Antimicrobial prophylaxis in canine and feline surgery

Antimicrobiële profylaxe bij chirurgie van honden en katten

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ABSTRACT

Antimicrobial prophylaxis aims at decreasing the risk of surgical site infections (SSI) by administration of antimicrobial drugs prior to surgery in animals at risk. Multiple risk factors for the development of SSIs have been determined in companion animals, and based on these risk factors, a flow diagram is proposed to identify dogs and cats that would benefit from antimicrobial prophylaxis. Furthermore, the most identified bacteria in healthy companion animals are listed per organ system with their recommended prophylactic antimicrobial drug(s). Besides administration of the optimal drug type, the route of administration, dose, dose interval, and duration of antimicrobial prophylaxis are important to help reduce the emergence of (multidrug-) resistant bacteria.

SAMENVATTING

Het doel van antimicrobiële profylaxe is om het risico op postoperatieve wondinfecties te verminderen, door het preoperatief toedienen van een antimicrobieel middel bij dieren die een risico lopen. Er zijn verschillende risicofactoren bekend die de kans op postoperatieve wondinfectie bij gezelschapsdieren vergroten. Gebaseerd op deze risicofactoren wordt er in dit artikel een stroomdiagram voorgesteld dat kan helpen bij het identificeren van honden en katten die al dan niet baat zouden kunnen hebben bij antimicrobiële profylaxe. Daarnaast worden de meest voorkomende bacteriën bij gezonde gezelschapsdieren weergegeven per orgaanstelsel met de bijhorende aanbevolen profylactische antimicrobiële middelen. Naast het toedienen van het correcte middel zijn de toedieningswijze, de dosis, het dosisinterval alsook de duur van toedienen van antimicrobiële profylaxe zeer belangrijk in de strijd tegen het ontstaan van (multi)resistente bacteriën.

INTRODUCTION

Antimicrobial prophylaxis is the preoperative administration of one or multiple antimicrobial drugs in a patient without pre-existing infectious disease. The aim is to reach a sufficiently high tissue concentration of the antimicrobial drug before the potential development of a surgical site infection (SSI), in order to prevent proliferation of contaminating bacteria without killing all of them (Boothe and Boothe, 2015). By definition, antimicrobial drugs are synthetic or natural products with an antimicrobial effect, whereas the term antibiotics is reserved for antimicrobial drugs that are produced by micro-organisms (Demain and Sanchez, 2009). Optimal use of antimicrobial prophylaxis implies not only a good patient selection, but also the administration of the appropriate antimicrobial drug at the correct dose, route, timing, and duration of administration (Burke, 2001). Possible side effects of antimicrobial drugs are anaphylactic reactions, especially when given in combination with other drugs, gastro-intestinal complaints, and the development of antimicrobial resistance (Prescott et al., 2002; Torres-Henderson et al., 2017; Gosling and Martínez-Taboada, 2018). In the past, the vast majority of published recommendations for the use of antimicrobial prophylaxis in companion animals were based on recommendations in human medicine. More recently, veterinary data have become available, but the information remains limited.

The terms wound inflammation and wound infection are often used interchangeably, although both are distinct disease entities. In case of mere wound inflammation, there is an absence of bacterial colonization. Wound inflammation is typically characterized by swelling, redness, heat and pain (tumor, rubor, calor and dolor) (Punchard et al., 2004). In a prospective observational study that was performed in intensive care units of four veterinary referral clinics, it has been shown that 2.8 dogs and 1.5 cats per 100 days developed an inflammation at the level of a surgical incision (Ruple-Czerniak et al., 2013). A certain level of inflammation is to be expected in all (surgical) wounds, as the inflammatory phase is the first sequence in wound healing. Excessive wound inflammation, however, can delay wound healing (Szpaderska and DiPietro, 2005). Wound infection is characterized by the local presence of bacteria, which multiply, and is usually accompanied by wound inflammation (Horan et al., 1992). Surgical site infections are infections that develop at the surgical site. A SSI is believed to be the result of an exaggerated inflammatory response, which is primed by a surgical insult, and perpetuated and aggravated by various factors such as immediate postoperative immune suppression and exposure to pathogens (Cui and Fang, 2015). Recently, large-scale studies investigating risk factors for SSIs in small animals have been published. In several studies, the administration of prophylactic antimicrobials has been shown to protect animals against the development of SSIs (Whittem et al., 1999; Eugster et al., 2004). Nevertheless, in other studies, it has been shown that omitting prophylactic antimicrobials does not increase the risk of SSIs in clean surgeries if performed by graduated veterinarians (Vasseur et al., 1985; Vasseur et al., 1988; Brown et al., 1997; Stetter et al., 2021). Although the use of prophylactic antimicrobials is undeniably very important in some animals, misuse is to be avoided in the fight against increasing antimicrobial resistance. In this article, all risk factors for the development of SSIs identified in the veterinary literature are discussed, and a flow diagram is proposed as a guide to help determine which dogs and cats may or do not require prophylactic antimicrobials. Furthermore, it is discussed which antimicrobial drugs are most ideal before surgeries of specific organ systems and at what posology.

