Infection following operations on the central nervous system: deconstructing the myth of the sterile field

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Neurosurgical patients are at a high risk for infectious sequelae following operations. For neurosurgery in particular, the risk of surgical site infection has a unique implication given the proximity of the CSF and the CNS. Patient factors contribute to some degree; for example, cancer and trauma are often associated with impaired nutritional status, known risk factors for infection. Additionally, care-based factors for infection must also be considered, such as the length of surgery, the administration of steroids, and tissue devascularization (such as a craniotomy bone flap). When postoperative infection does occur, attention is commonly focused on potential lapses in surgical “sterility.” Evidence suggests that the surgical field is not free of microorganisms. The authors propose a paradigm shift in the nomenclature of the surgical field from “sterile” to “clean.” Continued efforts aimed at optimizing immune capacity and host defenses to combat potential infection are warranted.

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THE world comprises innumerable bacterial species, all having highly evolved genomes that enable them to occupy specialized niches. Even when we limit our analysis of bacteria to the human body, there is a vast diversity of environments, each with a specific microbiome.⁷⁴ The human skin alone exhibits regional microbiome differences, and the NIH has recently launched a \$140 million dollar project aimed at characterizing 3000 reference genomes isolated from various body sites (http://www.hmpdacc.org/reference_genomes/reference_genomes.php). Given the distribution of the microbiome, one might expect a difference in the susceptibility and the type of surgical wound infection based on the local bacterial population alone. Indeed, data of surgical site infections suggest a correlation between surgery site and infectious organism.¹⁰⁶ Therefore, surgery can be viewed not only as a disruption in the homeostatic state of host defenses, but also as a disruption in the normal activity of regionally specific bacteria. It is only when the balance of host defenses and the expression of bacterial virulence factors is altered that a clinical state of infection can exist.^{56,62,64} Humans and bacteria typically exist in either a state of mutualism or commensalism; there-

fore we must recognize the existence of bacteria, even in the surgical field.

Clean, but Not Sterile

It is impossible to eradicate all microbes from the surgical field. Ultrastructurally, the skin surface contains crevices, including the sweat glands, that are incompletely accessible to commonly used skin preparation solutions or scrub techniques.⁶⁵ The degree to which our standard surgical skin preparation fails to sterilize the surgical field is highlighted in a recent publication by Shiono et al.⁸³ In this study, the authors obtained cultures at various time points during spine deformity operations. They demonstrated that 31% of skin cultures were positive immediately after patient skin cleansing with a povidone-iodine scrub solution. Not surprisingly, 25% of wound cultures were positive immediately after the initial exposure. This suggests that bacteria penetrate the wound at the time of the initial surgical exposure. It is likely that most wound infections are the result of direct contamination with the local microbiome, although several other sources of bacteria exist in the operating room. “Lapses” in sterile technique, such as the use of contaminated in-

struments and touching of unclean surfaces, certainly do exist and may introduce a greater inoculum and different microorganisms to the surgical field.

Evidence That We Are Not Alone

The theory of surgical asepsis was introduced more than 100 years ago.⁸ Since then, great strides have been made in decreasing bacterial presence in surgical wounds. Technological advancements such as the use of continuous video recording of surgical technique have been used to identify obvious breaks in sterile technique,⁹¹ but total surgical field sterility is not achievable. From the moment a surgeon performs the ritualistic surgical scrub, bacteria are present in the water.^{17,42,58,77} Swab studies and settle plate techniques demonstrate that microbes abound in the operating room. Even the air itself contains aerosolized microorganisms. During routine joint arthroplasty operations, a standard particle analyzer identified an average of 1786 colony forming units (primarily gram-positive cocci) from the air over a 10-minute capture period.⁹⁰ Other studies have used air sampler/settle plate techniques to assess the effect of different variables during simulated lumbar discectomies on microbe prevalence.¹⁰² During simulated operations, more than half of the samples in groups using the operative microscope or headlamp and loupes demonstrated bacterial growth (mainly coagulase negative *Staphylococcus*), significantly more than the control group.¹⁰² The efficacy of routine cleaning of surgical loupes, headlamps, and operating microscopes on the quantity of aerosolized microbes is not known, yet it is a minimal resource and no-risk intervention that may decrease the wound inoculum. With airborne bacteria, it is not surprising that many should end up on the “sterile” field.

