



Medical Committee
The University of Jordan



SLIDE



SHEET

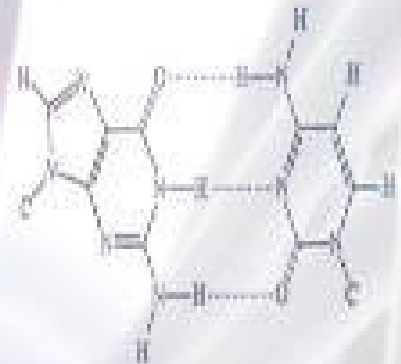


SLIDE : 27



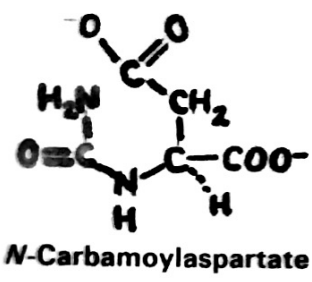
DR.NAME: Dr. Nayef

Biochemistry



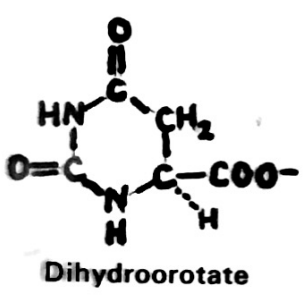
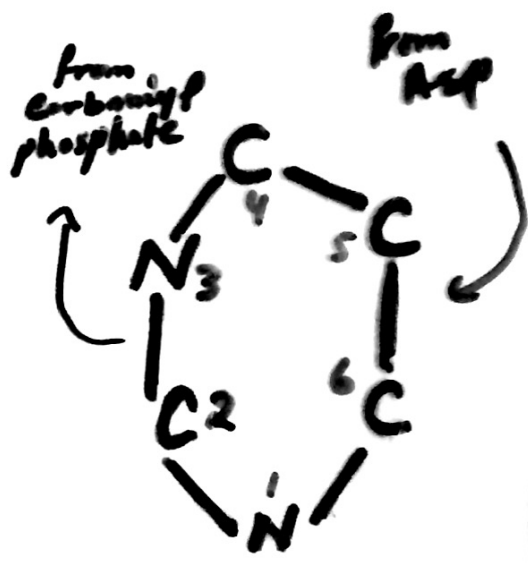
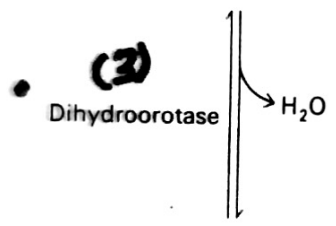
Majida Al-Foqaraa'

PYRIMIDINE NUCLEOTIDE SYNTHESIS



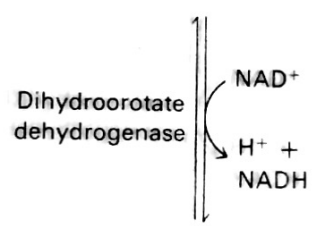
CPS II

- In cytosol
- uses Glu, not NH₄⁺
- Not activated by N-acetyl glutamate
- inhibited by UTP



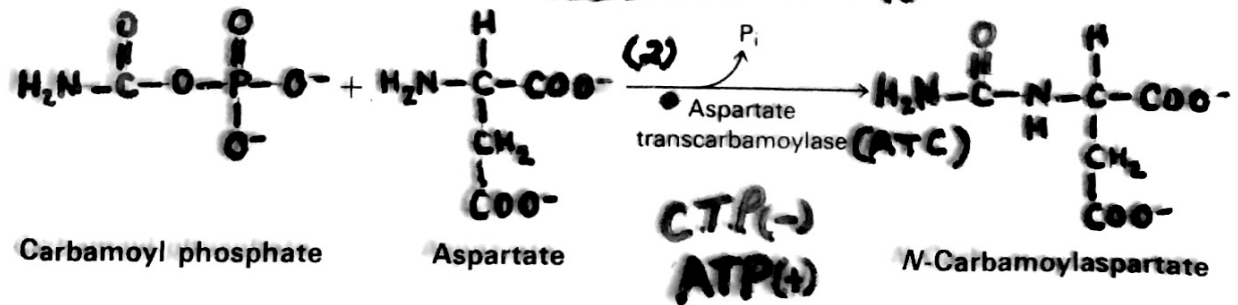
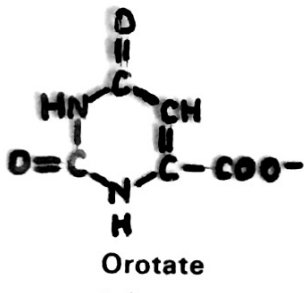
ATC