CLASSIFICATION OF SURGICAL SITE INFECTIONS

Different classification systems have been described for SSIs. Those classification systems originate from human medicine but are also used in veterinary medicine.

Depth of wound infection

Surgical site infections can be divided into superficial (skin and subcutaneous tissue) and deep infections (muscles and fasciae) at the level of the surgical incision, but SSIs can also occur at the level of an organ that was manipulated during surgery (e.g. arthritis) or in the body cavity where the surgery took place (e.g. peritonitis) (Nelson, 2011). Surgical site infections are defined as wound infections related to the surgery that typically occur within thirty days (Weese, 2008). In case an implant has been applied and infection appears related to the surgery, infections that occur within one year postoperatively still qualify as SSIs (Weese, 2008). At the level of implants, a biofilm can develop which may cause recurrent infections that only become apparent after many months (Khatoon et al., 2018). Superficial and deep wound infections are by far the most common presentation of SSIs in companion animals; they occur in 42.0-81.3% and 6.3-50.0% of cases with SSI, respectively (Turk et al., 2015; Espinel-Rupérez et al., 2019). Only in 6.3-8.0% of all SSIs, organs or body cavities are involved (Turk et al., 2015; Espinel-Rupérez et al., 2019).

Type of surgery

Surgeries can be classified according to the degree of contamination that occurs during surgery. Clean surgeries are typically non-traumatic surgeries in non-contaminated or -infected areas (e.g. elective surgeries). After a clean surgery, 2.0-7.9% of dogs and cats develop a SSI (Vasseur et al., 1988; Brown et al., 1997; Eugster et al., 2004; Turk et al., 2015; Espinel-Rupérez et al., 2019; Stetter et al., 2021), and in a prospective randomized blind clinical trial, no difference was found in infection rate between dogs and cats receiving either prophylactic ampicillin or a placebo prior to clean surgery (Vasseur et al., 1985). In clean-contaminated surgeries, a hollow organ is opened in a controlled manner without leakage (e.g. surgical intestinal biopsies) and SSIs have been described in 3.5-8.6% of dogs and cats (Vasseur et al., 1988; Brown et al., 1997; Eugster et al., 2004; Turk et al., 2015; Espinel-Rupérez et al., 2019). When an active inflammation is present or in case of an open traumatic wound, surgeries are classified as contaminated and in case of an infection or in the presence of perforation of the gastro-intestinal tract, surgeries are classified as dirty (Weese, 2008; Nelson, 2011). After contaminated and dirty surgeries, SSIs have been described in 0-12.0% and 6.7-20.0% of dogs and cats, respectively (Vasseur et al., 1988; Brown et al., 1997; Eugster et al., 2004; Turk et al., 2015; Espinel-Rupérez et al., 2019).

RISK FACTORS FOR SURGICAL SITE INFECTIONS

Risk factors can be classified as factors related to the patient, the environment and the treatment, and as pre-, peri-, intra- and postoperative factors. Taking different risk factors into account, the authors propose a flow diagram that can help to define the risk of an individual dog or cat to develop SSI, and consequently the need for prophylactic antimicrobials (Figure 1).

