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Recent advances in the treatment of biofilms induced surgical site infections

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Annually, more than 10 million in-patients (or more than a quarter of all hospital stays) undergo surgical treatments. Cesarean sections, orthopedic surgeries, neurosurgery treatments, and intra-abdominal operations are some common surgical procedures. Ambulatory surgical centers (facilities specifically designed for certain types of surgery after which the patient can be discharged directly home) are also seeing an increase in patients. The Centers for Disease Control and Prevention defines a surgical site infection (SSI) as an infection at or near the site of a surgical incision that develops within 30 days after surgery or within 90 days if prosthetic material is inserted during surgery[1]. Two to four percent of all in-hospital surgery patients get SSIs. Despite the effectiveness of antibiotics in managing infection, SSIs continue to be a major contributor to postoperative illness and death. Biofilm-associated SSIs do not respond to conventional antibiotic therapy due to multiple tolerance mechanisms devised by resistant bacteria[2]. An estimated 3% of patients who get an SSI may die as a result, and they are the primary cause of readmissions to the hospital following surgery. SSIs are a prominent cause of morbidity in patients despite being less common after ambulatory surgery than after in-patient treatments. Superficial incisional SSIs are those limited to the skin and subcutaneous tissues, whereas deep incisional SSIs extend into the deeper, softer tissues of the incision. Abscesses, anastomotic leaks after abdominal procedures, and infections caused by implants are all examples of infections that can occur in other organs or spaces.

Objective criteria have been used to characterize SSIs with the help of other technologies. Both a patient-centered wound questionnaire primarily intended for retrospective identification of SSI and the ASEPSIS (additional treatment, the presence of serous discharge, erythema, purulent exudate, separation of the deep tissues, isolation of bacteria, and the duration of in-patient stay) scoring system[3] were developed to evaluate sternal wounds. As opposed to the Centers for Disease Control and Prevention classifications, there was a higher inter-rater agreement for ASEPSIS in evaluating SSIs after colorectal surgery[4]. Such devices can be used to evaluate signs, symptoms, and wound care procedures by patients or medical staff both in the hospital and after discharge.

Patient characteristics (such as age, cigarette use, diabetes, and malnutrition) and procedural risk factors contribute to the likelihood of SSI occurring (including emergency surgery and the degree of bacterial contamination of the surgical wound at the time of the procedure). However, even though many of these risk factors are immutable, the vast majority of SSIs are considered preventable. In addition, recent research has increased our understanding of how hospitals can systematically prevent these infections[5].

In order to survive, many bacteria form dense colonies called biofilms, which adhere to inanimate or living surfaces and surround themselves with a matrix of extracellular polymeric substances they manufacture. This provides structural support for the biofilms and protects them from external stresses while allowing them to obtain nutrition. In addition, biofilms are protected from neutrophil attacks and antimicrobial agents and can survive in extremely harsh environments[2]. Endogenous microorganisms such as *Staphylococcus aureus*, coagulase-negative staphylococci, *Enterococcus*, and *Escherichia coli* are prominent causes of SSIs, although the prevalence of these bacteria varies[6]. In contrast, the air, surgical equipment, materials, and personnel in an operating room are all common external sources of bacteria. *Staphylococci* and *Streptococci* are the most prevalent microbes found outside the body.

Novel antimicrobial and antibiofilm treatment techniques are needed because the survival of biofilm-forming bacteria and the establishment of new resistant bacterial illnesses constitute a severe danger to public health[7]. Inhibiting microbial adhesion to the substratum, utilizing chemicals that interfere with and unsettle biofilm structure, and disturbing biofilm in its nascent phases are some of the methods now used to treat SSIs linked to biofilm development[5,8]. In addition, several classes of agents, such as nitric oxide-releasing antibiotics, antimicrobial peptides, antimicrobial lipids, extracellular polymeric substance-targeting

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enzymes, and quaternary ammonium compounds, have been considered as potential biofilm eradicators[9].

