

Infection control in colon surgery

Donald E. Fry^{1,2,3}

Received: 7 June 2016 / Accepted: 16 June 2016 / Published online: 27 June 2016
© Springer-Verlag Berlin Heidelberg 2016

Abstract

Purpose The aim of this study is to provide a comprehensive review of strategies that should be employed in the prevention of infection at the surgical site in patients undergoing colon surgery.

Methods The world's literature on the pathogenesis and prevention of infections at the surgical site in colon resection were reviewed to identify those methods that are associated with improved rates of infection at the surgical site. The pathogenesis, microbiology, diagnosis, and surveillance of surgical site infection have been reviewed in the context of better understanding the accepted methods for prevention. Recommendations are provided based upon evidence-based information when available.

Results Surgical site infection rates in colon surgery have been reduced consistently over the last 60 years of surgical practice. Preoperative and intraoperative techniques are described which have been useful in this improvement, while postoperative methods including the extension of postoperative systemic antibiotics have not been of value.

Conclusions Many methods have been demonstrated to improve surgical site infection rates in colon surgery. However, consistent and standardized applications of these principals in prevention currently do not exist. Application of evidence-based practices can further reduce the morbidity and cost of infection following colon surgery.

Keywords Preventive antibiotics · Oral antibiotic bowel preparation · Mechanical bowel preparation · Surgical infection control · Colon surgery

Infection continues to be a major source of morbidity in the patient undergoing elective colon surgery. Among all planned operations, infections following colon surgery are the most frequent. Infections in the colon surgery patient have proven to be very costly, result in prolonged hospitalization time, and are major causes of readmissions following discharge from the hospital. There has been an extensive effort over 80 years of clinical investigations and research to refine methods in the prevention of surgical site infection (SSI) in these patients.

In a historical review of his lifetime work in the prevention of SSI in colon surgery, Poth [1] noted that colon surgery in the 1930s was associated with a 10–12 % surgical mortality rate and that over 80 % of resection cases were complicated by incisional infection, leakage of the colonic anastomosis, or both. Progress in the prevention of SSI has been considerable with current infections being reported at rates less than 10 % [2] and anastomotic leak rates that may approach 3–6 % [3]. Despite these results, considerable improvement is necessary. It will be the objective of this presentation to provide an understanding of the pathogenesis of infection in the colon surgery patient and to identify those methods that are proven or are expected to improve rates of infections in these patients.

✉ Donald E. Fry
dfry@consultmpa.com

¹ MPA Healthcare Solutions, 1 East Wacker Drive, Suite 1210, 60601 Chicago, IL, USA

² Department of Surgery, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

³ Department of Surgery, University of New Mexico School of Medicine, Albuquerque, New Mexico

Microbiology of the human colon

There are more bacterial cells within the lumen of the colon than there are eukaryotic cells in the host [4]. When the succus entericus reaches the cecum, the vast majority of nutrients have been absorbed and the colon function becomes one of

water and electrolyte absorption. The intraluminal environment of the colon is largely anaerobic. These conditions lead to proliferation of bacteria to very large concentrations, and only the barrier functions of the colon prevent dissemination of the colonization. Bacterial concentration at the cecum is 10^5 – 10^6 colony forming units (cfu)/ml, and the colonization is largely gram-negative facultative bacteria (e.g., *Escherichia coli* and *Klebsiella pneumoniae*) (Fig. 1). As the luminal content progresses distally in the colon, solid stool content is formed. The bacterial density progressively increases to 10^{10} – 10^{12} cfu/ml, and the gram-negative bacterial colonists become predominantly an array of anaerobic species of which *Bacteroides fragilis* is most notable (Fig. 1) [5]. *Enterococcus* sp. likewise increases in number. An important issue is that while the bacterial concentration in the formed stool is progressive increasing from the proximal colon to the rectosigmoid area, the concentration of bacteria within the mucus layer overlying the colonocyte is similarly increasing in number. With nearly one trillion bacterial/g in the stool and a similar number in the mucus at the distal colon, it should not be surprising that surgical intervention even with the best of techniques will result in the local release of millions of bacterial cells into the soft tissues and the surgical incision.

Pathogenesis of SSI

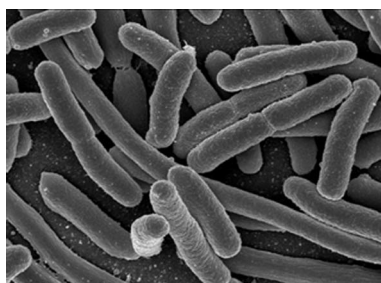
Because of the large numbers of bacteria that contaminate the surgical site with invasive operations of the colon, all surgical wounds have culturable bacteria at the termination of the procedure even when all appropriate infection control practices

are used. Only a minority develop clinical infection. The probability of infection is a function of multiple bacterial and host factors, and is not simply a matter of microbial presence in the tissue.

Knowledge of the pathophysiology of the surgical wound is important to understanding the emergence of infection [6]. With the surgical incision, blood vessels are disrupted and tissue factor is released. Cleavage products from the coagulation cascade, vasoactive products from platelet activation, activation of the bradykinin pathway (contact activating system), mast cells, and complement cleavage products all produce a local environment that is rich in initiator events and opsonins that launch the innate host response. The net effect is microcirculatory vasodilation, edema formation, and then phagocytic cell migration into the injured tissue in the quest to identify and eliminate foreign products (e.g., bacteria) that are present in the wound. Extravasation of serum results from increased microcirculatory permeability, and this leads to extravascular precipitation of fibrin on the wound interface as a nonspecific host mechanism to avoid microbial access to the soft tissues from the external environment. After wound closure, if the vascular and phagocytic functions of inflammation are effective in eradicating bacterial contamination of the surgical site, then wound healing proceeds without infection. If net microbial effects exceed the capacity of the host innate response to eradicate wound contaminants, then suppuration ensues and clinical infection is the result.

What are the determinants of infection following a colon resection; i.e., what are the net microbial effects that result in clinical infection? (Fig. 2) First, the most important determinant in the development of SSI is the inoculum of microbial

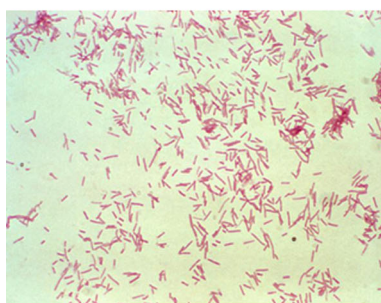
Fig. 1 The electron and photomicrographs of common pathogens in the surgical site infections that are observed of colon surgery patients



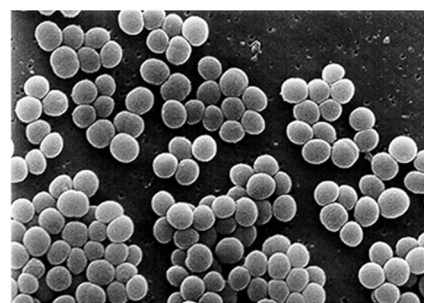
E. Coli; 15,000x



Klebsiella pneumoniae; 23,000x



Bacteroides fragilis; 1000x



Staphylococcus aureus; 10,000x

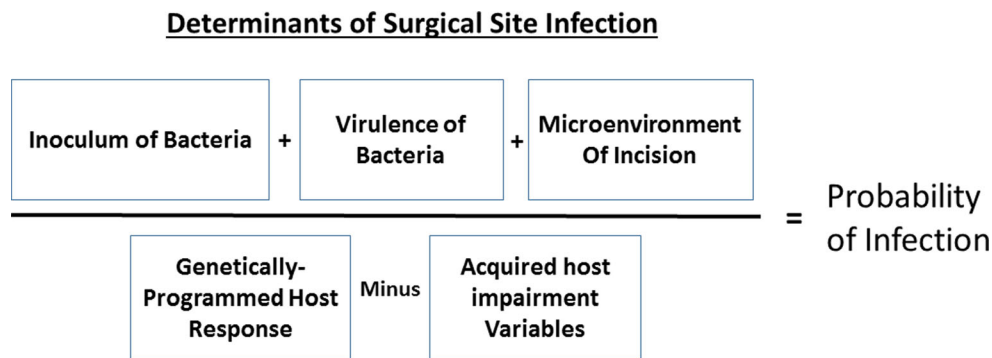


Fig. 2 The determinant of infection in the surgical site of colon surgery patients. The probability of infection is favored by the inoculum of contamination, the virulence of the contaminants, and the environment of the surgical incision. These variables that increase the probability of

infection are offset by the genetically programmed host defense of the patient. The host defense can be impaired by acquired acute and chronic conditions of the host

contaminants in the wound tissues. Many studies have validated that the probability of infection increases as the bacterial density per gram of tissue increases. Early studies identified that 10^5 bacteria/g of tissue was the critical threshold that resulted in infection [7]. With polymicrobial contamination as is seen in colon surgery, the synergistic interaction of different aerobic (*E. coli*, *Klebsiella* sp., and others) and anaerobic species (*B. fragilis*) may result in lesser concentrations of bacteria that are needed to achieve clinical infection [8]. Efforts to reduce the density of bacterial concentration become the most important strategy to reduce SSIs.

It must be emphasized that colonic bacteria are not the sole source of potential pathogens in colon surgery. Bacteria from the patient's skin and from the operating room environment add to the overall inoculum that may contribute to infection as an outcome. Skin colonization is with gram-positive bacteria (e.g., *Staphylococcus aureus*, [Fig. 1]) at the beginning of the procedure, and this source of contamination introduces another pathogen for the surgical site that may account for 20 % of observed SSIs in the colon surgery patient. The risk of methicillin-resistant *S. aureus* (MRSA) in particular looms as a major issue in colon and other surgical procedures [9].

A second determinant of SSI is the virulence of the bacterial contamination. Each bacterial species has an intrinsic virulence that is dictated by the various endotoxins, exotoxins, antimicrobial resistance patterns, and other factors. The unique virulence characteristics of the contaminant of the surgical site are important features in dictating which organism emerges as a pathogen, and which organism is eradicated by the innate inflammatory response. The individual virulence characteristics will result in far fewer bacteria that are necessary to contaminate the wound to result in clinical infection. While little can be done to manage the random bacteria that will contaminate the wound, future strategies in the prevention of infection will need to focus upon efforts to modulate the effects of the virulence factors and not necessarily be designed to kill the organism.