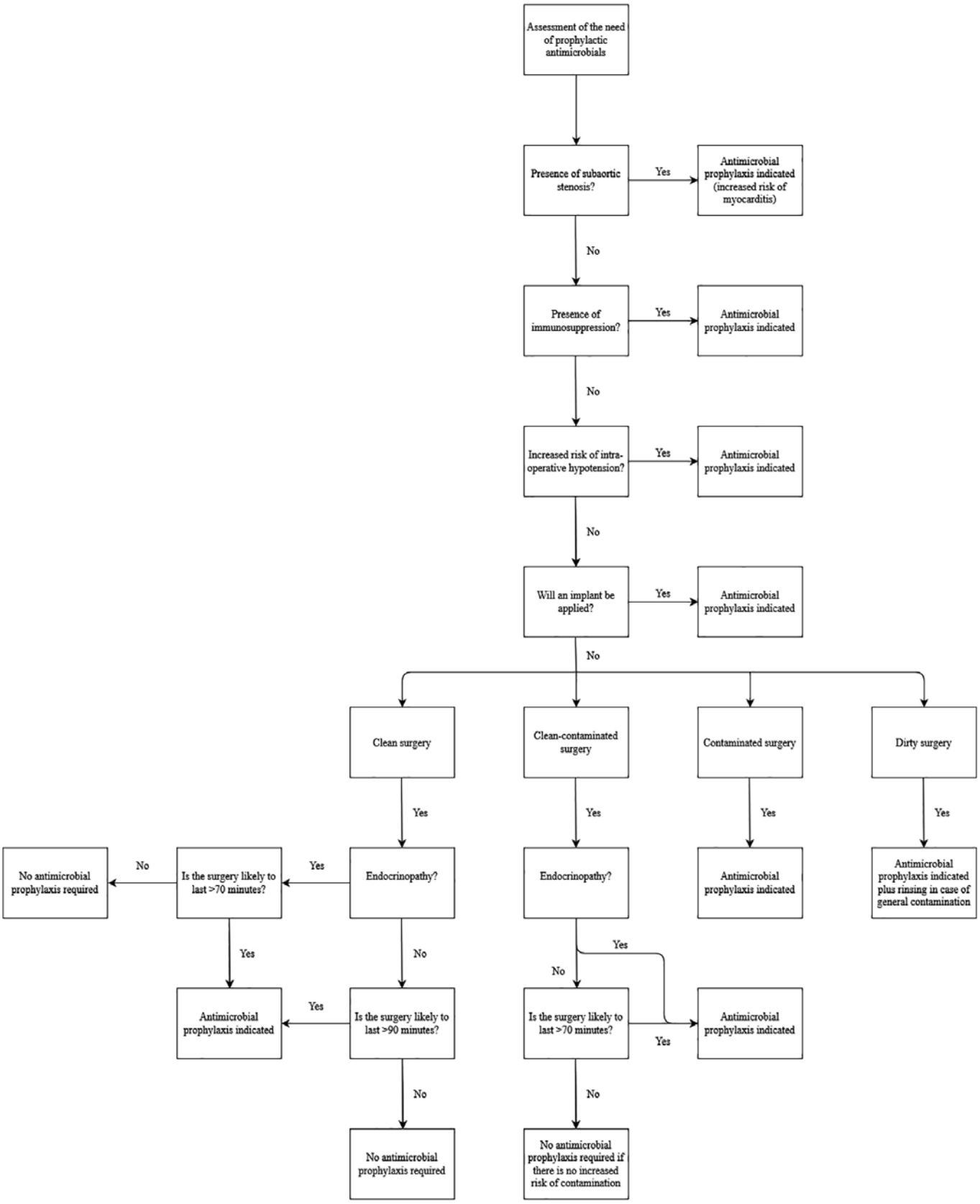

Figure 1. Flow diagram to help define the risk of an individual animal to develop a surgical site infection, and the need for the use of prophylactic antimicrobial drug(s).

Patient-related factors

In a retrospective study by Nicholson et al. (2002) on risk factors for the development of SSIs in dogs and cats after clean-contaminated surgeries, it was found that male intact animals had an increased risk to develop SSIs. This finding was confirmed in a large-scale retrospective study in dogs with cranial cruciate rupture undergoing tibial plateau levelling osteotomy (TPLO) surgery (Fitzpatrick and Solano, 2010). The latter study also identified heavier dogs to be significantly more likely to develop SSI (Fitzpatrick and Solano, 2010). The association between SSI risk and body weight in both dogs and cats had been documented before (Eugster et al., 2004). In dogs with cruciate disease, the breed is also identified as a risk factor; Labrador retrievers seem to have significantly less SSIs, whereas bulldogs have a significantly higher risk of developing SSIs after TPLO surgery (Fitzpatrick and Solano, 2010; Nazarali et al., 2015). In a recent prospective, randomized study performed in dogs undergoing orthopedic surgery, in which implants were applied, the risk of developing SSI increased 1.5 times for each year increase in age (Aiken et al., 2015).