Regulatory Enz. in bacteria
 Inhibited by CTP
 Activated by ATP



(4) the only Mitochondrial ENZ. (inner membrane)

(1), (2) + (3) are trifunctional protein



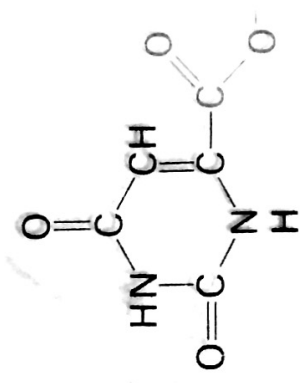
cluster of 3 domains (1+2+3)

15a

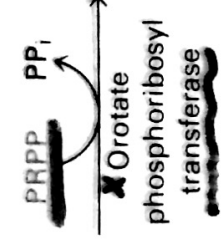
OROTIC Aciduria:-

low activity of transferase & decarboxylase or any one
 → abnormal growth & severe anemia, excretion of urinary orotate
 → treatment diet rich in uridine or cytosine

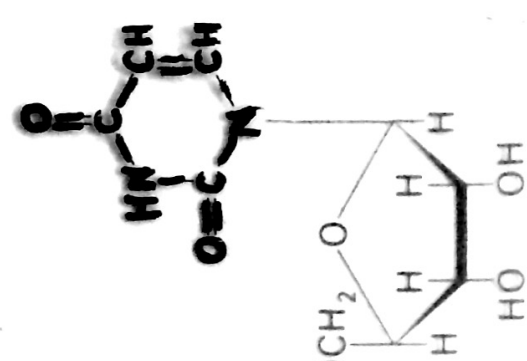
(5) and (6) are two domains in one bifunctional enzyme called UMP Synthase



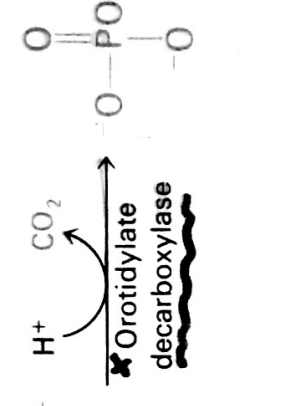
(5)



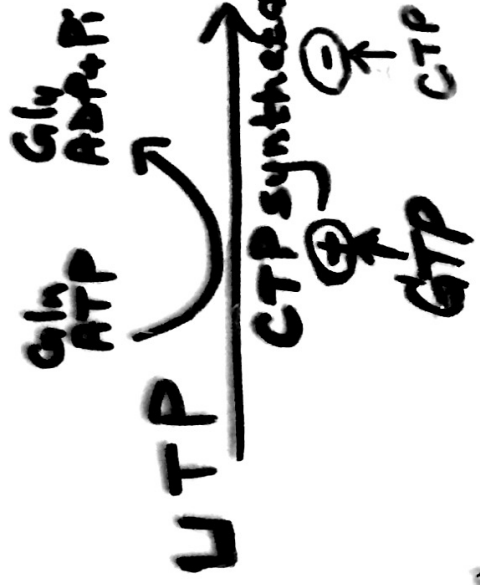
Orotate



(6)



Orotidylate (UMP)



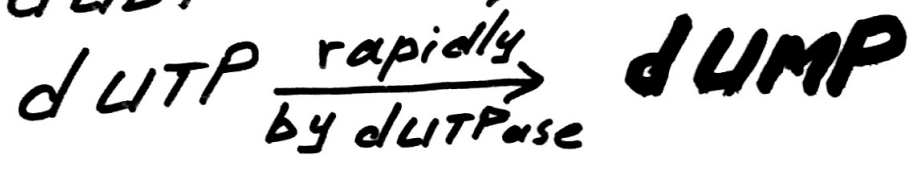
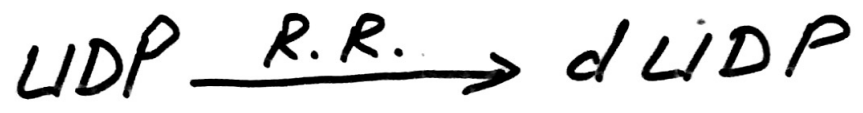
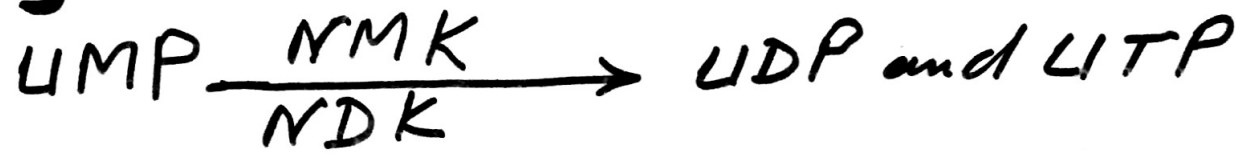
Pyrimidine bases

