# Nitrogen & Nucleotide Metabolism

BCH 100 — Introductory Biochemistry · Dr. Radi

# By the end of this unit, you can…

- Describe amino-acid catabolism — transamination and oxidative deamination — and where the carbon skeletons go
- Walk the urea cycle and how the body disposes of toxic ammonia as urea
- Explain nitrogen balance and the essential amino acids
- Identify nucleotide structure and the purine/pyrimidine bases, and outline nucleotide biosynthesis

# Today's route

1. **Amino Acid Catabolism**
2. **The Urea Cycle**
3. **Nitrogen Balance**
4. **Nucleotides & the Bases**
5. **Making & Breaking Nucleotides**

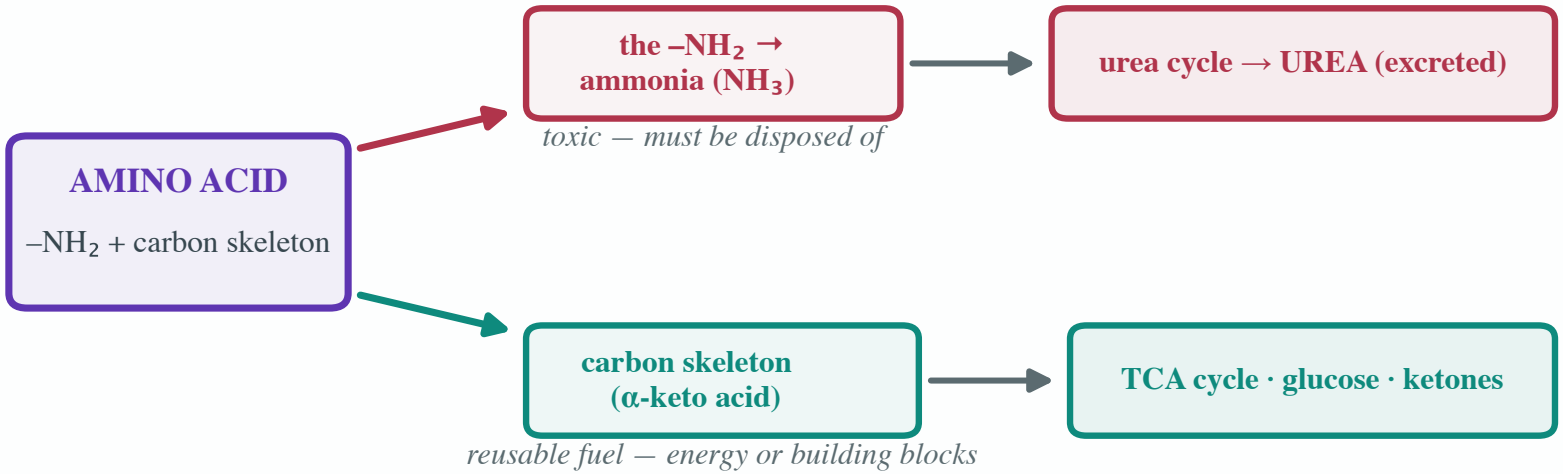
# 1 · Amino Acid Catabolism

"Unlike fat and sugar, protein carries nitrogen — and nitrogen can't just be burned. Step one of using an amino acid for fuel is prying that nitrogen off."

# Two problems in one molecule

When you burn **carbs or fat**, the atoms are just **C, H, and O** – they leave as $CO_2$ and water. But an **amino acid** also carries **nitrogen** in its amino group, and nitrogen has nowhere clean to go. So catabolizing an amino acid **splits into two jobs**. The **carbon skeleton** – an **α-keto acid** – is a normal fuel: it feeds the **TCA cycle**, or becomes **glucose** or **ketones**. The **amino group** is the problem child: pulled off as **ammonia ($NH_3$)**, which is **toxic**, and must be shipped to the **urea cycle** for disposal.