Nearly all surgical gowns used in the operating room contain the presence of microorganisms. Systematic swab studies have demonstrated varying degrees of areas of cleanliness at the end of spinal operations. The presence of bacteria has been demonstrated to be lowest in the region between the chest and operative field, indicating that this may be the cleanest area of the surgical gown.¹¹ The applicability of this statement must take into consideration the type of operation being performed, because the ergonomic positions used to perform a spinal operation are distinctly different from those used when performing a retrosigmoid craniotomy. These surgical positioning factors may influence a surgical gown’s regional propensity for cleanliness.

The operating microscope drape is also frequently inhabited by microorganisms during operations. While negative control drapes have demonstrated no bacterial growth, microscope drapes used in spine operations have been shown to approach 100% contamination.¹² By using swabs obtained from different regions of the microscope drape, investigators in the study by Bible et al.¹² attempted to quantify regions of relative cleanliness. The “dirtiest” regions included the shafts of the optic eyepieces for the primary surgeon, the forehead portion on both viewing stations, and the overhead portion of the drape. This was hypothesized to occur due to inadvertent touching of the sterile portion of the drape by the surgeon. Interventions such as changing gloves after eyepiece adjustment and

avoiding handling anything above the eyepieces may decrease wound inoculum, although these measures have not been evaluated.

Information regarding the relative cleanliness of other areas of the surgical field is less well known. For example, light handle covers are potential sources for inadvertent contamination, yet a literature search reveals no information other than data from dental operations. Other potential high-risk areas exist in the surgical field, such as frameless stereotactic reference systems, because they traverse layers of the surgical drapes. There is also a paucity of data regarding the sterility of methods to drape the intraoperative CT or MRI scanners. Information from other intraoperative imaging techniques such as fluoroscopy can be extrapolated in these cases for estimation purposes, although it is not implied to be applicable. In a swab study, nearly all the drapes from a C-arm fluoroscopy machine were positive for bacterial growth after being used in a spinal operation.¹³ As the number of intraoperative imaging operations increases, it is important to optimize and standardize draping to minimize bacterial inoculum.

Preoperative Interventions

While the great majority of surgical wounds are contaminated, infections are still a relatively rare event. This indicates that the vast majority of bacteria are successfully cleared by the host. Multiple actions taken by the surgeon can be aimed at reducing the bacterial inoculum, which in turn may prevent the development of infection. Other actions taken by the surgeon can be aimed at optimizing host defense, something that is potentially the most significant aspect preventing surgically related infection (Table 1).

Preoperative Factors

The avoidance of surgical site infection begins in the preoperative period with several modifiable risk factors. The complex interplay between nutritional status and immune function cannot be understated.^{31,47} In a series of patients undergoing total joint arthroplasty, preoperative serum albumin levels < 3.5 g/dl (controversially used as a surrogate marker of nutritional status) were associated with a 7-times greater frequency of wound complication.³¹ For this reason, patients scheduled for elective or selective surgery could benefit from screening for impaired nutritional status. Identifying cachectic patients with malignancy or advanced age may allow for generalized nutritional optimization prior to surgery, thereby avoiding a known risk factor for infection.

In addition to optimizing the general nutritional state of patients prior to surgery, implementation of so-called immunonutrition supplements may improve rates of surgical infection. Preoperative supplementation with omega-3 fatty acids, arginine, glutamine, and nucleotides has been shown to boost immune function in clinical trials of surgical patients. Evidence for this benefit resides in their beneficial effect on known biomarkers of immune capacity and function, such as HLA-DR epitopes on monocytes and serum levels of interleukin-6 in high-risk surgical patients.^{66,95} Healthy volunteer studies have also

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TABLE 1: Common infection prevention strategies

