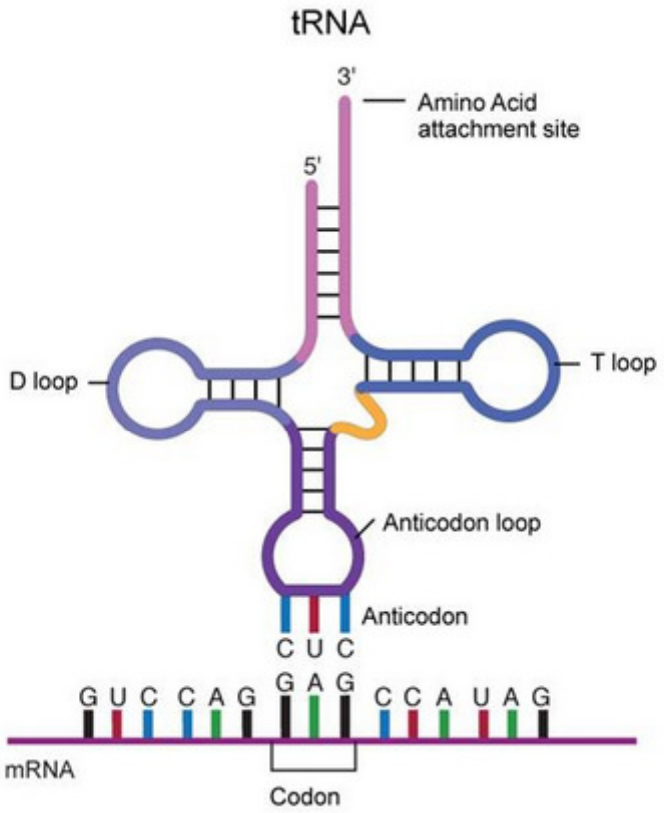


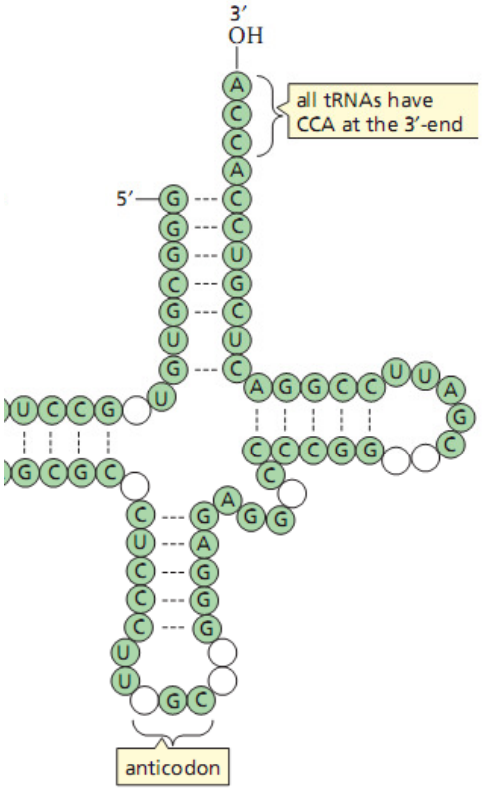
▲ **Figure 27.12**
Transcription: using DNA as a blueprint for RNA.



