

Objective 6: The team will consistently use methods known to minimize the risk for surgical site infection.

An infection that occurs in surgical patients at the site of operation is known as surgical site infection. These infections occur after invasive procedures in the superficial or deep layers of the incision or in the organ or space that was manipulated or traumatized, such as the peritoneal space, pleural space, mediastinum or joint space. These problems are serious and costly, and are associated with increased morbidity and mortality as well as with prolonged hospitalization (1–3). Recently, their prevalence has been used as a marker for the quality of surgeons and hospitals (4–7).

Surgical site infection accounts for about 15% of all health-care-associated infections and about 37% of the hospital-acquired infections of surgical patients (8,9). Two thirds of surgical site infections are incisional and one third confined to the organ space (9). In western countries, the frequency of such infections is 15–20% of all cases, with an incidence of 2–15% in general surgery (3,10–12). Surgical site infections lead to an average increase in the length of hospital stay of 4–7 days. Infected patients are twice as likely to die, twice as likely to spend time in an intensive care unit and five times more likely to be readmitted after discharge (11,13–15).

Health-care costs increase substantially for patients with surgical site infections. The severity of the effects depends on the extent of the surgical procedure, the country and the method used to calculate costs (3,12,16–18). In the United States, at least 780 000 surgical site infections occur each year, with rates as high as 13% for high-risk colon surgery (19,20). Such infections resulted in 3.7 million excess hospital days and US\$ 1.6–3 billion in excess hospital costs per year (15,21). In the United Kingdom, the excess cost has been calculated to be about £ 1594 per infection (3). In the European Union, surgical site infections exact an economic toll of € 1.5–19.1 billion per year (12). The prevalence and consequences of surgical site infections are illustrated in Tables II.6.1 and II.6.2.

Table II.6.1 – Prevalence of surgical site infections in certain countries

Country (Reference)	Setting (Number of centers involved)	Study period	Study design	Surgical site infections	
				No.	%
Australia (26)	Hospitals (28)	1992	Retrospective	5 432	7.9
Brazil (27)	University hospital (1)	1993–1998	Retrospective	9 322	6.8
France (24)	Hospital network (67 surgical wards)	1998–2000	Prospective	26 904	3.3
Italy (23)	Public hospitals (31)	1 month (date not given)	Prospective	6 167	3.3
Spain (25)	Tertiary-care hospital (1)	1992–1994	Prospective	1 483	10.5
Thailand (29)	General and regional hospitals (33)	1992	Prevalence	15 319	2.7
Thailand (30)	University hospitals (9)	2003–2004	Prospective	4 764	1.4
United States (20)	NNIS hospitals (225)	1992–1998	Prospective	738 398	2.6
Viet Nam (28)	Tertiary-care hospitals (2)	1999	Prospective	697	10.9

NNIS, National Nosocomial Surveillance System

Table II.6.2 – Consequences of surgical site infections

Reference	Type of operation	Consequence studied	Excess stay, cost or mortality
Asensio, Torres (31)	Heart	Length of postoperative stay	21 days
Kasatpibal et al. (18)	General surgery, neurosurgery	Length of postoperative stay; cost	14 days; bhat 31 140
Astagneau et al. (13)	Gastrointestinal, orthopaedic, gynaecology	Length of postoperative stay	8.5 days
Coello et al. (32)	General surgery, orthopaedic, gynaecology	Length of postoperative stay; cost	8.2 days; UK£ 1798
Poulsen et al. (33)	All surgery	Length of postoperative stay	6 days
Kirkland et al. (15)	All surgery	Length of postoperative stay; mortality	5 days; 4.3%
Whitehouse et al. (2)	All surgery	Length of postoperative stay	1 day
Plowman et al. (34)	General surgery, orthopaedic, obstetrics and gynaecology	Cost	UK£ 1618
Whitehouse et al. (2)	Orthopaedic	Cost	US\$ 17 708

Pathogenesis and microbiology

Microbial contamination during a surgical procedure is a precursor of surgical site infection. Most surgical wounds are contaminated by bacteria, but only a minority progress to clinical infection (35). Infection does not occur in most patients because their innate host defences eliminate contaminants at the surgical site efficiently (36). There are at least three important determinants of whether contamination will lead to surgical site infection: the dose of bacterial contamination, the virulence of the bacteria and the resistance of the patient (37). This is demonstrated in the following formula (38):

$$\frac{\text{Dose of bacterial contamination} \times \text{Virulence of bacteria}}{\text{Resistance of host}} = \text{Risk of surgical site infection}$$

Other factors that affect the probability of infection are depicted in the following hypothetical equation (36):

$$\frac{\text{Inoculum of bacteria} + \text{Virulence of bacteria} + \text{Adjuvant effects}}{\text{Innate and adoptive host defence} - \text{Acute and chronic host liabilities}} = \text{Probability of infection}$$

The probability of infection increases proportionally as the number and virulence of the bacteria increase. Local characteristics of the wound, such as residual dead tissue, sutures or other foreign material or the presence of drains, will amplify the consequence of the bacterial inoculum.

