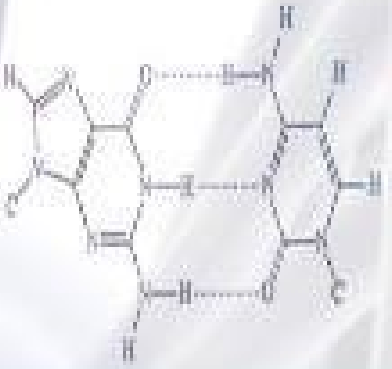
Medical Committee
The University of Jordan

SLIDE ○ SHEET

SLIDE : 24

DR.NAME: Dr. Nayef

Biochemistry



Majida Al-Foqaraa'

# NUCLEOTIDE METABOLISM

**Nucleotides are essential :-**

- .DNA + RNA .— protein synthesis
- .Energy currency
- .Carriers & activated intermediates
- .Components & essential cofactors: CoA, FAD, $NAD^+$, $NADP^+$
- .Regulatory compounds cAMP, ATP, cGMP

**Synthesis :-**

I → **De novo synthesis**

II → **Salvage pathway :-**

III → Degradation of Nucleotides (DNA + RNA) in G.I.T → bases + nucleoside (little only) → Blood
→ Uric acid

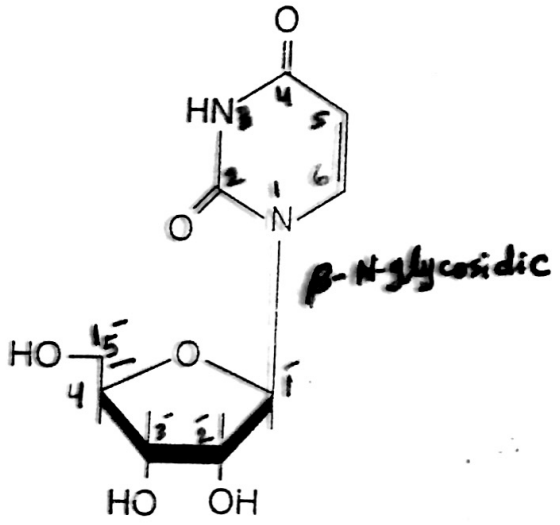
# Pyrimidine Nucleosides

- major Pyrimidine nucleotides are those of Uracil & Cytosine, thymine.

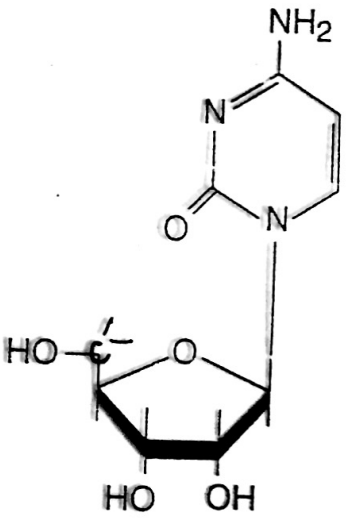
β-N-Glycosidic bond
- Stable to Alkali
- Stable to Acid treatment
- 60% PCA +100°C release bases

Nucleotides (more polar) more soluble than nucleosides & free bases

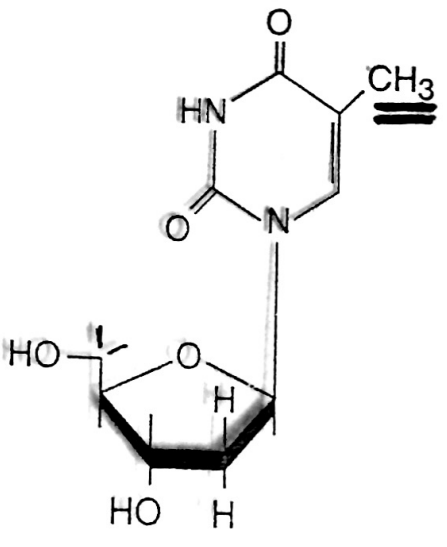
Nucleosides are more stable than free bases




