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Nucleic acid metabolism and genetic information transfer

Presented By;-

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Nucleic acid metabolism

Nucleic acid metabolism refers to the **synthesis and degradation of nucleotides** (purines & pyrimidines) that form DNA and RNA.

It includes:

- **Synthesis of nucleotides**
- **Breakdown of nucleotides**

Biosynthesis of Purine Nucleotides (De-novo Pathway)

1. Formation of PRPP

- **Ribose-5-phosphate** (from HMP shunt pathway) is the starting molecule.
- Enzyme: **PRPP synthetase**
- Uses: **ATP** (Adenosine Triphosphate)
- Product formed: **PRPP (5-Phosphoribosyl-1-pyrophosphate)**

2. Rate-Limiting Step (Most Important)

- Enzyme: **Glutamine-PRPP amidotransferase**
- PRPP + Glutamine → **5-Phosphoribosylamine**
- This is the **committed & rate-limiting step**

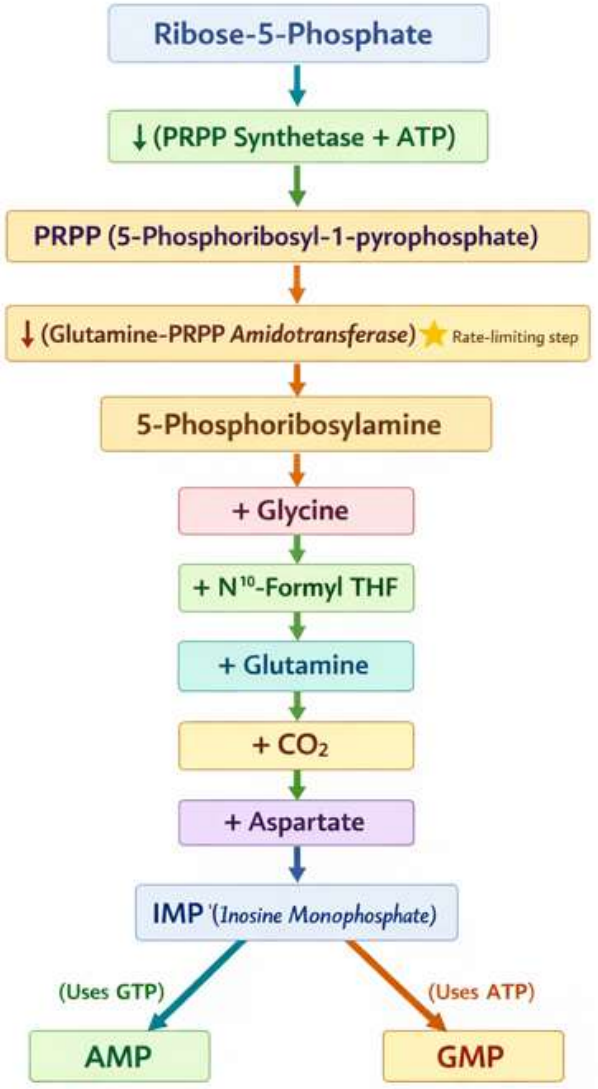
3. Stepwise Ring Formation on Ribose

- The purine ring is built **directly on ribose sugar**.
- Substrates added sequentially:
  - **+ Glycine**
  - **+ N^{10}-Formyl Tetrahydrofolate**
  - **+ Glutamine**
  - **+ CO_2**
  - **+ Aspartate**
  - **+ N^{10}-Formyl Tetrahydrofolate**

☞ After these additions → **IMP (Inosine Monophosphate)** is formed.

4. IMP Conversion

- IMP is the **parent purine nucleotide**.
  - AMP formation uses **GTP** (Guanosine Triphosphate)
  - GMP formation uses **ATP** (Adenosine Triphosphate)



