BIOCHEMISTRY

UNIT 4 NOTES

IMPORTANT TOPICS

Rx Pharma Education

Biosynthesis Of Purine Nucleotides

There are mainly two methods of biosynthesis of Purines :

① De Novo Pathway
② Salvage Pathway

De Novo Pathway

- In denovo pathway purine nucleotides are synthesized not free purine bases
- Ribose - 5 - Phosphate used as precursor in de novo pathway :

α - D - Ribose - 5 - Phosphate

ATP, AMP — PRPP Synthase

5 - Phosphoribosyl - α - Pyrophosphate

Glutamine + H_2O, Glutamate + PPi — PRPP Glutamyl Amidotransferase

5 - Phospho - β - D - Ribosylamine

Glycine + ATP, ADP + Pi — Phosphoribosyl Glycinamide Synthase

Glycinamide ribosyl - 5 - Phosphate

N^5, N^{10} - Methenyl THF, THF — Formyl transferase

Formylglycinamide ribosyl - 5 - Phosphate

Glutamine + ATP + H_2O, Glutamate + ADP + Pi — Synthase

Formylglycinamidine ribosyl - 5 - Phosphate

ATP, ADP — Synthase

5 - Aminoimidazole ribosyl - 5 - Phosphate

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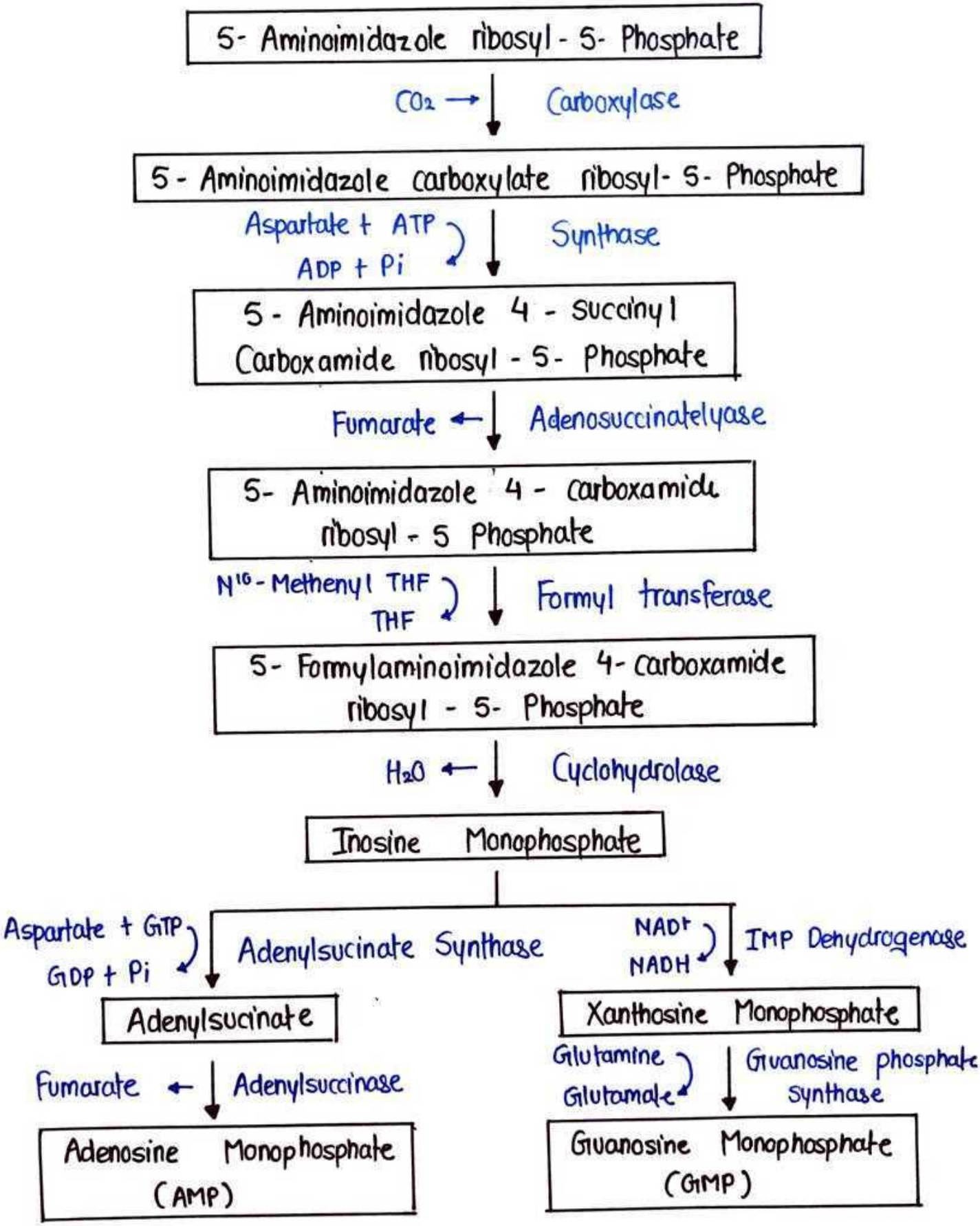
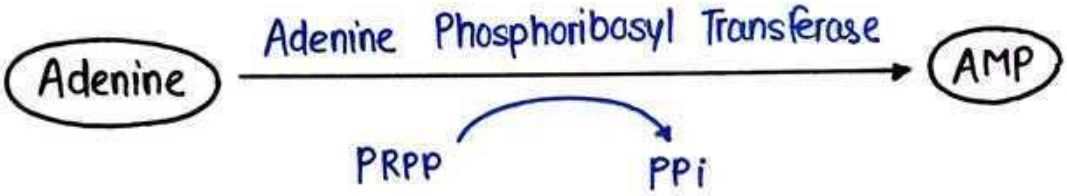
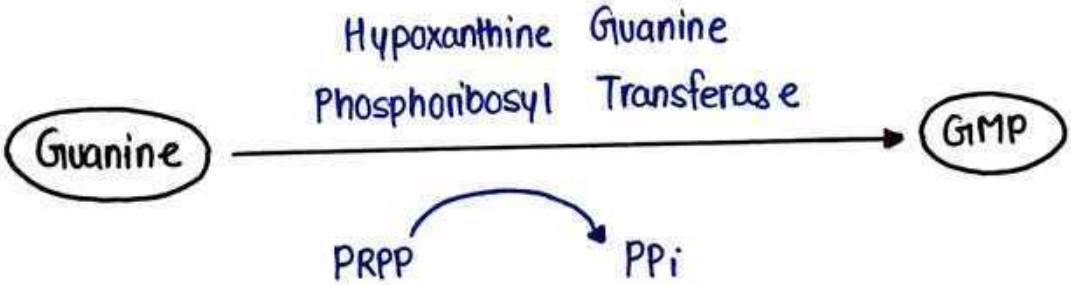
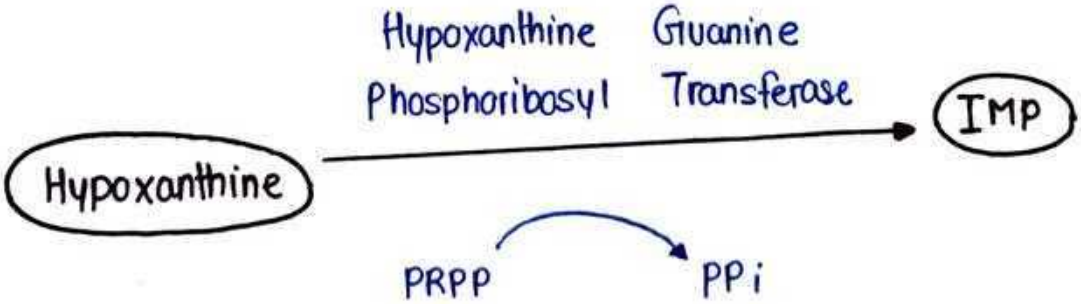

5- Aminoimidazole ribosyl - 5- Phosphate
CO_2 →
Carboxylase
5 - Aminoimidazole carboxylate ribosyl- 5- Phosphate
Aspartate + ATP
ADP + Pi
Synthase
5 - Aminoimidazole 4 - Succinyl Carboxamide ribosyl - 5- Phosphate
Fumarate ←
Adenosuccinatelyase
5- Aminoimidazole 4 - carboxamide ribosyl - 5 Phosphate
N^{10} - Methenyl THF
THF
Formyl transferase
5- Formylaminoimidazole 4- carboxamide ribosyl - 5- Phosphate
H_2O ←
Cyclohydrolase
Inosine Monophosphate
Aspartate + GTP
GDP + Pi
Adenylsucinate Synthase
NAD+
NADH
IMP Dehydrogenase
Adenylsucinate
Xanthosine Monophosphate
Fumarate ←
Adenylsuccinase
Glutamine
Glutamate
Guanosine phosphate synthase
Adenosine Monophosphate (AMP)
Guanosine Monophosphate (GMP)

