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Evaluation of Available Diagnostic Techniques for Feline Infectious Peritonitis

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INTRODUCTION

In most cats, feline coronavirus (FCoV) is transmitted by fecal-oral contamination at an early age and causes subclinical disease or mild, transient enteritis. However, when the virus mutates within a susceptible host, the ability of the virus to replicate in macrophages can be enhanced. The mutated forms of FCoV develop in fewer than 5% of cats with FCoV, but this process causes a fatal disease — feline infectious peritonitis (FIP).[1] Mutated forms of FCoV that cause FIP are renamed feline infectious peritonitis virus (FIPV).

Clinically, two forms of FIP are recognized: the "wet" form and the "dry" form. Fever, inappetence, lethargy, and jaundice can be observed in cats with either form of FIP.[2] Animals with the wet form of the disease have ascites and/or pleural effusion. Evaluation of these fluids can aid in the diagnosis of FIP, but there is significant overlap in findings associated with FIP and those associated with other causes of effusion. In cats with the dry form of FIP, granulomas form in a variety of organs, making the dry form FIP even more difficult to diagnose.

There is no good way to prevent FCoV infection at this time. Exposure to FCoV does not lead to the production of protective antibodies against FCoV or FIPV. Therefore, vaccination against FCoV is ineffective. It is also believed that T-cell immunity directly contributes to clinical signs associated with FIPV. Cats with the wet form of FIP mount relatively poor, ineffective T-cell immune responses against FIPV. Whereas animals with the dry form of FIP seem to mount an enhanced T-cell immune response against the virus. This enhanced response prevents formation of effusions, but leads to a more chronic granulomatous response to infection.[3]

Very low numbers of FIPV particles are shed in the feces of cats with FIP. Therefore, FIPV is rarely (if ever) transmitted between cats. Although horizontal transmission is not a critical issue, the clinical signs of FIP become severe quickly which necessitates rapid and accurate diagnosis of the disease.

DIAGNOSTIC TESTING FOR FIP

Certain routine diagnostic test abnormalities can help support a clinical diagnosis of FIP.[2,4] These tests must be used in conjunction with more specific tests for FIP as well as with diagnostic tests to rule out appropriate differential diagnoses. The most consistent routine test abnormality is hyperglobulinemia which is observed in approximately 89% of cats with FIP. An albumin to globulin ratio <8.0 also occurs in approximately 85% of affected cats. An increased total protein concentration is present in as few as 18% of cats with FIP. Additionally, hyperbilirubinemia is detected in ≥50% of cats with FIP. Abnormalities in complete blood counts in cats with FIP include anemia, lymphopenia, and/or an inflammatory leukogram with or without band neutrophils.

The sensitivity and specificity of routine diagnostic test results for diagnosis of FIP are listed in Table 1. It is critical to remember that sensitivity and specificity results change with changes in cut-off values assigned to the test, number of healthy animals sampled, number of diseased animals sampled, and the overall composition of the population sampled. Therefore, these values can vary greatly between studies. Sensitivity and specificity are too low for any single routine diagnostic test to be definitive for the diagnosis of FIP.

Theoretically, tests designed to detect FIPV or antibodies to FIPV should be more sensitive and/or specific. Often, this is not the case, because the genes, antigens, and antibodies associated with FIPV are also present in cats with FCoV. Many diagnostic tests for FIPV have a low specificity due to large numbers of false-positive tests caused by a high prevalence of FCoV (up to 90% in some cat populations).[1]

Serum, effusions, and other body fluids (e.g., cerebrospinal fluid) can be evaluated for FCoV/FIPV antibody titers. Clinically available tests include indirect immunofluorescence assays (IFAs) and enzyme-linked immunosorbent assays (ELISAs). Sensitivity and specificity of these tests vary with the specific test used and the prevalence of FCoV in a population. The sensitivity of these tests ranges from 67 to 100%, and the specificity ranges from 57 to 100%. Most ELISAs are slightly less sensitive but are more specific than IFAs. A titer ≥1:1600 in an effusion supports a diagnosis of FIP. The absence of antibody in an effusion has a good negative predictive value.[1]

Reverse transcriptase polymerase chain reaction (RT-PCR) to detect specific mutations in the FIPV genome can be performed on serum, effusions, and other body fluids. However, test sensitivity as low as 42% has been reported, because the mutations amplified by the RT-PCR may not be present in the individual cat being tested. The specificity of this test is good (88 to 100%).[6]

Immunocytochemistry can be performed on effusions to detect FIPV antigen within cells. However, the sensitivity for this test is relatively low (as low as 57%), because false negative results are likely if the cellularity of the sample is low. Specificity ranges from 71 to 100% for this test.

Table 1. Sensitivity and Specificity of Diagnostic Test Findings for Feline Infectious Peritonitis (FIP)[2,4,5]

Diagnostic Test Findings	Sensitivity for FIP	Specificity for FIP
Serum Chemistry		
[Total protein] >8.0 g/dL	62%	60%
Albumin:globulin <0.8	80%	82%
[γ-globulin] >2.5 g/dL	70%	86%
Effusion Chemistry		
[Total protein] >3.5 g/dL	87%	60%
Albumin:globulin <0.9	86%	74%
[γ-globulin] >0.1 g/dL	82%	83%
Effusion Cytology		
[Total protein] >3.5 g/dL and 1,300-12,800 nucleated cells/μL (predominantly neutrophils)	90%	71%
Rivalta's Test		
Effusion clumps when added to dilute acetic acid solution	65-98%	63-80%

CONCLUSIONS

Although diagnostic tests for FIP lack the high sensitivity and specificity desired, judicious use of multiple tests can help support a diagnosis of FIP. It is important to note that histology is still the gold standard for FIP testing. Lesions with classic histologic evidence of FIP (granulomatous phlebitis) and concurrent detection of FCoV antigen within granulomas is considered definitive for the diagnosis of FIP.

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