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Use of liposomal bupivacaine in dogs and cats undergoing gastrointestinal surgery is not associated with a higher rate of surgical site infections or multidrug-resistant infections

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Received August 18, 2023
Accepted September 30, 2023

doi.org/10.2460/javma.23.08.0463

OBJECTIVE
To report the rate of surgical site infections (SSIs) after clean-contaminated and dirty gastrointestinal surgery in dogs and cats that did and did not receive incisional infiltration of Nocita and report the bacteria isolated.

ANIMALS
Client-owned dogs (n = 211) and cats (78).

METHODS
Records of dogs and cats that underwent gastrointestinal surgery at the Matthew J. Ryan Veterinary Hospital of the University of Pennsylvania and the University of Florida Small Animal Hospital between July 1, 2020, and April 1, 2023, were reviewed for surgical procedures, presence of preoperative septic peritonitis, use of Nocita, perioperative antibiotics administered, postoperative antibiotic use, SSI development postoperatively, and aerobic bacteria isolated.

RESULTS
7 of 124 (5.6%) dogs that received Nocita and 9 of 87 (10.2%) that did not receive Nocita developed an SSI. No dogs presenting with septic peritonitis and given Nocita (n = 5) developed an SSI. Two of 55 (3.6%) cats that received Nocita and 1 of 23 (4%) that did not receive Nocita developed an SSI. Multidrug-resistant (MDR) *Escherichia coli* was the most common aerobic bacteria isolated from SSIs (n = 3), and MDR bacteria were isolated commonly from both groups (4).

CLINICAL RELEVANCE
Use of Nocita for gastrointestinal surgery in dogs and cats is not associated with higher rates of SSI than published rates of SSI after gastrointestinal surgery. Use of Nocita in dogs with preoperative septic peritonitis is not associated with the development of SSI. MDR bacteria are commonly isolated via culture from both dogs that received Nocita and those that did not.

Keywords: Nocita, gastrointestinal surgery, surgical site infection, soft tissue surgery, MDR bacteria

Gastrointestinal surgery in dogs and cats is extremely common in both elective and nonelective scenarios. Gastrointestinal surgery is most commonly classified as a clean-contaminated procedure (surgery under normal conditions involving entry into the respiratory, gastrointestinal, or genitourinary tracts), based on the wound classification system developed by the National Academy of Sciences National Research Council.[1] However, in the presence of septic peritonitis, these procedures are considered to be dirty.[1] Common indications in veterinary medicine for gastrointestinal surgery are for the removal of obstructive foreign bodies, gastrointestinal masses, intussusceptions, and obtaining full-thickness gastrointestinal biopsies for diagnosis of common medical problems like inflammatory bowel disease, and more. Gastrointestinal surgery may involve entering the stomach or small or large intestine and may involve the resection and subsequent anastomosis of viscera.

A major consideration in the postoperative period for animals undergoing gastrointestinal surgery is surgical site infections (SSIs). Antibiotics are commonly used perioperatively, but antibiotics are not

routinely prescribed postoperatively. Indications for postoperative antibiotic administration include the degree of contamination or presence of infection before surgery (as with a diagnosis of septic peritonitis), degree of contamination or break in sterility during surgery, presence of infection in the immediate postoperative period, or certain individual risk factors (degree of immunocompromise, age, and more).[2] High mortality rates (17%) and excessive cost are associated with SSIs.[3] It has been shown that SSIs cost hospitals $1.6 billion annually and may accumulate an extra 1 million days of stay in hospital.[3] The rate of SSI after gastrointestinal surgery in humans is especially high, with studies finding that the rate is between 15% and 20%, depending on the segment of the gastrointestinal tract involved.[3] It has been well documented that clean-contaminated SSI rates are between 4.5% and 5% in veterinary medicine.[4] A recent veterinary study[3] identified an incisional infection rate of 7% for gastrointestinal surgery specifically, but infection rates were not reported for specific regions of the gastrointestinal tract. Risk factors of SSIs, specifically pertaining to clean-contaminated surgery, include length of anesthesia, length of surgery, and incidence of underlying disease, specifically endocrinopathies in intact males.[2] Other studies have shown that density, virulence, synergism of bacterial inoculum, local environment, hypothermia under anesthesia, and other host factors contribute to the incidence of SSI.[3] The most common flora from an SSI, cultured 10 to 14 days after gastrointestinal surgery, are normal gastrointestinal flora including *Escherichia coli*, *Enterobacter*, and more.[3] Many of these commonly cultured bacteria are multidrug resistant (MDR), or resistant to > 1 class of antibiotic agents and therefore not susceptible to commonly administered perioperative antibiotics, necessitating either the use of second- or third-line antibiotics, extended hospital stays, or repeat surgery.[5]

