# AMINOTRANSFERASE

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November 10, 2025



RECOMMENDED CITATION

mohammad looti (2025). *AMINOTRANSFERASE*. PSYCHOLOGICAL SCALES. Retrieved from https://scales.arabpsychology.com/?p=69267

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**Primary Disciplinary Field(s): Biochemistry**, **Enzymology**, **Clinical Pathology**

## 1. Core Definition

Aminotransferase, often referred to as a **transaminase**, is a critical category of enzymes belonging to the transferase class (EC 2.6.1.x). These enzymes are fundamentally responsible for catalyzing the reversible transfer of an **alpha-amino group** (NH2) from an alpha-amino acid to an alpha-keto acid. This vital metabolic process is known as **transamination**. Through this reaction, the original amino acid is converted into its corresponding keto acid, and the receiving keto acid is converted into a new amino acid. Aminotransferases thus serve as crucial metabolic intermediaries, linking the pathways of amino acid catabolism and synthesis with those of carbohydrate and lipid metabolism. The overall function of these enzymes is essential for maintaining the balance of nitrogen within the cell and ensuring the appropriate availability of precursors for gluconeogenesis and energy production, particularly during periods of fasting or high protein intake.

The catalytic activity of all known aminotransferases is absolutely dependent upon a specific organic cofactor: **pyridoxal phosphate (PLP)**, which is the biologically active derivative of **vitamin B6** (Pyridoxal phosphate). PLP is tightly bound to the enzyme's active site via a Schiff base linkage with a specific lysine residue. During the transamination reaction, PLP acts as a temporary carrier for the amino group. The enzyme reaction proceeds via a two-step mechanism, frequently described as a **ping-pong bi-bi reaction**. The first half-reaction involves the amino acid donating its amino group to PLP, forming the keto acid product and converting PLP into pyridoxamine phosphate (PMP).

In the second half-reaction, the newly formed PMP, which now carries the amino group, interacts with a different alpha-keto acid substrate. The amino group is then transferred from PMP to the keto acid, forming the new amino acid product and simultaneously regenerating the original PLP cofactor, allowing the enzyme to catalyze another reaction cycle. This robust, reversible mechanism allows the cell to rapidly adjust its amino acid pool, enabling the synthesis of non-essential amino acids when required or the breakdown of excess amino acids when they are used for energy. The omnipresence and high concentrations of these enzymes in metabolically active organs underscore their centrality to overall systemic homeostasis and nitrogen management.

## 2. Etymology and Historical Development

The understanding of transamination and the enzymes responsible for it began in the 1930s. The process was first systematically described by the Russian biochemists **Alexander E. Braunstein** and **Maria G. Kritzmann** in 1937, who demonstrated that amino groups could be rapidly and reversibly transferred between amino acids and keto acids in animal tissues, initially focusing on muscle extracts. This discovery fundamentally altered the comprehension of nitrogen metabolism, moving away from the previous view that amino acid breakdown required direct deamination, demonstrating instead a cyclical shuttling mechanism. Their initial observations paved the way for the biochemical identification and isolation of the specific enzymes responsible for this activity.

Following the foundational work on the transamination process itself, the specific enzymes were isolated and characterized. The two most clinically significant forms, Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT), were originally designated as Glutamic-Oxaloacetic Transaminase (GOT) and Glutamic-Pyruvic Transaminase (GPT), respectively. Their critical role transcended basic biochemistry when researchers realized their utility as diagnostic tools. In the 1950s, particularly through the work of LaDue, Wroblewski, and Karmen, it was observed that elevated levels of these enzymes in the serum correlated strongly with tissue damage, especially **myocardial infarction** (heart attack) and **liver disease**.

The introduction of reliable quantitative assays for serum aminotransferases revolutionized clinical diagnostics. While initially highly valued for detecting heart damage, advancements in specialized biomarkers (like cardiac troponins) later refined their use. Today, aminotransferases are most recognized as primary components of the battery of tests used to assess liver health, often inaccurately termed "liver function tests," though they technically measure **cellular injury** rather than functional capacity. Their historical trajectory illustrates a movement from elucidating fundamental metabolic processes to developing routine, essential clinical markers of cellular integrity.

## 3. Major Isoforms: ALT and AST

While a wide variety of aminotransferases exist, each specific to a different pair of amino/keto acids, two isoforms hold paramount importance in clinical and metabolic contexts: Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST). These enzymes are differentiated by their specific substrates and their primary subcellular and tissue locations. Understanding these distinctions is crucial for interpreting clinical test results and determining the source and nature of tissue damage within the body. Both enzymes utilize the glutamate/alpha-ketoglutarate pair in their reactions, but differ in their secondary substrates.

**Alanine Aminotransferase (ALT)**, which catalyzes the reversible transfer of an amino group between **alanine** and **alpha-ketoglutarate** to produce **pyruvate** and **glutamate**, is found predominantly in the **cytosol** and is highly concentrated within the **liver**. This high specificity makes serum ALT levels an exceptionally sensitive and specific marker for **hepatocellular injury**. Even relatively minor damage to liver cells can lead to the release of ALT into the bloodstream. Furthermore, ALT plays a central role in the **glucose-alanine cycle**, which allows muscles to transfer nitrogen to the liver safely for detoxification via the urea cycle, while providing the liver with pyruvate for gluconeogenesis.