Timing	Focus	Intervention	Level of Evidence*
preop	antibiotics	administration of antibiotics in the 2 hours before surgery reduces the risk of wound infection ¹⁸	II
preop	checklist	implementation of the checklist was associated w/ concomitant reductions in the rates of death & complications (including surgical site infection) among patients at least 16 yrs of age who were undergoing noncardiac surgery ⁴¹	II
preop	skin prep	there is insufficient research examining the effects of preoperative skin antiseptics to allow conclusions to be drawn regarding their comparative effects on postop surgical wound infections; ²²	I
		there was no evidence of a benefit in 4 trials associated w/ the use of iodophor-impregnated drapes ²²	I
intraop	gloving	there is no direct evidence that additional glove protection worn by the surgical team reduces surgical site infections in patients, but the review has insufficient power for this outcome; ⁹²	I
		perforation indicator systems result in significantly more innermost glove perforations being detected during surgery ⁹²	I
intraop	antibiotics	intraop redosing of cefazolin was associated w/ reduction in the overall risk for surgical site infection after cardiac surgery ¹⁰⁸	III
postop	antibiotics	antibiotics administered beyond 48 hours after cardiac surgery are ineffective in reducing surgical site infection & increase antimicrobial resistance; ³⁷	III
		prophylactic antimicrobials should be discontinued within 24 hours after the end of surgery ¹⁵	V

* Level of evidence assessed by the Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence (<http://www.cebm.net/index.aspx?o=5653>).

been performed that have demonstrated the beneficial effect of immune-boosting supplementation on experimental models of surgical wound healing and immune function.^{7,46} The most compelling evidence for their routine use in surgical patients comes from prospective, randomized, double-blind trials in which preoperative supplementation with arginine, omega-3 fatty acids, and dietary nucleotides resulted in a significantly reduced incidence of postoperative infection.^{20,86}

Overnutrition of the patient is also a concern to the neurosurgeon. Obesity is associated with an increased incidence of infection in patients undergoing spinal arthrodesis surgery.⁶¹ Specifically, the distribution of central obesity is more predictive of surgical site infection than body mass index alone. This can be measured on preoperative imaging by the length from the skin to the lamina distance at the L-4 level.⁶¹ Other methods to evaluate central obesity include the W-index (measured as the skin–spinous process distance to the anterior vertebral body–spinous process distance ratio). The influence of subcutaneous fat on surgical site infection is likely multifactorial, with increased operative difficulty, longer operative time, impaired tissue perfusion, higher proportion of diabetes mellitus, and impaired postoperative mobility contributing to varying degrees. Obesity may also impair tissue penetration of prophylactic antibiotics in a dose-independent fashion, limiting their efficacy in preventing surgical infections.⁹⁷ Facilitating preoperative weight loss in obese and super-obese patients in the preoperative setting is indicated not only for general health purposes, but it has also been shown to decrease surgical complications.^{3,89}

Other techniques for infection risk reduction in the preoperative period relate to reducing bacterial flora in the patient. Several studies have examined the influence of preoperative whole-body bathing with chlorhexidine or other wash products on surgical infection; a systematic review of 7 trials encompassing over 10,000 operations provides no clear evidence of benefit.¹⁰¹ However, direct efforts to eliminate *S. aureus* nasal carriage in the preop-

erative setting have been shown to be effective in decreasing surgical site infections in cardiac surgery patients.⁸¹ Efforts at evaluating the effect of surveillance and eradication of bacterial carriage in a neurosurgical-specific population have not yet been undertaken.

Another potential opportunity for preoperative intervention resides in determining the optimal order of surgical cases performed in a day by any particular surgeon. It has been shown that procedures performed later in the day carry a higher risk for postoperative infection.³³ Factors postulated to contribute to this phenomenon include the progressive deterioration of operating room cleanliness as the day progresses, cross contamination between health care providers during the course of the day, the use of flash sterilization for surgical instruments, and even nursing shift changes.³³ It should be noted that none of these factors has been validated in prospective trials. Scheduling patients that are anticipated to undergo longer operations and who possesses more patient-centered risk factors for infection to undergo surgery first in the day is a systems-based intervention that may be beneficial to overall infection rates. Given the limitations of study design, it is unlikely that this hypothesis could be practically evaluated.

