UNCOVERING THE CAUSE OF FEVER IN CATS
Uncovering the Cause of Fever in Cats

Kenneth R. Harkin, DVM, DACVIM (Small Animal Internal Medicine)  
Kansas State University

The normal body temperature range in cats is 38.1°C to 39.2°C (100.5°F–102.5°F). Fever of unknown origin (FUO) in cats is classified as a temperature higher than 39.7°C (103.5°F) measured at least 4 times in a 2-week period without an identified cause.

**TERMINOLOGY**

The term **FUO** is often overused in veterinary medicine, as the number of patients in which a true case of fever cannot be uncovered is relatively small.

Veterinary patients are often described incorrectly as having FUO when routine diagnostic testing yields negative results. The term FUO should be reserved for patients in which no etiology is revealed after an extensive workup.

FUO is also applied incorrectly when used to describe a fever that does not respond to empiric antibiotics. A response to antibiotics does not prove a bacterial cause for fever because a transient response may be associated with an anti-inflammatory effect of the antibiotic or the waxing/waning course of disease.

It is important to remember that fever implies an internal resetting of the hypothalamic set point, whereas the elevated body temperature in **hyperthermia** results from outside causes.

**DIAGNOSTIC APPROACH**

In cats, the diagnostic approach to fever varies from that typically followed for dogs: In dogs, the approach tends to be orderly and algorithmic. In cats, diagnosis requires both categorical and algorithmic approaches.

For many cats that present with fever, a thorough physical examination often
reveals clues as to the etiology or, at least, to the organ system involved. For example:

• Purulent discharge or evidence of pain and bite marks can suggest a cat bite abscess.

• Lymphadenomegaly is not pathognomonic for any one disease, but it points to a specific diagnostic test (lymph node aspiration) that may provide the diagnosis.

• Icterus in a febrile cat should prompt a complete blood count (CBC) and blood smear evaluation (which may reveal the etiology, such as hemotropic mycoplasmosis or cytauxzoonosis) or serum biochemistry profile (which may help support a diagnosis of acute cholangiohepatitis).

• Dyspnea or dull or absent lung sounds on thoracic auscultation should lead to a consideration of pyothorax, which warrants further evaluation with thoracic radiography and thoracentesis.

• Renomegaly, hepatomegaly, or mesenteric lymphadenomegaly may prompt the need for abdominal imaging (radiographs or ultrasound) or fine-needle aspiration for cytologic evaluation.

In some cats, however, the cause cannot be identified even after an extensive medical investigation that includes a thorough history and physical examination, imaging, and culture of various body fluids when indicated.

LITERATURE REVIEW

Despite the notion that fever is a common clinical sign in cats, retrospective studies detailing the diagnostic workup in cats with FUO are lacking.

Identifying Cause

In their study of factors associated with toxic neutrophils in cats, Segev and colleagues found fever in 14% of patients (21/150). The authors named several diseases that would be expected to cause fever (but were not named specifically as the causes of fever in these patients), including pneumonia, feline immunodeficiency virus (FIV) infection, upper respiratory tract infection, bite wounds, peritonitis, pleural effusion, panleukopenia, and sepsis.

In their retrospective study of severe neutrophilia (40 × 10^9/L–76 × 10^9/L), Langenstein and colleagues found that only 2 of 24 cats had a fever (>39.3°C [102.7°F]), despite 21 of 28 cats having an inflammatory disease.

In most of the cats in these studies, diagnosis of the cause of fever would likely have been straightforward, with physical examination findings and/or results of routine testing (CBC, serum biochemistry profile, urinalysis, feline leukemia virus [FeLV] and FIV testing) guiding the diagnosis.
In a case series of 6 cats with renal abscess, only 3 cats were febrile, but renomegaly was a consistent finding, as was active sediment on urinalysis, further emphasizing the ability to localize findings based on physical examination and routine testing.3

Infectious Disease

Based on review of published case studies, retrospectives, case reports, and review articles (cited throughout this text) in which fever is listed as a finding on physical examination, infectious disease appears to be the most common cause of fever in cats (Box 1).

Bacterial Disease

Some of the published reports on bacterial infections describe a clinical presentation that does not follow what is generally expected for the organism.

• Dow and colleagues reported on 6 cats with salmonellosis. Four of the 6 cats were febrile, yet 2 had no signs referable to the gastrointestinal tract and a third had findings more consistent with acute kidney injury.4

• Giovannini and colleagues5 also reported on an outbreak of salmonellosis characterized by fever and anorexia without diarrhea in cats suspected of eating passerine birds (songbirds).

In some instances, the clinical signs of a generalized bacterial infection are caused by an unexpected organism.

