Antibiotic Prophylaxis of Surgical Site Infections – Some Latest Guidelines

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ABSTRACT

Background and Objective: Surgical site infections (SSIs) have an enormous impact over the operative intervention outcome. In the last 20 years the use of antibiotic prophylaxis (ABP) has been greatly improved as regards appropriate choice of antibacterial drugs, timing of initial dose and precised duration of the administration scheme.

Methods: The study should be considered a compiling work (references review), reviewing some latest original statements on antibiotic prophylaxis in surgery of experienced centers and a society of anesthesiology and reanimation. The recommendations discussed were selected with the presumption of demonstrating practical guidelines of highly interested in antibiotic prophylaxis institutions. The analysis takes into consideration the specific definitions and risk-related factors for SSI. Thus the recommended new (2010) algorithms of the strategy for antibiotic prophylaxis are presented in the context of, and in compliance with the classification systems of wounds, and with respect to the major surgical clinical specialities.

Results The study presents some new recommended regimens (2010) for antibiotic prophylaxis administration considering surgical wounds classifications (by anatomical location, class of the wound), and major surgical specialities practice, substantiated by the practical experience of leading medical centers and a society of anesthesiology and reanimation.

Conclusion: These guidelines should be treated as general statements regarding the appropriate practices for ABP, based on the current available medical references and the clinical experience in the course of time of their development. They could be considered a guidance applying to the elaboration of antibiotic policy for surgical wards and critical care units as resuscitation, intensive care units, in particular the responsible original decisions for the individual patients considering their general health and surgical status.

Key words: surgical site infections (SSIs), surgical wound infections (SWIs), operative wound infections (OWIs), antibiotic prophylaxis (ABP), antibiotics (Abs).
Introduction

Surgical site infections (SSIs), earlier described as surgical wound infections (SWIs) have an enormous impact on the operative intervention outcome. According to Nichols RL (1) data as of 2001, postoperative surgical site infections remain a major source of illness and a less frequent cause of death in the surgical patient. These infections have numbered approximately 500,000 per year, among an estimated 27 million surgical procedures, and have accounted for approximately one quarter of the estimated 2 million nosocomial infections in the United States each year.

The latest data of the Procedure-associated Module, SSI, Surgical Site Infection (SSI) Event.- 2010 (SSI module) within the National Healthcare Safety Network (NHSN)1, indicate that SSIs have been the most common healthcare-associated infections, accounting for 31% of all hospital-acquired infections (HAIs) among hospitalized patients (2). NHSN data for 2006-2008 (16,147 SSIs following 849,659 operative procedures) showed an overall SSI rate of 1.9% while advances have been made in infection control practices, including improved operating room ventilation, sterilization methods, barriers, surgical technique, and availability of antimicrobial prophylaxis, SSIs remain a substantial cause of morbidity, prolonged hospitalization, and death. SSI is associated with a mortality rate of 3%, and 75% of SSI-associated deaths are directly attributable to the SSI (2). R. Holzheimer (3) reports that wound infections are responsible for extension of hospital stay on an average of 1 week and for increase in hospital costs by 20%.

To the present time two versions of CDC and Healthcare Infection Control Practices Advisory Committee guidelines for the prevention of surgical site infection have been issued (1985 and 1999), the newest version scheduled for publication in 2014, still not published. The currently available revised guideline (1999) treats in details all factors affecting the development of infection with a special accent on antibiotic prophylaxis (ABP) as a reliable tool for prevention of postoperative infectious complications (4,2).

The use of antibiotic prophylaxis before surgery has evolved greatly in the last 20 years. Improvements in the timing of initial administration, the appropriate choice of antibiotic agents, and shorter durations of administration have defined more clearly the value of this technique in reducing postoperative wound infection(1).

