

Revised Reprint

Textbook of **BIOCHEMISTRY** for Medical Students

10th Edition

*A Clinically Integrated Approach with
Case Scenarios & Clinical Applications*

As per the Competency-based Medical Education Curriculum (NMC)

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Nucleotides: Chemistry and Metabolism

Specific Learning Objectives

The learner will be able to:

- ❖ Enumerate purines and pyrimidines
- ❖ Nucleosides and nucleotides
- ❖ Outline the de novo synthesis of purine nucleotides
- ❖ Indicate the origin of the different atoms of the purine ring
- ❖ Describe the degradation of purine nucleotides
- ❖ The disorders associated with hyperuricemia and gout
- ❖ The laboratory tests used in gout and their interpretation
- ❖ Describe the salvage pathway, its significance and associated disorders
- ❖ De novo synthesis of pyrimidine nucleotides
- ❖ Enumerate the disorders of pyrimidine metabolism
- ❖ Describe the regulation of purine and pyrimidine metabolism and their interrelationships

INTRODUCTION

BI-6.4: Discuss the laboratory results of analytes associated with gout and Lesch Nyhan syndrome.

In 1868, Frederich Miescher isolated **nucleic acid** (then called nuclein) from pus cells (Fig. 33.1). Albrecht Kossel (Nobel Prize: 1910) differentiated ribonucleic acid (RNA) and deoxyribonucleic acid (DNA) in 1882 (Fig. 33.2). In 1906, Kossel described the four bases in nucleic acids.

Nucleotides are the precursors of the nucleic acids, DNA, and RNA. The nucleic acids are concerned with the storage and transfer of genetic information. The universal currency of energy, namely adenosine triphosphate (ATP), is a nucleotide derivative. Nucleotides are also components of important coenzymes like nicotinamide adenine dinucleotide (NAD⁺) and flavin adenine dinucleotide (FAD), and metabolic regulators such as cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (cGMP).



Fig. 33.1:

Johannes Friedrich Miescher
(1844–1895).



Fig. 33.2:

Albrecht Kossel
Nobel Prize: 1910 (1853–1927).

COMPOSITION OF NUCLEOTIDES

A nucleotide is made up of three components:

1. Nitrogenous base (a purine or a pyrimidine)
2. Pentose sugar, either ribose or deoxyribose
3. Phosphate groups esterified to the sugar. When a base combines with a pentose sugar, a **nucleoside** is formed.

When the nucleoside is esterified to a phosphate group, it is called a **nucleotide** or nucleoside monophosphate. When a second phosphate gets esterified to the existing phosphate group, a nucleoside diphosphate is generated. The attachment of a third phosphate group results in the formation of a nucleoside triphosphate. The nucleic acids (DNA and RNA) are polymers of nucleoside monophosphates.

FUNCTIONS OF NUCLEOTIDES

1. Building blocks for DNA and RNA
2. Energy source (As ATP)
3. Intracellular signaling pathways (as various second messengers, e.g. cAMP)

Bases Present in the Nucleic Acids

Two types of nitrogenous bases—the purines and pyrimidines—are present in nucleic acids.

Purine Bases

The purine bases present in RNA and DNA are the same; **adenine** and **guanine**. Adenine is 6-amino purine and guanine is 2-amino, 6-oxypurine. The numbering of the purine



Fig. 33.3: Structure of purines.

ring with the structure of adenine and guanine are shown in Figure 33.3.

Minor Purine Bases

Some bases may be found in small amounts in nucleic acids and hence called minor bases. These are hypoxanthine (oxopurine) and xanthine (di-oxopurine; Fig. 33.4). Uric acid (tri-oxopurine) is formed as the end product of the catabolism of other purine bases. It can exist in the “enol” as well as “keto” forms (tautomeric forms; Fig. 33.4). Keto form is by far the predominant type under physiological conditions.

Pyrimidine Bases

The pyrimidine bases present in nucleic acids are cytosine, thymine, and uracil. **Cytosine** is present in both DNA and RNA. **Thymine** is present in DNA and **uracil** in RNA. Structures are shown in Figure 33.5. See also Box 33.1. A few other modified pyrimidine bases like dihydrouracil and methylcytosine are also found rarely in some types of RNA (Fig. 33.6).

NUCLEOSIDES

Nucleosides are formed when bases are attached to the pentose sugar, D-ribose or 2-deoxy D-ribose (Fig. 33.7). All the bases are attached to the corresponding pentose sugar by the beta-N-glycosidic bond between the first carbon of the pentose sugar and N9 of a purine or N1 of a pyrimidine.

The carbon atoms of the pentose sugar are denoted by attaching a priming sign to the numbers to avoid confusion with

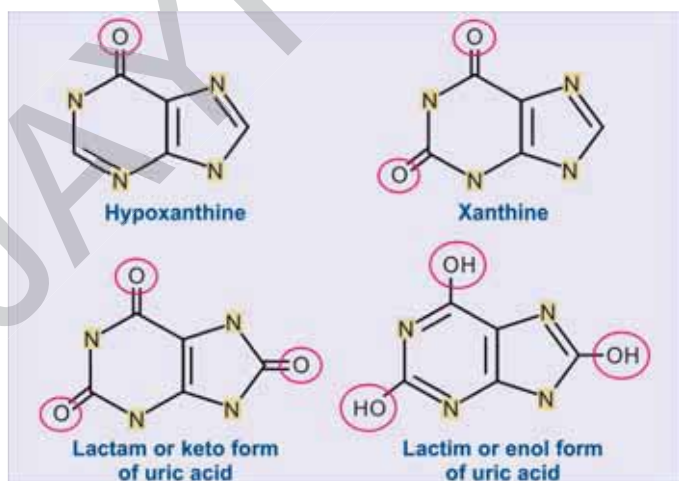


Fig. 33.4: Minor bases seen in nucleic acids.

Box 33.1 These two words are often confused.

- **Thymine** is the base present in DNA.
- **Thiamine** is a member of vitamin B complex.