Operative Preparation

While infection avoidance begins with optimizing preoperative host defenses, operations themselves are the setting in which bacteria infiltrate into surgical wounds and therefore play a key role in the balance between bacterial contamination and infection. Operations begin with both patient and surgeon skin preparation to reduce microbial load. While one may assume that decreased microbial load, particularly on the patient's skin, would be an independent risk factor for infection following neurosurgical operations, a prospective study found that microbial counts from preoperative (postpreparation) skin cultures were not associated with surgical site infec-

tions.¹⁹ In that study, obesity, duration of surgery, and age were independent statistically significant risk factors for infection following craniotomy.¹⁹ Although there is little controversy as to whether skin preparation is effective compared with no treatment at all, this finding supports the premise that bacteria abound in the surgical field even after patient skin cleansing. It also gives support to the notion that patient-centered variability in host defense plays a significant role in the development of infection in the setting of bacterial contamination. Additionally, there may be features of the skin preparation solution beyond its initial bactericidal effect that are unique to the durability and duration of its action.^{30,44} There are high quality data that preoperative cleansing with a chlorhexidine-alcohol solution is superior to povidone-iodine for preventing surgical site infections.²¹ These data provide evidence that differences in patient skin preparation do matter and directly contribute to the incidence of postoperative infections. The absolute microbial load just prior to incision may not be as influential as the duration of action of the antibacterial agent.

Another major component of patient skin preparation is the decision regarding the amount of hair removal. Practice patterns vary from wide hair removal from the scalp to no hair removal at all. In a large neurosurgical series, the practice of hair removal did not lower the risk of surgical wound infection.¹⁰⁴ In a review of more generalized surgical procedures,⁹⁴ there was no difference found in surgical site infections for those with hair removed prior to surgery compared with those who did not. When hair is removed, there is evidence that using a razor increases the rate of surgical wound infection when compared with using electric clipper devices,^{1,94} likely related to damage that a razor produces in the epidermis more so than electric clippers. Razors should not be used to remove hair in neurosurgical patients. Emphasis must also be placed on having electric clippers accessible to surgeons requiring hair removal when performing bedside procedures, such as ventriculostomy.

In addition to patient skin preparation, the surgeon's hand scrub is one of the most ritualistic portions of an operation and is routinely performed to prevent surgical site infection. Even though the surgeon's skin does not come into contact with the surgical field under ideal conditions, there is potential to transmit microbes through defects in surgical gowns or gloves. Therefore, the hypothesis exists that reducing the surgeon's microbial load can limit the potential for microbe transmission to the surgical field if defects exist. Methods of surgical scrub generally include the use of alcohol rubs or aqueous scrubs. Alcohol rubs are at least equivalent to aqueous scrubbing,⁶⁹ yet no superiority of one method over the other exists.⁹³ Because the alcohol-based rubs are potentially better tolerated and can be performed in less time, compliance may be improved. Similar to patient skin preparation, evidence from multiple studies suggests that chlorhexidine-based scrubs are more effective than povidone-iodine-based scrubs.⁹³ There exists no Class I or II evidence regarding the efficacy of scrub duration or mechanical adjuncts (such as brushes and sponges).⁹³

The air in the operating room itself has the potential

to contribute to surgical site infection given the known presence of aerosolized microbes. In high-risk, high-consequence surgical settings, joint replacement surgeons have turned to the concept of ultraclean air in the operating room to mitigate this factor. Using "space suits" and laminar airflow, the amount of microbes that are aerosolized can be reduced. In an analysis of thousands of operations, those performed in ultraclean air had a substantially reduced incidence of joint and major wound infection.^{52,53} Even the concept of ultraviolet light to kill aerosolized microbes has been proposed, yet is recommended against due to the documented potential health risks to surgical personnel.²⁵

As part of the patient preparation on the day of an operation, preoperative antibiotics are administered just prior to the incision to reduce the risk of subsequent surgical site infection. This practice has been widely adopted and is even recognized as a core component in surgical "time-out" checklists as a testament to the magnitude of their efficacy.^{14,15,18,41} The timing of administration is optimally within 60 minutes before skin incision.¹⁶

Surgical draping follows skin preparation and is one of the most variable practices in neurosurgery. The common goal is to provide a barrier between areas that have not undergone skin preparation with those that have, thereby establishing the surgical field.

