Epidemiology of feline infectious peritonitis among cats examined at veterinary medical teaching hospitals

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Objective—To determine proportions of cats in which feline infectious peritonitis (FIP) was diagnosed on an annual, monthly, and regional basis and identify unique characteristics of cats with FIP.

Design—Case-control study.

Sample Population—Records of all feline accessions to veterinary medical teaching hospitals (VMTH) recorded in the Veterinary Medical Data Base between January 1986 and December 1995 and of all feline accessions for necropsy or histologic examination at 4 veterinary diagnostic laboratories.

Procedure—Proportions of total and new feline accessions for which a diagnosis of FIP was recorded were calculated. To identify characteristics of cats with FIP, cats with FIP were compared with the next cat examined at the same institution (control cats).

Results—Approximately 1 of every 200 new feline and 1 of every 300 total feline accessions at VMTH in North America and approximately 1 of every 100 accessions at the diagnostic laboratories represented cats with FIP. Cats with FIP were significantly more likely to be young, purebred, and sexually intact males and significantly less likely to be spayed females and discharged alive than were control cats. The proportion of new accessions for which a diagnosis of FIP was recorded did not vary significantly among years, months, or regions of the country.

Conclusions and Clinical Relevance—Results indicated that FIP continues to be a clinically important disease in North America and that sexually intact male cats may be at increased risk, and spayed females at reduced risk, for FIP. The high prevalence of FIP and lack of effective treatment emphasizes the importance of preventive programs, especially in catteries. (*J Am Vet Med Assoc* 2001;218:1111–1115)

Evidence suggests that **feline infectious peritonitis virus (FIPV)** is the result of a mutation of **feline enteric coronavirus (FECV)**.[1] The 2 viruses are antigenically and morphologically similar and indistinguishable by current test procedures. Feline infectious peritonitis virus and FECV are grouped together as **feline coronavirus (FCoV)**.

Indirect immunofluorescent assays (IFA) and ELISA are commonly used to detect antibodies to FCoV in cats. Most cats residing in households where FECV is present develop antibodies to FCoV, regardless of whether they eventually develop **feline infectious peritonitis (FIP)**. Serologic surveys indicate that approximately 25% of domestic (nonpurebred) cats in pet households and 75 to 100% of purebred cats in catteries have antibodies to FCoV.[2] In a study of 73 households, 22 of 282 (7.8%) kittens seropositive for FCoV developed FIP.[3] Presently, there is no effective treatment for FIP,[4] and the mortality rate for cats with clinical disease is greater than 95%.[5]

The unique characteristics of the effusive fluid facilitate diagnosis of the "wet" form of FIP; however, antemortem diagnosis of the noneffusive, or "dry," form is a challenge, and histologic examination of biopsy specimens is needed to confirm the diagnosis.[6,7] The ratio of effusive to noneffusive cases is reported to be approximately 3:1; however, this may be misleading, because a greater proportion of noneffusive cases may go undetected.[8]

Knowing the prevalence and patterns of prevalence of FIP may allow veterinary clinicians to adjust their index of suspicion, thereby increasing recognition of cats with FIP. The purposes of the study reported here were to estimate prevalence of FIP in cats, identify unique characteristics of cats with FIP, and determine proportions of cats in which FIP was diagnosed on an annual, seasonal, and geographic basis.

Materials and Methods

Case and control selection—Data for all feline accessions recorded in the **Veterinary Medical Data Base (VMDB)** between Jan 1, 1986 and Dec 31, 1995 were obtained from the processing center at Purdue University. Information obtained for each accession included patient identification, institution, age, weight, sex, breed, diagnoses (up to 10), diagnostic procedures (including histologic and gross pathologic examinations), consultations, anesthetic procedures, date of discharge, duration of hospitalization, discharge status, and zip code. Data were also obtained from 4 diagnostic laboratories[a] on all feline accessions for necropsy or histologic examination (including histologic examination of biopsy specimens) from 1995 through 1998.

