Emerging Paradigms in the Prevention of Surgical Site Infection: The Patient Microbiome and Antimicrobial Resistance

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Healthcare-associated infection has emerged as the most frequent complication of modern surgery, led by surgical site infection, which alone is second only to transfusion among outcomes measured by the National Surgical Quality Improvement Program (fig. 1). As a result, surgical site infections have become the leading cause of postoperative readmission and carry the greatest economic cost of all healthcare-associated infections.[1,2] At the patient level, surgical site infection increases mortality and postoperative pain and decreases quality of life, mental health, and satisfaction with medical treatment.[3–5]

While rates of other adverse hospital-acquired conditions monitored by the Agency for Healthcare Research and Quality (Rockville, Maryland; *e.g.*, falls, medication errors, postoperative thromboembolism, and other classes of healthcare-associated infection) have gradually improved over time, surgical site infection has seen little progress in recent years and by some measures even worsened.[6] The limitations of traditional infection prevention measures in achieving significant further improvement have led to a fundamental reexamination of the causes of surgical site infection, yielding new conceptual models of pathogenesis with important clinical implications. Two emerging paradigms at the center of this development are (1) *the role of the patient microbiome* and (2) *the spread of antimicrobial resistance into the general population*. The relationship of these factors to surgical site infection is influenced by a range of microbiologic, metabolic, immune, and socioecological factors (fig. 2) that introduce new layers of biologic complexity to the traditional view of "hospital-acquired infection," but provide novel avenues for prevention and quality improvement.

Other important aspects of perioperative infection prevention have been covered in recent Anesthesiology reviews and expert guidance documents, including cleanliness of the anesthesia workspace,[7] hand hygiene,[8] prevention of healthcare-associated infection in critical care environments,[9] and controversies in surgical antimicrobial prophylaxis.[10] This review focuses specifically on the prevention of surgical site infection,[1,2] covering new scientific evidence on pathogenesis and changing clinical approaches to prevention.[6]

Paradigm 1: Role of the Patient Microbiome in Surgical Site Infection

Germ theory, modern hospital sanitation measures, and advances in operating room sterility have led to substantial declines in perioperative infection over the preceding centuries. These improvements arose primarily from targeting environmental reservoirs of "exogenous" infection. Under this traditional model, surgical site infections are "healthcare-associated" *via* a causal relationship with nosocomial pathogens in the healthcare environment (fig. 3A). The ongoing importance of preventing exogenous infection continues to be underscored by studies demonstrating the role of perioperative sources such as the anesthesia workspace[11] and ultrasound probes[12] in clusters of common-source infection.

While maintaining clean perioperative environments, sterile technique, and hand hygiene remain cornerstones of infection prevention,[13] attention has increasingly turned to another important source as key to achieving further improvements in surgical site infection: the patient's own microbiome.[14–16] Under this complementary model, patients "bring their own" bacteria to the hospital, and "endogenous" infection occurs when commensal microbes shift from states of colonization to infection because of factors that perturb the microbiome (fig. 3B). While not arising from pathogens newly acquired from the hospital environment, these endogenous infections retain their classification as "healthcare-associated" events because of their relationship with procedures, medications, and physiologic stresses that uniquely occur in healthcare settings.

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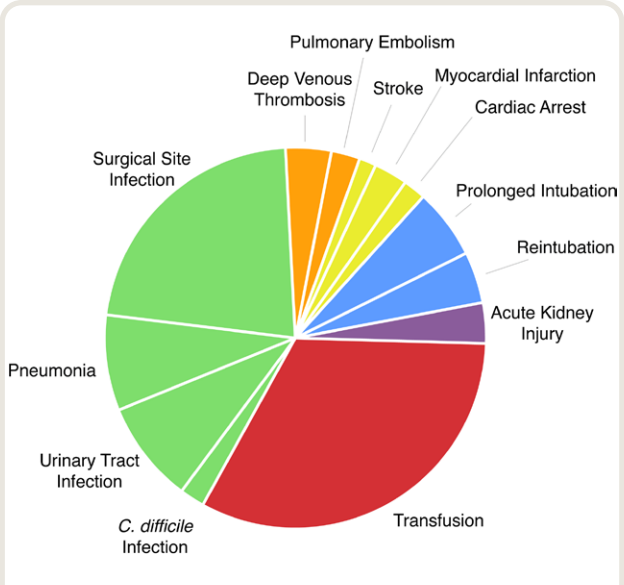


Fig. 1. Relative frequency of adverse perioperative events reported in most recent National Surgical Quality Improvement Program registry data. Healthcare-associated infection (*green*) is the most common overall class of postoperative complication measured by the American College of Surgeons National Surgical Quality Improvement Program, driven largely by surgical site infection, which is second only to bleeding as the most common single adverse event type reported. American College of Surgeons National Surgical Quality Improvement Program 2019 Participant Use File, https://www.facs.org/quality-programs/acs-nsqip/participant-use, accessed September 2, 2021. Detailed data descriptions available in "2019 PUF User Guide" accessible at this site.