The local environment of the surgical wound and the host tissues becomes a third determinant of infection. To paraphrase a quote attributed to Pasteur, “the pathogen is nothing, the terrain is everything [10].” While the number and virulence of microbes at the surgical site are important, there is no question that the pathophysiologic effect of the pathogens is amplified by local conditions of the soft tissues. Sub-infective inocula of bacteria result in infection when free hemoglobin or hematoma in the wound tissues or wound interspace provides a ready source of iron to promote microbial proliferation [11]. Dead tissue within the wound from overly aggressive use of the electrocautery, or from other local insults, cannot be penetrated by phagocytic cells and becomes a haven for bacterial proliferation. Foreign bodies (e.g., braided silk sutures) provide a surface that harbors bacteria and is a surface that impairs phagocytic function [12]. Selected bacteria on foreign body surfaces will produce a biofilm that functionally serves as a protective shield against humoral and cellular host defense mechanisms [13]. Finally, the adverse “terrain” is further identified by wound dead space where serum, inflammatory exudates, and red cells are sequestered dependently and becomes an ideal environment to foster microbial proliferation and infection.

The fourth determinant of SSI is the integrity of the host immune response [14]. Host responsiveness can be viewed as having an intrinsic and an acquired effectiveness. Every patient has a genetically programmed intrinsic inflammatory response. Polymorphism in genetic expression yields different clinical phenotypes of the initiator events discussed above, in the efficiency of phagocytic cell functions, and in the pro-inflammatory signals that govern effectiveness in the eradication of bacteria. Intrinsic effectiveness is poorly measured because acquired variables modulate the innate response. Hypoxemia, core body temperature, glucose concentrations, current medications (e.g., corticosteroids), acidosis, anemia, and preexisting infection all impair host responsiveness and contribute to SSI as an outcome. As opposed to the intrinsic

host variability, these acquired conditions are actionable by the clinician as will be addressed subsequently.

Thus, the determinants of infection allow a hypothetical equation to be developed for the prediction of SSI (Fig. 2). If excessive net effect of the inoculum, the virulence of the contaminant, or the hostility of the surgical site environment exceeds the host response, then infection is the response. Prevention requires measures to reduce the net microbial effect, and perhaps interventions to enhance the responsiveness of the host.

Diagnosis and surveillance of SSI

A consistent standard for the definition of SSI has remained elusive. In Table 1, the Centers for Disease Control and Prevention (CDC) definition of the three categories of superficial, deep, and organ/space SSI is presented [15]. A feature of this definition is that a surgical site is infected when the surgeon declares it to be infected. A converse to this statement is also true: If the surgeon states that the site is not infected, then it is recorded as not infected. Consistency in reporting SSI rates clouds efforts at surveillance and confounds efforts to identify whether measures to improve results are effective. If obvious pus is discharged from the wound, then infection is generally agreed to be present. A small discharge from a small section of the incision becomes problematic. Serous discharge from a section of the wound that may grow a few colonies of *Staphylococcus epidermidis* and spontaneously resolves is even more problematic. The greater the rigor with which the surgical site is evaluated, the higher will be the observed infection rate.

This is illustrated by different observers reporting different rates of SSI. My research identified a 3.9 % SSI rate among elective colon resections from the National Inpatient Sample, a rate that I viewed as not being valid and stated so in the published manuscript [16]. For approximately the same period, SSIs were self-reported at between 4 and 10 % depending upon the four risk tiers of patients by the National Healthcare Surveillance Network (NHSN) in the USA [17]. A published report on data from the National Surgical Quality Improvement Project identified an overall 9–11 % SSI rate depending upon whether a right or left colon resection was performed [18]. Finally, three prospective studies with postdischarge follow-up in elective colon surgery during the 1990s and 2000s demonstrated SSI rates > 20 % [19–21]. Does anyone know the real SSI rate for elective colon surgery or any other surgical procedure? Clearly, different groups are declaring infection rates for the same population of patients with different definitions.

In addition to inconsistent definitions among observers, effective surveillance is another major issue in the highly variable rates of SSI that are reported. The momentum for shorter hospital lengths-of-stay of surgical care has resulted in the majority of infections not being identified until the postdischarge period of time, and many of these may be identified by providers other than those from the site of the index procedure. Many postdischarge events are not reported, and many may not even be recognized by the operating surgeon. Identification of infections is very problematic after hospital discharge [22], and it is likely that SSI rates are linked to the vigilance of surveillance.

A final consideration in understanding and interpreting reported SSI rates is risk adjustment. There are a multitude of patient and treatment-associated risk factors that can influence the rate of SSIs in colon surgery (Table 2). All variables that are beyond the control of the surgeon and the hospital may well influence infection rates. Chronic diseases such as diabetes and chronic lung disease may create acquired pathophysiologic consequences that influence SSIs. The presence of the underlying disease (e.g., advanced-stage colon cancer) will influence different infection rates from those having an elective procedure for less onerous conditions. The American Society of Anesthesiology Physical Status Classification System has been an effective way to provide a coarse method to estimate risk (Table 3) [23] and has been used by the NHSN with the presence of gross contamination and the duration of the operative procedure to create a four-tier system for risk adjustment [24]. More recently, the NHSN has developed a national risk calculator that permits the computation of a predicted SSI rate from the risk profile of the patients within a given institution. This risk tool employs a more sophisticated logistic prediction model [25]. A Standardized Infection Ratio (SIR) can be calculated by the observed-to-predicted ratio of SSIs within an institution [26]. A SIR above 1.0 reflects performance that is poorer than the national predicted rate, and a SIR less than 1.0 represents a superior performance. The variability of surveillance and the local interpretation of definitions for SSI leave this methodology of uncertain value, especially when these data are used for public reporting of hospital and surgeon performance.

With all of these uncertainties about definitions and surveillance, SSI rates can only be interpreted within an institution or collaborating group of institutions dedicated to improved care. Standardized definitions and surveillance need to be established. Collaboration with other institutions is essential to identify postdischarge emergency department visits and readmissions to other facilities. As electronic medical records proliferate, capturing the use of postdischarge antibiotics may be a tell-tale sign that infection has occurred. A given rate of risk-adjusted SSIs can really only be interpreted and tracked within an institution over time when the same definitions and surveillance methods are utilized.

Table 1 Definitions of superficial, deep, and organ/space SSIs as defined by the National Healthcare Safety Network

Definition	Comments specific for elective colon surgery
<p>Superficial SSI: Infection occurs within 30 days after any colon resection procedure. Infection involves only skin or subcutaneous tissue of the incision. The patient must have at least one of the following:</p> <ol style="list-style-type: none"> 1. Purulent drainage, with or without laboratory confirmation, from the superficial incision. 2. Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision. 3. Superficial incision is deliberately opened by a surgeon and is culture-positive or not cultured, and patient has at least one of the following signs or symptoms: pain or tenderness; localized swelling, redness, or heat. A culture negative finding does not meet this criterion. 4. Diagnosis of superficial incisional SSI by the surgeon or attending physician, or other designee (nurse practitioner or physician's assistant). 	<ol style="list-style-type: none"> 1. There are two specific types of superficial incisional SSIs: <ul style="list-style-type: none"> • Superficial Incisional Primary (SIP): a superficial incisional SSI that is identified in the primary incision in a patient that has had an operation with one or more incisions (e.g., primary laparotomy site in a colectomy). • Superficial Incisional Secondary (SIS): a superficial incisional SSI in a secondary incision (e.g., second incision site of a colostomy closure). 2. Do not report stitch abscess (minimal inflammation and discharge confined to the points of suture penetration). 3. Do not report a localized stab wound or drain site infection as an SSI. 4. Do not report cellulitis by itself as an SSI. 5. Incisional SSI that extends into the fascial and muscle layers is reported as a deep incisional SSI, not a superficial SS.
<p>Deep SSI: Infection occurs within 30 days after elective colon resection <i>and</i> involves deep soft tissues of the incision (e.g., fascial and muscle layers), <i>and</i> the patient has one of the following:</p> <ul style="list-style-type: none"> • Purulent drainage from the deep incision (i.e., pus) • A deep incision that spontaneously dehisces or is deliberately opened by a surgeon and is culture-positive or not cultured, <i>and</i> the patient has at least one of the following signs and symptoms: fever (>38 °C); localized pain or tenderness. A culture-negative finding does not meet this criterion. • An abscess or other evidence of infection involving the deep incision that is found on direct examination, during invasive procedure, or by histopathologic examination or imaging test. • Diagnosis of a deep incisional SSI by a surgeon or attending physician or other designee (nurse practitioner or physician's assistant). 	<ul style="list-style-type: none"> • There are two types of deep incisional SSIs: <ul style="list-style-type: none"> ○ Deep Incisional Primary (DIP): a deep incisional SSI that is identified in a primary incision where multiple incisions exist (e.g., midline laparotomy and colostomy closure site). ○ Deep Incisional Secondary (DIS): a deep incisional SSI that is identified in the secondary incision where multiple incisions may exist (e.g., colostomy closure site). • Infections involving both superficial and deep sites should be classified as deep incisional SSIs. • The attending physician is interpreted to mean: <ul style="list-style-type: none"> ○ Surgeon ○ Infectious disease specialist ○ Other physician on the case ○ Emergency physician ○ Physician's designee
<p>Organ/space SSI: Infection occurs within 30 days after elective colon resection <i>and</i> infection involves any part of the body, excluding the skin incision, fascia, or muscle layers that is opened or manipulated during the operative procedure, <i>and</i> the patient has at least one of the following:</p> <ul style="list-style-type: none"> • Purulent drainage from a drain that is placed into the organ/space. • Organisms isolated from an aseptically obtained culture of fluid or tissue in the organ space. • An abscess or other evidence of infection involving the organ/space that is found on direct examination, during invasive procedure, or by histopathologic examination or imaging test. • Diagnosis of an organ/space SSI by a surgeon or attending physician or other designee (nurse practitioner or physician assistant). 	<ul style="list-style-type: none"> • Because an organ/space SSI involves any part of the body (excluding skin incision, fascia, or muscle layers) that is manipulated during the operative procedure, criterion for infection at these body sites must be met in addition to the organ/space SSI criteria. • If a patient has an infection in the organ/space being operated on and the surgical incision was closed primarily, subsequent continuation of this infection type during the remainder of the surveillance period is considered an organ/space SSI, if organ/space SSI and site-specific infection criteria are met. • Occasionally, an organ/space infection drains through the incision and is considered a complication of the incision. Therefore, classify it as a deep incisional SSI (e.g., sub-fascial abscess).

From [15]. The comments are specifically applied to elective colon surgery

Prevention of surgical site infections

There are an extensive number of preoperative and intraoperative measures that are necessary to prevent SSIs. Failure to comply with any of these subsequently detailed preventive measures means that infection is a potential outcome. The numerous measures and risks that can potentially lead to infection underscore that compliance with only antibiotic use, or correct application of antiseptics at the surgical site by themselves will not dramatically reduce SSI rates if other preventive strategies are ignored.