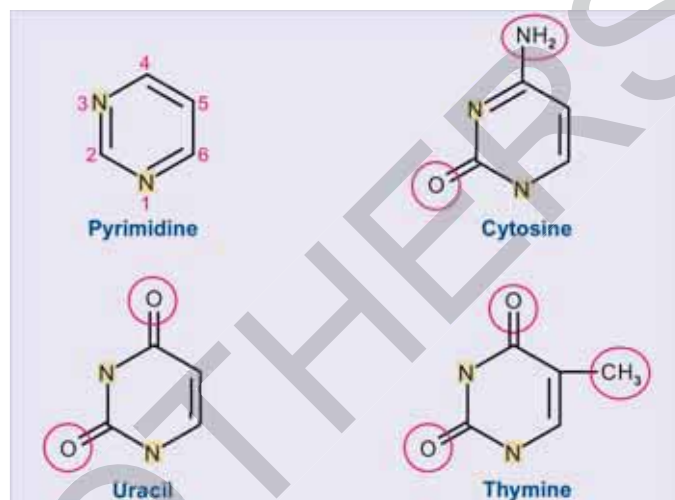


Fig. 33.5: Common pyrimidines.

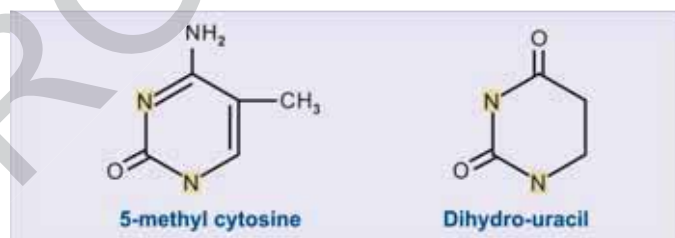


Fig. 33.6: Modified pyrimidine bases.

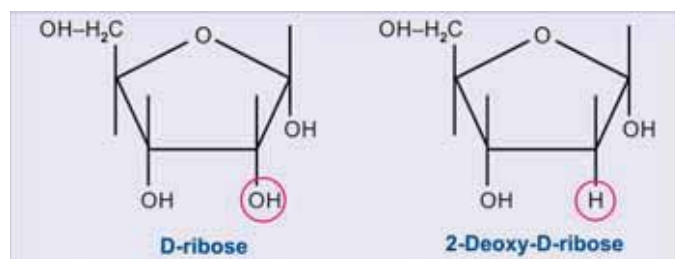


Fig. 33.7: Sugar groups in nucleic acids.

the carbon atoms of the purine or pyrimidine ring (Fig. 33.8). The names of the different nucleosides are given in Table 33.1.

The deoxynucleosides are denoted by adding the prefix *d-* before the nucleoside. Nucleosides with purine bases have the suffix **-sine**, while pyrimidine nucleosides end with **-dine**. Uracil combines with ribose only; and thymine with deoxyribose only (Table 33.1).

NUCLEOTIDES

These are phosphate esters of nucleosides. Base plus pentose sugar plus phosphoric acid is a nucleotide. The esterification occurs at the 5th or 3rd hydroxyl group of the pentose sugar. Most of the nucleoside phosphates involved in biological function are 5'-phosphates (Table 33.2).

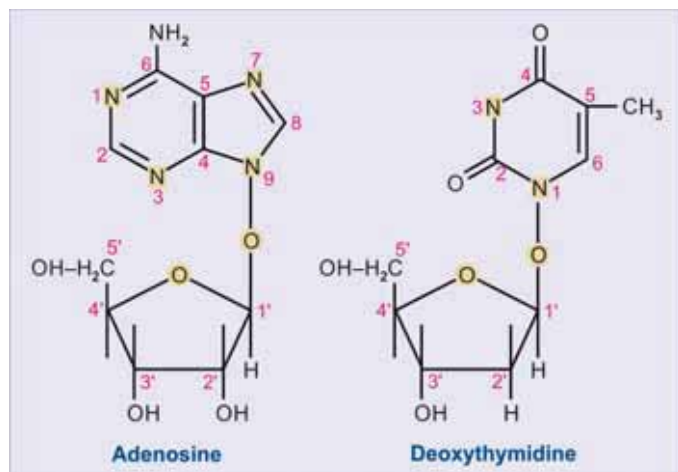


Fig. 33.8: Numbering in base and sugar groups. Atoms in sugar are denoted with primed numbers.

TABLE 33.1 Base + sugar are nucleosides.

<i>Ribonucleosides</i>		
Base	Sugar	Nucleoside
Adenine	Ribose	Adenosine
Guanine	Ribose	Guanosine
Uracil	Ribose	Uridine
Cytosine	Ribose	Cytidine
Hypoxanthine	Ribose	Inosine
Xanthine	Ribose	Xanthosine
<i>Deoxyribonucleosides</i>		
Base	Sugar	Nucleoside
Adenine	Deoxyribose	Deoxyadenosine (d-adenosine)
Guanine	Deoxyribose	d-guanosine
Cytosine	Deoxyribose	d-cytidine
Thymine	Deoxyribose	d-thymidine

Since 5'-nucleotides are more often seen, they are simply written without any prefix. For example, 5'-AMP is abbreviated as AMP; but 3' variety is always written as 3'-AMP. Moreover, a base can combine with either ribose or deoxyribose, which in turn can be phosphorylated at 3' or 5' positions. One purine and one pyrimidine derivative are given as examples in Table 33.3.

Many coenzymes are derivatives of adenosine monophosphate. Examples are NAD⁺, NADP, FAD, and coenzyme A. Nucleotides and nucleic acids absorb light at a wavelength of 260 nm; this aspect is used to quantitate them. As nucleic acids absorb ultraviolet light, chemical modifications are produced leading to mutation and carcinogenesis.

NUCLEOSIDE TRIPHOSPHATES

Corresponding nucleoside diphosphate and triphosphate are formed by esterification of further phosphate groups to the existing ones. In general, any nucleoside triphosphate is abbreviated as NTP or d-NTP (Table 33.4).