CO₂, NH₄, β-alanine and β-amino isobutyrate

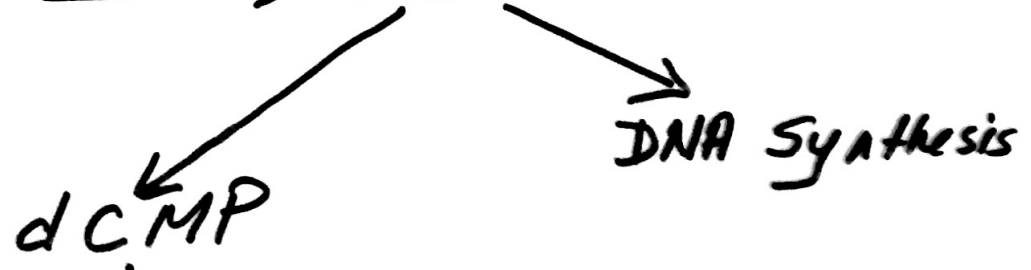
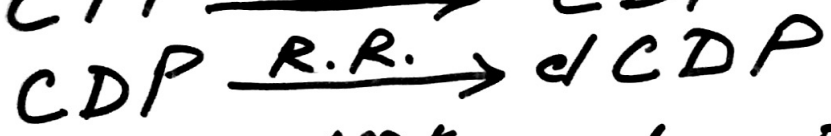
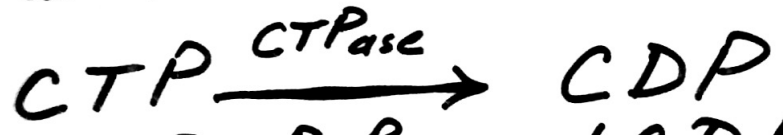
CO₂, H₂O, NH₄/urea