Bacterial contamination is a necessary precursor to surgical site infection. Skin bacteria are always present, despite thorough skin preparation. In addition, numerous bacteria contaminate any operation involving a body structure ordinarily colonized by bacteria, such as the bowel. Quantitatively, the risk for surgical site infection is markedly increased if the surgical site is contaminated with $> 10^5$ microorganisms per gram of tissue (38); however, the dose of contaminating microorganisms required to produce infection might be much lower when foreign material is present at the surgical site (e.g. 100 staphylococci per gram of tissue introduced on silk sutures).

The aggressiveness of many invasive microorganisms is often a function of their biology. Many bacteria that cause surgical site infections contain or produce toxins and other substances that increase their ability to survive on or in host tissue and invade and damage the host. The more virulent the bacterial contaminant, the greater the probability of infection.

Some bacterial surface components, notably polysaccharide capsules, inhibit phagocytosis, a critical and early host defence response to microbial contamination. Certain strains of clostridia and streptococci produce potent exotoxins that disrupt cell membranes or alter cellular metabolism (39). A variety of microorganisms, including Gram-positive bacteria such as coagulase-negative staphylococci, produce glycocalyx and an associated component called slime, which physically shields bacteria from phagocytes or inhibits the binding or penetration of antimicrobial agents (40). Although these and other virulence factors are well defined, their mechanistic relationship to surgical site infection has not been fully determined.

The source of the pathogens that cause most surgical site infections is the endogenous flora of the patient's skin, mucous membranes or hollow viscera. When a mucous membrane or skin is incised, the exposed tissues are at risk for contamination. The organisms are usually aerobic Gram-positive cocci (e.g. staphylococci) but may include faecal flora (e.g. anaerobic bacteria and Gram-negative aerobes) when the incision is made near the perineum or groin. When a gastrointestinal organ is opened during an operation and is the source of pathogens, Gram-negative bacilli (e.g. *Escherichia coli*), Gram-positive organisms (e.g. enterococci) and sometimes anaerobes (e.g. *Bacteroides fragilis*) are the typical isolates.

Bacterial contaminants may also enter the wound from exogenous sources, including the air in the operating room, instruments, prostheses or other implants or the surgical team that comes into contact with the wound (41-44). The exogenous flora are primarily aerobes, especially Gram-positive organisms (e.g. staphylococci and streptococci). Fungi from endogenous and exogenous sources rarely cause surgical site infections, and their pathogenesis is not well understood (45,46).

Pathogens isolated from the surgical site vary according to the type of surgery as well as the organ and location. The distribution of pathogens isolated from the surgical site in the National Nosocomial Infections Surveillance (NNIS) system in the United States between 1986 and 1996 is shown in Table II.6.3. The pathogen most frequently isolated was *Staphylococcus aureus*, followed by coagulase-negative staphylococci, *Enterococcus* spp., *E. coli* and *Pseudomonas aeruginosa*. There was a notable increase over this time period in antimicrobial-resistant pathogens, such as methicillin-resistant *S. aureus* and fungal pathogens, especially *Candida albicans* (46,47). This increase might reflect inappropriate use

of antimicrobial medication because not all specimens can be sent to laboratories for isolation of pathogens, and some pathogens are difficult to identify in some laboratories. Moreover, some surgeons prefer to use broad-spectrum antibiotics instead of drugs with a narrower susceptibility profile (48). The increase in fungal pathogens might also reflect an increase in the number of immunocompromised surgical patients.

Table II.6.3 – Distribution of pathogens isolated from surgical-site infections in the National Nosocomial Infections Surveillance system (9,49)

Pathogen	Percentage of isolates	
	1986–1989 (n = 16 727)	1990–1996 (n = 17 671)
<i>Staphylococcus aureus</i>	17	20
Coagulase-negative staphylococci	12	14
<i>Enterococcus</i> spp.	13	12
<i>Escherichia coli</i>	10	8
<i>Pseudomonas aeruginosa</i>	8	8
<i>Enterobacter</i> spp.	8	7
<i>Proteus mirabilis</i>	4	3
<i>Klebsiella pneumonia</i>	3	3
Other <i>Streptococcus</i> spp.	3	3
<i>Candida albicans</i>	2	3
Group D streptococci, other (non-enterococci)	–	2
Other Gram-positive aerobes	–	2
<i>Bacteroides fragilis</i>	–	2