Animals with an endocrinopathy, such as diabetes mellitus, hyperadrenocorticism, hypothyroidism and hyperthyroidism, have been found to have 8.2 times more risk to develop a SSI after undergoing a clean-contaminated surgery (Nicholson et al., 2002). Dogs and cats that were preoperatively treated with corticosteroids and animals with a urinary catheter are also at increased risk (Ruple-Czerniak et al., 2013; Espinel-Rupérez et al., 2019). Furthermore, the presence of preoperative hyperglycemia or a higher body temperature are risk factors for SSI development (Espinel-Rupérez et al., 2019; Piirainen et al., 2019). Dogs with subaortic stenosis are suggested to be at increased risk to develop postoperative infectious endocarditis (Muna et al., 1978). Finally, carriers of multidrug-resistant *Staphylococcus* species have an increased risk of developing a SSI (Nazarali et al., 2015; Piirainen et al., 2019; Välkki et al., 2020).

Environment-related factors

Presurgical hand antisepsis, preoperative surgical site preparation and glove use are crucial components of surgical asepsis that reduce the risk of SSIs (Verwilghen and Singh, 2015; Burgess, 2019). For each additional person in the surgical theatre, the risk of SSI increases by a factor 1.3 (Eugster et al., 2004).

Treatment-related factors

In a recent retrospective study by Piirainen et al. (2019) in 406 dogs, there was no increased risk of SSIs in clean orthopedic or neurosurgeries when no prophylactic antimicrobials were administered, irrespective of whether an implant was applied or not. In a prospective study in 846 dogs by Turk et al. (2015) on the other hand, surgeries in which an implant was placed, were found to have a 5.6 times higher risk of developing a SSI compared to surgeries without implants. However, in a recent large prospective multicenter study by Stetter et al. (2021) including 1550 dogs, the incidence of SSIs was similar in dogs undergoing soft tissue procedures (5.7%) or orthopedic and neurosurgeries (5.0%). Animals in which a passive drain is placed, have an increased risk of a SSI (Eugster et al., 2004). This can be explained by the presence of a foreign object in the wound on the one hand and the fact that the open drain can give rise to an ascending infection on the other hand. Finally, in a study by Frey et al. (2010), it has been shown that the use of stainless-steel staples for skin closure compared to suturing means an increased risk for the development of SSIs after cranial cruciate ligament surgery, making suturing the preferred method to close the skin.

Preoperative risk factors

It has been shown that shaving >4 hours prior to surgery increases the risk of a SSI by four times (Mayhew et al., 2012). However, it has also been found that the timing of preoperative shaving is less important than the fact that it has already been performed before induction, and that the risk of a SSI is significantly decreased if animals are only shaved after induction. This can most likely be explained by the decreased risk of trauma secondary to shaving when animals are under general anesthesia (Brown et al., 1997). Surgical sites clipped before anesthetic induction are three times more likely to become infected than sites clipped after induction (Brown et al., 1997).

Propofol is a fat emulsion, being an ideal culture medium for bacteria. In a retrospective study (1994-1995) by Heldmann et al. (1999), dogs and cats induced with propofol had a 3.8 times higher risk to develop a SSI after a clean surgery. It is important to realize however, that nowadays, preservatives are added to most propofol formulations, which reduce that risk (Feng et al., 2017). An increased risk of developing a SSI is present when multidose vials are used, since they carry a higher risk to become contaminated (Mattner and Gastmeier, 2004).

Perioperative risk factors

The longer the duration of anesthesia and surgery, the higher the risk of a SSI (Brown et al., 1997; Eugster et al., 2004; Nicholson et al., 2002; Stetter et al., 2021). Several studies indicated different durations of anesthesia and surgery, after which the risk of SSI doubles. In a recent prospective study including 184 dogs that underwent soft tissue surgery, it has been shown that the risk of developing a SSI is higher if a surgery takes more than sixty minutes (Espinel-Rupérez et al., 2019). In an older study by Eugster et al.

