Biochemistry1 For First Year Medical Students
Lecture 5: Nucleic acids; Nucleotides and Nitrogen bases:

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Learning Objectives

- **Study the constituents, chemistry & types of Nucleic acids**
- **Learn the biologically important nucleotides and their functions.**
- **Study the structure of two major purines and three major pyrimidines**
- **Correlate clinically with hyperuricemia & gout.**

Q&A

Q1: What are the Nucleic acids?

Nucleic Acids (NA) are polymers made up of repeating monomers (nucleotides), and they are responsible for transmitting the characteristics of a species from one generation to the next. There are two types of nucleic acids, ribonucleic acids (RNA) and deoxyribonucleic acids (DNA).

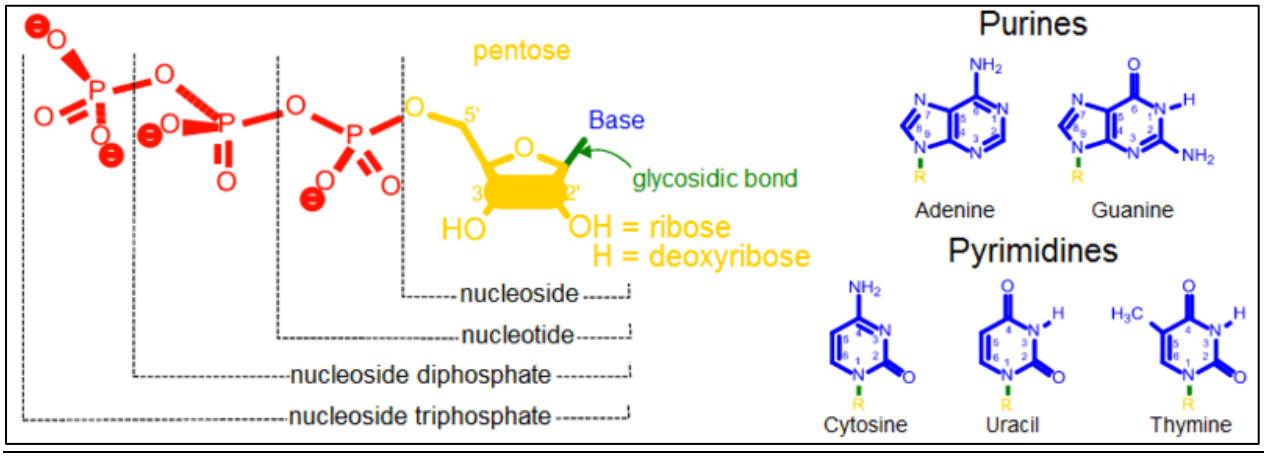
Q2: What is the composition of NA?

Nucleic Acids are made of nucleotides which are composed of three parts:

1- Phosphoric acid (phosphate group).

2- The smaller part called (nucleoside = a pentose sugar and a heterocyclic compound (nitrogen base)

The heterocyclic compounds (nitrogen base) are derivatives of either pyrimidine or purine.



Q3: What is the importance of nucleotides?

- **Nucleotides involved in synthesis of NA. Also play a central role in the metabolism at the cellular level. They carry chemical energy in the form of the nucleoside triphosphates ATP, GTP, CTP and UTP throughout the cell in many cellular functions that demand energy, which include synthesizing amino acids, proteins and cell membranes .**
- **In addition, nucleotides participate in cell signaling (cGMP and cAMP), and are incorporated into important coenzymes of enzymatic reactions (e.g. coenzyme A, FAD, NAD, and $NADP^+$).**

Q4: What is the structure of DNA?