Nucleoside diphosphate contains one high energy bond and triphosphates have two high energy bonds. ATP is the

TABLE 33.2 Base + sugar + phosphate = nucleotide.

<i>Ribonucleotides</i>		
Base	Phosphate	Nucleotide
Adenosine	Pi	Adenosine monophosphate (AMP; adenylic acid)
Guanosine	Pi	Guanosine monophosphate (GMP; guanylic acid)
Cytidine	Pi	Cytidine monophosphate (CMP; cytidylic acid)
Uridine	Pi	Uridine monophosphate (UMP; uridylic acid)
Inosine	Pi	Inosine monophosphate (IMP; inosinic acid)

Deoxyribonucleotides

Base	Phosphate	Nucleotide
d-adenosine	Pi	d-AMP (d-adenylic acid)
d-guanosine	Pi	d-GMP (d-guanylic acid)
d-cytidine	Pi	d-CMP (d-cytidylic acid)
d-thymidine	Pi	d-TMP (d-thymidylic acid)

TABLE 33.3 Nucleosides and nucleotides.

Base	Sugar	Nucleoside	Phosphoric acid at	Nucleotide
Adenine	Ribose	Adenosine	5' position	AMP
Adenine	Ribose	Adenosine	3' position	3'-AMP
Adenine	Deoxyribose	d-adenosine	5' position	d-AMP
Adenine	Deoxyribose	d-adenosine	3' position	d-3'-AMP
Cytosine	Ribose	Cytidine	cytidine 5' position	CMP
Cytosine	Ribose	Cytidine	3' position	3'-CMP
Cytosine	Deoxyribose	d-cytidine	5' position	d-CMP
Cytosine	Deoxyribose	d-cytidine	3' position	d-3'-CMP

(AMP: adenosine monophosphate; CMP: cytidine monophosphate)

TABLE 33.4 Nucleoside triphosphates.

Nucleoside	Nucleoside monophosphate	Nucleoside diphosphate (NDP)	Nucleoside triphosphate (NTP)
<i>Ribonucleoside phosphates</i>			
Adenosine	Adenosine monophosphate (AMP)	Adenosine diphosphate (ADP)	Adenosine triphosphate (ATP)
Guanosine	GMP	GDP	GTP
Inosine	IMP	IDP	ITP
Cytidine	CMP	CDP	CTP
Uridine	UMP	UDP	UTP
<i>Deoxyribonucleoside phosphates</i>			
d-adenosine	d-AMP	d-ADP	d-ATP
d-guanosine	d-GMP	d-GDP	d-GTP
d-cytidine	d-CMP	d-CDP	d-CTP
d-thymidine	d-TMP	d-TDP	d-TTP

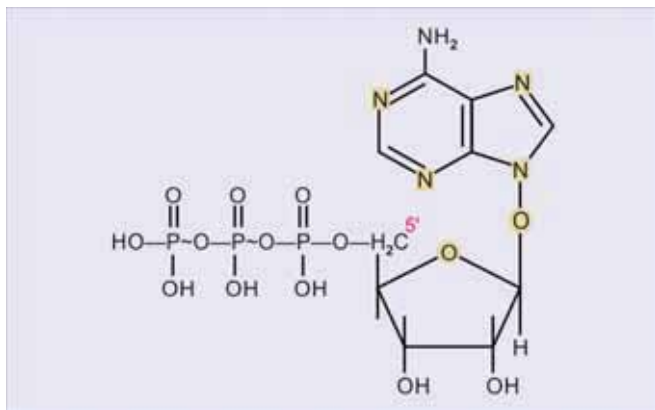


Fig. 33.9: Adenosine triphosphate (ATP).

universal energy currency (Fig. 33.9). It is formed during oxidative processes by trapping the released energy in the high energy phosphate bond. More details on high energy bonds are given in Chapter 7.

■ CYCLIC NUCLEOTIDES

A phosphodiester linkage may be formed between the 3' and 5' positions of ribose group. Such compounds are called cyclic nucleotides (Fig. 33.10). The 3', 5'-**cyclic AMP** or cAMP is a major metabolic regulator. Cyclic GMP also behaves similarly. These are second messengers in mediating the action of several hormones.

Deoxyribonucleotides are used for synthesis of DNA and ribonucleotides for RNA. In pseudouridylic acid (found in tRNA) uridine is attached to ribose phosphate in a C-C bond instead of C-N bond in UMP (Fig. 33.11).

High energy compounds are listed in Table 7.4. Please note that active methionine, amino acid adenylates, active sulfate, etc. are higher energy compounds containing adenosine monophosphate.

■ DIGESTION OF NUCLEIC ACIDS

The nucleic acids in the diet are hydrolyzed to a mixture of nucleotides by **ribonuclease** and **deoxyribonuclease** present in pancreatic and intestinal secretions. Then nucleotidases liberate the **phosphate** from nucleotides. The resulting nucleosides are hydrolyzed by nucleosidases forming free



Fig. 33.10: 3', 5'-cyclic adenosine monophosphate or cAMP.

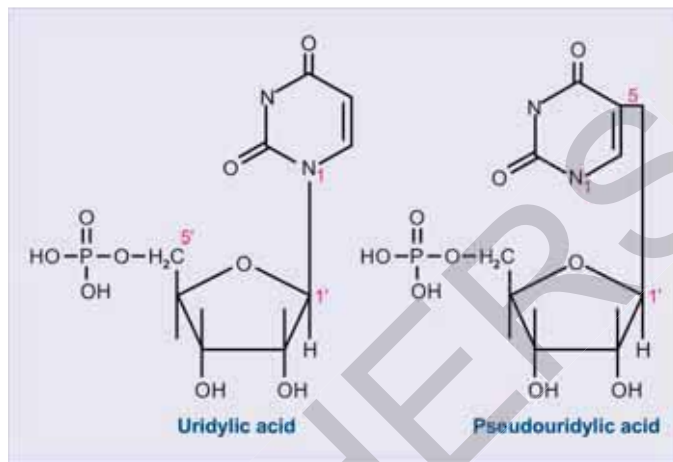


Fig. 33.11: Different attachment of uracil to sugars.

bases and pentose sugars. However, the dietary purines and pyrimidines are **neither converted to nucleotides nor incorporated into nucleic acids**. They are directly catabolized.