Exogenous and endogenous infection may be caused by similar organisms (*e.g.*, *Staphylococcus*, *Klebsiella*, *Escherichia*, *Enterococcus*, and *Proteus* species) and cannot reliably be distinguished based on taxonomy or antimicrobial resistance patterns. However, studies using molecular techniques capable of tracking individual strains of *Staphylococcus aureus* have shown that *upward of 80% of surgical site infections arise from the preoperative patient microbiome.* This finding has been consistent across a range of patient, procedural, and geographic contexts.[17–20] While *S. aureus* is simpler to selectively isolate from preoperative patient samples for comparison with subsequent infection, accumulating evidence suggests that endogenously acquired infection may be the predominant mode of surgical site infection generally (not unique to *S. aureus*).[14,15,21] From this perspective, wound infection in the era of modern surgical practice has been described as a "failure to control the host-microbiome during surgery."[15]

The host microbiome may contribute to surgical site infection in the following ways.

Direct Contamination

The composition of the human microbiome varies dramatically by anatomic site, even differing significantly across various regions of the skin[22] (fig. 2C). Procedures such as surgical incision, intubation, and intravascular or urinary catheter insertion disrupt the normal anatomic separation of these compartments, resulting in mechanical translocation of bacteria from their normal sites of colonization (skin, oropharynx, gut) into new anatomic niches (deep tissue, lung, bloodstream, urinary tract; fig. 3B1). In this new microenvironment with differences in temperature, nutrient availability, immune activity, and competition from other species, quiescent bacteria can rapidly evolve to express pathogenic phenotypes and hence become "pathogens."

Prevention measures targeting endogenous wound contamination (*e.g.*, skin preparation, antibiotic prophylaxis) are highly effective, but have important limitations. For example, traditional approaches to surgical skin preparation effectively sterilize the epidermis; however, the skin microbiome extends into subepidermal layers, with pathogens such as *Pseudomonas aeruginosa* observed as deep as dermal or adipose tissue.[23] This limitation is particularly well described in shoulder surgery: *Cutibacterium acnes*, which heavily colonizes the shoulders of male patients and is a leading cause of chronic infection and arthroplasty failure, evades topical antiseptics through sequestration in sebaceous glands.[15]

Trojan-Horse Hypothesis

In addition to direct contamination of the surgical field, bacteria from anatomically distant compartments of the human microbiome may indirectly seed an otherwise sterile operative site (fig. 3B2). The "Trojan-horse hypothesis" is based on the observation that some pathogens, most notably *S. aureus,* can invade neutrophils at remote sites of colonization (*e.g.*, nares, gastrointestinal tract) and remain viable intracellular pathogens after re-entering systemic circulation.[14] As part of the normal immune response to surgery, these pathogen-laden neutrophils migrate to sites of traumatized tissue and foreign material (which may be sterile in the case of a surgical procedure), where they release this infectious payload in parallel with other inflammatory mediators *via* exocytosis.[24,25]

"Awakening" the Microbiome

Bacteria already natively present within the microbiome of the surgical site may also undergo phenotypic switching from commensalism to virulence without the need for translocation (fig. 3B3). Common perioperative exposures such as opioids,[26] anesthetic agents,[27,28] increased fraction of inspired oxygen (F_{IO_2}),[29] and physiologic stress[30] may dramatically impact the microbiome, triggering expression of pathogenic phenotypes among "normal" microbes resident in the surgical site.