Uridine



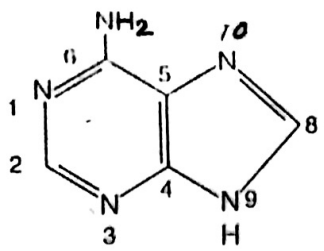
Cytidine



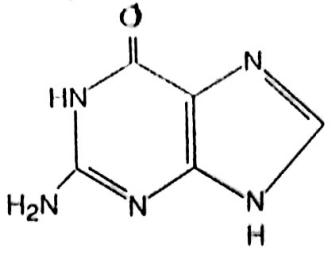
Thymidine

# Chemistry of Nucleotides:-



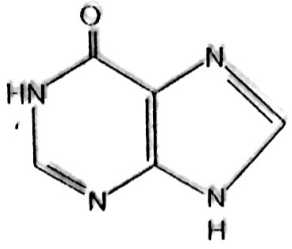


Adenine

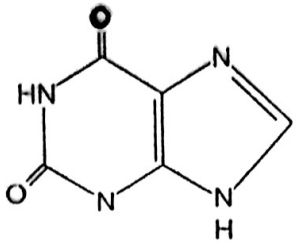


Guanine

} major

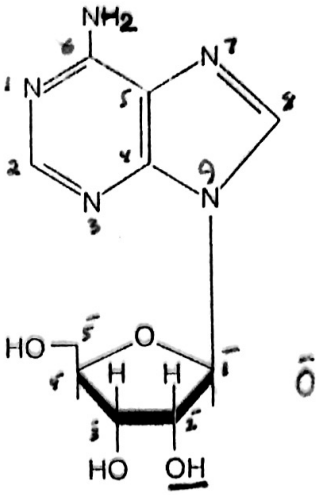


Hypoxanthine

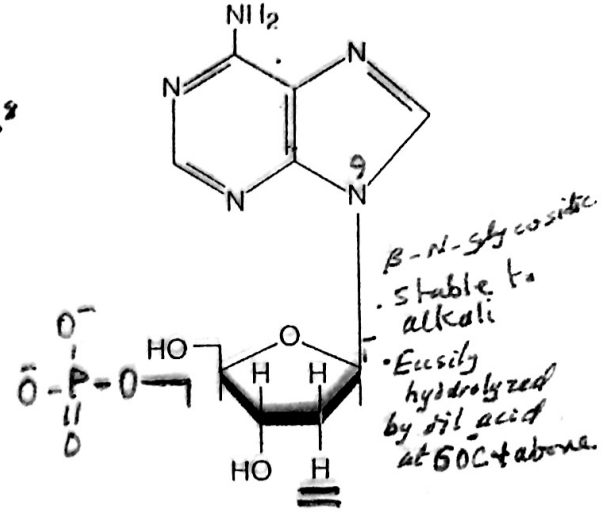


Xanthine

FIGURE 12.1
Purine bases.



Adenosine



Deoxyadenosine

β-N-glycosidic
· Stable to alkali
· Easily hydrolyzed by dil acid at 60°C + above.

FIGURE 12.2
Adenosine and deoxyadenosine.

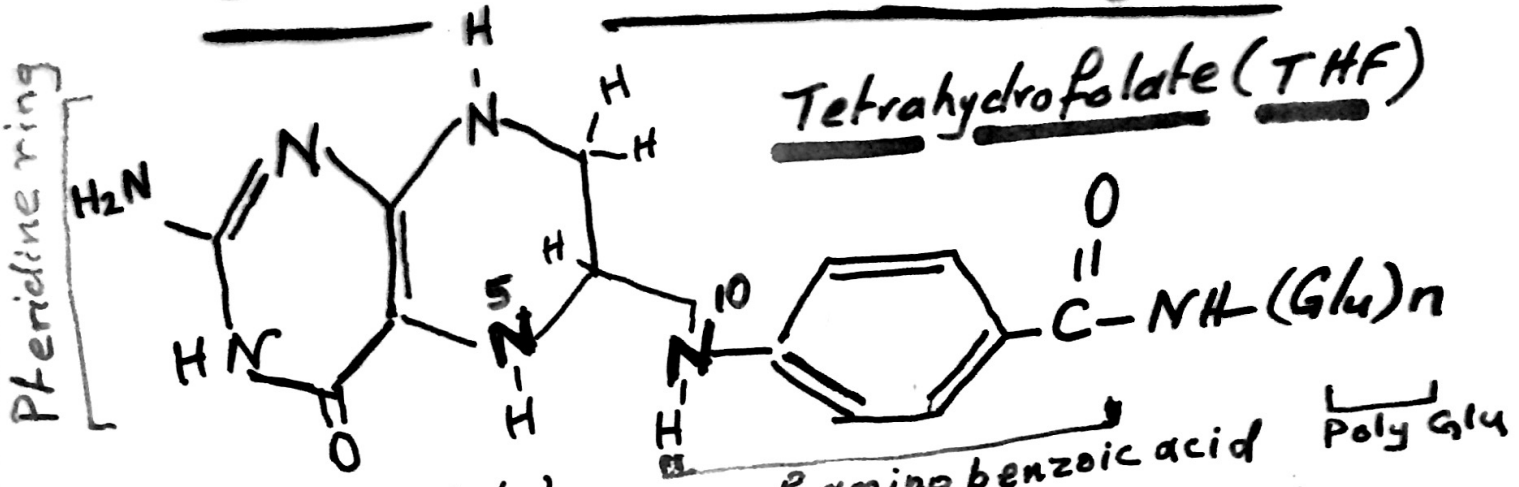
Nucleotides

- Di + tri-phosphates more than mono-, nucleosides & free bases
- ATP is found highest
- Conc. varies with cell type.
- Ribonucleotides > Deoxy-

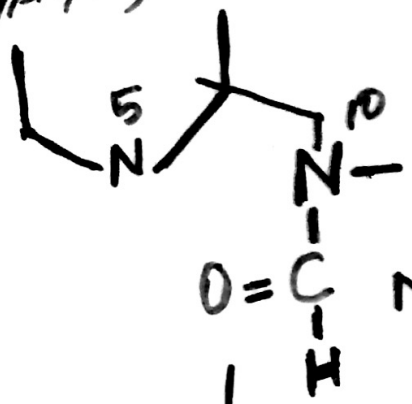
Absorption of light in U.V. at 260nm
Purine derivatives have stronger absorption than pyrimidine derivatives