• In a retrospective case study, persistent fever was a prominent feature in 2 Siamese cats ultimately diagnosed with disseminated Mycobacterium avium complex infection. Diagnosis was straightforward, with identification of the organisms in aspirates of the spleen and/or lymph nodes.6 Lymphadenomegaly was not pathognomonic for this infection, but provided the target for making the diagnosis.

• Fever can be seen with tuberculous or non-tuberculous mycobacterial infections in cats, and although organisms are commonly seen in aspirate or biopsy samples of affected organs or subcutaneous nodules (Figure 1), it is possible for the organisms to be lost during processing of histology samples.7

Fungal Disease

Histoplasmosis can present with relatively vague clinical signs. In one study, 34% of cats with histoplasmosis were reported to be febrile.8 Only half of the cats had recognized pulmonary involvement, and only 25% had peripheral lymphadenomegaly.

When pulmonary involvement and lymphadenomegaly are not present in a cat with histoplasmosis, the clinician may be faced with a febrile cat and no apparent diagnostic direction. In these patients, a liver, bone marrow, or splenic aspirate may be necessary to establish a diagnosis (Figures 2 and 3).

Box 1: Infectious Disease

- Salmonellosis
- Histoplasmosis
- Mycobacterium avium complex infection
- Tuberculous or non-tuberculous mycobacterial infections
- Fungal infections
FIGURE 1. Cytology of a lymph node aspirate demonstrating long, negative-staining bacilli within macrophages (arrows) from a cat with *Mycobacterium* species infection.

FIGURE 2. Cytology of a bone marrow aspirate from a cat with pancytopenia demonstrating multiple *Histoplasma capsulatum* organisms (arrows).

FIGURE 3. Cytology of a lymph node aspirate from a cat with histoplasmosis demonstrating large numbers of *H. capsulatum* organisms within macrophages (arrows).

FIGURE 4. Cytology of a lymph node aspirate from a cat with *Cytauxzoon felis* infection. The macrophages are laden with schizonts (short arrow) and the macrophage on the left is rupturing to release merozoites, which will infect more macrophages (long arrow).

FIGURE 5. *C. felis* piroplasms are seen on this blood smear from a cat (arrows).

FIGURE 6. Histology of a liver biopsy sample from a cat with toxoplasmosis demonstrating a hepatocyte containing numerous tachyzoites (arrow).
Protozoal & Parasitic Disease

Cytosporidiosis most commonly presents as a rapidly fatal febrile illness characterized by hemolytic anemia, lethargy, and icterus. In these patients, organisms are often found in red blood cells or tissue macrophages (Figure 4), but the organism is not always identified on a blood smear (Figure 5), resulting in lack of, or delayed, diagnosis.9

Toxoplasmosis (Figure 6), although typically an asymptomatic infection, can result in acute or chronic disease. Fever is common in both presentations, but with such an array of nonspecific clinical signs that diagnosis is often delayed.10 In a retrospective study of 100 cases of toxoplasmosis in cats in which the diagnosis was confirmed histologically over a 39-year period, fever was identified in 49 of 67 cats (73%) for which a rectal temperature was recorded.11

Viral Disease

Various viral diseases of cats can cause transient or persistent fever. Feline infectious peritonitis (FIP) was reported to result in fever in 120 of 215 cats (55.8%) in a recent retrospective study, with 43 of the cats presenting with a fever in excess of 40°C (104°F).12

In that study, 89% of cats with FIP had elevated globulins, although the degree of hyperglobulinemia may have been relatively subtle in some (median, 51.78 g/L; upper reference interval, 50 g/L). FIP was significantly more common in cats younger than 2 years.12

In the initial stage of infection, FIV may present with fever that persists for a few weeks before resolving, regardless of therapy.13 FeLV infections are associated with fever when the cat acquires a secondary infection or as a component of a paraneoplastic syndrome; however, fever is not typically caused by the primary viral infection itself.13

Although fever is a common component of the respiratory syndrome caused by herpesvirus and calicivirus infections, chronic persistent fever does not occur in the absence of upper respiratory disease and diagnosis is typically obtained with minimal testing.14,15

Borna disease virus, although rare, is reported to be present with fever in some cats, in addition to gait disturbances and behavioral changes.16 Avian influenza virus (H5N1) infection in cats reportedly produces fever, severe respiratory signs, and neurologic signs (convulsions and ataxia), but it is also rare.17

Zoonotic Disease

Bartonellosis is recognized as a zoonotic disease in which the cat plays an important role. Experimental inoculation in cats, whether by blood transfusion or flea inoculation, has been shown to result in transient febrile illness, but it remains unclear what role chronic infection with Bartonella henselae or other Bartonella species would play in recurrent or persistent fever in cats.18
DIFFERENTIAL DIAGNOSIS: CATEGORICAL APPROACH

The categorical approach to fever in cats involves stratifying the risks for various diseases based on a number of parameters. The emphasis is on differentials for fever when the diagnosis is not immediately obvious (eg, the kitten with a severe upper respiratory tract infection caused by herpesvirus or calicivirus).