In mice, morphine administration has been shown to rapidly induce a state of gut dysbiosis (reduced diversity, predominance of *Enterococcus faecalis*),[26] and trigger *P.*

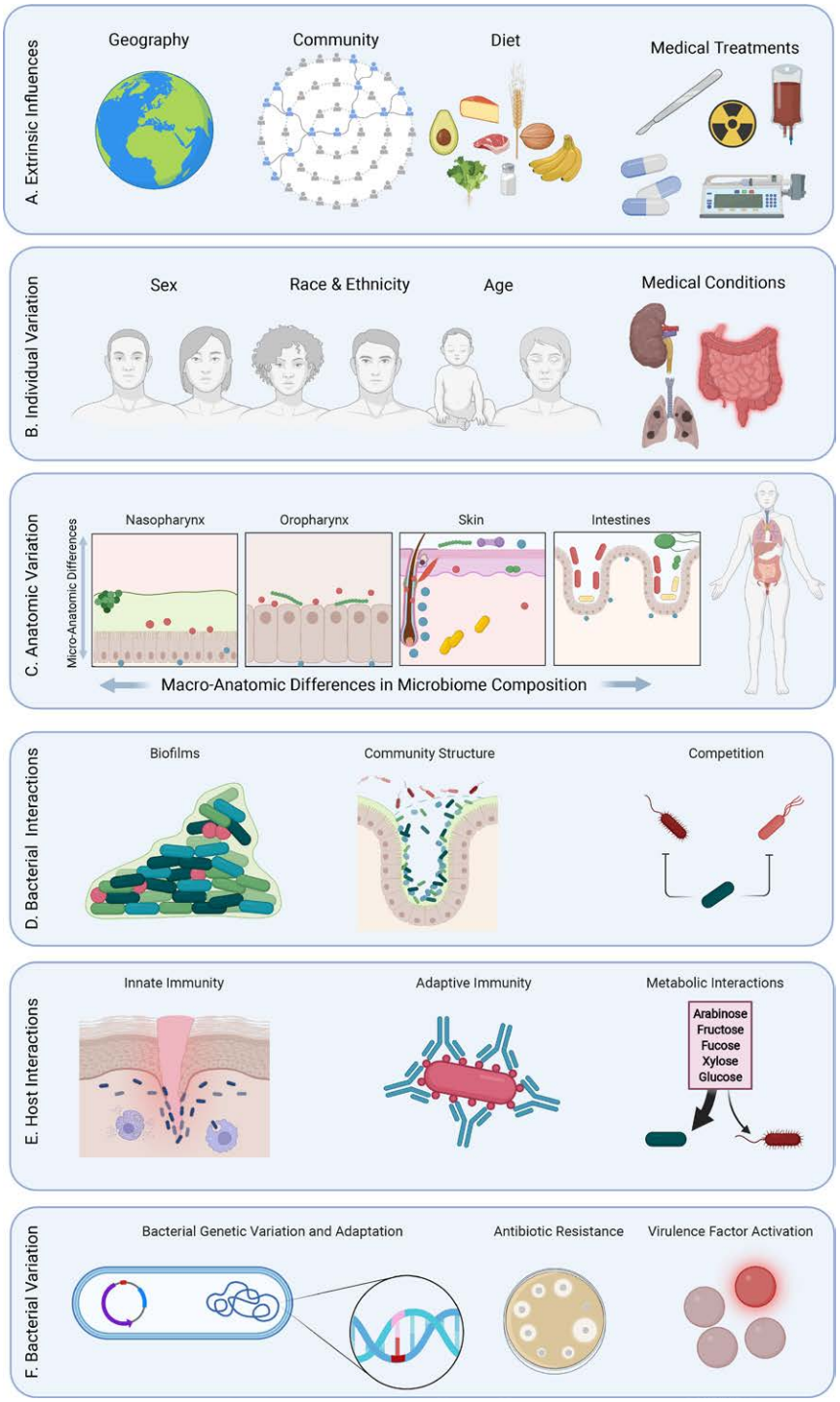
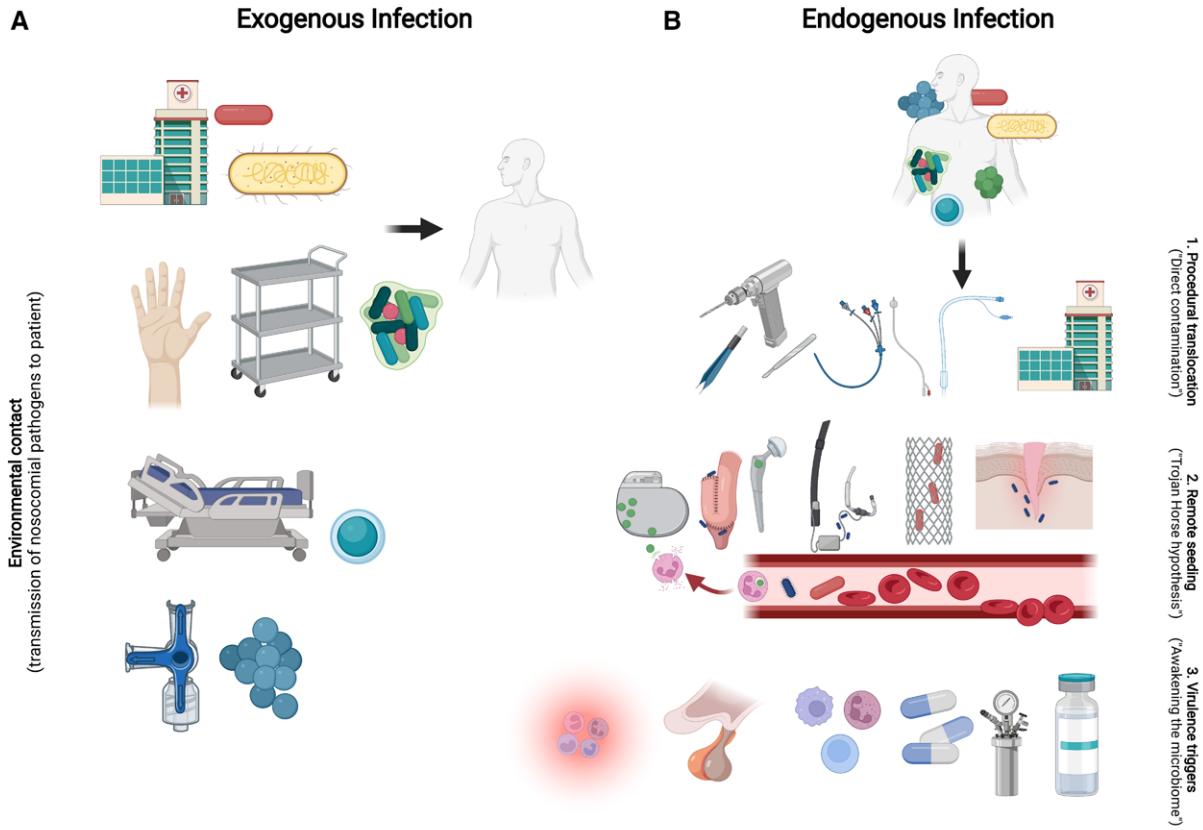