Calculation of proportions of cats with FIP—Twenty-four North American **Veterinary Medical Teaching Hospitals (VMTH)** have contributed information to the VMDB for various periods since the database was established in 1964. Annual, seasonal, and regional proportions of cats in which

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FIP was diagnosed were determined, using data from the 11 VMTH that contributed information to the VMDB for each of the 10 years of the study period. Proportion of cats in which FIP was diagnosed was calculated for all accessions by dividing the number of feline accessions for which a diagnosis of FIP was recorded[b] by the total number of feline accessions during the same period. Proportion of cats in which FIP was diagnosed was calculated for new accessions by dividing the number of cats for which FIP was a new diagnosis by the number of individual cats examined during the same period; for this calculation, each cat was counted only once during the specified period.

The frequency of various diagnostic procedures and characteristics of cats with FIP were determined, using data from all 24 VMTH that contributed information to the VMDB any time during the 10-year study period. To identify unique characteristics of cats with FIP, cats with FIP were compared with the next cat examined at the same institution (control cats).

Data analysis—A categorical data analysis model was used to evaluate differences in age, sex, breed, and discharge status between cats with FIP and control cats. **Odds ratios (OR)** were calculated, and **confidence intervals (CI)** were adjusted according to the method of Bonferroni. A second categorical model was used to evaluate the effects of the independent variables region, year, and month and of their 2-way interactions on the proportion of cats in which FIP was diagnosed. The Mantel extension for analysis of trends in proportions was used to analyze seasonal changes in proportions of cats in which FIP was diagnosed during the 10-year study period.[9] Proportions of cats in which FIP was diagnosed by the 4 diagnostic laboratories were compared among years, using a mixed-model procedure. Year was the independent variable, and laboratory was included as a random factor in the model. The Pearson product-moment method was used to determine whether the proportion of cats in which FIP was diagnosed by the **Michigan State University (MSU)** VMTH correlated with the proportion in which FIP was diagnosed by the MSU Animal Health Diagnostic Laboratory. Statistical analyses were performed with commercially available software.[c,d] Values of $P \leq 0.05$ were considered significant.

Results

Information on 397,182 feline accessions was entered in the VMDB during the 10-year study period, and a diagnosis of FIP was recorded for 1,420 (0.36%). There were 226,720 new feline accessions, with a diagnosis of FIP recorded for 1,250 (0.55%).

The 11 VMTH that contributed data each year during the 10-year study period accounted for 242,467 feline accessions, with a diagnosis of FIP recorded for 797 (0.33%). These 11 VMTH accounted for 61% (242,467/397,182) of the feline accessions during the study period. For these 11 VMTH, there were 137,326 new accessions, with a diagnosis of FIP recorded for 707 (0.51%). The proportion of new accessions for which a diagnosis of FIP was recorded ranged from a low of 0.37% in 1995 to a high of 0.60% in 1986 and 1989. The ratio of the number of cats for which FIP was a new diagnosis (701) to number of cats for which FeLV was a new diagnosis (2,330) during the 10-year study period was 1:3.3.

Data from all 24 VMTH that contributed information to the VMBD were used to determine characteristics of cats with FIP. Information was available for 1,237 cats for which FIP was a new diagnosis and for 1,226 control cats (ie, the next cat examined after a cat with FIP at each institution). Cats with FIP were significantly more likely to be younger (**Fig 1**), purebred, and sexually intact male and significantly less likely to be spayed female and discharged alive than were control cats (**Table 1**). Cats with FIP also weighed significantly less than control cats.

The diagnosis of FIP was made on the basis of results of clinical examination alone in only 146 of the 1,237 (12%) cats for which FIP was a new diagnosis, and in most cats a variety of diagnostic procedures was performed (**Table 2**). Six hundred fifty-one of the

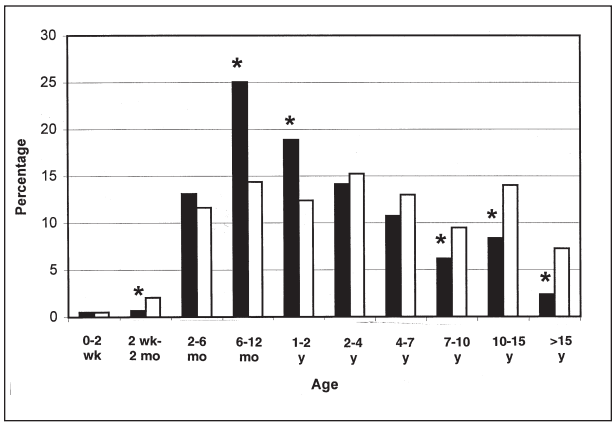

Figure 1—Age distribution of 1,182 cats with feline infectious peritonitis (FIP; solid bars) and 1,160 control cats without FIP (open bars) examined at veterinary medical teaching hospitals (VMTH) in North America during a 10-year period. *Significantly ($P < 0.05$) different from percentage for control cats.