(2004), the risk of a SSI doubled after seventy minutes of surgery. In two more studies, the risk doubled only after ninety minutes of surgery (Brown et al., 1997; Mayhew et al., 2012). In an additional study, the duration of anesthesia was identified as a risk factor, irrespective of the duration of surgery itself (Beal et al., 2000).

Intraoperative risk factors

After dirty surgeries, there is an increased risk of SSI (Eugster et al., 2004; Turk et al., 2015). Animals that are hypotensive intraoperatively have a 27 times higher risk to develop a SSI (Turk et al., 2015). An excellent surgical technique with strict adherence to Halsted principles (Table 1) is believed to reduce SSIs (Verwilghen and Singh, 2015).

Postoperative risk factors

Long hospital stays increase the risk of SSIs (Ruple-Czerniak et al., 2013). For each day a dog or cat stays in an intensive care unit, the risk of SSIs increases by 1.16 (Eugster et al., 2004). Although prophylactic antimicrobials should typically be discontinued after surgery (see below), continued administration of antimicrobial drugs has a protective effect against the development of SSIs after TPLO surgery (Fitzpatrick and Solano, 2010; Frey et al., 2010; Nazarali et al., 2015; Solano et al., 2015). Nevertheless, in another prospective, randomized study performed in dogs undergoing orthopedic surgery, in which implants were applied (including TPLO), no benefits were revealed of continuing antimicrobial administration postoperatively (Aiken et al., 2015). Finally, not wearing an Elizabethan collar increases the risk of automutilation and consequently the risk of a SSI after any type of surgery (Espinel-Rupérez et al., 2019).

WHAT TYPE(S) OF PROPHYLACTIC ANTIMICROBIAL(S) SHOULD BE ADMINISTERED?

Depending on the organ systems involved during the surgical procedure, a different choice of prophylactic antimicrobial should be made (Table 2).

The most common bacteria on the skin of healthy dogs are *Staphylococcus* spp. (Cox et al., 1988), whereas the most abundant bacteria on the skin of healthy cats are *Bacteroides* spp., bacteria that are typically associated with the oral cavity thus most likely transferred via grooming (Older et al., 2017). To reduce the number of bacteria on the skin, it is crucial to antiseptically prepare the skin prior to surgery (Verwilghen and Singh, 2015). In case of wounds, antimicrobials can never replace proper wound management, including wound lavage and debridement (Nakamura and Daya, 2007). If correctly applied, most commonly used skin preparations (e.g. chlorhexidine and povidone iodine-based preparations) will efficiently reduce the amount of skin bacteria, rendering prophylactic antimicrobials unnecessary (Verwilghen and Singh, 2015). Entering the abdominal or thoracic cavity as such, are clean surgeries in which the only possible contaminating bacteria are skin bacteria. Also, most orthopedic or neurosurgeries without implant placement are regarded as clean surgeries. In the past, it has been argued that antimicrobial prophylaxis in this type of surgeries is advised because of the devastating consequences in case a SSI would occur (Verwilghen and Singh, 2015). In case antimicrobial prophylaxis would be required in these kinds of surgeries, antimicrobials should then be directed against *Staphylococci* spp. (Verwilghen and Singh, 2015). However, a recent retrospective study including 154 dogs revealed that the risk of a SSI after neurosurgery without the use of prophylactic antimicrobials is only 0.6% (Dyall and Schmökel, 2018). Cases included in that study underwent anesthesia for a duration between 60-250 minutes, and the few affected cases only experienced superficial SSIs (Dyall and Schmökel, 2018), suggesting the routine use of prophylactic antimicrobials is unjustified in dogs undergoing neurosurgery.

Table 1. Halsted principles.

Strict aseptic technique
Gentle tissue handling
Meticulous hemostasis
Preservation of blood supply to tissues
Elimination of dead space
Accurate apposition of tissues
Minimal tension on tissues

The oral cavity of dogs and cats is known for its variety of bacterial species, the most important ones being *Staphylococcus* spp, *Streptococcus* spp., *Pasteurella* spp. and anaerobes such as *Bacteroides* spp. (Bailie et al., 1978). Nevertheless, for strictly oral procedures (including dental procedures), prophylactic antimicrobials are not needed because of the excellent blood supply and the antibacterial properties of saliva (Radice et al., 2006; Anderson, 2018). A retrospective study in 375 dogs undergoing oromaxillofacial oncologic surgery revealed that whether or not antimicrobials are administered before, during and/or after surgery, the incidence of SSIs does not change, leading to the recommendation that prophylactic antimicrobials are also not routinely necessary when performing this type of surgery (Rigby et al., 2021).

