

# Compendium

## Septic Peritonitis: Treatment and Prognosis

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**Abstract:** *Septic peritonitis is an inflammatory condition of the peritoneum that has a wide variety of clinical courses. The etiology and pathophysiology of this condition and its diagnosis in small animals are reviewed in a companion article. This article addresses the treatment of septic peritonitis and prognosis in small animals.*

Septic peritonitis is an inflammatory condition of the peritoneum that occurs secondary to microbial contamination.<sup>1</sup> Septic peritonitis may have a wide variety of clinical courses and outcomes, with high morbidity and mortality. The definitive diagnosis usually relies on the identification of toxic and/or degenerate neutrophils with foreign debris and/or intracellular bacteria in the peritoneal fluid. A thorough understanding of the treatment options and prognosis is crucial to decision making and comprehensive care.

### Treatment

#### Circulatory Shock and Fluid Therapy

Although surgery is the definitive treatment once the diagnosis of septic peritonitis has been made, establishing vascular access and initiating aggressive fluid resuscitation is the first priority.<sup>1</sup> Volume replacement fluids are given to correct hypovolemia and metabolic changes. An isotonic electrolyte solution (e.g., lactated Ringer solution, Normosol-R, Plasmalyte A, 0.9% sodium chloride) is usually administered. Total doses for crystalloid fluid therapy of patients in shock are 90 mL/kg in dogs and 50 mL/kg in cats. About 25% of the calculated total shock volume is administered rapidly, and subsequent boluses are adjusted based on the patient's response.<sup>1</sup> Appropriate fluid therapy can produce marked improvements in the patient's condition.

The patient's response to fluid therapy should be monitored by periodic cardiovascular evaluation (heart rate, mucous membrane color, central venous pressure, arterial blood pressure) and measurements of oxygen content (partial oxygen pressure [PaO<sub>2</sub>], oxygen saturation [SaO<sub>2</sub>]). Rapid redistribution of crystalloids and vascular leakage accompanying sepsis can lead to limited success when crystalloid fluids are used alone. If the patient's condition fails to stabilize after administration of a shock dose of crystalloids, or if the patient is hypoalbuminemic, colloids should be used as part of the resuscitation plan.

Hypoproteinemia and increased vessel permeability are common in patients with septic peritonitis. They can lead to a reduced osmotic pressure that can be corrected by administration of synthetic or natural colloids. The dose of colloids for patients in shock is 10 to 20 mL/kg in dogs and 15 mL/kg in cats, usually given as 5-mL/kg boluses.<sup>2</sup> Because shock increases the metabolic oxygen demand, patients are additionally treated with supplemental oxygen and respiratory function is assessed with pulse oximetry and blood gas analysis.

Resuscitation end points include normal perfusion parameters (pink mucous membranes, capillary refill time [CRT] of 1 to 2 seconds, strong and regular peripheral pulses), normal heart rate (100 to 140 bpm in dogs, 140 to 225 bpm in cats), and a normal mean arterial pressure (>70 mm Hg). The patient's mental status should be improved, the urine output should be >1 to 2 mL/kg/h, and the serum lactate level in dogs should be <2.5 mmol/L. Serum lactate level is not a sensitive end-point parameter in cats. Occasionally,

### Key Points

- Stabilization of patients with septic peritonitis is critical before surgical intervention.
- Presurgical stabilization includes fluids, broad-spectrum antibiotics, pain management, and oxygen supplementation.
- Disseminated intravascular coagulation should be suspected if coagulation parameters are elevated and the platelet level is decreased.
- Surgery is focused on treating the inciting cause as well as aggressive abdominal lavage.
- Controversy exists about the need for and methods of postoperative drainage.
- Postoperative hypoproteinemia is common and should be managed in severely affected patients by using early enteral nutrition and colloids.