■ BIOSYNTHESIS OF PURINE NUCLEOTIDES

BI-6.2: Describe and discuss the metabolic processes in which nucleotides are involved.

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 is denoted as **de novo synthesis**, because the purine ring is synthesized from different small components. Since the human beings can synthesize the purine and pyrimidine bases de novo, they are said to be prototrophs.

The contribution of different atoms from different sources for the formation of the purine ring is shown in the Figure 33.12. During the de novo synthesis, **purine ring is built upon a ribose-5-phosphate molecule**. Hence nucleotides are the products of the de novo synthesis.

There are ten steps in the de novo synthesis pathway. The enzymes catalyzing these reactions are existing as a multienzyme complex in eukaryotic cells; this arrangement increases the efficiency of the pathway. The names of the enzymes catalyzing the purine synthesis steps are shown under the Figure 33.13.

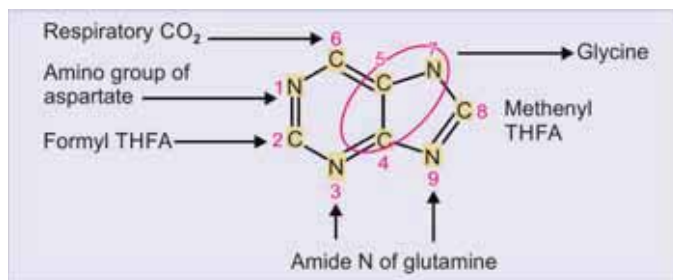


Fig. 33.12: The assembly of purine ring is from various sources. (THFA: tetrahydrofolic acid)

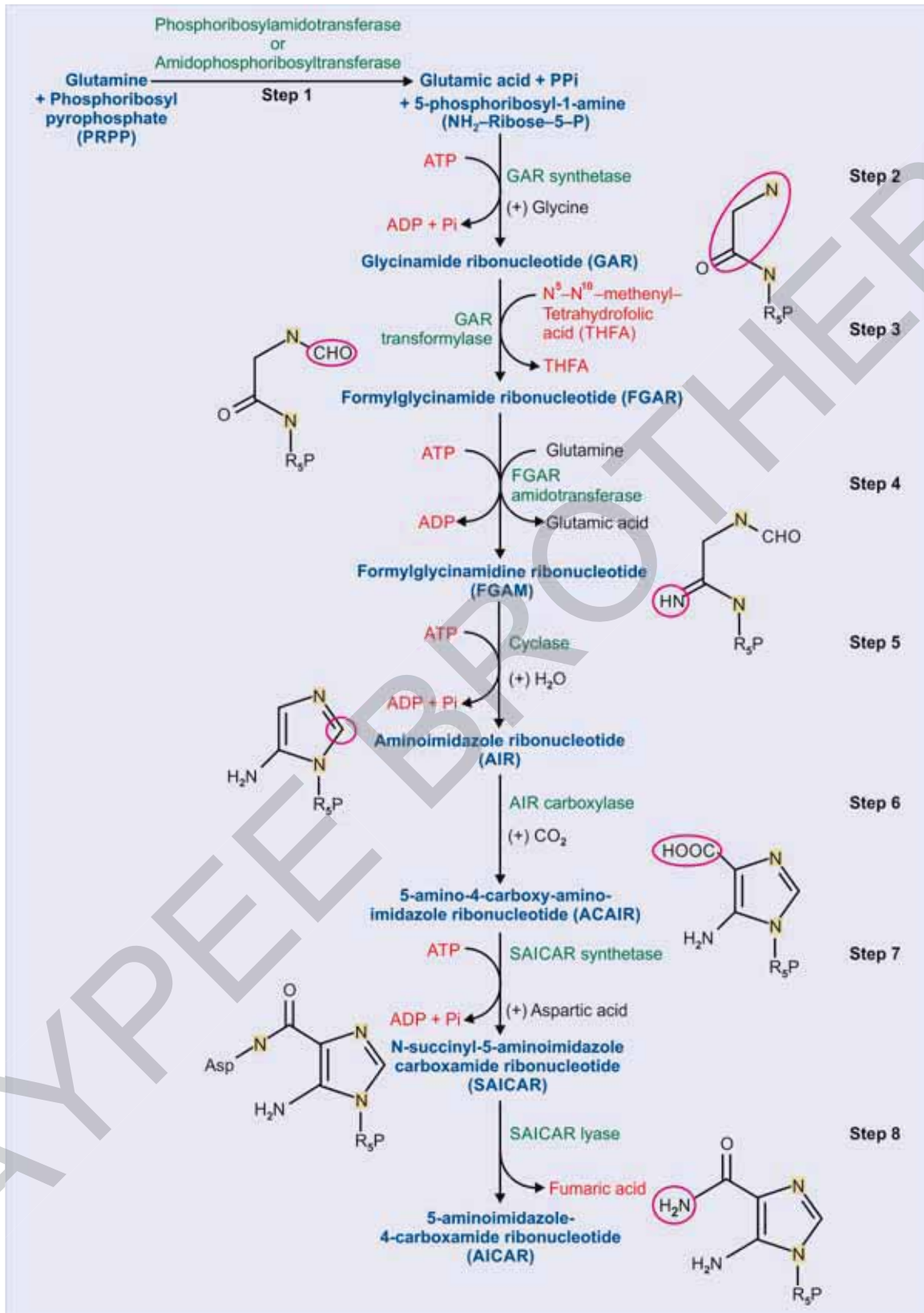


Fig. 33.13: Contd...