The use of injectable liposomal bupivacaine has increased in veterinary medicine since its development in 2011 and FDA approval in dogs and cats. The FDA-approved product Nocita has been approved for a single dose by infiltration injection at the time of incisional closure of cranial cruciate ligament surgery and for feline declaw procedures.[6,7] The off-label use of incisional infiltration of Nocita at the time of incisional closure for gastrointestinal surgery, however, is common at the authors' institutions. In a recent study,[8] the incisional complication rate (infection, seroma, and dehiscence) was 10.8% in 65 dogs that received Nocita during foreign body surgery, higher than reported for dogs that did not receive Nocita (n = 140) during foreign body surgery. The SSI rate was also higher in dogs that received Nocita, as 1.5% of the 65 dogs developed an SSI, compared to 0.7% of 140 dogs that did not receive Nocita.[8] This study did not report the bacterium isolated, nor did it indicate whether dogs diagnosed with SSI had surgeries performed under clean-contaminated or dirty conditions. Another study[9] found that the incidence of wound complications after infiltration of liposomal bupivacaine in dogs did not vary significantly between clean, clean-contaminated, and dirty surgeries but that the overall wound complication rate was 19.7%, with contaminated and clean-contaminated surgeries having high complication rates of 30.8% and 23.1%, respectively. The overall rate of SSI reported was 5%, but the rate of SSI for clean, clean-contaminated, or contaminated surgeries was not reported.[9]

In human medicine, SSI is listed as a potential complication of liposomal bupivacaine administration. Some reports support an increased risk of SSI with use of liposomal bupivacaine, particularly in skin graft donor sites and after arthroplasty.[10,11] However, 1 study[12] found no significant difference in SSIs rates between a group receiving liposomal bupivacaine and a control group during abdominal surgery. In a laboratory setting, 1 study[10] inoculated 6 common bacterial isolates of SSIs in humans (methicillin-resistant *Staphylococcus aureus*, methicillin-sensitive *S aureus*, coagulase-negative staphylococci, *E coli*, and *Enterococcus*) into liposomal bupivacaine, finding that the antibacterial effects seen with traditional local anesthetic agents (bupivacaine) are not seen with liposomal bupivacaine. They concluded that an animal model would be a critical next step.[10] This study suggests that MDR bacteria may more easily grow in incisions after incisional infiltration with Nocita compared to a typical line block of bupivacaine.

Considering the morbidity, mortality, and cost associated with SSIs in a veterinary setting, it is important to document whether incisional infiltration of Nocita at the time of closure of gastrointestinal surgery is a risk factor for incisional infections. No studies in veterinary medicine have assessed the SSI rate in cats that have received Nocita for gastrointestinal surgery, the SSI rate of dogs that received Nocita undergoing gastrointestinal surgery for indications other than foreign body retrieval, or whether the presence of septic peritonitis or dirty abdominal surgery affects SSI rate in dogs and cats receiving Nocita. Additionally, no paper in veterinary medicine has discussed specific isolates of SSIs in animals that received Nocita for gastrointestinal surgery and compared them to animals that did not receive Nocita. Our objectives were to (1) report the incidence of SSI rate after gastrointestinal surgery in dogs and cats that received Nocita and (2) report the aerobic bacteria isolated from cultures obtained of those patients with incisional infections. We hypothesized that the rate of incisional infection would be similar between patients receiving Nocita and those that did not. We also hypothesized that similar species of causative bacteria isolated would be similar to those that have been reported previously for incisional infections following gastrointestinal surgery. However, we also hypothesized that MDR bacteria would be isolated more frequently from SSIs in patients receiving Nocita than those that did not.

