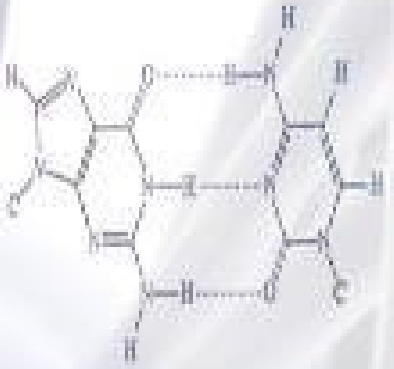
Medical Committee
The University of Jordan

SLIDE ○ SHEET

SLIDE : 25

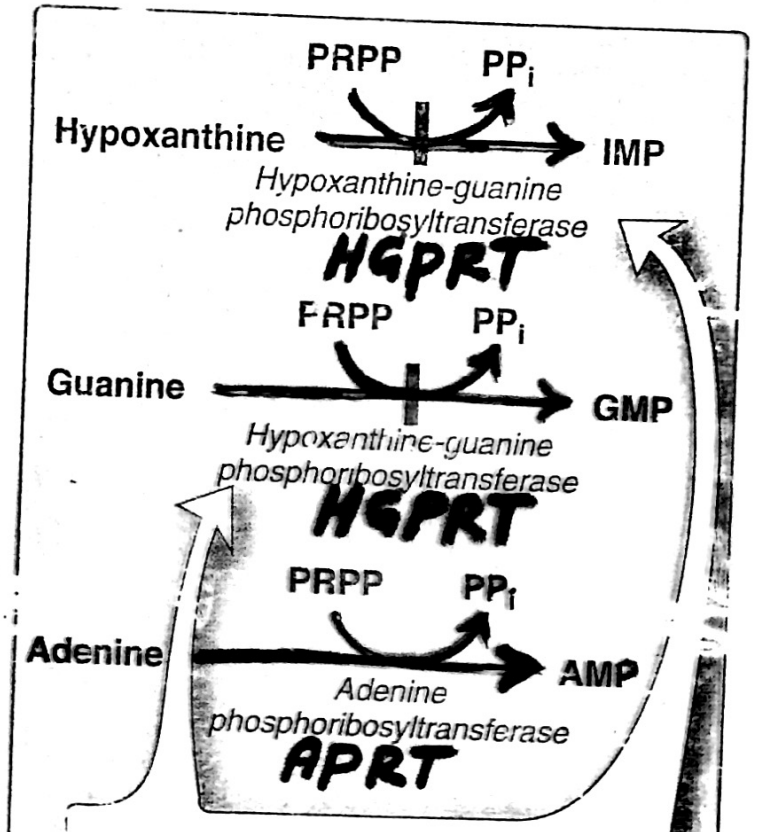
DR.NAME: Dr. Nayef

Biochemistry



Majida Al-Foqaraa'

Disorder of purines salvage pathway



LESCH-NYHAN SYNDROME

- This is an X-linked, recessive, inherited disorder associated with a virtually complete deficiency of *hypoxanthine-guanine phosphoribosyltransferase* and, therefore, the inability to salvage hypoxanthine or guanine.
- The enzyme deficiency results in increased levels of PRPP and decreased IMP and GMP, causing increased de novo purine synthesis.
- This results in the excessive production of uric acid, plus characteristic neurologic features, including self-mutilation and involuntary movements.

Hyperuricemia:
→ uric acid stones in kidneys (urolithiasis)
→ deposition of urate crystals in the joints (gouty arthritis) and in soft tissues

→ motor dysfunction
Cognitive deficits
behavioral disturbances
e.g. self mutilation
involuntary movements