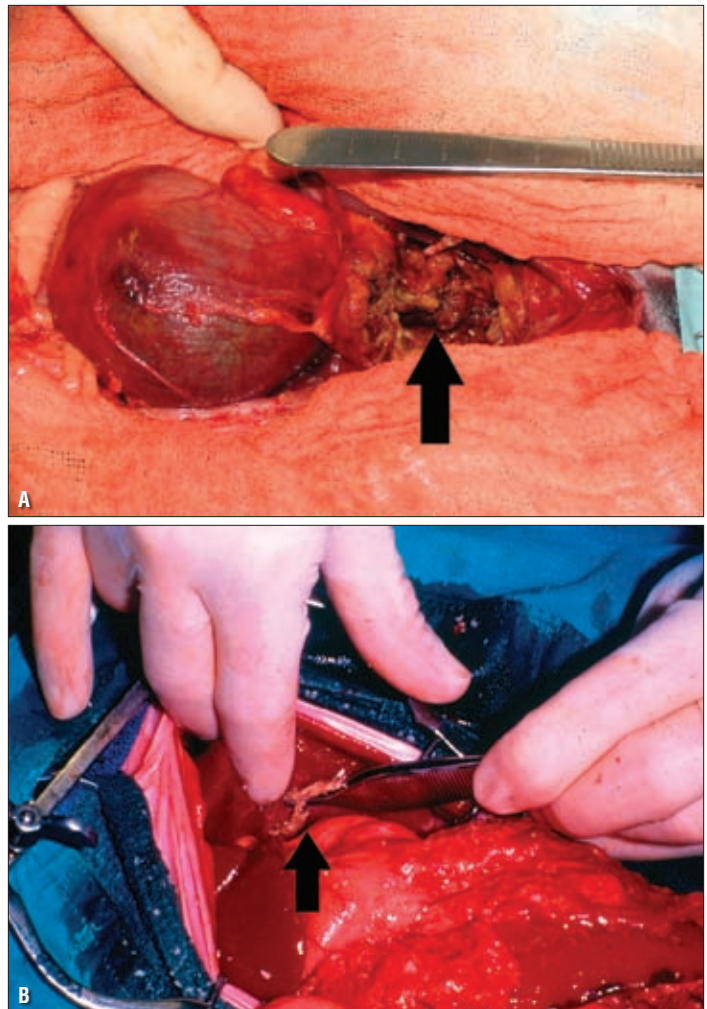
**Table 1. Antibiotics and Dosages Recommended for Treating Dogs and Cats With Septic Peritonitis<sup>4</sup>**

Drug	Dosage	Antimicrobial Coverage
Ampicillin	20–40 mg/kg IV q8h	G+: ++ G-: + Anaerobes: +
Cefaxolin	20 mg/kg IV q8h	G+: ++ G-: ± Anaerobes: +
Cefotaxime	20–80 mg/kg IV or IM q8h	G+: + G-: ++ Anaerobes: +
Ceftiofur	2.2–4.4 mg/kg SC q12h	G+: ++ G-: ++ Anaerobes: +
Enrofloxacin	5–20 mg/kg IV q24h	G+: ++ G-: ++
Amikacin	10–15 mg/kg IV q24h	G+: ++ G-: ++
Metronidazole	10 mg/kg IV q8h	Anaerobes: ++

G+ = gram positive, G- = gram negative.

an animal fails to reach end points of stabilization within the first hour despite fluid administration at shock levels. These patients should be reassessed for possible undiagnosed or contributing factors, such as ongoing hemorrhage, primary heart disease, sepsis-induced cardiac depression, severe vasodilation, hypoglycemia, hypokalemia, or arrhythmias.

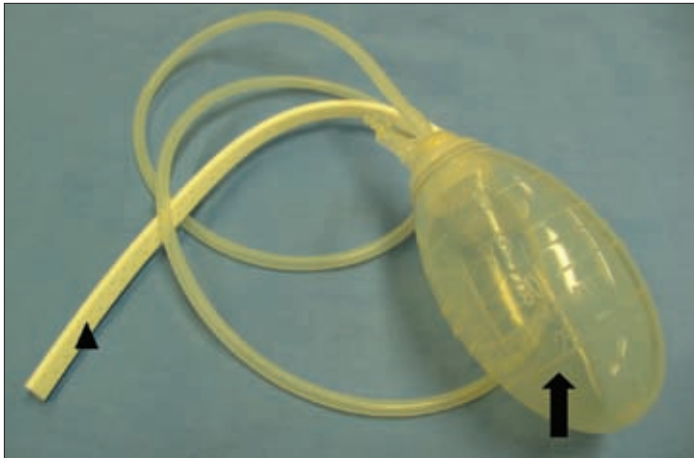
If the resuscitation fluid volume appears adequate and the patient is still hypotensive, the patient is a candidate for vasopressor or inotrope therapy. In human medicine, dopamine and norepinephrine are considered the vasopressors of choice for treating septic shock.<sup>3</sup> Vasopressin is also considered a good choice, as endogenous vasopressin levels have been shown to decrease in septic human patients.<sup>4</sup> The positive inotrope dobutamine may also be effective in treating the cardiac depression and decreased contractility induced by sepsis. Dopamine (5 to 15 µg/kg/min) or norepinephrine (0.05 to 0.3 µg/kg/min) is administered as a constant-rate infusion, starting at the low end of the range and titrating upward until the desired blood pressure is reached (usually a mean of approximately 70 mm Hg). The rate is usually gradually decreased once the animal can maintain normal blood pressure for a minimum of 4 hours. In septic patients not responding to fluids and vasopressors, relative adrenal insufficiency might be a contributing factor.<sup>5</sup> A physiologic dose of corticosteroids, the equivalent of 0.25 mg/kg of prednisone, may be beneficial in these patients.



