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Definition, prevention, and management of surgical site infections

Definizione, prevenzione e gestione delle infezioni del sito chirurgico

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Anno Accademico 2022-2023

SUMMARY

ABSTRACT

Surgical site infection (SSI) is one of the most common complications in veterinary medicine. Surgical site infections are a major cause of morbidity and mortality across the world.

It is essential to follow standard guidelines when conducting studies on the incidence of surgical site infections to obtain consistent data across studies.

It is also important to know the risk factors that can predispose to the onset of a surgical site infection (SSI). This knowledge allows for action to prevent or stem the onset of SSI, which is crucial to improving the outcome of surgical patients.
The identification of patients at high risk of contracting SSI, the application of correct aseptic rules, close surveillance of the incidence of SSIs in the clinic, and moderate use of antimicrobials are the basis of the correct management of the surgical patient.

It's important to note that not all surgical site infections require antimicrobial therapy. Ideally, antimicrobial therapy should only be considered after conducting culture and sensitivity tests to minimize the unjustified use of antimicrobials. The unregulated use of antimicrobials has contributed to the rise in antimicrobial resistance. Therefore, it's ethically crucial for all veterinarians to use antimicrobials more consciously to combat this global issue.

INTRODUCTION

Healthcare-associated infections (HAI) are one of the major threats to patient's health and are one of the biggest challenges for healthcare in both human beings and animals. Among HAIs, surgical site infection (SSI) is one of the most common complications in both human and veterinary medicine. Surgical site infections are a major cause of morbidity and mortality across the world. [1]

Surgical site infection was the most surveyed and most frequent healthcare-associated infection in low-income and middle-income Countries, affecting up to one third of human patients undergone surgery. The incidence is much lower in high-income Countries, but it is still the second most common cause of health-care-associated infection in Europe and the USA.[2] Furthermore, data from the USA showed that up to 60% of the microorganisms isolated from infected surgical wounds have antibiotic resistance patterns. [2]

The veterinary literature dealing with SSI is far less rich compared to the human counterpart, and many items of the veterinary guidelines are mediated from there. In addition, studies in veterinary medicine can present highly variable data since the same criteria are not internationally adopted for defining a surgical site infection. Data from the veterinary literature report an incidence of SSI varying from 3% to 10% in dogs and cats.[3] Many factors in the patient's journey through surgery contribute to the risk of SSI, and prevention is complex and requires the integration of a range of measures before, during, and after surgery. Although some of the factors contributing to SSI cannot be influenced, there are measures that can be undertaken perioperatively to prevent them. All the people of the team working around the patient must know the causes that increase the risk of developing an SSI, so that they can take actions to reduce the prevalence.

In recent years, several studies in veterinary medicine have begun to follow the guidelines adopted in human medicine for the definition of SSIs, in order to present uniform data and discriminate self-limiting, mild inflammation.[3] Different definitions of SSI have been developed, different risk factors have been identified, and different guidelines have been drawn up over the last few decades. On the one hand, studies carried out in the past have made it possible to incredibly reduce the prevalence of certain risk factors, e.g. by implementing rules of asepsis and surgical site preparation, in both human and veterinary hospitals. On the other hand, the most recent studies have brought to light new factors to be considered in the prevention of SSIs. Continuing vigilance is therefore required, applying a systematic approach, with attention to multiple risk factors related to the patient, the procedure, and the hospital environment. In addition to documenting a relevant part of the healthcare system, the surveillance adopted in each clinical practice itself, even without any specific intervention, has been associated with a reduction in SSI incidence.[4]

This thesis aims to provide an overview of the definitions of surgical site infection and to indicate which risk factors have been recognized, to have a clearer vision of how to prevent them with regard to the importance of surveillance in the prevention of surgical site infections.

Finally, this thesis aims to highlight the guidelines for the treatment of SSIs, with regard to the use of antibiotics, also considering the worldwide increase in antibiotic resistance.

DEFINITION OF SURGICAL SITE INFECTION (SSI)

One of the most complex challenges in managing SSIs is recognizing them. Therefore, it is essential to have guidelines that allow to differentiate infection from inflammation. This makes it possible to identify the correct therapy and to have uniform data in studies reporting cases of SSI. The United States public control centers for human infectious diseases (Centers for Disease Control and Prevention [CDC]) drew the Guidelines for the prevention of SSIs in 1999[5], and divided the surgical wounds into four classes: clean, clean-contaminated, contaminated, and dirty or infected (Table 1). In veterinary medicine, this classification has often been considered the only factor in selecting antibiotic prophylaxis. More recent studies, which will be discussed later, have shown that other factors must be considered when choosing antibiotic prophylaxis.

Table 1.Standard Definitions of Surgical Wound adapted from Johnston, Tobias, Veterinary Surgery Small Animal, 2018[6]; Mangram et al., 1999[5]; Burgess et al., 2019[7]

Clean	An uninfected surgical wound in which no inflammation is encountered, and the respiratory, alimentary, genital or uninfected urinary tracts are not entered. In addition, clean wounds are primarily closed and, if necessary, drained with closed drainage. Surgical incisional wounds that follow non-penetrating trauma should be included in this category if they meet the criteria.
Clean-contaminated	Surgical wounds in which the respiratory, alimentary, genital or urinary tracts are entered under controlled conditions and without unusual contamination. Specifically, surgeries involving the biliary tract, vagina and oropharynx are included in this category, provided no evidence of infection or major break in technique is encountered.
Contaminated	Open, fresh, accidental wounds. In addition, surgeries with major breaks in sterile technique or gross spillage from the gastrointestinal tract, and incisions in which acute, non-purulent inflammation is encountered, including necrotic tissue without evidence of purulent discharge.
Dirty or infected	Old traumatic wounds with retained devitalized tissue and those that involve existing clinical infection or perforated viscera. This definition suggests that the organisms causing postoperative infection were present in the operative field before the operation.