Materials and Methods

The study should be considered a compiling work (references review), reviewing some latest original statements on antibiotic prophylaxis in surgery of experienced centers and a society of anesthesiology and reanimation. The recommendations discussed were selected with the presumption of demonstrating practical guidelines of highly interested in antibiotic prophylaxis institutions. The analysis takes into consideration the specific definitions and risk-related factors for SSI. Thus the recommended new (2010) algorithms of the strategy for antibiotic prophylaxis are

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presented in the context of, and in compliance with the classification systems of wounds, and with respect to the major surgical clinical specialties.

Result

According to former prevalence studies\(^2\) in France (2001, 2006) surgical site infections (SSIs) rank third by frequency among the nosocomial infections. Data of the Department of Anesthesiology and Reanimation, University Hospital Center, Amiens, France, indicate a considerable percentage of the hospitalized patients receiving antibiotics (30-40%), antibiotic prophylaxis accounting for 30-50% of antibiotics prescriptions. It is estimated that the treatment with antibiotics is a field of action not adequately controlled - 20-50% of the prescriptions are inappropriate, and up to 90% of the prescriptions as ABP (5).

A figure adapted from Rabaud C\(^3\) (6) indicates the rising percentage of the patients with a registered operative wound infection (OWI) depending on the increase in the number of hospitals, having participated in four consecutive pilot studies of the National Nosocomial Infections Surveillance System (NNIS), USA. At the present state of knowledge, however, in the field of SSI prophylaxis, the statement of Johns Hopkins POC-IT Center is that the appropriate ABP and the other interventions for perioperative care would contribute to a diminution in SSI rates by more than 50% (7). The main objective of ABP is to decrease the incidence of SSI development, opposing to bacterial proliferation (5).

The factors of importance for SSI development are generalized by H. Singhal as a complex interplay between host, microbial, and surgical factors (8).

The host (systemic) factors include age, malnutrition, hypovolemia, poor tissue perfusion, obesity, diabetes, steroids, and other immunosuppressants, etc.

The microbial factors that influence the establishment of a wound infection are the bacterial inoculum, virulence, and the effect of the microenvironment (8).

Most SSIs are contaminated by the patient's own endogenous flora, which are present on the skin, mucous membranes, or hollow viscera, the mechanisms of infection being invasion through the skin during the surgical incision or in the course of the procedure and the postoperative period. The normal flora comprises conditionally pathogenic\(^4\) or opportunistic microorganisms\(^5\) which may act as pathogens in case of SSI (9,10).

The usual pathogens on skin and mucosal surfaces are Gram-positive cocci (notably staphylococci); however, Gram-negative aerobes and anaerobic bacteria

2. prevalence studies – determining the frequency (rates) of nosocomial infections (NI) as of definitive moment, the registration protocols being filled in by a team not associated with the system of the healthcare facility studied.


4. Conditionally pathogenic bacteria are only pathogenic under certain conditions, such as a wound that allows for entry into the blood, or a decrease in immune function. (9).

5. Opportunistic microorganisms are usually found in the environment or as part of the normal flora. In normal individuals, they are harmless, but they may cause severe disease in immunocompromised patients or if they penetrate a territory from which they are usually excluded (as a result, for example, of trauma or surgery) - definition of G. Virella (10). Both terms are usually compatible.

contaminate skin in the groin/perineal areas. The contaminating pathogens in gastrointestinal surgery are the multitude of intrinsic bowel flora, which include Gram-negative bacilli (eg, *E. coli*) and Gram-positive microbes, including enterococci and anaerobic organisms (8) – Table 1. In case of breached integrity of the tissues and unnatural conditions (presence of pus, blood) the multiplication of the bacteria contaminants of the digestive tract may lead to the development of infection.

Strictly pathogenic species, eg, *S. aureus*, are among the primary causative agents of SSIs, other strict pathogens as some streptococci and anaerobes are also involved in the etiology of SSIs – Table 2. The inoculum (microbial concentration) highly associated with SSIs is that of bacterial counts higher than $10^3$ organisms per gram of tissue (or in the case of burned sites, organisms per cm$^2$ of wound) (8).