Fig. 2. Conceptual model of the human microbiome and layered factors influencing health and disease. The human microbiome can be conceptualized as having nested layers spanning epidemiologic to microscopic levels of organization, each of which can influence health and clinical outcomes such as infection. Community, diet, and medical treatments are among the most significant extrinsic factors (*A*) impacting the composition and function of the microbiome. Acute and chronic medical conditions as well as sociodemographic differences produce additional diversity in the microbiomes of individual patients (*B*). Within an individual, the distribution of microbes varies at anatomic and tissue levels (*C*), adding a spatial context to the dynamics of infection for surgeries performed on various body regions. The function and regulation of these communities are further affected by interactions between microbes (*D*) and with the host (*E*). At the level of an individual organism (*F*), differences in gene content, antimicrobial resistance, and virulence factor expression are clinically important determinants of infection that can be characterized and targeted.



C

Evolution of Surgical Site Infection Prevention Strategies by Route of Infection

	Exogenous	Both	Endogenous
Past	Focus on operating room attire	Increased FIO_2 Avoidance of perioperative glucocorticoids Clean surgical instruments on closing	Mechanical bowel preparation Iodine-based skin antisepsis
Present	Targted surface decontamination Sterile processing Ventilation/airflow Selective use of contact precautions	Hand hygeine Temperature management Glucose control Surgical antibiotic prophylaxis Sterile procedure IV system stewardship	Mechanical & antimicrobial bowel preparation Chlorhexidine-based skin antisepsis Preoperative methicillin-resistant *S. aureus* screening Nasal decolonization Reduced postoperatve prophylaxis
Future	Broad surface decontamination? Single-use devices? Equipment covers? Universal contact precautions?	IV system filtration/sterilization systems? Microbiome-concordant medication selection? Closed incision negative pressure wound therapy? Far-ultraviolet-C light systems?	Antimicrobial-only bowel preparation? Individualized surgical antibiotic prophylaxis? Improved preoperative screening, decolonization? Dietary prehabilitation? Elimination of routine postoperatve prophylaxis? Probiotics and/or fecal autotransplantation?