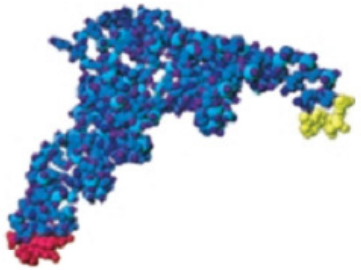
NTP = nucleoside triphosphates

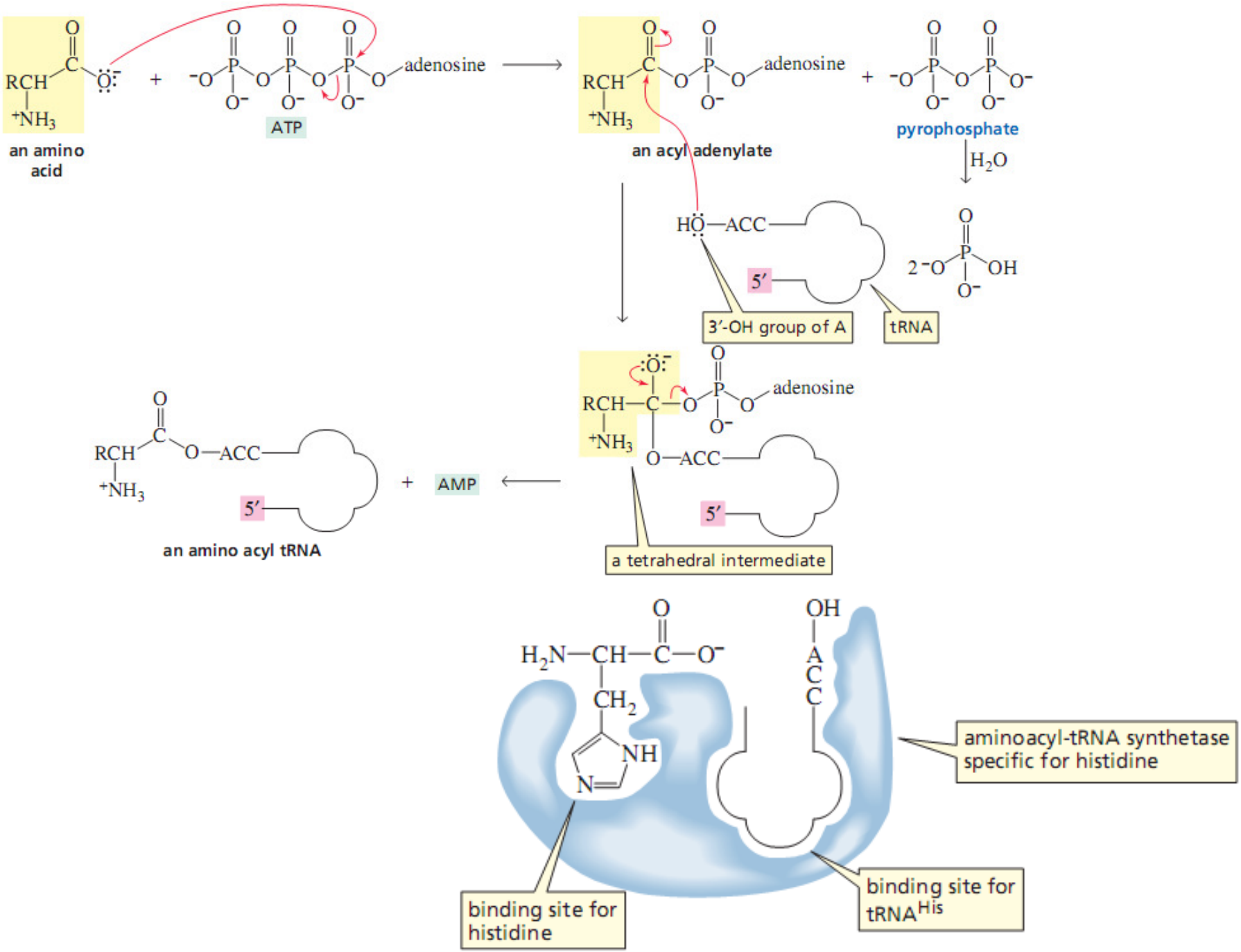
Transfer RNA



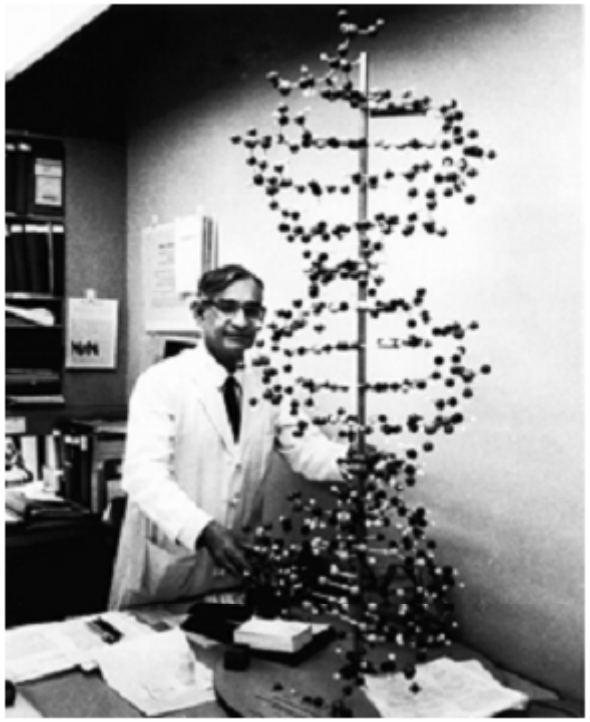


b.




an amino acid
ATP
adenosine
an acyl adenylate
pyrophosphate
H_2O
3′-OH group of A
tRNA
5′
a tetrahedral intermediate
AMP
an amino acyl tRNA
aminoacyl-tRNA synthetase specific for histidine
binding site for histidine
binding site for $tRNA^{His}$

Biosynthesis of Proteins: Translation



Har Gobind Khorana *was born in India in 1922. He received a bachelor's and a master's degree from Punjab University and a Ph.D. from the University of Liverpool. In 1960 he joined the faculty at the University of Wisconsin and later became a professor at MIT.*

Table 27.2 The Genetic Code

5′-Position	Middle position				5′-Position
	U	C	A	G	
U	Phe	Ser	Tyr	Cys	U
	Phe	Ser	Tyr	Cys	C
	Leu	Ser	Stop	Stop	A
	Leu	Ser	Stop	Trp	G
C	Leu	Pro	His	Arg	U
	Leu	Pro	His	Arg	C
	Leu	Pro	Gln	Arg	A
	Leu	Pro	Gln	Arg	G
A	Ile	Thr	Asn	Ser	U
	Ile	Thr	Asn	Ser	C
	Ile	Thr	Lys	Arg	A
	Met	Thr	Lys	Arg	G
G	Val	Ala	Asp	Gly	U
	Val	Ala	Asp	Gly	C
	Val	Ala	Glu	Gly	A
	Val	Ala	Glu	Gly	G

Translation is the process by which the genetic message in DNA that has been passed to mRNA is decoded and used to build proteins. Each of the approximately 100,000 proteins in the human body is synthesized from a different mRNA. Don't

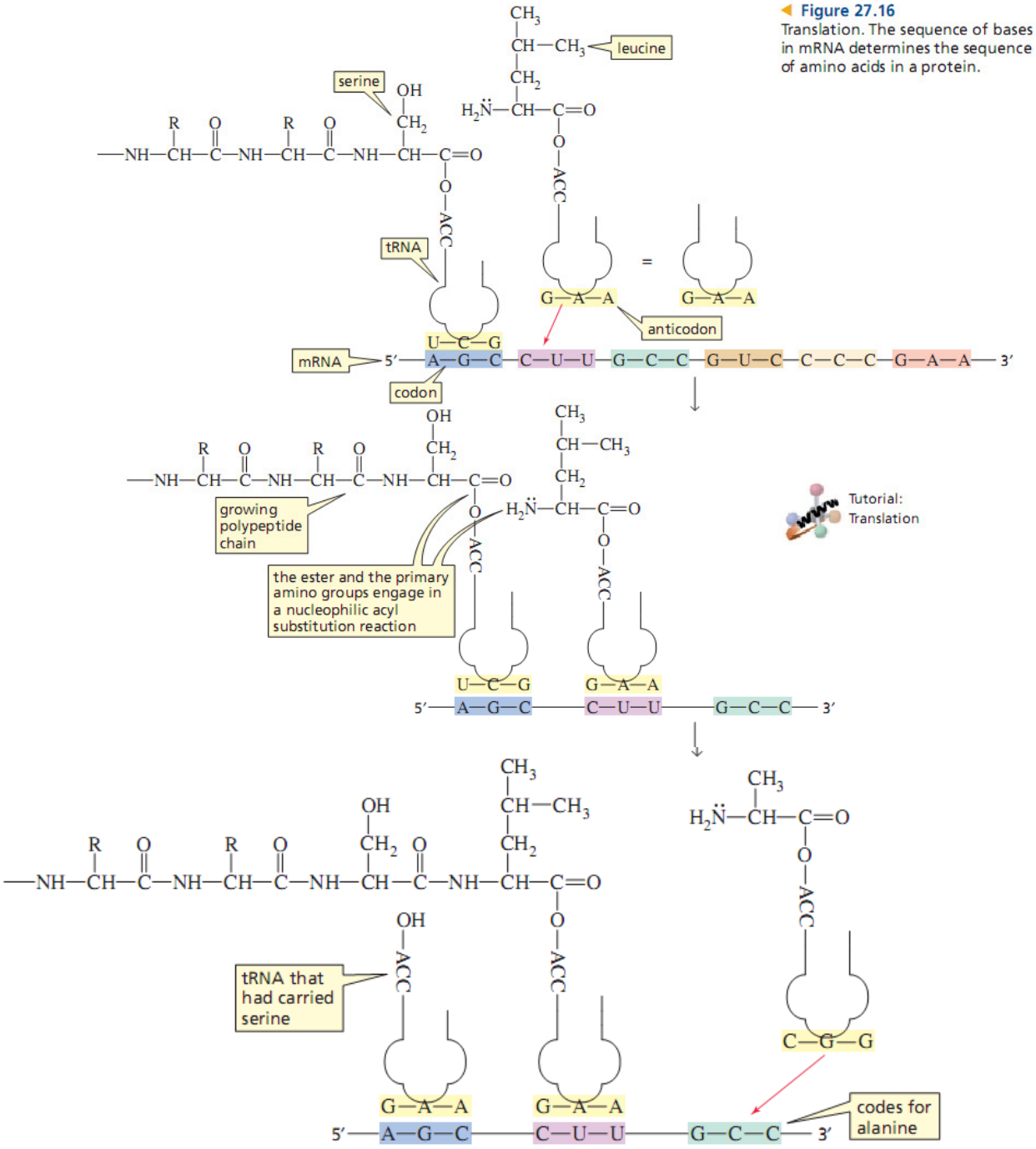
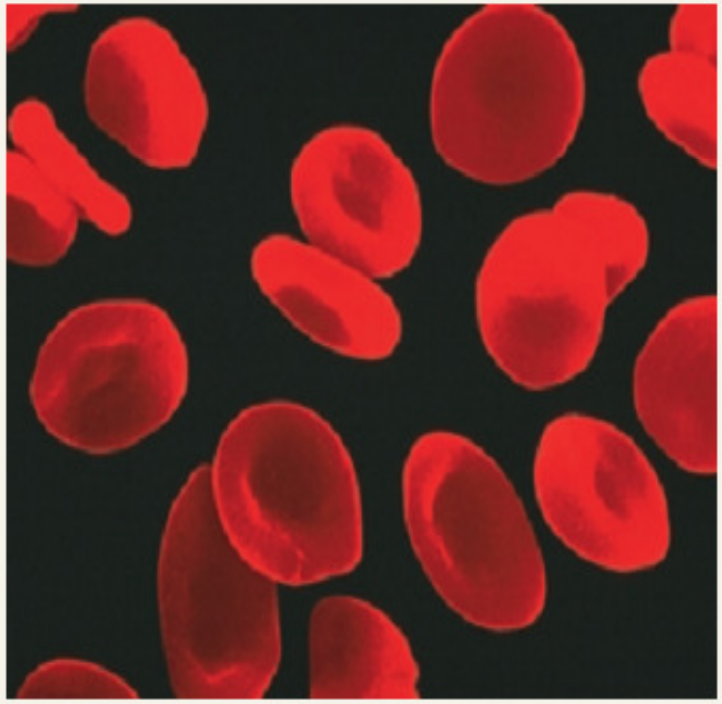