**Breaking down an amino acid — split the nitrogen from the carbon**

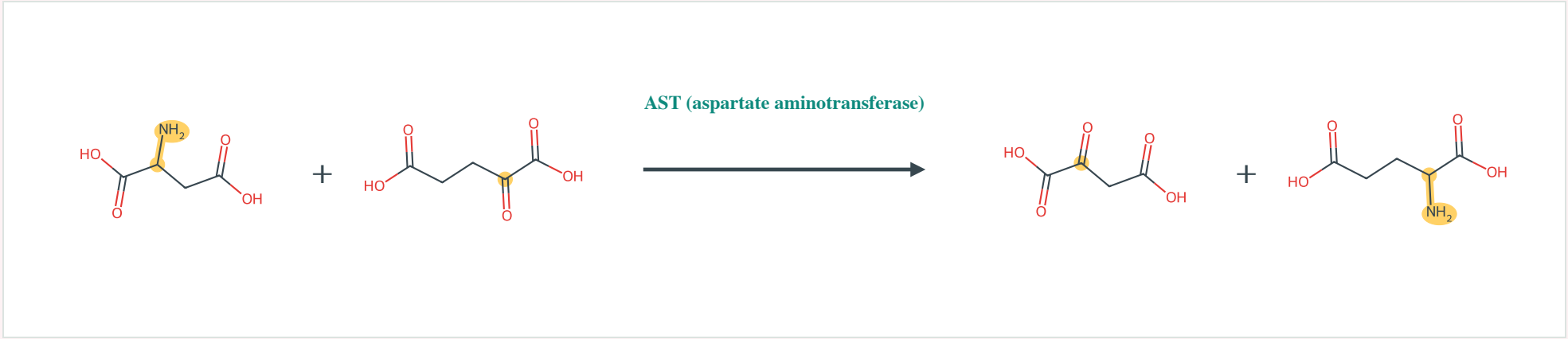


# Transamination: passing the nitrogen

The cell doesn't just rip the amino group off and release ammonia everywhere — that would be dangerous. Instead it **hands the nitrogen off** in a controlled swap called **transamination**. An **aminotransferase** enzyme takes the amino acid's **–$NH_2$** and transfers it onto **α-ketoglutarate**, producing **glutamate** and leaving the original amino acid as its **α-keto acid**. Here **ALT** does it to **alanine** — turning it into **pyruvate** while making glutamate. (All these enzymes use the vitamin-$B_6$ cofactor **PLP**.)

# ALT and AST: the enzymes in a blood test

The two transaminases you'll actually meet again are **ALT** (alanine) and **AST** (aspartate) — shown here handing aspartate's nitrogen to α-ketoglutarate. They matter clinically because they normally live **inside liver cells**. When the liver is **damaged** — hepatitis, fatty liver, a paracetamol overdose — those cells **leak**, and **ALT and AST spill into the blood**. That's why "**liver enzymes**" on a blood panel **are** these two: a routine test that reads out cell damage through the biochemistry of nitrogen handling.



# 2 · The Urea Cycle

"Ammonia is poison — especially to the brain. So your liver runs a five-step loop that locks two waste nitrogens into one safe molecule you can pee out: urea."

# What to do with the nitrogen

Once transamination has funneled waste nitrogen into **ammonia**, the body has to **get rid of it** – and different animals solve this differently. **Fish** just dump **ammonia** straight into the water; it's toxic but they have an ocean to dilute it. **Birds and reptiles** convert it to **uric acid**, a nearly **solid** paste that wastes almost no water (handy inside an egg). **Mammals – you – make urea**: far less toxic than ammonia, freely water-soluble, built in the **liver** and flushed out by the **kidneys**. The choice is a trade-off between **toxicity, water, and energy**.