Because of the acidity of the gastric secretions, only a relatively small number of bacteria is present in the stomach of dogs and cats, with *Helicobacter* spp. being most prevalent (Garcia-Mazcorro et al., 2012). Prophylactic antimicrobials in case of gastric surgery are only needed in case of obstructive dis-

Table 2. Most commonly identified bacteria in different organ systems with the recommended prophylactic antimicrobial(s).

Most common bacteria	Recommended antimicrobials	Remarks
Skin surgery		
Staphylococcus spp. (dogs) *Bacteroides* spp. (cats) Antimicrobials can never replace wound lavage and debridement	* (First generation cephalosporins)	Importance of local disinfection
Cardiac and thoracic surgeries		
Staphylococcus spp.	* (First generation cephalosporins)	
Head and oral surgery (including dental procedures)		
Staphylococcus spp. *Streptococcus* spp. *Pasteurella* spp. Anaerobes	* (First generation cephalosporins) * (Clindamycin)	Because of excellent blood supply and antibacterial properties of saliva, usually no antimicrobials needed
Gastric surgery		
Helicobacter spp.	* (First generation cephalosporins)	Relatively small number of bacteria Only if obstructive disease or perforation
Small intestinal surgery		
Gram-positive cocci Enteric gram-negative anaerobes	* (First generation cephalosporins)	Only if obstructive disease or perforation
Colonic surgery		
Enterococci Gram-negative bacilli Anaerobes	* Second generation cephalosporins * First generation cephalosporins combined with metronidazole	Avoid enema <24h prior to surgery
Anorectal surgery		
Enterococci Gram-negative bacilli Anaerobes	* Second generation cephalosporins which can be combined with metronidazole	Avoid enema <24h prior to surgery Place purse string suture whenever possible
Hepatobiliary surgery		
Clostridium spp. *Staphylococcus* spp. *Escherichia coli* *Enterococcus* spp. *Bacteroides* spp.	* Second generation cephalosporins * Fluoroquinolones combined with penicillin and metronidazole * Fluoroquinolones and potentiated amoxicillin * Fluoroquinolones and clindamycin	
Urinary tract surgery		
Proteobacteria (dogs) *Escherichia coli* (cats) *Enterococcus* spp. (cats)	* (First generation cephalosporins) * (Ampicillin)	
Orthopedic and neurological surgeries without implant placement		
Staphylococcus spp.	* (First generation cephalosporins)	

ease (e.g. gastric dilation volvulus), because bacterial overgrowth can occur, or in case of gastric perforation (Cornell, 2018).

The type and number of bacteria in the small intestinal tract of dogs and cats are different in the proximal versus the distal part (Suchodolski et al., 2005). A retrospective study in 210 dogs and 66 cats revealed that *Escherichia coli* was most commonly cultured from SSIs following gastro-intestinal surgery (Williams et al., 2020). Antimicrobial prophylaxis in clean-contaminated surgeries is not routinely indicated; however, it should be administered in case of obstruction as this causes an increase and shift in bacterial flora (Hicks et al., 1969; Giuffrida and Brown, 2018).

The colon contains a large number of bacteria, with *enterococci*, gram-negative bacilli and anaerobes being the most prevalent microorganisms (Suchodolski et al., 2005; Verwilghen and Singh, 2015). Consequently, antimicrobial prophylaxis is mandatory in any type of colonic surgery and needs to cover a larger spectrum than needed for other gastro-intestinal surgeries (Table 2). Similar bacteria are expected when performing anorectal surgery; however, the risk of bacterial contamination can be limited compared to colonic surgeries by placing a purse string suture on the anus (Suchodolski et al., 2005; Verwilghen and Singh, 2015). In addition, one should be very cautious with enemas prior to colonic or anorectal surgery, as liquid fecal content increases the risk of contamination of the surgical field. In the veterinary literature, no studies have been published on that topic, but there is no proven advantage of preoperative mechanical bowel cleansing in human medicine (Saha et al., 2014).