The following discussion will address methods that are not always applied. There will be no discussion about wearing protective head gear, surgical masks, eye shields, and other

attire of the operating room environment. These are uniformly accepted practices even though many (e.g., shoe covers) may not have clinical evidenced to proof efficacy.

Pre-incisional methods

Prolonged preoperative hospitalization

Beginning with the landmark contributions of Cruse and Foord [27], several publications have highlighted that prolonged hospitalization before the operative procedure will increase infectious complications with major surgical procedures [28, 29]. Prolonged preoperative hospitalization is a surrogate marker for case complexity and is usually attended

Table 2 The intrinsic patient risk factors and the treatment-related risk factors that are associated with surgical site infections in colectomy patients

Intrinsic patient risk factors		Treatment-related risk factors	
Advanced age	Obesity	Length of operation	Hair removal strategy
Alcoholism	Drug abuse	OR traffic	Glove/barrier failure
HIV disease	Chronic liver disease	Poor antibiotic timing	Wrong antibiotic choice
Chronic renal disease	Corticosteroids	Intraoperative “spill”	Excessive electrocautery
Chronic tobacco use	Diabetes	Skin antiseptics	Adhesive drapes
Hyperglycemia	Chronic lung disease	Contaminated instruments	Contaminated irrigation solution
Hypoalbuminemia	Malignancy	Preoperative showers	Braided suture material
Nasal colonization	Preoperative nursing home	Excessive traction/wound trauma	Wound dead space
Chronic hemodialysis	Recent hospitalization	Transfusion	Drains
Presence of Stoma	ASA score	Wound hematoma	Glove starch
Resistant bacterial colonization	Virulent colonization	Intraoperative hypothermia	OR air handling systems
Prehospitalization antibiotics	Inflammatory bowel disease	Antibacterial sutures	Wound sealants
Prior surgical site infections	Preoperative anemia	Patient controlled analgesia	Pulsed-lavage of the surgical site
Nonsteroidal anti-inflammatory agents	Recent weight loss	Mechanical bowel preparation	Oral antibiotic bowel preparation

The list constitutes the most common risk factors identified by the author and is not inclusive of all possibilities

by multiple preoperative diagnostic studies and perhaps management of medical conditions to optimize the outcome. The patient may have received a course of antibiotics or other pharmaceutical agents that potentially impact the host. The commonly accepted reason for increased infections with 3 days or more of preoperative hospitalization is that the patient will become colonized with resistant hospital microflora. MRSA colonizes the patient’s skin and mucus membranes. Gut microflora change to resistant gram-negative species. Additional exposure to *Clostridium difficile* spores and other hospital-acquired microflora may have ramifications for infections other than those at the surgical site. Obviously, many operations need to be performed with several days of preoperative hospitalization, but truly elective procedures may benefit from hospital discharge and rescheduling the patient for a subsequent elective procedure when prolonged inpatient care exceeds 3 days. When operations must proceed following three or more days of inpatient care, the surgeon should make adjustments to preventive antibiotic choices to compensate for adverse patient colonization.

Prehospitalization cleansing of the surgical site

A controversial area for prevention has been the use of antiseptic soaps and solutions at the proposed surgical site prior to hospital admission. Instructing the patient to shower/bath and diligently scrub the surgical site has been documented to reduce the density of skin microflora, but not been consistently demonstrated to reduce SSI rates [30]. There is always the issue of whether the patient was compliant in the application of the antiseptic soap or solution, and whether recolonization occurs prior to the actual surgical incision. Studies with chlorhexidine have identified binding of the antiseptic to skin

surface and a sustained antibacterial action well after application [31]. Repeated scrubbing or application of the antiseptic has been documented to provide concentrated antimicrobial activity. These data make the case that repeated prehospitalization scrubs or skin applications at the surgical site may be of benefit. Additional studies are necessary to document the intuitive concept that prehospitalization antiseptic use at the surgical site should be effective.

Hair removal

There is a long-standing tradition in surgical lore that body hair at the surgical site promotes infection and should be removed. Current evidence indicates that for most patients, hair does not promote infection and does not need to be removed [32]. Operations on the scalp and those procedures performed in very hirsute patients require hair removal for logistical reasons. When necessary, hair removal should be performed with electric shaving devices in the operating room immediately prior to initiation of the procedure [33]. Using straight razors to remove hair results in minor cuts and abrasions that become sites for microbial proliferation. Hair removal should not be performed the night before the operative procedure even with electric clippers since minor abrasions from the process may lead to adverse colonization by the following day. Depilatory agents have been used for hair removal, but evidence to support this method is lacking.

Pre-incisional skin preparation

The use of antiseptics for the preparation of the surgical site before incision remains somewhat controversial and confusing. The 1999 recommendations by the CDC in the USA did

Table 3 Descriptor of the six categories that currently comprise the American Society of Anesthesiology Physical Status Classification System

ASA score	Description of classification	Patient example in colon surgery
1	Normal healthy patient	A 55-year-old patient with recurrent diverticulitis episodes with an ideal body weight, no co-morbid conditions, no history of tobacco use.
2	Patient with mild systemic disease	A 62-year-old woman with mild but controlled hypertension who walks 8 km/day. She is 2 kg over ideal body weight.
3	Patient with severe systemic disease	A 53-year-old man with insulin-dependent diabetes, 12 kg over ideal body weight, and stable coronary artery disease undergoing a right hemicolectomy for a sessile cecal polyp.
4	Patient with severe systemic disease that is a constant threat to life	A 70-year-old woman on chronic renal hemodialysis is undergoing a sigmoid colectomy for a partially obstructing adenocarcinoma.
5	Moribund patient who is not expected to survive without the operation	A 58-year-old man with morbid obesity, type 2 diabetes, septic shock undergoing colon surgery for a free perforation of a sigmoid colon cancer.
6	Patient declared brain-dead whose organs are being removed for donor purposes	Not applicable in colon resection.

From [23]. Examples are provided that are relevant to colon surgery patients

not make a specific recommendation and basically concluded that chlorhexidine, povidone iodine, and isopropyl alcohol were all equivalent [34]. Isopropyl alcohol is generally viewed as having superior antibacterial action, but its flammability creates a certain anxiety when the electrocautery is being used in the procedure [35]. Chlorhexidine has better antiseptic effect than povidone iodine and has been the preferred preparation for prevention of intravascular device infections [36] and in selected studies of surgical site infections [37, 38].

There has been a trend to add isopropyl alcohol to either chlorhexidine or povidone iodine. The addition of the isopropyl alcohol not only has a major antiseptic effect but also facilitates the drying process of the chlorhexidine or povidone iodine to enhance antibacterial effects. One study demonstrated superiority of the chlorhexidine-isopropyl alcohol combination when compared to povidone iodine alone in abdominal surgery [39]. A study with isopropyl alcohol added to the povidone iodine would have been a better comparison, and the benefits of adding the isopropyl alcohol to chlorhexidine need to be compared to chlorhexidine alone. A review of most studies on the use of topical antiseptics at the surgical site indicates that many are underpowered to demonstrate a difference, and many have design flaws that may bias the outcomes. At present, any of the three identified skin antiseptics or combinations can be used if applied appropriately and permitted to dry before the skin incision. Discriminating evidence in favor of one preparation or combination over another requires further elucidation. An important consideration in pre-incisional skin preparation is that the application of the selected antiseptic be consistent with recommended practices. Failure to

completely apply the antiseptic across the entire field, or using towels to remove the antiseptic before drying will compromise the benefits of the antiseptic [40].

Adhesive plastic skin drapes/skin sealants

Adhesive skin drapes placed over the patient's skin with the subsequent incision passing through the plastic has been used for decades to reduce SSI rates. The concept is that adherent plastic prevents bacteria that colonize skin pores and crevices from reaching the subcutaneous tissues of the incision. Early models of these drapes failed to improve infection rates probably because dense adherence of the plastic to the skin diminished as the procedure progressed. Newer versions of adhesive plastic applications have a much more resilient adherence, and many have an antiseptic coat to further control potential bacterial contamination. A meta-analysis failed to document reductions in SSIs with the newer versions of the adhesive plastic skin drape [41].

A variant of the adhesive skin drape is to apply a cyanoacrylate skin sealant over the surgical site before the incision. This is done after the skin antiseptic has been applied and has dried. Like the adhesive drape, the theory behind the skin sealant is that it will reduce bacterial access to the surgical wound and reduce SSI rates by entrapment of remaining bacteria after antiseptic application in the follicles and pores of the skin. While the sealant has been shown to reduce bacterial colon counts in the incision [42], reductions in SSI rates have not been validated.

Preventive systemic antibiotics

With the introduction of antibiotics into medical practice in the late 1940s and 1950s, there has been the promise that the use of preventive antibiotics especially in colon surgery would reduce or eradicate infection at the surgical site. Early efforts at using preventive systemic antibiotics failed because the drugs were not administered until after the operation was completed and the wound was closed. It was the experimental studies of Miles et al. [43], followed by additional experimental studies in clinically relevant models by Burke [44] that clearly identified that the antibiotic with activity against the contaminating bacteria had to be present in the tissue prior to the contaminating event. Another important observation in these experimental studies was the lack of benefit in the prevention of infection for antibiotics given systemically after soft tissue contamination had occurred. Studies by Bernard and Cole [45] in abdominal surgery without colon cases were the first to demonstrate potential benefit to the administration of antibiotics prior to the surgical incision.

The first study with a major cohort of colon resection patients for systemic preventive antibiotics was Polk and Lopez-Mayor [46]. For colon surgical cases, the use of preoperative cephaloridine was associated with a reduction of SSIs from 30 to 7 %. Subsequent studies by Stone and associates identified that antibiotics started after the operation had no benefit in the prevention of SSIs [47] and that preoperative antibiotics that were supplemented with five postoperative days of the drug were no better than the preoperative drugs alone [48]. Baum et al. [49] in 1981 summarized the clinical trials that validated the use of preoperative systemic antibiotics in colon surgery and concluded that no further trials needed to be conducted using placebo controls. Song and Glennly [50] summarized the literature on the comparisons of preoperative antibiotics alone compared to postoperative extension of the drugs in colon surgery and concluded that no value can be associated with systemic antibiotics given after wound closure. McDonald et al. [51] did a meta-analysis of gastrointestinal operations including colon resections and similarly concluded that additional benefits are not derived by continuing systemic antibiotics beyond the time of wound closure.