Methods

Data collection

Medical records were evaluated of dogs and cats that had gastrointestinal surgery at the Matthew J. Ryan Veterinary Hospital of the University of Pennsylvania

and University of Florida Small Animal Hospital between July 1, 2020, and April 1, 2023. The criteria for inclusion included any animal undergoing a procedure in which a full-thickness incision was made in the stomach, small intestine, or large intestine. All subjects were hospitalized after the procedures in either traditional patient wards or the ICU depending on their stability before and during surgery. Antibiotic choice during surgery was determined by the primary surgeon. Only subjects that were either humanely euthanized before discharge or died of natural causes before discharge or those that did not return for follow-up within 10 to 14 days of their surgery were disqualified from the study pool. Surgeries were performed by board-certified surgeons or surgical residents who were either supervised by board-certified surgeons or unsupervised. Postoperative care (appearance of the incision, medication administration, and continuation of antibiotics) was determined by either a board-certified surgeon or by a surgery resident under the supervision of a board-certified surgeon.

Subjects were initially divided into 2 groups: those that received Nocita at the time of surgery and those that did not. Species, surgery performed, indication for gastrointestinal surgery, perioperative antibiotic used, presence of preoperative septic peritonitis, whether an antibiotic was sent home at the time of discharge, and the choice of that antibiotic were recorded. Additionally, presence of incisional infection before or at the time of routine recheck examination, whether an antibiotic was prescribed at that time, and isolates after culture and sensitivity testing were recorded. Aerobic culture results were recorded for dogs and cats that developed incisional infections, when available. Aerobic cultures were obtained via a direct swab of the subcutaneous tissues, using aseptic technique. Routine follow-up was conducted 10 to 14 days following surgery. If a patient presented prior to the scheduled recheck examination, due to suspicion of an incisional complication, this information was recorded. Presence of incisional infection was determined by clinicians utilizing criteria determined by the CDC.[13] More specifically, this criteria included the presence of at least one of the following: purulent drainage from the superficial incision, organism(s) identified from an aseptically obtained specimen, and localized pain or tenderness, swelling, erythema, or heat. Deep incisional infections were also identified by criteria determined by the CDC. This specifically included purulent drainage from the deep incision; a deep incision that spontaneously dehisces or is deliberately opened or aspirated by a surgeon or physician and organisms identified from the deep soft tissues via culture; clinical signs of fever, localized pain, or tenderness; or an abscess or other evidence of infection involving the deep incision detected grossly or via imaging.

Statistical analysis

Frequencies and descriptive data were determined using Excel (version 16.37; Microsoft Corp). Data were coded such that the procedures that patients underwent were divided into the following groups: gastrotomy or gastrectomy, enterotomy, intestinal resection and anastomosis (RA), full-thickness gastrointestinal biopsies, 2 or more of the above procedures, or 2 or more of the above procedures including an RA. Indications for gastrointestinal surgery were also categorized to reflect the following groups: foreign body obstruction, gastrointestinal mass, intussusception, perforation or ulceration, a problem at a previous surgical site (namely dehiscence or stricture), a mix of the categories described above, or for a reason other than those described above (including primary medical issues, bite wounds, diaphragmatic hernia, mesenteric torsion, and more).

Results

Study population

Eight hundred twenty-three dogs and cats underwent gastrointestinal surgery during the study period. Of these, 211 dogs and 78 cats returned for reevaluation of their incision at these institutions and were included in the final study population. Of the final study population, 124 of the 211 (58%) dogs received Nocita during gastrointestinal surgery and 55 of 78 (71%) cats received Nocita during gastrointestinal surgery. Fifty-two of 78 (66.7%) cats and 123 of 211 (58.3%) dogs underwent surgery at the Matthew J. Ryan Veterinary Hospital at the University of Pennsylvania, and 26 of 78 (33.3%) cats and 88 of 211 (42.7%) dogs underwent surgery at the University of Florida Small Animal Hospital.