The distribution of pathogens that cause surgical site infections is similar in many countries. In a study of these infections in the European Union, 27–40% were due to *S. aureus*, 6–11% to coagulase-negative staphylococci, 3–15% to *E. coli* and 7–10% to *Pseudomonas* (12). A study in Turkey showed that *S. aureus* accounted for 50% of 621 pathogens isolated from surgical site infections, *E. coli* for 8%, *S. pyogenes* and *Ps. aeruginosa* each for 7% and coagulase-negative staphylococci for 6% (50). In Thailand, the most common causative pathogens identified in surgical site infections were *E. coli* (15.3%), *S. aureus* (8.5%), *Ps. aeruginosa* (6.8%), *K. pneumoniae* (6.8%) and *Acinetobacter baumannii* (3.4%) (30).

Prevention and surveillance of surgical site infections

The Study on the Efficacy of Nosocomial Infection Control (SENIC) showed that about 6% of all nosocomial infections can be prevented with minimum intervention (51,52). Simple methods that can be used to limit risk include:

- complete assessment of all surgical patients preoperatively;

- reduced preoperative hospitalization;
- evaluation and treatment of remote infections;
- weight reduction (for obese patients);
- cessation of tobacco use;
- control of hyperglycaemia;
- restoration of host defences;
- decreased endogenous bacterial contamination;
- appropriate methods of hair removal;
- administration of appropriate and timely antimicrobial prophylaxis;
- confirmation of proper asepsis and antisepsis of skin and instruments;
- maintenance of meticulous surgical technique and minimization of tissue trauma;
- maintenance of normothermia during surgery;
- shortened operating time; and
- effective wound surveillance.

Effective surveillance systems and feedback to surgeons on their infection rates have been shown to improve the prevention of surgical site infection (53–55). The rates can be reduced by one third or more with programmes and personnel trained in infection control and surveillance (51). In studies in Brazil, the Netherlands, the United Kingdom and the United States, surgical site infection rates were reduced by 33–88% when a surgeon-specific feedback system was used, with strategies such as organized surveillance and control, an adequately trained staff, education and standardized infection control policies (56–60). In many of these studies, the follow-up period was more than 2 years. Surgeon-specific infection rates could be calculated and reported not only to the surgeons but also to the head of the department of surgery (52,59). Collaboration by surgeons in research projects as the principal or co-investigator was instrumental in their success (52). A study in Thailand showed that feedback on surgical site infection rates to surgeons alone did not affect the rate (55) but could give rise to self-assessment and rigorous prevention practices. To ensure acceptance by staff, infection prevention measures should be designed and implemented by a multidisciplinary team, as sustainable changes in procedure and behaviour require commitment from all the disciplines involved.

The methods of surveillance include chart review, medication review, laboratory-based ward surveillance, laboratory-based telephone surveillance, ward liaison surveillance, treatment and temperature chart surveillance, risk factor surveillance, antimicrobial use monitoring and microbiology reports (8). While the details of these methods are beyond the scope of this document, the principles of an effective surveillance system are:

- to maintain accurate, efficient, confidential data collection;
- to provide data on final infection rates stratified by multivariate risk for each surgeon and patient;
- to use clear, consistent definitions of infection; and

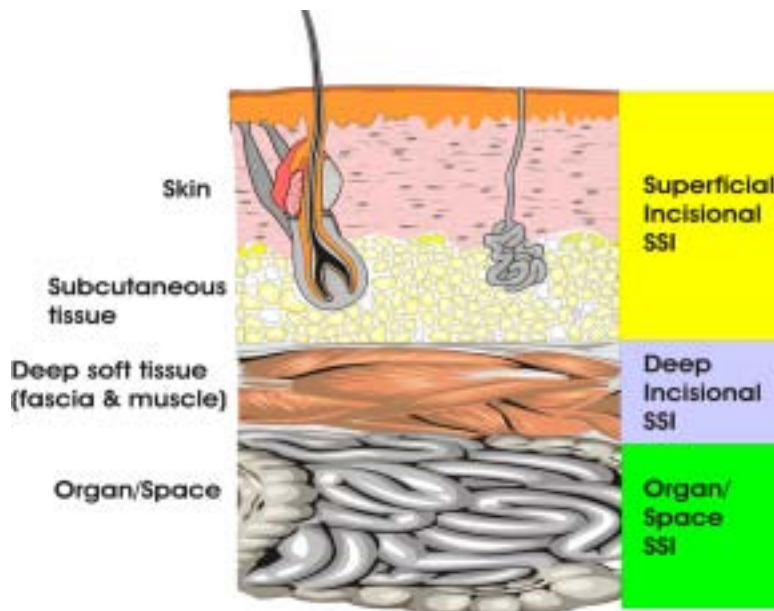
- to use standardized post-discharge follow-up protocols and proper maintenance of data.