Table 1—Characteristics of 1,237 cats examined at veterinary medical teaching hospitals (VMTH) in North America in which feline infectious peritonitis (FIP) was diagnosed and of 1,226 control cats* without FIP

Characteristic	No. of cats (%)		Odds ratio	Confidence interval†
	Cats with FIP	Control cats		
Sex				
Sexually intact male	329 (27)	186 (16)	2.0	1.6–2.6
Sexually intact female	266 (22)	216 (18)	1.3	1.0–1.7
Spayed female	215 (18)	381 (32)	0.5	0.4–0.6
Castrated male	401 (33)	417 (35)	0.9	0.7–1.2
Purebred	403 (33)	190 (16)	2.6	2.2–3.2
Alive at discharge	586 (53)	1,137 (86)	0.07	0.05–0.10

*Control cats were the next cat examined at each veterinary medical teaching hospital after a cat with FIP was examined. †Confidence intervals were adjusted for multiple comparisons by use of the Bonferroni method.

Table 2—Diagnostic procedures performed on 1,237 cats with FIP examined at VMTH in North America

Procedure	No. of cats	Percentage
Clinical examination only	146	12
Gross necropsy	525*	42
Histologic examination	422*	34
Serologic testing	349	28
Microbial culture	210	17
Radiography	424	34
Electrocardiography	69	6
Hematologic testing	626	51
Urinalysis	343	28
Serum biochemical testing	554	45
Testing for parasites	81	7
Other or not specified	592	48

*No. includes 26 gross necropsies and 64 histologic examinations that were done subsequent to the initial visit.

1,237 cats for which FIP was a new diagnosis and 89 of the 1,226 control cats died or were euthanatized. Gross necropsy, histologic examination of tissues, or both was performed on 519 (80%) of the cats with FIP that died or were euthanatized and on 45 (51%) of the control cats (**Table 3**). The odds that a cat with FIP that died or was euthanatized would undergo necropsy or histologic examination of tissues were significantly higher than the odds that a control cat would (OR, 3.8; 95% CI, 2.4 to 6.2).

The proportion of new accessions for which a diagnosis of FIP was recorded did not vary significantly among years when values were adjusted for season and region (**Fig 2**). Although there appeared to be a steady decline in the proportion of new accessions for which a diagnosis of FIP was recorded from 1992 through 1995, mean proportion for this 4-year period (259/52,527; 0.49%) was not significantly ($P > 0.4$) different from that for the previous 4-year period (306/57,898; 0.53%).

The monthly proportion of new accessions for which a diagnosis of FIP was recorded ranged from a low of 0.31% in July to a high of 0.51% in February and April (**Fig 3**). We did not detect any significant difference in proportions among months; however, there was a significant ($P < 0.001$) linear trend in the monthly proportion of new accession for which a diagnosis of FIP was recorded from June through April.

The 11 VMTH that contributed information to the VMDB each year of the 10-year study period were assigned to regions on the basis of the Centers for Disease Control and Prevention classification of states. Regions consisted of the east-north central (Michigan, Purdue, Illinois, Wisconsin), east-south central (Tennessee), mountain (Colorado), south Atlantic (Georgia, Florida), west-north central (Missouri, Iowa), and west-south central (Texas). The proportions of new accessions for which a diagnosis of FIP was recorded did not vary significantly with region. However, there was a significant ($P = 0.001$) interaction between region and year, indicating an inconsistent pattern among regions across years. The proportions of new accessions over the 10-year period for which a diagnosis of FIP was recorded were 0.43% for the east-north central region, 0.48% for the east-south central region, 0.58% for the mountain region, 0.60% for the south Atlantic region, 0.50% for the west-north central region, and 0.64% for the west-south central

Table 3—Frequency of gross and histologic examinations performed on cats (651 at first diagnosis of FIP and 89 control cats) that died or were euthanatized during a 10-year period at VMTH in North America

Procedure	No. of cats (%)		Odds ratio	Confidence interval*
	Cats with FIP	Control cats		
Gross necropsy alone	161 (25)	17 (19)	1.4	0.7–2.8
Histologic examination alone	20 (3)	4 (5)	0.7	0.2–2.7
Gross necropsy and histologic examination	338 (52)	24 (27)	2.9	1.6–5.5
Neither	132 (20)	44 (49)	0.3	0.1–0.5

*Adjusted for multiple comparisons by use of the Bonferroni method; $\alpha = 0.0125$.