Indications for surgery were recorded. Among dogs, 181 of 211 (85%) underwent surgery for a foreign body obstruction, 16 (7.6%) underwent surgery for a gastrointestinal mass, 2 (0.94%) underwent surgery for an intussusception, 3 (1.4%) underwent surgery for a gastrointestinal perforation or ulceration, 2 (0.94%) underwent surgery for a mix of the above categories, and 3 (1.9%) underwent surgery for another problem (primary medical issue such as inflammatory bowel disease, diaphragmatic hernia requiring gastrointestinal surgery, or mesenteric torsion). Among cats, 59 of 78 (75%) underwent surgery for a foreign body obstruction, 11 (14.1%) for a gastrointestinal mass, 4 (5.1%) for an intussusception, 3 (3.8%) for a problem related to a previous surgery site (stricture or dehiscence), and 1 (1.3%) for a problem that was unrelated to those described above.

Specific surgical interventions were also recorded. For dogs, 78 of 211 (36.9%) underwent a gastrotomy, 62 (29.4%) underwent an enterotomy, 31 (14.7%) underwent an intestinal RA, 25 (11.8%) underwent 2 or more procedures not including an RA, and 15 (7.1%) underwent 2 or more procedures including an RA. For cats, 30 of 78 (38.5%) underwent a gastrotomy, 19 (24%) underwent an enterotomy, 15 (19%) underwent an intestinal RA, 8 (10%) underwent 2 or more procedures not including an RA, and 6 (7.7%) underwent 2 or more procedures including an RA.

Surgical site infection rate

Sixteen of 211 (8%) of canine patients were diagnosed with SSI. Of the canine patients that received

Nocita, 7 of 124 (5.6%) were diagnosed with an SSI and 1 (0.8%) patient was diagnosed with septic peritonitis postoperatively. After this diagnosis, this patient was lost to follow-up. Of the canine patients that did not receive Nocita, the SSI rate was 9 of 87 (10.2%; **Table 1**).

Table 1—Canine surgical site infection (SSI) frequency after clean-contaminated gastrointestinal surgery.

Groups	Subjects	SSI	Percentage (%)
Nocita	124	7	4.2
No Nocita	87	9	10.2
Totals	**211**	**16**	**8**

Fourteen canine patients, 5 of which received Nocita and 9 of which did not, presented with preoperative septic peritonitis. Of these patients, 1 of 14 (7%) was diagnosed with an SSI and 1 (7%) was diagnosed with septic peritonitis postoperatively. Both of these patients did not receive Nocita at the time of gastrointestinal surgery. None of the 5 (0%) patients with preoperative septic peritonitis that were administered Nocita developed a superficial SSI **(Table 2)**.

Table 2—Canine SSI frequency after gastrointestinal surgery for septic peritonitis.

Groups	Subjects	SSI	Percentage (%)
Nocita	5	0	0
No Nocita	9	1	11
Totals	**14**	**1**	**7**

Of the canine patients that developed SSI, the most common surgical indication was a foreign body obstruction making up 15 of 16 (93%) of incisional infections in this study. Eight of 16 (50%) underwent a gastrotomy, which represented the most common procedure of those canine patients that developed SSI.

Three of 78 (3.8%) feline patients were diagnosed with SSI. Two of 55 (3.6%) feline patients that received Nocita were diagnosed with an SSI, compared to 1 of 23 (4%) of those that did not receive Nocita. No feline patients were diagnosed with preoperative or postoperative septic peritonitis. All feline patients diagnosed with an SSI underwent surgery for a foreign body obstruction. Of feline patients that developed an SSI, 2 underwent 2 or more procedures not including an intestinal RA and 1 cat underwent an enterotomy **(Table 3)**.

Table 3—Feline SSI frequency after clean-contaminated gastrointestinal surgery.