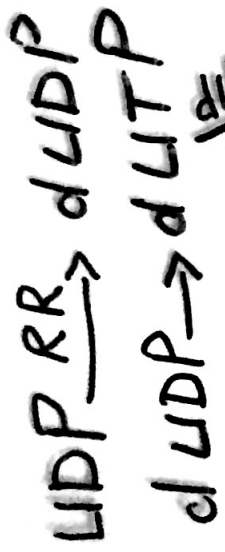
Sources of dUMP

1- Major source



Or 2- another source





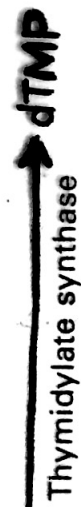
to prevent
 incorporation
 into DNA

$dUTPase$
 (phosphatase)
 rapidly

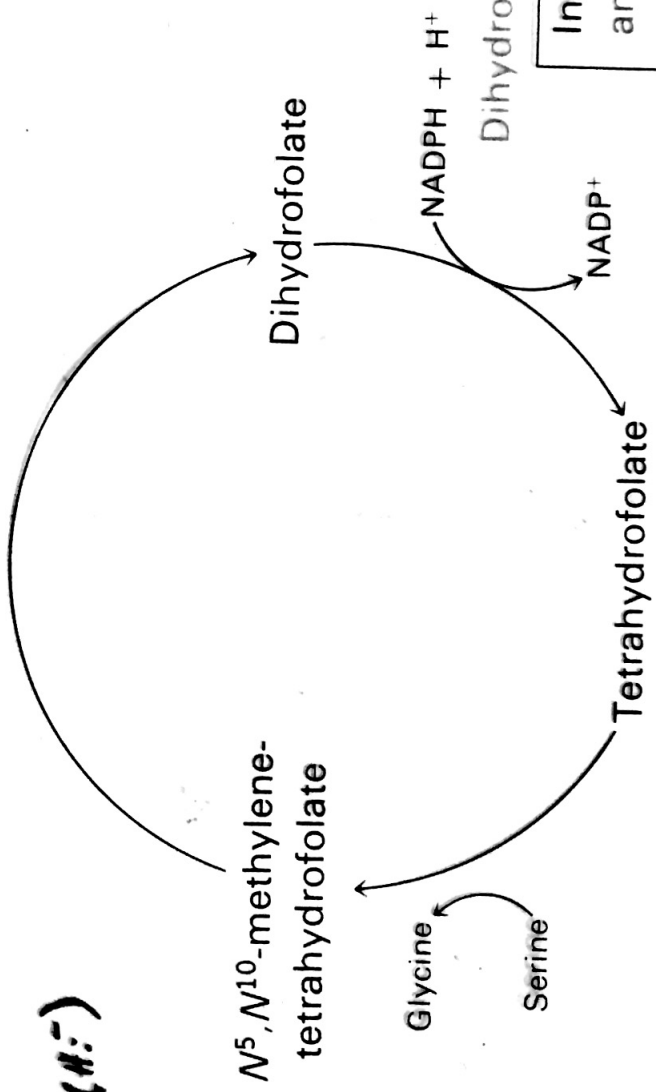


Fluorouracil
 ↓
 Fluorodeoxyuridylate
 (Suicide inhibitor)

(s-FdUMP)



electron donor (H:-)
 and one-carbon
 donor.
only reaction



Dihydrofolate reductase

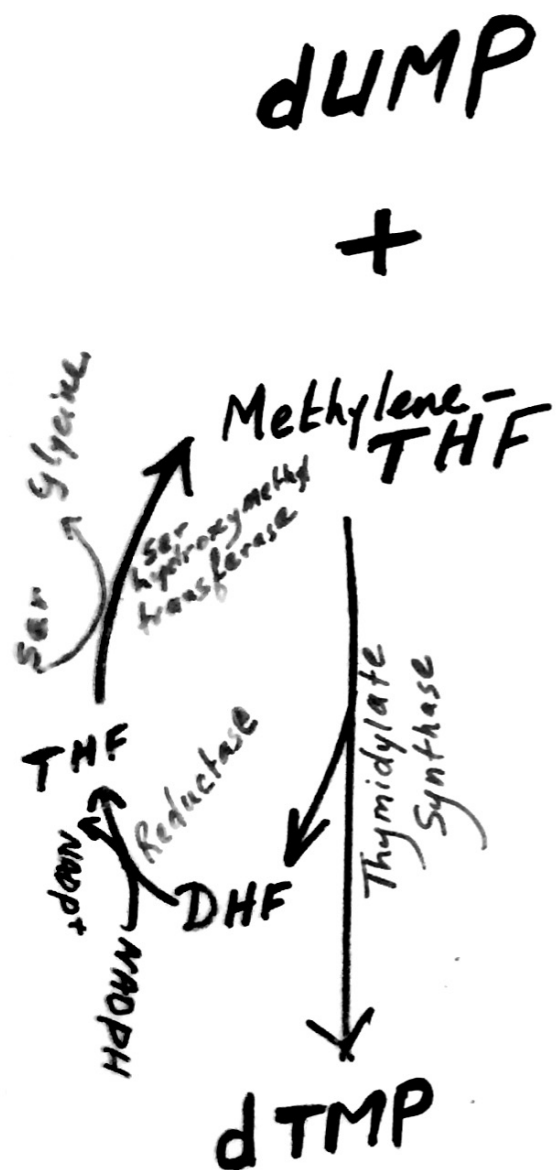
Inhibited by
 aminopterin
 and
 amethopterin
 (methotrexate)