The above mentioned prevalence studies in France (2001, 2006) established as major etiologic agents *E. coli* in 24% and *S. aureus* in 23%, both determining about a half of SSIs. Of basic importance as etiologic agents as well have been other Enterobacteriaceae – 19%, other Gram (+) cocci – 25%, nonfermentative Gram (-) bacilli as *Pseudomonas* spp. – 5%, anaerobes – 3%, fungi – 1% (5). The opportunistic bacteria as Enterobacteriaceae and *Pseudomonas* spp. play a very important role as SSIs causative agents. The above cited structure of the most frequent isolates coincides to a great extent with the data of the Computerized Information System – Nosocomial Infections (CIS-NI) in our country (11).

There are still many controversies as regards the microbiological diagnostic of SSI. For instance as skin sites are normally colonised by a variety of organisms, positive wound cultures in the absence of clinical signs are rarely indicative of SSI (12). The isolation of skin colonizers, eg, *S. epidermidis*, usually in a polymicrobial culture, and evident local symptomatology for SSI is still controversial in view of its suspected etiological role (13).

The surgical factors influencing the development of SSI include:
- Wound characteristics - nonviable tissue in wound, hematoma, foreign material (eg, drains and sutures, dead space, poor skin preparation (eg, shaving), and preexistent sepsis (local or distant)
- Operative characteristics - poor surgical technique; lengthy operation (>2 hours); intraoperative contamination (eg, from infected theater staff and instruments or inadequate theater ventilation), prolonged preoperative stay in the hospital, hypothermia, etc.

The relationship between the above-mentioned factors is illustrated in Appendix 1 - adapted from Wound Infection Clinical Presentation - Medscape Reference (8).

In view of systematizing the basic characteristics of SSI two classifications are adopted and used universally by the systems for nosocomial infections control and specialized studies (2, 4, 6, 13):

The latest CDC classification (Guideline of 1999), based on the anatomical location of the affected during the intervention tissues’ layers and organs, classifies the infections into:

*incisional*, including superficial ones.
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(affecting skin and subcutaneous tissue) and deep incisional (penetrating into fascia and muscle), and organ/ space or organ/cavity type – out of the wall of the incised opened or manipulated part of the human body, usually requiring surgical therapy to drain infected organs or body cavities (4). This classification meets the NHSN (former NNIS) criteria, endorsed by CDC, for defining of Surgical Site Infections (SSIs) – Appendix 2 - adapted from Wound Infection Clinical Presentation - Medscape Reference (13).

There exist modifications of the indicated classification, eg, the definition of the postoperative infections of P. Tulkens and A. Spinewine - University of Leuven, Belgium, as follows:

– Superficial incisional (skin and subcutaneous tissue) or deep incisional (fascia and muscle),
– (Peri)visceral infections at the level of the reached organs, spaces between the organs and other manipulated sites during the operation
– Systemic infections and infections in the operated patient appearing at a distance from the surgical site. These infections do not represent a part of the primary task of the surgical antibiotic prophylaxis (ABP) (14).

Depending on the degree of bacterial contamination the surgical wound is subject to classification in classes ranging from I to IV. The latest surgical wound classification of the National Center for Biotechnology Information (NCBI) is based on the following criteria for defining the class of the surgical wound (15):

![Figure 1](image)

**Figure 1.** Percentage of SSIs in four consecutive NNIS pilot studies, 2001-2002.

**Surgical Wound Classification**

**Clean** – an incision in which no inflammation is encountered in a surgical procedure, without a break in sterile technique, and during which the

respiratory, alimentary and genitourinary tracts are not entered.

**Clean-contaminated** – an incision through which the respiratory, alimentary or genitourinary tract is entered under controlled conditions but with no contamination encountered.