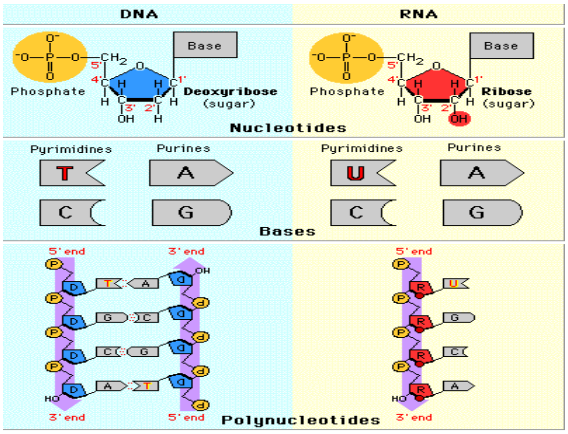
- **DNA molecule consists of two chains of polynucleotides.**
- **Each chain is coiled in a right-hand helix, and the two chains wind around each other to form a (double helix).**
- **The double helix is stabilized by the (hydrogen bonds) between pairs of complementary bases on opposite strands (A=T; G≡C). There for 2 strong hydrogen bonds between A and T and (3 bonds between G and C).**
- **The sequence of bases in the structure of DNA that contains the genetic information of a particular species.**
- **Genetic information must be reproduced exactly each time a cell divides. This is done by making an exact copy of DNA molecule. (The process by which DNA molecules reproduce themselves in the molecules of cell is called DNA replication).**

Q5: What is the structure of RNA?

- **RNA contains ribose instead of 2-deoxyribose as the sugar**
- **The base uracil (U) is present in RNA instead of thymine (T).**
- **RNA is made up of a single polynucleotides chain rather than a double helix.**
- **The genetic information carried by DNA is incorporated into the structure of RNA. The RNA molecules use this information to specify and synthesize the amino acid sequence in proteins.**
- **The enzyme RNA polymerase catalyzes the reaction that joins the nucleotides together into the RNA chain with elimination of pyrophosphate.**

Q6: What are the main differences in the structures of DNA and RNA?

You can write the structure of DNA and RNA same answer in Q4&Q5.



Q7: What is the central dogma?

The central dogma describes the two-step process, transcription and translation, by which the information in genes flows into proteins:

DNA → RNA → Protein.

Transcription is the synthesis of an RNA copy of a segment of DNA.

Q8: What are the types of RNA?

- **DNA is used as a template to make three kinds of RNA:**
- **rRNA: ribosomal RNA is the largest in both size and amount between 60 and 80% of the total RNA in cells. rRNA combines with protein to form (ribosomes the intracellular substructure where proteins are synthesized = protein factory).**
- **Messenger RNA (mRNA): genetic information needed for protein synthesis is transcribed from DNA into mRNA.**
- **Transfer RNA: the Smallest of the three kinds of RNA is (tRNA).**

Q9: What is the genetic code?

The genetic information needed for protein synthesis is transcribed from DNA to mRNA. Translation is the process by which the three-base code in mRNA is turned into a 20-unit code needed to specify the amino acid sequence in proteins. Translation occurs by using a specific sequence of three nucleotide bases on mRNA called (a base triplet or codon).

Q10: What are the pathways for purine nucleotide synthesis?

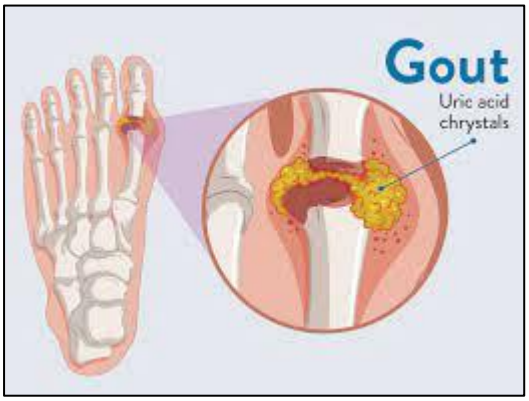
- **The purine nucleotides are synthesized by most of the tissues. However, the major site is the liver. This pathway operates in the cytoplasm.**
- **The major pathway (called de novo synthesis): purine ring is built up on a ribose-5-phosphate molecule. There are ten steps in the de novo synthesis pathway. Major site is the liver.**
- **Salvage Pathway: This pathway ensures the recycling of purines formed by degradation of nucleotides. (5-phosphoribosyl-1-pyrophosphate) PRPP is the starting material in this pathway; it is also a substrate for *de novo* synthesis pathway.**
- **The free purines are salvaged by two different enzymes; adenine phospho ribosyl transferase (APRTase) and hypoxanthine guanine phosphoribosyl transferase (HGPRTase).**
- **The pathway is of special importance in tissues like RBCs and brain where the *de novo* pathway is not operating.**
- **Deficiency of HGPRTase is inherited as an X-linked trait causing (Lesch-Nyhan syndrome).**