The definition of surgical site infection was first described in human medicine[5]. In recent years, the CDC criteria for defining surgical site infection have also been adopted in veterinary medicine. Nowadays, most studies in veterinary medicine use the following definition for SSIs. Although 1999's guidelines are outdated and developments have been made regarding the discovery of risk and prevention factors, the criteria for defining an SSI that they propose are still used today. A SSI is defined as an infection occurring within 30 days from a surgical procedure or 1 year from a surgical procedure if an implant is used. Surgical site infections are divided based on location into superficial, deep, and organ/space (Figure 1). To define the category to which they belong, they must meet one or more of the following clinical aspects:

- Superficial incisional SSIs are those affecting only the skin or subcutaneous tissues at the incision site. At least one of the following clinical aspects must be present:
    - Purulent discharge
    - Organisms isolated from an aseptically collected sample of fluid or tissue
    - Pain, heat, redness, or localized swelling, and the surgeon decides to operate on the wound. The presence of any of these factors justifies the presence of an infection unless the culture test is negative.
- Deep incisional SSIs are SSIs that affect deep soft tissues at the incision site. At least one of the following clinical aspects must be present:
    - Purulent discharge from the deep incision but not from organ/space
    - Deep incision spontaneously dehisces or is deliberately opened when the patient has one or more of fever, localized pain, or tenderness. The presence of any of these factors justifies the presence of an infection unless the culture test is negative.
    - Abscess or other evidence of infection on direct exam, during revision surgery, or by histopathology or radiology.
- Organ/space incisional SSIs are SSIs affecting any area other than the incision that was opened or manipulated during surgery. At least one of the following clinical aspects must be present:
    - Purulent discharge from the drain that is placed into the organ/space
    - Organisms isolated from aseptically collected samples from organ/space

- Abscess or other evidence of infection on direct exam, during revision surgery, or by histopathology or radiology
- Diagnosis of organ/space SSI by attending clinicians.

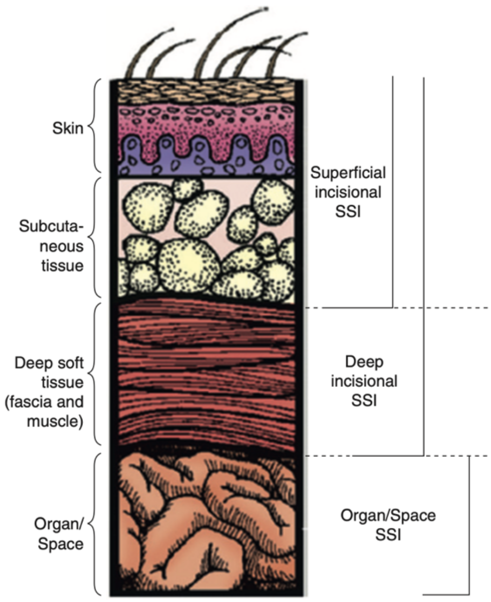

Figure 1

Cross-section of the abdominal wall depicting Centers for Disease Control and Prevention classifications of surgical site infection *(SSI)*.[6]

A recent study proposed to grade post-operative wound infections from 1 to 5 based on the severity of the infection in accordance with the Veterinary Cooperative Oncology Group—Common Terminology Criteria for Adverse Events (VCOG-CTCAE v2) guidelines[8]:

- Grade 1: localized infection in which local intervention is indicated
- Grade 2: oral antimicrobial administration is indicated
- Grade 3: infection in which antibiotic administration and invasive intervention are required (e.g., debridement, drainage, or repair)
- Grade 4: the infection has caused life-threatening consequences, and urgent action is needed
- Grade 5: patient's death

INCIDENCE OF SURGICAL SITE INFECTIONS

Although the studies regarding the incidence of SSIs in veterinary medicine are much lower than in human medicine, the incidence of infection in veterinary medicine is comparable.[6] Studies about the epidemiology of SSIs are difficult because of the heterogeneous nature of these infections. The incidence varies considerably between procedures, hospital, surgeon, and patient.[9]

The risk of development of an SSI after microbial contamination of a surgical site depends on the dose and virulence of the pathogen and on the patient's resistance.

$$Risk\ of\ SSI = \frac{\text{dose of bacterial contamination x virulence}}{\text{Resistance of the patient}}$$

The risk of SSI is considered elevated when the level of contamination exceeds 10^5 organisms per gram of tissue.[9] This threshold can be lower if foreign materials such as sutures are present. [5]
A study about the global incidence of SSI among human patients reported a worldwide incidence of 2.5%. Based on subgroup analysis by survey year, studies conducted between 2014 and 2022 had the lowest pooled incidence of surgical site infections among patients (0.4%), while studies conducted between 1996 and 2004 had the highest (3.2%).[1] The same study highlighted that SSI is substantially higher in low-income and middle-income Countries compared to high-income ones.

No studies have been carried out in veterinary field comparing the difference in the incidence of SSIs between low-income and high-income Countries, but it can be assumed that the trend is similar, since the difference in the incidence of SSIs between the two areas has also been associated with a different application of common hygiene and prevention standards.
In veterinary medicine, reported rates are variable, and it is difficult to compare studies because of different (or inadequately described) criteria for the identification of SSIs. A prospective study carried out in 2004 on the incidence of SSIs in dogs and cats showed that when evaluating the same sample of animals, the results differed in the case of a strict consideration of surgical infection (3%) or when also mild inflammation was included among the complications (5.8%).[10]
In addition, other studies[11–15] focused their research on single surgical procedures, making it

difficult to assess the overall incidence of SSIs (Table 2). Despite the difficulty in finding homogeneous data, the trend of the last decades, as shown in human medicine, seems to be moving toward a global decrease in SSIs, as reported in two large studies (Table 3).

Table 2. SSI rates in different veterinary surgical procedures adapted from S. A. Johnston, K. M. Tobias, Veterinary surgery Small Animal, 2018[6]; *Vasseur et al., 1988*[16]; *Eugster et al., 2004*[10]; *Nicholson et al., 2002*[17]; *Tracy et al., 2010*[11]; *Fitzpatrick et al., 2010*[12]; *Mayhew et al., 2012*[18]; *Turk et al., 2015*[3]; *Williams et al., 2020*[13]; *Spåre et al., 2021*[14]; *Turkki et al., 2023*[15].