**Figure 1.** (A) Septic uroabdomen secondary to urinary tract infection and bladder rupture (arrow). (B) Septic peritonitis secondary to grass awn (arrow) migration through the gastrointestinal tract. The awn was free floating in the abdomen.

### Antimicrobial Therapy

Antimicrobials are administered as soon as the diagnosis of septic peritonitis is made and samples of the peritoneal fluid have been obtained for aerobic and anaerobic culture and susceptibility testing. Although antibiotic selection is initially empirical, it should be rational. The antibiotic chosen should cover a broad spectrum, as the bacteria in most cases are from gastrointestinal (GI) leakage containing a combination of aerobic and anaerobic organisms. Cytology and Gram staining may help with choosing the initial antibiotics. Recommendations for the best combination of antibiotics vary<sup>1,6</sup> (TABLE 1). Common antibiotics used include a β-lactam (e.g., ampicillin) combined with an aminoglycoside or a fluoroquinolone.<sup>7–9</sup> Due to the critical condition of most patients with septic peritonitis and the risk of acute renal failure, aminoglycosides may not be ideal.<sup>8</sup> Fluoroquinolones should be used judiciously based on emerging resistance.<sup>1</sup> If an anaerobic infection is suspected, metronidazole may be added to this antibiotic protocol; however, this does not increase coverage much because its



**Figure 2.** A Jackson-Pratt (Cardinal Health, Dublin, OH) silicone drain with a multifenestrated drain (arrowhead) and a reservoir (arrow).

spectrum for anaerobes is similar to that of  $\beta$ -lactams, with additional coverage for *Bacteroides* spp.

A new trend is emerging toward using single-drug therapy in the treatment of people with septic peritonitis.<sup>10</sup> Treatment options recommended by the Surgical Infection Society that are applicable to veterinary patients include the use of extended-range  $\beta$ -lactam agents such third-generation cephalosporin (e.g., ceftiofur, cefotaxime) alone or in combination with metronidazole.<sup>10</sup>

### Surgery

Abdominal surgery is performed as soon as the patient reaches the desired end-point parameters for stabilization. The surgical goals in patients with diffuse peritonitis include (1) identification and correction of the underlying cause (**FIGURE 1A** and **FIGURE 1B**), (2) lavage of the peritoneal cavity, (3) consideration for postoperative drainage, and (4) provision of an avenue to ensure nutritional support (feeding tube) postoperatively.

Surgical therapy for the underlying disease is focused on either repair or removal of the inciting cause. After addressing the cause of the peritonitis, lavage is crucial to remove debris, bacteria, and toxic by-products. Lavage with warm isotonic saline solution at 200 mL/kg has been shown to improve the outcome of patients with septic peritonitis.<sup>11</sup> As much fluid as possible is removed from the abdomen because residual fluid can serve as a source of infection and decreases opsonization and chemotaxis by neutrophils.

Controversy exists regarding provisions for postoperative abdominal drainage.<sup>7,12-15</sup> No statistically significant difference in survival rate (29% to 46%) was found in studies evaluating drainage techniques.<sup>7,12-15</sup> Primary closure of the abdomen is acceptable once the source of contamination has been isolated and controlled.<sup>7</sup> Peritoneal drainage has been promoted by some authors for the removal of foreign material, toxins, and bacteria.<sup>12-14</sup> Types of peritoneal drainage include open peritoneal drainage, passive drainage, and active drainage.