→ Increased Purine synthesis

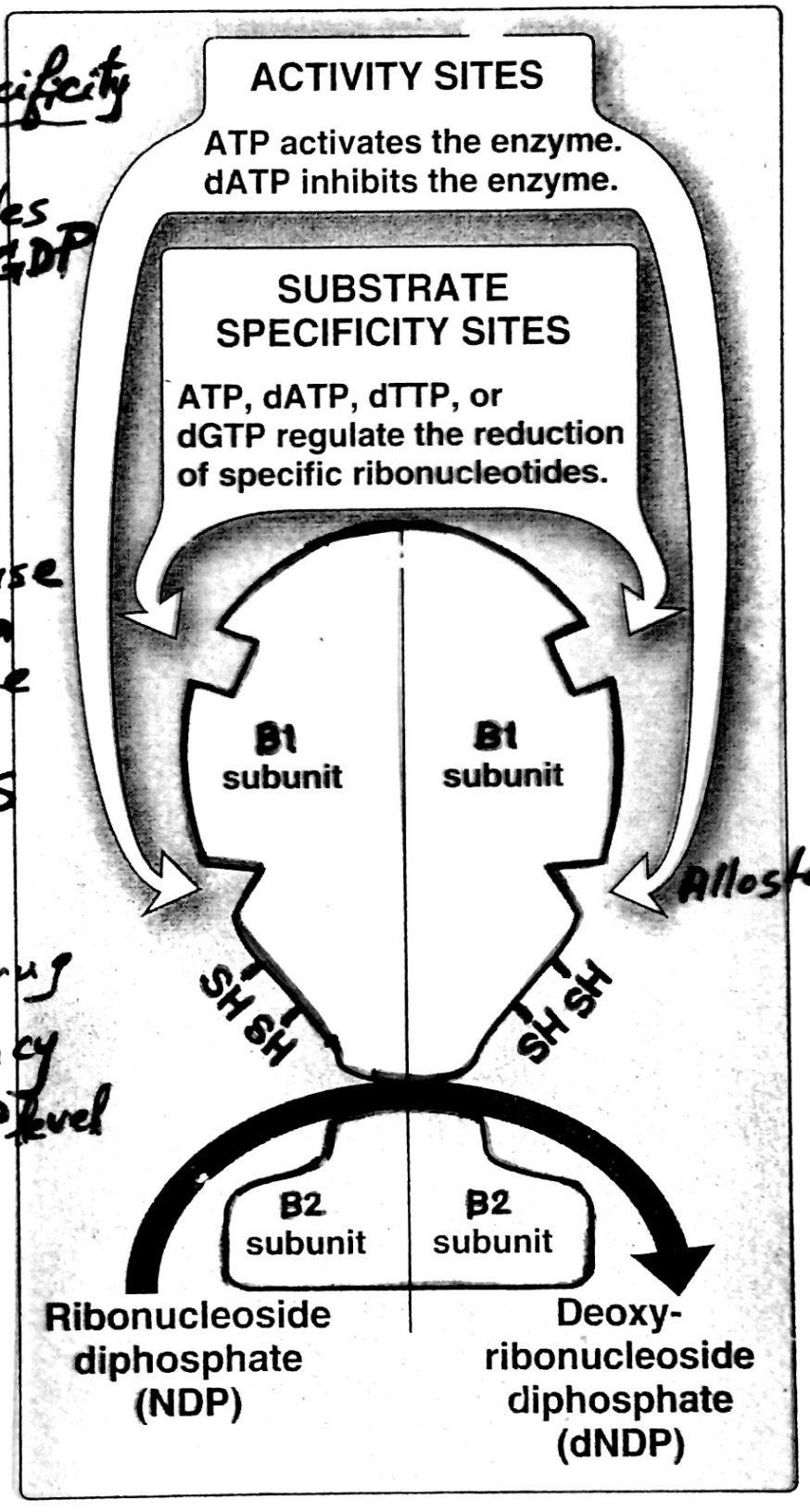
→ Increased Uric acid (Gout)

Substrate Specificity

e.g..
dTTP activates reduction of GDP

Hydroxy urea
- inhibit RRase by destroying a required free radical
- treating HbS disease by increasing HbF level
- Anti cancer drug