# One-Carbon Unit Carried by THF

## Tetrahydrofolate (THF)

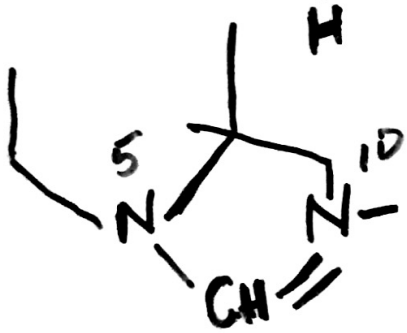



Formate (from tryptophan) + THF → Purines



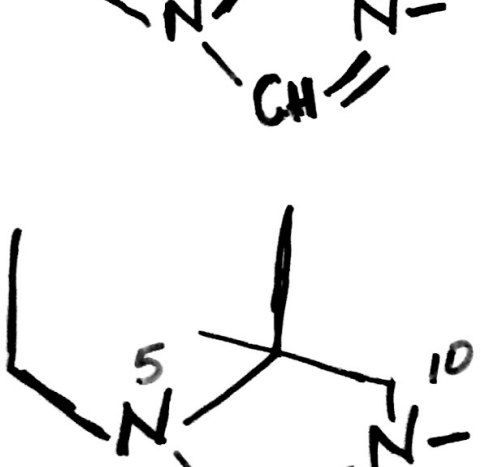

$N^{10}$-Formyl-THF

Histidine + THF →



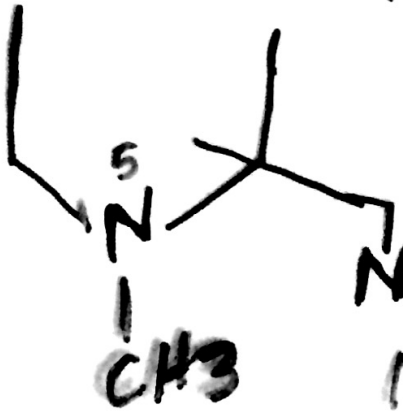

$N^5, N^{10}$-methenyl-THF

Glycine, Serine + THF →




→ TMP (from dUMP)

$N^5, N^{10}$-methylene-THF

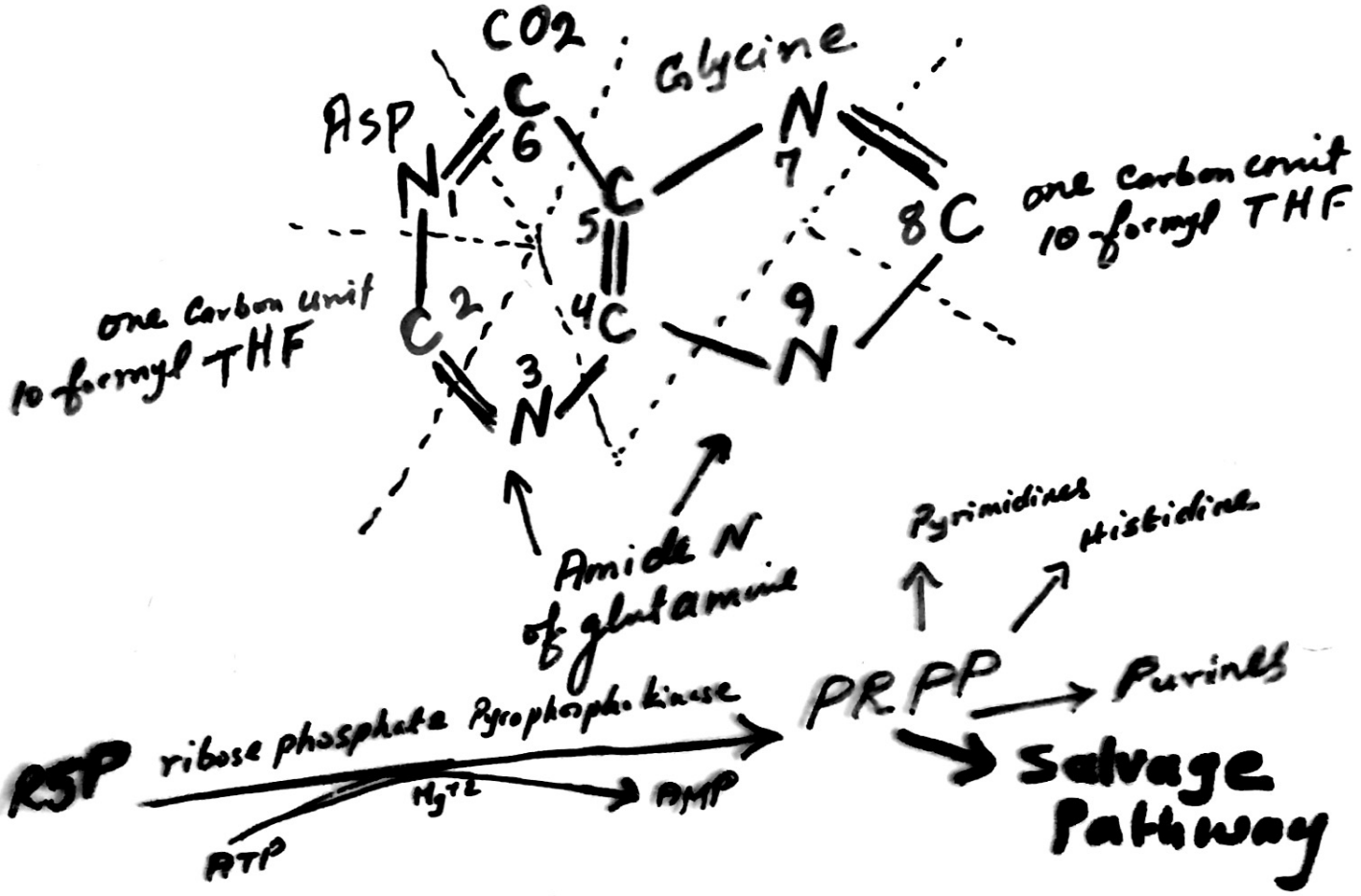



→ Methionine (from homocysteine)

