Surgical site infections – review of current knowledge, methods of prevention

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ABSTRACT: Introduction: Surgical site infections have accompanied humanity since the dawn of time. Development of medicine has reduced their percentage, but still they are a huge problem to face with. Surgical site infections cause a significant increase in a cost of hospitalization. This is the main reason why the whole scientific world is looking for prevention of these complications.

Materials and methods: The aim of the paper is to present current views on the etiology and methods of prevention of surgical site infection.

Results: Patients own pathogens are most often responsible for surgical site infections. In hospitalizations over 5–7 days exogenous and hospital flora have the advantage. The most common isolated pathogen is Staphylococcus aureus. The percentage of MRSA – resistant methicillin strains is increasing. Pre-operative antibiotic therapy reduces the frequency of surgical site infection in many surgical procedures. Time of administration, type and dose of antibiotic play an important role in preventing post-operative infections. Pre-operative skin antiseptic is also important. The two most commonly used ingredients are chlorhexidine gluconate and povidone iodine. Recent reports point the chlorhexidine alcohol solution as an agent with a higher degree of efficacy.

Conclusions: In 2017 Centers for Disease Control and Prevention published the new guidelines for prevention of surgical site infections. This practical tips and tricks should be implemented to every surgical procedure.

KEYWORDS: chlorhexidine, perioperative antibiotic therapy, Staphylococcus aureus, surgical site infections

INTRODUCTION
Surgical site infection (SSI) is one of the most common hospital-acquired infections, and according to recent studies its incidence is estimated to be 2–11% for all surgical interventions [1]. SSIs are associated with increased treatment costs, prolonged hospital stay and increased mortality. They can also cause disfiguring scars, which can be problematic, especially for young women.

DEFINITION, HISTORICAL BACKGROUND, CLASSIFICATION
Surgical site infection has replaced previously used term surgical wound infection. The name SSI was introduced by the US Center for Diseases Control and Prevention (CDC) in 1992.

According to historical sources, even the early man practiced wound treatment. It is evidenced by cave paintings found in Spain dated back to 2–30 thousand years BCE [2]. However, the first written sources trace back to Hammurabi’s reign (approx. 2000 BCE). In ancient Greece and Rome, wound healing was practiced by Hippocrates, Celsus and Galen. The saying pus bonum et laudabile literally translated as ‘good and praiseworthy pus’ was a surgical dogma at the time. The presence of pus was considered a sign of normal healing [3]. Hippocrates commented on wound healing saying – ‘if the pus is white and not heinous, the health shall come; but if it is ichorous and muddy, the death will ensue’ [4]. It was not until the 19th century that a breakthrough took place that eradicated the term pus laudabile from the medical literature [2, 5]. It was then that a Hungarian obstetrician Ignaz Philipp Semmelweis (1818–1865) recommended that physicians wash their hands in chlorinated water before examining patients, which led to a drastic decrease in mortality [6]. Nevertheless, it is the British surgeon Joseph Lister who would spray phenol over surgical field, and is now considered the father of modern asepsis [6]. Despite the passing of time and enormous advances in medical technology, the problem of surgical site infections is still valid and hard to fight, although various methods are now used, including e.g. air conditioning in operating rooms, antibacterial foils and perioperative antibiotic prophylaxis.

According to the CDC definition, SSIs can be divided as follows:
1. Superficial – develop within 30 days since surgery and involve skin and subcutaneous tissue;
2. Deep – develop after 30 days or within one year if a foreign body was implanted and involve fascia and muscles;
3. Organ or body cavity infection in close proximity to the surgical site – developing within 30 days or one year if a foreign body was implanted.