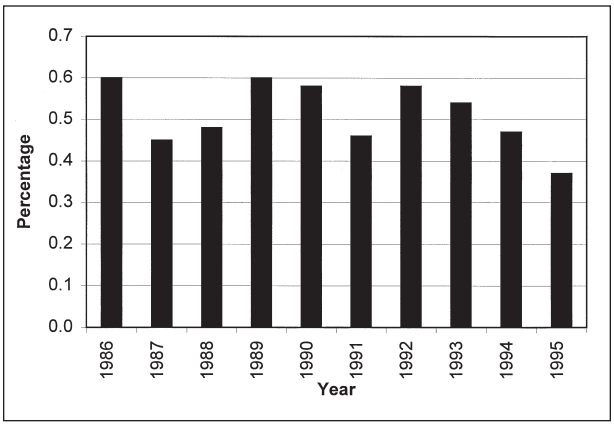

Figure 2—Annual proportions of new feline accessions at VMTH in North America for which a diagnosis of FIP was recorded.

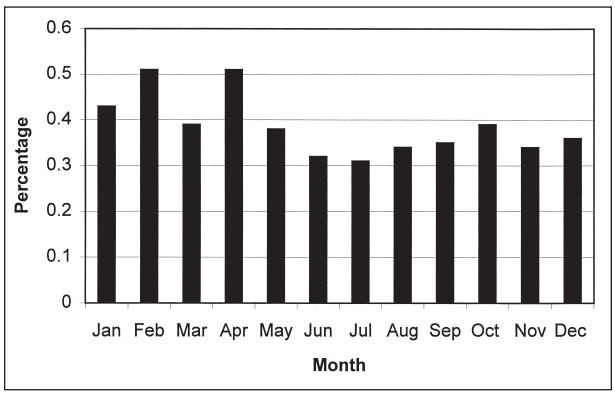

Figure 3—Monthly proportions of new feline accessions at VMTH in North America during a 10-year period for which a diagnosis of FIP was recorded.

Table 4—Proportions of feline accessions for 4 veterinary diagnostic laboratories for which a diagnosis of FIP was assigned

Laboratory*	No. with FIP/No. of accessions (%)				
	1995	1996	1997	1998	Total
Cornell	18/929 (1.94)	13/902 (1.44)	8/820 (0.98)	12/724 (1.66)	51/3,375 (1.51)
Georgia	NA	6/487 (1.23)	22/1,168 (1.88)	9/666 (1.35)	37/2,321(1.59)
Michigan	12/1,738 (0.69)	19/1,946 (0.98)	12/2,028 (0.59)	14/984 (1.42)	57/6,696 (0.85)
Tennessee	NA	15/771 (1.95)	7/933 (0.75)	21/978 (2.56)	43/2,683 (1.60)

*Diagnostic Laboratory, Cornell University, Ithaca, NY; Veterinary Diagnostic and Investigational Laboratory, University of Georgia, Tifton, Ga; Animal Health Diagnostic Laboratory, Michigan State University, East Lansing, Mich; and C. E. Kord Animal Disease Diagnostic Laboratory, Tennessee Department of Agriculture, Nashville, Tenn.
NA = Not available.

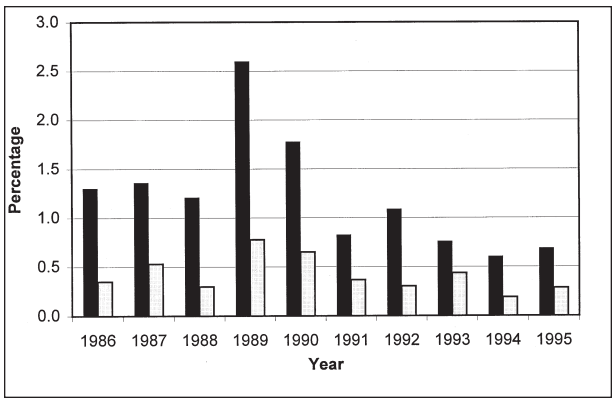

Figure 4—Proportions of cats in which FIP was diagnosed by the Michigan State University Animal Health Diagnostic Laboratory (solid bars) and by the Michigan State University VMTH (open bars).

region. Within regions, monthly and annual proportions of new accessions for which a diagnosis FIP was recorded varied greatly, with no observable patterns.