**Contaminated** – an incision undertaken during an operation in which there is a major break in sterile technique or gross spillage from the gastrointestinal tract, or an incision in which acute, non-purulent inflammation is encountered. Open traumatic wounds that are more than 12–24 hours old also fall into this category.

**Dirty or infected** – an incision undertaken during an operation in which the viscera are perforated or when acute inflammation with pus is encountered during the operation (for example, emergency surgery for faecal peritonitis), and for traumatic wounds where treatment is delayed, and there is faecal contamination or devitalised tissue present.

Other practical definitions of the four classes of wounds are developed by K Sheetz et al. - Appendix 3 – adapted from Surgical Wound Classification. Michigan Apps for Surgical Trainees 2012 (16). No matter of the variety of risk factors, NNIS employs the calculation of a risk index on the basis of three determinants, i.e. - underlying disease status or ASA score, eg. diabetes mellitus; prolonged operations, and contaminated or dirty wounds. The risk index is calculated as a score, gaining 1 point for:
- ASA three or more;
- operations of duration > 75th percentile of the mean duration of the intervention, and
- contaminated or dirty procedure (7, 17)

The points scores (ASA, CEPOD scores) are necessary for the determination of the risk for infection. ASA and CEPOD scores are endorsed for practical application:
1. ASA score – The scheme of the American Association of Anaesthetists (ASA);
2. CEPOD or NCEPOD score - National Confidential Enquiry into Patient Outcome and Death (NCEPOD) – UK (18)

- The latest guidelines on ABP of three leading medical institutions have been reviewed as follows (posted in Appendix 4):

- General recommendations and concrete guidelines according to the type of intervention and the isolated microbial flora from the corresponding surgical site - Department of Surgical Education, Orlando Regional Medical Center (19);
- 2010 recommendations of the Johns Hopkins POC-IT Center relevant to the type (Class) of the operative wound (the four classes of wounds) (7).
- The updated 2010 recommendations for ABP of the Guidance Committee of the French Society for anesthesiology & reanimation (SFAR - Comité de pilotage Société française d’anesthésie et de réanimation) in accordance with surgical specialties specificity: Antibiotic prophylaxis (ABP) in surgery and interventional medicine (adult patients) (20).

**Discussion**

The prophylactic use of antibiotics in the surgical patient evolves in stages of first
clinical trials in the 1950s; experimental studies in the 1960-1970s, having defined appropriately the quantititative and qualitative nature of the endogenous flora in conditions of health and illness, eg, gastrointestinal flora of importance for abdominal surgery; and randomised (blinded) control trials (RCT) in the 1980s, the 1990s and the following years. The latest demonstrated the successful usage of antibiotic prophylaxis in appropriately selected patients and reasonable choice out of the disposable antibacterial drugs, and stimulated the elaboration of concrete recommendations regarding the correct approaches for ABP in surgery. The choice of the parenteral drugs, the administration regimen with an initial dose and secondary injections, and the mode of administration are standardized on the basis of well-planned clinical trials (1, 21). The routine usage of ABP in surgery has overcome some controversial statements related predominantly to bacterial resistance.

The general recommendations on antibiotic prophylaxis are summarized by NICE Clinical Guidelines as follows (12):

Give antibiotic prophylaxis to patients before:
- clean surgery involving the placement of a prosthesis or implant
- clean-contaminated surgery
- contaminated surgery.

Do not use antibiotic prophylaxis routinely for clean non-prosthetic uncomplicated surgery.

Use the local antibiotic formulary and always consider potential adverse effects when choosing specific antibiotics for prophylaxis.

Consider giving a single dose of antibiotic prophylaxis intravenously on starting anaesthesia. However, give prophylaxis earlier for operations in which a tourniquet is used.

Before giving antibiotic prophylaxis, consider the timing and pharmacokinetics (for example, the serum half-life) and necessary infusion time of the antibiotic. Give a repeat dose of antibiotic prophylaxis when the operation is longer than the half-life of the antibiotic given.

