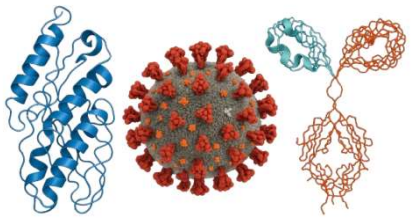
The Albumin-to-Globulin Ratio in FIP

Albumin and globulin are the two principal components of plasma proteins, and their ratio (A/G ratio) provides an integrated overview of inflammation, infection, and hepatic function. Albumin is a negative acute-phase protein synthesized by the liver; its production is suppressed during inflammatory responses (Fong et al., 2024). In contrast, globulin fractions increase in association with immune activation, with immunoglobulin G (IgG) and α1-acid glycoprotein (AGP) showing marked elevations in chronic inflammatory diseases such as FIP (Donato et al., 2023; Murphy et al., 2024).

In cats, the hypoalbuminemia combined with hyperglobulinemia pattern is a typical laboratory finding in feline infectious peritonitis (FIP). As a consequence, the albumin/globulin (A/G) ratio decreases. Pedersen (2014) emphasized that the A/G ratio has diagnostic value but is not pathognomonic, meaning that it cannot establish a definitive diagnosis when used in isolation.



The Albumin/Globulin Ratio in the Diagnosis of FIP

In cases of feline infectious peritonitis (FIP), the albumin/globulin (A/G) ratio is often below 0.6. According to the European Advisory Board on Cat Diseases (EABCD), an A/G ratio < 0.6 is associated with a high likelihood of FIP, whereas an A/G ratio > 0.6 reduces the probability of FIP but does not exclude the disease, particularly in cats under treatment or in partial remission. Jeffery et al. (2012) demonstrated that the positive predictive value of an A/G ratio < 0.6 is only approximately 25%, indicating that this parameter has a high negative predictive value but a low positive predictive value. These findings support the use of the A/G ratio as a helpful tool for ruling out FIP, while highlighting its limited utility as a standalone diagnostic criterion.

Dynamics of the Albumin/Globulin Ratio and Its Clinical Significance in FIP Treatment

1) Antiviral Phase

Nucleoside analogues used in FIP therapy suppress viral replication within a few days. During the first 1–2 weeks of treatment, acute-phase proteins such as serum amyloid A (SAA) and α1-acid glycoprotein (AGP) decline rapidly, while the A/G ratio often remains low (approximately 0.4–0.5) (Katayama et al., 2024). This period is defined as an "immune residual phase," in which viral replication is controlled but the inflammatory response persists.

2) Immune–Pathological Residual Phase

Despite effective antiviral therapy, macrophage infiltration, residual granulomatous lesions, and fibrosis may persist for several weeks (Murphy et al., 2024). This ongoing tissue-level inflammation leads to delayed normalization of serum protein balance. Residual inflammation in organs such as the liver and intestines particularly contributes to the slow recovery of albumin synthesis.

3) Delayed Recovery of Albumin As albumin is a negative acute-phase protein, its synthesis is suppressed during inflammation. Pedersen (2014) and Fong et al. (2024) have reported that recovery of albumin production may require 6–8 weeks. In contrast, the decline of globulin fractions often occurs even more slowly; consequently, the A/G ratio may normalize weeks after apparent clinical improvement.

4) Treatment Duration and Remission Monitoring

The A/G ratio is a valuable parameter for monitoring resolution of inflammation and recovery of albumin synthesis in FIP. However, an increase above 0.6 should not be considered sufficient justification for early discontinuation of therapy. Due to the immune-pathological nature of FIP, tissue repair lags behind biochemical improvement. Accordingly, a minimum antiviral treatment duration of 84 days (12 weeks) is consistent with clinical, laboratory, and histopathological evidence.

Multiple clinical studies have demonstrated that an **A/G ratio > 0.6 is not sufficient to justify shortening the duration of therapy, as biochemical normalization lags behind clinical remission**, and **tissue repair and restoration of protein balance occur with delay**. The European Advisory Board on Cat Diseases (EABCD) has emphasized that while an A/G ratio above 0.6 indicates improvement, it does not guarantee complete viral clearance.

- Kamiyoshi et al. (2025)**:** In a cat with FIP, the baseline A/G ratio was 0.5, increasing to 0.7 after 12 weeks of antiviral therapy. Relapse was observed in some cats when treatment was discontinued solely on the basis of A/G > 0.6.
- Zwicklbauer et al. (2023)**:** Even in cats in which the A/G ratio normalized by weeks 8–9, antiviral treatment was completed to 12 weeks.
- de Witt Curtius et al. (2025)**: Relapse rates were higher in cats receiving antiviral therapy for less than 84 days.**
- Sase et al. (2024)**:** A 17% relapse rate was reported in cats in which treatment was discontinued based on biochemical remission alone.

Collectively, these clinical studies demonstrate that the **A/G ratio reflects biochemical remission but does not ensure virological remission**. Therefore, **antiviral therapy should be continued even after the A/G ratio exceeds 0.6**.

An upward trend in the A/G ratio is consistent with remission; however, a single measurement is insufficient for clinical decision-making. During clinical remission, **acute-phase proteins may normalize while the A/G ratio remains within the 0.6–0.7 range** (Sase, 2024; Larson, 2025).

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The Albumin/Globulin Ratio After Treatment

Murphy et al. (2024) demonstrated that viral antigens disappear rapidly following antiviral therapy, whereas granulomatous lesions persist for several weeks in organs such as the liver, kidneys, and colon. During this so-called "sterile inflammatory tail" phase, protein metabolism remains disrupted in hepatic and renal tissues. These residual lesions are associated with ongoing local immune stimulation and continued IgG production, despite effective virological suppression.

In the study by Katayama et al. (2024), a decline in globulin concentrations and a subsequent increase in the A/G ratio were observed with a delay of approximately 4–6 weeks. Notably, this change was not primarily driven by a synchronous increase in albumin, but rather by a gradual reduction in globulin levels.

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