Nucleotides: Chemistry and Biological Significance

- # Basic Structure

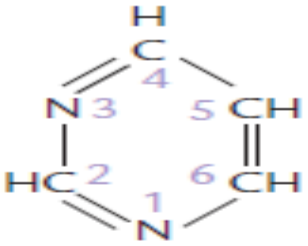
  A nucleotide has three structural components: a heterocyclic compound termed nitrogenous base, a five carbon (pentose) sugar, and at least one phosphate group.

- The nitrogenous bases belong to either **purines or pyrimidines**.
- When the nitrogenous bases are combined with a pentose sugar, they are known as ***nucleosides***.
- Phosphate group can be attached either at the 5’-position or the 3’-position of the pentose, and the nucleoside-phosphate thus formed is known as ***nucleotide***.
- ***Nucleic acids*** are polymers of several nucleotide units, hold together by covalent linkages

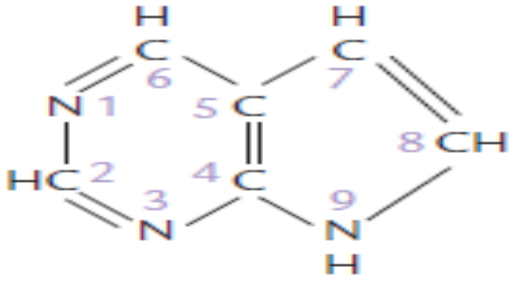
$$\text{Nucleoside} = \text{Base} + \text{Sugar}$$

$$\text{Nucleotide} = \text{Base} + \text{Sugar} + \text{Phosphate(s)}$$

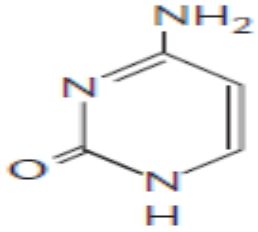
- **Nitrogenous Bases**
  The bases are derivatives of purines or pyrimidines.
- **Purines** are numbered in **anti-clockwise direction**, and the **pyrimidines** are numbered in the **clockwise direction**.
  Major Bases
  The major purines of both DNA and RNA are guanine (G) and adenine (A).
- In DNA, the major pyrimidines are thymine (T) and cytosine (C), while in RNA the major pyrimidines are uracil (U) and cytosine (C).



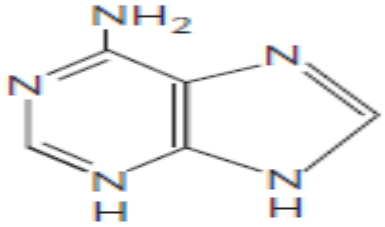
Pyrimidine, the parent compound of the pyrimidine bases



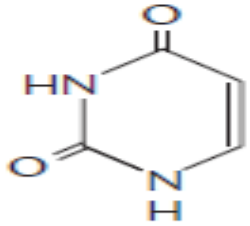
Purine, the parent compound of the purine bases



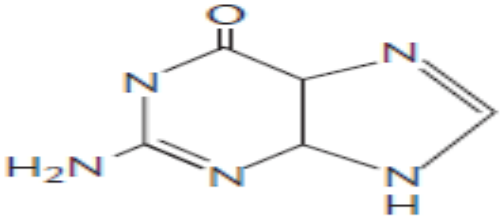
Cytosine



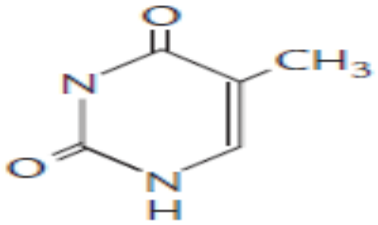
Adenine



Uracil



Guanine



Thymine

- ***Chemical Properties of Bases***
  Nitrogenous bases include highly conjugated double bond systems within the ring structures.
- **Sugars**
  The 5-carbon sugar found in nucleotides is either ***D-ribose or D-2'-deoxyribose***. Each occurs in furanose form
- **D-Ribose** is present in **RNA**, while **D-2'- deoxyribose** is present in **DNA**. **Deoxyribose, as the name suggests, differs from ribose in having one oxygen less (at C-2).**
  Nucleosides
  A nucleoside is a compound of **base** and **sugar** linked by an *N-glycosidic linkage* (a carbon-nitrogen bond). The bond is formed between C-1 of sugar and nitrogen atom 1 of pyrimidine base or nitrogen atom 9 of purine base.
- If the sugar is *ribose,* the compound is **ribonucleoside** and if the sugar is *deoxyribose*, the compound is **deoxyribonucleoside**.
- Adenosine (adenine + ribose), guanosine (guanine + ribose), cytidine (cytosine + ribose) and uridine (uracil + ribose) are the ribonucleosides of A, G, C and U, respectively.
- Similarly, deoxyadenosine, deoxyguanosine, deoxycytidine and deoxythymidine are the deoxyribonucleosides of A, G, C and T.

- # Nucleotides

  nucleotide is nucleoside plus phosphate.