Important factors used to determine the relative risk for various diseases include (Box 2):

- Age, environment, travel history, and retrovirus status
- Whether cat lives exclusively indoors or is allowed outside
- If the cat goes outdoors, the extent of its roaming behavior (because the risk for certain infectious diseases increases dramatically in the roaming, active hunter)
- Number of cats in the household
- In multicat households, status of the colony (eg, number of cats, hierarchy of the colony, retroviral status, recent additions); for example, FIP would be high on the differential list for a 9-month-old kitten with persistent fever (>2 weeks) that lives in a multicat household, but would be considered unlikely in a 12-year-old cat that has been living with 4 other cats of roughly the same age for its entire life.

While this approach can include many different categories of cats, the following discussion focuses on the most common: young and older indoor cats in single-cat and multicat households and outdoor cats of all ages.

Category 1: Young Cat, Lives Indoors, No Other Pets

Given that infection is the most common cause of fever in cats, cats in this category are infrequently evaluated for disease that results in fever. Foreign body ingestion is more common in young, curious cats. Foreign bodies (eg, needles) that penetrate the oral cavity can result in secondary abscessation or cellulitis with resultant fever. While vomiting and inappetance—rather than fever—are the most common signs seen with a gastrointestinal foreign body, peritonitis can develop subsequent to perforation. The clinician should perform a careful inspection of the oral cavity, especially if the client reports that the cat is pawing at the mouth, drooling, or showing other signs of oral discomfort, and palpate the abdomen and intestinal tract if vomiting is present.

FeLV and FIV testing should be performed if the status of the cat is unknown.

FIP must be considered high on the list of differentials as a cause of persistent fever in cats younger than 1 year of age. Index of suspicion for FIP is even greater if hyperbilirubinemia and/or hyperglobulinemia is noted on a serum biochemistry profile. In cats that do not have an effusion, the diagnosis can be impossible to confirm except through biopsy (eg, liver).

Although it is beyond the scope of this article to discuss pros and cons of serologic testing for FIP, I prefer confirmation using polymerase chain reaction (PCR) assay for coronavirus.
on an effusion or histologic confirmation. Still, in most cases of FIP, the clinician should be able to collect enough supporting evidence for a presumptive diagnosis of FIP with a high level of confidence.

**Histoplasmosis** has been documented in cats housed exclusively indoors and should also be a consideration, but this diagnosis does not typically come to mind in the absence of respiratory signs with associated radiographic changes, ocular abnormalities, or lymphadenomegaly.

In some cats, the disease may be localized primarily to the bone marrow with some degree of bicytopenia or pancytopenia evident on CBC; in others, the organism may be found in aspirates of the spleen or liver, even in the absence of elevated liver enzymes. The clinician should consider including a urine antigen test (or urine and blood) for the detection of histoplasmosis in cats with vague clinical signs and persistent fever.

**Surgical site infection** should be investigated as a possible cause of fever if the cat has had prior surgery (eg, ovariohysterectomy), especially recently.

Other infectious causes are rare in this category, and immune-mediated disease is an uncommon cause of fever in cats.

**Category 2: Young Cat, Lives Indoors, Multicat Household**

All of the diseases listed in the previous category should also be considered in young, indoor cats living in multicat households (**Table 1**).

**FeLV and FIV** testing is one of the first steps in the diagnostic workup.

**FIP** should receive more consideration in this category, given the ubiquitous nature of feline enteric coronavirus. Even something as simple as evaluating packed cell volume (PCV) and total solids (TS) using a microhematocrit tube and refractometer may provide a rapid screen to include FIP on the differential list, if the TS count is elevated.

In a multicat household where flea infestation is problematic, rapid screening of PCV and TS also provides information as to the possibility of infection by hemotropic mycoplasmal organisms (anemia and icteric serum). Of course, in both scenarios, additional testing is necessary to confirm the diagnosis or arrive at an alternate diagnosis.

**Bartonellosis** is more likely in cats with flea infestation. Although serologic testing is of questionable value in understanding the relative risk of clinical bartonellosis, the clinician should consider some level of testing (PCR on blood, fluids, or tissue, with or without serologic testing) if:

- A diagnosis is elusive
- Multiple cats have a febrile illness
- Pyogranulomatous disease is found on histology
Cat bite abscesses or cellulitis may result from intercat aggression, which depends on the stability of the relationships among the cats in the household (or in spite of it), and the clinician should evaluate the cat for evidence of these causes of fever.

Pyothorax may also result from intercat aggression. In one study, pyothorax was reportedly more common in cats from multicat households, with an almost fourfold increased risk compared with cats in single-cat households. The mean age of cats diagnosed with pyothorax was 3.8 years, and there was no difference in prevalence between indoor and outdoor cats.

