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Comparison of Peritoneal Fluid and Peripheral Blood pH, Bicarbonate, Glucose, and Lactate Concentration as a Diagnostic Tool for Septic Peritonitis in Dogs and Cats

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Objective—To establish a reliable diagnostic tool for septic peritonitis in dogs and cats using pH, bicarbonate, lactate, and glucose concentrations in peritoneal fluid and venous blood.
Study Design—Prospective clinical study.
Animals—Eighteen dogs and 12 cats with peritoneal effusion.
Methods—pH, bicarbonate, electrolyte, lactate, and glucose concentrations were measured on 1- to 2-mL samples of venous blood and peritoneal fluid collected at admission. The concentration difference between blood and peritoneal fluid for pH, bicarbonate, glucose, and lactate concentrations were calculated by subtracting the peritoneal fluid concentration from the blood concentration. Peritoneal fluid was submitted for cytologic examination and bacterial culture. Peritonitis was classified as septic or nonseptic based on cytology and bacterial culture results.
Results—In dogs, with septic effusion, peritoneal fluid glucose concentration was always lower than the blood glucose concentration. A blood-to-fluid glucose (BFG) difference $>$ 20 mg/dL was 100% sensitive and 100% specific for the diagnosis of septic peritoneal effusion in dogs. In 7 dogs in which it was evaluated, a blood-to-fluid lactate (BFL) difference $<$ −2.0 mmol/L was also 100% sensitive and specific for a diagnosis of septic peritoneal effusion. In cats, the BFG difference was 86% sensitive and 100% specific for a diagnosis of septic peritonitis. In dogs and cats, the BFG difference was more accurate for a diagnosis of septic peritonitis than peritoneal fluid glucose concentration alone.
Conclusions—A concentration difference $>$ 20 mg/dL between blood and peritoneal fluid glucose concentration provides a rapid and reliable means to differentiate a septic peritoneal effusion from a nonseptic peritoneal effusion in dogs and cats.
Clinical Relevance—The difference between blood and peritoneal fluid glucose concentrations should be used as a more reliable diagnostic indicator of septic peritoneal effusion than peritoneal fluid glucose concentration alone.

SEPTIC PERITONITIS is a common life threatening condition with a mortality rate as high as 68% in dogs.[1] A rapid and accurate diagnosis is essential to initiate appropriate medical and surgical therapy. The history, clinical signs, physical examination, and radiographic and ultrasonographic findings in patients with septic peritonitis are nonspecific; therefore, abdominal fluid cytology is the most common diagnostic tool used. A diagnosis of septic peritonitis is based on identification of toxic neutrophils with intracellular bacteria.[2] Intracellular bacteria occasionally are not identified. Peritoneal fluid cytology has been reported to be 57%-87% accurate in the diagnosis of septic peritonitis.[3-5] Bacterial culture (and susceptibility test-

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ing) of peritoneal fluid is considered the gold standard for diagnosis of septic peritonitis, but may take days to yield a result.

In 14 dogs and 2 cats, a peritoneal fluid pH $<$ 7.2, pCO_2 $>$ 55 mm HG, glucose concentration $<$ 50 mg/dL, and lactate concentration $>$ 5.5 mmol/L were specific for a septic peritoneal effusion.[6] In horses, a peritoneal fluid pH $<$ 7.3 and a fluid glucose concentration $<$ 30 mg/dL were significantly correlated with septic peritonitis.[7] It was reported also that the difference between blood glucose and peritoneal fluid glucose concentrations was more sensitive and specific than peritoneal fluid glucose concentration alone for detection of septic peritonitis.[7] With this background, we were interested in determining if differences between blood and peritoneal fluid pH, bicarbonate, glucose, and lactate concentrations of peritoneal fluid could be used as a reliable diagnostic tool for septic peritonitis in dogs and cats.