Not all studies, however, show a reduction in surgical site infection rates after continuous surveillance. Standardized definitions of infection and objective criteria should be used whenever possible. The most widely used definition is that of the NNIS system of the Centers for Disease Control and Prevention in the United States (61).

Definitions of surgical site infection

A precise definition of surgical site infection is vital for personnel measuring infection rates. It should be simple and accepted by nurses and surgeons. Use of a standard definition allows comparison of rates across surgeons and hospitals. In the NNIS definition, surgical site infection is divided into two main groups, incisional and organ–space. Incisional infections are further subdivided into superficial (skin and subcutaneous tissue) and deep (deep soft tissue such as fascia and muscle layers). Organ–space surgical site infection involves any part of the anatomy other than the incision that is opened or manipulated during an operation (Figure 6.1). The criteria for the different sites of infection are given below.

Figure 6.1 – Cross-section of abdomen depicting classification of surgical site infection according to the Centers for Disease Control and Prevention (United States)



SSI, surgical-site infection

Superficial incisional surgical site infection: Infection occurs at the incision site within 30 days of surgery and involves only skin or subcutaneous tissue at the incision and at least one of the following:

- purulent drainage from the superficial incision;
- an organism isolated by culturing fluid or tissue from the superficial incision;
- deliberate opening of the wound by the surgeon because of the presence of at least one sign or symptom of infection (pain, tenderness, localized swelling, redness or heat), unless the wound culture is negative; or
- diagnosis of superficial incisional surgical site infection by the surgeon or attending physician.

The following conditions are generally not reported as surgical site infection:

- stitch abscess with minimal inflammation and discharge confined to the points of suture penetration;
- infection of an episiotomy site;
- infection of a neonatal circumcision site; or
- infected burn wound.

Deep incisional surgical site infection: Infection occurs at the site of operation within 30 days of surgery if no implant (non-human-derived foreign body permanently placed in the patient during surgery) is left in place and within 1 year of surgery if an implant is left in place. In addition, infection appears to be related to surgery and involves deep soft tissue (muscle and fascia layers) and at least one of the following:

- purulent drainage from deep incision but not from the organ–space component of the surgical site;
- wound dehiscence or deliberate opening by the surgeon when the patient has fever ($> 38\text{ }^{\circ}\text{C}$) or localized pain or tenderness, unless the wound culture is negative;
- an abscess or other evidence of infection involving the deep incision seen on direct examination during surgery, by histopathological examination or by radiological examination; or
- diagnosis of deep incisional surgical site infection by the surgeon or attending physician.

Organ–space surgical site infection: Infection occurs within 30 days of surgery if no implant (non-human-derived foreign body permanently placed in the patient during surgery) is left in place and within 1 year of surgery if an implant is left in place. In addition, infection appears to be related to surgery and involves any part of the anatomy other than the incision that is opened or manipulated during an operation and at least one of the following:

- purulent drainage from a drain placed through a stab wound into the organ–space;
- an organism isolated from an aseptically obtained culture of fluid or tissue in the organ or space;

- an abscess or other evidence of infection involving the organ or space seen on direct examination during surgery, by histopathological examination or by radiological examination; or
- diagnosis of an organ–space surgical site infection by the surgeon or attending physician.

Methods of scoring infection

Several different scoring systems have been described that objectively evaluate wound status or risk of infection. The ASEPSIS (Additional treatment, Serous discharge, Erythema, Purulent exudates, Separation of deep tissues, Isolation of bacteria and Stay duration as inpatient) scoring system was devised in 1986 by Wilson and co-workers in England (62). This scale can be used to monitor and record the rate and severity of surgical site infections. It was initially designed for evaluating the effectiveness of antibiotic prophylaxis before cardiac surgery but has been proposed for comparing outcomes at different institutes (63–65). The surgical site is inspected on five of the first seven days after surgery, and the wound scored is based on the findings of serous exudates, erythema, purulent exudate and separation of deep tissue. The findings are scored as shown in Table II.6.4.