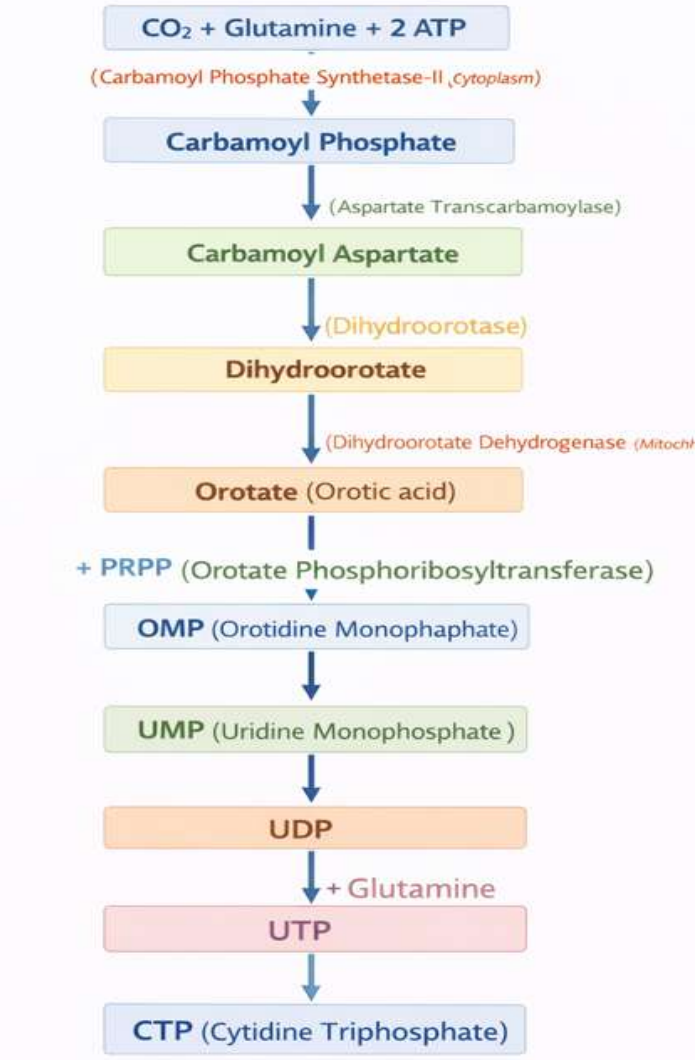
Biosynthesis of Pyrimidine Nucleotides (De-novo Pathway)

De-novo Pyrimidine Synthesis – Explanation

De-novo pyrimidine synthesis begins in the **cytoplasm** with the formation of carbamoyl phosphate from **CO_2, glutamine, and 2 ATP**. This reaction is catalyzed by **Carbamoyl Phosphate Synthetase-II (CPS-II)** and is the **rate-limiting and committed step** of the pathway. CPS-II is activated by PRPP and ATP, while it is inhibited by UTP through feedback regulation. Carbamoyl phosphate then combines with aspartate in a reaction catalyzed by **Aspartate Transcarbamoylase**, forming carbamoyl aspartate. This compound is cyclized by **Dihydroorotase** to produce dihydroorotate.

Dihydroorotate is then oxidized to orotate (orotic acid) by **Dihydroorotate Dehydrogenase**, which is the only mitochondrial enzyme in this pathway. Orotate subsequently reacts with PRPP in the presence of **Orotate Phosphoribosyltransferase** to form OMP (orotidine monophosphate). OMP is then decarboxylated by **OMP Decarboxylase** to produce **UMP (uridine monophosphate)**, which is the first pyrimidine nucleotide formed in this pathway. UMP is further phosphorylated to UDP and then to UTP using ATP. Finally, UTP is converted into **CTP (cytidine triphosphate)** by the addition of an amino group from glutamine in a reaction catalyzed by **CTP Synthetase**.