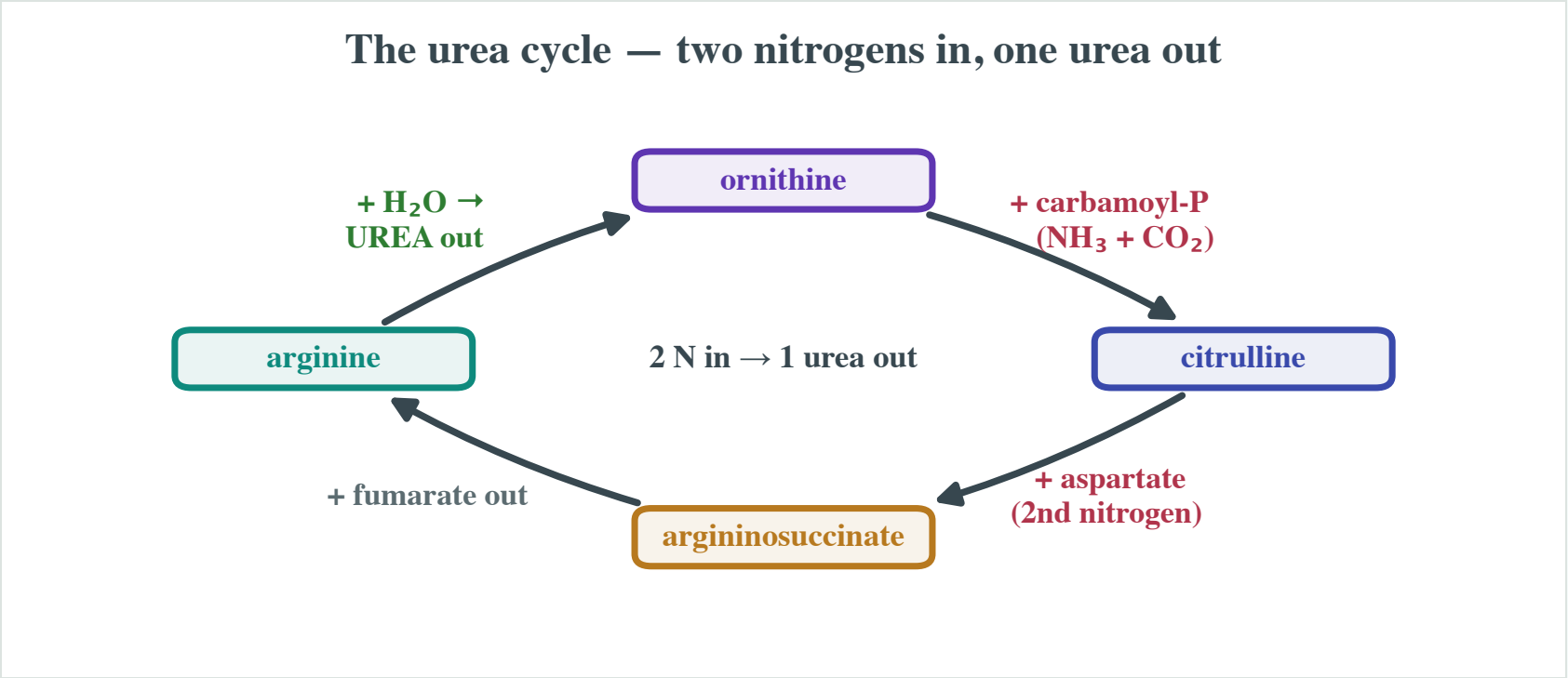
**Three ways to dump waste nitrogen**

| AMMONIA | UREA | URIC ACID |
|---|---|---|
| *fish* | *mammals (you)* | *birds, reptiles, insects* |
| very toxic · needs lots of water to flush | much less toxic · water-soluble, made in liver | nearly insoluble solid · saves water |
| **cheap to make** | **moderate cost** | **costly to make** |

**You are ureotelic: your liver packages waste nitrogen as safe, soluble urea for the kidneys to excrete.**

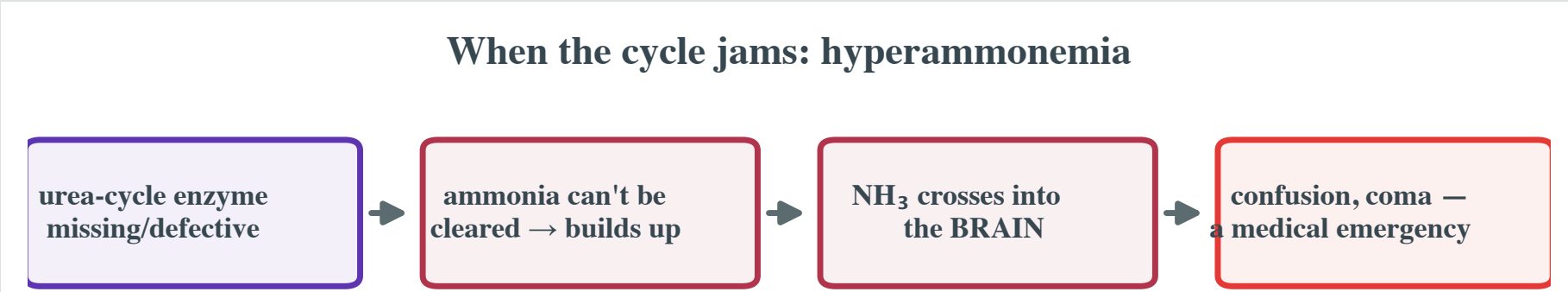
# The urea cycle

Making urea takes a **five-step loop** in the liver, and the key is that it **loads two nitrogens** from two different sources. The **first** nitrogen enters as **carbamoyl phosphate** (built from **ammonia + $CO_2$**), which joins **ornithine** to make **citrulline**. The **second** nitrogen is donated by **aspartate**. A couple of steps later, the enzyme snips out **urea** — carrying **both** waste nitrogens — and regenerates **ornithine** to run the loop again. Two toxic nitrogens in, one harmless **urea** out.



# When the cycle jams

This loop isn't optional — and you can see why when it **fails**. If a baby is born missing one of the **urea-cycle enzymes**, ammonia has **nowhere to go**: it **builds up in the blood** (**hyperammonemia**) and, because **ammonia is a potent brain toxin**, causes vomiting, lethargy, seizures, and — untreated — **coma**. There's no way to make the missing enzyme, so treatment is about **buying time**: a **low-protein diet** to make less nitrogen, plus drugs that escort nitrogen out by an **alternate route**. The whole disease is a **backed-up cycle**.