Groups	Subjects	SSI	Percentage (%)
Nocita	55	2	3.6
No Nocita	23	1	4
Totals	**78**	**3**	**3.8**

Postoperative antibiotic use

Thirty-eight of 211 (18%) canine patients were discharged with antibiotics. Specific antibiotics that were prescribed at the time of discharge included Clavamox, enrofloxacin, amoxicillin, metronidazole, cefpodoxime, azithromycin, cephalexin, and meropenem in 1 dog. Of the patients that were discharged with antibiotics, 2 of 38 (5%) were diagnosed with an SSI. One of these patients received Nocita at the time of surgery, and the other did not. The one that did not receive Nocita required additional wound debridement for treatment of the infection. Nine of 78 (12%) of feline patients were discharged with antibiotics. Specific antibiotics that were prescribed included only Clavamox. No feline patient discharged with antibiotics developed an SSI.

Culture and sensitivity results

Aerobic culture and antibiotic sensitivity results of those patients that were diagnosed with an incisional infection were available for 6 dogs and 1 cat. For dogs that were administered Nocita and underwent culture and susceptibility testing at the time of diagnosis of an SSI (n = 1), the isolated bacteria were MDR *E coli* (1) and MDR *Beta streptococcus* (1). For animals that did not receive Nocita and underwent culture and susceptibility testing at the time of diagnosis of an SSI (n = 5), the isolated bacteria included *E coli* (2), *Pseudomonas aeruginosa* (1), MDR *Enterococcus faecium* (1), MDR *Enterobacter cloacae* (1), and MDR *Streptococcus equi zooepidemicus* (1). Three of 5 (60%) of these patients grew MDR bacteria. All bacteria isolated from dogs were resistant to the perioperative antibiotic chosen. *E coli* was cultured from a feline patient that did not receive Nocita. The *E coli* grown was susceptible to the perioperative antibiotic chosen.

Discussion

Off-label use of Nocita for incisional infiltration at the time of closure of gastrointestinal surgery is becoming increasingly common in veterinary medicine. The information presented in this manuscript is novel and builds upon previously published work regarding incisional infections and the use of Nocita for abdominal procedures. This was the largest-scale study to date evaluating the rate of SSIs in dogs receiving Nocita for gastrointestinal surgery and the only study to do so in cats. The overall SSI rate was 5.8% in dogs receiving Nocita for gastrointestinal surgery, compared to 10.2% for dogs that did not receive Nocita in this study. The SSI rate among cats that received Nocita for gastrointestinal surgery was 3.6%, compared to 4% for those that did not receive Nocita. Not only was there no association between higher infection rates and administration of Nocita, but the infection rates presented here mirror published rates of SSIs for clean-contaminated surgeries.[4] As a result, the authors propose that the use of Nocita following gastrointestinal surgery poses no increased risk for the development of an SSI in both dogs and cats.

No dogs that received Nocita after dirty gastrointestinal surgery due to septic peritonitis developed an SSI. Although there was a larger population of patients presenting with preoperative septic peritonitis that did not receive Nocita (n = 9) than those that

did receive Nocita (5), the rate of SSI reported here in patients presenting with septic peritonitis is much lower than previously published rates of wound complications in contaminated surgeries in which patients received Nocita.[9] On the basis of this information, the authors suggest that the use of Nocita in dirty gastrointestinal surgery presents a low risk for the development of SSIs in dogs and cats; however, further prospective clinical trials are indicated to further investigate its use in these cases.

Isolates of aerobic culture and antibiotic sensitivity were recorded. In both dogs and cats, the most common isolates were similar to those previously reported, most commonly normal gastrointestinal flora (*E coli*, *Enterococcus*, and more).[3] It was noted, as was reported previously, that many of the isolates were resistant to the perioperative antibiotic used in surgery and commonly prescribed antibiotics for SSIs (Clavamox and cefalexin). While an MDR bacterium was grown from the dog that received Nocita, MDR bacteria were also isolated in most of the cases in dogs that did not receive Nocita. Our study suggests that MDR bacteria are very commonly cultured from SSI of both canine patients that receive Nocita and those that do not. A larger study population is needed to determine whether MDR pathogens are more commonly isolated from patients that received Nocita at the time of gastrointestinal surgery.