Different types of drains are suitable for use in the peritoneal cavity.<sup>16</sup> Multiluminal (sump) or column disk catheters are passive

drains that can be used. Active drainage requires an external vacuum to create negative pressure within the peritoneal cavity. Active peritoneal drains, such as Jackson-Pratt (**FIGURE 2**), flat suction, or Hemovac drains, have a one-way valve to prevent fluid reflux and decrease the risk of iatrogenic contamination. Advantages of drains include removal of bacteria, toxins, foreign debris, and abdominal effusion; they also allow quantification of abdominal effusion. Disadvantages include the potential for drain occlusion, ascending nosocomial infection, accidental premature removal, hypoproteinemia, and electrolyte imbalances. Nosocomial infections have been documented to occur within 24 hours after drain placement, with an incidence as high as 90%.<sup>7,12-14</sup> Controversy exists as to whether patients with abdominal drains have an increased risk of hypoproteinemia.<sup>12</sup>

The linea alba and skin are left open for open peritoneal drainage (**FIGURE 3**). The tissues are covered with sterile absorbent dressings that are changed once or twice daily, when fluid from the abdomen has penetrated all layers of the bandage or when the bandage becomes wet or soiled from the outside. The decision about whether to leave the abdomen open at the end of surgery for septic peritonitis is governed by the nature and severity of peritonitis, the perceived ability to control continued contamination, the finances of the owner, the availability of intense postoperative monitoring, the serum albumin concentration, the temperament of the patient, and the surgeon's personal experience and preference.<sup>7,12-14</sup> The greatest advantages of open peritoneal drainage stem from improved drainage and alteration of the anaerobic environment of the peritoneum. Potential disadvantages include fluid loss, hypoproteinemia, evisceration, continued sepsis, nosocomial infection, increased cost, increased need for intensive care, and the need for repeat sedation and anesthesia during bandage changes and when the incision is eventually debrided and closed.

### Other Supportive Therapy

If coagulation parameters are elevated (prothrombin time [PT], >1.5 times high normal of the reference range; activated partial thromboplastin time [aPTT], >1.5 times high normal; and D-dimers, >1000 U) and platelet numbers are decreased (<145,000/ $\mu$ L in dogs; <190,000/ $\mu$ L in cats), disseminated intravascular coagulation (DIC) is likely.<sup>8,17,18</sup> Unquestionably, removing or eliminating the precipitating cause is a primary therapeutic goal in patients with



**Figure 3.** Linea alba closure for open abdominal drainage.

DIC. Different treatments have been used to limit intravascular coagulation. Antithrombin activity in animals with DIC is usually low as a result of consumption and possibly inactivation. Fresh frozen plasma, frozen plasma, or cryoprecipitate can be used to correct the antithrombin level, but multiple doses are often required.<sup>8,17,19</sup> Heparin therapy in the treatment of DIC is controversial; heparin is a cofactor for antithrombin and may be less effective in preventing the activation of coagulation when there is insufficient antithrombin activity in the plasma.<sup>20</sup>

Pain may be severe because the abdomen has a large number of sympathetic efferent pain fibers. A comprehensive analgesic plan includes a combination of drugs that are adjusted to the patient's needs and responses. Opioids are often used as a first choice. Continuous intravenous (IV) infusion of multimodal agents is very effective and convenient in animals being treated with IV fluids.<sup>21</sup> Drugs most commonly used in continuous IV infusions for dogs and cats include fentanyl, buprenorphine, ketamine, and medetomidine; morphine, hydromorphone, and lidocaine are used only in dogs.<sup>21</sup> Commonly used analgesic continuous-infusion combinations include morphine (0.05 to 0.2 mg/kg/h), lidocaine (2 to 4 mg/kg/h), and ketamine (0.2 to 0.6 mg/kg/h) for dogs and fentanyl (2 to 4 µg/kg/h) and ketamine (0.05 to 0.2 mg/kg/h) for cats.<sup>21</sup> The drugs used for analgesia have many potential side effects, but the dosages for each of those drugs can be at the low end of the suggested range when used in combination. It is almost always possible to provide meaningful and safe analgesia to even critically ill patients.