Salvage Pathway For Purines

- This pathway provides purine nucleotide for the tissues which are incapable of their biosynthesis by denovo pathway.
- example : human brain has low levels of PRPP amidotransferase & also RBCs cannot synthesize 5- phosphoribosylamine.
- Now these tissues mainly depends on salvage pathway for purine nucleotide synthesis.
- This is much simpler & required less energy.







Biosynthesis Of Pyrimidine Nucleotides

Biosynthesis of pyrimidine nucleotides occured by :

① De Novo Pathway
② Salvage Pathway

De Novo Pathway

- The pyrimidine nucleotides are :

① Cytidine Monophosphate
② Uridine Monophosphate.
③ Thymidine Monophosphate.

- Unlike the synthesis of purine nucleotide, pyrimidine ring is made first & then attached to ribose phosphate., which is donated by PRPP.

CO_2 + Glutamine + ATP

2 ATP + H_2O → 2 ADP + Pi : Carbamoyl Phosphate Synthase II

Carbamoyl Phosphate

Aspartic Acid, Pi : Aspartate Transcarbomylase

Carbamoyl Aspartate

NAD+ → NADH : Dihydroorotase

Orotate

PRPP → PPi : Orotate Phosphoribosyl Transferase

Oritidine Monophosphate

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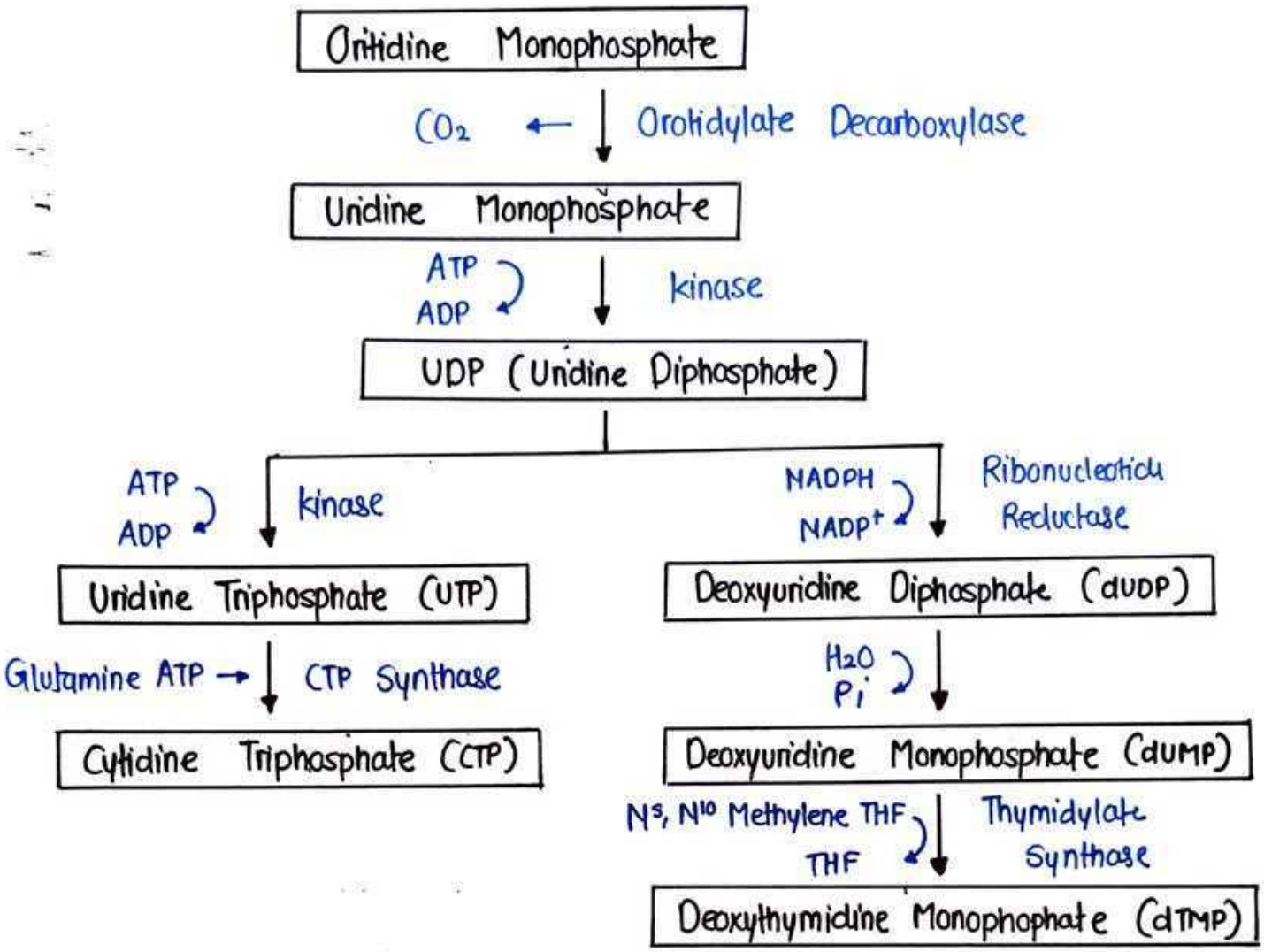
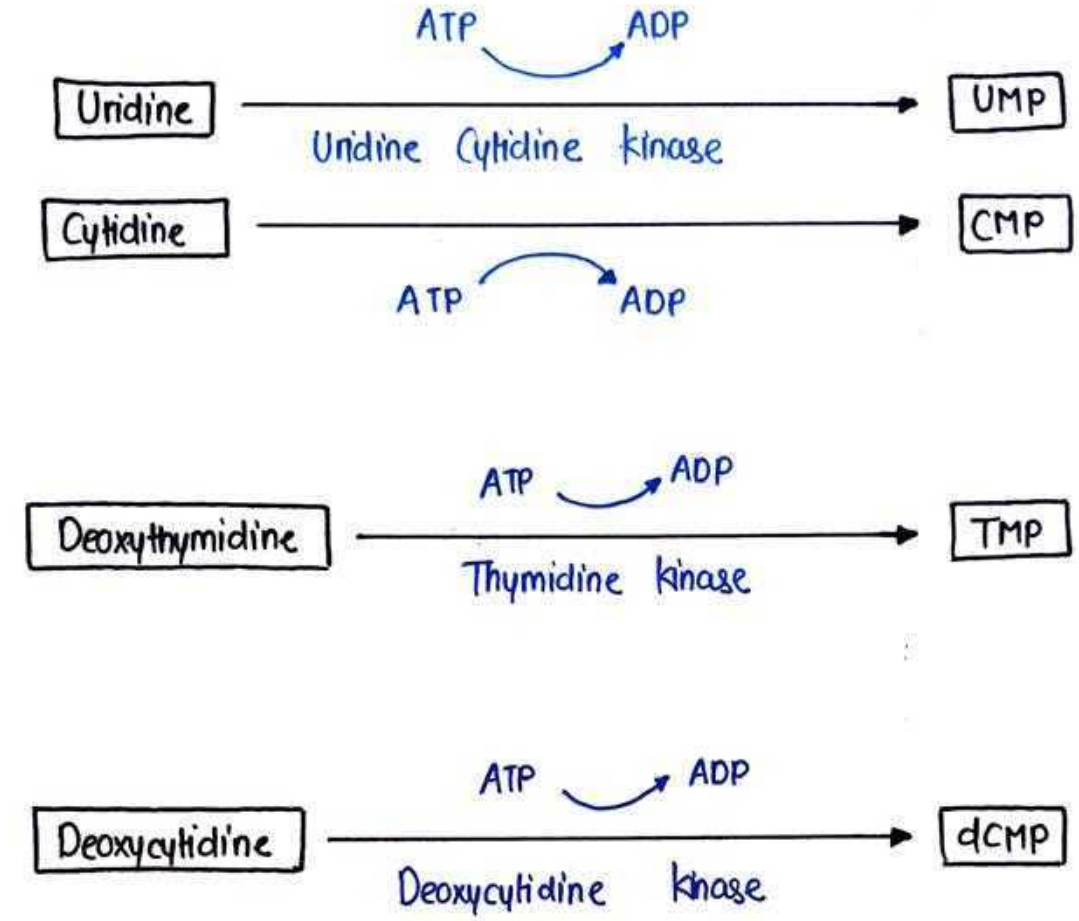