PROCEDURE	**SSI rate (%)**	**Author**
All clean procedures	2.5%	Vasseur et al., 1988[16]
All dirty procedures	18.1%	Vasseur et al., 1988[16]
All surgical procedures	3%	Eugster et al., 2004[10]
Clean-contamined procedures	5.9%	Nicholson et al., 2002[17]
ECLS	4.2%	Tracy et al., 2010[11]
TPLO	8.4%	Tracy et al., 2010[11]
TPLO	6.6%	Fitzpatrick et al., 2010[12]
Minimally invasive procedures	1.7%	Mayhew et al., 2012[18]
Open surgery procedures	5.5%	Mayhew et al., 2012[18]
All surgical procedures	3%	Turk et al., 2015[3]
Gastrointestinal surgery	7%	Williams et al., 2020[13]
Mastectomy	8.9%	Spåre et al., 2021[14]
OHE in dogs with pyometra	7.1%	Turkki et al., 2023[15]

ECLS= extracapsular lateral suture; TPLO= tibial plateau leveling osteotomy; OHE= ovariohysterectomy

Table 3. SSI rates by wound classification

Procedures classification	**Infection rates Vasseur et al., 1988**[16]	**Infection rates Eugster et al., 2004**[10]
Clean	2.5%	2%
Clean-contaminated	4.5%	3.5%
Contaminated	5.8%	4%
Dirty	18.1%	6.7%

RISK FACTORS OF SURGICAL SITE INFECTION

When managing the risks associated with the occurrence of SSIs, 3 key factors must be considered in the development of the disease: the agent, the host, and the environment.

- The **agent** is the microorganism that causes the SSI. Agents described as risk factors are biological factors, including the pathogens associated with the surgical site, which can be endogenous or exogenous microorganisms. Endogenous microorganisms are those commonly found on the surgical site, and they may be pathogens or not; exogenous microorganisms usually derive from the environment. The agents can also be physical or chemical agents that predispose to secondary bacterial infection from the aforementioned microorganisms. Chemical agents can be, for example, agents that alter the integrity of the skin. Some animals may develop a skin reaction following the surgical scrub with povidone-iodine that increases the chance of contracting an SSI. Physical agents may be an overly aggressive surgical scrub or a shear that alters the integrity of the skin.[6] The implantation of metal prosthesis may predispose to the nesting of circulating bacteria coming from different sites of the body, thus causing contamination of the surgical site.
- The **host** factors can be intrinsic or extrinsic. Intrinsic factors are directly related to the patient, such as the age or the BCS; extrinsic factors come from the external environment, such as from other hospitalized patients.
- **Environmental** factors are usually considered as extrinsic factors. They can be animated environmental factors, such as the personnel working in the hospital or the other patients, and inanimated environmental factors, such as surgical instruments, operating room and recovery units. When considering SSI, the literature consistently reports an increased risk associated with the duration of surgery, the time of perioperative clipping, and the number of persons in the operating room.[7] These risk factors are all related to the environment since they affect the time of exposure to environmental bacterial contamination (in the case of increased surgery time) and the amount of bacterial contamination present in the environment (in the case of the number of people present in the operating room).

The risk factors can also be divided into patient-related factors and surgery-related factors. Table 4 provides some examples of themes.

Table 4. Patient-related and procedure-related factors that may influence the risk of surgical site infection adapted from Stetter et al., 2021[19]

Patient-related risk factors	**Procedure-related risk factors**
Age	Duration of anesthesia
American Society of Anesthesiologists (ASA) status	Duration of surgery
Hypotension	Use of surgical implants
Presence of endocrine disease	Use of perioperative antimicrobial prophylaxis (AMP)
Body condition score (BCS)	Time of preoperative hair clipping
	Number of persons in the operating room
	Post-operative use of antimicrobials
	Skin antisepsis
	Preoperative skin preparation
	Use of surgical drains

PATIENT-RELATED RISK FACTORS

Patient-related risk factors are often uninfluenced; they cannot be acted upon to prevent them. Knowing them is important for recognizing patients most at risk of contracting an SSI following surgical procedures.

It has been seen that the sex of an animal can be a risk factor towards which no precautions can be taken. In 2002 a study reported that **intact males** were at a higher risk for postoperative wound infections after clean-contaminated surgeries.[17] For this reason, every time a intact male undergoes a surgical procedure, it must be taken into account that he may have a greater chance of developing an SSI and consequently more care must be taken in acting on all the risk factors that can be prevented.

In 2004 **elevated BCS** of the dogs was found to be a risk factor.[10] The same study demonstrated that an **increasing American Society of Anesthesiologists (ASA) score** was associated with an increasing wound infection rate.[10]

The infection rate also increases as the degree of **bacterial contamination** of skin, environment, and surgical site increases.[10,16,20] The microorganisms are often endogenous and related to the surgical site. Table 5 reports some examples of surgical site bacterial species.

Table 5. Bacterial species colonizing different surgical sites in small animals.[21]

Site	**Bacterial species**
Skin	*Staphylococci, Streptococci, Corynebacteria*
Elective orthopedics	*Staphylococci, Streptococci, Corynebacteria*
Neurosurgery	*Staphylococci, Streptococci, Corynebacteria*
Oral cavity	*Pasteurellae, Streptococci, Corynebacteria, Actinomycetes Fusobacteria, Porphyromonas, Prevotella, Bacteroides*
Upper GI tract	*Staphylococci, Streptococci, Enterococci, Clostridia, Bacteroides, Fusobacteria*, other aerobic and anaerobic gram-positive cocci and rods, coliforms
Lower GI tract	*Clostridia, anaerobic positive Cocci, Bacteroides, Fusobacteria, Coliforms, Enterococci, Streptococci,* gram-positive Rods
Urinary tract	*Coliforms, Enterococci, Staphylococci*
Reproductive trat	*Coliforms, Streptococci, Pasteurellae, Staphylococci*

Risk factors such as sex, age, BCS, and ASA score cannot be modified by the team working for the patient, therefore, the only thing that can be done is to be very careful in preventing other risk factors, such as the presence of concomitant diseases, the occurrence of hypotension at any time during the procedure, or bacterial contamination of the surgical site. A careful monitoring of blood pressure during surgery and perioperatively, also by the administration of drugs that contrast hypotension, and therapies to control concomitant diseases may contribute to the control of SSIs. Any **disease or treatment** that compromises the patient's overall health status can potentially impact the surgical site infection risk.[6] A study demonstrated that dogs with hypotension at any point of the surgery have an increased rate of SSIs[3]for this reason, it is important to act by counteracting hypotension pharmacologically. The presence of concomitant diseases can increase the risk of contracting an SSI both because of the patient's compromised state of health and because some therapies could affect causing immune depression and increasing the risk of contracting an infection. Several studies have shown that **concurrent endocrinopathies** increase the risk of contracting SSI by 8.2 times.[17,18,22]

Finally, it is important that an adequate surgical scrub is carried out to minimize bacterial contamination of the incision site and that appropriate measures are used in case of concomitant bacterial contamination in other areas.