The liver contains a large number of bacteria. In a study by Niza et al. (2004) on normal canine hepatic flora, 12 out of 20 dogs (60%) had positive cultures when liver tissue was immediately cultured on special blood agar plates and on enriched broth. The most common isolate was *Clostridium perfringens* followed by *Staphylococcus* spp. Approximately half of the positive samples grew a single isolate, and the others grew multiple isolates (Niza et al., 2004). In a clinical study in 248 dogs and cats with confirmed hepatobiliary disease where liver and bile were cultured after being placed in transportable culture media, cats were identified to have more positive culture results in liver tissue than dogs (14% vs. 5%) and more single isolates in liver or bile (cats; 83% single isolate; dogs, 50% single isolate). The majority of cultured organisms were of enteric origin (*Escherichia coli*, *Enterococcus* spp., *Bacteroides* spp., and *Clostridium* spp.) and the high likelihood of multiple isolates warrants broad-spectrum antibacterial coverage in these animals (Wagner et al., 2007). Biliary culture results in dogs and cats were significantly more likely to be positive (30%) than hepatic cultures (7%) in the same study. In none of the cases where the bile culture result was negative, a positive hepatic culture result was obtained (Wagner et al., 2007).

The urogenital tract has long been suggested to be a sterile environment. However, a recent study in dogs revealed that the urinary bladder has a diverse and rich bacterial microbiota, with Proteobacteria being the most prevalent (Burton et al., 2017). This microbiota is different from the genital microbiota, where *Pseudomonas* spp. are the most abundant bacteria (Burton et al., 2017). The most common pathogens identified in dogs with urinary tract infections are *E. coli*, *Staphylococcus intermedius*, *Enterococcus* spp. and *Proteus* spp. (Ball et al., 2008). In cats, subclinical bacteriuria has been identified in 6.2% (31/500) of cases, with the most common bacteria being *E. coli* and *Enterococcus* spp. (Puchot et al., 2017). In the genital tract of healthy cats, *E. coli*, *Staphylococcus* spp. and *Streptococcus canis* are the most abundant bacteria (Clemetson and Ward, 1990; Holst et al., 2003).

Whenever implants are placed, there is a risk of biofilm formation. A biofilm is formed by bacteria and protects them physically against antimicrobials and host mechanisms (Khatoon et al., 2018). Furthermore, biofilms capture and concentrate nutrients for bacteria, and bacteria can change to a quiescent growth pattern while protected by the biofilm. Once a biofilm is formed, it is very difficult to disrupt it and remove all potential bacteria hosted within the biofilm (Khatoon et al., 2018). The results of an in vitro study by Ferran et al. (2016) suggested that marbofloxacin prevents biofilm formation better than amoxicillin, cephalexin, doxycycline or clindamycin. However, no in vivo studies have been performed to confirm these data. Based on the available literature, it is currently not advised to give marbofloxacin to every animal receiving an implant.

A serious threat is the emergence of multidrug-resistant bacteria and their association with SSIs. In a recent prospective study by Turk et al. (2015), *Staphylococcus* spp. were found in 73.3% of dogs that developed a SSI, and 63.2% of those were multidrug-resistant strains. A potential history of prior antimicrobial therapy was not mentioned. In a study by Windahl et al. (2015), the resistance to penicillin and ampicillin in case of SSIs in dogs was investigated. They found that two thirds of the bacteria involved in SSIs were *Staphylococci*, of which 80% were resistant to penicillin and ampicillin. In that study, 36% of the dogs that had received antimicrobial therapy prior to surgery, had multidrug-resistant bacteria causing the SSI (Windahl et al., 2015). This underlines the importance of avoiding antimicrobial overuse.

For most surgical procedures, first generation cephalosporins (e.g. cefazolin) are the first choice (Rosin et al., 1993). Although potentiated amoxicillin (amoxicillin/clavulanic acid) is still one of the most used antimicrobials in clinical practice, it is not recommended, not only because of the increased resis-

Table 3. Important questions to ask in regard to prophylactic antimicrobials.