Orotidine Monophosphate
CO_2
Orotidylate Decarboxylase
Uridine Monophosphate
ATP
ADP
kinase
UDP (Uridine Diphosphate)
ATP
ADP
kinase
Uridine Triphosphate (UTP)
Glutamine ATP
CTP Synthase
Cytidine Triphosphate (CTP)
NADPH
$NADP^+$
Ribonucleotide Reductase
Deoxyuridine Diphosphate (dUDP)
H_2O
P_i
Deoxyuridine Monophosphate (dUMP)
N^5, N^{10} Methylene THF
THF
Thymidylate Synthase
Deoxythymidine Monophosphate (dTMP)

Salvage Pathway for Pyrimidines



Structure Of DNA & RNA

DNA

- The word DNA stands for deoxyribonucleic acid.
- It contains Deoxyribose sugar.
- DNA is made up of monomeric units called nucleotides, hence it is polymer of nucleotide or polynucleotide.

Components

- A DNA molecule consist of double stranded nucleic acid chain which is linked via hydrogen bonds with base pairs projecting inwards.
- The hydrogen bonds attach only to specific base pairs depending on the structure of four bases.
- The Nitrogenous bases in DNA are :

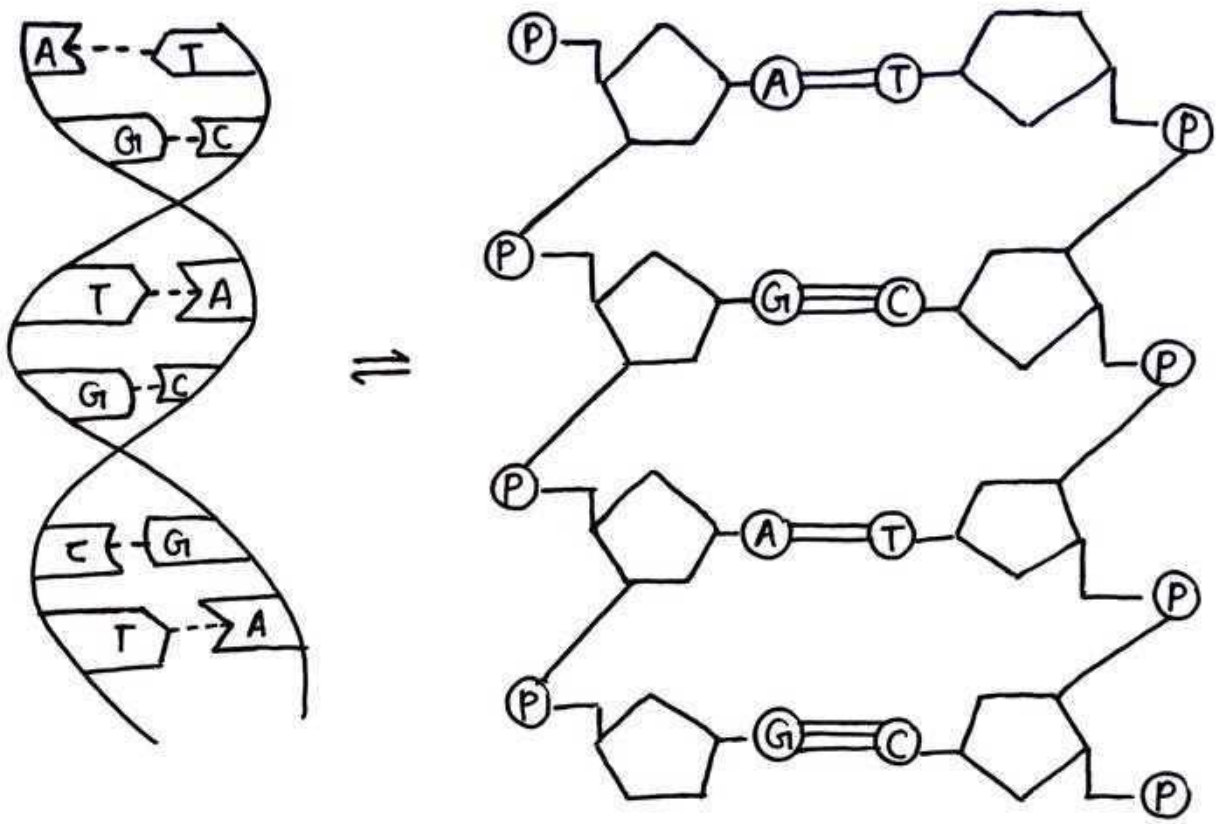
① Adenine
② Guanine
③ Thymine
④ Cytosine