Figure 27.16
Translation. The sequence of bases in mRNA determines the sequence of amino acids in a protein.

SICKLE CELL ANEMIA

Sickle cell anemia is an example of the damage that can be caused by a change in a single base of DNA (Problem 55 in Chapter 23). It is a hereditary disease caused when a GAG triplet becomes a GTG triplet in the sense strand of a section of DNA that codes for the β-subunit of hemoglobin. As a consequence, the mRNA codon becomes GUG—which signals for incorporation of valine—rather than GAG, which would have signaled for incorporation of glutamic acid. The change from a polar glutamic acid to a nonpolar valine is sufficient to change the shape of the deoxyhemoglobin molecule and induce aggregation, causing it to precipitate in red blood cells. This stiffens the cells, making it difficult for them to squeeze through a capillary. Blocked capillaries cause severe pain and can be fatal.

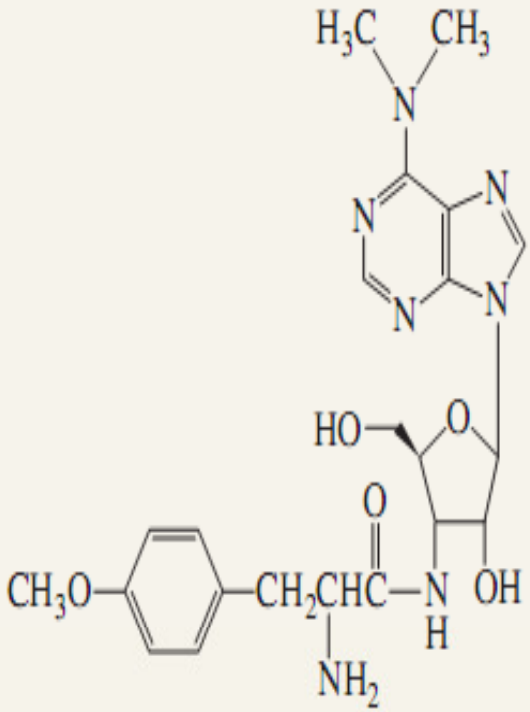


Normal red blood cells

Sickle red blood cells

ANTIBIOTICS THAT ACT BY INHIBITING TRANSLATION

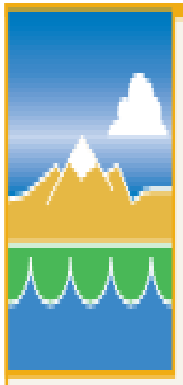
Puromycin is a naturally occurring antibiotic. It is one of several antibiotics that act by inhibiting translation. Puromycin mimics the 3′-CCA-aminoacyl portion of a tRNA. If, during translation, the enzyme is fooled into transferring the growing peptide chain to the amino group of puromycin rather than to the amino group of the incoming 3′-CCA-aminoacyl tRNA, protein synthesis stops. Because puromycin blocks protein synthesis in eukaryotes as well as in prokaryotes, it is poisonous to humans and therefore is not a clinically useful antibiotic. To be clinically useful, an antibiotic must affect protein synthesis only in prokaryotic cells.



puromycin

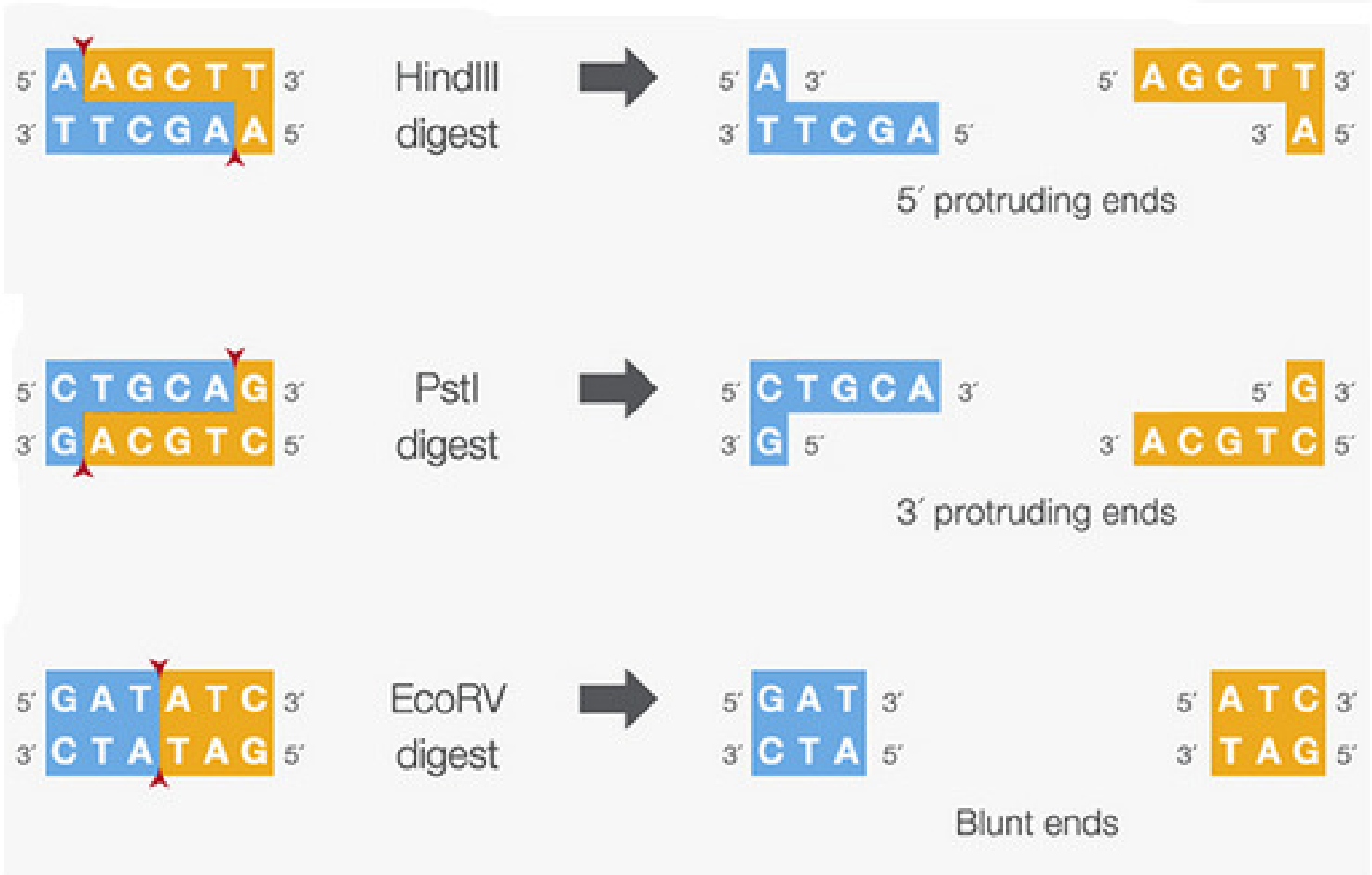
Clinically useful antibiotics	Mode of action
Tetracycline	Prevents the aminoacyl-tRNA from binding to the ribosome
Erythromycin	Prevents the incorporation of new amino acids into the protein
Streptomycin	Inhibits the initiation of protein synthesis
Chloramphenicol	Prevents the new peptide bond from being formed