Antimicrobial prophylaxis required?	See Figure 1
Type of prophylactic antimicrobial drug(s) recommended?	See Table 2
Timing and route of prophylactic antimicrobial drug(s) administration?	30-60 minutes before the start of surgery; intravenous administration
Dose interval of prophylactic antimicrobial drug(s)?	First generation cephalosporins: 4 hours, if surgery is still ongoing *(in veterinary medicine, data are only available for first generation cephalosporines)*
Duration of prophylactic antimicrobial drug(s) administration	Ideally stop immediately after surgery (maximum 24 hours postoperatively)

tance of bacteria against (potentiated) amoxicillin, but also because clavulanic acid is an emerging drug used in human medicine in patients with multidrug-resistant bacteria (Davies and Davies, 2010). For similar reasons, fluoroquinolones (enrofloxacin, marbofloxacin, pradofloxacin) should be used with the utmost prudence (Davies and Davies, 2010). In selected cases, depending on the organ(s) involved during the surgical procedure, another choice than first generation cephalosporins might be more appropriate (Table 2).

In dogs or cats that already have an infection prior to surgery and in which antimicrobial susceptibility testing has been performed, the appropriate antimicrobial drug might need to be continued during and after surgery.

WHEN AND FOR HOW LONG DO PROPHYLACTIC ANTIMICROBIALS NEED TO BE ADMINISTERED?

Besides determining the need and type of prophylactic antimicrobials, the timing, dosage, dose interval and duration are important (Table 3). The prophylactic antimicrobial drug needs to be efficacious against the most likely bacteria present within the surgical field. It is not only important to have sufficiently high plasma concentrations prior to the start of surgery, the local concentration of the antimicrobial drugs in the wound bed needs to be adequate as well. In order to obtain appropriate plasma concentrations at the time of surgery, prophylactic antimicrobials need to be administered thirty to sixty minutes before the start of surgery. Antimicrobials need to be administered every two half-lives of the drug used (Boothe and Boothe, 2015). In veterinary medicine, in only one study, the pharmacokinetics of a prophylactic antimicrobial has been investigated. In that study, it was demonstrated that cefazolin, a first generation cephalosporin, given at a dose of 22 mg/kg intravenously, needs to be repeated four hours after the first intravenous administration, if the surgery is still ongoing at that time (Gonzalez et al., 2017).

Prophylactic antimicrobials should not be continued after surgery and should be stopped 24 hours postoperatively the latest (Aiken et al., 2015). In a retrospective study by Välkki et al. (2020) including 406 dogs undergoing clean orthopedic and neurosurgeries, in which 92.1% of the dogs received prophylactic antimicrobials and 1.1% also received postoperative antimicrobials, the rate of SSIs was 6.3%, suggesting that using only perioperative antimicrobial prophylaxis (without postoperative continuation) does not increase the risk of developing a SSI. In a retrospective study by Korytárová et al. (2022) including 158 dogs undergoing neurosurgery, in which all dogs received prophylactic antimicrobials and 58.2% also received postoperative antimicrobials, a similar rate of SSIs in both groups was found (1.1% in dogs receiving postoperative antimicrobials versus 1.5% in dogs only receiving prophylactic antimicrobials).

CONCLUSION

Based on the published risk factors, the authors propose a flow diagram to help decide which animals most likely would or would not benefit from antimicrobial prophylaxis. Nevertheless, an individual approach remains necessary and advantages and disadvantages of the use of prophylactic antimicrobials need to be outweighed in each animal. If possible, prophylactic antimicrobials should be omitted to help reduce antimicrobial (multidrug-) resistance formation. Importantly, antimicrobial prophylaxis can never replace aseptic surgical techniques with correct tissue handling, respecting the Halsted principles.

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Oproep

Vragen uit de dierenartsenpraktijk

De vraag- en antwoordrubriek behandelt reeds lang probleem- en vraagstellingen waarmee de dierenarts-practicus te maken krijgt. Het is een graag gelezen rubriek en om haar succes staande te houden, zijn wij immer op zoek naar vragen die oprijzen tijdens de praktijk.

Indien u met een dergelijk probleem of vraag geconfronteerd werd/wordt, dan kunt u ze te allen tijde doorsturen naar nadia.eeckhout@ugent.be Ze worden door een expert (Faculteit Diergeneeskunde of elders) van een deskundig antwoord voorzien dat samen met de vraag in het tijdschrift gepubliceerd wordt.