Why are preventive antibiotics given after wound closure not of value in colon surgery? It is somewhat counter-intuitive that the drug with activity against the likely pathogens would be effective if given before the incision but has no impact if administered after wound closure. The answer is an extension of the prior discussion about inflammation and the pathogenesis of wound infection [52]. Organisms that are present at the surgical site following operation are imbedded in the soft tissues of the wound interface and in the fibrin layer overlying the incised tissue. With wound closure, the inflammatory process continues with edema developing in the wound and the continued deposition of fibrin between the two coated edges

of the wound. The dense fibrin matrix which has surface contamination from the procedure becomes impervious to systemic antibiotics. The only antibiotics present will be drug that was present at the time the fibrin was deposited. The edema process of the wound interface increases the tissue hydrostatic pressure after wound closure, and systemically administered drugs following closure will not gain access. Additional antibiotics after closure do not penetrate the wound and the fibrin matrix and have no benefit.

From the above discussion of experimental and clinical data, conclusions can be drawn about the use of systemic preventive antibiotics for colon surgery, and other surgical procedures as well: First, the antibiotic(s) should be given before the incision and the drugs should be in therapeutic concentrations within the wound soft tissues at the time that potential contamination begins; second, the antibiotic(s) used should have biological activity against the likely pathogens to be encountered during the operation; and third, the preventive antibiotics should not be continued after primary closure of the wound since the opportunity for antimicrobial prevention has passed. These three principles for the administration of preventive antibiotics have been adopted by the Surgical Infection Prevention Project and the Surgical Care Improvement Projects in the USA [53].

A critical consideration in colon surgery is the selection of a specific preventive antibiotic choice that has activity against the likely pathogens to be encountered in the procedure. The antibiotics should have activity against *E. coli* and *B. fragilis* as the target organisms for consideration. This can be achieved by using any one of the choices that are identified in Table 4. Beta-lactam antibiotics either with or without a beta-lactamase inhibitor are single drugs that have been demonstrated to be effective in elective colon surgery. Combination of quinolone antibiotics with metronidazole is a common choice when multiple drugs are preferred. Aminoglycosides (e.g., gentamicin) when used with clindamycin have been a well-established combination for prevention in colon surgery, but both have fallen into disfavor because of issues of resistance and potential drug toxicities.

While the identified antibiotic choices in Table 4 are appropriate for the majority of patients, recent exposure to the healthcare environment will change colonization and the pathogens that can be anticipated. Recent hospitalization, outpatient antibiotic exposure, nursing home patients, and those receiving hemodialysis for chronic renal failure will be colonized with MRSA and resistant gram-negative organisms that would not ordinarily be a concern. Both gut and skin colonization with resistant organisms may necessitate choosing broader spectrum antibiotics for both MRSA and gram-negative bacteria.

It is reasonable to modify the original dose of the preventive antibiotic choice because of the patient having an increased body-mass index (BMI) [54]. The increased volume

Table 4 Systemic preoperative antibiotic choices for prevention of surgical site infection in elective colon surgery

Drug choice (dose)	Advantages	Disadvantages
Cefoxitin (1 g)	Low toxicity cephalosporin; extensive use for colon surgery prophylaxis; aerobic and anaerobic coverage.	Short biological elimination half-life (45 min); concerns about resistance from many years of usage.
Cefotetan (1 g)	Low toxicity cephalosporin; extensive use for prophylaxis in colon surgery; aerobic and anaerobic coverage. Long biological elimination half-life (4 h)	Concerns about bacterial resistance from years of usage.
Ampicillin/sulbactam (1.5–3.0 g)	Extensively used penicillin with a beta-lactamase inhibitor; good anaerobic coverage.	Short biological elimination half-life (1 h); emerging <i>E. coli</i> resistance in up to 40 % of isolates.
Ertapenem (1 g)	Extended gram-negative coverage (not <i>Pseudomonas</i> spp.); long biological elimination half-life (3.5 h).	Expense. Concern about carbapenem resistance with preventive use.
Cefazolin (1 g) and metronidazole (500 mg)	Good bacteriological coverage of anticipated pathogens	Limited clinical data to show effectiveness in elective colon surgery
Cefuroxime (500 mg) and metronidazole (500 mg)	Good bacteriological coverage of anticipated pathogens	Limited clinical data to show effectiveness in elective colon surgery
Aminoglycoside (gentamicin or tobramycin; 1 mg/kg) and clindamycin (300–600 mg)	A good choice for patients needing extended gram-negative coverage (e.g., nursing home patients)	Unpredictable aminoglycoside pharmacology. Clindamycin resistance.
Quinolone (ciprofloxacin; 500–750 mg, or levofloxacin; 500–750 mg) and clindamycin (300–600 mg)	Comprehensive antimicrobial coverage of anticipated pathogens.	Limited data to validate use for prophylaxis in elective colon surgery
Aztreonam (1 g) and clindamycin (300–600 mg)	Good antimicrobial coverage of anticipated pathogens.	Aztreonam has no gram-positive coverage and should not be used with metronidazole
Aminoglycoside (gentamicin or tobramycin; 1 mg/kg) and metronidazole (500 mg)	A good choice for patients needing extended gram-negative coverage (e.g., nursing home patients)	Unpredictable aminoglycoside pharmacology.
Quinolone (ciprofloxacin; 500–750 mg, or levofloxacin; 500–750 mg) and metronidazole (500 mg)	Comprehensive antimicrobial coverage of anticipated pathogens.	Gram-negative resistance looms as a threat.

From [52]

of distribution for antibiotics in large patients has the risk that concentrations of the drug in the surgical wound will not be sufficient for the entire duration of the procedure to provide adequate prevention. While the data on this subject is limited, doubling the initial dose of a beta-lactam antibiotic may be a necessary consideration.

Another consideration is to re-dose antibiotics in operations that have an extended duration. Antibiotic elimination begins from the time of administration. When procedures last beyond two half-lives of the antibiotic, then wound concentrations may decrease below that level necessary to prevent infection [55]. When procedures are anticipated to be lengthy, a preoperative strategy that is coordinated with nursing or anesthesiologists for re-dosing the patient is a wise choice. It should be emphasized that antibiotics given several hours prior to the incision because of surgical delays in initiating the procedure means that re-dosing needs to be referenced to the time of first administration rather than the beginning of the operation. To maximize the duration of antibiotic availability, it is wise to give the intravenous preoperative antibiotic just before the induction of anesthesia in the operating room. It is

generally advisable to give the antibiotic prior to anesthesia to avoid the unanticipated hypersensitivity reaction which may only be identified with bleeding problems if the drug is administered after induction.

Much has been written about preoperative screening of patients for MRSA before major operations [56]. The rationale is that patients identified as carriers of staphylococci but particularly MRSA could then have nasal decontamination with mupirocin before the operation or that antibiotic selections that cover MRSA could be implemented. In elective colon surgery with a positive nasal culture, MRSA coverage would need to be included. From cardiac surgery studies, it has been learned that if vancomycin is used for prevention in the hopes of covering all gram-positive organisms in addition to MRSA, then coverage of methicillin-sensitive *S. aureus* (MSSA) may be necessary because of the failure of vancomycin to cover the full gram-positive spectrum [57]. Vancomycin could be added to most of the choices identified in Table 4 with the exception of aztreonam and metronidazole which would have no MSSA coverage. While the focus of coverage for these patients is still primarily enteric colonists of the

human colon, the MRSA colonized patient is a significant risk and should be covered.

Mechanical/antibiotic bowel preparation

Early in the experience of surgery on the colon, it was appreciated that fecal contamination of the surgical site was associated with subsequent infection. It was intuitive that removal of gross fecal material would be a strategy to reduce infections in colon surgery. However, mechanical cleansing of the colon did not reduce SSIs because the concentration of the bacteria in the surface mucus was not diminished. Mechanical preparation alone did not and has never been shown to reduce SSI rates [58–61]. Accordingly, when antibiotics were first introduced into medicine with the sulfanilamide group of drugs, many surgeons hoped that these poorly absorbed drugs could be used to reduce the microbial concentration in the colon before operation.

Numerous studies were conducted in the late 1930s and early 1940 to use poorly absorbed sulfa compounds [62, 63]. While some reduction in bacterial concentrations was achieved, scientific validation of improved infection rates was not seen. Cohn and associates demonstrated that intraluminal antibiotics protected the colon against ischemia [64] and, in the early 1950s, used oral tetracycline for the antibiotic bowel preparation [65]. Because they associated tetracycline use with staphylococcal overgrowth in the colon, they transitioned to oral kanamycin as a nonabsorbed preoperative antibiotic [66]. It became somewhat fashionable to use kanamycin even though scientific rigor was lacking in the validation of this method in the actual reduction of SSI.

Clinical trials finally were attempted with oral antibiotics in the early 1970s. Rosenberg et al. studied a sulfa derivative with and without neomycin in a three-armed clinical trial [67]. The study showed no benefit from the addition of neomycin, and it had numerous scientific flaws including a small number of total cases and the fact that 40 % of randomized cases did not have a colon resection. Finally, Washington et al. [68] conducted a three-armed clinical trial where colon surgery patients received either oral neomycin alone, neomycin plus tetracycline, or a placebo in the 48 h leading to the procedure. All patients received mechanical cleansing. The results demonstrated equal infection rates with neomycin alone compared to the control group. However, a dramatic reduction to 5 % SSIs was seen with neomycin and tetracycline when compared to the controls (43 %). The rationale of adding tetracycline was its coverage of anaerobic species that was not achieved with neomycin alone.

Nichols and Condon proposed substituting tetracycline with oral erythromycin base because of its superior antimicrobial activity against *B. fragilis* and because it was a poorer-absorbed antibiotic and resulted in higher intraluminal concentrations [69]. A prospective randomized trial demonstrated

significant reduction in both SSI rates and in anastomotic leak rates [70]. Recognition of these observations led to oral neomycin-erythromycin being commonly employed with mechanical bowel preparation in the USA. With the simultaneously developed strategy of preventive systemic antibiotics for colon surgery, the two methods were used together. Selected studies showed that adding systemic antibiotics to the oral antibiotic bowel preparation further reduced SSI rates [71, 72]. And conversely, adding the oral antibiotic bowel preparation to both arms of a clinical trial where all patients received an appropriate systemic antibiotic likewise demonstrated the benefit of both methods being employed together [73, 74]. By the mid-1990s, the combination of systemic and oral antibiotic bowel preparation was the most common antimicrobial strategy used in elective colon surgery [75–77].

However, disillusionment with the oral antibiotic bowel preparation began with the managed care movement in the USA. A preoperative day of bowel preparation was no longer compensated by health insurers which required that mechanical preparation and the administration of the oral antibiotics be performed by patients at home. Discomfort with large volumes of polyethylene glycol and the gastrointestinal discomfort from the erythromycin base preparation led to a decline in patient compliance with the preparation protocol. The result was suboptimal preparation, retained stool, intraluminal liquid contents from delay in the ingestion of the polyethylene glycol, and poor propagation of the oral drugs resulted in poorer results. At the same time in the early 2000s, a host of studies reiterated the findings of Poth and others from the late 1930s which demonstrated the lack of benefit of mechanical preparation alone [78–86]. Several meta-analyses similarly identified that mechanical preparation alone did not reduce SSI rates [87–89], even though research from the 1930s has never contended that SSI reduction was the product of mechanical preparation.