PROCEDURE-RELATED RISK FACTORS

Procedure-related risk factors are factors that may depend on the procedure itself, therefore cannot be influenced (e.g. the use of a surgical implant) or factors that can be influenced, e.g. the decision of when to perform preoperative clipping or the number of people present in the operating room.

In 1997 **preoperative clipping** immediately before surgery has been shown to decrease the risk of infection in small animals.[20] In dogs, clipping before anesthetic induction was associated with an increased risk of SSI. In this case, the increased risk of a surgical site infection may be related to the fact that clipping a conscious animal can increase the risk of causing trauma to the skin.[6]

The **duration of surgery** as a risk factor for infection has been investigated in many studies. It has been shown that longer surgical procedures (>90 minutes) have a greater risk of infection, [10,16,20] with the risk doubling for each hour of surgery.[6] Prolonged surgery allows the surgical site to be exposed to bacteria for a longer period of time, and increases their chance of adhesion. In addition, more complex surgeries are associated with longer surgical times and, likely, result in progressive wound desiccation and trauma, thus weakening the host immune response and making it more likely that the surgical site is contaminated by bacteria.[6] The duration of the surgery may depend both on the type of procedure itself and on the surgeon's experience. Moreover, an increased rate of SSIs is associated with a longer **anesthesia time**. The risk in clean wounds increases by 30% for each additional hour of anesthesia.[10]

Another risk factor is the **number of people present in the operating room**.[20] For each additional person in the surgical room, the risk of SSI is 1.3 times higher.[10] In addition, a study aiming at evaluating the difference in the prevalence of SSIs between minimally invasive and open surgeries showed that minimally invasive surgeries are associated with a lower rate of SSIs, but some confounding factors, such as the different length of the procedures, may have played a role. Therefore, the **surgical approach** cannot be identified as an independent risk factor.[18]

The risk of developing SSI for dogs with implanted medical devices is 5.6 times that of dogs without surgical implants. **Surgical implants** can become colonized with bacteria and are a recognized risk factor for SSI.[3]

The use of an adhesive incise drape did not significantly reduce the frequency of bacterial contamination of canine clean surgical wounds in a study conducted in 2009 out of 100 dogs submitted to ovariohysterectomy (76 dogs) or stifle surgery (24 dogs).[23] The surgical procedures were carried out uniformly, and the dogs were divided into two groups; one group was given an incise drape after surgery so as to cover the surgical wound, and the other was not. Incise drapes work by creating a barrier between the wound and the external environment, preventing exogenous bacteria from contaminating the wound. Since most bacteria that cause surgical site infections on the skin are commensal bacteria, the percentage of SSIs did not differ between the two groups. A sample taken from positive SSI cases in both groups showed a prevalence of Staphylococcus *spp*, a common skin bacterium. This demonstrates the usefulness of adhesive incise drapes in preventing contamination by exogenous bacteria but, at the same time, shows that they are not useful in the prevention of skin SSIs since the bacteria that cause them are endogenous most of the time.

Another very important risk factor is the use of **antibiotic prophylaxis** and post-operative antibiotics. The next chapters will cover the use of antimicrobials in preventing SSIs and their importance in the increase of antibiotic-resistant microorganisms.

PATHOGENS IN SURGICAL SITE INFECTIONS

Pathogens responsible for SSIs could be endogenous or exogenous. The former could be microorganisms that can be found as common inhabitants in some districts of animal bodies, or they can be microorganisms that are translocated from infections in other districts. Exogenous pathogens are environmental microorganisms that can somehow colonize the wound during the perioperative time.

For most SSIs, pathogens are of endogenous origin and derive from the patient's endogenous flora of the skin, membranes, and hollow viscera (Table 5). When the skin or membranes are incised, the tissues are exposed to endogenous bacterial flora that can contaminate them. These pathogens are usually aerobic gram-positive cocci (e.g., staphylococci) but may include fecal flora, when incisions are made in the digestive tract. When the gastrointestinal tract is opened during surgery, the source of pathogens can include gram-negative bacilli (e.g. *E. coli),* gram-positive organisms (e.g., enterococci), and sometimes anaerobes. In addition to the microorganisms present at the surgical site, a concurrent infection in another district can cause contamination of the surgical site, especially in the case of surgeries where an implant is positioned.[5]
A prospective study conducted on dogs and cats who underwent gastrointestinal surgery investigated microorganisms associated with SSIs. Bacteria native from the gastrointestinal tract were the most frequently isolated.[13]

Exogenous pathogens isolated from SSI may derive from surgical personnel (surgical team members), the operating room environment, and all tools, instruments, and objects brought into the sterile field during an operation. Exogenous flora is composed primarily by aerobes, especially gram-positive organisms (e.g., Staphylococci and Streptococci).[5]

In 2016, a study investigated intraoperative bacterial contamination in dogs during clean orthopedic procedures. Eighty-one percent of the procedures had some degree of bacterial contamination. Sixty-three percent had low contamination, 31 had moderate contamination, and 8% had high contamination. *Staphylococcus* spp. was the most recovered bacteria from surgical gloves, hands, and dogs' skin, suggesting that the human and canine microbiomes are predominant contributors to the intraoperative bacterial load. Despite 81% of cases presenting intraoperative contamination rates, the contamination was low in most cases, and there was no association between intraoperative bacterial contamination and postoperative SSI.[24] This indicates that, while it is impossible to completely eradicate the environmental contamination, following aseptic procedures during surgery can avoid most of the infections of the surgical site.