For the 4 diagnostic laboratories, yearly proportions of feline accessions for which a diagnosis of FIP was recorded ranged from a low of 0.59% (Animal Health Diagnostic Laboratory, 1997) to a high of 2.56% (C. E. Kord Diagnostic Laboratory, 1998; **Table 4**). For all 4 laboratories and all 4 years, the proportion was 1.25% (188/15,075; 95% CI, 1.07 to 1.42%).

The proportion of cats in which FIP was diagnosed by the MSU VMTH between 1986 and 1995 was significantly ($r = 0.79$; $P < 0.007$) correlated with the proportion in which FIP was diagnosed by the MSU Animal Health Diagnostic Laboratory. However, the correlation was inconsistent during some years (**Fig 4**).

Discussion

Results of the present study suggest that approximately 1 of every 200 new feline accessions and 1 of every 300 total feline accessions at VMTH in North America represent cats with FIP. Cats with FIP were younger and significantly more likely to be sexually intact male and purebred, and less likely to be spayed female, than were cats in the general hospital population that did not have FIP. There was a gradual increase in the proportion of cats for which a diagnosis of FIP was recorded from June through April. Although we did not detect any significant differences in proportions of cats with FIP among regions, seasons, or years, there was a great deal of variability from region to region across years. The proportion of feline accessions for which a diagnosis of FIP was recorded was higher for the diagnostic laboratories than for the VMTH and was approximately 1 of every 100 accessions.

Exposure to FCoV is required for development of FIP, and the high potential for exposure of cats to FCoV is, in part, responsible for the high proportion of cats with FIP. The seroprevalence of antibodies to FCoV is estimated to be 25% for single-cat households and 75 to 90% for multiple-cat households.[2] One study[10] reported that 41% of fecal samples from cats in multiple-cat households contained infectious amounts of coronavirus. Another study[3] reported that 22 of 282 (7.8%) kittens seropositive for FCoV in 73 households developed FIP. An FIP mortality rate of 1:5,000 was reported for cats in pet households with 1 or 2 older cats, and a mortality rate of 5% was common in densely housed groups of cats.[3,11,12] Feline infectious peritonitis is thought to be the leading cause of death among cats in purebred catteries, shelters, and other large multiple-cat households.[13]

The accuracy of the diagnosis of FIP for records submitted to the VMDB was supported by the fact that 80% of cats that died or were euthanatized were submitted for necropsy, histologic examination, or both and that a diagnosis of FIP was made on the basis of results of clinical examination alone in only 12% of cats. Cats with clinical signs of FIP, lymphopenia ($< 1.5 \times 10^3$ lymphocytes/μl), a FCoV antibody titer > 1:160, and hyperglobulinemia (> 5.1 g/dl) have an 89% probability of having FIP confirmed at necropsy.[14] On the other hand, cats without antibodies to FCoV are rarely found to have FIP at necropsy (negative predictive value, 96.6%).[14]

Recording and transposing data from clinical records to the VMDB can result in errors, but we would expect the error rate to be < 5%. In addition, the diagnosis may have been erroneous for cats in which the diagnosis was made on the basis of results of clinical examination alone because of the difficulty of diagnosing the dry form of FIP. However, we do not believe that these sources of error had a meaningful effect on this study's results.

In the present study, the proportion of cats with FIP that were between 6 months and 2 years old was significantly higher than the proportion of control cats that were in this age group, and the proportion of cats with FIP that were > 7 years old was significantly lower than the proportion of control cats that were. A previous study[15] reported that cats between 6 and 12 months old have the highest incidence of FIP and that FIP is fairly common up to 5 years of age. In that study, there was a decrease in incidence among middle-aged cats and an increase in cats > 13 years old that was thought to be attributable to a decrease in cell-mediated immunity. In the present study, except for a slight nonsignificant increase in the proportion of cats with FIP that were 10 to 15 years old, the proportion of cats with FIP in each age group declined steadily, casting doubt on the importance of an age-mediated decrease in cell-mediated immunity as a risk factor for FIP.