RISK FACTORS
Surgical wounds are traditionally classified into four classes based on how clean or contaminated they are according to the CDC definition [7]:

- Class I: clean wound: infection risk <2%, e.g. laparotomy, breast resection, vascular interventions;
- Class II: clean/contaminated wound: infection risk <10%, e.g. elective cholecystectomy, small bowel resection, laryngectomy;
• Class III: contaminated wound: risk infection of about 20%, e.g. appendiceal phlegmon, gangrenous cholecystitis;
• Class IV: dirty/infected wound: risk infection >40%, e.g. infected traumatic wounds, pus collections such as testicular abscess. The appropriate evaluation for surgical site infection risk is not based solely on wound classification. There is a number of other risk factors (Tab. I) contributing to SSI.

**MICROORGANISMS RESPONSIBLE FOR SSI**

The skin is the largest human organ colonized by various microorganisms, which in majority are harmless or even beneficial to the host. It is estimated that 1 cm² of skin contains up to three million bacteria [8]. Skin colonization is highly variable and depends on topographic location, host’s endogenous as well as exogenous environmental factors. Some skin areas are folded, e.g. armpit or groin. Those areas have higher temperature and humidity, which promotes growth of bacteria that develop well in humid environment (e.g. *Gram-negative bacilli*, *Corynebacterium spp.*, *S. aureus*). The skin of the back and chest contains a great number of sebaceous glands, which makes perfect conditions for lipophilic microorganisms (*Propionibacterium spp.*, *Malassezia spp.*). The major role of skin as a physical barrier is to protect the body against potential attacks by harmful microorganisms or substances. Symbiotic microorganisms residing on skin play a role in maturation of millions of T cells, thus preventing invasion of other pathogenic organisms [9]. The most common skin pathogens and their disease-inducing potentials are summarized in Tab. II.

Endogenous pathogens are the main culprits responsible for surgical site infections. Those include bacteria that normally reside on the skin or within the operated organ (e.g. gut bacteria in gastrointestinal surgery) [10]. The most commonly isolated pathogens responsible for SSI are listed in Tab. III. According to studies by the European Center for Disease Prevention and Control (ECDC), *Staphylococcus aureus* has become the most common cause of SSI in the recent years [11]. Almost half of the cases are caused by methicillin-resistant *S. aureus* (MRSA) strains [12]. Upper airway colonization of surgical patients with MRSA is associated with an increased risk of SSI [5]. In a study on 9006 patients, MRSA colonization in the anterior nasal passages was found in 4.3%. In that group, MRSA was responsible for 1.86% of SSIs compared to 0.20% in non-colonized patients [13].

Routine eradication with chlorhexidine or mupirocin poses a risk of inducing drug-resistant strains. Therefore, it is recommended to conduct active screening and to decolonize nasal passages only in subjects that test positive [14].

**PREVENTING SURGICAL SITE INFECTIONS**

**Preoperative phase**

**Surgical site shaving**

A few randomized controlled trials were conducted to evaluate hair shaving around the surgical site. The results are ambiguous. It has been established, however, that the use of safety razors causes epithelial microinjuries and hence increases the area for potential infection [15]. Hair removal should be done only using an electric razor with a single-use tip, optimally right before transferring the patient to the OR [16].

**Nutrition**

Malnutrition is a common problem in surgery and has a negative effect on patient’s condition and surgical outcomes. According to the definition by ESPEN (European Society for Clinical Nutrition and Metabolism), malnutrition is, a condition resulting from malabsorption or inappropriate supply of nutrients, which leads to changes in body composition, impaired physical and mental function and has a negative effect on treatment outcomes for the underlying disease” [17]. Two tools can be used to evaluate patient’s nutritional status, namely the Nutritional Risk Screening (NRS-2002) or Nutritional Risk Index (NRI) questionnaires [17]. NRS 2002 was introduced by ESPEN and is calculated based on four variables: percentage weight loss, BMI, general condition (severity of the underlying disease) and food intake during the week prior to surgery. The end score is a sum of points (0–3) for nutritional impairment and points for disease severity (0–3). There is also an additional point for patients aged over 70. The score of three or more means that the patient is at high risk of malnutrition-induced complications. On the other hand, the Nutritional Risk Index is based on serum albumin and a ratio of the actual to predicted body weight, which can be expressed in the form of an equation: NRI = (1.519 × albumin g/L) + (41.7 × actual/predicted body weight). The score of 97.5 or less denotes high-risk patients [18].