Adhesive drapes applied directly to the surgical site have been the subject of debate with regards to surgical site infection. In neurosurgery, adhesive drapes may not even be technically possible given the presence or absence of hair. When looking at studies that compared the effect of adhesive drape with no adhesive drape, a significantly higher proportion of patients in the adhesive drape group developed a surgical site infection.¹⁰⁰ Therefore, it appears that there is at least preliminary evidence that adhesive drapes may increase infection rates.

Intraoperative Interventions

Antibiotic Administration

Given that it is known that bacteria are introduced into wounds by the act of surgery, certain actions taken by the surgeon can minimize the bacterial inoculum experienced by patients. Local antibiotics, in addition to systemically delivered prophylactic antibiotics, are a promising and low-risk intervention. In a large cohort of neurosurgical patients undergoing implantation of hardware, the infection rate was lowest (effectively zero) in those treated with local neomycin/polymixin treatment in addition to systemic antibiotics.⁶³

The old adage that "the solution to pollution is dilution" may hold true, although caveats exist. Local wound irrigation, particularly with detergent additives, is effective at cleansing surgical wounds.⁵ The aim of local wound irrigation is to remove, rather than kill, bacteria. While the volume of irrigation appears to be an important factor, the optimal volume or duration of irrigation is not known. In fact, high-pressure lavage has been shown to damage bone structure and disrupt soft tissue, possibly causing deeper penetration and retention of harmful

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bacteria.⁴⁰ Therefore, low-pressure lavage, combined with detergent or antibiotic agents, is indicated in the intraoperative care of routine surgical wounds.

As neurosurgical operations progress in length, the cumulative time possible for bacteria to mount an invasion accumulates. Some of the initial interventions such as preoperative antibiotic dosing lose their efficacy in a pattern related to the particular pharmacokinetics of the antibiotic administered.^{45,59} Therefore, redosing antibiotics in long-duration procedures at routine intervals is recommended to maintain antimicrobial action at the internal tissue level.¹⁰⁸ Automation with computerized prompts in the anesthesia record system is efficacious in increasing compliance with this redosing and should be routinely employed.^{88,107} Perioperative antibiotics are therefore those that are administered immediately before surgery, during surgery, and following an operation, and their proven efficacy is sufficient enough to warrant systems-based approaches to ensure timely consideration and dosing in all 3 time periods.

Additional Gloving

Other aspects of long duration procedures have implications given the mechanical wear and tear on surgical gowns, draping, and gloves. Some surgeons have advocated for the changing of surgical gloves to a fresh pair just prior to handling implantable hardware as a means to decrease infection risk.⁷² In theory, this does little to alter microbes that are already in the wound or microbes that are located on the surgical instruments, drapes, or surgical gown. Changing gloves prior to handling hardware may be effective in unknown ways, such as preventing the further introduction of bacteria as a result of occult perforations in surgical gloves. These perforations occur commonly in surgery and typically an hour after the initial incision.³⁵ Perforations can be minuscule and require water leakage or air-inflation tests to detect. Perforation indicator systems result in better detection of these acquired defects.⁹² Double gloving can reduce perforations to the innermost glove, yet its efficacy to reduce surgical site infections has yet to be observed.⁹² Procedures that place more mechanical stress on surgical gloves, such as instrumented spinal fusions, warrant consideration for more than 1 layer of glove or more robust material.