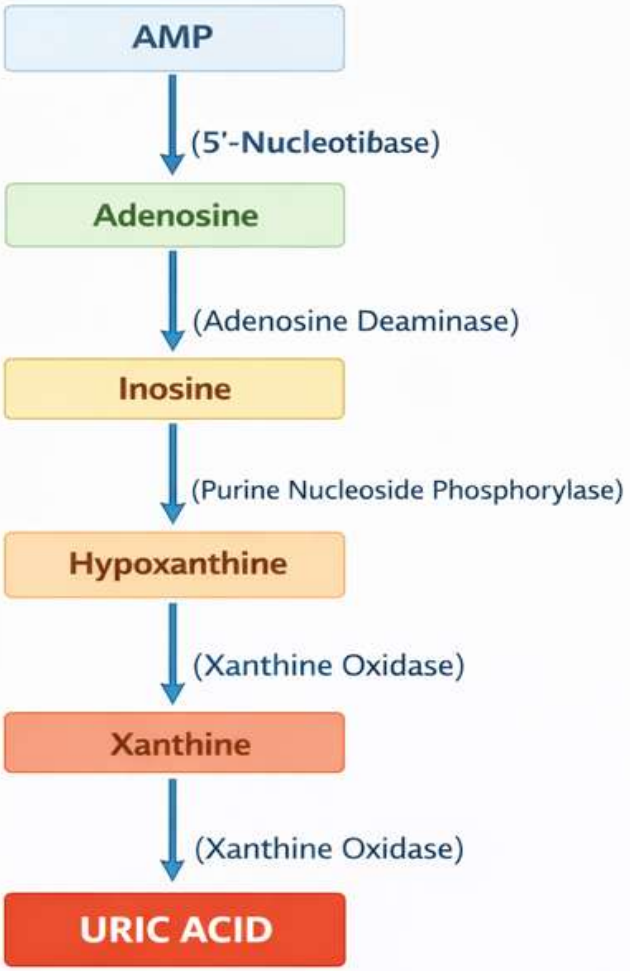
An important distinguishing feature of pyrimidine synthesis is that the pyrimidine ring is synthesized first and then attached to PRPP, unlike purine synthesis where the ring is built directly on the ribose sugar.

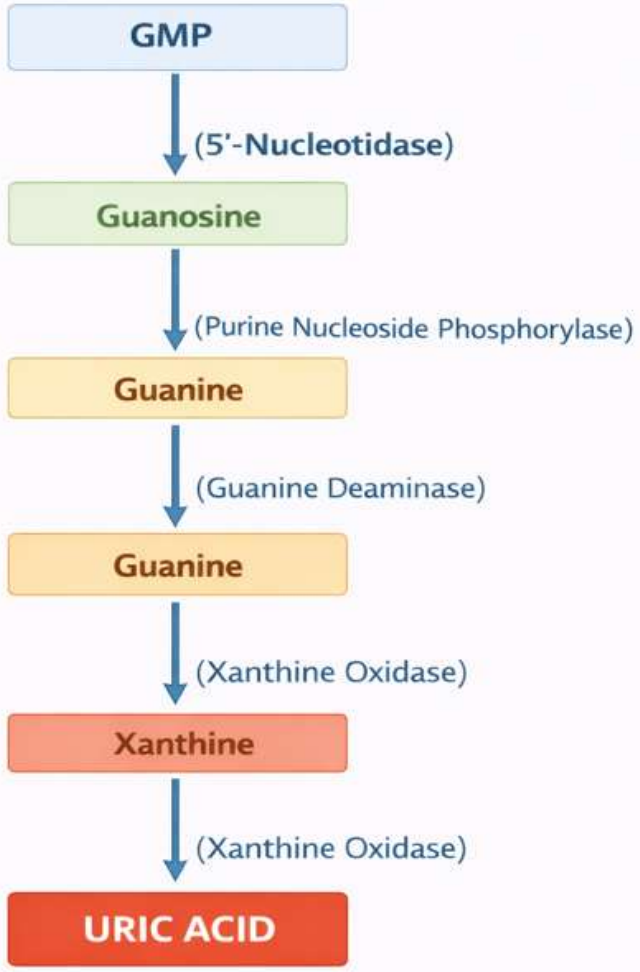


Catabolism of Purine Nucleotides

Purine catabolism is the breakdown of purine nucleotides **(AMP & GMP)** into **uric acid** (end product in humans).

Site: Mainly **liver**





Gout Disease

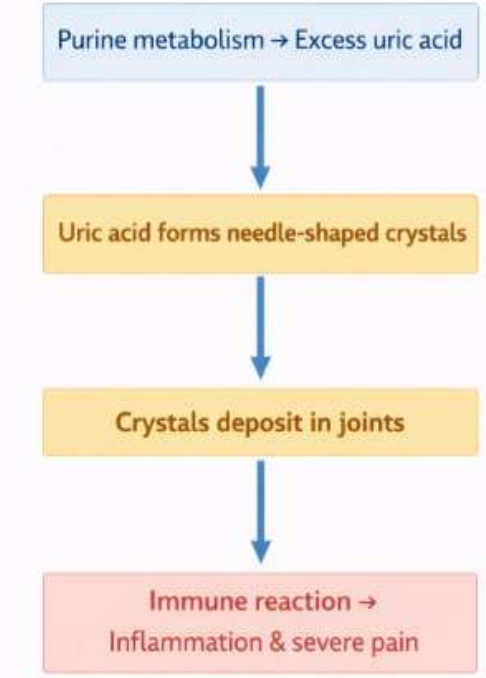
Definition:-

Gout is a metabolic disorder characterized by **painful inflammation of joints** due to deposition of **monosodium urate crystals**, caused by **hyperuricemia** (high uric acid in blood).