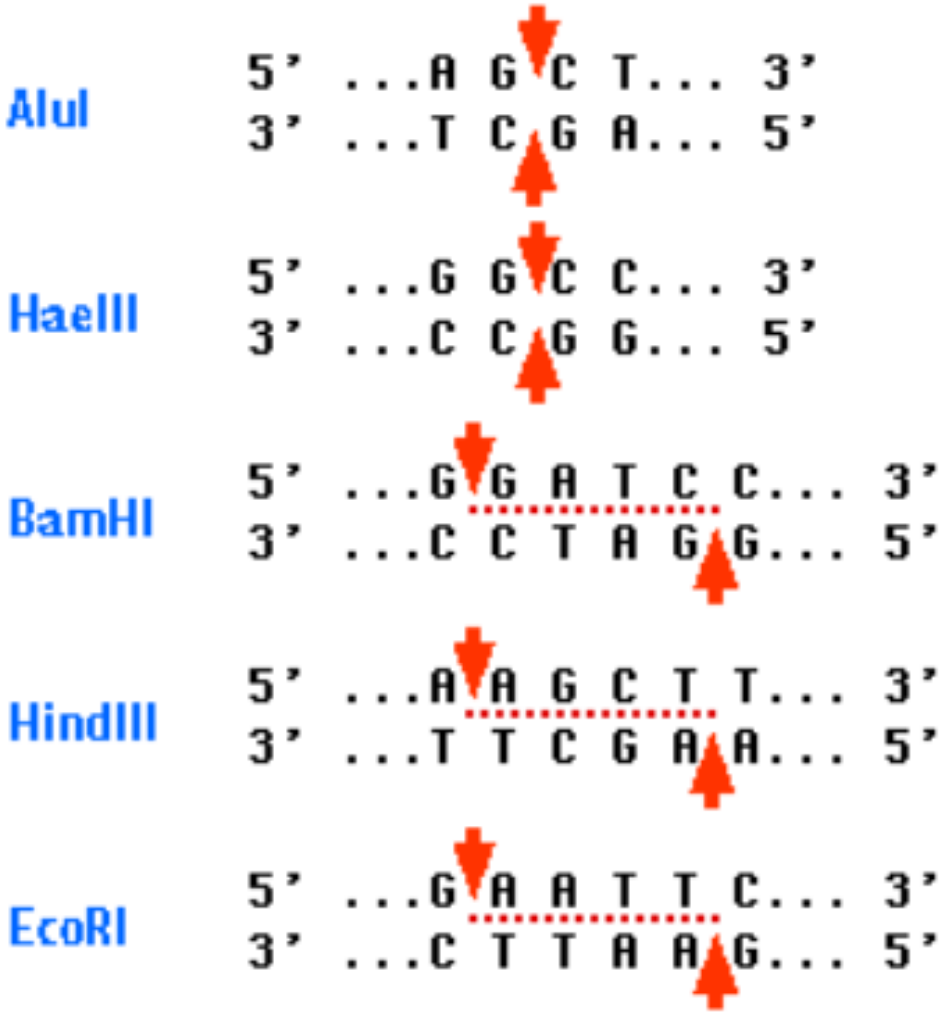
Prokaryotic and Eukaryotic



DNA FINGERPRINTING

The base sequence of the human genome varies from individual to individual, generally by a single base change every few hundred base pairs. Because some of these changes occur in base sequences recognized by restriction endonucleases, the fragments formed when human DNA reacts with a particular restriction endonuclease vary in size depending on the individual. It is this variation that forms the basis of DNA fingerprinting (also called DNA profiling or DNA typing). This technique is used by forensic chemists to compare DNA samples collected at the scene of a crime with the DNA of the suspected perpetrator. The most powerful technique for DNA identification analyzes restriction fragment length polymorphisms (RFLPs) obtained from regions of DNA in which individual variations are most common. This technique takes four to six weeks and requires a blood stain about the size of a dime. The chance of identical results from two different persons is thought to be one in a million. The second type of DNA profiling uses a polymerase chain reaction (PCR), which amplifies a specific region of DNA and compares differences at that site among individuals. This technique can be done in less than a week and requires only 1% of the amount required for RFLP, but does not discriminate as well among individuals. The chance of identical results from two different people is 1 in 500 to 1 in 2000. DNA fingerprinting is also being used to establish paternity, accounting for about 100,000 DNA profiles a year.