Skeie et al. evaluated the nutritional status of 1194 patients undergoing colorectal surgery and showed that malnutrition was an important risk factor for surgical site infections [19]. On the other hand, Pacelli et al. analyzed the nutritional status of patients undergoing gastric tumor resection and did not find any correlation between malnutrition and surgical site infections [20]. Therefore, any evaluation of the relationship between malnutrition and surgical site infection should include type and extent of surgical intervention.

Obesity (BMI > 30) affects wound healing in many ways. Subcutaneous vascular bed in obese individuals is insufficient and cannot provide adequate oxygen supply. Healing tissues have a high metabolic demand and an inadequate oxygen supply slows down the whole process. Immune cells also have a high oxygen demand, which is used e.g. to synthesize anitmicrobial reactive oxygen species [21]. Sufficient antibiotic concentration for perioperative prophylaxis is more difficult to achieve in obese patients compared to those with normal BMI. It is caused by higher distribution volume, which necessitates higher drug doses to obtain the same serum concentration as in non-obese patients [22]. All those factors have a negative effect on postoperative wound healing in obese patients.

**Immunosuppressive therapy**

There are no uniform guidelines as to managing surgical patients on immunosuppressive therapy. In the study by Berthold et al., it was established that immunosuppressive therapy impairs wound healing and increases the risk of infections [23]. On the other hand, discontinuation of immunosuppression can lead to exacerbation of the primary disease. Guidelines published by SHEA (Society for Healthcare Epidemiology of America) recommend stopping immunosuppressive treatment peroperatively as long as testicular abscess. The appropriate evaluation for surgical site infection risk is not based solely on wound classification. There is a number of other risk factors (Tab. I) contributing to SSI.

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as it is possible [24]. The risk associated with treatment cessation should be assessed individually for each patient including his or her treating physician, surgeon and patient him- or herself. Side effects, as a result of stopping therapy, can potentially overcome even an increased risk of surgical site infection. The risk of adverse outcomes is particularly high in post-transplant patients as well as those treated for rheumatoid arthritis, yet the risk is lower than in inflammatory bowel disease [25].

Antibiotic prophylaxis

Antibiotic prophylaxis is indicated for clean/contaminated wounds as well as clean wounds with implanted foreign objects (e.g. vascular or joint prosthesis). For contaminated and dirty wounds, the patient should be given not a prophylactic dose but rather a full course of antibiotics. A widely-used tool for assessing the need for perioperative antibiotics is the NNIS (National Nosocomial Infections Surveillance) scale. It includes three features. The first feature is wound classification regarding infection risk – for a contaminated or dirty wound the patient scores one point. The next stage is patient evaluation using ASA score (American Association of Anesthesiologists). For ASA 3, 4 or 5, the patient is given one point. The third feature is duration of surgery – when it exceeds 75% of time estimated by NNIS, the patient receives 1 point. For instance, predicted duration of appendectomy is 1 hour, colorectal surgery – 3 hours, pancreatic and liver surgeries – 4 hours. When the overall score is one or more points, the patient should be given antibiotic prophylaxis. Although a single dose is preferred, next doses should be given depending on the duration of surgery, drug’s half-life time or excessive blood loss. In most cases, the antibiotic should be active against methicillin-sensitive Staphylococci, Gram-negative bacteria (community-acquired or endogenous pathogens) and anaerobes. For prophylaxis, the most widely used antibiotic is cefazolin, which is active against the above-listed pathogens except for anaerobes. Types of antibiotics and their dosage are summarized in Tab. IV.