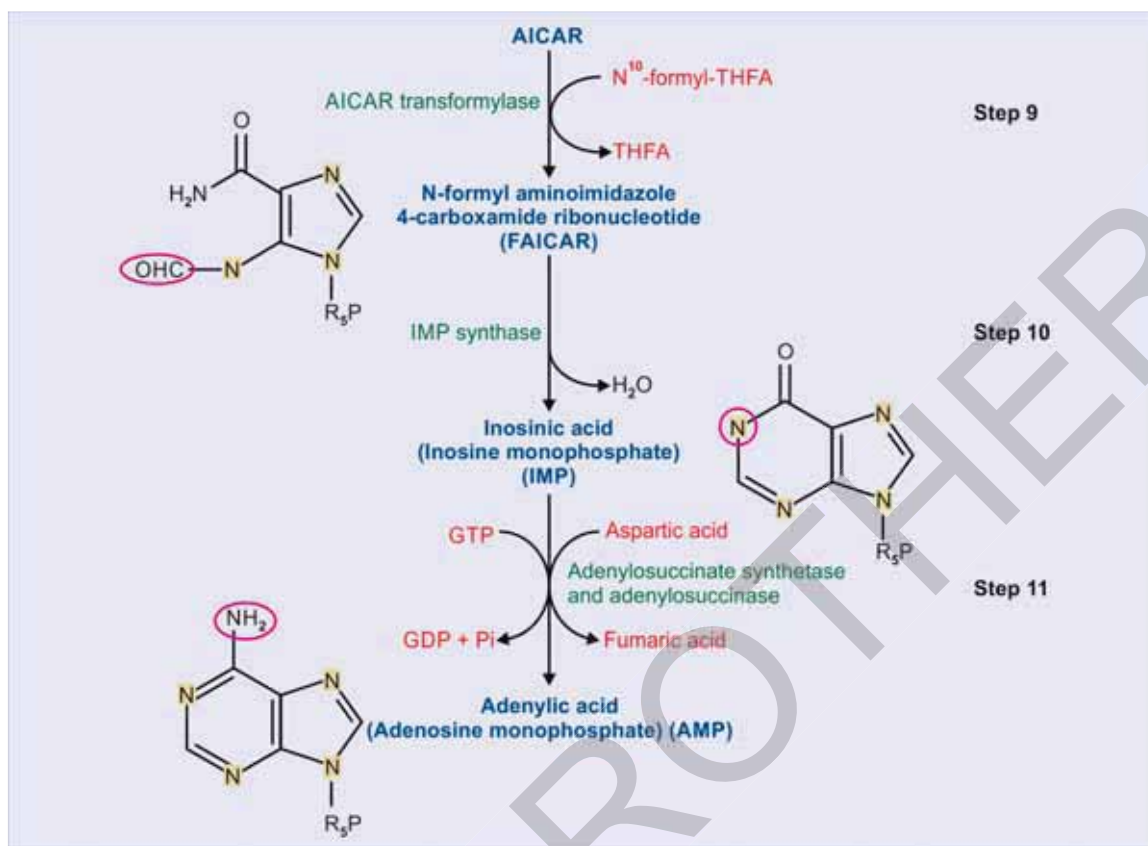


Fig. 33.13: Steps of purine synthesis.

Note: The purine ring is built upon a ribose-5-phosphate.

Step 0 (Preparatory Step): Phosphoribosyl Pyrophosphate Synthesis

Phosphoribosyl pyrophosphate (PRPP) is the donor of ribose-5-phosphate for de novo synthesis. The reaction is:



The structure of PRPP is shown in Figure 33.14. The purine ring is later on assembled on the ribose-5-phosphate. PRPP is also used for the synthesis of pyrimidine nucleotides, nucleotide coenzymes and also for the salvage pathway. Hence the synthesis of PRPP is not considered as a step in the de novo synthesis of purine nucleotides; it is called a preliminary or preparatory step.

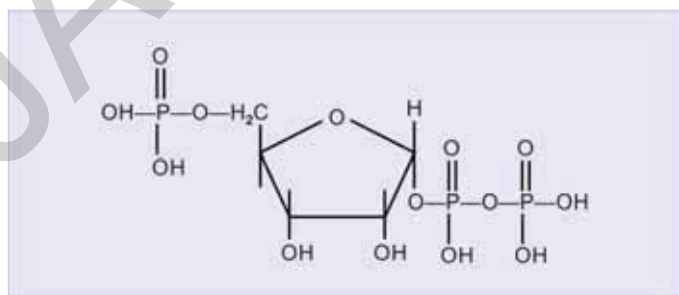


Fig. 33.14: Phosphoribosyl pyrophosphate.

Formation of AMP

Steps 1 to 10 are summarized in Table 33.5. Flow diagrams of these steps are shown in Figure 33.13. The de novo synthesis of one molecule of purine nucleotide requires 6 ATP.

TABLE 33.5 Summary of steps of purine synthesis.

Donor	Added atom	Product
Glutamine	N9 (rate limiting)	PRA
Glycine (ATP required)	C4, 5, N7	GAR
Methenyl-THFA	C8	FGAR
Glutamine	N3 (ATP required)	FGAM
–	Ring closure (ATP)	AIR
Carbon dioxide	C6	ACAIR
Aspartic acid	N1 (ATP required)	SAICAR
–	Fumarate removed	AICAR
Formyl-THFA	C2	FAICAR
–	Ring closure	IMP

(ACAIR: amino carboxyamino imidazole ribonucleotide; AICAR: amino imidazole carboxamide ribonucleotide; AIR: amino imidazole ribonucleotide; FAICAR: formyl aminoimidazole carboxamide ribonucleotide; FGAR: formyl glycinamide ribonucleotide; FGAM: formyl glycinamide ribonucleotide; GAR: glycinamide ribonucleotide; IMP: inosine monophosphate; PRA: phosphoribosyl amine; SAICAR: succinylaminoimidazole carboxamide ribonucleotide.)