MATERIALS AND METHODS

Thirty consecutive dogs and cats with peritoneal effusion, admitted between January and December, 2001, were studied. Patients were included if at least 1 mL of peritoneal fluid was obtained for analysis. Patients were excluded if dextrose was administered within 24 hours before peritoneal fluid sampling or if there was hemoabdomen from trauma or splenic rupture.

At admission, venous blood was collected in a 1 mL heparinized syringe and at least 1 mL of peritoneal effusion was collected by abdominocentesis and placed into a heparinized syringe. Samples were analyzed within 15 minutes of collection. Blood and peritoneal fluid sample pH, bicarbonate, and electrolytes were measured with a blood gas analyzer (Rapidlab 850 or 860; Bayer Corporation, Tarrytown, NY). During the study, the Rapidlab 860 blood gas analyzer was acquired, which enabled lactate concentration to be measured in 14 patients (7 dogs, 7 cats). Glucose concentrations were measured with Vet Test 8008 analyzer (Vet Test Analyzer; Idexx Laboratories, Westbrook, ME). The blood-to-peritoneal fluid pH (BFpH), blood-to-fluid glucose (BFG), and blood-to-fluid lactate (BFL) concentration differences were calculated by subtracting the concentration in peritoneal fluid from the blood concentration.

A peritoneal fluid sample was evaluated for fluid type, nucleated cell count, and protein concentration. Although samples were evaluated at admission by the attending clinician to guide treatment, the results used in this report were based on peritoneal fluid samples stored and evaluated within 24 hours by one cytologist (AL), only aware of the source of the fluid and the patient's signalment. Peritoneal fluid was submitted also for aerobic and anaerobic bacterial culture and susceptibility testing.

Peritoneal fluid was considered septic if intracellular bacteria were identified on cytologic examination or if the bacterial cultures were positive with a confirmed source of contamination at surgery or necropsy. Animals were considered to have a nonseptic peritoneal effusion if no bacteria were identified on cytologic examination or by bacterial culture. The source of the nonseptic peritoneal effusion was documented by abdominal ultrasound, echocardiography, clinical pathology, surgery, or necropsy.

Statistical Analysis

Data from dogs and cats were evaluated separately. Statistical analysis was performed with a Mann-Whitney test with the level of significance set at $P < .05$. Sensitivity, specificity, positive and negative predictive values, and diagnostic accuracy were calculated for variables that were significantly different and considered clinically relevant.[8,9]

RESULTS

There were 18 dogs (7 septic peritoneal effusion, 11 nonseptic) and 12 cats (7 septic, 5 nonseptic). The median age for dogs with septic effusion was 7 years (range, 3-14 years) and for nonseptic effusion was 11 years (range, 8-15 years) whereas for cats, the median age of the septic effusion group was 4 years (range, 8 months-12 years) and for the nonseptic group was 12 years (range, 7-12 years). Patients with septic peritoneal effusion were significantly younger (dogs, $P = .02$; cats, $P = .03$) than patients with nonseptic effusion. Septic effusions were caused by intestinal perforation associated with intestinal neoplasia (2 dogs, 2 cats) or foreign body (1 dog, 2 cats), postoperative enterotomy dehiscence (1 dog, 1 cat), hepatic abscess (1 dog), duodenal feeding tube leakage (1 dog), pancreatic abscess (1 dog), mesenteric lymph node abscess (1 cat), and contamination from the urinary bladder (1 cat). The peritoneal fluid from the cat with suspected contamination from the urinary bladder had intracellular bacteria on cytologic examination and a positive bacterial culture. Bacteria isolated from peritoneal fluid were identical to those isolated from the bladder. Multiple attempts to collect urine by cystocentesis were performed before surgery. On exploratory celiotomy, the bladder was very irritated but no leaks were detected.