Without mechanical preparation, oral antibiotics are not propagated distally in the colon that is full of stool. The bacterial burden of organisms within the unprepared colon lumen will bind all oral antibiotics in the proximal colon. Complete evacuation insures that oral antibiotics will actually access the full length of the colon. The studies of the last several years from multiple centers have reaffirmed the value of systemic and oral antibiotics together in elective colon surgery but only when mechanical bowel preparation is complete before oral antibiotics are administered [90–96]. Several meta-analyses have likewise confirmed the value of oral antibiotics added to mechanical preparation [97–99].

There are key issues to effective execution of the oral antibiotic bowel preparation. The mechanical preparation must be completed before administration of the oral antibiotics. If active purging of the colon is ongoing at the time of oral antibiotic administration, the associated enhanced gut motility will result in undissolved tablets and capsules passing through the

colon without antimicrobial benefit. Another issue that is unresolved is the preferred method for mechanical preparation. While polyethylene glycol is commonly used, sodium phosphate was demonstrated in one study to have lower SSI rates [100]. Supplemental phosphate in the colon lumen may suppress the virulence of gram-negative organisms and be a positive influence on SSI rates [101]. The use of sodium phosphate is associated with complications [102] but may have utility in the prevention of SSIs and deserves further clinical study. While many issues need further study in the implementation of the oral antibiotic bowel preparation, the current objective evidence strongly supports that it is an effective strategy when combined with systemic antibiotics to reduce SSI rates in elective colon surgery.

Intraoperative preventive measures

Technical issues

The technical management of the wound during the procedure is of paramount importance in the prevention of SSI. Hematoma in wound tissues or in the wound space at closure will increase SSI rates. Over-exuberant use of the electrocautery that leaves singed and devitalized tissue has consequences. Avoiding suture material especially braided and non-absorbable materials (e.g., silk) is recommended. Managing dead space in obese patients with closed suction drains that exit the skin through a separate stab wound can prevent abscess formation in the dependent portion of the incision. Drains are two-way streets that should be avoided for most cases, should never exit through the incision, and must be removed as soon as their purpose has been served. Overly aggressive retraction traumatizes the wound edges and pushes surface microbes into the soft tissues.

Wound protection devices

Expandable wound protection devices made with a plastic interface to cover the wound edges during the procedure are commonly used and have some clinical trial evidence in open abdominal surgery that supports their use [103–105]. The plastic wound cover is supported by two circular rings at the skin and at the peritoneal surface that keeps the protective barrier in place. Care must be taken at the conclusion of the procedure, least major wound contamination occurs with removing the barrier device, and benefit of wound protection is compromised.

Anti-bacterial suture

Suture material that is coated with triclosan as a locally released antiseptic has been shown to reduce bacterial growth associated with wound closure and hemostatic stitches.

Several meta-analyses have documented the merits of this method in the reduction of SSI rates in several different surgical settings [106–109]. Large randomized clinical trials across multiple participating centers would further help settle the questions about the general utility of this method. A strong case can be made that antibacterial sutures are of value in high-risk surgical cases such as colon resections.

Air handling

Air-borne bacteria have been a long-standing source of concern for contamination of the surgical site and subsequent infection. Surgical face masks are testimony to the concern about airborne bacteria. Laminar-flow air handling devices have been used but largely have testimonial evidence for the reduction of SSIs [110]. Ultraviolet irradiation of the operating room would presumably sterilize air and avoid wound contamination. Ultraviolet irradiation was of potential value in refined-clean operations [111]. The most cost-effective way to reduce bacterial “fall out” at the surgical site is to restrict traffic in and out of the operating room. For colon surgery, the role of contamination from colonic and skin colonization is such an overwhelming factor in SSI, and it is hard to image that the summed effects of any of these air-handling or air-modification methods would have an effect on outcomes.

Glucose control

Hyperglycemia is recognized as a suppressant of the innate immune response [112]. Hyperglycemia in both diabetic and non-diabetic patients has been associated with increased SSIs [113]. Reduction in blood sugar with insulin titration has been shown to reduce SSI rates [114], although some have argued that this may be a consequence of the insulin and not just reduction in the blood sugar. Managing blood sugar to a level ≤ 150 mgs% is desirable, but efforts to reduce glucose concentration beneath this level are of uncertain value and risk the serious complication of hypoglycemia [115]. A meta-analysis has identified little evidence to support managing the blood sugar below 200 mgs% [116]. The development of “real-time” blood sugar measurement in the operating room should greatly enhance the effective management of glucose for the colon surgery patient.

Temperature control

Clinical hypothermia is associated with impaired phagocytic function and with coagulopathy [117]. Kurz et al. [118] randomized elective colon resection patients to temperature control of 36.5° versus those that were allowed to have their core body temperature decline to 34.5° before temperature enhancement strategies were employed. Normothermic patients had an SSI rate of 6 %, while hypothermic patients had infection in 19 % of cases. However, Lehtinen et al. [119] has presented data that

has challenged the merits of maintaining normothermia, and Melton et al. [120] has studied SSI in over 1000 colon resection patients and did not find hypothermia to be predictive of SSI. Other studies have challenged [121], and others have confirmed the effects of hypothermia upon SSI rates [122]. Additional studies are warranted to evaluate whether the efforts and the degree of intraoperative warming are of value.

Oxygen supplementation

Supplemental oxygen has been shown to enhance the host response and to prevent infection after soft tissue contamination [123]. Greif et al. [124] reported on a prospective randomized clinical trial of 500 colon resection patients which compared 80 to 30 % inspired oxygen during the procedure and for 2 h postoperatively. The 80 % inspired oxygen group had an SSI rate of 5 %, while the 30 % oxygen group had 11 % infection rates. However, Pryor et al. [125] demonstrated increased SSI rates in general surgery abdominal operations with a similar 80 versus 35 % inspired oxygen protocol. A number of subsequent studies have demonstrated variable results but generally favor supplemental oxygen compared to conventional 30 % inspired oxygen during the operation [126–128]. The studies have been complicated by heterogeneous populations of patients and variable associated methods employed in patient management. Additional studies are necessary to define the desired inspired oxygen concentration and which patient population is most likely to benefit from this treatment strategy. For colon resection, supplemental oxygen would appear to be of benefit in the reduction of SSI.

Wound irrigation

Irrigation of the surgical wound at the conclusion of the operation has been a method that is widely employed to potentially reduce infection after colon surgery. Washing the wound with saline from a bulb syringe or from a basin will remove clot and loose debris that is present in the wound but has generally been viewed to not reduce the bacterial burden that is bound to the wound surface. The minimal benefits of saline lavage alone have led to the evaluation of pressure lavage of the wound and to the use of antimicrobials in the irrigation solution.

Experimental studies have demonstrated benefit of pressure lavage in reducing the number of bacteria in the wound and in reducing actual infections [129, 130]. Pressure lavage has been widely deployed in large numbers of surgical wounds despite limited clinical evidence to demonstrate efficacy. Abdominal surgery studies have only been in hepatobiliary and foregut operations [131, 132], where pulsed lavage has been shown to reduce SSI. No studies have been done in the use of pressure lavage in either elective or emergency colon resection. Randomized clinical trials are needed

to validate this method that is widely employed at the conclusion of colon operations. The addition of antibiotics to wound irrigation solutions is commonly employed. The traditional approach has been to use any of a number of different antibiotics that are placed in varying concentrations into the irrigation solution and to complete a quick wash of the wound space at the completion of the operation. There remains no evidence that topical antibiotics in the irrigation solution result in a reduction in SSI. The transient exposure of contaminating bacteria within the fibrin matrix of the wound for a period of time that is beneath the necessary exposure necessary to get an effect is unlikely to influence infection rates.

Delayed primary closure

A method used in the prevention of contaminated or dirty surgical wounds has been delayed primary closure [133]. When operative contamination in colon surgery has been clinically obvious from either an intraoperative spill or from colonic perforation from underlying disease, surgeons have elected to close the fascia of the abdominal incision, but to leave the skin and subcutaneous tissue open. The theory behind this strategy has been that the contaminated wound that is left open can be topical cleansed, debrided, and perhaps treated with either saline dressings or topical antimicrobials. With diligent wound management, the incision can then be closed in a delayed fashion at 3–5 days following the procedure. The reality is that severely contaminated wounds are seldom amenable for delayed closure and have the additional insult of continued interval contamination from the environment. It is uncommon for open wounds to have delayed primary closure but rather they are subject to secondary closure. In essence, the intent for delayed primary closure results in a duration of treatment that extends for a length of time that is the same as closing the wound and then opening it on the three to five postoperative day because of infection. If one assumes a 30 % infection rate for contaminated wounds, leaving all wounds open results in the equivalent morbidity of a superficial wound infection for 100 % of cases managed in this fashion if delayed primary closure is not achieved.

The published evidence that delayed primary closure has value is conflicting [134–137] and has been challenged by mathematical modeling as having any value [138]. It is time for a large, multicentered randomized clinical trial in a relatively homogenous population of patients (elective colon resection or penetrating abdominal trauma with colon injury) where primary closure is compared to delayed primary closure.

Postoperative preventive measures

There are limited interventions that have been demonstrated to be effective in prevention of SSI in colon surgery after the

incision has been closed. Conventional wound dressings will absorb serum or blood-tinged drainage to avoid accumulation over the surface of the wound. The fibrin seal of the closed wound is complete by 24 h, and external skin contamination should not have access to the wound space if no mechanical disruption of the closed wound has occurred following closure. Collodion seal over the wound may be of value in pediatric patients to avoid mechanical separation of the wound edges by the child. Other wound sealants have been used but are not of proven value.

The latest but unproven postoperative method is to place a wound vacuum device over the closed wound. This suction device is unlikely to provide evacuation of serum or other accumulated debris/contamination from the wound for a depth or more than 1–2 mm of depth. The use of the wound vacuum device for multiple days after the operation will certainly increase the cost of care without any evidence or rationale for its use. At present, only expert opinion without meaningful data supports the use of this method [139].

Secondary contamination with resultant infection from distant sources following wound closure has been the source of speculation but is likely to be a rare event. There is no justification for the continuation of postoperative systemic antibiotics with the speculation that this will avoid wound contamination from a remote source via blood borne or lymphatic dissemination.

