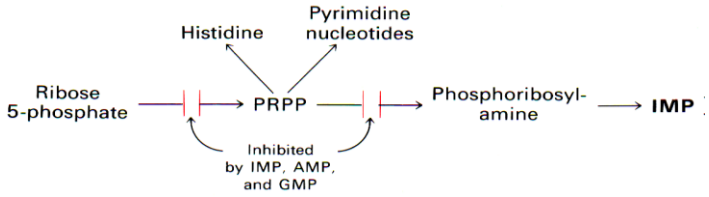
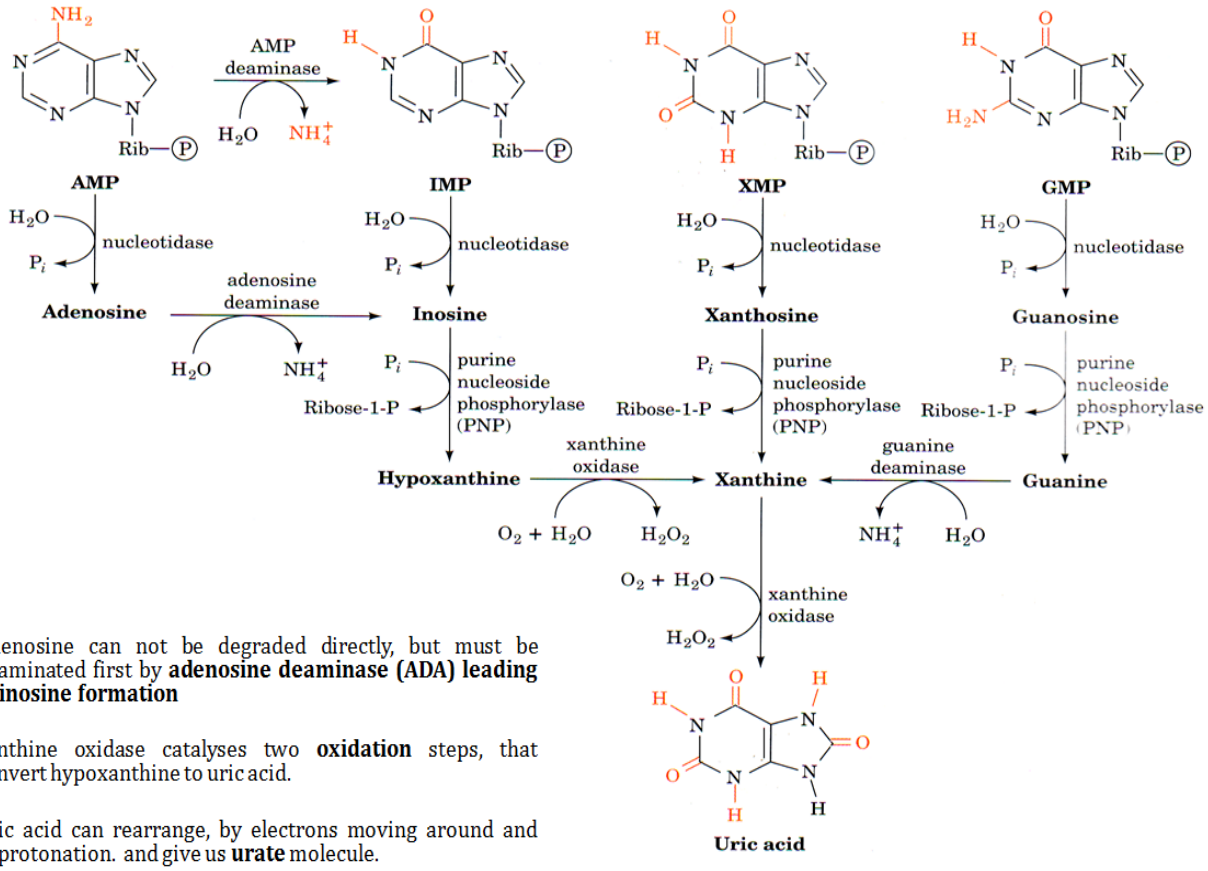
Problem 3 – Unit 6 – Biochemistry: uric acid and hyperuricemia

- **Nucleotides are:**
  - Purines (A & G).
  - Pyrimidines (T & C).

  And they are composed of:
  - Nitrogenous base.
  - Pentose monosaccharide
  - One, two or three phosphate groups.
- **Purine synthesis:**

De Novo pathway	Salvage pathway
* Using amino acids as nitrogen and carbon donors. * Expensive pathway (6ATP/1IMP). * IMP synthesized from PRPP is the precursor of both AMP & GMP. * AMP & GMP converted to ATP and GTP by mono & diphosphate kinase. --- * **Synthesis of IMP:** Ribose-5-phosphate (from PPP) → addition of 2 phosphate using ATP molecule → PRPP → addition of amino group from glutamine → 5-phosphoribosyl-1-amine → 8 reactions → IMP  	* Purines are formed by the degradation of nucleic acids & nucleotides from: - Normal turnover of cellular nucleic acids. - Diet. * Effective pathway (less energy is used than in De Novo pathway).

- **AMP and GMP formation:**
  - These two are synthesized from IMP in 2 steps:
    - ✓ IMP → addition of aspartate and GTP → adenylosuccinate (by the enzyme adenylosuccinate synthetase) → AMP will be generated (by the action of the enzyme adenylosuccinate lyase).
    - ✓ IMP → IMP dehydrogenase → xanthosine monophosphate (XMP) → addition of glutamine and ATP → GMP (by the action of the enzyme GMP synthase).
  - AMP synthesis needs GTP while GMP synthesis needs ATP.
  - If AMP & GMP are present in adequate amounts, the De Novo pathway of purine synthesis is turned off at an earlier step.
- **Purine catabolism:**



Adenosine can not be degraded directly, but must be deaminated first by **adenosine deaminase (ADA) leading to inosine formation**

xanthine oxidase catalyses two **oxidation** steps, that convert hypoxanthine to uric acid.

Uric acid can rearrange, by electrons moving around and deprotonation. and give us **urate** molecule.