In the meta-analysis, Liu et al. proved the effectiveness of preoperative antibiotic administration versus placebo for inguinal hernia, breast cancer or colorectal surgery as well as Caesarean section [26]. Combined antibiotic prophylaxis (intravenous + oral) is more effective at preventing SSIs. Nelson et al. conducted a meta-analysis, which showed that combined therapy is associated with 4.14–6.87% risk of surgical site infection compared to intravenous (12.76%) or oral (7.95%) routes only, the differences being statistically significant [27]. Perioperative antibiotic prophylaxis does not induce bacterial drug resistance [28]. The antibiotic should be given 30–60 minutes before skin incision, ideally during anesthesia induction. When vancomycin or fluoroquinolones have been chosen, the administration time should be expanded to 60–120 minutes before surgery [29]. The dose should be modified for GFR < 60 mL/min/1.73 m² [30].

Tab. I. Risk factors of surgical site infections.

<table>
<thead>
<tr>
<th>PATIENT-DEPENDENT</th>
<th>SURGERY-DEPENDENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Skin disinfection</td>
</tr>
<tr>
<td>Nutritional status</td>
<td>Hair shaving</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Perioperative antibiotics</td>
</tr>
<tr>
<td>Smoking</td>
<td>Duration of surgery</td>
</tr>
<tr>
<td>Obesity</td>
<td>Operating room air conditioning</td>
</tr>
<tr>
<td>Concomitant infections</td>
<td>Improper instrument sterilization</td>
</tr>
<tr>
<td>Colonization with drug-resistant pathogens</td>
<td>Foreign body within wound</td>
</tr>
<tr>
<td>Impaired immunity</td>
<td>Surgical site drainage</td>
</tr>
<tr>
<td>Duration of hospital stay before surgery</td>
<td>Insufficient hemostasis</td>
</tr>
<tr>
<td></td>
<td>„Dead space“</td>
</tr>
<tr>
<td></td>
<td>Significant surgical trauma</td>
</tr>
</tbody>
</table>

Tab. II. Skin pathogens.

<table>
<thead>
<tr>
<th>MICROORGANISM</th>
<th>INCIDENCE / VIRULENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus epidermidis</td>
<td>Common, sometimes pathogenic</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>Rare, pathogenic</td>
</tr>
<tr>
<td>Staphylococcus warneri</td>
<td>Rare, sometimes pathogenic</td>
</tr>
<tr>
<td>Streptococcus pyogenes</td>
<td>Rare, pathogenic</td>
</tr>
<tr>
<td>Streptococcus mitis</td>
<td>Common, sometimes pathogenic</td>
</tr>
<tr>
<td>Propionibacterium acnes</td>
<td>Common, sometimes pathogenic</td>
</tr>
<tr>
<td>Corynebacterium spp.</td>
<td>Common, sometimes pathogenic</td>
</tr>
<tr>
<td>Acinetobacter johnsonii</td>
<td>Common, sometimes pathogenic</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>Rare, sometimes pathogenic</td>
</tr>
</tbody>
</table>

The goal is to reduce the number of potential pathogens naturally residing on the skin and to limit their growth potential during and after surgery. Two most commonly used substances for preoperative skin decontamination are alcohol solutions of chlorhexidine gluconate and povidone iodine. Chlorhexidine is adsorbed by phosphorus-containing proteins of the bacterial cell wall. At bacteriostatic concentration, it penetrates and damages the cell membrane causing leakage of cytoplasmic structures. However, at bactericidal concentrations, it penetrates to the bacterial cell membrane causing leakage of cytoplasmic structures.
and irreversibly attaches to the ATP and nucleic acids [32]. Chlorhexidine also shows fungistatic and fungicidal properties and can neutralize some viruses. Minimal inhibitory concentration is lower for Gram-positive than for Gram-negative bacteria because chlorhexidine shows greater affinity to Gram-positive cell wall [32, 33]. Povidone iodine is a solution containing 1% of free iodine. Iodine molecules penetrate thorough the cell wall and cause cysteine oxygenation and iodination of other amino acids and unsaturated fatty acids [34]. It leads to reduced protein synthesis and cell wall damage. Iodine is effective against Gram-positive and Gram-negative bacteria, as well as some spore-forming bacteria, Mycobacteria, viruses and fungi [34, 35]. Mixing chlorhexidine with povidone iodine or ethanol, or isopropyl ethanol can widen the bactericidal spectrum. Alcohol denaturates proteins and provokes bacterial cell lysis. It is effective against methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococci* and *Mycobacterium tuberculosis* [36].