Table II.6.4 – Point scale for daily wound inspection for ASEPSIS scoring of surgical site infections

Wound characteristic	Proportion of wound affected (%)					
	0	< 20	20–39	40–59	60–79	≥ 80
Serous exudates	0	1	2	3	4	5
Erythema	0	1	2	3	4	5
Purulent exudates	0	2	4	6	8	10
Separation of deep tissue	0	2	4	6	8	10

The point scales for additional information on wound treatment, culture findings and delayed discharge are:

- antibiotic therapy for wound infection (additional treatment): not given = 0, given = 10
- drainage of pus under local anesthesia (additional treatment): not done = 0, done = 5
- debridement of wound under general anesthesia (additional treatment): not done = 0, done = 10
- isolation of pathogenic bacteria: none = 0, present = 10
- stay as inpatient: not prolonged = 0, prolonged = 5

ASEPSIS scores range from 0 to 70, with the following interpretation: 0–10, satisfactory healing; 11–20, disturbance of healing; 21–30, minor wound infection; 31–40; moderate wound infection; > 40, severe wound infection.

The risk index in the Study on the Efficacy of Nosocomial Infection Control (SENIC) is based on four clinical findings: abdominal operation, operation lasting more than 2 hours, surgical wound classed as contaminated, dirty or infected, and patient with three or more major pre-existing diagnoses (66). Each clinical finding adds one point to the total score, the minimum index value being 0 and the maximum 4; 0 denotes a low risk for surgical site infection, 1 point implies an intermediate risk, and 2–4 points indicate a high risk. While the SENIC risk

index is valid as a scoring system, it has not been popular because of the constant 2-hour cut-off point for the duration of the operation.

The NNIS risk index was based on the SENIC index (66), with three parameters: the American Society of Anesthesiologists (ASA) preoperative assessment classification, reflecting the patient's preoperative physical status; the duration of the procedure; and the surgical wound class. One point is scored for each finding: an ASA preoperative assessment classification of 3, 4 or 5; duration of surgery longer than 75% of similar cases; and a surgical wound classed as contaminated, dirty or infected. If a procedure is performed endoscopically, the NNIS risk index score is modified by subtracting one point; therefore, the NNIS risk index ranges from -1 to 3. An index of 0 is interpreted as a low risk for surgical site infection, an index of 1 means an intermediate risk, and an index of 2 or 3 equates to a high risk. The NNIS risk index is popular because it includes the specific duration of the operation being performed and replaces the severity of underlying disease in the SENIC risk index by the ASA classification. Moreover, it shows a linear trend with both crude and adjusted rates of surgical site infection. The NNIS risk index has therefore been applied to benchmarked surgical site infection rates by indirect standardization and reported in terms of a standardized infection ratio (24,67-70). This ratio can be a useful tool for comparing surgical site infection rates between institutions (30). The NNIS risk index has been shown to be more accurate than the simple preoperative wound classification of 'clean', 'clean-contaminated', 'contaminated' and 'dirty' described by the Centers for Disease Control and Prevention in the United States (see 'Antibiotic prophylaxis' below).

Surveillance of surgical site infections

Surveillance has been described as the on-going systematic collection, analysis, evaluation and dissemination of data. Monitoring systems use assessment criteria based on standard definitions, extent of coverage, adjustment for risk, ability to collect and validate data, ability to analyse data and provide feedback to clinicians, and wider dissemination to academic and clinical personnel (65,71). An active surveillance programme is necessary for accurate identification of surgical site infections (72).

The methods used for surveillance of surgical site infections were originally designed for monitoring inpatients only. Over the past decade, the shift from inpatient to outpatient surgical care has been dramatic (73), making traditional surveillance methods considerably more difficult to employ. Most hospitals do not have the resources to monitor all surgical patients all the time; therefore, they should target their efforts to high-risk procedures and combine computer-assisted, laboratory-based screening with case confirmation by surgeons (10,30,53,67,68,70,74). When the necessary technology is available, these methods can be reliable, accurate and less time-consuming than conventional methods of chart review.

Inpatients: Several methods have been used to identify inpatients with surgical site infections. Direct observation of the surgical site by the surgeon, a trained nurse or infection control personnel, and indirect detection by infection control personnel who review laboratory reports, patient records and hold discussions with primary-care providers are two of the most common strategies (38). Direct

observation of surgical sites is the most precise and accurate method for detecting surgical site infections (10), but several studies have utilized indirect methods (75,76). Because the hospital stay is often very short, post-discharge surveillance has become increasingly important to obtain precise infection rates.