Nonsurgical site infection in colon surgery

Infections other than those at the surgical site are of importance for colon surgery patients but generally do not get a lot of attention in discussions about the morbid events in these patients. These non-SSI infections include pneumonia, urinary tract infections, central line catheter infections, and *C. difficile* infections. These non-SSI infections may occur during the hospitalization or may not be identified until after discharge. In the USA, postdischarge non-SSI infections have been identified with increased frequency in large part because patients are discharge from the hospital much earlier than in years past (Fig. 3) [140]. It is not the purpose of this presentation to cover the complete diagnosis, prevention, and management of these non-SSI infections; the clinician must be aware that these are significant events in the colon surgery patient.

Summary

Infection is a frequent, morbid, and costly complication of colon surgery. Understanding the pathogenesis and microbiology of these infections becomes a critical step in prevention. Improvement in SSIs in the colon resection patient requires a consistent definition for these infections and that a consistent surveillance program is in place to provide accurate assessment

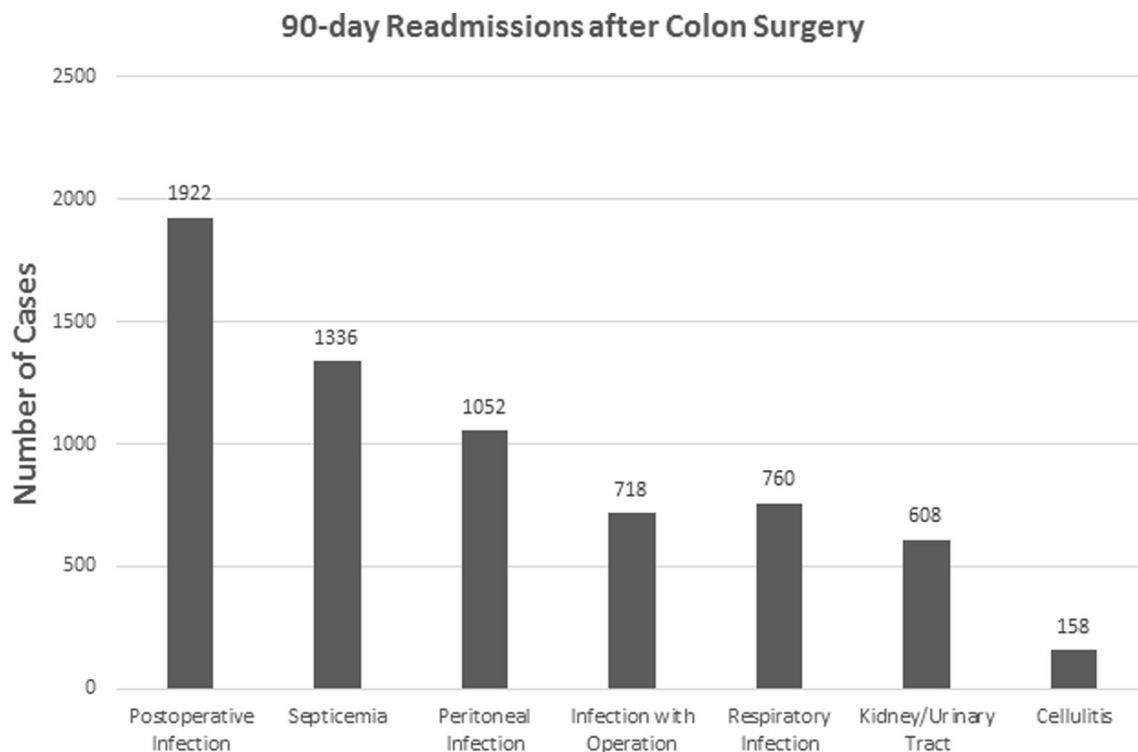


Fig. 3 The infections responsible for 6549 (23 %) readmissions among 28,073 patient readmitted patients following elective colon surgery [140]. Postoperative infections and infection with operation are readmissions for

SSIs. Peritoneal infections not only are for peritonitis but also included *C. difficile* infections. Septicemia is a diagnosis of readmission but does not specify the site of the infection

of these adverse events. In the contemporary environment, it is essential that SSIs be tracked into the postdischarge period of time to capture all events. There are a large number of preoperative and intraoperative methods that can reduce SSIs in the colon surgery patient. The time for prevention is before the operation and before the wound is closed in the operating room. Little evidence supports any preventive measure for SSIs in the postoperative period of time.

Compliance with ethical standards This study was totally financed by the author with no external funding sources.

Disclosure of potential conflicts of interest of the author:

IrriMax Corporation: Consultant (research grant)

CareFusion: Speakers Bureau (honorarium)

Prescient Surgical Co: Consultant (honorarium)

This article does not contain any studies with human participants or animals performed by the author.

There were no informed consent issues in this review article.

References

- Poth EJ (1982) Historical development of intestinal antisepsis. *World J Surg* 6:153–159
- Keenan JE, Speicher PJ, Thacker JKM et al (2014) The preventive surgical site infection bundle in colorectal surgery: an effective approach to surgical site infection reduction and health care cost savings. *JAMA Surg* 149:1045–1052
- Kingham TP, Pachter HL (2009) Colonic anastomotic leak: risk factors, diagnosis, and treatment. *J Am Coll Surg* 208:269–278
- Savage DC (1977) Microbial ecology of the gastrointestinal tract. *Annu Rev Microbiol* 31:107–133
- Ahmed S, Macfarlane GT, Fite A et al (2007) Mucosa-associated bacterial density in relation to human terminal ileum and colonic biopsy samples. *Appl Environ Microbiol* 73:7435–7442
- Fry DE (2012) Sepsis, Systemic Inflammatory Response, and Multiple Organ Dysfunction: the mystery continues. *Am Surg* 78:1–8
- Krizek TJ, Robson MC (1975) Evolution of quantitative bacteriology in wound management. *Am J Surg* 130:579–584
- Onderdonk AB, Bartlett JG, Louie T et al (1976) Microbial synergy in experimental intra abdominal abscess. *Infect Immun* 13:22–26
- Fry DE, Barie PS (2011) The changing face of *Staphylococcus aureus*: a continuing surgical challenge. *Surg Infect* 12:191–203
- The Bovine (2016) Pasteur., <https://thebovine.wordpress.com/pasteur/>. Accessed 23 May 2016
- Polk HC Jr, Miles AA (1971) Enhancement of bacterial infection by ferric iron: kinetics, mechanisms, and surgical significance. *Surgery* 70:71–77
- Elek SD, Conen PE (1957) The virulence of *Staphylococcus pyogenes* for man; a study of the problems of wound infection. *Br J Exp Pathol* 38(6):573–586
- Percival SL, McCarty SM, Lipsky B (2015) Biofilms and wounds: an overview of the evidence. *Adv Wound Care* 4:373–381
- Sørensen TI, Nielsen GG, Andersen PK, Teasdale TW (1988) Genetic and environmental influences on premature death in adult adoptees. *N Engl J Med* 318:727–732
- Centers for Disease Control and Prevention (2016) Surgical Site Infection Event., <http://www.cdc.gov/nhsn/PDFs/pscManual/9pscSSICurrent.pdf>. Accessed 23 May 2016
- Fry DE, Pine M, Jones BL, Meimban RJ (2012) Control charts to identify adverse outcomes in elective colon resection. *Am J Surg* 203:392–396
- Edwards JR, Peterson KD, Mu Y et al (2009) National healthcare safety network (NHSN) report: data summary for 2006 through 2008, issued December 2009. *Am J Infect Control* 37:783–805
- Kwaan MR, Al-Refaie WB, Parsons HM et al (2013) Are right-sided colectomy outcomes different from left-sided colectomy outcomes?: study of patients with colon cancer in the ACS NSQIP database. *JAMA Surg* 148:504–510. doi:10.1001/jamasurg.2013.1205
- Milsom JW, Smith DL, Corman ML et al (1998) Double-blind comparison of single-dose alatrofloxacin and cefotetan as prophylaxis of infection following elective colorectal surgery. *Am J Surg* 176(Suppl 6A):46S–52S
- Smith RL, Bohl JK, McElearney ST et al (2004) Wound infection after elective colorectal resection. *Ann Surg* 239:599–607
- Itani KMF, Wilson SE, Awad SS et al (2006) Ertapenem versus cefotetan prophylaxis in elective colorectal surgery. *N Engl J Med* 355:2640–2651
- Petherick ES, Dalton JE, Moore PJ, Cullum N (2006) Methods for identifying surgical wound infection after discharge from hospital: a systematic review. *BMC Infect Dis* 6:170
- American Society of Anesthesiologists (2016) ASA Physical Status Classification System., <http://www.asahq.org/resources/clinical-information/asa-physical-status-classification-system>. Accessed May 23, 2016
- Culver DH, Horan TC, Gaynes RP et al (1991) Surgical wound infection rates by wound class, operative procedure, and patient risk index. *Am J Med* 91(suppl 3B):152S–157S
- Mu Y, Edwards JR, Horan TC et al (2011) Improving risk-adjusted measures of surgical site infection for the National Healthcare Safety Network. *Infect Control Hosp Epidemiol* 32:970–986
- National Healthcare Safety Network. Your guide to the Standardized Infection Ratio (SIR). http://www.cdc.gov/nhsn/PDFs/Newsletters/NHSN_NL_OCT_2010SE_final.pdf. Accessed 24 May 2016.
- Cruse PJ, Foord R (1980) The epidemiology of wound infection. A 10-year prospective study of 62,939 wounds. *Surg Clin North Am* 60:27–40
- Vogel TR, Dombrovskiy VY, Lowry SF (2010) In-hospital delay of elective surgery for high volume procedures: the impact on infectious complications. *J Am Coll Surg* 211:784–790
- Fry DE, Pine M, Locke D, Pine G (2015) Prediction models of Medicare 90-Day post-discharge deaths, readmissions, and costs in bowel operations. *Am J Surg* 209:509–514. doi:10.1016/j.amjsurg.2014.12.005, Epub 2014 Dec 20
- Webster J, Osborne S (2012) Preoperative bathing or showering with skin antiseptics to prevent surgical site infection. *Cochrane Database Syst Rev* 9:CD004985
- Edmiston CE Jr, Krepel CJ, Seabrook GR et al (2008) Preoperative shower revisited: can high topical antiseptic levels be achieved on the skin surface before surgical admission? *J Am Coll Surg* 207:233–239
- Tanner J, Norrie P, Melen K (2011) Preoperative hair removal to reduce surgical site infection. *Cochrane Database Syst Rev* 11:CD004122
- Alexander JW, Fischer JE, Boyajian M et al (1983) The influence of hair-removal methods on wound infection. *Arch Surg* 118:347–352
- Mangram AJ, Horan TC, Pearson ML et al (1999) The Hospital Infection Control Practices Advisory Committee. Guidelines for prevention of surgical site infection, 1999. *Infect Control Hosp Epidemiol* 20:247–280