Studies comparing chlorhexidine and povidone iodine proved that both substances show similar antibacterial spectrum. However, chlorhexidine acts longer by covalently bonding to skin and mucous membrane proteins. Contrary to povidone iodine, its action is unaffected by blood or other bodily fluids, and hence it is commonly used to protect vascular catheters [37]. There are contradictory reports on the effectiveness of chlorhexidine and povidone iodine. In the meta-analysis by Lee et al. including 9 randomized controlled trials, the greater effectiveness of chlorhexidine was concluded [38]. However, the quality of the analysis has been debated due to the fact that some studies compared alcohol chlorhexidine solution with povidone iodine only, which distorted the analysis.

In the meta-analysis by Priviter et al. aimed at comparing alcohol solutions of chlorhexidine and povidone iodine, it was established that chlorhexidine use resulted in lower rate of surgical site infections [39].

### Hand disinfection

The bacteria on the hands of the medical staff can be a source of hospital-acquired infections. *Staphylococcus aureus* and Gram-negative bacilli are the main components of the superficial skin bacterial flora [40]. Chlorhexidine solution is used to provide surgical sterility by reducing bacterial count. The effectiveness of disinfection is measured by logarithmic decrease in microbe number. A decrease by 1-log in the number of bacteria means a 10-fold reduction (i.e. elimination of 90% of population), while 2-log denotes a 100-time reduction (i.e. eliminating 99%) [41]. According to the US Food and Drug Agency (FDA), effective disinfectants are characterized by a 1-log reduction in bacterial count within one minute and a 2-log reduction over 5 minutes [42]. Chlorhexidine is characterized by a wide spectrum and long-lasting antibacterial effect, while alcohol rapidly starts to act. Products containing chlorhexidine and alcohol combine rapid start by the alcohol with the long-lasting effect of chlorhexidine, and therefore are considered the most effective [43].

### Blood transfusion

According to the American College of Surgeons (ACS), an extensive blood loss is defined as a loss of 30–40% of the total blood volume (TBV). Perioperative blood loss leads not only to circulatory failure, but also to a significant loss of proteins, antibodies and coagulation factors. On the other hand, blood transfusion leads to two types of immune response in humans, namely immunosuppression and immunization. Probably, it results from a reduced cell-mediated immunity with simultaneous increase in humoral immunity. It was observed that blood transfusion causes an increase in Th2 cell population compared to Th1 cells, as well as their reduced cytotoxic activity and a shift in the CD4+/CD8+ cell ratio [4]. Hypoxia, deficiency of protein and albumin, which act as drug carriers, as well as changes in immune response all predispose to impaired wound healing and surgical site infections.

### Maintaining patient’s homeostasis

According to the European Center for Disease Prevention and Control 2017 Guidelines, it is recommended to maintain perioperative glucose level at <200 mg/dL in both diabetic and non-diabetic patients (recommendation level IА). The guidelines, however, do not state precisely when and at what intervals glucose level should be measured. Glucose monitoring applies not only to diabetics but to all surgical patients. Stress hyperglycemia is a condition in which glucose level rises in response to a stressful factor e.g. surgical intervention. Hyperglycemia >180 mg/dL within 48 h after operation is associated with an increased risk of complications including surgical site infections [45]. Body temperature should be maintained within normal limits (recommendation level IА). Temperature drop by 1.6°C leads to coagulation disturbances, excessive intraoperative blood loss and impaired peripheral circulation [46]. Hypothermia can also promote surgical site infections [47]. Patients with normal respiratory function, who undergo general or endotracheal anesthesia, should be given...
increased FiO2 during surgery and after extubation immediately after the procedure. In order to optimize oxygen supply, perioperative normothermia and adequate volume exchange should be provided (recommendation level IA).