Nanoparticle-equipped antibiofilm implants are a relatively new invention. In a well-controlled animal investigation, Hassani Besheli *et al.*[10] demonstrated the efficacy of silk fibroin nanoparticles in the treatment of severe osteomyelitis. As a result of a recent study, a titanium pedicle screw coated with silver nanoparticles has been developed, which can prevent biofilm formation on implanted titanium screws in rabbits[11]. Infection management facilitated by nanotechnology has great potential for preventing acute postoperative infections in trauma and spinal implants and joint replacements. Hydrogels are another option available for wound healing[12–14]. Chopra *et al.*[15] formulated honey-based hydrogels with chitosan and polyvinyl alcohol for antimicrobial action on wound healing, which was supported by in-vitro and in-silico research. In addition to nanotechnology-based therapeutic strategies, natural plant-based products are also being evaluated as a novel approach for managing biofilm-associated SSIs[2]. These plant-based products, including plant extracts and essential oils, contains several novel compounds or phytochemicals that can be used to manage multidrug-resistant bacteria[16]. The bioactive non-nutrient secondary metabolites (phytochemicals) present in the plant-based products possess antibacterial, antiviral, antifungal, anti-inflammatory, antioxidant, and immunosuppressive properties that will be useful to treat SSIs linked to biofilm development[16,17].

An accurate diagnostic technique for evaluating bacterial infections is needed for an hour. A machine-learning system can help estimate the number of bacteria present in the biofilm. Further, these artificial intelligence-based deep learning models can be taught to identify polymicrobial biofilms with 90% accuracy, compared to 50% when compared to human specialists, providing a reliable alternative to conventional, time-consuming biochemical procedures. This method, in conjunction with other significant developments of ultrasonic contrast agents such as encapsulated gas microbubbles and nanobubbles, provides an advantage for real-time monitoring of biofilm creation and progression and for differentiating infected from healthy tissues. In addition, sensor-based approaches are gaining momentum as novel and accurate detection methods that can identify and monitor biofilm formation at wound sites[7]. Such techniques are easy to use and can be translated to point-of-care settings.

Avoiding elective surgery on patients with active infection, using prophylactic antibiotics at the appropriate times, ensuring proper skin preparation, and keeping operating rooms clean can help surgeons reduce the incidence of SSI. Adopting safe surgical practices is another way to lessen the likelihood of a SSI. Soft traction, successful hemostasis, the removal of necrotic tissue, the elimination of dead space, the irrigation of tissues with saline to prevent excessive drying, tension-free wound closure, and shortening the time needed for closed-suction drainage are all examples of best practices. Using electrosurgery with care can lessen the risk of burning off healthy tissue. Overuse can damage surrounding tissue, which makes it easy for infections to spread.

Antibiotic irrigation, topical antimicrobial drugs, antibiotic sutures, and antimicrobial dressings are some local and topical antibiotic administration strategies employed to lower SSI rates. There are many different ways to administer antibiotics, but only a few routes are used regularly to give antibiotics close to implants. Different types of surgical drains, such as closed-suction drains placed inside an anatomic region, have also been utilized to reduce the risk of SSI. In addition, surgical drains, either open or closed, have also been utilized in the subcutaneous region to help prevent SSIs. However, the routine use of drains to prevent SSI is not supported by the available data[18,19].

It has been documented how prophylactic negative pressure wound care can be used to avert SSI[20]. The available evidence shows that it can be used in high-risk procedures and on infected wounds, but the evidence is not very strong. Results are probably different depending on the level of contamination and incision site characteristics[21,22]. Despite the many antibiofilm approaches that have been devised, there is still a need for further research to address problems caused by insufficient mechanistic and biological knowledge of the chemical activity and biofilm interactions. Since in-vitro results do not always anticipate in-vivo outcomes, evaluating the antibacterial and antibiofilm activities of the studied drugs requires further in-vivo investigations and the standardization of the in-vitro methodology. Last but not least, future clinical trials would help us better understand the function of biofilms in SSIs since real-world situations, such as postoperative surgical wound infections, are linked to substantial microbial diversity, in contrast to laboratory investigations employing specific bacterial cultures.

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Data statement

The data in this correspondence article is not sensitive in nature and is accessible in the public domain. The data is therefore available and not of a confidential nature.

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