Fig. 3. Exogenous and endogenous routes of infection and evolving approaches to surgical site infection prevention. Traditional conceptions of healthcare-associated infection are hospital-centered, emphasizing the role of "exogenous" infection with bacteria newly acquired through contact with the hospital environment (*A*). Under this model, infection occurs when pathogens are transmitted from nosocomial reservoirs (surfaces, hands, ventilation systems, instruments) to the patient through contact that occurs in the course of clinical care. Exogenous sources are frequently implicated in common-source outbreaks, which attract significant attention; however, bacterial genetic analyses now demonstrate that, in routine clinical circumstances, the vast majority of healthcare-associated infections are "endogenous," arising from the patient microbiome rather than the hospital environment (*B*). Under this complementary model, bacteria colonizing the patient before contact with the healthcare system become pathogens when procedures (*1*), exposures (*2*), and stresses (*3*) that occur in the hospital disrupt normal regulation of the microbiome. The evolution of surgical site infection prevention strategies over time (*C*) can be conceptualized through this perspective. Fio_2, fraction of inspired oxygen; IV, intravenous.

aeruginosa virulence and gut-derived sepsis.[31] These effects can be attenuated by administration of opioid-receptor antagonists such as methylnaltrexone.

Brief periods of volatile anesthetic exposure, on par with a typical anesthetic, have also been shown to collapse microbiome diversity with reductions in protective organisms

such as *Lactobacillus* and selection for potential pathogens such as *Bacteroides* species. These changes begin within a day of exposure, peak at approximately 1 week, and are similar for sevoflurane[27] and isoflurane.[28] Delivery of increased F_{IO_2}, once recommended as a routine prevention measure, has recently been demonstrated to increase proliferation of aerobic bacteria (*e.g.*, *S. aureus*) and pathologic inflammation in the lung and gut[29] with little or no overall impact on rates of surgical site infection.[32,33]

In addition to their direct influences on the microbiome, many of these same factors simultaneously affect the host immune response (fig. 2E). Commonly used intravenous opioids[34] and volatile anesthetics[35] have potent immunosuppressive potential, the clinical sequelae of which have not been adequately studied. Soluble factors in plasma and wound fluids from trauma patients that peak within the first day of injury in response to tissue damage suppress neutrophil function,[36] and may similarly increase susceptibility to infection after major surgery. Interestingly, recent proteomic analyses have demonstrated that the immunologic stage for postoperative surgical site complications may be set well in advance of surgery. In a study of patients undergoing noncancer bowel resection, individual differences in preoperative immune and inflammatory phenotypes improved prediction of postoperative outcomes compared with the National Surgical Quality Improvement Program Surgical Risk Calculator, which utilizes traditional clinical predictors.[37]

Paradigm 2: Antimicrobial Resistance and Surgical Antibiotic Prophylaxis

Surgical antibiotic prophylaxis remains a pillar of prevention and is one of the most profound, broadly applicable, and cost-effective measures of preventing both exogenous and endogenous wound infection. When the addition of routine prophylaxis was initially studied in the 1960s to 1980s, infection rates were reduced approximately 50 to 60% across a wide range of surgical procedure groups.[38] However, since that time, the global burden of antimicrobial resistance has significantly increased and is now a leading cause of mortality worldwide.[39] Resistance has outpaced development pipelines for novel antimicrobial agents and has expanded beyond the confines of the healthcare setting into the general population through sustained community transmission, agricultural and commercial products, and outpatient prescribing practices. The impact on efficacy of current standard surgical prophylaxis regimens has been modeled for U.S. surgical populations, estimating that (1) approximately 40 to 50% of surgical site infections are currently resistant to standard prophylactic agent(s) for the procedure, and (2) continuation of these trends in the United States could result in tens or hundreds of thousands of additional infections per year.[38] The presence of diverse antimicrobial-resistant strains within the microbiomes of patients presenting for care now poses a complex set of challenges for prophylaxis against endogenous infection in procedures such as surgery and cancer treatment, potentially necessitating individualized approaches tailored to the patient "resistome"[40] (fig. 2F).

The rise of antimicrobial resistance has widely been referred to as the "next pandemic,"[41] with the potential to disrupt current approaches of infection prevention and broadly impact healthcare systems. As tragically experienced in the current pandemic, existing sociodemographic disparities may similarly be exacerbated by differences in resistance and microbiome health in our communities.[39,41] The burden of surgical site infection is known to be elevated in low- and middle-income countries, partially driven by higher rates of prophylaxis-resistant Gram-negative infection in these regions.[39,42] Similar resistance-associated disparities in surgical outcomes are likely to develop, or may already exist, within the United States but have not been studied.