Tissue Handling Techniques

There are other less tangible aspects of neurosurgery that may predispose to infection, such as tissue handling techniques. Forceps destruction of skin edges, electrocautery, and retractor-related soft tissue ischemia are difficult to study, yet may be major determinants in preventing wound infection. Because the surgical incision is a controlled wound, surgeons must control the aspects that contribute to wound healing as much as possible in the patient's favor.⁸⁴ The use of Bovie electrocautery is commonplace in neurosurgical operations,⁷⁸ given its ease of use and efficiency in providing pinpoint hemostasis. The local tissue destruction caused by the Bovie impairs local blood flow and, in turn, the accessibility of the operative bed to the circulating immune system. The

same can be said for other means of surgical hemostasis, such as bipolar cautery and radiofrequency ablation.^{99,109} The formation of coagulated tissue in conjunction with impaired local immunity may predispose the patient to infection. Relatively few studies exist on the effects of Bovie electrocautery usage, yet their preliminary findings are important to consider. In a study of patients undergoing laparotomy, Bovie use increased the rate of postoperative infection.⁸⁷ Adverse effects of excessive Bovie use were also noted with seroma formation following mastectomy.⁷³ For patients undergoing median sternotomy, discriminate use of electrocautery decreased infection rates.⁶⁷ A major confounding factor with these studies is the very tissue operated on. In highly vascularized tissue, such as the posterior spine, Bovie use does not appear to have adverse effects.⁴⁸ Meanwhile, median sternotomy and craniotomy both entail the dissection of well-vascularized soft tissue overlying a devascularized, approximated bone incision. Other hemostatic adjuncts must be considered as well (such as bone wax) that have been demonstrated to increase the rate of sternotomy infection and dehiscence.^{39,55} New wax substitutes such as alkylene oxide copolymer bone hemostatic material are highly biocompatible, absorbed, and do not inhibit bone healing.^{57,103}

Local Tissue Perfusion and Oxygenation

Although deliberate alteration of perfusion and oxygenation during neurosurgical operations is common to provide the goal of neural protection,^{34,50,68,96} there may be consequences from these manipulations in terms of postoperative infection rates. Physiologically, hypothermia induces peripheral vasoconstriction that reduces oxygen tension in the subcutaneous tissues.^{54,82} Because phagocytes and neutrophils require relatively high oxygen content for antimicrobial activity,^{2,6,27} it has been postulated that artificial augmentation may improve surgical infection rates. In selected studies, intraoperative and postoperative high-concentration oxygen administration has been associated with a significant reduction in postoperative surgical wound infections.^{9,32} Consistent with this hypothesis, maintenance of normothermia has also been associated with a reduction of surgical site infection.⁴⁹ However, these studies were performed in a very small subgroup of patients undergoing colon surgery, making their applicability to the general neurosurgical population difficult. Follow-up studies have demonstrated that the use of induced perioperative high-oxygen delivery in a general surgical population does not reduce the overall incidence of surgical site infection.⁷⁵ Further study is necessary in regional tissue oxygenation in the neurosurgical population, particularly considering the unique variable of neural protection.

Wound Closure and Dressing Techniques

At the conclusion of the procedure, most wounds are dressed with a bandage. This variable practice serves to aesthetically improve the patient's condition following surgery and to provide some barrier to further microbial invasion. Because the wound is not completely epithelial-

ized for several days,⁸⁴ there is some vulnerability to further bacterial infiltration, and whether a bandage prevents this infiltration is not proven. There is also a hypothesis that surgical dressings provide a milieu for accelerated bacterial growth.

In a large series of neurosurgical patients, antibiotic ointment was applied in lieu of a bandage with comparable infection rates to historical controls.¹⁰⁵ Other than gauze dressings, other options for dressing surgical wounds include the use of tissue adhesives such as octyl cyanoacrylate. In vitro experiments have demonstrated that octyl cyanoacrylate is an effective barrier to microbial penetration by gram-positive, gram-negative, and nonmotile species for at least 72 hours.¹⁰ It has also been widely used in neurosurgical spine practice with low infection rates.³⁶ Other wound barriers include silver-impregnated dressings that have been used following lumbar fusion and are associated with a reduced incidence of infection.²³