**POSTOPERATIVE PHASE**

After operation, wound hygiene is crucial. The gold standard is ‘non-touch’ techniques, i.e. avoiding touching wounds and dressings with bare hands. Sterile saline should be used for rinsing the wound. After 48 h postoperatively, the patient should take a shower and wash his or her body with soap. It is not recommended to use local antimicrobial products to reduce the infection risk. In the randomized study by Kamath et al., local use of chloramphenicol had no effect on risk reduction of surgical site infection [48].

Clinical signs of infection traditionally include the following: local redness, pain, increased temperature, edema and purulent discharge [49]. In SSI treatment, it is necessary to open the infected area and drain the pus. Deep tissue infection requires drainage of the whole area, while superficial infections require only partial drainage. The remaining fibrin or sutures and staples should be removed or tissue debridement may be indicated in the case of necrosis. Infected wound should be treated with various antimicrobial products depending on surgeon’s preference (e.g. octenidine dihydrochloride, povidone iodine water solution). Concerns about antiseptics leading to bacterial resistance against them or even against antibiotics remain unsubstantiated. The concentrations of widely used antiseptics are even 100 times higher than their minimal inhibitory concentrations, and therefore they are capable of killing bacteria even after bacteria developing lower sensitivity to the antiseptic [50]. According to 2014 IDSA guidelines (Infectious Diseases Society of America), the use of antibiotics is unnecessary when there is minimal inflammatory infiltrate (less than 5 cm around the wound) with no signs of generalized infection defined as fever >38.5°C and heart rate >110/min. However, it is recommended to initiate antibiotics when the inflammation reaches beyond 5 cm and the above-listed signs of generalized inflammation are present [51]. When choosing the first-line treatment, local epidemiological situation and Gram staining of wound smears should be considered. Indications for microbiology studies in SSI patients include: severe clinical course, need for antibiotic therapy, suspected drug-resistant pathogens, allergy to first-line treatment. When staphylococcal infection is suspected, cefazolin, cefuroxime or cloxacillin can be used. For MRSA infection, it is justified to use linezolid or glycopeptides. When Gram-negative infection is suspected, the first-line antibiotic can be second or third generation cephalosporin or fluoroquinolones [51].

For complicated deep and non-healing wounds, negative pressure therapy should be considered. Negative pressure facilitates blood supply to the wound by promoting angiogenesis and increases the rate of granulomatous tissue formation. In the studies on rabbits, it was established that negative pressure accelerates blood flow through microcirculation and promotes vascular bed development [52]. Negative pressure therapy in infected wounds is safe. However, it must be preceded by debridement and initiation of targeted antibiotic therapy.

**SUMMARY**

Surgical site infections are not only a strictly medical but also a social problem. They are associated with prolonged hospital stay, increased mortality and disfiguring scars. Considering health outcomes and treatment costs, there is research being conducted all over the world together with causality analysis and search for methods for infection rate reduction. One very promising study is the multicenter SALT Europe trial. The main goal is to determine general and procedure-specific risk of surgical site infection caused by S. aureus in Europe. The study is to be published at the end of 2018.

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31. Rozporządzenie ministra zdrowia z dnia 10 listopada 2006 r. w sprawie wymagań, jakim powinno odpowiadać pod względem fachowym i sanitarnym pomieszczenia i urządzenia zakładu opieki zdrowotnej (Dz. U. z dnia 24 listopada 2006 r.).


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