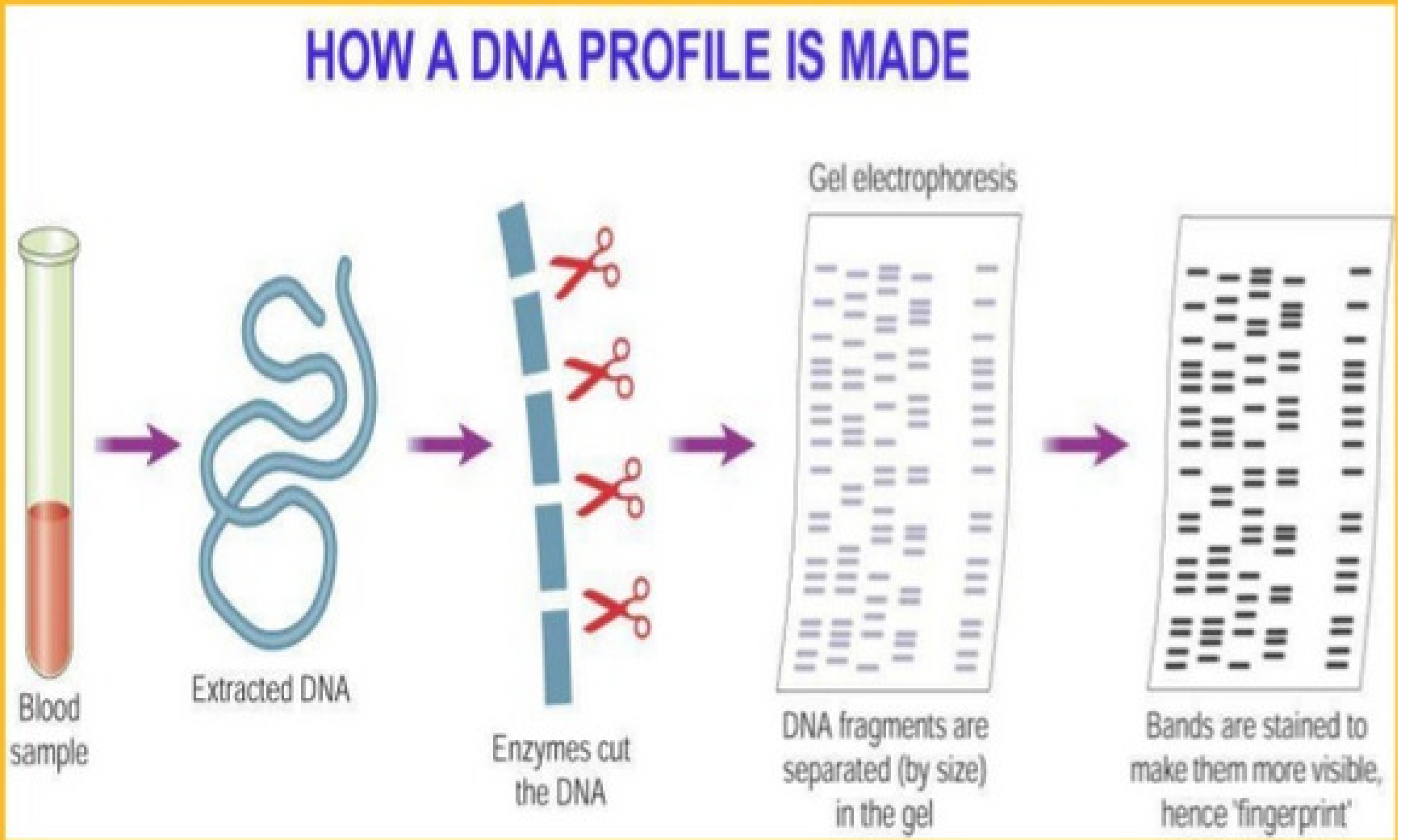

5′ A A G C T T 3′
3′ T T C G A A 5′
HindIII
digest
5′ A 3′
3′ T T C G A 5′
5′ A G C T T 3′
3′ A 5′
5′ protruding ends
5′ C T G C A G 3′
3′ G A C G T C 5′
PstI
digest
5′ C T G C A 3′
3′ G 5′
5′ G 3′
3′ A C G T C 5′
3′ protruding ends
5′ G A T A T C 3′
3′ C T A T A G 5′
EcoRV
digest
5′ G A T 3′
3′ C T A 5′
5′ A T C 3′
3′ T A G 5′
Blunt ends