Treatment (Basic Concept)

- **NSAIDs** – reduce pain
- **Colchicine** – reduces inflammation
- **Allopurinol / Febuxostat** – decrease uric acid formation
- Low purine diet

Cause (Pathogenesis)



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Hyperuricemia Disease

Definition:-

Hyperuricemia is a condition in which the level of **uric acid in blood is abnormally high**.

Normal serum uric acid:-

- ❑Men: **3.5–7.0 mg/dL**
- ❑Women: **2.5–6.0 mg/dL**
- ❑☞ Above this range = Hyperuricemia

Cause (Why it happens?)

Uric acid is the **end product of purine metabolism**.

Hyperuricemia occurs due to:

- ➢**Overproduction of uric acid**
  - Increased purine synthesis
  - Increased cell breakdown (e.g., leukemia)
- ➢**Decreased excretion by kidneys** (most common cause)

Treatment (Basic Concept)

Treatment (Basic Concept)

- ➢ **Allopurinol** – inhibits xanthine oxidase
- ➢ Increase water intake
- ➢ Low purine diet

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What is DNA?

What is DNA?

- **DNA** (Deoxyribonucleic Acid) is the molecule that stores the genetic instructions used by living organisms to grow, develop, function, and reproduce.
- It is found in the nucleus of most cells and is responsible for passing genetic information from one generation to the next.
- DNA controls everything from eye color to how your body works, by telling cells how to make proteins — the building blocks of life.

Structure of DNA

The structure of DNA was discovered by James Watson and Francis Crick in 1953. It has a unique shape known as a double helix, which looks like a twisted ladder.

Here are the key parts of DNA's structure:

1. Double Helix:

DNA has two long strands coiled around each other like a spiral staircase.

2. Nucleotides:

Each strand is made of units called nucleotides.

Each nucleotide has three parts:

- A sugar molecule (deoxyribose)
- A phosphate group
- A nitrogen base

3. Nitrogen Bases:

There are four types:

- Adenine (A)
- Thymine (T)
- Cytosine (C)
- Guanine (G)

These bases pair in a specific way:

- A pairs with T
- C pairs with G

4. Backbone:

The sugar and phosphate groups form the "sides" of the ladder.

The base pairs (A-T and C-G) form the "rungs" of the ladder.

What is RNA?

What is RNA?

- **RNA** stands for **Ribonucleic Acid**. It is a single-stranded molecule that plays a crucial role in the process of **coding, decoding, regulating**, and **expressing** genes.
- RNA works closely with DNA to help the cell produce proteins, which are essential for all biological functions.
- Unlike DNA, which mainly stays in the cell nucleus, **RNA can move between the nucleus and the cytoplasm** to carry out its functions

Structure of RNA

RNA is made up of smaller units called nucleotides, similar to DNA. However, there are a few key differences:

1. Single-Stranded
RNA consists of a **single strand** of nucleotides, not a double helix like DNA.

2. Nucleotide Components
Each RNA nucleotide has three parts:

a. A **phosphate group**
b. A **sugar** called **ribose** (unlike DNA, which has deoxyribose)
c. A **nitrogen base**

3. Nitrogen Bases
There are four nitrogen bases in RNA:

a. **Adenine (A)**
b. **Cytosine (C)**
c. **Guanine (G)**
d. **Uracil (U)** – replaces **Thymine (T)** found in DNA

Base pairing in RNA (when needed):

a. **A pairs with U**
b. **C pairs with G**

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Functions Of DNA And RNA

Feature	DNA (Deoxyribonucleic Acid)	RNA (Ribonucleic Acid)
Main Function	Stores and transmits genetic information	Helps in protein synthesis and gene expression
Role	Blueprint of life – long-term genetic storage	Acts as messenger and assistant in making proteins
Location	Mainly in the nucleus	In the nucleus and cytoplasm
Stability	Stable, long-lasting molecule	Less stable, short-lived molecule
Involvement in Protein Synthesis	Indirect (provides the code)	Direct (mRNA, tRNA, and rRNA are all involved)
Types	One main type (DNA)	Multiple types: mRNA, tRNA, rRNA
Replication	Can replicate itself	Synthesized from DNA during transcription
Transmission	Passed from parents to offspring	Not passed to offspring

DNA Replication by the Semi-Conservative Model

- **DNA Replication by the Semi-Conservative Model** refers to the process by which DNA makes an exact copy of itself before cell division, ensuring genetic information is passed on accurately.
- The term *semi-conservative* describes the mechanism of replication discovered by Meselson and Stahl in 1958.