Compared with control cats, cats with FIP in the present study had higher odds of being sexually intact male and lower odds of being spayed female, even after adjustment for age and breed in the multivariate model. To our knowledge, previous studies have not examined the effect of neutering status on risk of FIP. This effect likely represented a difference in behavioral patterns of spayed female versus sexually intact male cats.

Cats with FIP were significantly more likely to be purebred than were control cats (OR, 2.6). To our knowledge, no breed of domestic cats has been shown to have a predisposition for FIP; however, the genetically monomorphic cheetah is highly susceptible.[16,17] It is possible, therefore, that enhanced susceptibility or resistance to FIP is present in some highly inbred pop-

ulations of domestic cats. On the other hand, purebred cats are more likely to be housed in catteries containing large numbers of cats in close confinement, which may also predispose cats to FIP. Thus, it is difficult to separate genetic from nongenetic influences. Analysis of mode of inheritance suggests that susceptibility to FIP is best modeled as a polygenic trait.[16] Heritability of susceptibility to FIP was high in 1 study[16] and was reported to be > 54% for 4 Persian catteries and 52% for a Birman cattery.

The percentage of cats with FIP that were discharged alive (53%) was significantly lower than the percentage of control cats that were (86%). To our knowledge, a comparison of outcomes of cats with FIP versus control cats has not been reported previously. The low percentage of cats with FIP that were discharged alive likely reflected the limited treatment options and invariably fatal outcome for cats with FIP.[5]

In the present study, the annual proportion of new feline accessions for which a diagnosis of FIP was recorded appeared to rise and fall in 4- to 5-year cycles. Many diseases of wild animals in nature tend to follow long-term cycles; however, housed cats are exposed to a completely different set of environmental factors, and the limited 10-year period of the present study was insufficient to identify any long-term cycle. The monthly proportion of new feline accessions for which a diagnosis of FIP was recorded also varied considerably. Although significant differences in monthly proportions were not found, a gradual increase in proportion from June through April was identified, with the highest proportion of new feline accessions with FIP identified during January through April (winter). This may be attributable to the increased amount of time cats spend indoors during the winter months or the stress of cold temperatures, or it may simply be a reflection of the fact that most cats born during the summer would be between 6 and 12 months old during these months.

Overall, proportions of new feline accessions for which a diagnosis of FIP was recorded did not vary significantly with region of the country. The variability from region to region may have been a result of the small number of VMTH representing some regions and the fact that some VMTH see only referral patients, whereas others accept a mix of referral and regular patients.

The proportion of new feline accessions for which a diagnosis of FIP was recorded was higher for the diagnostic laboratories than for the VMTH. This could result from the increased likelihood that cats with a clinical diagnosis of FIP would be euthanatized or die while hospitalized and the fact that a definitive diagnosis of FIP requires a necropsy or histologic examination of tissues.

The proportion of cats examined that are sick is likely higher for VMTH than for general veterinary medical practices, because VMTH see a large number of referred cases. A diagnosis of FIP can be made in cats with the effusive form of disease based solely on results of physical examination and fluid evaluation. Because of the poor prognosis and limited options for long-term therapeutic success, cats with the effusive form of FIP are probably less likely to be referred to a VMTH for further evaluation. On the other hand, diagnosis is more difficult in cats with the dry form of FIP, which represent approximately 1 of 4 cats with FIP, and such cats are likely to be referred for further diagnostic testing. Therefore, the prevalence of FIP among sick cats examined at private veterinary practices may be similar to or greater than that among cats examined at VMTH.

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[a]Diagnostic Laboratory, Cornell University, Ithaca, NY; Veterinary Diagnostic and Investigational Laboratory, University of Georgia, Tifton, Ga; Animal Health Diagnostic Laboratory, Michigan State University, East Lansing, Mich; and CE Kord Animal Disease Diagnostic Laboratory, Tennessee Department of Agriculture, Nashville, Tenn.

[b]Veterinary Medical Data Base code 06001Y000.

[c]SAS, version 7, SAS Institute Inc, Cary, NC.

[d]EpiInfo, version 6.01, USD Inc, Stone Mountain, Ga.

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