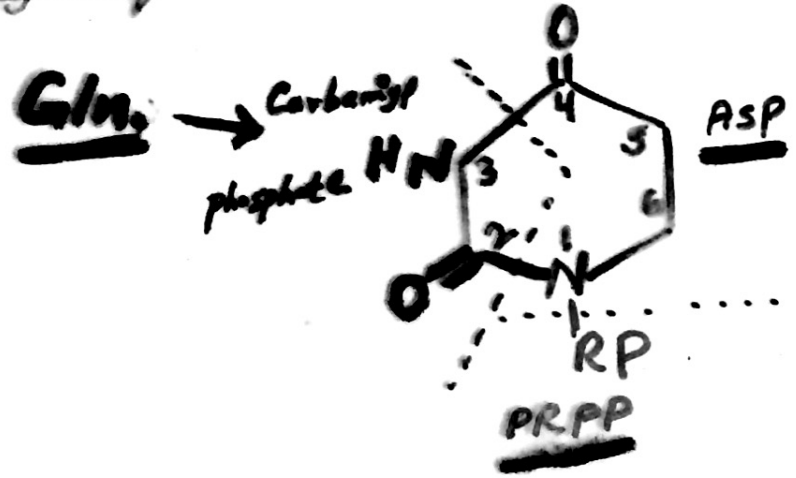
$N^5$-methyl-THF

# De Novo Synthesis of Purines

## → Origin of the ring atoms of purines

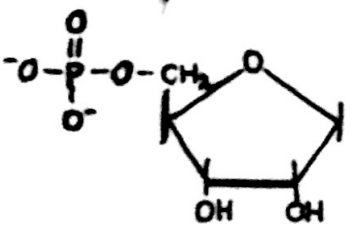



## → Origin of the ring atoms of pyrimidine



# Purine Biosynthesis

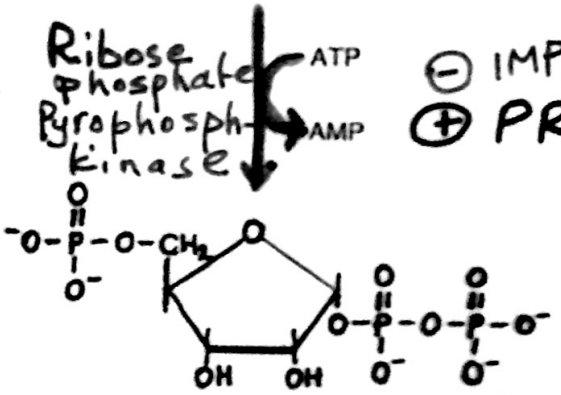
- Synthesis of PRPP



Ribose 5–phosphate

Source of ribose moiety for

- Purine Nucleotides ←
- Pyrimidine " ←
- Salvage Pathway ←

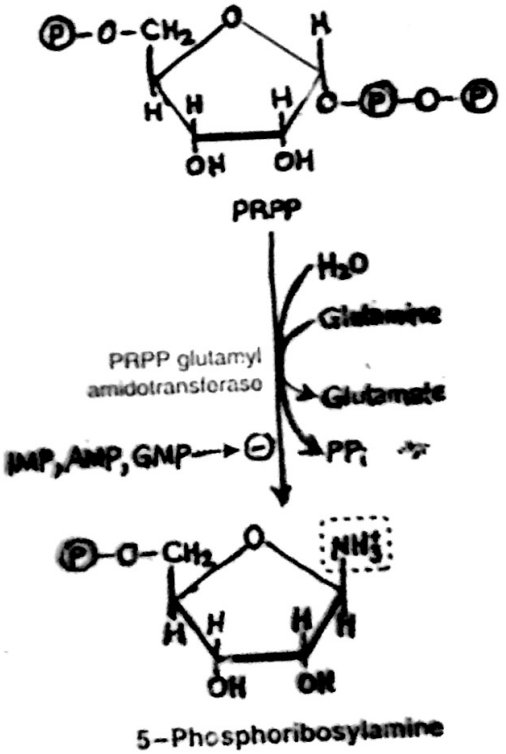



⊖ IMP, AMP & GMP
⊕ PRPP

5–Phosphoribosyl 1–pyrophosphate (PRPP)