Staphylococci are one of the most represented pathogens when an SSI occurs.[3,21,25] *S. pseudintermedius* and *S. aureus* are common opportunistic pathogens and leading causes of SSI in animals.[3,21] The risk of developing a SSI due to different bacteria can vary depending on the type of surgery performed. For instance, different types of bacteria may be involved in abdominal or orthopedic surgery. However, some leading causes of SSI are relatively predictable, since the primary pathogens responsible for the infection are typically present in the area of the body where the surgery is performed. The commensal bacteria in each district of the body are well-known (Table 6).

Table 6

Bacteria Commonly Responsible for Surgical Site Infections Associated with a Variety of Surgical Procedures and recommended perioperative antimicrobials.[6]

SURGICAL PROCEDURE	**ANTICIPATED BACTERIA**	***RECOMMENDED PERIOPERATIVE ANTIMICROBIAL***
Skin and reconstructive surgery	*Staphylococcus* spp.	Cefazolin
Head and neck surgery	*Staphylococcus* spp., *Streptococcus* spp., anaerobes	Cefazolin or clyndamicin
Orthopedic surgery - Elective procedures, closed fractures	*Staphylococcus* spp.	Cefazolin
Orthopedic surgery - Open fractures	*Staphylococcus* spp., *Streptococcus* spp., anaerobes	Cefazolin or clyndamicin
Thoracic surgery	*Staphylococcus* spp.	Cefazolin
Abdominal surgery (non-gastrointestinal)	*Staphylococcus* spp.	Cefazolin
Upper gastrointestinal surgery	Gram-positive cocci, enteric Gram-negative bacilli	Cefazolin
Hepatobiliary surgery	*Clostridium* spp., Gram-negative bacilli, anaerobes	Cefotixin

Lower gastrointestinal surgery	Enterococci, Gram-negative bacilli, anaerobes	Cefotixin
Urogenital surgery	*Streptococcus* spp., *Staphylococcus* spp., *Escherichia coli*, anaerobes	Cefazolin or ampicillin

As indicated in Table 6 and as a result of various studies about pathogens associated with SSIs, of particular concern are *Staphylococci, Enterococci, Pseudomonas*, and *Escherichia coli*, all of which can exhibit multidrug resistance and can persist in the hospital environment.[7]
An in-depth study of multidrug-resistant pathogens is necessary since they are increasingly important in small animal infections.

MULTIDRUG-RESISTANT PATHOGENS IN SURGICAL SITE INFECTIONS

Due to the emergence of multi-resistant bacteria as a global health concern, it is essential to understand further the factors associated with developing SSI and other postoperative complications in patients undergoing surgery, to reduce the routine use of antimicrobial perioperative prophylaxis. Increased antibiotic resistance has been related to inappropriate use of antibiotics. When an SSI occurs, antimicrobial treatment should be chosen based on the results of culture and sensitivity tests. The most critical multidrug-resistant pathogens in veterinary medicine are resistant strains of Staphylococci, Enterococci, and Pseudomonas.

1. METICILLIN-RESISTANT STAPHYLOCOCCI

Postsurgical infections with methicillin-resistant staphylococci (MRS) in dogs are usually caused by *Staphylococcus pseudintermedius* (MRSP) or Staphylococcus aureus (MRSA). These bacteria can be found in the nose, mouth, intestine, and skin of healthy dogs and human beings.[21] Staphylococci are bacteria that naturally live on the skin of both humans and animals. To prevent infections caused by these bacteria, it is essential to perform thorough surgical scrubs and follow strict aseptic protocols during the surgical procedures.

The emergence of multidrug-resistant *S. pseudintermedius* isolates in the last few years, particularly methicillin-resistant strains (MRSP), threatens small animal health and highlights the need for antimicrobial resistance surveillance to detect trends and potentially perform timely interventions.[26] The resistance problem is a major concern because of the limitation in the use of antimicrobial molecules in veterinary medicine due to the cross-resistance with the human counterpart. The major complexity in treating infections with methicillin-resistant strains is to identify an effective antimicrobial treatment and to do so, it is essential to rely on the sensitive test results.

The therapeutic approach for SSIs caused by MRS does not involve actions different from those taken for all other SSIs. Although systemic antimicrobial therapy is most often required, superficial infections might respond to local actions such as suture removal and local treatment with antiseptics and antimicrobials.

1.1. MRSA

Alongside the increasing number of MRSA-associated infections in human medicine, there has been much interest in animal MRSA infection. The prevalence of methicillin resistance in clinical veterinary *S. aureus* isolates has been reported to be approximately 25% to 35%.[27] MRSAs are resistant to almost all beta-lactam antimicrobials. Fluoroquinolones should also be avoided due to their unpredictability of treatment response and propensity to improve resistance during treatment. The phenomenon of resistance to clindamycin is a cause for concern as some susceptible strains in vitro develop resistance in vivo. Therefore, clindamycin should be avoided in erythromycin-resistant MRSA.[21] Depending on the results obtained from the sensitivity tests, they can be treated with trimethoprim or chloramphenicol.[28] Since they can cause zoonoses, the use of vancomycin in their treatment is restricted in veterinary medicine.

1.2. MRSP

The first methicillin-resistant *S. pseudintermedius* (MRSP) strains were isolated in France from healthy dogs and dogs with pyoderma in the mid-1980s. *Staphylococcus pseudintermedius* is a commensal and a common opportunistic pathogen mainly causing infections of the integumentary system in dogs. From that date, the isolation of MRSP in veterinary medicine has increased; the prevalence increased from 16-17% in the early 2000s to 30% in 2008, up to 80% in 2020. [27,29,30]

Unlike MRSA, MRSPs do not cause zoonoses, but transmission between dogs and cats living in the same environment has been demonstrated.[28] MRSPs are also often resistant to many antimicrobials, e.g., penicillin, ampicillin, tetracyclines, trimethoprim, chloramphenicol, erythromycin, clindamycin, aminoglycosides, and fluoroquinolones.[27,28] This can make identifying the correct antimicrobial treatment difficult. Systemic antimicrobial therapy is often required and should always be based on the results of susceptibility testing. MRSPs are resistant to almost all beta-lactam antimicrobials. Fluoroquinolones should also be avoided due to their unpredictability of treatment response and propensity to improve resistance during treatment.

