Nucleotide Catabolism
Purine Breakdown by Primates, Birds and Reptiles Produces Uric Acid

Most purine and pyrimidine molecules are salvaged; excess from diet or intracellular turnover are degraded.

For birds and reptiles, uric acid is also the excretion product for disposal of surplus nitrogen from amino acid breakdown (urea serves this function in primates).
*The first gene therapy was performed on a patient with a defective ADA gene. This patient had severe combined immunodeficiency syndrome.
Nucleotidase

\[
\text{Ribose-5-P} \xrightarrow{\text{Nucleotidase}} \text{Xanthosine} \xrightarrow{\text{Guanine deaminase}} \text{Guanine}
\]

\[
\text{Ribose-5-P} \xrightarrow{\text{Nucleotidase}} \text{Guanosine}
\]
Xanthine oxidase catalyzes the conversion of xanthine to uric acid.
Xanthine Oxidase:

- Present in large amounts in liver, intestinal mucosa and milk
- Oxidizes hypoxanthine to xanthine and xanthine to uric acid
- Gout is a disease in humans caused by overproduction or inadequate excretion of uric acid
- Uric acid crystallizes in cartilage and soft tissues, especially kidneys, toes and joints causing inflammation and pain
• Gout is treated with the drug **allopurinol**, a synthetic isomer of hypoxanthine that is a powerful inhibitor of xanthine oxidase:

![Allopurinol](image)

• Gertrude Elion and George Hitchings (of Glaxo-Wellcome) won the Nobel Prize for the development of allopurinol, as well as acyclovir used to treat AIDS, and other purine analogues used in cancer chemotherapy
Uric acid is further metabolized in most organisms:

Uric Acid

Excreted by primates, birds, reptiles, insects

urate oxidase

Excreted by other mammals

Allantoin

Allantoinase

Allantoic acid

Excreted by teleost fishes
Allantoicase converts allantoate to glyoxylate, which is then converted to urea by urease. Urea is excreted by cartilaginous fish and amphibia. Excreted by marine invertebrates.
Pyrimidines are catabolized to Acetyl CoA and Succinyl CoA:

- **CMP** \(\rightarrow\) nucleotidase \(\rightarrow\) **UMP**
- **Cytidine** \(\rightarrow\) **Uridine** \(\rightarrow\) **Uracil**
- **UMP** \(\rightarrow\) nucleotidase \(\rightarrow\) **dTMP**
- **Thymidine** \(\rightarrow\) **Thymine**

**Reactions:**
- Cytidine deaminase
- Nucleotidase
Uracil → O → HN → CH₂ → CH₂ → COO⁻

H₂N-C-NH-CH₂-CH₂-COO⁻  
(Pro ideopropionate)

H₂N-CH₂-CH₂-COO⁻  
(β-alanine)

many steps

H₂N-C-NH-CH₂-CH₂-COO⁻  
(Acetyl CoA)

Thymine → O → HN → CH → C → CH₃

H₂N-C-NH-CH₂-CH₂-COO⁻  
(Ureidopropionate)

H₂N-CH₂-CH-COO⁻  
(β-aminoisobutyrate)

H₂N-CH₂-CH-COO⁻  
(Succinyl CoA)

H₂N-C-NH-CH₂-CH₂-COO⁻  
(Ureidoisobutyrate)