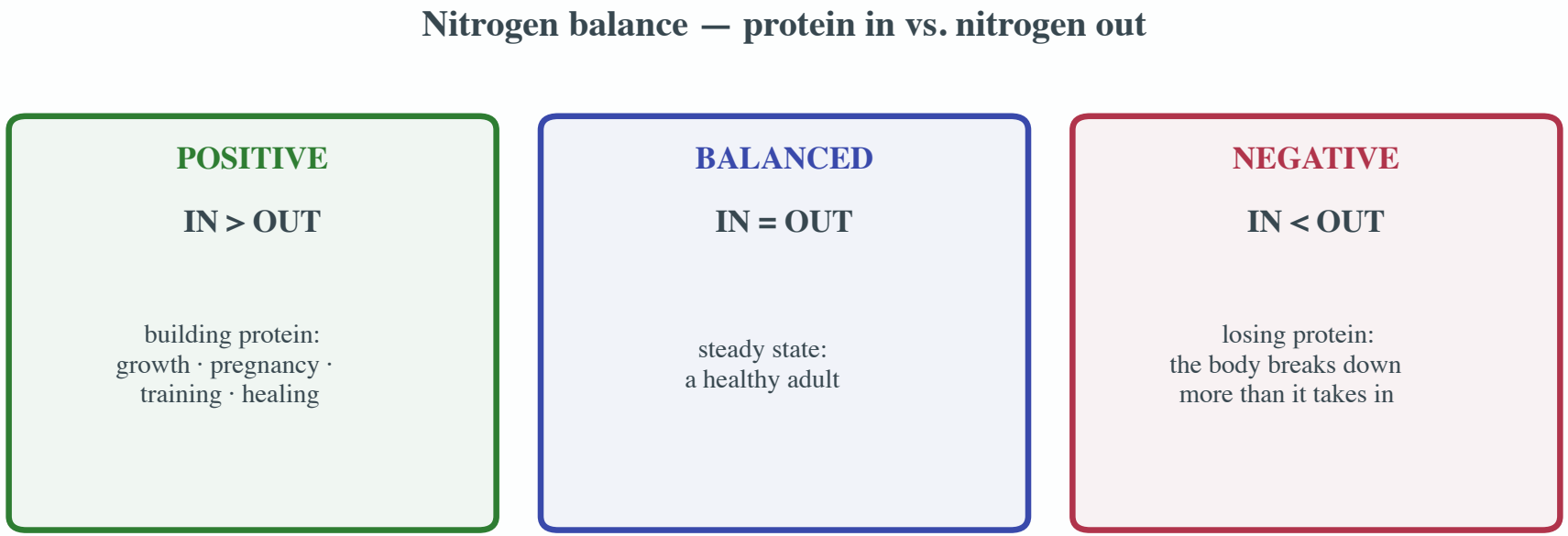

*Treatment buys time: a low-protein diet and drugs that mop up nitrogen by another route.*

# 3 · Nitrogen Balance

"You don't store protein the way you store fat. So whether you're building muscle or losing it comes down to a simple ledger: nitrogen in versus nitrogen out."

# The nitrogen ledger

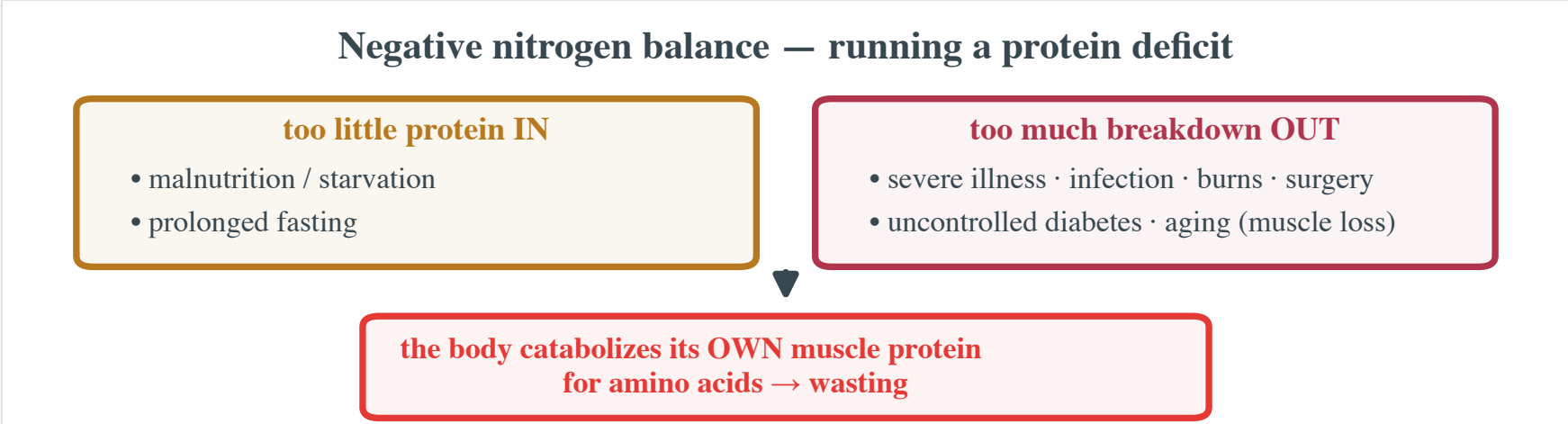
Because the body has **no dedicated protein store**, dietitians track protein status with a simple accounting trick: **nitrogen balance** — the **nitrogen you eat** (in protein) minus the **nitrogen you excrete** (as urea). It comes in three states. **Positive** balance (in > out) means you're **net building protein** — normal in **growth, pregnancy, training, and healing**. **Balance** (in = out) is the **steady state** of a healthy adult. **Negative** balance (in < out) means you're **losing protein faster than you replace it** — and that one is a warning sign.