Another complexity to consider when dealing with an MRSP is its ability to form biofilms.[31] Biofilm is often resistant to antimicrobials and plays an essential role as a reservoir in recurrent infections. A study comparing the minimum inhibitory concentration (MIC) of amikacin, cefazolin, enrofloxacin, and gentamicin to inhibit the growth of biofilm-producing bacteria (not to eradicate bacteria in the biofilm) between the planktonic form of *Staphylococcus* spp and the biofilm-associated form indicated that MIC was thousand times higher in biofilm-associated vs. planktonic bacteria for all antimicrobials.[31] This is one of the reasons why infections caused by biofilm are difficult to eradicate.

2. ENTEROCOCCI

Enterococci are Gram-positive bacteria, and antibiotic resistance is widespread among this class of microorganisms. They are commonly found in the gastrointestinal tract and can cause urinary tract infections. They can survive very well in the environment; therefore careful environmental sanitation is essential in preventing infections caused by Enterococci. Resistant strains to the most common antibiotics, such as cephalosporins, clindamycin, penicillin, and trimethoprim, have been identified. Vancomycin-resistant strains have also been identified. Antibiotic treatment should be chosen based on the sensitivity test and may vary between ampicillin and chloramphenicol.[28]

3. *PSEUDOMONAS* spp.

Pseudomonas spp. are pathogens that have a high resistance in the environment and to common disinfectants. They are gram negative bacilli and are commonly found in the skin, subcutaneous

tissues, urinary tract, lungs, and heart valves. To prevent *Pseudomonas* spp. contamination, thoroughly cleaning and sanitizing the environment is essential. Fluoroquinolone-resistant strains have often been found but they are usually sensitive to aminoglycosides.[28]
Moreover, this class of bacteria has the ability to form biofilms.[27] Therefore, it is essential to implement procedures that prevent their formation.

To reduce the spread of antibiotic resistance, a few things can be done. First, to prevent SSIs caused by MDR, all common SSI prevention practices must be strictly observed. In human medicine, screening is performed to identify patients who need to undergo a surgical procedure who are MRSA positive. Once identified, these patients undergo MRSA decolonization therapy. A similar approach could be useful with regard to the identification of MRSP-colonized patients in veterinary medicine, but there are currently no rapid tests that allow this. In addition, amikacin added to cefazolin could be administered during antimicrobial prophylaxis to prevent SSIs from MRSP in orthopedic procedures.[21]

Finally, one key principle in the fight against antimicrobial resistance is reducing and more conscious use of antimicrobials.
ACVIM's General Methods to Reduce Antimicrobial Resistance indicates three methods to reduce antimicrobial resistance: reducing the occurrence of diseases by implementing prevention whenever possible, reducing the administration of antibiotics, and improving the way antibiotics are administered. Not all animals with bacterial infections need to be treated with antimicrobials. Sometimes, bacterial infection is secondary to other causes and may be a remedy for the primary cause by avoiding the use of antimicrobials.[32]

PREVENTION OF SURGICAL SITE INFECTIONS

Not all SSIs are preventable, but many actions can be undertaken to reduce their incidence before, during, and after the surgical procedure.

PRE-OPERATIVE STRATEGIES

The first step is identifying animals at higher risk of developing SSIs. In previous chapters, the risk factors associated with the patient have been identified. The animals most at risk are those with concomitant diseases that worsen their health conditions, those with contaminated wounds, and those requiring surgical procedures involving orthopedic implants or drainage. Once these animals have been identified, special care must be taken in their management, and all the following strategies must be followed for each surgical procedure.

Adequate clipping of the surgical field (preferably within 4 hours before surgery), and a proper surgical scrub are essential. The surgical scrub can be done with Chlorhexidine gluconate 4% and 70% isopropyl alcohol or with povidone-iodine and 70% isopropyl alcohol. No differences in the incidence of SSIs between these two disinfectants have been demonstrated.[6] Some differences must be considered when choosing which substances to use in the surgical scrub. Both chlorhexidine and povidone-iodine are broad-spectrum actives, but betadine also acts against spores. They both have immediate activity, but only chlorhexidine has persistent activity for more than 6 hours and residual activity for up to two days. Finally, povidone-iodine can cause contact dermatitis, while chlorhexidine is ototoxic (use on perforated eardrum should be avoided) and neurotoxic (must not encounter the brain and meninges).
Surgical instruments must be properly sterilized, and the surgeon's hands must be washed appropriately.

Emphasis should be placed on the administration of antimicrobial prophylaxis (AMP). The antimicrobial should be chosen according to the pathogens expected at the site where the surgical procedure will be performed (Table 6). The first administration must be performed intravenously before the start of the surgical procedure to allow the drug to reach sufficient tissue concentrations at the surgical site before the incision is made.[33] The guidelines indicate that the first administration should be performed within 60 minutes before the start of the surgical procedure.[34] One of the most widely used antimicrobials for prophylaxis is cefazolin. This should be given within 60 minutes before incision, and subsequent doses should be given every 90 minutes of surgery.

Guidelines indicate antimicrobial prophylaxis should be undertaken in clean-contaminated, contaminated, or dirty procedures. Regarding clean procedures, the surgeon may choose to administer AMPs if the procedure is expected to last longer than 90 minutes, if the bone is incised, if implants are planned in orthopedic procedures, and in cases of high-risk patients. In clean-contaminated and contaminated procedures, AMP is justified and should be chosen according to the bacterial flora present at the site where the procedure is performed. When dirty or dirty-contaminated surgeries are suspected of infection or purulent exudate, a broad-spectrum therapeutic antimicrobial should be administered, and treatment should continue post-operatively.

These guidelines should be considered when choosing whether and which AMP to undertake, but they should not always be strictly followed. The surgeon must evaluate each case based on the patient's status and the surgical procedure.