ADA deficiency → ↑dATP level

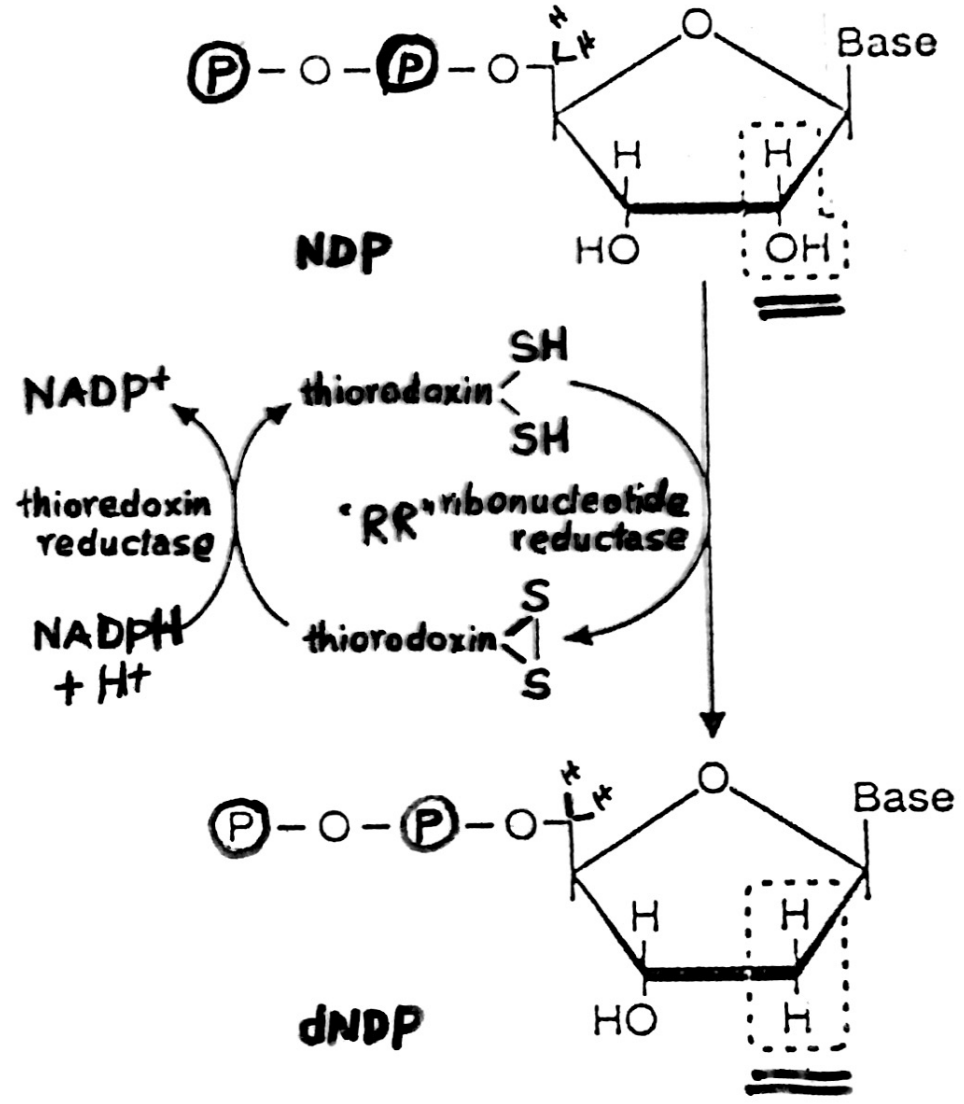


Allosteric sites

Figure 22.13
Regulation of *ribonucleotide reductase*.

Reduction of Ribose → deoxy Ribose

Synthesis of Deoxyribonucleotides:



Regulation of RR

- → balanced supply of dNDP
- → two Identical B_1 + two Identical B_2 subunits
- → one single active site
- → two regulatory site
  - . Activity site dATP↓ ATP↑
  - . substrate specificity site

Mechanism of Increased Uric acid production and de novo synthesis of purine nucleotides in deficiency of HGPRT