activated ribose

- First step in Purine biosynthesis




5–Phosphoribosylamine

6+7

# Synthesis of Purine Nucleotides



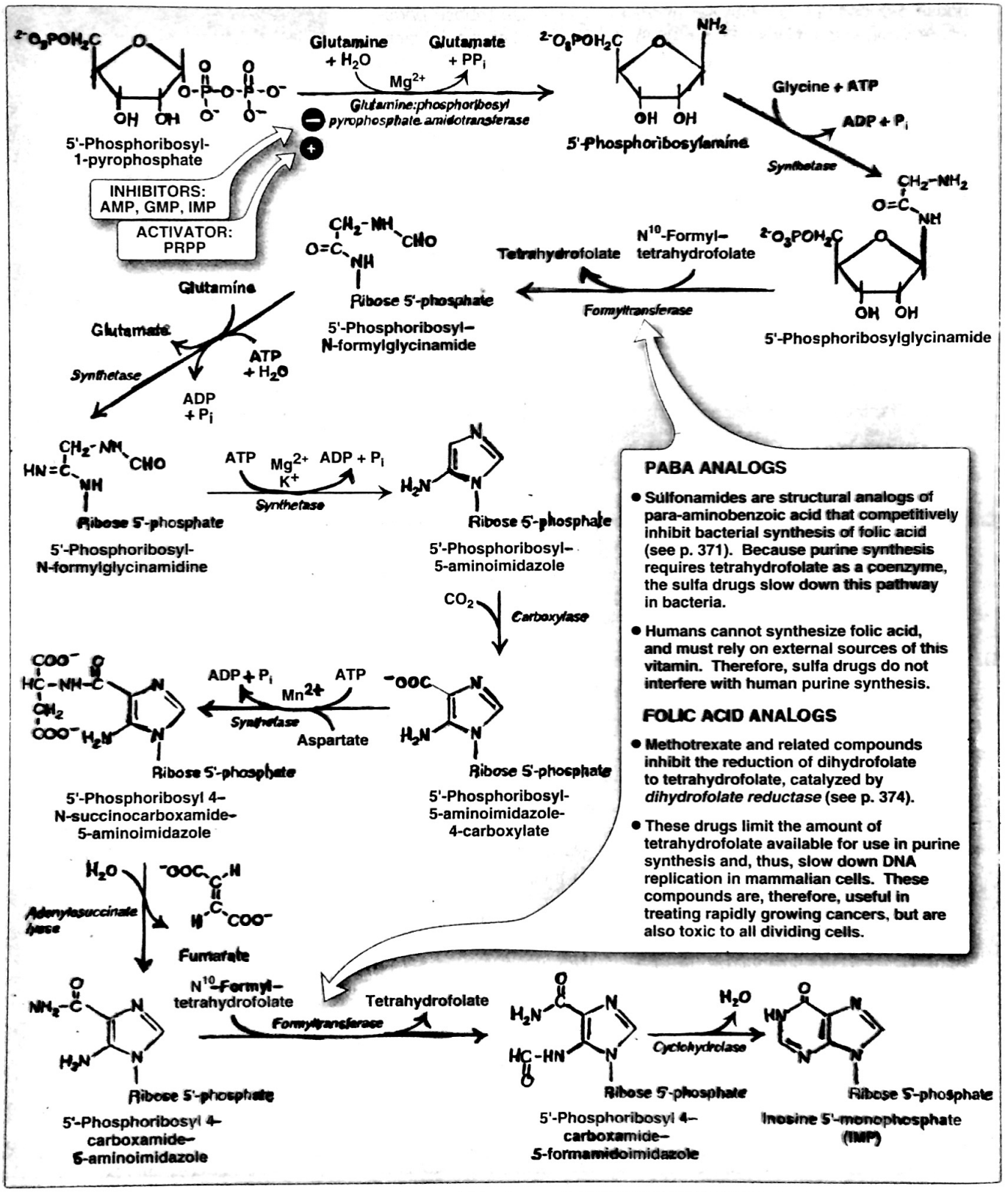



**Figure 22.7**
Synthesis of purine nucleotides, showing the inhibitory effect of some structural analogs