Interestingly, the majority of canine patients that developed an SSI, regardless of administration of Nocita, presented for foreign body obstructions. It is unclear whether this indicates that there is a higher risk of developing an SSI following surgery to retrieve a foreign body, given the limited number of cases that developed an infection. Given that the bacteria isolated from infections in this study were consistent with native gastrointestinal flora, suggesting that they are secondary to contamination at the time of surgery, it stands to reason that there may be increased spillage or contamination of tissues when retrieving a foreign body through a small incision into a hollow viscus compared to resecting a portion of an intestine for a gastrointestinal tumor that traditionally is performed with the use of atraumatic clamps to prevent spillage. Further studies are needed to investigate the association between indication for surgery and development of an incisional infection as well as the specific location of gastrointestinal tract operated on and development of an incisional infection.

Limitations of this study were inherent in its retrospective nature. Because of the retrospective nature of this study, the method in which Nocita was administered was unable to be standardized. While on-label use describes instillation of the drug either as a 4-point nerve block for onychectomy in cats or using an "infiltration injection technique" following tibial plateau–leveling osteotomy surgery in dogs, no such guidelines exist for administration following abdominal surgery. Some surgeons have reported injecting only into the subcutaneous tissues, while others report injecting into the rectus sheath as well. This was unable to be evaluated in this study. Additionally, the volume or method of postoperative lavage following the gastrointestinal-specific portion of surgery was unable to be appropriately quantified or standardized. While it is currently standard practice for the authors to lavage the subcutaneous tissues prior to closure, this was not something that was able to be assessed in this patient population and the potential impact of differing quantities or methods of lavage are unknown. Patient selection for Nocita administration was also not standardized and represents a potential source of bias. Additionally, few cultures were performed following diagnosis of an incisional infection. As a result, interpretation of the impact that administration of Nocita has on the bacterial population of incisional infections and presence of multidrug resistance is limited. Anaerobic cultures were also not routinely performed in these patients, so it is impossible to know the impact that opportunistic or commensal organisms had in the development of a postoperative infection. Furthermore, active surveillance was unable to be achieved due to its retrospective nature such that diagnosis of an SSI was dependent on owner observation and diagnosis at a follow-up appointment. In addition to this, the CDC states that SSIs may be diagnosed up to 30 days postoperatively. However, follow-up in veterinary surgical patients is often limited to 10 to 14 days. Many large-scale veterinary and human epidemiological studies of wound infection have used the presence of purulent discharge within 14 days as the definition of an infected wound; however, there is the possibility that SSIs were underdiagnosed as a result.[1,14–17] It is impossible to know what proportion of these patients had incisional infections outside of the study period but still within the time frame dictated by the CDC and how it would have altered our results. Lastly, the inoculation techniques and specifically count of bacteria that a microbiology lab deems as significant growth were not standardized across the 2 institutions in this study, such that a small degree of growth at 1 institution may have been inappropriately disregarded.

Overall, we found no evidence that Nocita leads to higher rates of SSIs, septic peritonitis, or growth of more MDR bacteria than in dogs and cats not receiving Nocita for both clean-contaminated and dirty gastrointestinal surgery.[4] The rates of SSIs of dogs and cats receiving Nocita are lower than published SSI rates for both clean-contaminated and dirty surgery. Further prospective clinical trials are needed to assess the impact of Nocita administration in a wide variety of surgeries and determine the influence of Nocita on the presence of MDR infections. Future study directions may include blinded, randomized clinical trials comparing the effect of no incisional block, traditional bupivacaine line blocks, and Nocita for the development of SSI and growth of MDR bacteria.

Acknowledgments

None reported.

Disclosures

The authors have nothing to disclose. No AI-assisted technologies were used in the generation of this manuscript.

Funding

The authors have nothing to disclose.