Single epidural injection of analgesics or repeated injections after temporary epidural catheterization have also proved to be safe in dogs. However, an epidural catheter is not recommended in patients with coagulopathies or bacteremia.<sup>22</sup>

### Postoperative Care

Intensive monitoring is the key to patient management after surgery. Volume status should be reassessed several times daily and fluid therapy adjusted as indicated. The ins-and-outs method of fluid administration is especially useful but should only be applied after rehydration is complete. Three components must be measured or estimated to use the ins-and-outs method: (1) insensible loss (fluid lost via respiration and normal stool = 22 mL/kg/d), (2) urine volume, and (3) ongoing losses (body cavity drainage, vomiting, diarrhea). These "outs" should be measured over a period of time (usually between 4 to 12 hours) and the new fluid administration rate based on the total volume lost (fluid rate [mL/h] = maintenance volume + [volume of fluid lost/number of hours]). In debilitated animals, a urinary catheter facilitates monitoring urine production and helps keep the patient clean. The mean arterial blood pressure should be maintained above 70 mm Hg at all times to ensure proper perfusion of the kidneys and brain. Due to abnormalities in vascular tone, blood pressure may be difficult to maintain with IV fluids alone and vasopressors may be needed. Antimicrobial drugs should be adjusted once the results of the aerobic and anaerobic culture and susceptibility testing are available.

If recumbent, the patient should be turned every 4 to 6 hours and kept clean to limit the development of decubitus ulcers and pulmonary atelectasis. The patient should be kept clean and dry, with strict attention to hand hygiene to prevent transmission of nosocomial infections at sites of drainage. Patients may be predisposed to GI ulcers secondary to poor perfusion and to the effects of endogenous corticosteroids on intrinsic gastric protectors. GI protectants (famotidine, sucralfate) may be used in these patients. Ileus is treated with motility enhancers. Metoclopramide stimulates and coordinates gastric, pyloric, and duodenal motor activity but is contraindicated in patients with GI hemorrhage or obstruction.

Postoperative hypoproteinemia is common in patients with septic peritonitis, affecting 12.5% to 69%.<sup>12-14</sup> Early nutritional support helps reduce the risk of hypoproteinemia.<sup>23</sup> Enteral nutrition also supports the enterocytes and aids in maintaining the integrity of the GI tract. Intact cell-to-cell junctions within the villi preserve the protective mechanism of the GI tract against lumen bacteria penetrating the wall.<sup>24</sup> A lack of nutrients in the lumen leads to a loss of mucosal integrity and bacterial translocation.<sup>24</sup> Enteral nutrition also minimizes the risk of delayed transit time and subsequent bacterial overgrowth contributing to increased bacterial migration through the bowel wall.<sup>24</sup> Surgical placement of an esophagostomy, gastrostomy, or enterostomy tube allows feeding of high-protein alimentation soon after surgery.<sup>11</sup> Gastrojejunostomy tubes have been shown to be effective for postoperative enteral nutritional supplementation in critically ill dogs when postgastric delivery is indicated.<sup>19</sup> The combination of partial enteral and partial parenteral nutrition is a reasonable option for patients that cannot tolerate total enteral nutrition.<sup>24</sup>

If hypoproteinemia becomes severe (albumin <1.5 mg/dL, total solids <3.0 mg/dL), IV colloids such as frozen plasma, fresh frozen plasma, or canine or human albumin can be administered. Other authors have recommended plasma transfusion,<sup>11</sup> but the effects on plasma osmolarity are minor (22 mL/kg of plasma is required to increase serum albumin by 0.5 g/dL).<sup>11</sup> Canine albumin is available, but studies on its use in dogs and cats are lacking. A dose of 1.4 g/kg of human albumin will increase the serum albumin level by 1.1 g/dL. It has been recommended that human albumin be diluted to 10% with saline solution and administered over a 12-hour period with a transfusion filter to decrease the risk or allow early detection of acute adverse reactions<sup>25</sup>; however, this will not reduce the risk of chronic adverse immunologic reactions. Current recommendations for human albumin are to use it cautiously and only for patients failing other therapies, as the risk of complications is high (up to 100% in some studies).<sup>25,26</sup> Further studies on the use of human albumin in animals are required to better define recommendations for its use.

Cytologic evaluation of abdominal effusion is a useful monitoring tool in the postoperative period. The number of toxic and/or degenerate neutrophils should decrease progressively after surgery, and no bacteria should be seen after 3 days.<sup>16</sup> Cytology can confirm the persistence of septic peritonitis (identification of foreign debris and/or intracellular bacteria), which could indicate either dehiscence of the surgical site, another leak, or the presence of



organisms resistant to the antibiotic regimen.<sup>11</sup> A second exploratory celiotomy is then warranted.