Details of the reactions is shown in Figure 33.13.

The first step is the rate-limiting enzyme. The step 4 is inhibited by **azaserine**, while **6-mercaptopurine** inhibits amination of inosine monophosphate (IMP) to AMP. So both are **anticancer drugs**.

Conversion of IMP to GMP

The conversion of IMP to guanosine monophosphate (GMP) involves two steps, in which the first step is the oxidation of IMP to xanthylic acid [xanthosine monophosphate (XMP)] by an NAD^+ dependent dehydrogenase. Then the NH_2 group from glutamine is transferred to XMP to form GMP by an amidotransferase. The ATP is hydrolyzed to AMP level in this reaction (Fig. 33.15). Both AMP and GMP can be converted to their corresponding di- and triphosphates. *Synthesis of one molecule of purine nucleotide requires 6 high energy phosphates.*

Regulation of Purine Synthesis

The committed step in de novo synthesis is the reaction catalyzed by amidotransferase (Step 1, Fig. 33.13). It is inhibited by AMP and GMP. They act as allosteric modifiers. Binding of AMP and GMP on the enzyme converts monomeric active form to a dimeric inactive form. Since both AMP and GMP can bind to the same enzyme molecule at different sites, they act synergistically.

Both, AMP and GMP, inhibit their own formation by feedback inhibition of adenylosuccinate synthetase and IMP dehydrogenase. The formation of AMP from IMP requires GTP; similarly formation of GMP requires ATP. Hence both GTP and ATP are made available in sufficient quantities (**coordinated regulation**).

The availability of PRPP is another important regulatory factor. The activity of PRPP synthetase is regulated by negative modifiers; purine and pyrimidine nucleotides. Since the salvage pathway provides inhibitory nucleotides and utilizes PRPP, the rate of operation of salvage pathway has a regulatory effect on de novo synthesis. A balance between the two pathways is essential to maintain the cellular pool of purine nucleotides.

Multifunctional Enzymes of Purine Nucleotide Synthesis

In prokaryotes, each reaction is catalyzed by a different polypeptide. But in eukaryotes gene fusion has taken place,

so that a single polypeptide has multiple catalytic functions. These multifunctional enzymes are:

- Reaction steps 3, 4 and 6—phosphoribosylglycinamide synthase, formyl transferase, aminoimidazole ribosyl 5 phosphate synthase
- Reaction steps 7 and 8—aminoimidazole ribosyl 5 phosphate carboxylase, aminoimidazole succinyl carboxamide ribosyl 5 phosphate synthase
- Reaction steps 10 and 11—formyltransferase, IMP cyclohydrolase.

Structural Analogues as Purine Synthesis Inhibitors

These structural analogues act as **competitive inhibitors** of the naturally occurring nucleotides that are used to synthesize DNA. When wrong bases are incorporated, the DNA becomes functionally inactive. There by cell division is arrested. So they are useful as anticancer drugs. A few examples are:

- Mercaptopurine (Fig. 33.16A) inhibits the conversion of IMP to GMP and AMP.
- Folate antagonists (methotrexate; Fig. 33.16B) would affect the reactions involving one carbon group transfers.
- Azaserine (diazoacetyl-L-serine; Fig. 16.10) is a glutamine antagonist and therefore inhibits reactions involving glutamine (Steps 1 and 4 in Figure 33.13).
- Other synthetic nucleotide analogues used as anticancer agents are thioguanine (Fig. 33.16C) and azaguanine (Fig. 33.16D).

Salvage Pathway

This pathway ensures the recycling of purines formed by degradation of nucleotides. Nucleosides and deoxynucleosides can also be salvaged. PRPP is the starting material in this pathway; it is also a substrate for de novo synthesis. Hence these two pathways are closely inter-related.

The free purines are salvaged by two different enzymes; adenine phosphoribosyltransferase (**APRTase**) and hypoxanthine guanine phosphoribosyl transferase (**HGPRTase**).

The pathway is of special importance in tissues like red blood cells (RBCs) and brain where the de novo pathway is not operating. The salvage pathway economizes intracellular energy expenditure. Absence of enzymes of salvage pathway produces specific clinical syndromes. Salvage pathway is summarized as:

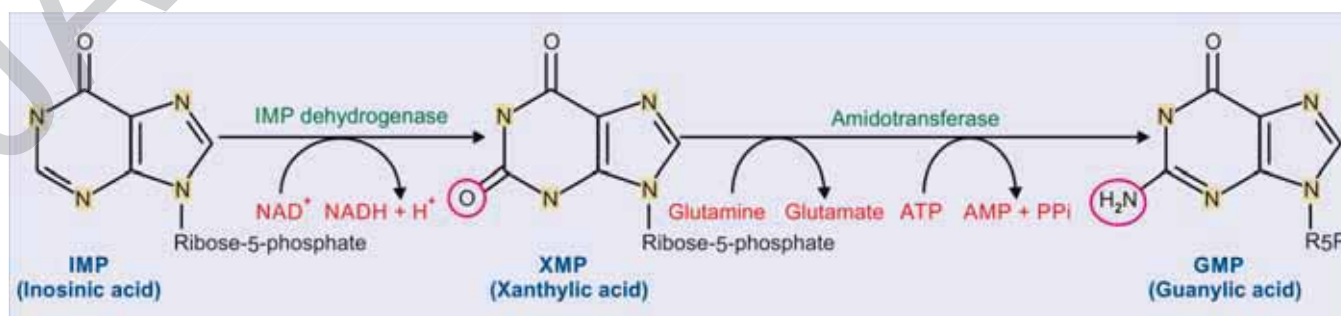
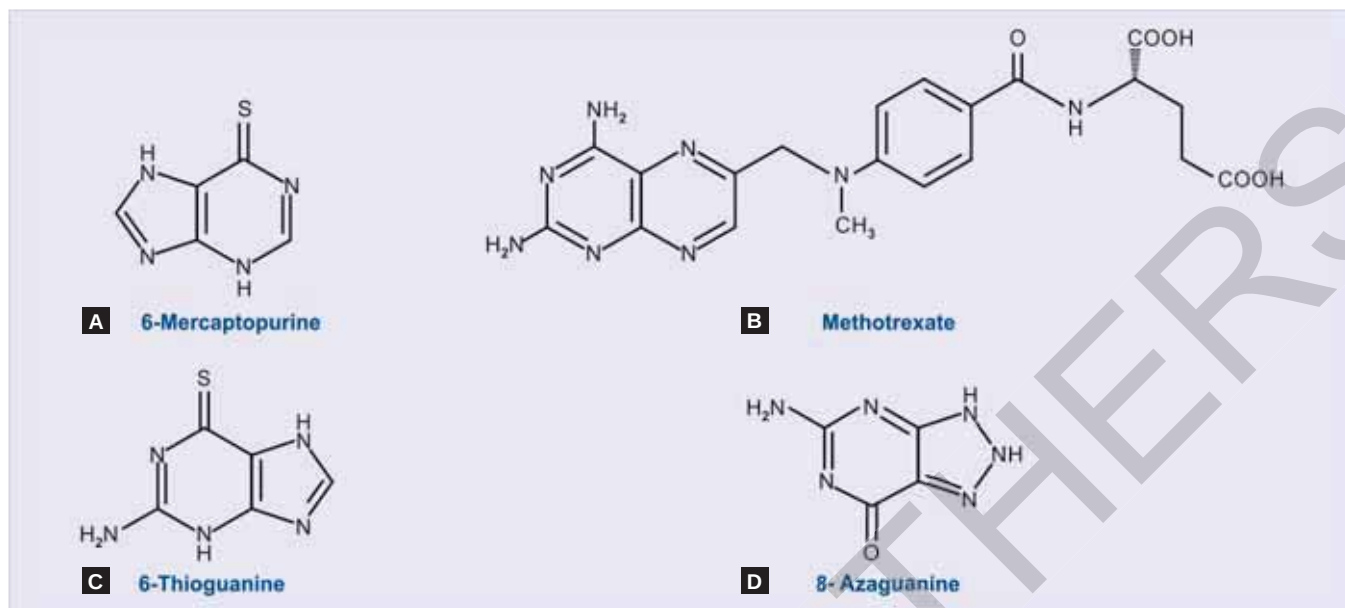
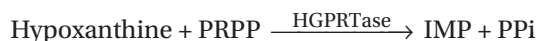


Fig. 33.15: Conversion of inosine monophosphate (IMP) to guanosine monophosphate (GMP).



Figs. 33.16A to D: Purine synthesis inhibitors.



Purine Nucleoside Di- and Triphosphates

These are synthesized by specific kinases and phosphate group is donated by ATP. One example is given below.



DEGRADATION OF PURINE NUCLEOTIDES

The end product of purine nucleotide catabolism is **uric acid** (urate). The structure is shown in Figure 33.4. This degradation is taking place mainly in the liver. The steps are shown in Figure 33.17. The major steps are deamination, removal of ribose 1 phosphate followed by two successive oxidation steps.

The xanthine oxidase is a metalloflavoprotein containing FAD, **molybdenum**, and iron. As xanthine is oxidized to uric acid, the electrons are transferred first to molybdenum, then to FAD, and finally to molecular oxygen, when **hydrogen peroxide** (one of the reactive oxygen species) is produced.

Species Difference

The end product of purine catabolism in human beings is uric acid. However, the total amount of nitrogen excreted as uric acid is very little, because human beings are **ureotelic**. The amino nitrogen is finally excreted as urea in mammals. The birds, amphibians, and reptiles are **uricotelic** because they

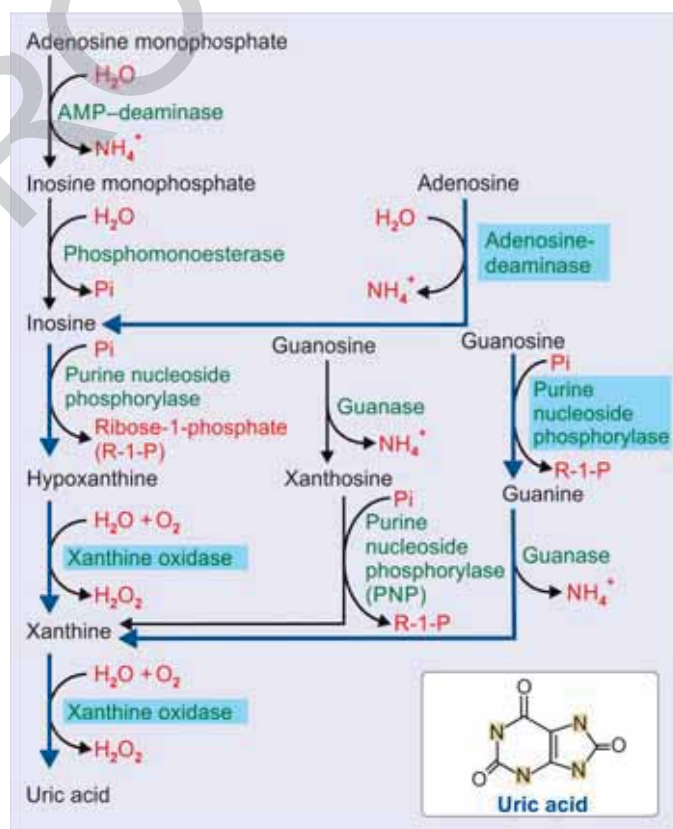


Fig. 33.17: Degradation of purine nucleotides. Main pathway is shown in blue arrows.

excrete uric acid as the major end product of purine as well as amino acid catabolism. The lower primates and some other mammals have the enzyme uricase which converts uric acid to allantoin and the final product excreted is allantoin which is more water soluble.