Diagnosis of pyothorax may be elusive if the volume of effusion is insufficient to result in significant respiratory compromise or abnormalities on thoracic auscultation. Considering that both histoplasmosis and pyothorax may present with vague and subtle signs early in the course of disease and that contents of the thorax cannot be palpated (in contrast to the abdomen), thoracic radiographs should be considered in the workup of a cat with FUO even in the absence of obvious respiratory signs.

**Category 3: Older Cat, Lives Indoors, Multicat or Single-Cat Household**

Most older cats have been exposed to common viral pathogens, mounted a normal immune response to eliminate them, and have limited or no susceptibility.

FeLV, FIV, and FIP are lesser considerations than in young cats, although testing for FeLV and FIV is always recommended in any sick cat if the retrovirus status is not known or in doubt.

Cat bite wounds may be a problem in the multicat household. A thorough evaluation, including CBC, serum biochemistry profile, and urinalysis, is indicated in these cats when the diagnosis is not immediately evident.

Pyelonephritis may be present in a cat with an obstructed ureter and a history of recurrent calcium oxalate urolithiasis, which is an example of how history may also help in the evaluation of potential differentials.

Acute cholangiohepatitis, pancreatitis (acute, acute on chronic, chronic smoldering), histoplasmosis, cancer unassociated with retroviral infection and, to a much lesser degree, immune-mediated disease are additional differentials to consider in this category of cats.

Fever was identified in 4 of 33 cats with pancreatitis (mean age, 12.7 years) in a study by Stockhaus and colleagues. Given the often vague clinical signs associated with pancreatitis (hyporexia or anorexia is the most frequent complaint and, sometimes, the only historical clinical finding), the veterinarian may need to consider additional diagnostics, such as measurement of feline
pancreatic lipase immunoreactivity or abdominal ultrasound, to confirm the diagnosis.\textsuperscript{20}

**Category 4: Cat of Any Age, Free to Roam Outdoors**

Cats that have free access to the outdoors are at highest risk for exposure to diseases associated with the predator–prey cycle, including vector-borne diseases. These cats may be more aggressively territorial and self-defensive and, thus, more prone to fighting with other cats.

**Cat bite abscess, tularemia, cytauxzoonosis, and salmonellosis** (a distant fourth) are, in my experience, the most common conditions in cats with a fever in excess of 40\(\degree\)C (104\(\degree\)F) and usually over 40.5\(\degree\)C (105\(\degree\)F).

Careful physical examination to look for cat-bite abscess, wounds, or cellulitis is the first step when evaluating cats in this category.

Although tularemia is most commonly reported in some midwestern states (ie, South Dakota, Kansas, Missouri, Oklahoma, Arkansas), the bacteria have been recognized throughout North America. Cats typically are infected through ingestion of infected rabbits, although tick-transmitted tularemia can occur.\textsuperscript{21}

Tularemia is typically confirmed by serologic evidence of seroconversion, although the organism can be seen on cytology from aspiration of regional lymphadenomegaly in the case of tick transmission. Tularemia is a zoonotic disease, and precautions should be taken when handling a cat if infection with this organism is suspected. However, I am unaware of any reports of zoonotic transmission resulting from performing fine-needle aspiration.

A blood smear is helpful to identify *Cytauxzoon felis* organisms in the red blood cells but is not always rewarding. If the cat is anemic, a blood smear can help identify hemotropic mycoplasma organisms, if present.

A fecal and/or blood culture can be performed to confirm a diagnosis of salmonellosis if ingestion of passerine birds is suspected.

**Toxoplasmosis** should also be considered as a differential for cats because of their predation.

Cats with multiorgan disease (any combination of pulmonary, hepatic, nervous system, and gastrointestinal signs), especially when combined with a persistent or relapsing fever, should be evaluated for toxoplasmosis. Serologic testing should document a high IgM (reciprocal titer &gt;64) or a fourfold rise in IgG over 2 to 3 weeks.\textsuperscript{10}

**IN SUMMARY**

The diagnosis of fever in cats often involves investigation directed toward an infectious etiology. For cats housed indoors, the diagnostic differential list is fairly limited and, for many young cats, a diagnosis of FIP is often made. The veterinarian should consider all risk factors for individual cats (indoor, outdoor, multicat household, predator, time of year) when deciding which diagnostics to pursue. Categorizing cats based on these risk factors should help the veterinarian narrow the focus, optimize testing, and achieve a diagnosis.

**REFERENCES**


**Glossary**

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<td>CBC</td>
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<td>FeLV</td>
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<td>FIP</td>
<td>feline infectious peritonitis</td>
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<td>FIV</td>
<td>feline immunodeficiency virus</td>
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<td>FUO</td>
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<td>PCR</td>
<td>polymerase chain reaction</td>
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<td>PCV</td>
<td>packed cell volume</td>
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