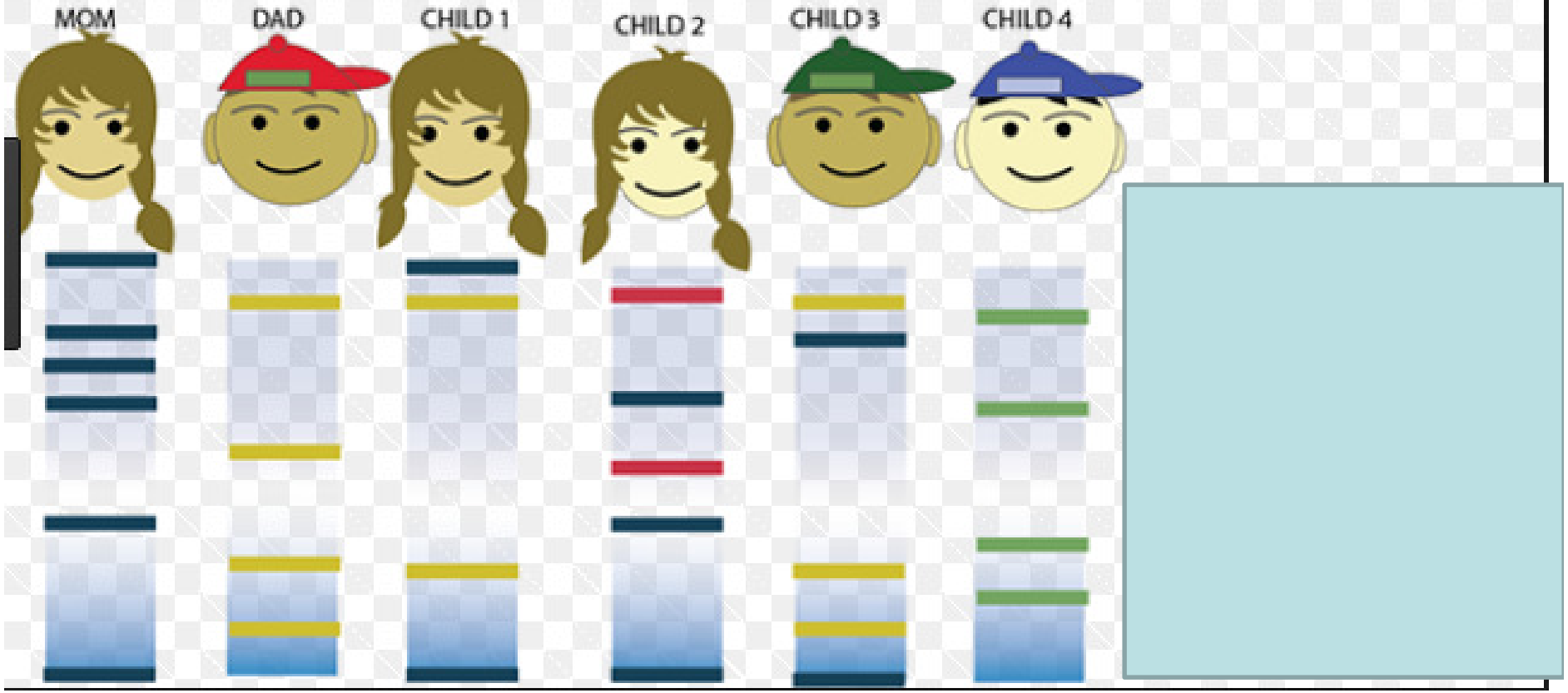
AluI and **HaeIII** produce blunt ends

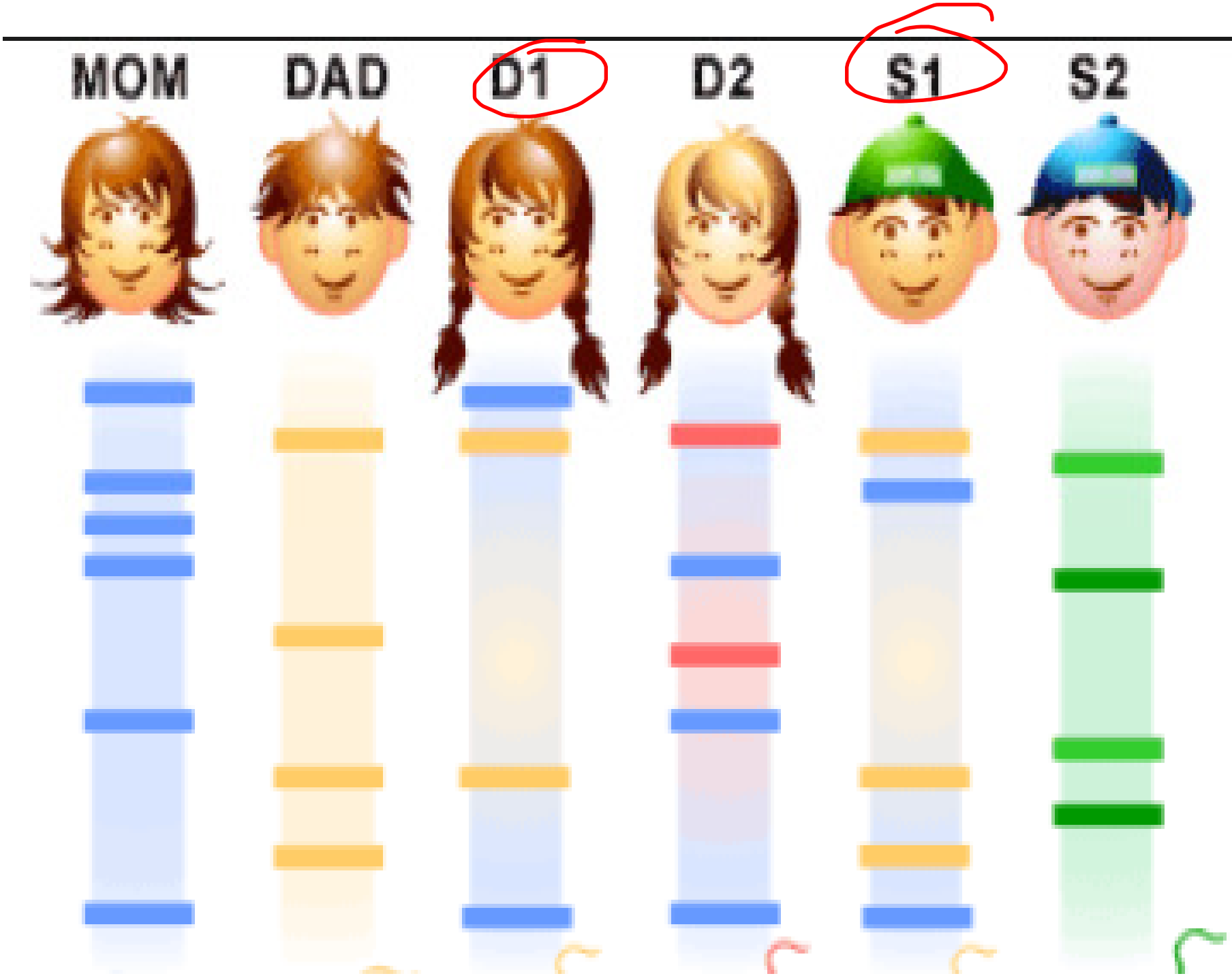
BamHI **HindIII** and **EcoRI** produce "sticky" ends

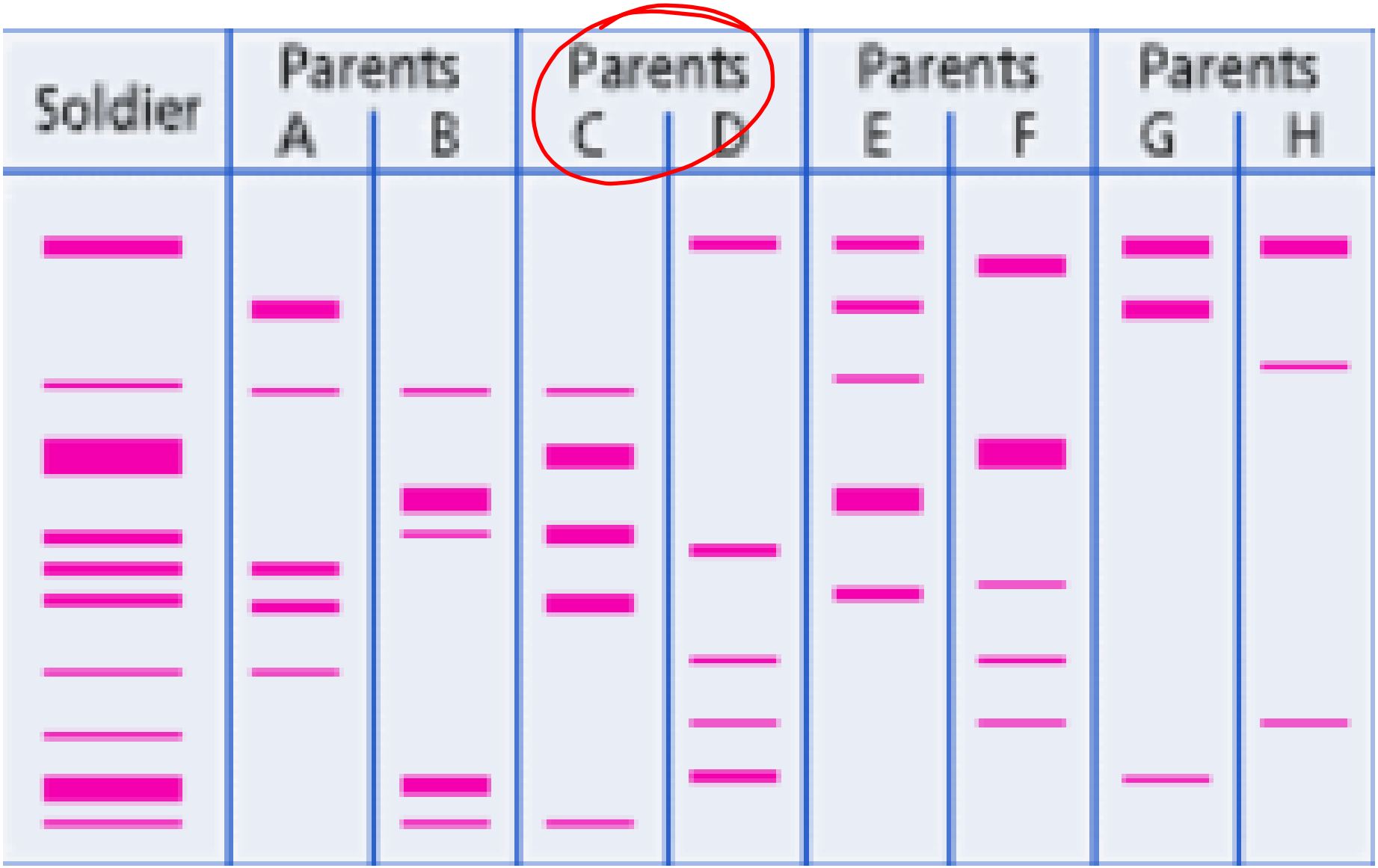
Stages of DNA Profiling



DNA FINGERPRINTING




MOM
DAD
D1
D2
S1
S2


Soldier
Parents
A
B
Parents
C
D
Parents
E
F
Parents
G
H

Few popular examples of individual DNA diagnostics

* Rajiv Gandhi Assassination Case (Chennai, Tamil Nadu),
* Naina Sahni or the Tandoor case (New Delhi
* Priyadarshini Mattoo (New Delhi),
* Sishu Vihar Child adoption case (Hyderabad, Andhra Pradesh),
* Black Buck killing case (Jodhpur, Rajasthan)
* Beanth Singh Assassination Case (Punjab)
* ND Tiwari – Biological father hood case