Postoperative Interventions

Direct Antimicrobial Interventions

Interventions in the period following an operation are necessary to reduce the incidence of surgical infections. Prolonged courses of antibiotics (beyond 24 hours postoperatively) are sometimes administered in a prophylactic fashion, yet evidence for the efficacy of this practice is lacking. In patients undergoing coronary artery bypass surgery, prolonged duration of prophylactic antibiotics was ineffective in reducing surgical site infection and also increased the incidence of antimicrobial resistance.³⁷ Microbial resistance is a growing problem in both the community and the hospital setting; therefore antibiotics should be administered judiciously.⁷⁹ Because most antibiotic resistance mechanisms are associated with a fitness cost of reduced bacterial growth rate, it is possible that susceptible bacteria will outcompete resistant bacteria if the selective pressure from antibiotics is reduced.⁴ Other “systemic” forms of antimicrobial treatment, such as daily chlorhexidine baths, have been shown to be effective in decreasing rates of methicillin-resistant *S. aureus* and *Acinetobacter* infection, in addition to lowering rates of catheter-related bloodstream infection.²⁴ There may be elements to carefully extrapolate from this trauma population, given the sample size and power limitations of performing separate neurosurgical studies. For example, catheter-related bloodstream infections share a similar physical mechanism with external ventricular catheters—both are indwelling conduits that traverse the skin. Introducing chlorhexidine into the daily postoperative bathing solution is safe, requires little additional resources, and has a proven efficacy in reducing infection in a high-risk intensive care population.²⁴

Optimizing Postoperative Host Defense

Besides direct antimicrobial interventions, other surgeon-directed efforts at optimizing host defense in the postoperative setting are beneficial. Optimizing chronic health conditions such as diabetes mellitus is one prevalent subject of ongoing study. Elevated serum glucose directly impairs neutrophil^{28,71} and dendritic cell

function,⁷⁶ the major orchestrators of innate and adaptive immunity, respectively. In clinical trials, the use of perioperative continuous intravenous insulin infusion in diabetic patients undergoing open heart surgery reduced major infection and hospital cost.²⁶ However, there are also drawbacks to intensive insulin therapy, such as episodes of hypoglycemia, increased length of hospital stay, and even possible effects on mortality.²⁹ Evidence from a study of patients with brain tumors identified the duration of surgery as more important than blood glucose levels in the development of surgical site infection.³⁸ There likely exists an as-yet-to-be-determined optimal protocol that maximizes the benefit of avoiding hyperglycemia associated with infection and avoiding episodes of hypoglycemia that can contribute to death. This is extremely difficult in the neurosurgical population, in which steroids are routinely administered (or are endogenously produced as part of their disease process) that can result in elevated serum glucose levels.⁷⁰

Steroids themselves are immunosuppressive, and their use can predispose individuals to infection. This is true in the case of endogenous steroid production (Cushing disease)^{80,98} and with exogenous steroid administration.⁴³ It is possible that steroid administration may contribute to a negative synergy with patient pathophysiology and nutritional status, as observed in the setting of spinal operations for metastases.⁶⁰

Judicious use of postoperative steroids may reduce wound infection rates, but randomization and accounting for covariates are difficult to accomplish in clinical trial design. Surveillance for postoperative wound infection is important in the immediate days following an operation. Additionally, some indolent organisms such as *Propionibacterium acnes* can cause delayed surgical site infections,⁵¹ highlighting the need for patient education prior to discharge from the hospital.

Because sufficiently powered studies require thousands of patients to identify even small differences in a heterogeneous population with an already low rate of infection, many of these hypotheses cannot be practically evaluated; however, their lack of proven benefit does not necessarily indicate lack of efficacy.⁸⁵ Evaluating the cumulative and subspecialty surgical experience alike is important, because many of the infectious-related concepts already tested in clinical trials may have applicability to neurosurgical patients.

Conclusions

Any single infection in a neurosurgical patient represents the perturbation of balance between host defenses, virulence of the microbiome, and the inoculum experienced at the time of surgery. Efforts from the surgical team must be directed at each one of these fronts; the emphasis on any 1 factor should not lead to neglect of the others. Optimization of infection risk factors based on these principles can reduce the incidence of infection, thereby avoiding significant morbidity and mortality.

Disclosure

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