35. Hart SR, Yajnik A, Ashford J et al (2011) Operating room fire safety. *Ochsner J* 11:37–42
36. Aly R, Maibach HI (1998) Comparative antibacterial efficacy of a 2 minute surgical scrub with chlorhexidine gluconate, povidone iodine, and chloroxylenol sponge brushes. *Am J Infect Control* 16:173–177
37. Dumville JC, McFarlane E, Edwards P et al (2013) Preoperative skin antiseptics for preventing surgical wound infections after clean surgery. *Cochrane Database Syst Rev* 3:CD003949
38. Lee I, Agarwal RK, Lee BY et al (2010) Systematic review and cost analysis comparing use of chlorhexidine with use of iodine for preoperative skin antisepsis to prevent surgical site infection. *Infect Control Hosp Epidemiol* 31:1219–1229
39. Darouiche RO, Wall MJ Jr, Itani KM, et al. (2010) Chlorhexidine-Alcohol versus Povidone-Iodine for Surgical-Site Antisepsis. *N Engl J Med*. 362:18–26.
40. Fry DE (2014) Pre-surgical skin antisepsis: a call to reduce variability to improve quality. *Becker's Infection Control & Clinical Quality*, September 17, 2014.
41. Webster J, Alghamdi A (2013) Use of plastic adhesive drapes during surgery for preventing surgical site infection. *Cochrane Database Syst Rev* 1:CD006353
42. Towfigh S, Cheadle WG, Lowry SF et al (2008) Significant reduction in incidence of wound contamination by skin flora through use of microbial sealant. *Arch Surg* 143:885–891
43. Miles AA, Miles ES, Burke J (1957) The value and duration of defense reactions of the skin to primary lodgment of bacteria. *Br J Exp Pathol* 38:79–96
44. Burke JF (1961) The effective period of preventive antibiotic action in experimental incisions and dermal lesions. *Surgery* 50:161–168
45. Bernard HR, Cole WR (1964) The prophylaxis of surgical infection: the effect of prophylactic antimicrobial drugs on the incidence of infection following potentially contaminated operations. *Surgery* 56:151–157
46. Polk HC Jr, Lopez Mayor JF (1969) Postoperative wound infection: a prospective study of determinant factors and prevention. *Surgery* 66:97–103
47. Stone HH, Hooper CA, Kolb LD et al (1976) Antibiotic prophylaxis in gastric, biliary and colonic surgery. *Ann Surg* 184:443–452
48. Stone HH, Haney BB, Kolb LD et al (1979) Prophylactic and preventive antibiotic therapy: timing, duration and economics. *Ann Surg* 189:691–699
49. Baum ML, Anish DS, Chalmers TC et al (1981) A survey of clinical trials of antibiotic prophylaxis in colon surgery: evidence against further use of no-treatment controls. *N Engl J Med* 305:795–799
50. Song R, Glennly AM (1998) Antimicrobial prophylaxis in colorectal surgery: a systematic review of randomized controlled trials. *Br J Surg* 85:1232–1244
51. McDonald M, Grabsch E, Marshall C et al (1998) Single-versus multiple-dose antimicrobial prophylaxis for major surgery: a systematic review. *Aust N Z J Surg* 68:388–396
52. Fry DE (2013) Surgical Site Infection. In: Fry DE (ed) *Surgical Infections*. JP Medical Publishers, London, pp 49–62, Chapter 4
53. Fry DE (2008) Surgical site infections and the surgical care improvement project (SCIP): evolution of national quality measures. *Surg Infect* 9:579–584
54. Janson B, Thursky K (2012) Dosing of antibiotics in obesity. *Curr Opin Infect Dis* 25:634–649
55. Fry DE, Pitcher DE (1990) Antibiotic pharmacokinetics in surgery. *Arch Surg* 125:1490–1492
56. Simor AE (2011) Staphylococcal decolonization: an effective strategy for prevention of infection? *Lancet Infect Dis* 11:952–962
57. Finkelstein R, Rabino G, Mashiah T et al (2002) Vancomycin versus cefazolin prophylaxis for cardiac surgery in the setting of a high prevalence of methicillin-resistant staphylococcal infections. *J Thorac Cardiovasc Surg* 123:326–332
58. Poth EJ (1934) A clean intestinal anastomosis: an experimental study. *Arch Surg* 28:1087–1094
59. Poth EJ (1935) A clean intestinal anastomosis, II: an experimental study. *Arch Surg* 31:579–586
60. Firor WM, Jonas AF (1941) The use of sulfanilylguanidine in surgical patients. *Ann Surg* 114:19
61. Garlock JH, Seley GP (1939) The use of sulfanilamide in surgery of the colon and rectum. *Preliminary Report Surgery* 5:787–788
62. Firor WM, Poth EJ (1941) Intestinal antisepsis with special reference to sulfanilylguanidine. *Ann Surg* 114:663–671
63. Poth EJ, Ross CA (1944) The clinical use of phthalylsulfathiazole. *J Lab Clin Med* 29:785–808
64. Cohn I Jr, Rives JD (1955) Antibiotic protection of colon anastomoses. *Ann Surg* 141:707–717
65. Cohn I Jr, Longacre AB (1956) Tetracycline (achromycin)-neomycin for preoperative colon preparation. *AMA Arch Surg* 72:371–376
66. Cohn I Jr (1958) Kanamycin for bowel sterilization. *Ann NY Acad Sci* 76:212–217
67. Rosenberg IL, Graham NG, de Dombal FT, Goligher JC (1971) Preparation of the intestine in patients undergoing major large-bowel surgery, mainly for neoplasm of the colon and rectum. *Brit J Surg* 58:266–269
68. Washington JA II, Dearing WH, Judd ES, Elveback LR (1974) Effect of preoperative antibiotic regimen on development of infection after intestinal surgery: prospective, randomized, double-blind study. *Ann Surg* 180:567–571
69. Nichols RL, Briodo P, Condon RE et al (1973) Effect of preoperative neomycin-erythromycin intestinal preparation on the incidence of infectious complications following colon surgery. *Ann Surg* 178:453–459
70. Clarke JS, Condon RE, Bartlett JG et al (1977) Preoperative oral antibiotics reduce septic complications of colon operations: results of prospective, randomized, double-blind clinical study. *Ann Surg* 186:251–259
71. Coppa GF, Eng K, Gouge TH et al (1983) Parenteral and oral antibiotics in elective colon and rectal surgery. A prospective, randomized trial. *Am J Surg* 145:62–65
72. Schoetz DJ Jr, Roberts PL, Murray JJ et al (1990) Addition of parenteral cefoxitin to regimen of oral antibiotics for elective colorectal operations. A randomized prospective study. *Ann Surg* 212:209–212
73. Matheson DM, Arabi Y, Baxter-Smith D et al (1978) Randomized multicentre trial of oral bowel preparation and antimicrobials for elective colorectal operations. *Br J Surg* 65:597–600
74. Wapnick S, Guinto R, Reizis I, LeVeen HH (1979) Reduction of postoperative infection in elective colon surgery with preoperative administration of kanamycin and erythromycin. *Surgery* 85:317–321
75. Solla JA, Rothenberger DA (1990) Preoperative bowel preparation. A survey of colon and rectal surgeons. *Dis Colon Rectum* 33:154–159
76. Nichols RL, Smith JW, Garcia RY et al (1997) Current Practices of Preoperative Bowel Preparation Among North American Colorectal Surgeons. *Clin Infect Dis* 24:609–619
77. Pollock AV, Arnot RS, Leaper DJ, Evans M (1978) The role of antibacterial preparation of the intestine in the reduction of primary wound sepsis after operations on the colon and rectum. *Surg Gynecol Obstet* 147:909–912
78. Contant CME, Hop WCJ, van't Sant HP et al (2007) Mechanical bowel preparation for elective colorectal surgery: a multicenter randomized trial. *Lancet* 370:2112–2117