Nonseptic peritoneal effusion resulted from hepatic disease (5 dogs, 1 cat), gastrointestinal neoplasia (1

Table 1. Comparative Value of Diagnostic Variables for the Detection of Septic Effusions in 18 Dogs

Test	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Diagnostic Accuracy
Cytology	71%	100%	100%	85%	89%
TNCC* >13,000 cells/μL	86%	100%	100%	92%	94%
Peritoneal Fluid (Glucose) < 50 mg/dL	57%	100%	83%	83%	83%
BFG Difference† > 20 mg/dL	100%	100%	100%	100%	100%
BFL Difference‡ < −2.0 mmol/L (n = 7)	100%	100%	100%	100%	100%

*Peritoneal fluid total nucleated cell count.
†BFG difference = difference between venous blood and peritoneal fluid glucose concentrations.
‡BFL difference = difference between venous blood and peritoneal fluid lactate concentrations.

cat), multicentric lymphoma (1 dog, 1 cat), splenic leiomyosarcoma (1 dog), pancreatitis (2 dogs), right-sided congestive heart failure (1 dog, 1 cat), volume overload and anuric renal failure (1 cat), and intact pyometra (1 dog).

Twelve of 14 (86%) patients with septic effusion and all patients with nonseptic effusion were correctly identified on cytologic examination. Intracellular bacteria were not observed in a dog with an abscess around the stoma of a duodenal feeding tube placed after removal of an esophageal foreign body; antibiotic therapy had been administered for 5 days before referral. Intracellular bacteria also were not identified on cytologic examination in a dog with intestinal adenocarcinoma that subsequently had a positive peritoneal fluid bacterial culture; antibiotics had been administered for 3 days before admission. Both dogs underwent surgery based on history, clinical signs, and BFG difference despite the lack of intracellular bacteria on cytologic examination.

There was no significant difference in peritoneal fluid protein concentration between septic or nonseptic effusion in either dogs ($P = .06$) or cats ($P = .055$). The median peritoneal fluid nucleated cell counts for septic effusion were significantly higher (dogs, $P = .001$; cats, $P = .006$) than for nonseptic effusion. The median peritoneal fluid nucleated cell count was 51,975 cells/μL (range, 12,100-205,000 cells/μL) in dogs with septic effusion and 3,285 cells/μL (range, 134-12,800) in nonseptic effusion. In cats, the median peritoneal fluid nucleated cell count was 81,150 cells/μL (range, 17,900-175, 000 cells/μL) for septic effusion and 939 cells/μL (range, 200-11,100 cells/μL) for nonseptic effusion. For dogs, a peritoneal fluid nucleated cell count cutoff value of 13,000 cells/μL was 86% sensitive and 100% specific for septic effusions whereas in cats, the same cutoff value was 100% sensitive and 100% specific for septic effusions (Tables 1, 2).

Mixed bacterial populations were isolated from 6 of 14 septic peritoneal effusion samples; no bacteria were isolated from nonseptic effusions. *Escherichia coli* was the most common isolate (7 samples) and other isolates were *Enterococcus* sp. (4 samples), *Enterobacter* sp. (2 samples), beta-hemolytic *streptococcus* (2 samples), *Clostridium* sp.(2 samples), *Klebsiella* sp. (1 sample), *Streptococcus angiosus* (1 sample), and one unidentified anaerobic gram-positive coccus.

In dogs and cats, blood pH, bicarbonate, glucose, lactate, pCO_2, Na^+, K^+, Ca^{++}, and Cl^- concentrations were not significantly different between animals with septic and nonseptic effusion. Likewise, there was no significant difference between peritoneal fluid bicarbonate, pCO_2, Na^+, K^+, Ca^{++}, and Cl^- concentrations in animals with septic and nonseptic effusions. In both dogs and cats, there was no significant differ-

Table 2. Comparative Value of Diagnostic Variables for the Detection of Septic Effusions in 12 Cats

Test	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Diagnostic Accuracy
Cytology	100%	100%	100%	100%	100%
TNCC* > 13,000 cells/μL	100%	100%	100%	100%	100%
BFG Difference† > 20 mg/dL	86%	100%	100%	83%	92%

*Peritoneal fluid total nucleated cell count.
†BFG difference = difference between venous blood and peritoneal fluid glucose concentrations.