### Prognosis

The overall prognosis for patients with septic peritonitis is a function of the underlying cause, the health of the patient, the initial medical treatment, the time until surgical intervention, and the effectiveness of surgery in treating the primary problem.<sup>7,8,12,13,27</sup> The reported mortality in veterinary patients treated for septic peritonitis ranges from 20% to 68%.<sup>7,8,12,13,28</sup> The source of contamination may not have a significant effect on the prognosis, although there is some evidence that septic bile peritonitis carries a poorer prognosis. In a retrospective study on bile peritonitis in dogs and cats,<sup>9</sup> 100% of patients (15/15) with negative culture results survived, whereas only 27% of patients (3/11) with septic bile peritonitis survived. In a retrospective study, no difference in survival rates was found between the primary and secondary peritonitis cases, but dogs undergoing surgery for primary septic peritonitis were less likely to survive to discharge than dogs treated medically for primary septic peritonitis.<sup>29</sup> Decreased initial, intraoperative, or postoperative blood pressure has been found to be a negative prognostic indicator.<sup>8,12</sup> One study<sup>8</sup> found some clinicopathologic parameters to be different between survivors and nonsurvivors: survivors had higher packed cell volume, total solids, and serum albumin concentrations but lower aPTT at presentation. Another study found that survival was low if the patient had evidence of DIC or if an ineffective antibiotic was selected before culture and sensitivity results were obtained.<sup>27</sup> In humans, positive prognostic indicators include focal septic peritonitis, which is usually secondary to the presence of an intraabdominal abscess.<sup>10</sup>

### Conclusion

In small animal practice, acute generalized septic peritonitis is a relatively common occurrence and a clinically important condition with high morbidity and mortality. Early diagnosis and appropriate initial management allow rapid stabilization. Surgical treatment of the primary cause is then indicated. Prognosis is affected by the underlying cause, the patient's status, and early appropriate medical and surgical therapies.

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**1. The total dose for crystalloid fluid therapy of patients in shock is**

- a. 50 mL/kg in dogs and cats.
- b. 90 mL/kg in cats and 50 mL/kg in dogs.
- c. 90 mL/kg in dogs and 50 mL/kg in cats.
- d. 90 mL/kg in dogs and cats.

**2. Common antibiotics used to treat septic peritonitis pending results of culture and susceptibility testing include**

- a. fluoroquinolones as sole therapy.
- b. doxycycline.
- c. a combination of a fluoroquinolone with rifampin.
- d. a combination of a  $\beta$ -lactam with a fluoroquinolone or an aminoglycoside.

**3. DIC should be suspected if**

- a. PT, aPTT, and D-dimers are elevated and platelets are decreased.
- b. PT, aPTT, D-dimers, and platelets are elevated.
- c. PT, aPTT, and platelets are decreased and D-dimers are elevated.
- d. platelets are decreased and other coagulation parameters are normal.

**4. End-point parameters for resuscitation include**

- a. heart rate <80 bpm in dogs.
- b. heart rate <140 bpm in cats.
- c. systolic blood pressure >70 mm Hg.
- d. mean arterial blood pressure >70 mm Hg.

**5. After the cause of the septic peritonitis is surgically addressed, lavage should be performed**

- a. only in severely affected patients.
- b. by instilling and then removing approximately 200 mL/kg of warm, sterile saline solution.
- c. by instilling and leaving warm, sterile saline solution in the abdomen to increase opsonization and chemotaxis by neutrophils.
- d. with chlorhexidine diluted in warm, sterile saline solution.

**6. Which statement regarding drainage of the abdomen is true?**

- a. It must be performed in all patients with septic peritonitis.
- b. Open peritoneal drainage can help recovery by altering the anaerobic environment.
- c. Nosocomial contamination has been documented after drain placement in <50% of cases.
- d. Penrose drains are usually recommended.

**7. Which drug should not be used as a continuous-rate infusion for analgesia in cats?**

- a. fentanyl
- b. ketamine
- c. medetomidine
- d. lidocaine

**8. Nutritional support is important postoperatively because \_\_\_\_\_ is a common postoperative complication.**

- a. hypokalemia
- b. hypoproteinemia
- c. ionized hypocalcemia
- d. dehydration

**9. The overall prognosis for small animals with septic peritonitis is \_\_\_\_\_, with a \_\_\_\_\_ mortality rate.**

- a. very good; 90%
- b. fair to good; 57% to 90%
- c. fair to poor; 20% to 68%
- d. poor; 18%

**10. Negative prognostic indicators in patients with septic peritonitis include**

- a. increased blood pressure with low heart rate at presentation.
- b. high packed cell volume with hypoalbuminemia.
- c. evidence of DIC.
- d. presence of primary septic peritonitis.