*"In" = the protein you eat; "out" = the nitrogen you excrete as urea. Which way it tips tells a story.*

# Negative balance: the body eats itself

**Negative nitrogen balance** happens two ways — **too little protein coming in**, or **too much breakdown going out**. The intake side is **malnutrition, starvation, or prolonged fasting**. The breakdown side is **stress catabolism** — **severe illness, infection, major burns, surgery**, uncontrolled **diabetes**, and the slow muscle loss of **aging**. Either way the result is the same and grim: with amino acids in short supply, the body starts **dismantling its own muscle protein** to get them — **wasting**. It's why serious illness costs you muscle, and why nutrition is part of the treatment.

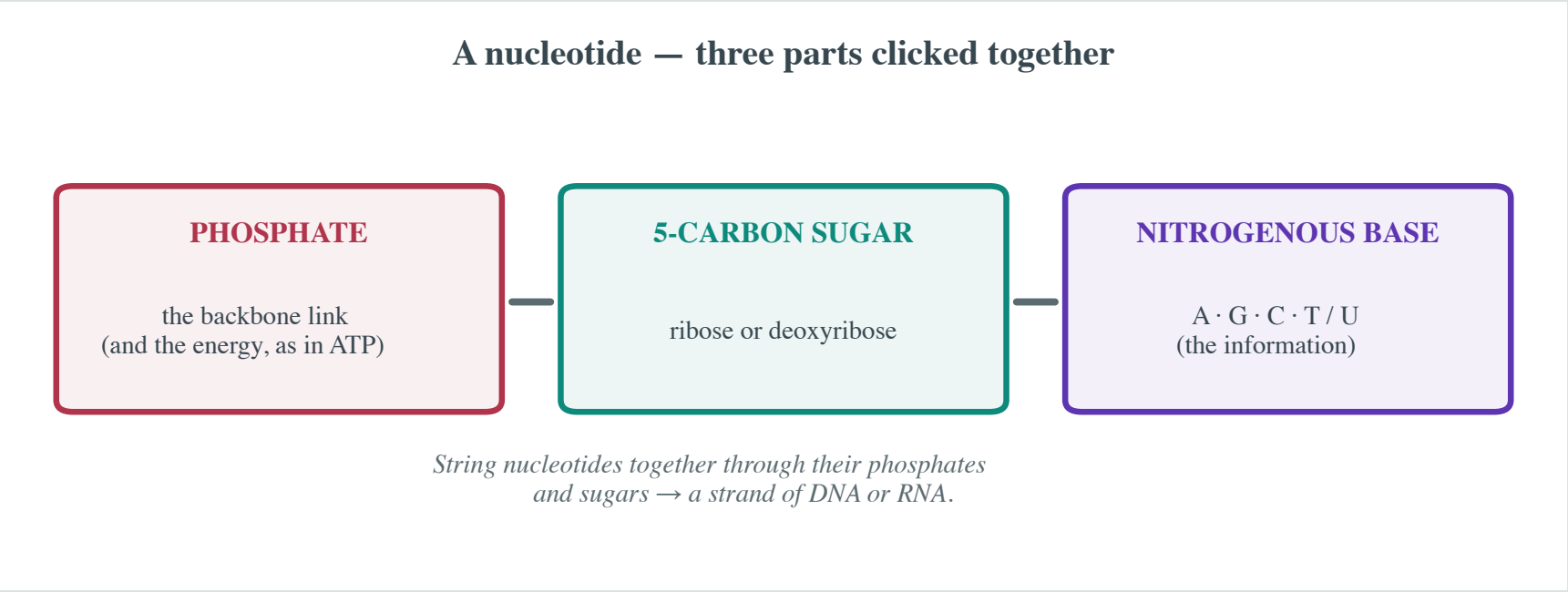


# 4 · Nucleotides & the Bases

"The molecules that store your genome are built from just three kinds of part — and the 'information' comes down to five nitrogen-rich rings."