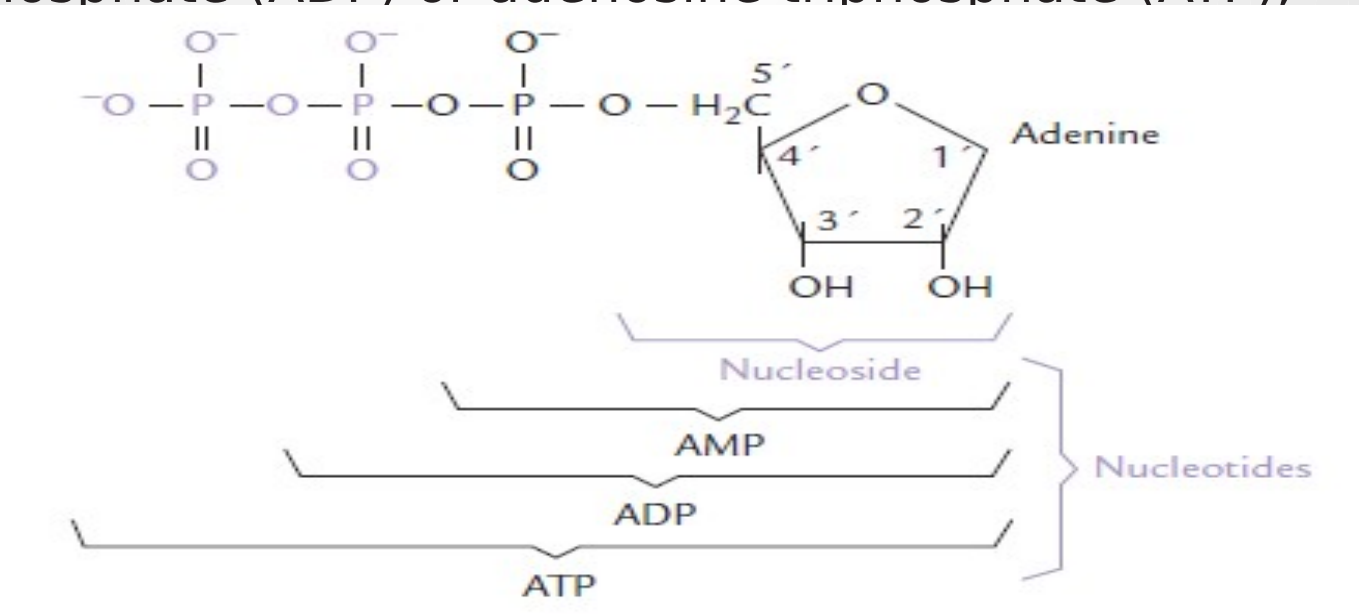
- The phosphate group is esterified to one of the hydroxyl groups of the sugar component of the nucleoside.
- Mostly it is the **hydroxyl group at the C-5** (less commonly C-3) that is phosphorylated.
- To avoid confusion between the numbering of various atoms in the base and carbon atoms of the sugar, the latter are represented with an associated prime. Thus, **carbons of sugar are numbered 1’, 2’, 3’**, etc.

- **Nomenclature**

  The nucleotides are named as phosphate derivatives of nucleosides.

- Thus, adenosine linked covalently with phosphate produces **adenosine monophosphate (AMP)**. It is a *mononucleotide*.
- Likewise, other mononucleotides, e.g. guanosine monophosphate (GMP), cytidine monophosphate (CMP), and uridine monophosphate (UMP) are formed by phosphorylation of guanosine, cytidine and uridine, respectively.
- **The phosphate group can be attached either at the 5’-position or the 3’-position of the pentose, and accordingly the mononucleotides formed are designated as 5’ or 3’-monophosphates, respectively.**
- However, attachment at the 5’-position is far more common, and therefore 5’ is usually omitted in the abbreviation.
- Thus, AMP means adenosine 5’-monophosphate, CMP means cytidine 5’-monophosphate, and so on.
- However, for adenosine 3’-monophosphate or cytidine 3’-monophosphate, the abbreviations 3’-AMP or 3’-CMP respectively are used.
- A mononucleotide is also called *nucleoside monophosphate*.

- ***Nucleoside-Diphosphate and Triphosphate***
  Additional phosphate groups may be attached to a mononucleotide.
- Addition of a second and a third phosphate to a nucleoside monophosphate yields a nucleoside-diphosphate, and triphosphate, respectively. AMP thus yields adenosine diphosphate (ADP) or adenosine triphosphate (ATP), resp



- **Functions**

  Nucleotides are central to maintenance and propagation of life.

- They are most versatile of all biomolecules, being involved in a number of reactions including the energy transfer reactions.
- Some important functions of nucleotides are:

  1. The ribonucleotides such as ATP, GTP, CTP and UTP are important **coenzymes** and provide the **basic unit of RNA**. The deoxyribonucleotides, dATP, dGTP, dCTP and dTTP are required for **DNA replication** and **DNA repair**.

- **2.** Nucleoside sugars are activated precursors which are used in **biosynthetic reactions**. For example:
  UDP-glucose is used in glycogen synthesis
  UDP-galactose is used in synthesis of ceramides
  CTP-choline is used in phospholipid synthesis.
  3. Nucleotides are the basis of high-energy compounds. The best known example is adenosine triphosphate (ATP), referred to as the **currency of free energy** in the body, which provides energy for all types of cellular activities. GTP is used as an energy source in protein synthesis.
  4. Regulation of enzyme activity involves certain nucleotides, such as cAMP and cGMP. They are signal conducting molecules, acting as **intracellular messengers** for certain hormones.
  5. The nucleic acids, DNA and RNA, are involved in **storage and decoding of genetic information**.