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Steps of DNA Replication (Semi-Conservative Model)

1. Initiation:

- The enzyme **helicase** unwinds and unzips the double helix at specific regions called **origins of replication**, forming a **replication fork**.
- **Single-strand binding proteins (SSBs)** stabilize the unwound DNA.

2. Primer Binding:

- **Primase** synthesizes a short RNA primer to provide a starting point for DNA synthesis.

3. Elongation:

- **DNA polymerase III** adds nucleotides in the 5' → 3' direction, complementary to the template strand.
- On the **leading strand**, DNA is synthesized continuously.
- On the **lagging strand**, DNA is synthesized in short fragments called **Okazaki fragments**.

4. Primer Removal and Replacement:

- **DNA polymerase I** removes RNA primers and replaces them with DNA.

5. Ligation:

- **DNA ligase** joins the Okazaki fragments into a continuous strand.

6. Termination:

- Replication ends when the entire DNA molecule is copied.

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Transcription in DNA

- **Transcription in DNA** is the process by which a segment of DNA is copied into **messenger RNA (mRNA)** by the enzyme **RNA polymerase**.
- This is the **first step of gene expression**, allowing genetic instructions stored in DNA to be converted into a format that can be used to build proteins.

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Steps of DNA Transcription

1. Initiation:

- RNA polymerase binds to a specific region called the **promoter** (often with the help of transcription factors).
- The DNA strands **unwind** near the gene to be transcribed, forming a **transcription bubble**.

2. Elongation:

- RNA polymerase reads the **template (antisense) DNA strand** in the 3′ → 5′ direction.
- It synthesizes a **complementary RNA strand** in the 5′ → 3′ direction using RNA nucleotides (A, U, C, G).
  - *Note:* Uracil (U) replaces thymine (T) in RNA.

3. Termination:

- Transcription continues until RNA polymerase reaches a **termination signal** (a specific DNA sequence).
- The newly formed **pre-mRNA** detaches from the DNA

What is RNA Synthesis?

What is RNA Synthesis?

Definition: The process of making an RNA strand from a DNA template using the enzyme RNA *polymerase.*

Purpose: To produce RNA that can perform functions in the cell (e.g., mRNA, tRNA, rRNA).

Location:

Eukaryotes: Nucleus

Prokaryotes: Cytoplasm

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Steps of RNA Synthesis

1. Initiation:

- RNA polymerase recognizes and binds to the promoter region of the DNA template.
- This binding leads to the unwinding of the DNA double helix, exposing the template strand.

2. Elongation:

- RNA polymerase moves along the DNA template strand, synthesizing an RNA molecule (usually mRNA, tRNA, or rRNA).
- It adds nucleotides to the growing RNA chain in a 5' to 3' direction, using the DNA template as a guide.

3. Termination:

- When RNA polymerase reaches a specific terminator sequence on the DNA template, it stops adding nucleotides.
- The newly synthesized RNA molecule is released, and the RNA polymerase dissociates from the DNA.

What is the Genetic Code?

- The **genetic code** is the set of rules by which the sequence of **nucleotides in mRNA** is translated into the sequence of **amino acids in a protein**.
- It is a **triplet code**, where each **codon** (a group of three nucleotides) codes for one specific amino acid.
- The genetic code is **universal**, **non-overlapping**, and **degenerate**, meaning that more than one codon can code for the same amino acid.

Protein synthesis

Protein synthesis is the process by which cells create proteins using the genetic information encoded in DNA.

It involves two main stages: Transcription And Translation.

1. Transcription occurs in the nucleus (in eukaryotes) and involves creating a messenger RNA (mRNA) copy of the DNA sequence.
2. Translation occurs at ribosomes, where the mRNA is decoded to build a protein chain, with the help of transfer RNA (tRNA) molecules and other proteins.

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Thank you

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