Post-discharge: As 96% of postoperative superficial surgical site infections occur within 28 days of surgery (77), 30 days has become the accepted length of surveillance for infections after operations that do not involve prosthetic implantation (61). Surgical site infections are frequently detected after patients have been discharged from hospital (17,78–82). Post-discharge surveillance methods have been used with varying degrees of success for different procedures and hospitals. The methods include direct examination of patients' wounds during follow-up visits, review of medical records and mail or telephone surveys with patients or surgeons (82). As integrated health information systems expand, tracking surgical patients throughout care may become easier and more practical and effective. There is currently no consensus on which post-discharge surveillance methods are the most sensitive, specific and practical. The method chosen will necessarily reflect the hospital's mix of operations, personnel resources and data needs.

Risk factors

Patient characteristics and comorbidity play an important role in determining the likelihood of infection after surgery. Coincident remote-site infections, colonization (in particular, nares colonization with *S. aureus*), diabetes, cigarette smoking, use of systemic steroids, obesity (body mass index ≥ 30 kg/m²), extremes of age, poor nutritional status, perioperative blood transfusion and prolonged preoperative stay have all been shown to increase the risk of surgical site infection (42,43,83–102). Prolonged postoperative hospital stay has also been frequently associated with increased surgical site infection risk (52,103,104). Length of stay is, however, probably a surrogate for severity of illness and comorbid conditions requiring inpatient work-up or therapy before or after the operation.

The characteristics of the operation can also affect the likelihood of surgical site infection. Preoperative preparation has a demonstrable role in preventing infection. Antiseptic showering, clipping (as opposed to shaving) for hair removal, skin preparation and hand and forearm scrub antiseptics are steps that can reduce infection rates. Several studies have shown that preoperative hair removal by any means is associated with increased surgical site infection rates and have suggested that no hair be removed (38,105,106). Appropriate antiseptic agents, scrubbing technique and duration of the scrub (both of the patient's skin and of the hands and forearms of the surgical team) result in decreased bacterial colony counts (107–111), although these practices have not been shown definitively to reduce surgical site infection rates (112,113).

Intraoperative factors such as the operating room environment (appropriate ventilation and cleanliness of environmental surfaces), sterilization of instruments, designated surgical attire (including masks, caps and shoe covers) and sterile drapes and scrub suits (including sterile gloves and gowns) also increase the likelihood of reducing contamination of the surgical wound. Antibiotic prophylaxis has the most evidence to support its use in the prevention

of surgical site infection. When used appropriately, infection rates can be significantly reduced (see 'Antibiotic prophylaxis' below).

The two most important principles of infection prevention, however, are related to the duration of the operation and the surgical aseptic technique (114,115). Minimizing the amount of time required for surgery is considered to be one of the principle means of preventing infections. Lack of adherence to the principles of asepsis during procedures has been associated with outbreaks of postoperative infections (116). Meticulous surgical technique is widely considered to reduce the risk for surgical site infection, and includes maintaining effective haemostasis while preserving an adequate blood supply, preventing hypothermia, handling tissues gently, avoiding inadvertent entries into a hollow viscus, removing devitalized tissue, using drains and suture material appropriately and eradicating dead space (117–119).

Appropriate postoperative management of the incision can reduce surgical site infection. The type of care is determined by whether the incision is closed or left open to heal by secondary intention. The evidence is inconclusive as to whether an incision should be covered with a dressing or whether showering or bathing is detrimental to healing. However, when a surgical incision is left open at the skin level for a few days before it is closed (delayed primary closure), the incision should be packed with sterile moist gauze and covered with a sterile dressing (110) or a hydrofibre dressing (120,121).

Blood glucose and risk of infection: Patients with diabetes have long been recognized as being at increased risk for infectious complications of all types, with surgical site infection rates two to three times higher than those of patients without diabetes after cardiac operations. The occurrence of hyperglycaemia (glucose > 200 or > 220 mg/dl) among patients undergoing gastrointestinal or cardiac operations has been correlated with a significant increase in surgical site infection rates (122,123). A recent report on patients with and without diabetes undergoing cardiac surgery showed that the risk for surgical site infection doubled when the postoperative glucose level was > 200 mg/dl in the first 48 hours. Half of all hyperglycaemic episodes occurred in patients without diabetes (124,125). Other surveys showed that hyperglycaemia is common in hospitalized patients (126). Furnary et al. demonstrated significant reductions in deep sternal wound infection and in mortality when perioperative insulin management was changed from subcutaneous administration on a sliding scale to continuous infusion (127,128). While the strongest evidence of benefit exists for patients undergoing cardiac surgery, it is likely that all surgical patients could benefit from perioperative screening of glucose level and continuous insulin infusion in the perioperative period when glucose levels are elevated (129). The American College of Endocrinology recently issued a position statement emphasizing the importance of glucose control in all hospitalized patients, including perioperatively (130).