- The sugar phosphate group attaches in an alternate arrangement.
- The deoxyribose sugars binds with phosphodiester bonds.
- Some common types of DNA are :

① Z - DNA
② B - DNA
③ A - DNA
④ C - DNA
⑤ D - DNA

DNA Double Helix

- The double helical structure of DNA was proposed by James Watson and Francis Crick in 1953 & also got nobel prize in 1962.
- The two strands of DNA are antiparallel to each other.



Functions Of DNA

- DNA serves as genetic material in living being.
- DNA carry specific information to an individual.
- DNA molecules provide genetic information which implies to characteristic feature of a living organism.
- Information of all cellular protein synthesis is carried by DNA.
- The parent transfer its DNA to the offspring, so the information moves from one generation to another.
- DNA molecule has the capability of replication & transcription.

RNA

- The word RNA stands for Ribonucleic Acid.
- It contains Ribose sugar.
- Structure of RNA is similar to DNA it is also a polymer of nucleotides.
- RNA in a cell is present in amount 10 times more than that of DNA, because RNA performs large no. of cellular functions.

Components

A RNA molecule consist of single stranded nucleic acid chain
The nitrogenous bases in RNA are :

- Adenine
- Guanine
- Cytosine
- Uracil

Types Of RNA

The three major types of RNA are :

① Messenger RNA
② Transfer RNA
③ Ribosomal RNA

Messenger RNA

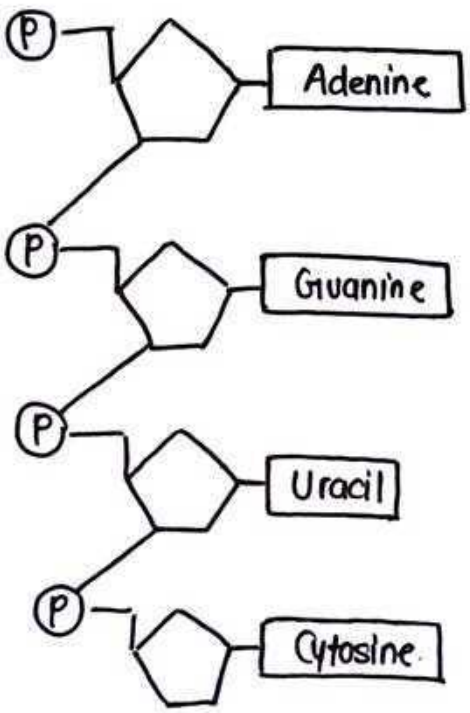
- Its cell composition is about 5-10%.
- It is synthesized in nucleus.
- mRNA has high molecular weight with a short life.
- mRNA of eukaryotes are more stable than prokaryotes.

Transfer RNA

- Transfer RNA contains about 71-80 nucleotides.
- Its cell composition is about 10-20%.
- The structure of tRNA, resembles that of a clever leaf.
- tRNA contains mainly four arms with a base pair

Ribosomal RNA

- Its cell composition is about 50-80%.
- They are the factory of protein synthesis.
- The rRNA has two subunits 50s & 30s, these subunits together form 70s ribosome



Functions

- RNA molecules are less stable than DNA molecules. In some organism RNA molecules also carry genetic information.
- The t- RNA transport specific amino acids to ribosomes
- The r- RNA provides structural framework to ribosomes.
- The m- RNA carries genetic information from nucleus to ribosomes

DNA REPLICATION

- It is the process in which DNA makes multiple copies of itself
- It is a biological polymerisation, that proceeds in the sequence of initiation, elongation & termination.
- It is an enzyme catalysed reaction.
- DNA Polymerase is the main enzyme in the replication process.

Models Of DNA Replication

There are basically 3 models of DNA replication:

① Conservative Model
② Dispersive Model
③ Semiconservative Model

Steps of DNA Replication

There are mainly 3 steps involved in the process of DNA replication:

① Initiation
② Elongation
③ Termination

INITIATION

- DNA replication demands a high degree of accuracy because even a minute mistake would result in mutations. Thus, replication cannot initiate randomly at any point in DNA.
- To begin the process of replication there is a particular region called origin of replication, this is the point where the replication originates.