GENETIC DISORDERS

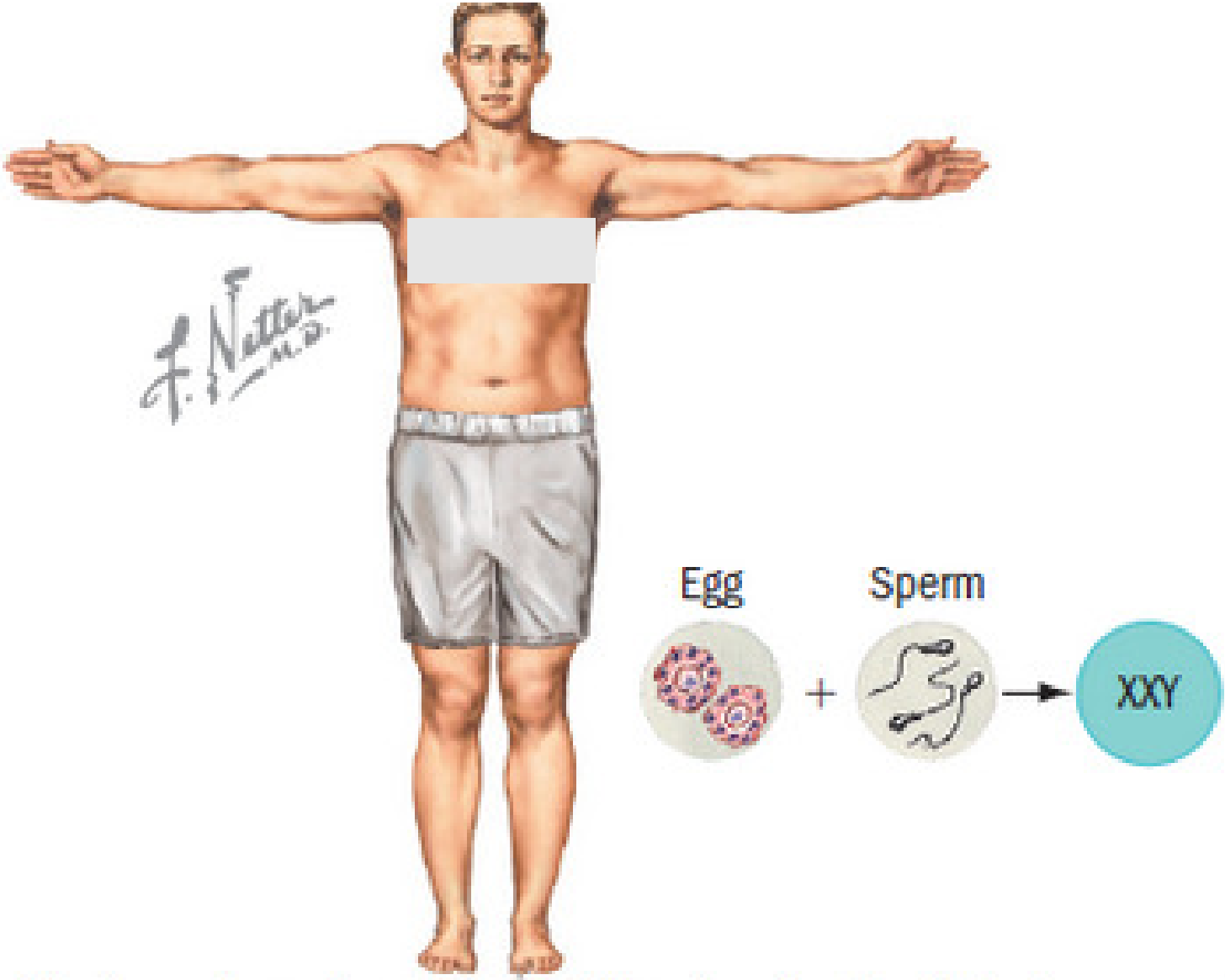
Mutations

- Gene mutations can be either inherited from a parent or acquired. A hereditary mutation is a mistake that is present in the DNA of virtually all body cells. Hereditary mutations are also called *germ line* mutations because the gene change exists in the reproductive cells and can be passed from generation to generation, from parent to newborn. Moreover, the mutation is copied every time body cells divide