In Northern Europe, guidelines for a lower use of antimicrobial prophylaxis associated with greater compliance with antiseptic regulations have been issued. Swedish guidelines advise against AMP in clean orthopedic procedures, even when orthopedic implants are used. In Finland, AMP is not recommended in clean, clean-contaminated surgical procedures lasting less than 60 minutes. However, using first-generation cephalosporins is recommended 30-60 minutes before an orthopedic procedure, even if clean, to be continued until the end of the surgical procedure.[33]

INTRA-OPERATIVE STRATEGIES

Observing the principles of asepsis during the entire surgical procedure is crucial. If a surgeon's glove breaks, these should be replaced immediately. In the case of clean-contaminated procedures (e.g., procedures on the digestive tract), it may be helpful to use a double surgical drape that isolates the intestine from the rest of the abdominal cavity. Sterile waterproof drapes are very useful as they prevent bacterial flora from contaminating the rest of the body cavity.[13] It is mandatory to replace sterile gloves before touching clean areas after touching potentially contaminated areas to avoid contamination. A lower incidence of SSIs is also found when peritoneal lavages with warm sterile saline are performed at the end of the procedure where bacterial contamination is suspected, although the volume of lavage to be used is controversial. These can affect reducing bacterial contamination in risky surgeries.[13]

If initiated before surgery, antimicrobial prophylaxis should be continued until the procedure is complete. It is crucial to keep the therapeutic levels of the antimicrobial stable throughout the whole surgical procedure by carrying out additional administrations depending on the duration of the surgery and the type of antimicrobial chosen. After the first antimicrobial administration, subsequent doses should be repeated every two half-lives of the antimicrobial used.[6]

POST-OPERATIVE STRATEGIES

Even in the case of post-operative norms, one of the main strategies for preventing SSIs is maintaining the proper cleanliness of the surgical wound and the environment in which the animal lives. Every time a clinician visits a pet, it is indicated to wear disposable gloves if the wound needs to be touched to prevent the bacterial flora on the vet's hands from contaminating the wound.

If AMP is administered in clean surgeries and clean-contaminated and contaminated surgeries, antimicrobial prophylaxis should be discontinued 12-24 hours after the end of the procedure. [28]
The postoperative use of AMP is not recommended unless a concurrent infection requires treatment.[33] The human medical literature does not support using postoperative antimicrobials for clean procedures, whereas its use in veterinary surgery, particularly following orthopedic procedures, is commonplace. [11,12,28] Two studies about orthopedic procedures describe a significant reduction in SSI occurrence in patients administered with postoperative antimicrobials.[11,12] The post-operative antimicrobials should only be administered if there is a demonstrated need for antimicrobial treatment. However, it can be used preventively if the surgeon deems it necessary in high-risk patients (for example, in orthopedic procedures).

Finally, surveillance is an essential strategy in the prevention of SSIs. On the one hand, it allows for early detection of SSI and intervention on a patient and, at the same time, enables an overview of the incidence of SSIs in the clinic so that corrective measures can be put in place if it is too high. Surveillance of surgical site infections can be active or passive. The key data to analyze is the number of procedures and surgical site infections that have occurred. In addition, other data can be entered according to what needs to be controlled in the clinic.

Active surveillance allows to determine the percentage of SSIs that occur. It is more expensive and takes longer since patients need follow-up. It requires an active study and follow-ups (physical or by telephone) must be scheduled at certain times. It is usually performed in large clinics where a study is to be carried out on the incidence and risk factors present in the clinic to have clear indications on which procedures should be implemented to reduce the incidence of SSIs in the clinic.

In this case, all procedures in a determinate period will be analyzed, and in these, we will take note of all the factors that could cause an increase in the rate of SSIs. Generic patient data, such as sex, age, species, and race, as well as more specific data, such as the presence of concomitant diseases, ASA status, and any allergies, will be analyzed. An analysis of factors that may influence the incidence of SSIs during the surgical procedure will then be carried out, such as the type of surgery itself, the antimicrobial prophylaxis used, the duration of anesthesia and surgery, the use of orthopedic implants and/or drains, etc. Subsequently, follow-ups will be agreed upon with the owner at pre-established times, during which the clinician will assess the patient's health and the possible presence of SSIs based on the criteria for defining an SSI seen previously. Once these data have been obtained, a statistical analysis should be carried out indicating the incidence of SSIs in the clinic and which factors influenced it the most.

Passive surveillance requires less expense and is easier to implement as it relies on data already collected for other studies or in medical records. It does not require an active study to be carried out on all surgical procedures in a period but requires a retrospective analysis of previously collected data. Therefore, all procedures performed in a specific period are analyzed, and the incidence of SSIs is determined based on the data collected about the patient, the procedure, and the follow-up visits. Usually, the number of follow-ups and the amount of data about the patient and the procedure are lower. The lower time and cost make this alternative valid in many situations.

Small animals often have a very short post-surgery hospitalization period that does not allow the presence of a surgical site infection to be detected. Therefore, it is essential to ensure that the small animal's owner is compliant and pays attention to his animal's health. The veterinarian should inform the owner about the risks and the importance of contacting the clinic immediately in case they suspect health problems with their pet.

For the passive surveillance model to provide reliable results, it is essential to standardize patient follow-ups and define a correct compilation of the medical record to have reliable data when determining the incidence of surgical site infections in the clinic.

However, its outcome varies greatly depending on how medical records are written, whether the presence of surgical site infections is correctly reported, and the follow-ups that are carried out on the patient.

MANAGEMENT OF SURGICAL SITE INFECTIONS

Once a surgical site infection has been identified, it is necessary to evaluate a series of parameters, such as where the infection is present and what caused it. In some cases, a physical examination of the patient may be sufficient; in others, in-depth examination is necessary, which may include cultural, hematological, or diagnostic imaging tests. It is also essential to assess the patient's general health condition (e.g. if there are concomitant pathologies), the type of surgical procedure performed, and the owner's compliance with specific post-operative prescriptions requested at home.

As seen above, the indiscriminate use of antimicrobials has increased the phenomenon of antimicrobial resistance. Therefore, it is essential to remember that not all infections must be treated with antimicrobials. A 2015 survey in Washington State revealed that 24% of participating veterinarians were not used to cultural testing when they suspect an infection. Of those who responded positively, only 36% request the culture test on a regular basis. Of these, only 10% replied that they used sensitivity tests in the definition of the antimicrobial therapy.[35] Although most respondents stated that antimicrobial resistance is an important phenomenon that needs to be addressed, the added cost often dictates veterinarians' disaffection with prescribing culture tests.