# Synthesis of Purine Nucleotides

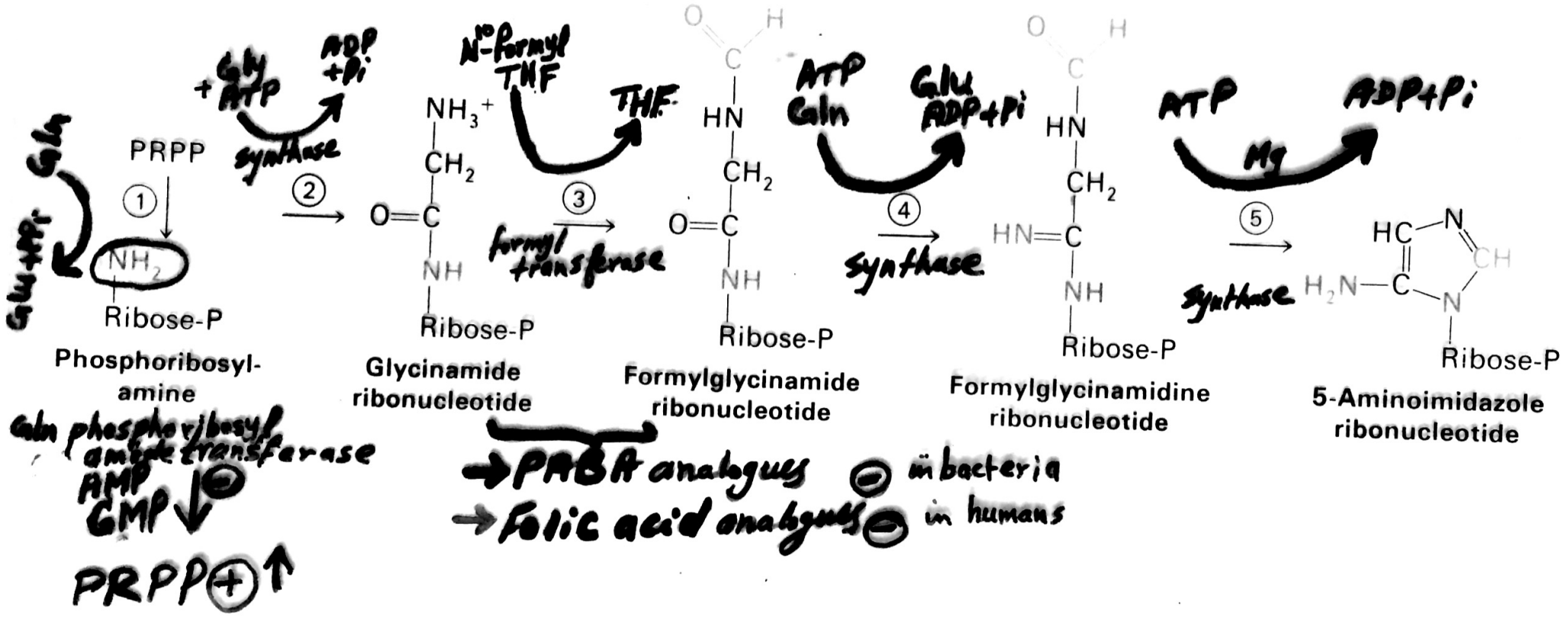



**Figure 25-4**

Stryer: *Biochemistry*, Third Edition

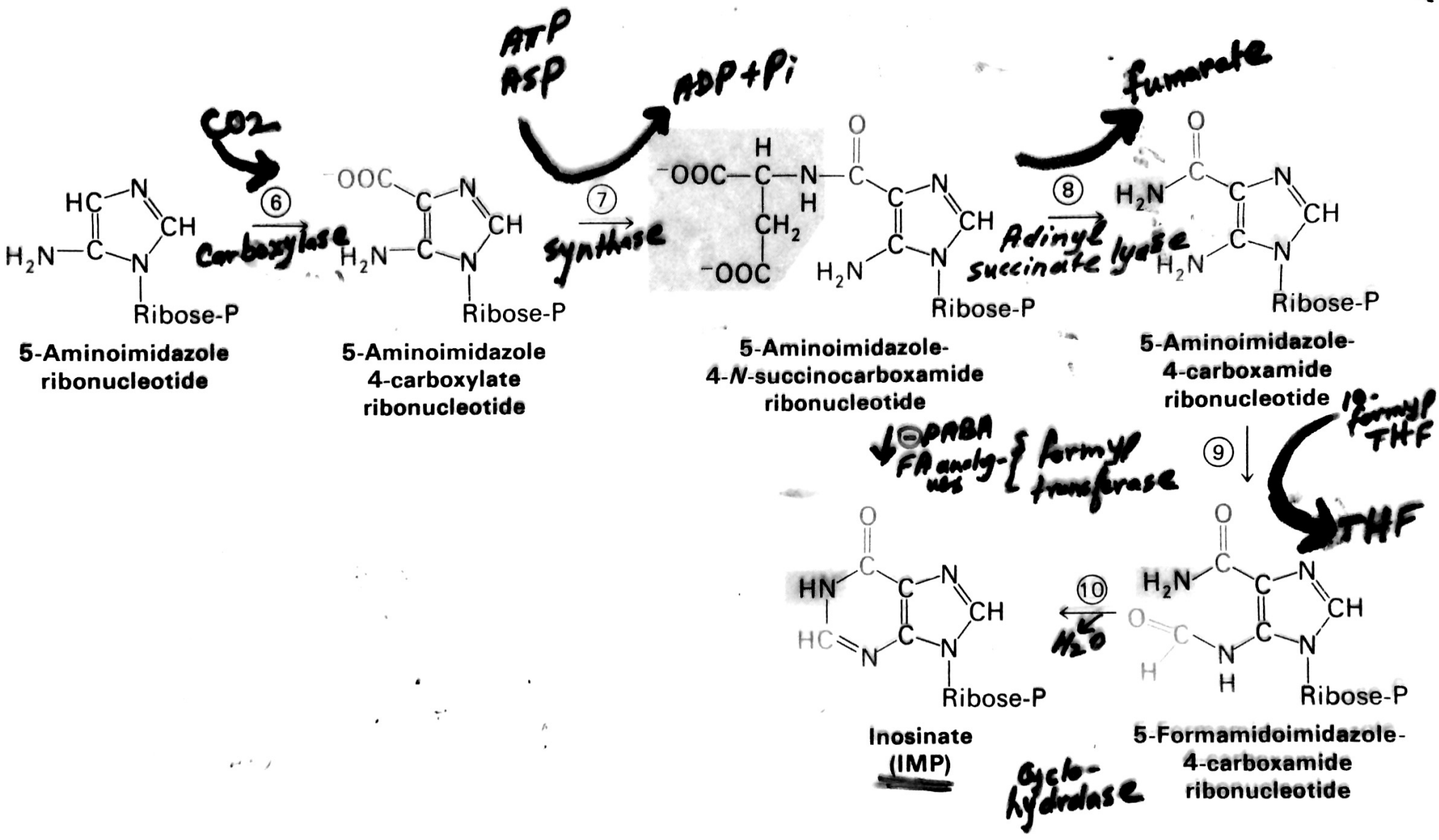
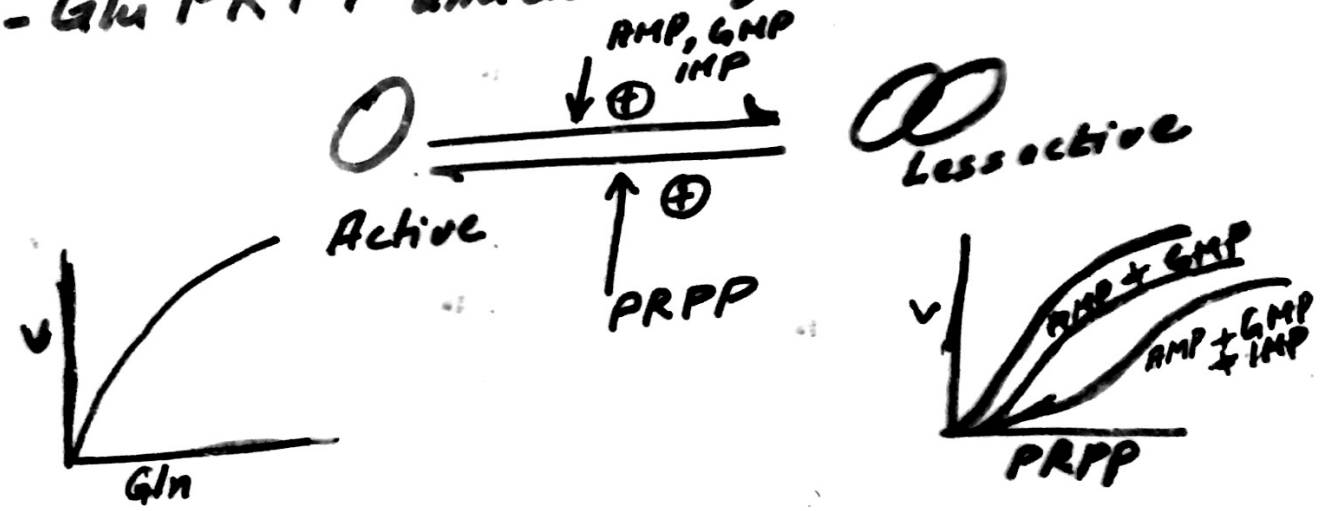