Oxygen tension and temperature in the perioperative period: All surgical wounds contain at least some bacteria at the end of the procedure (35). The balance between the number and virulence of bacteria and the resilience of host defences determines whether a surgical site infection will result. One of the key host defences is the action of leukocytes in the wound. White cells use activated oxygen to kill bacteria, and a number of studies in vitro and in experimental

animals have shown the importance of oxygen tension in supporting this process (131–135). Subsequent studies of postoperative patients showed that the risk for surgical site infection was associated with subcutaneous oxygen tension at the wound (136). Tissue warming improves tissue perfusion and tissue oxygen tension (137).

A multicentre trial in Europe of patients who had undergone colectomy showed that maintaining normothermia during the operation reduced the rate of infection (138), while a trial in the United Kingdom of smaller operations (on the breast, hernias and varicose veins) showed a lower infection rate when patients were warmed before the operation (139). Perioperative morbid cardiac events are also reduced by maintaining normothermia during major operations (140).

The benefit of increasing the level of inspired oxygen during surgery in order to increase tissue oxygen tension is less clear cut than that of maintaining normothermia. Three prospective randomized trials of patients undergoing colectomy or other major intra-abdominal procedures compared administration of an 80% or 30–35% fraction of inspired oxygen during the operation and for 2–6 hour afterwards (141–143). The first and third trials showed a benefit and the other trial showed an increased infection rate with a higher fraction of inspired oxygen. The two trials showing benefit were better designed and had more patients, but no conclusion can yet be drawn (144,145). Yet increasing the fraction of inspired oxygen might be beneficial and is almost certainly not harmful. Risk factors associated with surgical site infection are listed in Table II.6.5.

Table II.6.5 – Patient and operation characteristics that may be associated with surgical-site infection

<i>Patient characteristic</i>	<i>Operation characteristic</i>
Age	Preoperative skin preparation
Nutritional status	Preoperative shaving
Diabetes	Surgical team preoperative hand and forearm antisepsis
Smoking	Operating-room environment
Obesity	Surgical attire and drapes
Colonization with microorganisms	Sterilization of instruments
Coexisting infection at a remote body site	Duration of operation
Altered immune response	Surgical technique: haemostasis, hypothermia, tissue trauma, hollow viscus, removal of devitalized tissues, surgical drains and suture material, eradicating dead space
Length of preoperative stay	Antimicrobial prophylaxis

Presurgical skin disinfection

The aim of skin disinfection is to remove and rapidly kill skin flora at the site of a planned surgical incision. The antiseptics that are currently available do not eliminate all microorganisms (146), and coagulase-negative staphylococci can be

isolated even after three applications of agents such as iodine–alcohol to the skin (147).

The United States Food and Drug Administration defines a skin disinfectant as a “fast acting, broad-spectrum and persistent antiseptic-containing preparation that significantly reduces the number of microorganisms on intact skin” (148). There is no clear-cut level of bacterial skin load that should be removed or killed before surgery, and 80% of bacteria in surgical site infections originate from the skin of the patient (149). Therefore, the Food and Drug Administration and authorities in Europe and elsewhere have set standards that a disinfectant for presurgical skin preparation must meet before it can be legally marketed. The Food and Drug Administration requires testing at both 10 minutes and 6 hours: disinfectants should reduce colony-forming units (CFU) by more than 2 log₁₀ at dry sites (e.g. abdominal skin) and by 3 log₁₀ at moist sites (e.g. groin).

Most guidelines recommend a scrub-paint technique for applying a disinfectant. One study indicated, however, that spraying might be sufficient (150). The number of bacteria expected at a surgical site ultimately determines the number of disinfectant applications. As a general rule, three application are sufficient; however, in areas with high densities of bacteria, this might not be sufficient to kill all vegetative bacteria (151).

Before a patient’s skin is prepared for a surgical procedure, it should be cleansed of gross contamination (e.g. dirt, soil or any other debris) (38). Although preoperative showering has not been shown to reduce the incidence of surgical site infection, it might decrease bacterial counts and ensure that the skin is clean (152). The antiseptics used to prepare the skin should be applied with sterile supplies and gloves or by a no-touch technique, moving from the incision area to the periphery (38). The person preparing the skin should use pressure, because friction increases the antibacterial effect of an antiseptic. For example, alcohol applied without friction reduces bacterial counts by 1.0–1.2 log₁₀ CFU compared with 1.9–3.0 log₁₀ CFU when friction is used. Alcoholic sprays have little antimicrobial effect and produce potentially explosive vapours (153).