Q 11: What is the final degradation product of Purine Nucleotides?

- **Uric acid. And the enzyme responsible for formation of uric acid is called xanthene oxidase.**
- **This degradation is taking place mainly in the liver.**

Q12: What is uric acid?

- **Uric acid is a product of the metabolic breakdown of purine nucleotides, and it is a normal component of urine. Normal blood level of uric acid ranges from 2-5 mg/dl in females and 3-7 mg/dl in males.**
- **The most common abnormality is an elevation of uric acid level in blood, referred to as hyperuricemia. It is defined as serum uric acid concentration exceeding 7 mg/dl in male and 6 mg/dl in female. It may or may not be associated with increased excretion of uric acid in urine, which condition is called uricosuria.**
- **The manifestations are due to the low solubility of uric acid in water.**
- **Hyperuricemia may result from increased production or decreased excretion of uric acid.**
- **Uric acid is barely soluble in plasma, so even a moderate rise in its concentration leads to precipitation of uric acid crystals. This accounts for the development of characteristic features of gout, which include subcutaneous deposits of sodium urate crystals called tophi, arthritis and renal impairment. Gout is of two types: primary and secondary.**
- **In primary gout an inborn enzymatic defect leads to hyperuricemia.**
- **Secondary gout refers to a state where some other primary disorder leads to the increase of uric acid level.**



Q13: What is Lesch-Nyhan syndrome?

- **Lesch-Nyhan syndrome (LNS) is a rare, inherited disorder caused by a deficiency of the enzyme hypoxanthine-guanine phosphoribosyl transferase (HGPRTase).**
- **LNS is an X-linked recessive disease. The syndrome is characterized by neurological and behavioral abnormalities and the overproduction of uric acid in the body. It occurs almost exclusively in males. Signs and symptoms may include inflammatory arthritis (gout), kidney stones, bladder stones, and moderate cognitive disability.**

Q14: What are the pathways for pyrimidines nucleotide synthesis?

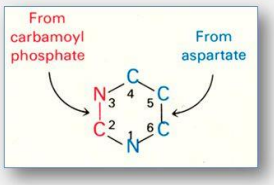
- **Make ring of base then attached to ribose 5 phosphate and combine with PRPP.**
- **Requires 6 steps enzymatic reaction.**

Q15: What are the final degradation products of Pyrimidine Nucleotides?

- **beta alanine converted to malonyl CoA (used in fatty acids synthesis for energy metabolism)**
- **beta-amino isobutyrate converted to methyl malonyl CoA (used in fatty acids synthesis for energy metabolism).**
- **Other products are carbon dioxide and ammonia (into urea cycle and converted to urea).**

Pyrimidine Denovo Synthesis

- ✓ It is a **shorter** pathway than for purines.
- ✓ **The base is made first**, then attached to ribose-P (unlike purine biosynthesis).
- ✓ Requires **6 steps** (instead of 11 for purine).
- ✓ The product is **UMP** (uridine monophosphate).
- ✓ **Only 2 precursors** (aspartate and glutamine, plus HCO_3^-) contribute to the 6-membered ring.



Review Questions:

- **What are the three parts of a nucleotide?**
- **Which nitrogen bases are purines and which are pyrimidines and what is the difference between them?**
- **What do we call a change in the nucleotide sequence?**
- **What is RNA primarily responsible for?**
- **What are the biochemical differences between RNA and DNA?**
- **What are the three types of RNA and their functions?**
- **What is translation and when does it begin?**