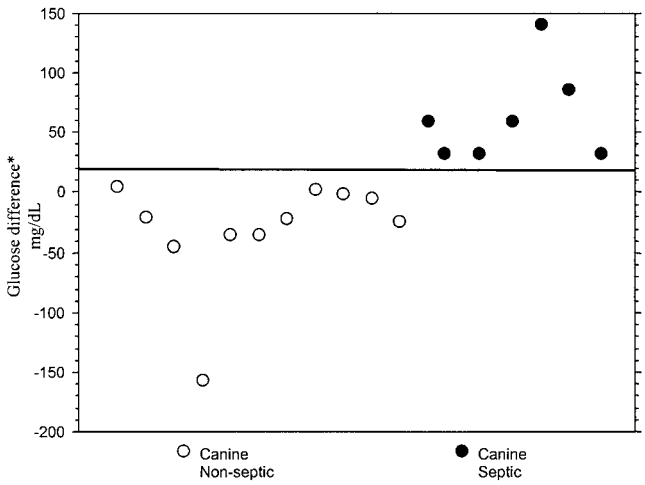

Fig 1. BFG difference in dogs. A cutoff value of 20 mg/dL (bold line) was 100% accurate in the detection of a septic effusion in dogs. *$[glu]_B$-$[glu]_F$ = BFG difference.

ence between blood and peritoneal fluid bicarbonate concentrations for septic and nonseptic effusions.

The median peritoneal fluid pH was significantly lower in cats with septic effusion than in nonseptic effusion (7.19 versus 7.32; $P = .04$), whereas in dogs, there was no significant difference in pH between septic and nonseptic effusions ($P = .44$). The BFpH difference was not significantly different for animals with septic or nonseptic effusions, for either dogs or cats.

Lactate concentrations were available for 14 patients, 7 dogs (4 nonseptic, 3 septic) and 7 cats (2 nonseptic, 5 septic). Peritoneal fluid lactate concentration was higher, but not significantly so, in cats and dogs with septic effusion than in nonseptic effusions. The median lactate concentration was 4.2 mmol/L (range, 3.8-8.4 mmol/L) in the dogs with septic effusion and 1.9 mmol/L (range, 1.1-5.7 mmol/L) in nonseptic effusion. In cats, the median lactate concentration was 6.2 mmol/L (range, 1.3-10.6 mmol/L) in septic effusion and 1.4 mmol/L (range, 1.2-1.6 mmol/L) in nonseptic effusion. The median BFL difference was significantly lower ($P = .03$) in dogs with septic effusion (median, −2.28 mmol/L; range, −6.6 to −2.1 mmol/L) than with nonseptic effusion (median, −0.375 mmol/L, range; −1.5-0 mmol/L) group (Fig 1). Using a cutoff value of < -2.0 mmol/L, the BFL difference was 100% sensitive and 100% specific for the diagnosis of a septic effusion in dogs (Table 1). In cats, the BFL difference was lower, but not significantly different ($P = .12$) in cats with a septic effusion (−3.0 mmol/L, range, −7.5 to −0.3 mmol/L) than with a nonseptic effusion (−0.1 mmol/L, range −0.3-0.2 mmol/L).

The peritoneal fluid glucose concentration was significantly lower ($P = .008$) in dogs with septic effusion than those with nonseptic effusion. The median peritoneal fluid glucose concentration in dogs with septic effusion was 57 mg/dL (range, 22-28 mg/dL) whereas in those with nonseptic effusion it was 136.7 mg/dL (range, 51-322 mg/dL). A cutoff value of < 50 mg/dL resulted in a 57% sensitive and 100% specific test for the diagnosis of a septic effusion in dogs (Table 1). Although the median peritoneal fluid glucose concentration was lower in cats with septic effusion (100mg/dL; range, 39-234 mg/dL) than those with nonseptic effusion (141 mg/dL; range, 107-224 mg/dL), the difference was not statistically significant ($P = .22$).