Evolving Clinical Approaches to Prevention

In light of these emerging paradigms and new clinical evidence, approaches to the prevention of surgical site infection are beginning to evolve (fig. 3C). Overall, this development is characterized by a shift from a hospital-centered to patient-centered model of pathogenesis and from aseptic to medical approaches to prevention. While some measures are procedure-specific, many elements are shared and span the entire perioperative period.

Preoperative. Because a significant proportion of surgical site infections are known to arise from bacteria colonizing the patient before surgery, numerous preventative opportunities exist to characterize and optimize the microbiome preoperatively.

Preoperative Microbiome Screening. Nasal swabbing for methicillin-resistant *S. aureus* represents an established approach to preoperative screening for resistant organisms in populations with high rates of endemicity, enabling personalization of prophylaxis based on the result (methicillin-resistant *S. aureus*–colonized patients should receive prophylaxis with vancomycin in addition to otherwise indicated agents such as cefazolin[10,43]). Various methods of methicillin-resistant *S. aureus* screening are currently utilized in the United States, with variable sensitivity (approximately 97% for polymerase chain reaction assays, approximately 77% for standard culture, and only approximately 15% for patient-reported history).[44,45] Limited efficacy data indicate that polymerase chain reaction–based preoperative screening is associated with lower rates of surgical site infection.[45] Clinical sensitivity of screening is further impacted by the number and location of sampling sites: approximately 30% of methicillin-resistant *S. aureus*–colonized patients are exclusive extranasal carriers,[46] and sampling of other anatomic sites such as the rectum or skin of the intended surgical site warrant consideration in high-risk groups.

This precedent for methicillin-resistant *S. aureus* screening can rationally be extended to preoperative screening for other organisms with high potential for causing infection, such as cefazolin-resistant Gram-negative bacteria.[47] Carriers of extended-spectrum β-lactamase–producing Enterobacterales have double the risk of surgical site infection after colorectal procedures, and a system of preoperative screening and tailored prophylaxis in regions with increased rates of carriage may reduce this risk[48] but remains a topic of debate. A recent anesthesiology-led study of preoperative nasal microbiome characterization builds upon this concept, demonstrating that, even after adjustment for *S. aureus* carriage, preoperative microbiome "cluster" is a stronger predictor of postoperative infection than traditional clinical factors such as age, procedure type, and medical comorbidity.[16]

Challenges to realizing the potential of preoperative screening include the growth of remote preoperative evaluation and actionable test turnaround times in cases of urgent or emergent surgery. Experience and innovation in high-reliability preoperative microbiologic screening developed during the COVID-19 pandemic may enable health systems to address these challenges more effectively: molecular diagnostic platforms acquired by many hospital laboratories for rapid preoperative SARS-CoV-2 screening can be repurposed for quick, highly accurate detection of methicillin-resistant *S. aureus* using alternative cartridges[49] (*e.g.*, to determine optimal prophylaxis for trauma patients requiring orthopedic implants shortly after admission). Cost-effective use of mail-in, patient-collected swabs has also demonstrated the feasibility of maintaining robust screening as an element of virtual preoperative evaluation and optimization.

Preoperative Decolonization. While laboratory evidence of methicillin-resistant *S. aureus* colonization should guide selection of surgical prophylaxis, guidelines for preoperative decolonization have shifted from targeted to universal approaches due to the practical limitations of current screening systems and extrapolation of data from intensive care environments.[50] Whether targeted or universal, evidence for the efficacy of nasal decolonization of *S. aureus* for the prevention of surgical site infection remains conflicted, even among well-designed trials.[19,51] As a result, current practice guidelines do not emphasize or delineate an optimal approach to preoperative *S. aureus* or methicillin-resistant *S. aureus* decolonization,[52] although the perceived low-risk, low-cost nature of this potentially beneficial intervention has favored its ongoing use. Mupirocin ointment was the most widely used agent when seminal studies of nasal decolonization were conducted in the preceding decades; however, concerns regarding development of mupirocin resistance and lack of an over-the-counter formulation have led to adoption of alternative, nonantibiotic treatments such as povidone-iodine and ethanol swabs. Despite their practical advantages, it is important to note that robust, unbiased outcome data for these products are lacking, and microbiologic data suggest an efficacy window as brief as several hours.[53] The mechanisms by which nasal decolonization may impact surgical site infection at a remote operative site are not well established, and the independent benefit of chlorhexidine-based skin decolonization protocols is also not well delineated.