# What a nucleotide is made of

Nucleic acids look complicated, but every **nucleotide** — the repeating unit of DNA and RNA — is just **three parts** snapped together: a **phosphate**, a **five-carbon sugar**, and a **nitrogenous base**. The **phosphate** and **sugar** alternate to form the strand's **backbone**; the **base** sticks out to the side and carries the **information**. (And notice the sugar–phosphate piece is exactly what makes **ATP** an energy molecule too — same parts, different job.)



# DNA vs. RNA

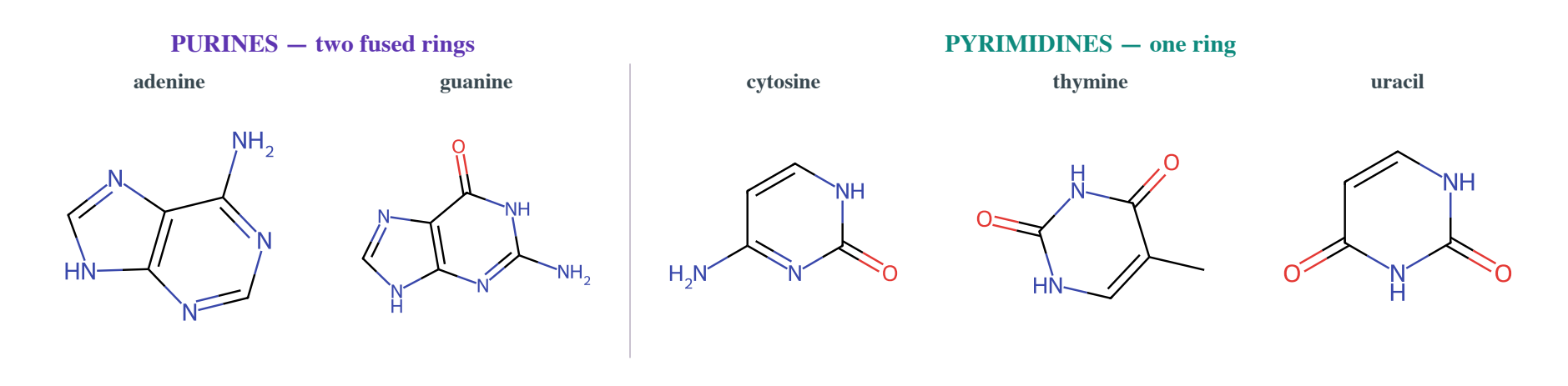
DNA and RNA are built the same way but differ in **four** telling spots. Their **sugar**: DNA uses **deoxyribose** (missing an oxygen at the 2′ position), RNA uses **ribose** (which keeps that **2′-OH**) — one atom, and it's what makes DNA the more **stable, long-term** molecule. Their **bases** are almost the same set, except DNA uses **thymine (T)** where RNA uses **uracil (U)**. And their **shape and job**: DNA is a **double** helix that **stores** the genome; RNA is usually **single**-stranded and **carries and translates** the message.

**DNA vs. RNA — four differences**

| | DNA | RNA |
|---|---|---|
| *sugar* | deoxyribose (no 2′-OH) | ribose (has 2′-OH) |
| *bases* | A · G · C · T | A · G · C · U |
| *strands* | double (the double helix) | usually single |
| *job* | stores the genome | carries & translates it |

# The five bases: purines vs. pyrimidines

The "information" in a nucleic acid is spelled with just **five** nitrogenous bases, and they come in **two shapes**. **Purines** — **adenine (A)** and **guanine (G)** — are the **big** ones: **two fused rings**. **Pyrimidines** — **cytosine (C)**, **thymine (T)**, and **uracil (U)** — are the **small** ones: a **single ring**. An easy way to keep them straight: **"PY-rimidines are the smaller CUT"** (**C, U, T**), and the purines are the two that are left. In the double helix, a big purine always pairs with a small pyrimidine.