Inhibit
 dTMP formation
 and Purines
 synthesis

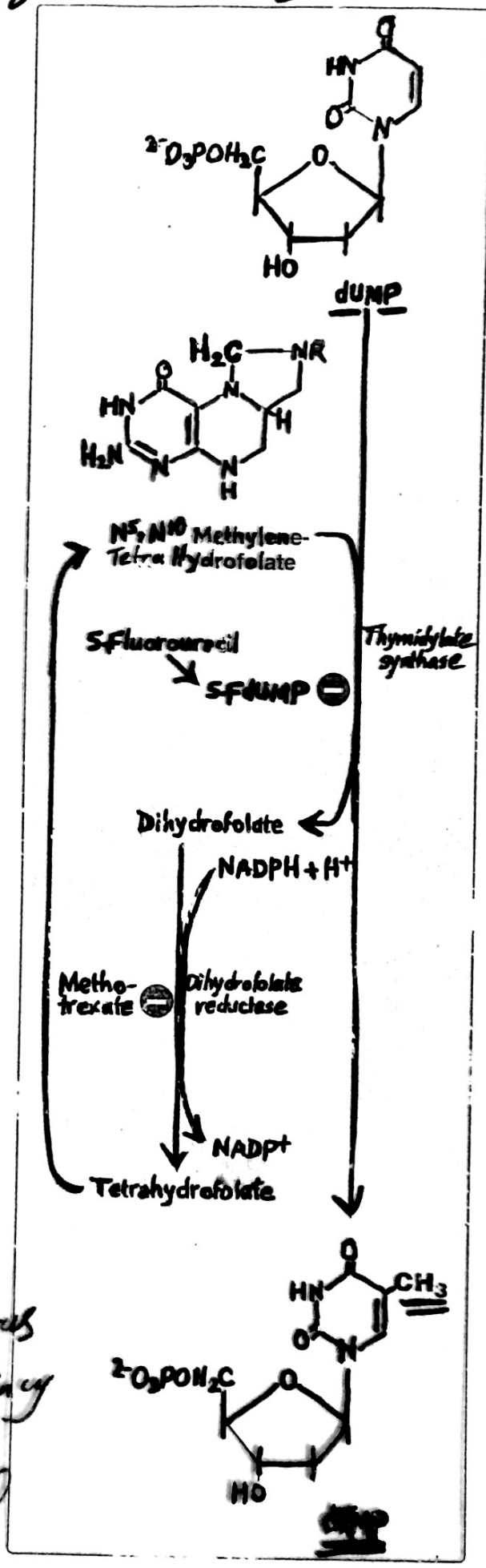
Synthesis of dTMP from dUMP

Figure 25-16

Synthesis of dTMP from dUMP



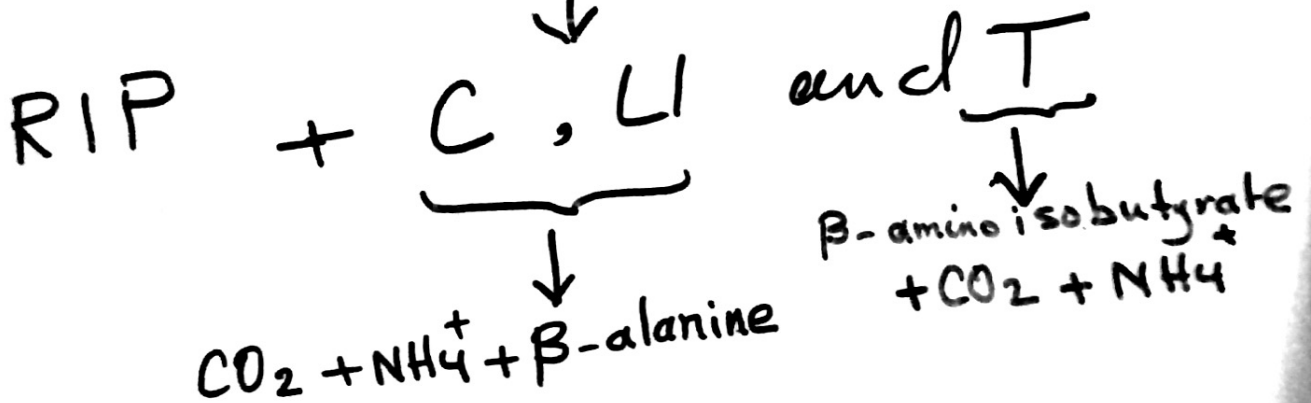
Other Drugs:-
 Acyclovir - Purine analogue
 AZT (3-azido-2-deoxythymidine) - Pyrimidine analogue
 Treat herpes simplex virus & human immunodeficiency virus
 Both inhibit viral DNA polymerase



Degradation and Salvage¹⁸ of Pyrimidines

Pyrimidine nucleotides

↓
nucleosides



Salvage

Pyrimidine base can be salvaged to nucleosides

Nucleosides $\xrightarrow{\text{phosphorylated}}$ Nucleotides