11. Which property of uric acid is responsible for the manifestations of gout?
 - A. Keto-enol tautomerism
 - B. Acidic nature
 - C. Reducing action
 - D. Solubility constant
12. Which compound is not derived from purine nucleotides?
 - A. Uric acid
 - B. Beta aminoisobutyric acid
 - C. Allantoin
 - D. Xanthic acid
13. Uric acid is the end product of breakdown of all the following, *except*:
 - A. AMP
 - B. IMP
 - C. Xanthosine
 - D. CMP
14. Secondary hyperuricemia is seen in all the following conditions, *except*:
 - A. Leukemia
 - B. Psoriasis
 - C. Hepatitis
 - D. Cytotoxic drug therapy
15. Which is correct regarding thymine synthesis?
 - A. Fourth carbon is donated by carbamoyl phosphate
 - B. Third nitrogen is donated by aspartate
 - C. Methylation is taking place on dUMP and not on UMP
 - D. First nitrogen is donated by glutamine
16. Regarding gout, all are true, *except*:
 - A. It is seen in HGPRT deficiency
 - B. There is deposition of urate in joints
 - C. Can be treated using allopurinol
 - D. It is seen in PRPP synthetase deficiency
17. If a cell is unable to synthesise PRPP, synthesis of which is likely to be directly affected?
 - A. Pyridoxal
 - B. OMP
 - C. CoASH
 - D. FAD
18. During de novo synthesis of pyrimidine, which nucleotide is first formed?
 - A. TMP
 - B. OMP
 - C. UMP
 - D. CMP
19. The drug of choice for primary gout is:
 - A. Allopurinol
 - B. Aspirin
 - C. Colchicine
 - D. Probenecid
20. All manifestations are seen in Lesch-Nyhan syndrome, *except*:
 - A. Self-mutilation
 - B. Immunodeficiency
 - C. Hyperuricemia
 - D. X-linked inheritance
21. All are true regarding pyrimidine nucleotide synthesis, *except*:
 - A. The reactions occur in the cytoplasm
 - B. CTP is a negative modifier
 - C. Glutamine and aspartic acid are used
 - D. Pyrimidine ring is built up on a ribose-5-phosphate
22. Formation of dTMP requires:
 - A. S-adenosylmethionine
 - B. NADPH
 - C. Adrenodoxin
 - D. Molybdenum
23. Orotic aciduria is characterized by all the findings, *except*:
 - A. Megaloblastic anemia
 - B. Response to oral uridine
 - C. Failure to thrive
 - D. Deficiency of HGPRTase
24. Which of the following condition is not associated with hyperuricemia?
 - A. Multiple myeloma
 - B. Xanthinuria
 - C. Psoriasis
 - D. Polycythemia vera

ANSWERS OF MULTIPLE CHOICE QUESTIONS

- | | | | | | | | | |
|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| 1. B | 2. B | 3. B | 4. B | 5. D | 6. D | 7. A | 8. D | 9. C |
| 10. C | 11. D | 12. B | 13. D | 14. C | 15. C | 16. A | 17. B | 18. B |
| 19. A | 20. B | 21. D | 22. B | 23. D | 24. B | | | |

VIVA VOCE QUESTIONS AND ANSWERS

1. What is a nucleotide?
Nitrogenous base + sugar + phosphate.
2. What is a nucleoside?
Nitrogenous base + sugar.
3. What are the sugars in nucleic acids?
Ribose in RNA and deoxyribose in DNA.
4. What are the bases present in nucleotides?
Purines and pyrimidines.
5. Name the common purines.
Adenine and guanine.
6. Name the common pyrimidines.
Cytosine, uracil, thymine.
7. What are the bases present in DNA?
Adenine, guanine, cytosine, thymine.
8. Which base is absent in DNA?
Uracil.
9. Which base is found exclusively in DNA and not in RNA?
Thymine.
10. Which base is found exclusively in RNA?
Uracil.
11. Which amino acid is required for both purine and pyrimidine synthesis?
Aspartic acid and glutamine.
12. N3 of purine ring is donated by what?
Glutamine.
13. Glycine donates what part of the purine ring?
C4, C5, N7 atoms.
14. What is the key enzyme of de novo synthesis pathway of purines?
Phosphoribosyl amidotransferase (Step 1).
15. How is de novo synthesis of purine regulated?
Amidotransferase enzyme is inhibited by AMP and GMP.

- 16. Give a few examples of purine analogues, used as anticancer drugs.**
6-mercaptopurine, cytosine arabinoside, methotrexate, azaserine.
- 17. What is the end product of catabolism of purines in human beings?**
Uric acid.
- 18. Name an enzyme containing molybdenum.**
Xanthine oxidase contains FAD, molybdenum, and iron.
- 19. What is the normal uric acid level in blood?**
2–5 mg/dL in females and 3–7 mg/dL in males.
- 20. What is gout?**
It is a disease associated with hyperuricemia, deposit of urate crystals in joints and excruciating joint pain.
- 21. When is increased uric acid level seen?**
Gout, pre-eclampsia, Hodgkin's lymphoma, leukemia.
- 22. Hyperuricemia is observed in which conditions?**
Gout, Lesch-Nyhan syndrome, von Gierke's disease.
- 23. What is the reason for severe combined immunodeficiency?**
Adenosine deaminase deficiency.
- 24. What are starting materials for pyrimidine synthesis?**
Carbamoyl phosphate and aspartic acid.
- 25. What is the rate limiting step in pyrimidine synthesis?**
Aspartate transcarbamoylase.
- 26. How is pyrimidine synthesis pathway regulated in mammals?**
CPS II is inhibited by CTP.
- 27. Orotic aciduria is a feature of deficiency of which enzymes?**
OMP decarboxylase, OPRTase, ornithine transcarbamoylase.
- 28. What are the characteristic features of orotic aciduria?**
Megaloblastic anemia.
- 29. What is the mechanism of methotrexate?**
It inhibits dihydrofolate reductase and thereby reduces the regeneration of THFA; it is a powerful anticancer agent.

Textbook of BIOCHEMISTRY for Medical Students

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