LEARNING OBJECTIVE

At the end of lecture students will be able to describe the:
- Pathway of purine catabolism.
- Salvage pathway of purine metabolism.
- Clinical disorders related to purine metabolism.

CATABOLISM OF PURINE BASES

- The purine bases arising from the degradation of nucleic acids (exogenous or endogenous) are conveyed to liver by blood.
- Catabolized through a series of reaction resulting in the formation of Uric Acid.

PURINE NUCLEOTIDE CATABOLISM

![PURINE NUCLEOTIDE CATABOLISM Diagram]
CATABOLISM OF ADENOSINE NUCLEOTIDE
{ADENYLIC ACID (AMP)}

REACTION # 1 HYDROLYSIS
AMP → Adenine nucleoside (adenosine)

REACTION # 2 Deamination
AMP → Inosine

REACTION # 3 Phosphorylation
AMP → Ribose-5-P + Hypoxanthine

REACTION # 4 & 5 Oxidation
AMP → Uric Acid

CATABOLISM OF ADENOSINE NUCLEOTIDE
{ADENYLIC ACID (AMP)}

REACTION # 1 Hydrolysis
Adenine nucleotide (AMP) + HOH → Adenine nucleoside (Adenosine)
**CATABOLISM OF ADENOSINE NUCLEOTIDE**

**REACTION # 2 Deamination**
Adenine nucleotide (Adenosine)

Deaminase

Inosine

\[ \text{H}_2\text{O} \]

\[ \text{NH}_3 \]

**CATABOLISM OF ADENOSINE NUCLEOTIDE**

**REACTION # 3 Phosphorylation**
Inosine

Nucleoside

Phosphorylase

Ribose-1-

Phosphate

Hypoxanthine

\[ \text{H}_3\text{PO}_4 \]
CATABOLISM OF ADENOSINE NUCLEOTIDE

REACTION # 4,5 Oxidation

Hypoxanthine

HOH + O₂ → Xanthine

Xanthine Oxidase

Xanthine

H₂O₂ → Uric Acid

MINOR PATHWAY OF ADENINE CATABOLISM
Conversion to Hypoxanthine
REACTION # 1; Hydrolysis of Guanine Nucleotide is catalyzed by hydrolase

Guanine Nucleotide (GMP)

Hydrolase

Guanine Nucleotide (Guanosine)

HOH

PO₄

Uric Acid → Xanthine → Guanine

Adenosine Nucleotide → Adenosine Nucleoside → Inosine → Hypoxanthine

Guanine Nucleotide → Guanine Nucleoside → Guanine

PURINE NUCLEOTIDE CATABOLOISM GROSS OVERVIEW
REACTION # 2; Phosphorylation is Catalyzed by Nucleoside Phosphorylase

Guanosine $\xrightarrow{\text{Nucleoside Phosphorylase}}$ Ribose-1-Phosphate

$\text{Guanine} \quad \text{H}_3\text{PO}_4$

REACTION # 3
Deamination is Catalyzed by Deaminase

Guanosine $\xrightarrow{\text{Deaminase}}$ Xanthine

$\text{NH}_3 \quad \text{H}_2\text{O}$
REACTION # 4
Catalyzed by Xanthine Oxidase

Xanthine Oxidase

Xanthine

HOH+O₂

Xanthine

H₂O₂

Uric Acid

GUANINE NUCLEOTIDE CATABOLISM
GROSS OVERVIEW

Guanine Nucleotide

Guanine Nucleoside

Guanine

Xanthine

Uric Acid

CONCLUSION OF PURINE CATABOLISM
- Both adenine & guanine bases arising from the degradation of nucleic acids (exogenous or endogenous) are catabolized
through a series of reactions resulting in the formation of Uric Acid.

- Hydrolysis
- Deamination
- Phosphorylation
- Oxidation
Reutilization (Recycling) of catabolic intermediates for synthesis of purine nucleotides

- **Salvage Pathway**
- During purine nucleotides salvage pathway, catabolic intermediates are saved from destruction or waste and put to further use.
**SALVAGE PATHWAY:**
Intermediate of cellular Nucleic Acids
Catabolism & digestion of dietary Nucleic Acids are reconverted to AMP & GMP

**SALVAGE PATHWAY:**
Products of cellular Nucleic Acids
Catabolism & digestion of dietary Nucleic Acids are converted to AMP & GMP
1. Adenine Phosphoribosyl Transferase (APRT)
2 & 3. Hypoxanthine-Guanine Phosphoribosyl Transferase (HGPRT).
4. Adenosine Kinase.

Purine Salvage Pathway

Decreases the Metabolic Load

- Recycle of catabolic intermediates:
  - Therefore recycle of purines rather than to form new purines.
  - Conclusively over production of purines is controlled.
- Decrease uric acid synthesis.
- Because of recycling catabolic intermediates of purines.
- Consumes less energy.
- Prevents loss of usable compounds.

Hyperuricemia (Increased Blood Uric Acid Level) May be due to genetic defects or Acquired

- Genetic Enzymatic defects:
  - HGPRT deficiency (Gout & Lesch-Nyhan Syndrome).
  - Phosphoribosylpyrophosphate synthetase
  - over-activity (Gout).
- Glucose-6-Phosphate Phosphatase deficiency (Von Gierk’s disease).
- Secondary hyperuricemia:
  - Cancer (e.g., Leukemia)
  - Psoriasis
  - Renal Disorders.

**BIOCHEMICAL UPSET IN LESCH-NYHAN SYNDROME**

- HGPRT deficiency results in failure of the salvage pathway for hypoxanthine and guanine.
- These purines are therefore degraded to uric acid.
- Additionally, a decrease in IMP & GMP leads to an increase in conversion of PRPP to Phosphoribosylamine, which further exacerbates uric acid overproduction.

**XANTHINE OXIDASE DEFICIENCY**

- Causing formation of stones.
- Diagnosis:
  - Low plasma uric acid.
  - High urine and plasma hypoxanthine and xanthine.
  - Enzyme determination requires liver or intestinal mucosal biopsy.
- Treatment:
  - High fluid intake to minimize likelihood of stone formation.
USE OF PURINE SYNTHESIS INHIBITORS IN CLINICAL PRACTICE

- Inhibition of folic acid synthesis by sulfonamide antibiotics.
- Inhibition of synthesis of purines & nucleic acids by cytotoxic (Anti-Cancer) Drugs.

THANKYOU