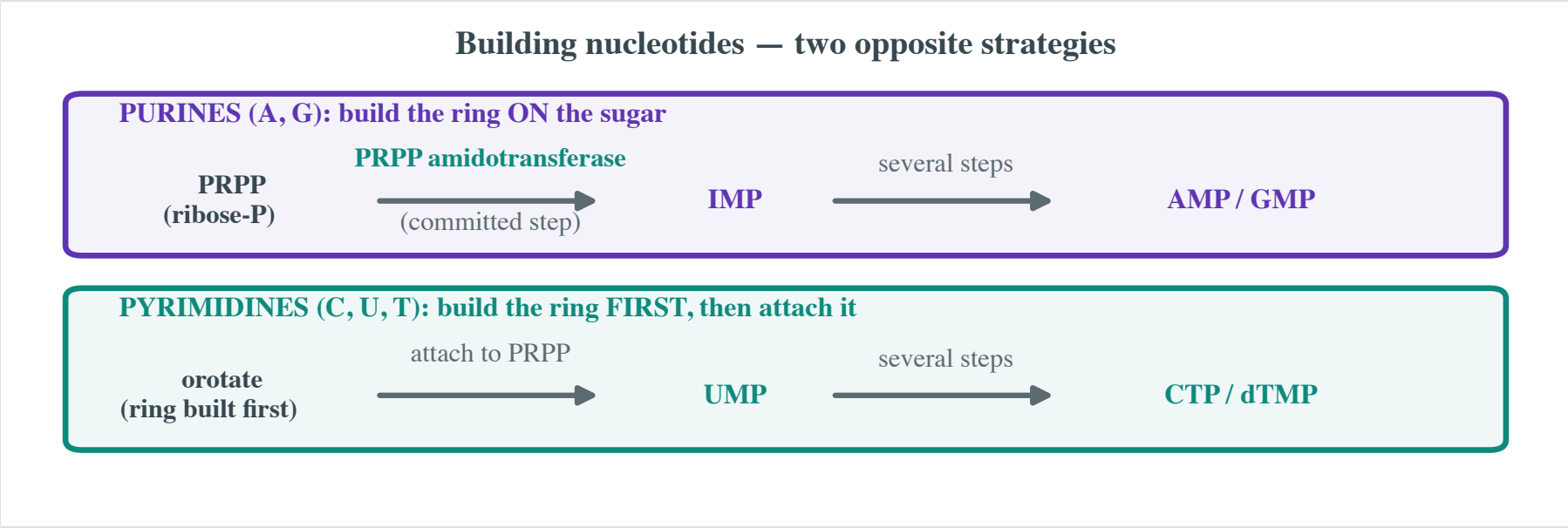


# 5 · Making & Breaking Nucleotides

"Cells build nucleotides two different ways, convert them into DNA's building blocks with a single pivotal enzyme, and — when they break the leftovers down — occasionally give someone gout."

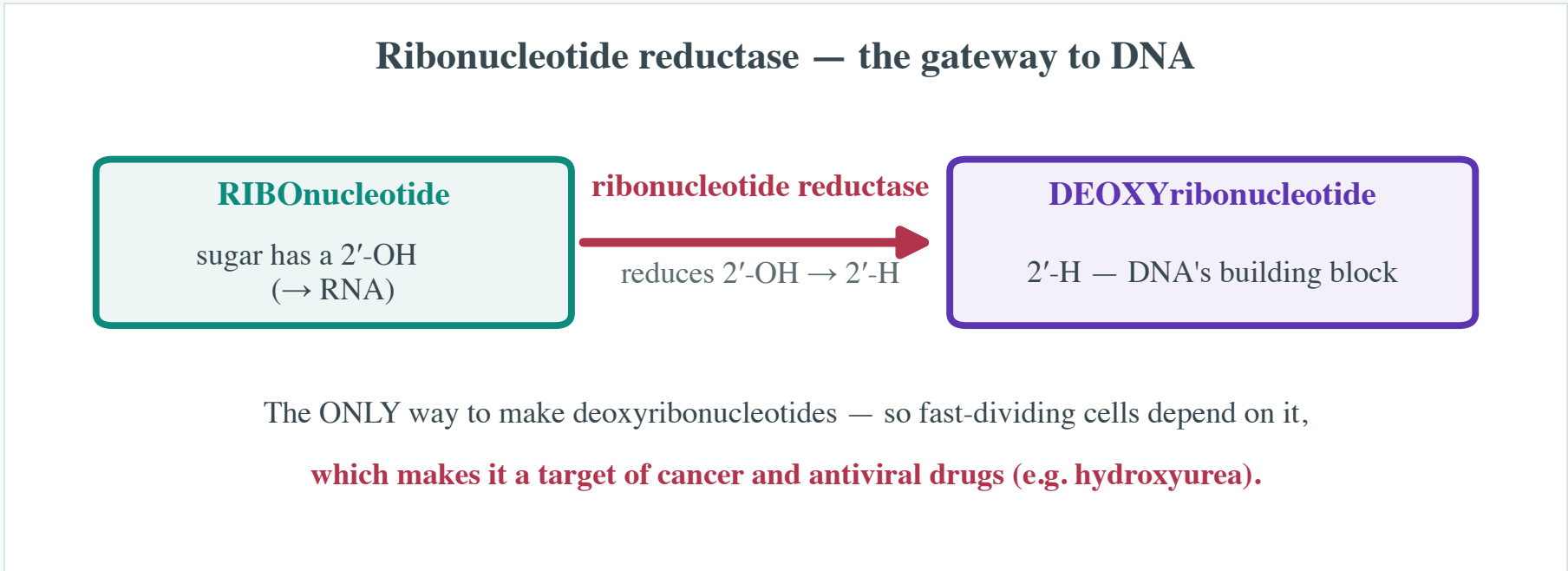
# Building the two kinds of base

Cells make nucleotides **from scratch** (**de novo**) by two **opposite** strategies. For **purines** (**A, G**), the ring is **built directly onto the sugar** — atom by atom, starting from an activated ribose called **PRPP** — to make **IMP**, which then becomes **AMP** or **GMP**. For **pyrimidines** (**C, U, T**), it's reversed: the **ring is built first** (as **orotate**), then **attached** to PRPP to make **UMP**, and onward to CTP and dTMP. (In practice, most cells prefer the cheaper **salvage** route — recycling free bases rather than building new ones.)