References

1. Nicholson M, Beal M, Shofer F, Brown DC. Epidemiologic evaluation of postoperative wound infection in clean-contaminated wounds: a retrospective study of 239 dogs and cats. *Vet Surg*. 2002;31(6):577–581. doi:10.1053/jvet.2002.34661
2. Jessen L, Damborg P, Spohr A, et al. *Antibiotic Use Guidelines for Companion Animal Practice*. 2nd ed. Companion Animal Group, Danish Veterinary Association; 2018.
3. Williams RW, Cole S, Holt DE. Microorganisms associated with incisional infections after gastrointestinal surgery in dogs and cats. *Vet Surg*. 2020;49(7):1301–1306. doi:10.1111/vsu.13495
4. Brown DC, Conzemius MG, Shofer F, Swann H. Epidemiologic evaluation of postoperative wound infections in dogs and cats. *J Am Vet Med Assoc*. 1997;210(9):1302–1306.
5. Siegel JD, Rhinehart E, Jackson M, Chiarello L; Healthcare Infection Control Practices Advisory Committee. Management of multidrug-resistant organisms in healthcare settings. *Am J Infect Control*. 2007;35(10 suppl 2):S165–S195. doi:10.1016/j.ajic.2007.10.006
6. US FDA. *NADA 141–461 Nocita Dog. Freedom of Information Summary: Original New Animal Drug Application*. US FDA; 2016.
7. US FDA. *NADA 141–461. Nocita Cat. Freedom of Information Summary: Original New Animal Drug Application*. US FDA; 2018.
8. Rahn AP, Moore GE, Risselada M. Postoperative injectable opioid use and incidence of surgical site complications after use of liposomal bupivacaine in canine gastrointestinal foreign body surgery. *Vet Surg*. 2023;52(7):1024–1031. doi:10.1111/vsu.13976
9. Power AM, McKee T, Jordan K, Bergman PJ, Davis KM. Incidence and severity of short-term incisional complications after intraoperative local infiltration of liposomal bupivacaine in dogs. *Vet Surg*. 2022;51(4):674–681. doi:10.1111/vsu.13803
10. Callahan ZM, Roberts AL, Christopher AN, et al. The effect of commonly used local anesthetic on bacterial growth. *J Surg Res*. 2022;274:16–22. doi:10.1016/j.jss.2021.12.040
11. Artz CE, Ward MA Jr, Miles MP, et al. 239 Intraoperative Liposomal Bupivacaine for Skin Graft Donor Site Analgesia. *J Burn Care Res*. 2019;40(suppl 1):S99–S100. doi:10.1093/jbcr/irz013.165
12. Joshi GP, Janis JE, Haas EM, Ramshaw BJ, Nihira MA, Dunkin BJ. Surgical site infiltration for abdominal surgery: a novel neuroanatomical-based approach. *Plast Reconstr Surg Glob Open*. 2016;4(12):e1181. doi:10.1097/GOX.0000000000001181
13. National Healthcare Safety Network. Surgical site infection (SSI) event. CDC. Accessed September 26, 2023. https://www.cdc.gov/nhsn/pdfs/pscmanual/9pscssicurrent.pdf
14. Espinel-Rupérez J, Martín-Ríos MD, Salazar V, Baquero-Artigao MR, Ortiz-Díez G. Incidence of surgical site infection in dogs undergoing soft tissue surgery: risk factors and economic impact. *Vet Rec Open*. 2019;6(1):e000233. doi:10.1136/vetreco-2017-000233
15. Vasseur PB, Levy J, Dowd E, Eliot J. Surgical wound infection rates in dogs and cats. Data from a teaching hospital. *Vet Surg*. 1988;17(2):60–64. doi:10.1111/j.1532-950x.1988.tb00278.x
16. Wenzel RP, Hunting KJ, Osterman CA. Postoperative wound infection rates. *Surg Gynecol Obstet*. 1977;144(5):749–752.
17. Leissner KH. Postoperative wound infection in 32,000 clean operations. *Acta Chir Scand*. 1976;142(6):433–439.