Bowel Preparation. In contrast to mixed data on preoperative nasal and skin decolonization, recent data on the impact of various bowel preparation regimens in colorectal surgery are comparatively robust: mechanical bowel preparation alone does not reduce the risk infection, but the addition of a preoperative oral antibiotic cuts rates roughly in half.[54] This regimen should include agents with Gram-negative and anaerobic activity (*e.g.*, neomycin plus either metronidazole or erythromycin) administered in three doses over the day before surgery, in addition to standard intravenous prophylaxis before incision. The comparative efficacy of oral antibiotics alone (without mechanical bowel preparation) has not been directly studied and is not currently recommended.[54,55] Preoperative probiotic administration is a promising future adjuvant to bowel preparation. The ideal timing and composition of such therapy in relation to traditional bowel regimens, to the native host microbiome, and to the specific surgical procedure (gastric, small bowel, large bowel, cancer *vs.* noncancer, among others) remain unresolved scientific questions and clinical studies to date remain limited.

Nutritional Prehabilitation. In addition to screening and eliminating bacteria with pathogenic potential, it may also be possible to influence the preoperative microbiome toward health. Diet has been shown to be among the most influential factors shaping one's microbiome (fig. 1A), and mice fed meals simulating the Western diet have greatly increased mortality after normally survivable abdominal surgery.[56] This effect can be reversed by "dietary prehabilitation" with a low-fat, high-fiber, plant-based diet over the course of 1 week, potentially consistent with the scheduling of a typical surgical procedure. Such microbiome-directed dietary interventions may be complementary to enhanced recovery and prehabilitation programs targeting physical frailty and age-associated vulnerability. These preoperative factors, as well as the influences of perioperative enteral feeding, may modulate the complex postoperative interplay between ileus, anastomotic leak, and systemic bacterial gut translocation.[57–59]

Intraoperative. Timely and appropriate antibiotic prophylaxis remains a key aspect of intraoperative prevention and has been comprehensively covered in a recent Anesthesiology review.[10] Since the time of that publication, interim data from a randomized trial of topical vancomycin in neurosurgery have been updated showing no substantial difference in infection rates after enrollment of approximately 1,000 patients (NCT02284126). A large randomized controlled trial of cefoxitin *versus* piperacillin–tazobactam in pancreatoduodenectomy has also completed

enrollment, and forthcoming results will represent the largest head-to-head comparison of intravenous prophylactic regimens in modern surgical practice (NCT03269994). Other essential clinical points covered in that resource, but worthy of emphasis, include the following:

1. Antibiotic allergies should be critically assessed with patients before induction of anesthesia as the risk of infection is substantially increased with use of alternative agents such as vancomycin or clindamycin.
2. Vancomycin prophylaxis for methicillin-resistant *S. aureus* positivity should be administered in addition to (not as a substitute for) cefazolin. Many methicillin-resistant *S. aureus*–colonized patients are co-colonized with methicillin-susceptible *S. aureus*, and vancomycin is substantially less effective against methicillin-susceptible *S. aureus* with no activity against Gram-negative organisms.
3. Improved clinical protocols are likely needed in many practice settings to achieve earlier initiation of antibiotics requiring administration as an infusion (*e.g.*, vancomycin) to ensure effective tissue concentrations by the time of incision.

Other traditional elements of intraoperative infection prevention remain unchanged, but are supported by new mechanistic evidence. Avoidance of intraoperative hypothermia is known to reduce surgical site infections and support the host immune response, but a key mechanistic connection may be the improved ability of skin-derived bacteria to replicate at lower temperatures, comparable to that of the skin surface.[60] Perioperative glucose management has long been associated with postoperative infection in patients with diabetes mellitus, with an emphasis on preoperative hemoglobin A1c. Avoidance of hyperglycemia during the intraoperative and postoperative periods has now been shown to be similarly important for patients both with and without diabetes.[61] Anesthesia workspace cleanliness and hand hygiene remain foundational in preventing direct transmission of nosocomial bacteria to patients and have been addressed in a recent expert guidance document collaboratively developed between leading infection preventionists and anesthesiologists with expertise in this area.[7] Their importance is further underscored by the role of horizontal resistance gene transfer within healthcare environments (in addition to transmission of resistant bacteria themselves) as contributors to healthcare-associated infection.[62]