Down's Syndrome

Symptoms of down syndrome

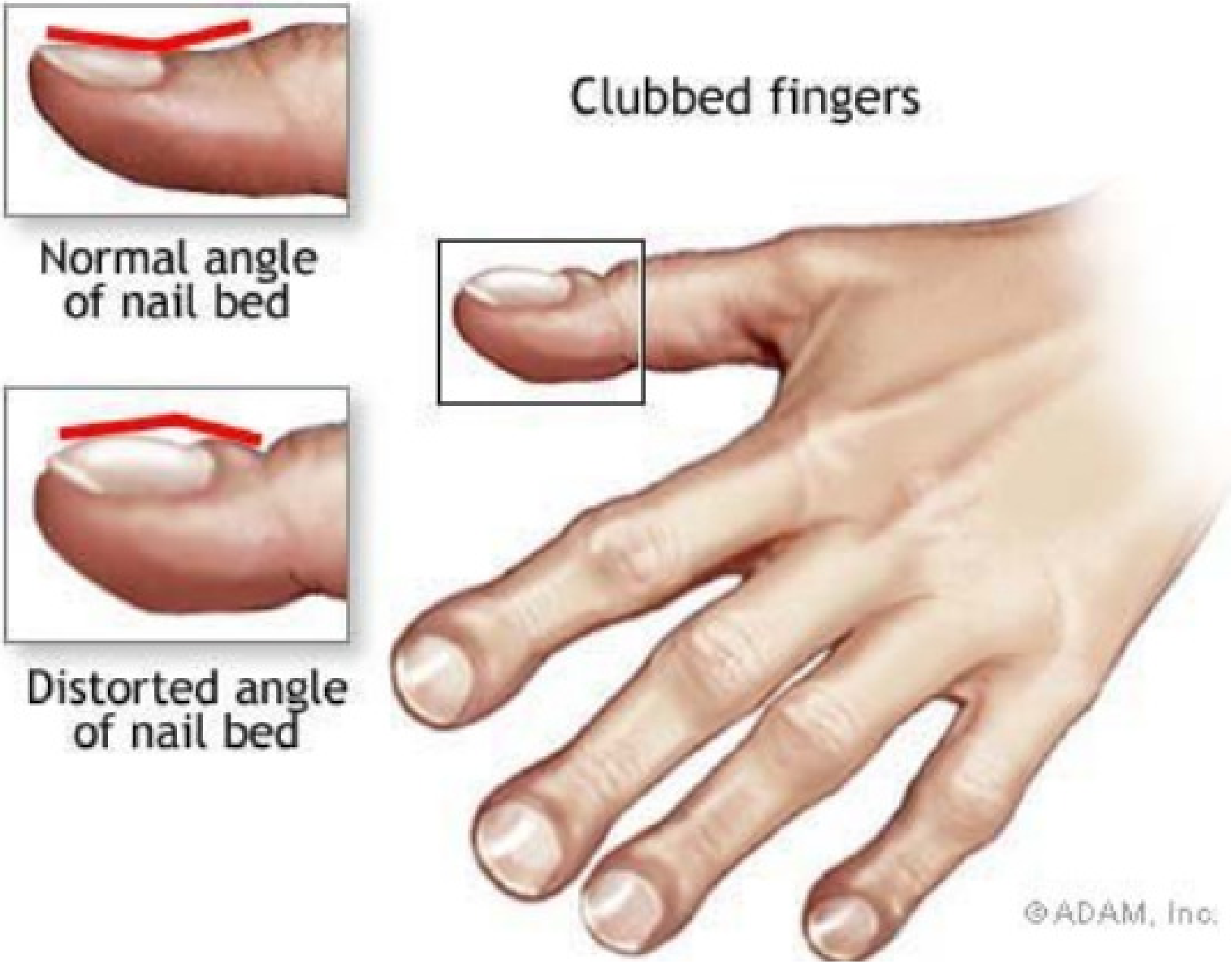
- Eyes that slant upward and outward
- Narrow eye openings
- A face that seems to be flattened
- A small head compared to body size
- Broad feet with short toes
- Ears that are small and set low
- Short arms and legs compared to length of body
- Broad hands with short fingers and a single crease across the palm
- Small nose and small mouth, in which the tongue may be relatively large
- Lack of muscle tone
- Ability to extend body joints; extreme flexibility



Klinefelter's syndrome is an inherited disorder of males. Males have an extra X chromosome and don't develop normal male sexual characteristics of puberty; however, most men with Klinefelter's syndrome can live normal lives.


True Story: *I Have Turner Syndrome*

Cystic Fibrosis



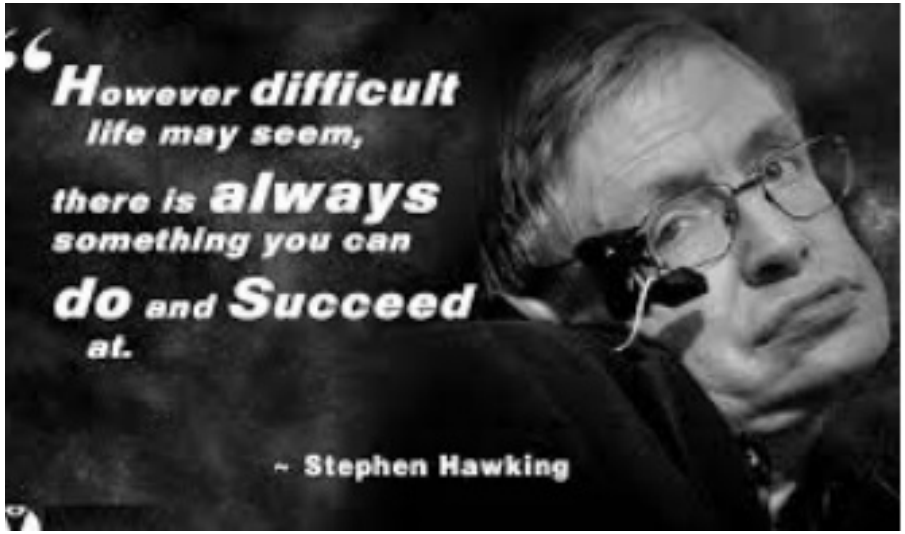
Symptoms of Infantile Tay-Sachs include:

- deafness
- blindness
- decreased muscle tone
- increased startle response
- paralysis or loss of muscle function
- seizures
- delayed mental and social development

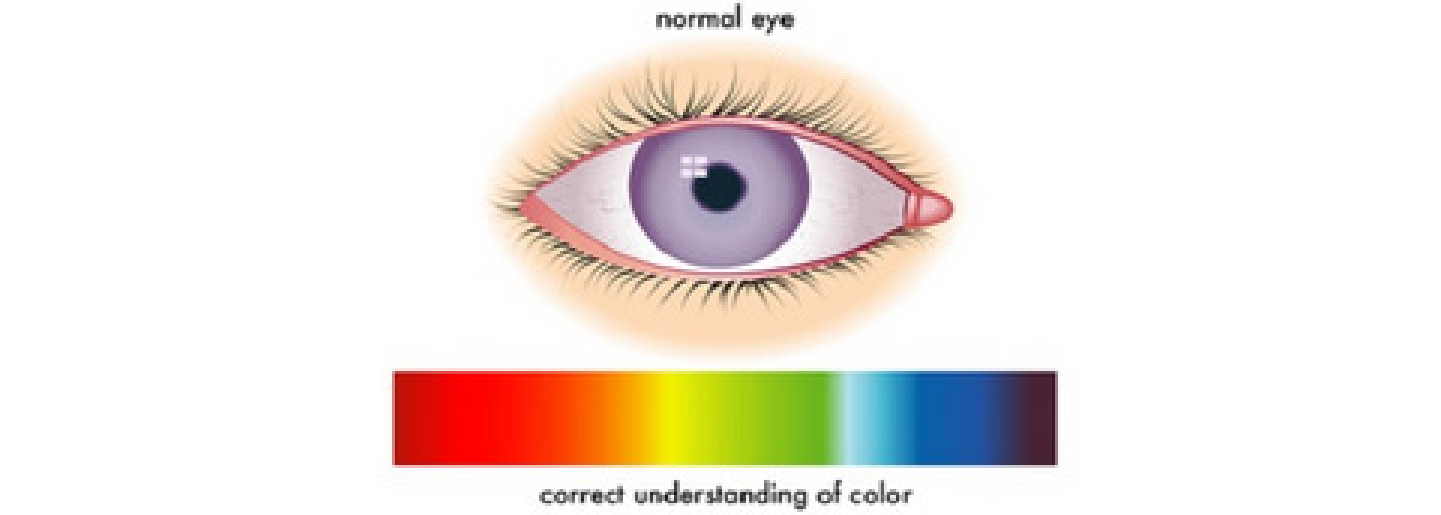
SYMPTOMS OF HEMOPHILIA:

- Spontaneous bleeding
- Prolonged bleeding from cuts
- Nosebleeds with no known cause
- Tightness in your joints
- Internal bleeding

Huntington's Disease



Color Blindness



Albinism

- Patients are unable to produce skin or eye pigments, and thus are light-sensitive