In dogs with septic effusion, the peritoneal fluid glucose concentration was always lower than the blood glucose concentration. Only 1 cat with a septic effusion did not have a peritoneal glucose concentration lower than the blood glucose concentration. In animals with nonseptic effusion, the peritoneal fluid glucose concentration was similar to (BFG difference $<$ 5mg/dL) or higher than the blood glucose concentration. In dogs ($P = .0005$) and cats ($P = .04$), the median BFG difference was significantly higher with septic effusion than those with nonseptic effusion (Figs 1, 2). The median glucose difference was 60 mg/dL (range, 20.2-141.4 mg/dL) in dogs with septic effusion and −21.6 mg/dL (range, −156.2-5 mg/dL) in those with nonseptic effusion. In dogs, a cutoff value for BFG difference set at $>$ 20mg/dL was 100% sensitive and 100% specific for the identification of a

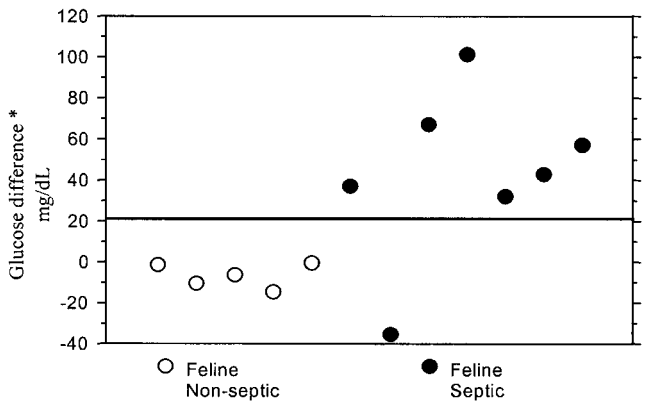

Fig 2. BFG difference in cats. A cutoff value of 20 mg/dL (bold line) was 92% accurate in the detection of a septic effusion in cats. *$[glu]_B$-$[glu]_F$ = BFG difference

septic effusion (Table 1). In cats, the median BFG difference was 43.4 mg/dL (range, −34.7-101.7 mg/dL) with septic effusion and −5.7 mg/dL (range, −14.0-0.100 mg/dL) for nonseptic effusion. In cats, a cutoff value set at > 20 mg/dL was 86% sensitive and 100% specific for the detection of a septic effusion (Table 2).

DISCUSSION

Patients with septic peritonitis often present with nonspecific clinical signs; therefore, the diagnosis of a septic effusion is usually made from abdominal fluid cytology. Cytology may not always be accurate because of concurrent antibiotic administration, a localized infection, inadequate staining, or technical experience. Abdominal fluid cytology results have been reported to be 57%-87% accurate in the diagnosis of septic peritonitis.[3-5] We obtained a similar result with 86% accuracy. Whereas, the gold standard for diagnosis of a septic effusion is bacterial isolation, these results often are not timely in terms of patient management. Therefore, it would be useful to have more rapid and accurate screening tests to facilitate immediate treatment. In humans, dogs, and horses, various peritoneal fluid variables and cutoff values have been identified as criteria for the diagnosis of a septic effusion.[6,7,10-12]

To our knowledge there is no reported cutoff value for peritoneal fluid nucleated cell count to diagnose septic effusion. It has been reported that > 2,000 nucleated cells/μL in presurgical and > 9,000 nucleated cells/μL in postsurgical patients were indicative of marked peritonitis, but this did not differentiate between septic and nonseptic effusions.[13] We found that peritoneal fluid nucleated cell count was one of the most reliable diagnostic variables for septic effusion in dogs and cats. All dogs or cats with a nonseptic effusion had a nucleated cell count < 13,000 nucleated cells/μL. We had 1 dog with a septic effusion and carcinomatosis that had only 12,100 nucleated cells/μL. This dog was being administered antibiotics before admission, which may have contributed to the absence of intracellular bacteria and a low nucleated cell count.