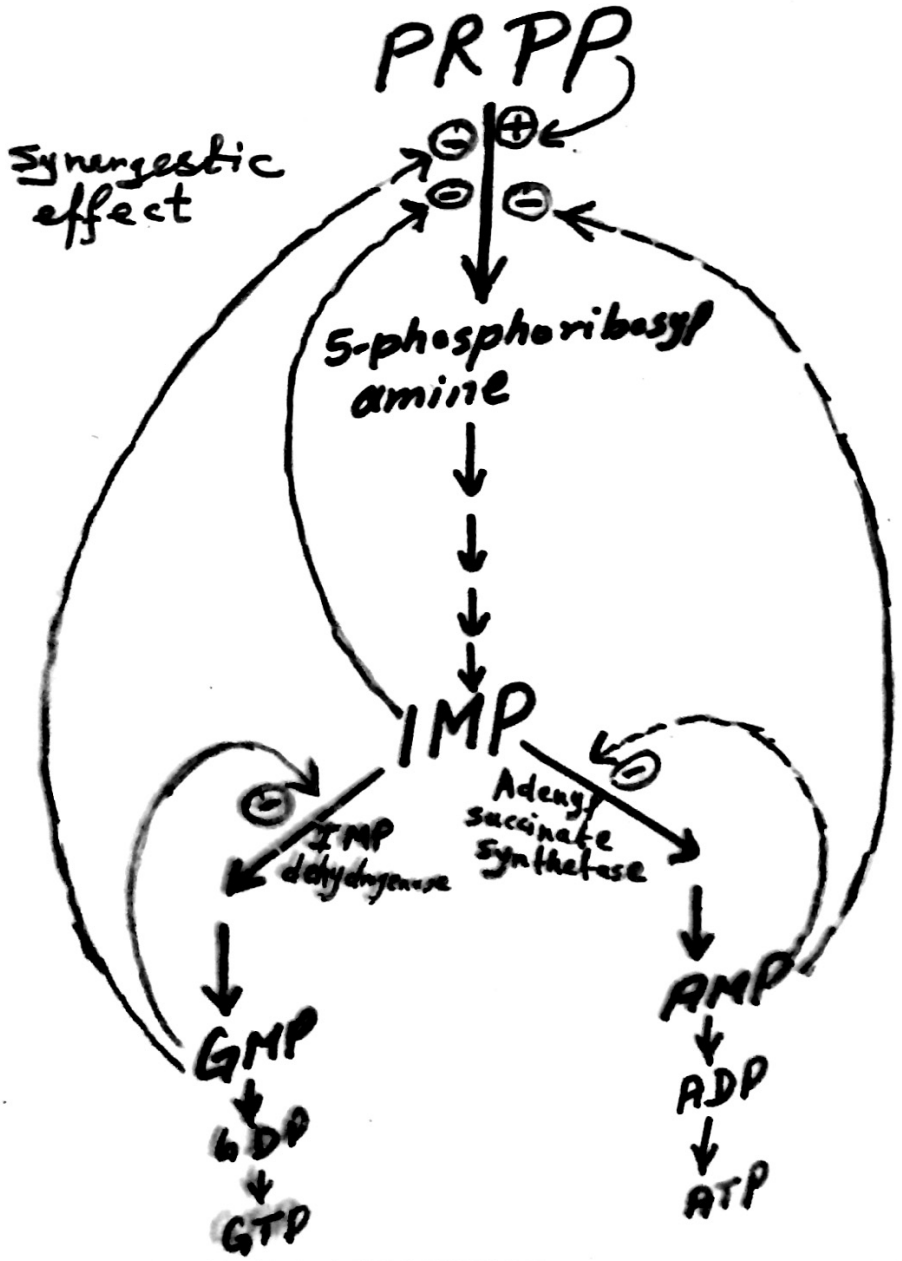

**Figure 25-5**

Stryer: *Biochemistry*, Third Edition

# - Purine Nucleotide Synthesis is Highly Regulated:-

- Glu PRPP amidotransferase is rate-limiting



# Nucleoside & Nucleotide Kinases

de novo synthesis → NMP

I Endogenous Nucleosides —(nucleoside kinase, ATP → ADP)→ NMP } kinase shows high specificity toward base & sugar

Exogenous [Adenosine the only purine nucleoside is salvaged]

II Nucleoside monophosphate kinase

(d) NMP + ATP ⇌ (d) NDP + ADP (NMK)

specific toward base but not sugar
Four different kinases

e.g. ATP + AMP ⇌ 2 ADP (A.K.)

Adenylate kinase

III Nucleoside diphosphate kinase

$N_2DP + \underbrace{N_1TP}_{TP} \underset{NDK}{\rightleftharpoons} N_2TP + N_1DP$

Present in high conc.
Non-specific toward base & sugar
10–100 fold > active than NMK