Cotinues.....

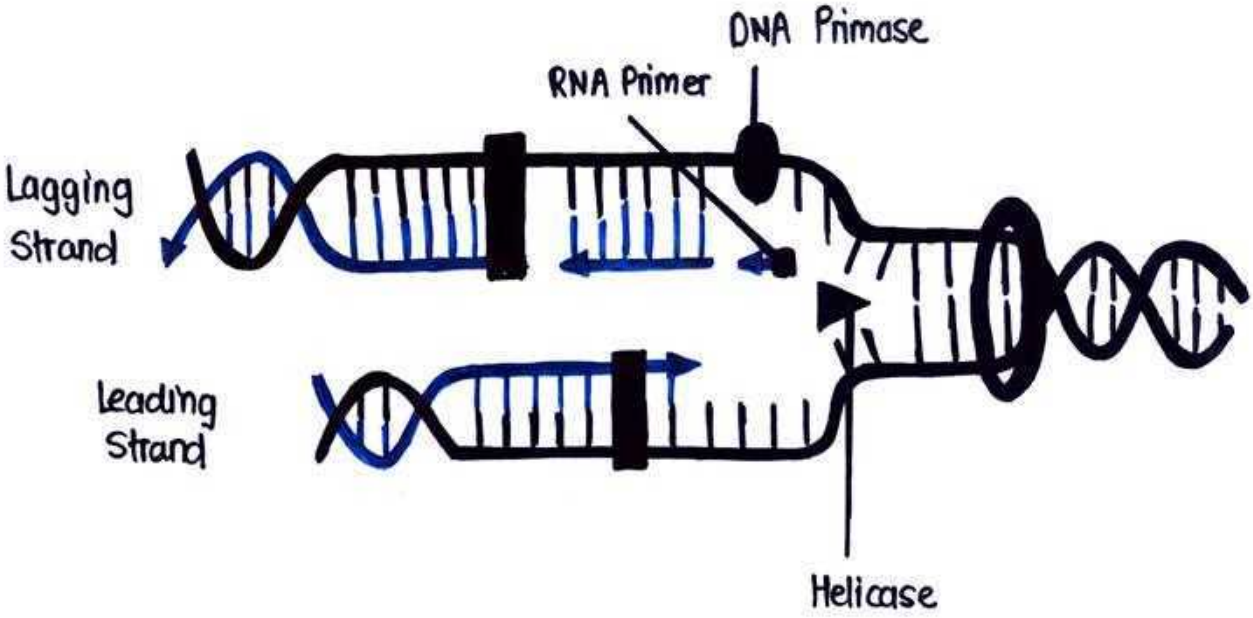
- Replication begins with the spotting of this origin followed by the unwinding of two DNA strands.
- Unzipping of DNA strands in their entire length is not feasible due to high energy input. Hence, first, a replication fork is created catalysed by helicase enzyme that unzips the DNA strands.

ELONGATION

- As the strands are separated, the polymerase enzymes start synthesizing the complementary sequence in each of the strands.
- The parental strands will act as a template for newly synthesising daughter strands.
- It is to be noted that elongation is unidirectional i.e. DNA is always polymerised only in the 5' to 3' direction.
- In one strand it is continuous, called continuous replication while in other strand it is discontinuous, called discontinuous replication.
- They occur as fragments called Okazaki fragments.
- The enzyme called DNA ligase joined them later.

TERMINATION

- Termination of replication occurs in different ways in different organisms.
- An enzyme, called exonuclease removes all the RNA poimers from original strand after the formation of continuous & discontinuous strands.



DNA REPLICATION

ENZYMES INVOLVED IN DNA REPLICATION

DNA Replication is a highly enzyme dependent process.
There are so many enzymes involved in DNA Replication as follows:

① DNA Polymerase

- It helps in polymerisation, catalyses & regularises the whole process of DNA replication with support of other enzymes.
- DNA polymerase is of three types:

(i) DNA Polymerase I
(ii) DNA Polymerase II
(iii) DNA Polymerase III

② Helicase

Helicase is the enzyme that unzips the DNA strands by breaking the hydrogen bonds between them.

③ **Ligase**

Ligase is the enzyme which joins the okazaki fragments together of discontinuous DNA strands.

④ **Primase**

The enzyme helps in the synthesis of RNA primer.

⑤ **Endonucleases**

These produce a single stranded or double stranded cut in a DNA molecule.