Give antibiotic treatment (in addition to prophylaxis) to patients having surgery on a dirty or infected wound.

Inform patients before the operation, whenever possible, if they will need antibiotic prophylaxis, and afterwards if they have been given antibiotics during their operation.

The principle formulations are expressed in details in CDC guidelines of 1999. Two types of guidelines should be differentiated – generalized and concrete ones, depending on:
- type of the intervention (anatomical location, surgical speciality respectively), and taking into consideration the microbial flora being isolated normally from the corresponding surgical site;
- the type (class) of the surgical wound

The review performed of the above cited issues of leading institutions for the recent years, and principally 2010, indicates that ABP is recommended for administration for a short period – within 24-48 hours perioperatively. As a summary of the updated guidelines of two medical centers of a considerable capacity (USA, UK) and the French anesthesiology & reanimation society, the following is recommendable (7,19,20) – Appendix 4:

In general, in most procedures with clean, clean-contaminated, and contaminated wounds (Class I, II and III) is recommended the administration of:
- A single dose of cephalosporin (CEFAZOLIN 1-2 g IV) within 60 minutes prior to the incision. Additional doses are
considered in case the operation lasts longer than 2 to 3 hours, and in the presence of:

- risk factors of surgical or anesthesiological type
- interventions related to a high risk of infection of the operative wound depending on the categorization (class) of the wound
- patients with high risk index (ASA score);

- In case of β-lactam allergy or with a high risk of Methicillin-resistant Staphylococcus aureus (MRSA) – VANCOMYCIN 15 mg/kg IV;
- CEFOXITIN or CEFOTETAN 1-2g IV, CEFAZOLIN 1-2 g IV + METRONIDAZOLE 500 mg, ERTAPENEM 1000 mg, or beta-lactam/beta-lactamase inhibitor combination (eg, AMPICILLIN-SULBACTAM) in case of high risk of anaerobic SSI, for instance colorectal operations;
- Mechanical bowel preparation (MBP) and oral antibiotics are considered prior to colorectal surgery procedures, eg, NEOMYCIN plus ERYTHROMYCIN.

For infected wounds (Class IV) the antimicrobial coverage is considered a treatment, not prophylaxis. The duration of treatment depends on the severity of the infection, the surgical debridement and the clinical reaction. The antibiotic coverage should include Gram (+) microorganisms, and in special circumstances Gram (-) microorganisms and anaerobes (eg, perforated organ).

- For simple wound infections CEFAZOLIN 1-2 g IV per 8 hours;
- VANCOMYCIN, LINEZOLID, TIGECYCLINE or DAPTOMYCIN in case of risk for Gram (+) infections (eg, MRSA) or with β-lactam allergies;
- In case of increased risk of Gram (-) and anaerobic infection: beta-lactam/beta-lactamase inhibitor combination (eg, PIPERACILLIN-TAZOBACTAM), CEFOTETAN or CEFOTETAN, CEFAZOLIN + METRONIDAZOLE, or CLINDAMYCIN + GENTAMICIN.

**Conclusion**

The recent recommendations regarding ABP in surgery launch antibacterial drugs and regimens of administration for the prevention of infectious complications of critical importance for the results and outcome of the operative interventions. A special coverage is envisaged for conditions of allergy (β-lactam allergy) and multiresistant bacteria. The guidelines have been worked out and updated by Advisory Committees of Surgery, Anaesthesiology, Reanimation and Intensive Care, assuming the responsibility of updating and precision of the recommendations of exclusively practical value. These guidelines should be treated as general statements regarding the appropriate practices for ABP, based on the current available medical references and the clinical experience in the course of time of their development. They could be considered a guidance applying to the elaboration of antibiotic policy for surgical wards and critical care units as resuscitation, intensive care units, in particular the responsible original decisions for the individual patients considering their general health and surgical status.

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