79. Fa-Si-Oen P, Roumen R, Buitenweg J et al (2005) Mechanical bowel preparation or not? Outcome of a multicenter, randomized trial in elective open colon surgery. *Dis Colon Rectum* 48:1509–1516
80. Jung B, Pahlman L, Nyström P-O et al (2007) Multicentre randomized clinical trial of mechanical bowel preparation in elective colon resection. *Br J Surg* 94:689–695
81. Miettinen RPJ, Laitinen ST, Mäkelä JT, Pääkkönen ME (2000) Bowel preparation with oral polyethylene glycol electrolyte solution vs. no preparation in elective open colon resection. *Dis Colon Rectum* 43:669–675
82. Pena-Soria MJ, Mayol JM, Anula R et al (2008) Single-blinded randomized trial of mechanical bowel preparation for colon surgery with primary intraperitoneal anastomosis. *J Gastrointest Surg* 12:2103–2109
83. Ram E, Sherman Y, Weil R et al (2005) Is mechanical bowel preparation mandatory for elective colon surgery? *Arch Surg* 140:285–288
84. van't Sant HP, Weidema WF, Hop WCJ et al (2010) The influence of mechanical bowel preparation in elective lower colorectal surgery. *Ann Surg* 251:59–63
85. Bucher P, Gervaz P, Soravia C et al (2005) Randomized clinical trial of mechanical bowel preparation versus no preparation before elective left-sided colorectal surgery. *Br J Surg* 92:409–414
86. Zmora O, Mahajna A, Bar-Zakai B et al (2006) Is mechanical bowel preparation mandatory for left-sided colonic anastomosis? Results of a prospective randomized trial. *Tech Coloproctol* 10: 131–135
87. Cao F, Li J, Li F (2012) Mechanical bowel preparation for elective colorectal surgery: updated systematic review and meta-analysis. *Int J Colorectal Dis* 27:803–810, Epub 2011 Nov 23
88. Guenaga KF, Matos D, Wille-Jorgensen P (2011) Mechanical bowel preparation for elective colorectal surgery. *Cochrane Database Syst Rev* 1544:CD001544.pub4. doi:10.1002/14651858
89. Dahabreh IJ, Steele DW, Shah N, Trikalinos TA (2015) Oral mechanical bowel preparation for colorectal surgery: systematic review and meta-analysis. *Dis Colon Rectum* 58:698–707
90. Lewis RT (2002) Oral versus systemic antibiotic prophylaxis in elective colon surgery: a randomized study and meta-analysis send a message from the 1990s. *Can J Surg* 45:173–180
91. Englesbe MJ, Brooks L, Kubus J et al (2010) A statewide assessment of surgical site infection following colectomy: the role of oral antibiotics. *Ann Surg* 252:514–520
92. Krapohl GL, Phillips LRS, Campbell DA et al (2011) Bowel preparation for colectomy and risk of *Clostridium difficile* infection. *Dis Colon Rectum* 54:810–817
93. Hendren S, Fritze D, Banerjee M et al (2013) Antibiotic choice is independently associated with risk of surgical site infection after colectomy: a population-based cohort study. *Ann Surg* 257:469–475. doi:10.1097/SLA.0b013e31826c4009
94. Toneva GD, Deierhoi RJ, Morris M et al (2013) Oral antibiotic bowel preparation reduces length of stay and readmissions after colorectal surgery. *J Am Coll Surg* 216:756–763
95. Scarborough JE, Mantyh CR, Sun Z, Migaly J (2015) Combined mechanical and oral antibiotic bowel preparation reduces incisional surgical site infection and anastomotic leak rates after elective colorectal resection: an analysis of colectomy-targeted ACS NSQIP. *Ann Surg* 262:331–337
96. Kiran RP, Murray AC, Chiuhan C et al (2015) Combined preoperative mechanical bowel preparation with oral antibiotics significantly reduces surgical site infection, anastomotic leak, and ileus after colorectal surgery. *Ann Surg* 262:416–425
97. Fry DE (2011) Colonic preparation and surgical site infection. *Am J Surg* 202:225–232
98. Bellows CF, Mills KT, Kelly TN, Gagliardi G (2011) Combination of oral non-absorbable and intravenous antibiotics versus intravenous antibiotics alone in the prevention of surgical site infections after colorectal surgery: a meta-analysis of randomized controlled trials. *Tech Coloproctol* 15:385–395, Epub 2011 Jul 23
99. Chen M, Song X, Chen LZ et al (2016) Comparing mechanical bowel preparation with both oral and systemic antibiotics versus mechanical bowel preparation and systemic antibiotics alone for the prevention of surgical site infection after elective colorectal surgery: a meta-analysis of randomized controlled clinical trials. *Dis Colon Rectum* 59:70–78
100. Itani KMF, Wilson SE, Awad SS et al (2007) Polyethylene glycol versus sodium phosphate mechanical bowel preparation in elective colorectal surgery. *Am J Surg* 193:190–194
101. Zaborin A, Defazio JR, Kade M et al (2014) Phosphate-containing polyethylene glycol polymers prevent lethal sepsis by multidrug-resistant pathogens. *Antimicrob Agents Chemother* 58:966–977. doi:10.1128/AAC.02183-13, Epub 2013 Nov 25
102. Ezri T, Lemer E, Muggia-Sullam M et al (2006) Phosphate salt bowel preparation regimens alter perioperative acid-base and electrolyte balance. *Can J Anesth* 53:153–158
103. Gheorghe A, Calvert M, Pinkney TD et al (2012) Systematic review of the clinical effectiveness of wound-edge protection devices in reducing surgical site infection in patients undergoing open abdominal surgery. *Ann Surg* 255:1017–1029
104. Mihaljevic AL, Schirren R, Ozer M et al (2014) Multicenter double-blinded randomized controlled trial of standard abdominal wound edge protection with surgical dressings versus coverage with a sterile circular polyethylene drape for prevention of surgical site infections: a CHIR-Net trial (BaFO; NCT01181206). *Ann Surg* 260:730–737
105. Mihaljevic AL, Muller TC, Kehl V et al (2015) Wound edge protectors in open abdominal surgery to reduce surgical site infections: a systematic review and meta-analysis. *PLoS One* 10(3): e121187. doi:10.1371/journal.pone.0121187, eCollection 2015
106. Daoud FC, Edmiston CE Jr, Leaper D (2014) Meta-analysis of prevention of surgical site infections following incision closure with triclosan-coated sutures: robustness to new evidence. *Surg Infect* 15:165–181
107. Edmiston CE Jr, Daoud FC, Leaper D (2013) Is there an evidence-based argument for embracing an antimicrobial (triclosan)-coated suture technology to reduce the risk for surgical-site infections?: a meta-analysis. *Surgery* 154:89–100. doi:10.1016/j.surg.2013.03.008
108. Guo J, Pan LH, Li YX et al (2016) Efficacy of triclosan-coated sutures for reducing risk of surgical site infection in adults: a meta-analysis of randomized clinical trials. *J Surg Res* 201:105–117. doi:10.1016/j.jss.2015.10.015, Epub 2015 Oct 23
109. Apisarnthanarak A, Singh N, Bandong AN, Madriaga G (2015) Triclosan-coated sutures reduce the risk of surgical site infections: a systematic review and meta-analysis. *Infect Control Hosp Epidemiol* 36:169–179. doi:10.1017/ice.2014.22
110. Gastmeier P, Breier AC, Brandt C (2012) Influence of laminar airflow on prosthetic joint infections: a systematic review. *J Hosp Infect* 81:73–78
111. National Academy of Sciences, National Research Council, Division of Medical Sciences, Ad Hoc Committee of Trauma (1964) Postoperative wound infection: the influence of ultraviolet irradiation of the operating room and of various other factors. *Ann Surg* 160:1–192
112. Turina M, Fry DE, Polk HC Jr (2005) Acute hyperglycemia and the innate immune system: clinical, cellular, and molecular aspects. *Crit Care Med* 33:1624–1633
113. Ramos M, Khalpey Z, Lipsitz S et al (2008) Relationship of perioperative hyperglycemia and postoperative infections in patients who undergo general and vascular surgery. *Ann Surg* 248:585–591

114. Kwon S, Thompson R, Dellinger P et al (2013) Importance of perioperative glycemic control in general surgery: a report from the surgical care and outcomes assessment program. *Ann Surg* 257:8–14
115. The NICE-SUGAR Study Investigators (2009) Intensive versus Conventional Glucose Control in Critically Ill Patients. *N Engl J Med* 360:1283–1297. doi:10.1056/NEJMoa0810625
116. Kao LS, Meeks D, Moyer VA, Lally KP (2009) Peri-operative glycaemic control regimens for preventing surgical site infections in adults. *Cochrane Database Syst Rev* 3:CD006806. doi:10.1002/14651858.CD006806.pub2
117. Billeter AT, Rice J, Druen D et al (2016) Warming to 39°C but Not to 37°C Ameliorates the Effects on the Monocyte Response by Hypothermia. *Ann Surg* 263:601–607
118. Kurz A, Sessler DI, Lenhardt R (1996) Perioperative normothermia to reduce the incidence of surgical wound infection and shorten hospitalization. *N Engl J Med* 334:1209–1215
119. Lehtinen SJ, Onicescu G, Kuhn KM et al (2010) Normothermia to prevent surgical site infections after gastrointestinal surgery: holy grail or false idol? *Ann Surg* 252:696–704
120. Melton GB, Vogel JD, Swenson BR et al (2013) Continuous intraoperative temperature measurement and surgical site infection: analysis of anesthesia information system data in 1008 colorectal procedures. *Ann Surg* 258:606–613
121. Walz JM, Paterson CA, Seligowski JM, Heard SO (2006) Surgical site infection following bowel surgery: a retrospective analysis of 1446 patients. *Arch Surg* 141:1014–1018
122. Tsuchida T (2016) Influence of Peri-Operative Hypothermia on Surgical Site Infection in Prolonged Gastroenterological Surgery. *Surg Infect*. [Epub ahead of print]
123. Qadan M, Battista C, Gardner SA et al (2010) Oxygen and surgical site infection: a study of underlying immunologic mechanisms. *Anesthesiology* 113:369–377
124. Greif R, Akca O, Horn EP et al (2000) Supplemental perioperative oxygen to reduce the incidence of surgical wound infection. *N Engl J Med* 342:161–167
125. Pryor KO, Fahey TJ 3rd, Lien CA et al (2004) Surgical site infection and the routine use of perioperative hyperoxia in a general surgical population: a randomized controlled trial. *JAMA* 291:79–87
126. Belda FJ, Aguilera L, Garcia de la Asuncion J et al (2005) Supplemental perioperative oxygen and the risk of surgical wound infection: a randomized controlled trial. *JAMA* 294:2035–2042
127. Mayzler O, Weksler N, Domchik S et al (2005) Does supplemental perioperative oxygen administration reduce the incidence of wound infection in elective colorectal surgery? *Minerva Anesthesiol* 71:21–25
128. Gardella C, Goltra LB, Laschansky E et al (2008) High-concentration supplemental perioperative oxygen to reduce the incidence of postcesarean surgical site infection: a randomized controlled trial. *Obstet Gynecol* 112:545–552
129. Gross A, Cutright DE, Bhaskar SN (1972) Effectiveness of pulsating water jet lavage in treatment of contaminated crushed wounds. *Am J Surg* 124:373–377
130. Rodeheaver GT, Pettry D, Thacker JG et al (1975) Wound cleansing by high pressure irrigation. *Surg Gynecol Obstet* 141:357–362
131. Nikfarjam M, Kimchi ET, Gusani NJ et al (2009) Reduction of surgical site infections by use of pulsatile lavage irrigation after prolonged intra-abdominal surgical procedures. *Am J Surg* 198:381–389
132. Nikfarjam M, Weinberg L, Fink MA et al (2014) Pressurized pulse irrigation with saline reduces surgical-site infections following major hepatobiliary and pancreatic surgery: randomized controlled trial. *World J Surg* 38:447–455
133. Collier FA, Valk WL (1940) The delayed primary closure of contaminated wounds. *Ann Surg* 112:256–262
134. Bhangu A, Singh P, Lundy J, Bowley DM (2013) Systemic review and meta-analysis of randomized clinical trials comparing primary vs delayed primary skin closure in contaminated and dirty abdominal incisions. *JAMA Surg* 148:779–786
135. Duttaroy DD, Jitendra J, Duttaroy B et al (2009) Management strategy for dirty abdominal incisions: primary or delayed primary closure? A randomized trial. *Surg Infect* 10:129–136
136. Siribumrungwong B, Noorit P, Wilasrusmee C, Thakkinstian A (2014) A systematic review and meta-analysis of randomized controlled trials of delayed primary wound closure in contaminated abdominal wounds. *World J Emerg Surg* 9:49. doi:10.1186/1749-7922-9-49, eCollection 2014. Review
137. Cohn SM, Giannotti G, Ong AW et al (2001) Prospective randomized trial of two wound management strategies for dirty abdominal wounds. *Ann Surg* 233:409–413
138. Brasel KJ, Borgstrom DC, Weigelt JA (1997) Cost-utility analysis of contaminated appendectomy wounds. *J Am Coll Surg* 184:23–30
139. Willy C, Agarwal A, Andersen CA, et al (2016) Closed incision negative pressure therapy: international multidisciplinary consensus recommendations. *Int Wound J*. doi: 10.1111/iwj.12612. [Epub ahead of print]
140. Fry DE, Pine M, Nedza SM et al (2016) The appropriate measurement of post-discharge readmissions in Medicare colon surgery. *Am J Surg* 211:577–582