In contrast, the significance of other traditional intraoperative factors has been de-emphasized. Use of increased F_{IO_2} was previously recommended as a routine infection prevention measure, but recent re-analyses indicate little or no benefit.[32,33] As described in the section "Awakening" the Microbiome, increased F_{IO_2} may also favor some pathogens over others and promote harmful inflammation.[29] In 2020, the World Health Organization (Geneva, Switzerland) downgraded its recommendation for this practice; however, comparable Centers for Disease Control and Prevention (Atlanta, Georgia) guidelines have not been updated since 2017 and therefore do not yet reflect this revised perspective. Association of periOperative Registered Nurses (Denver, Colorado) guidelines for surgical attire such as head coverings were previously stringent but were revised in 2020 in light of new studies showing no association with surgical site infection. Intraoperative dexamethasone administration for postoperative nausea and vomiting prophylaxis has historically raised concerns in patients at high risk for infection, but robust safety data now exist from the large, multicentered Perioperative Administration of Dexamethasone and Infection trial of intraoperative dexamethasone, which showed no increase in the primary endpoint of surgical site infection.[63] Finally, the practice of changing to fresh operative instruments at the end of colorectal procedures to avoid contamination of the wound during closure was also shown to have no effect on surgical site infection in a recent randomized trial.[64]

Postoperative. Factors in the postoperative period continue to influence the risk of infection after completion of a surgical procedure. In addition to maintenance of intraoperative measures such as glucose and temperature management, the use of negative pressure dressings and postoperative antibiotic prophylaxis are common practices that can be guided by new clinical evidence.

Prophylactic use of closed incision negative pressure wound therapy involves placement of a small, negative pressure system over a closed surgical wound as an alternative to a standard surgical dressing. This approach allows continuous efflux of fluid and cellular material from the wound, resulting in reduced edema and accelerated tissue healing. The most recent update to the Cochrane Review on this topic reports an increase in the overall quality of evidence supporting efficacy in prevention of surgical site infection[65]; however, data from individual high-quality trials in specific populations (*e.g.*, obese patients undergoing cesarian section[66]) indicate that this benefit varies by patient, procedure, and wound type.

The continuation of antibiotic prophylaxis into the postoperative period represents a significant opportunity for improved antimicrobial stewardship. Trials across a wide range of surgical specialties comparing shorter *versus* longer (greater than 48-h) courses of postoperative prophylaxis in the absence of established preoperative infection have consistently shown that longer durations do not prevent surgical site infection, but predispose to antimicrobial resistance when infection does occur and increase rates of *C. difficile* infection and acute kidney injury.[67–69] For patients with clean or adequately debrided open surgical wounds, meticulous wound care (potentially including negative pressure therapy) remains preferred over extension or escalation of antimicrobial prophylaxis.

Conclusions and Future Opportunities

This emerging model of surgical site infection, influenced by the patient microbiome and the changing landscape of antimicrobial resistance, introduces new complexities and

opportunities for the field of perioperative medicine, both now and in the future.

Currently, emphasis in the preoperative period should be placed on consistent and timely collection of preoperative samples for methicillin-resistant *S. aureus* screening in endemic regions, nasal decolonization, and antimicrobial bowel preparation. On the day of surgery, optimal antibiotic selection should be determined before induction of anesthesia, informed by the results of methicillin-resistant *S. aureus* screening, the planned procedure, and discussion of relevant allergies with the awake patient. Prophylactic vancomycin infusions should be initiated before case start to ensure adequate levels by the time of incision and should be given in addition to standard agents for the planned procedure (*e.g.*, cefazolin) with rare exception. Temperature and glucose management should span the entire perioperative period, with increased attention to detecting hyperglycemia in nondiabetic patients. Anesthesiology departments should work closely with hospital infection prevention and control teams to identify resources and practical approaches to implementing recommended anesthesia workspace hygiene measures.[7] After surgery, select patient groups may benefit from prophylactic use of close incision negative pressure wound therapy devices, and postoperative continuation of antibiotics use should be avoided or limited to a maximum of 24 to 48 h in the absence of established preoperative infection.

Looking forward, opportunities for practice improvement include areas such as enhanced preoperative screening and nutritional optimization, evaluating sociodemographic disparities in perioperative infection, postoperative stewardship in the intensive care unit, and advancement of institutional and public policy related to perioperative healthcare quality. The status quo of one-size-fits-all prophylaxis guidelines will increasingly be challenged by the spread antimicrobial resistance and the need for personalization. Tailored approaches targeting the individual patient microbiome hold promise in achieving a balance of antimicrobial efficacy and stewardship. Incorporation of infection prevention topics into Accreditation Council for Graduate Medical Education (Chicago, Illinois) training programs and academic collaboration through established networks such as the Multicenter Perioperative Outcomes Group (Ann Arbor, Michigan) represent significant opportunities for our specialty to contribute to the future safety, equity, and quality of surgical care.

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Competing Interests

The authors declare no competing interests.

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