The sample for a culture test should be as representative as possible. Therefore, deep swabs should be preferred to surface swabs that could be contaminated by bacteria that are not the cause of the infection. Antimicrobial treatment should be started after the culture result or at least after the sample has been taken to avoid interference with the diagnostic results.
Although systemic antimicrobial treatment is the most frequently used approach, other treatments may be undertaken.

MANAGEMENT OF SUPERFICIAL AND DEEP SURGICAL SITE INFECTIONS

The American College of Veterinary Internal Medical (ACVIM) sustains that not all animals with bacterial infections should be treated with systemic antimicrobials. Sometimes, a localized abscess incision and drainage are considered sufficient.[32]

Systemic antimicrobial therapy is not always necessary in patients who do not show deep or systemic infection signs. Antimicrobial ointments with topical action can be used, or a thorough cleaning of the wound with biocides such as chlorhexidine can be carried out. It has been shown that high concentrations of local antimicrobials at the site of infection can affect bacteria that are not susceptible to systemic therapy and, in some cases, can penetrate the biofilm in the case of surgical site infections that occur after orthopedic surgeries in which an implant is used.[25]

In the case of superficial and particularly extensive lesions, the antimicrobial properties of honey or sugar can be exploited. In addition, local injections of antimicrobials can be given in the case of infections in well-defined sites, such as the articulations.[6,21] In other cases, revision surgery may be considered to remove debris or foreign materials or to drain abscesses.

In the case of surgical site infections, when orthopedic surgery has been performed with an orthopedic implant, a biofilm could colonize the implant. Antimicrobial treatment may be attempted, but in most cases, the cure is reached only by the removal of the implant.

If the surgeon decides to operate again an SSI, drainage, debridement of the wound, or both may be performed. The wound must be reopened if drainage is chosen by removing the sutures to drain the purulent material. Once this has been done, the wound should be covered with sterile material. If the infection involves a large portion of the soft tissues, bone, or an orthopedic implant, surgical exploration of the wound with consequent debridement of the necrotic and devitalized material may be warranted, and tissue washes may be performed with sterile isotonic saline or local antiseptics, such as 0.05% chlorhexidine.[21]

If a systemic antibiotic is necessary, ideally, it should be chosen based on the results of culture tests. If the antibiotic must be administered immediately, the one that influences the pathogens most likely to have caused the infection should be chosen (Table 6). Then, the therapy should be adapted or modified according to the results obtained from cultural and sensitive tests. In addition, supportive treatment for pain control should be performed if necessary.

MANAGEMENT OF ORGAN/SPACE SURGICAL SITE INFECTIONS

For organ/space surgical site infections, exploratory laparotomy is required.

In septic peritonitis, exploratory laparotomy with peritoneal lavages has been found useful. A study conducted on 40 dogs affected by septic peritonitis aimed at assessing aerobic and anaerobic bacterial isolate type, susceptibility, and change in bacterial resistance on pre- and post-lavage culture samples showed that peritoneal lavage with 200 to 300 mL/kg of 0.9% NaCl sterile saline solution reduced bacterial contamination. Pre-lavage samples indicated a total of 109 isolated bacteria; post-lavage samples detected 14 fewer (with the appearance of 46 new isolated bacteria). As for MDRs, the post-lavage samples with MDRs were one-third of those pre-lavage.[36] The lavage is not able to completely eradicate the bacterial infection, but it may reduce the contamination to a manageable level.

Evaluating the patient's status, not just the laboratory result, is also essential. If the clinician decides to use a systemic antimicrobial treatment, this must be done at appropriate doses and intervals. For example, when the same antimicrobial used during surgery has also been used as post-operative prophylaxis, it is good to continue administering it even in the case of an SSI and consider whether to add or modify the therapy based on the results of the laboratory tests. Whenever possible, narrow-spectrum antimicrobials should be used based on laboratory results, and they should not be susceptible to antimicrobial resistance by isolated microorganisms.[7]

Few studies have been carried out in veterinary medicine regarding the duration of therapy. The ACVIM consensus statement on therapeutic antimicrobial use in animals and antimicrobial resistance sustains that therapy should be continued for as long and at the doses necessary to eradicate the infection. Antimicrobial therapy should be discontinued once the infection has ceased, even if the antimicrobial label indicates longer dosing periods. In the past, there was a tendency to always observe the timing of administration of antimicrobials for fear that shorter administrations could favor the onset of resistance. To date, there is no scientific evidence that stopping antimicrobial therapy early, in the face of negative cultures, can promote the onset of antibiotic resistance.[32]

CONCLUSION

The prevention of surgical site infections is crucial to improve the outcome of surgical patients. The concept of "prevention is better than cure" should be always applied facing the problem of the nosocomial infections. Proper pre-, intra- and post-operative management of these patients is the cornerstone of the prevention strategy to minimize the incidence of this complication. Not all surgical site infections can be prevented, but it is essential to understand the risk factors and all the prevention practices to reduce the complication rate as much as possible. It is necessary to train all staff in contact with the surgical patient to follow appropriate protocols. In this case, the formulation of a hospital protocol could be helpful to decrease the incidence of surgical site infections. An example of this is the daily use of surgical check lists.

Although there are no international guidelines on this subject in the veterinary field, it is important to standardize the definition of surgical site infections as much as possible and have homogeneous parameters to be evaluated in prospective studies. Surveillance of surgical site infections in veterinary medicine is necessary to understand which critical points need to be modified to lower the incidence of infections.

Significant attention must be paid to the use of antimicrobials, both as a prophylaxis and as a therapy. Guidelines that indicate the proper use of antimicrobial prophylaxis should always be considered.

Finally, it is important to remember that not all surgical site infections require antimicrobial therapy. Ideally, antimicrobial therapy should only be undertaken following culture and sensitivity tests to reduce unjustified antimicrobial use. The uncontrolled use of antimicrobials has led to an increase in the phenomenon of antimicrobial resistance, and it is ethically necessary that all veterinarians use antimicrobials more consciously to face this global problem.

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