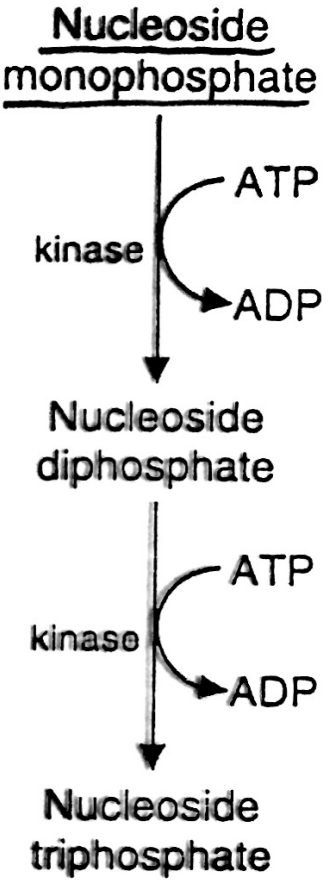



**Fig. 41.18.** Phosphorylation of nucleosides.

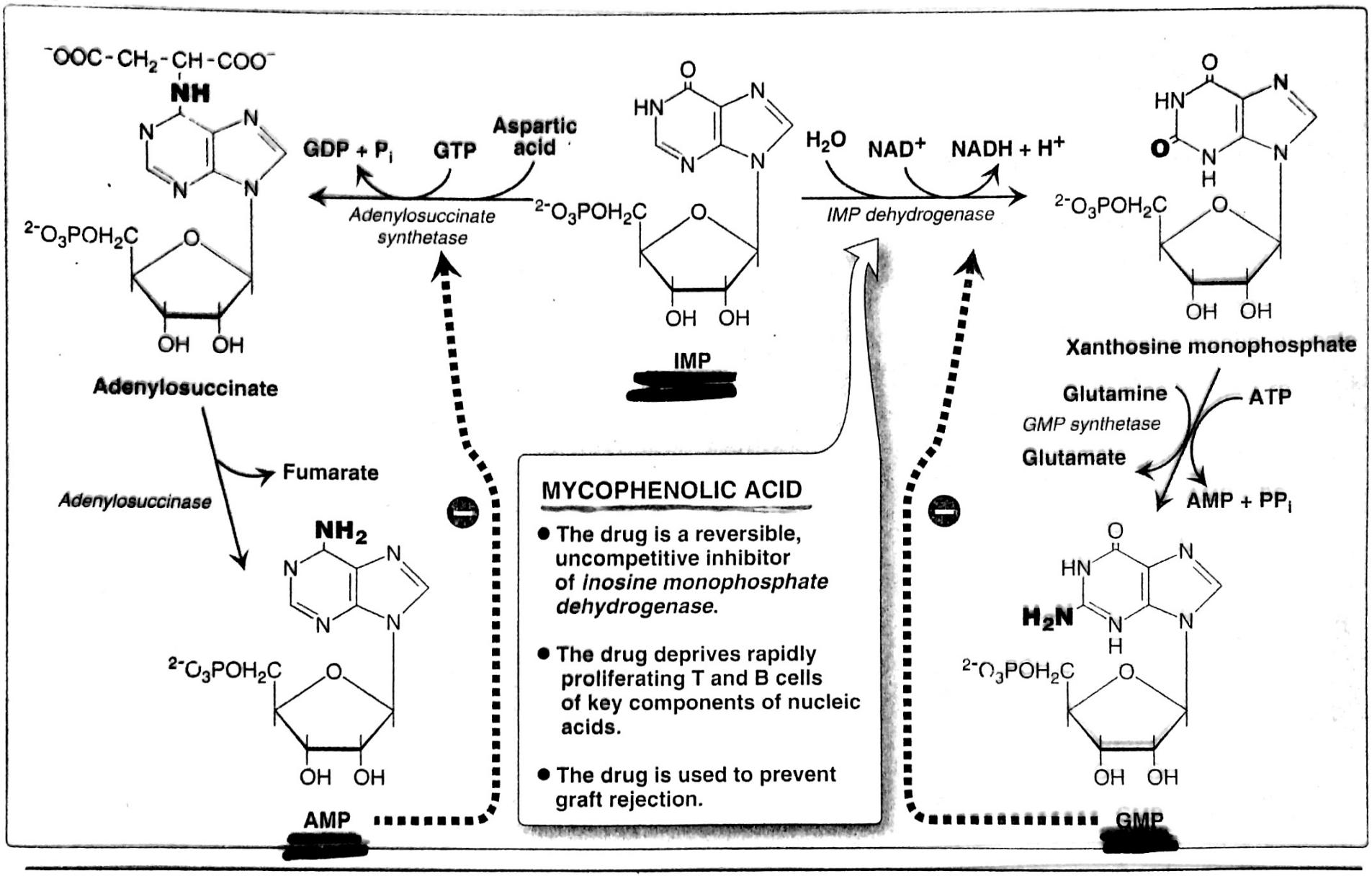
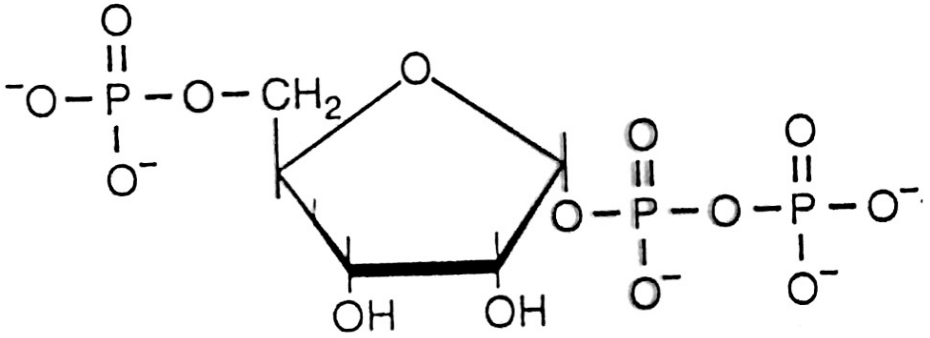



**Figure 22.8**
Conversion of IMP to AMP and GMP showing feedback inhibition.

# Salvage of the Bases



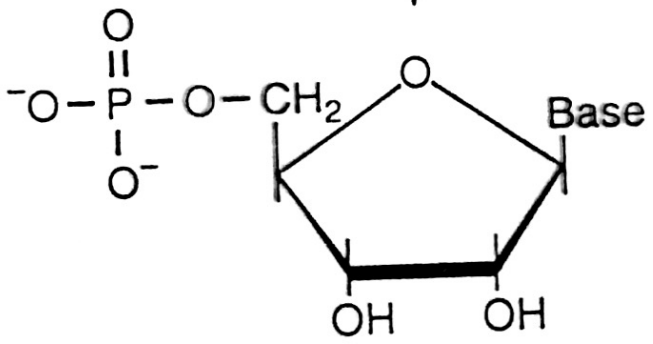
5-Phosphoribosyl 1-pyrophosphate (PRPP)

**HGPRT**
**APRT**

phosphoribosyl-transferase

Base

$H_2O$



Nucleotide

- Most of the de novo synthesis of bases & nucleotides in liver and to some extent in brain, neutrophils & other cells of Immune System

nucleotides → nucleoside → bases

↓ Blood

Other tissues

Bases + PRPP —salvage→ nucleotides