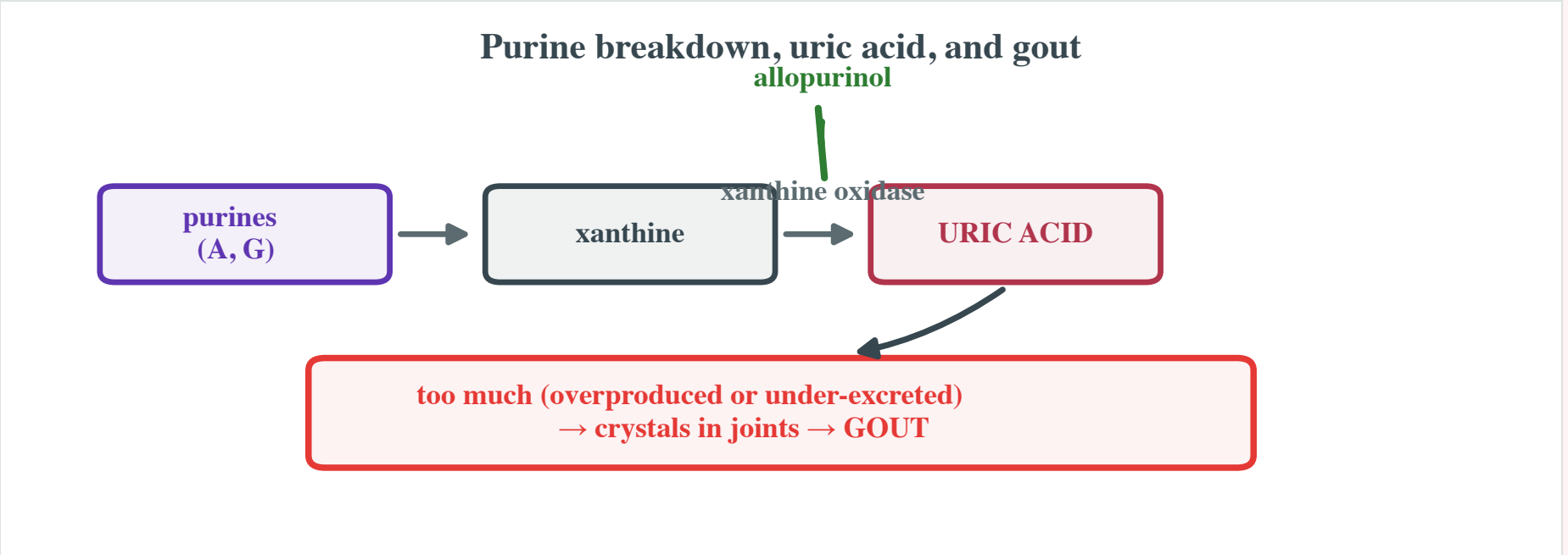
# From RNA parts to DNA parts

Notice that everything so far makes **ribonucleotides** – the units of **RNA**, with a **2′-OH** on the sugar. So how does a cell get the **deoxy** version for **DNA**? One enzyme does it: **ribonucleotide reductase**, which **reduces the 2′-OH to 2′-H**. It's the **single gateway** to every DNA building block – which makes it a **choke point**. Fast-dividing cells (like a tumor, or a replicating virus) need **huge** amounts of dNTPs, so ribonucleotide reductase is a favorite **drug target** (e.g. hydroxyurea).



# The leftovers: uric acid and gout

Finally, what happens to **old purines**? They're **broken down** — through **xanthine** — to **uric acid**, which you normally excrete. The catch: uric acid is **barely soluble**. If you make **too much** or **excrete too little**, it **precipitates** into **needle-sharp crystals** that lodge in a joint (classically the **big toe**), triggering the sudden, brutal inflammation of **gout**. The fix follows straight from the pathway: **allopurinol** blocks **xanthine oxidase**, the enzyme that makes uric acid — less uric acid, no crystals. Metabolism, all the way down to a sore toe.



# Can you…?

- ☐ describe amino-acid catabolism — transamination and oxidative deamination — and where the carbon skeletons go?
- ☐ walk the urea cycle and how the body disposes of toxic ammonia as urea?
- ☐ explain nitrogen balance and the essential amino acids?
- ☐ identify nucleotide structure and the purine/pyrimidine bases, and outline nucleotide biosynthesis?

If any box stays empty, the practice site has a drill for it.
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