**Aspartate Aminotransferase (AST)**, which catalyzes the transfer of the amino group between **aspartate** and **alpha-ketoglutarate** to produce **oxaloacetate** and **glutamate**, has a broader tissue distribution compared to ALT. High concentrations of AST are found in the liver, but also significantly in the **heart muscle**, **skeletal muscles**, **kidneys**, and **red blood cells**. AST exists in two distinct forms: a cytosolic isoform and a mitochondrial isoform. Because of its wide distribution, elevated AST levels in the blood are less specific for liver damage alone than ALT. However, the presence of mitochondrial AST in the serum, often measured alongside total AST, suggests more severe cellular damage (necrosis), as the mitochondria are only compromised in severe injury. The AST/ALT ratio is a key diagnostic tool, often used to differentiate types of liver disease; for instance, a ratio greater than 2:1 is highly suggestive of alcoholic liver damage.

## 4. Biological Roles and Metabolic Function

The physiological importance of aminotransferases extends far beyond their use as clinical markers. They are integral to the dynamic flow of nitrogen throughout the body, acting as metabolic conduits that regulate the supply of keto acids and amino acids necessary for synthesis and energy generation. Their primary metabolic function is to collect amino groups from various amino acids and concentrate them, usually onto alpha-ketoglutarate to form glutamate. Glutamate then serves as the primary substrate for further nitrogen processing, either through direct utilization in biosynthesis or through oxidative deamination, which releases free ammonium ions that enter the urea cycle for detoxification and excretion.

Furthermore, aminotransferases are deeply involved in **gluconeogenesis**, the pathway by which the body synthesizes new glucose from non-carbohydrate sources, such as amino acids, especially during prolonged fasting. By converting amino acids into their corresponding alpha-keto acids (e.g., alanine to pyruvate, aspartate to oxaloacetate), these enzymes supply critical intermediates that feed directly into the tricarboxylic acid (TCA) cycle or the gluconeogenic pathway. This interconversion ensures that the energy released from protein breakdown can be efficiently utilized to maintain blood glucose levels, which is vital for tissues like the brain that rely almost exclusively on glucose for fuel.

The specific function of certain aminotransferases highlights their specialized roles in different organs. The source content notes that Alanine aminotransferase (ALT) is vital to the proper functioning of the **muscles** and **kidneys**. In muscle, ALT is critical for the glucose-alanine cycle, transporting potentially toxic nitrogen away from muscle tissue to the liver without accumulating free ammonia. In the kidney, aminotransferases are essential for the production of ammonia, which is crucial for acid-base balance and the excretion of excess hydrogen ions. Thus, these enzymes are far more than just indicators of disease; they are essential workhorses of metabolic adaptability and nitrogen homeostasis across multiple organ systems.

## 5. Clinical Significance and Diagnostic Utility

The clinical measurement of serum aminotransferase activity is one of the most frequently performed laboratory tests worldwide. Elevated levels of AST and ALT in the blood are considered reliable **biomarkers of tissue injury**, particularly concerning the liver, heart, and skeletal muscle. When cells are damaged, their membranes become permeable or rupture (necrosis), leading to the leakage of intracellular components, including these enzymes, into the systemic circulation. Therefore, the magnitude of the enzyme elevation generally correlates with the extent and severity of the cellular damage.

In modern medicine, aminotransferases are primarily utilized in the diagnosis and monitoring of **hepatic diseases**. Conditions such as acute viral hepatitis, chronic hepatitis (B or C), alcoholic liver disease, non-alcoholic fatty liver disease (NAFLD), drug-induced liver injury, and cirrhosis all result in elevated ALT and AST levels. The pattern of elevation, the ratio between AST and ALT (De Ritis ratio), and the concurrent levels of other liver markers (like alkaline phosphatase and bilirubin) help clinicians pinpoint the specific etiology of the liver disorder. For instance, massive elevations (often >10 times the upper limit of normal) typically suggest acute viral hepatitis or severe toxic injury, whereas mild or moderate chronic elevations are common in NAFLD or chronic hepatitis C.

Although their role in diagnosing **myocardial infarction** has been largely superseded by the use of highly sensitive troponin assays, AST was historically a primary marker for heart damage. Today, if AST is elevated without a corresponding spike in ALT, clinicians must consider non-hepatic causes, such as muscle trauma, strenuous exercise, hemolysis, or musculoskeletal disorders, reflecting the broader tissue distribution of AST. Consequently, the interpretation of aminotransferase results requires a comprehensive clinical context, combining the enzyme profile with the patient's history and physical examination findings to accurately diagnose the underlying organ pathology.



## 6. Key Characteristics and Regulatory Factors

**Coenzyme Requirement:** All aminotransferases absolutely require pyridoxal phosphate (PLP), a derivative of Vitamin B6, as a prosthetic group for activity. PLP deficiency severely limits the body's ability to perform transamination reactions, impacting both amino acid metabolism and neurotransmitter synthesis.

**Substrate Specificity:** While all aminotransferases participate in the transamination of alpha-amino acids and alpha-keto acids, each enzyme exhibits high specificity for a second pair of substrates (e.g., ALT for the alanine/pyruvate pair; AST for the aspartate/oxaloacetate pair).

**Reversibility:** The reactions catalyzed by aminotransferases are **reversible**, allowing them to participate in both anabolic (synthesis) and catabolic (breakdown) pathways, enabling the cell to maintain metabolic equilibrium according to nutritional demand and energy status.

**Cellular Location:** Aminotransferases are distributed between the **cytosol** and the **mitochondria**. Cytosolic forms are often released during mild cell damage, while the presence of mitochondrial forms (particularly AST) in the serum indicates more severe, irreversible cell damage.

**Regulation:** The activity of aminotransferases is regulated primarily by the concentration of their substrates and products, ensuring that the flux through transamination pathways responds directly to the cellular amino acid load and the availability of alpha-ketoglutarate, which serves as the primary amino group acceptor.

## 7. Further Reading

Alanine aminotransferase
Aspartate aminotransferase
Pyridoxal phosphate
Urea cycle