Serological and Biochemical Diagnostic Approach in Feline Infectious Peritonitis (FIP)

1) FCoV antibody positivity is not merely an indicator of "exposure"

Although FCoV antibody tests demonstrate prior contact with the virus, high-titer seropositivity is typically associated with ongoing viral replication and an increased risk of environmental transmission. Kipar and Meli (2014) and Pedersen (2019) reported that high antibody titers are most often detected in cats harboring substantial viral loads during the enteric phase, creating a permissive environment for mutation and emergence of FIP-associated strains.

2) The incidence of FIP is higher than commonly assumed

Most FCoV infections remain asymptomatic; however, multiple studies report that:

- The overall FIP development rate in the general feline population is 5–12%,
- In multi-cat households and shelters, this rate may rise to 10–14% (Pedersen, 2019; Addie et al., 2020).
- Thus, assuming a "low risk" for FIP progression solely based on seropositivity is not epidemiologically justified.

3) Antibody test negativity may occur in asymptomatic or early infection

Seronegativity does not necessarily indicate absence of infection. It may reflect:

- Delayed antibody production (early infection phase),
- Immunosuppression or corticosteroid administration,
- Viral replication restricted to the intestinal epithelium.

Felten and Hartmann (2019) emphasized that serological sensitivity is reduced during early infection; therefore, supplemental tests such as RT-PCR or the A/G ratio should be considered in suspect cases.

4) Tropism shift and early pathogenesis are not detectable by serology

FIP pathogenesis begins when enteric FCoV acquires monocyte–macrophage tropism. This shift is molecular—frequently involving mutations such as M1058L—and is not detected by antibody assays. Chang et al. (2012) demonstrated that this mutation enhances replication within macrophages and initiates systemic dissemination.

5) Correlating clinical and laboratory findings is essential

Serology alone does not establish a diagnosis. Notably, FIP likelihood increases when antibody positivity is accompanied by:

- A/G ratio < 0.6,
- SAA > 200 µg/mL,
- Globulin > 50 g/L.

De Bonis et al. (2023) identified these parameters as strongly correlated with confirmed FIP cases.

6) Values within the reference interval do not always indicate “normal”

Pedersen (2019) and Felten & Hartmann (2019) highlighted that hematologic and biochemical abnormalities may develop within reference limits during early FIP, yet show a directional trend over days to weeks.

Clinicians should focus on trends rather than static results:

- Progressive lymphopenia and reduced hematocrit with rising neutrophils → early immune activation + chronic inflammation,
- Increasing globulins and total protein → early humoral response,
- Declining albumin → negative acute-phase reaction,
- Mild increases in SAA, AGP, or bilirubin → subclinical inflammation.

7) Biochemical “signals” fluctuate during the subclinical FIP phase

Recent investigations (De Bonis et al., 2023; Moyadee et al., 2024) reported the following early laboratory patterns in pre-treatment FIP cases:

- Mild reduction in A/G ratio (0.6–0.8 is often considered the “gray zone”),
- Globulin levels trending toward or above the upper reference limit (≥ 50 g/L),
- ALT, AST, BUN, and creatinine values mildly elevated, indicating early hepatic and renal involvement secondary to viral replication.

8) Subtle deviations within “normal limits” may have prognostic value

Kipar and Meli (2014) described early endothelial activation and monocyte infiltration during the transition to systemic FIP, leading to microvascular leakage.

This process may manifest as:

- Decreasing hematocrit,
- Gradual increases in total protein and globulin,
  even before clinical signs emerge.

Thus, even when biochemical parameters remain within the reference interval:

- A declining A/G ratio,
- Slowly increasing globulin concentration,
  combined with FCoV seropositivity, can support suspicion of asymptomatic or preclinical FIP.

Acute-phase proteins such as SAA, AGP, LDH, and others may assist in early-stage risk assessment even in outwardly healthy cats (Riemer et al., 2016; Dewerchin & Cornelissen, 2021).

Conclusion

FCoV antibody testing confirms viral exposure but does not discriminate active infection, mutation events, or progression to FIP. Therefore, serological findings must be integrated with the A/G ratio, acute-phase protein

levels (SAA, AGP), hematological trends, and clinical presentation. A single negative serological test does not rule out infection, especially during early phases or under immunosuppressive conditions.

References

Addie, D. D., Belák, S., Boucraut-Baralon, C., Egberink, H., Frymus, T., Gruffydd-Jones, T., Hartmann, K., Hosie, M. J., Lloret, A., Lutz, H., Marsilio, F., Pennisi, M. G., Radford, A. D., Thiry, E., Truyen, U., & Horzinek, M. C. (2020). Feline coronavirus infection: ABCD guidelines on prevention and management. Journal of Feline Medicine and Surgery, 22(8), 747–761.

Chang, H. W., Egberink, H. F., Halpin, R., Spiro, D. J., & Rottier, P. J. M. (2012). Spike protein fusion peptide and the pathogenesis of feline infectious peritonitis. Virology, 434(2), 295–303.

De Bonis, A., Donato, G., Guglielmini, C., and Boari, A. (2023). A retrospective comparative evaluation of selected blood cell ratios and their association with SAA, albumin, globulins, and A/G ratio in cats. Animals, 13(5), 612.

Dewerchin, H. L., and Cornelissen, E. (2021). Feline infectious peritonitis: insights into pathogenesis and diagnostic advances. Viruses, 13(6), 1138.

Felten, S., and Hartmann, K. (2019). Diagnosis of feline infectious peritonitis: a review of the literature. Journal of Feline Medicine and Surgery, 21(10), 1027–1038.

Kipar, A., and Meli, M. L. (2014). Feline infectious peritonitis: still an enigma? Journal of Feline Medicine and Surgery, 16(7), 529–541.

Moyadee, W., Sunpongsri, S., Choowongkomon, K., & Rattanasrisomporn, A. (2024). Feline infectious peritonitis: A comprehensive evaluation of clinical manifestations, laboratory diagnosis, and therapeutic approaches. J Adv Vet Anim Res, 11(1), 19–26.

Pedersen, N. C. (2019). A review of feline infectious peritonitis virus infection: Pathogenesis and immunity. Viruses, 11(9), 835.

Riemer, F., Kuehner, K. A., Ritz, S., Sauter-Louis, C., & Hartmann, K. (2016). Clinical and laboratory features of cats with feline infectious peritonitis – A retrospective study. BMC Veterinary Research, 12(1), 158.