Measurements of pH have been reported to be a reliable index for septic effusion in horses, dogs, and humans.[6,7,11-12] The lower pH in a septic effusion is likely because of the production of lactate from neutrophilic glycolysis and bacterial metabolites in the peritoneal fluid.[14,15] We found that peritoneal fluid pH was significantly lower in septic effusions than nonseptic effusions in cats but not in dogs. A clinically useful cutoff value in cats could not be selected because of the overlap of pH measurements within the 2 groups. In humans, the BFpH difference was reported to be more accurate as a diagnostic tool than absolute pH[10]; however, we did not detect any significant difference in BFpH difference between septic and nonseptic effusions in either dogs or cats.

Dogs with septic peritonitis had a higher lactate concentration in peritoneal fluid than in blood and, therefore, when the BFL difference was calculated, the result was more negative. There was no overlap in BFL difference between septic and nonseptic effusions in dogs and a BFL difference of < −2.0 mmol/L was suggestive of septic peritonitis. Unfortunately, lactate concentrations were only measured 14 patients, so another study with a higher number of animals is needed to evaluate peritoneal fluid lactate concentration and BFL difference as potential diagnostic indices of septic peritonitis.

In horses and dogs, a low peritoneal fluid glucose concentration was an accurate tool for the diagnosis of septic effusion, but was unreliable in humans.[6,7,10] It is hypothesized that the glucose concentrations decrease in the abdominal fluid as bacterial invasion increases.[14,15] This may be because of glucose use by bacteria and phagocytic cells, glycolysis in the peritoneal fluid, or low BFG transport.[14,15] As others have reported,[6] we found that peritoneal fluid glucose concentration was significantly lower in dogs with septic effusion. A peritoneal fluid glucose concentration < 50 mg/dL was specific for septic effusion; however, because of low sensitivity, peritoneal fluid glucose concentration should not be used as a single index for septic effusion. In cats, the peritoneal fluid glucose concentration also was lower in septic effusion but this was not significantly different from nonseptic effusion.

As reported in horses,[7] we confirmed that the BFG difference was one of the most reliable diagnostic variables to differentiate septic effusion from a nonseptic effusion in dogs and cats. In dogs and cats with septic effusion, the peritoneal fluid glucose concentration was consistently lower than the blood glucose concentration. There was no overlap of BFG difference between dogs with a septic or nonseptic effusion (Fig 1), whereas in cats, there was only 1 patient that contributed to a BFG difference overlap between

groups (Fig 2). The peritoneal fluid from this cat had intracellular bacteria that were identical to bacteria isolated from the urine with no apparent leakage identified at surgery. It is unknown if the urine contamination developed because of multiple attempts to collect urine or if translocation of bacteria occurred from the urinary bladder. Possible reasons for the failure of the BFG difference to detect a septic effusion in this patient may be that the contamination of the peritoneum was acute or the infection was low-grade.

A dog or cat with a BFG difference $>$ 20 mg/dL had a septic peritoneal effusion. In dogs, BFG difference was more accurate than peritoneal fluid nucleated cell count or cytology for identification of septic peritonitis. Two dogs with a septic effusion were incorrectly identified by cytology but were correctly explored based on the BFG difference. The BFG difference provides an objective test for the diagnosis of a septic effusion and may aid clinicians inexperienced in evaluating fluid cytology. However, in this population of cats, fluid cytology and nucleated cell count were more accurate than BFG difference.

We evaluated variables in peritoneal fluid and blood to aid in the diagnosis of septic peritonitis. We established that BFG difference was 100% accurate and more useful than peritoneal fluid glucose concentration alone for the diagnosis of septic peritonitis in dogs. This finding was similar in cats; however, peritoneal fluid glucose concentration had no correlation with septic effusion, and BFG difference did have a 92% accuracy rate for the detection of a septic effusion in cats. In addition to abdominal fluid cytology, we confirmed that calculation of the BFG difference provides an objective, rapid, and reliable method to differentiate between septic and nonseptic effusions in dogs and cats.

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