Alcoholic compounds: For centuries, alcohols have been used for their antimicrobial properties. Ethanol and isopropanol act within seconds, are minimally toxic to the skin, do not stain and are not allergenic. They evaporate readily, which is advantageous for most disinfection and antiseptics procedures. The uptake of alcohol by intact skin and the lungs after topical application is negligible. Alcohols have better wetting properties than water due to their lower surface tensions, which, with their cleansing and degreasing actions, make them effective skin antiseptics. Alcoholic formulations used to prepare the skin before invasive procedures should be filtered to ensure that they are free of spores; otherwise, 0.5% hydrogen peroxide should be added (153).

Alcohols have some disadvantages. If alcoholic antiseptics are used repeatedly, they may dry and irritate the skin. In addition, they are flammable (the flash-point should be considered) and cannot penetrate protein-rich materials.

The exact mechanism by which alcohols destroy microorganisms is not fully understood. The most plausible explanation for their antimicrobial action is that they coagulate (denature) proteins, such as enzymatic proteins, thus impairing

specific cellular functions (154). Ethanol and isopropanol at appropriate concentrations have broad spectra of antimicrobial activity that include vegetative bacteria, fungi and viruses. Their antimicrobial efficacies are enhanced in the presence of water, with optimal alcohol concentrations being 60–90% by volume.

Alcohols such as 70–80% ethanol kill vegetative bacteria such as *S. aureus*, *Streptococcus pyrogenes*, *Enterobacteriaceae* and *Ps. aeruginosa* in 10–90 s in suspension tests (155). Isopropanol is slightly more bactericidal than ethanol (154) and is highly effective against vancomycin-resistant enterococci (156). It also has excellent activity against fungi such as *Candida* spp., *Cryptococcus neoformans*, *Blastomyces dermatitidis*, *Coccidioides immitis*, *Histoplasma capsulatum*, *Aspergillus niger* and dermatophytes and mycobacteria, including *Mycobacterium tuberculosis*. Alcohols generally do not, however, destroy bacterial spores, and fatal infections due to *Clostridium* species have occurred when alcohol was used to sterilize surgical instruments.

Both ethanol and isopropanol inactivate most viruses with a lipid envelope (e.g. influenza virus, herpes simplex virus and adenovirus). Several investigators found that isopropanol had less virucidal activity against naked, nonenveloped viruses (157). In experiments by Klein and DeForest (158), 2-propanol, even at 95%, did not inactivate nonenveloped poliovirus type 1 or coxsackievirus type B within 10 min, whereas 70% ethanol inactivated these enteroviruses. Neither 70% ethanol nor 45% 2-propanol killed hepatitis A virus when their activities were assessed on stainless-steel discs contaminated with faecally suspended virus. Of the 20 disinfectants tested, only three reduced the titre of hepatitis A virus by more than 99.9% in 1 min (2% glutaraldehyde, sodium hypochlorite with > 5000 ppm free chlorine, and a quaternary ammonium formulation containing 23% HCl) (159). Bond et al. (160) and Kobayashi et al. (161) showed that 2-propanol (70% for 10 min) or ethanol (80% for 2 min) rendered human plasma contaminated with hepatitis B virus at high titre non-infectious for susceptible chimpanzees. Both 15% ethanol and 35% isopropanol readily inactivated human immunodeficiency virus (HIV), and 70% ethanol rapidly inactivated high titres of HIV in suspension, independent of the protein load (162). The rate of inactivation decreased when the virus was dried onto a glass surface and high levels of protein were present (163). In a suspension test, 40% propanol reduced the rotavirus titre by at least 4 log₁₀ in 1 min, and both 70% propanol and 70% ethanol reduced the release of rotavirus from contaminated fingertips by 2.7 log₁₀ units (164), whereas the mean reductions obtained with liquid soap and an aqueous solution of chlorhexidine gluconate were 0.9 and 0.7 log₁₀ units, respectively (165).

Alcohol is thus the most widely used skin disinfectant. Alcohols used for skin disinfection before invasive procedures should be free of spores; although the risk of infection is minimal, the low additional cost for a spore-free product is justified. One study indicated that isopropanol in a commercial hand rub could be absorbed dermally, transgressing the religious beliefs of some health-care workers (166), although the results have been put into question by a recent trial (167). WHO resolved the issue in their most recent guidelines on hand hygiene by carefully analysing the available information and concluding that use of alcoholic compounds for patient care does not transgress religious beliefs (168). Alcoholic compounds are not suitable for use during surgery at or in close proximity to mucous membranes or the eyes.

Chlorhexidine: Chlorhexidine gluconate, a cationic bisbiguanide, has been widely recognized as an effective, safe antiseptic for nearly 40 years (169,170). Chlorhexidine formulations are used extensively for surgical and hygienic hand disinfection; other applications include preoperative showers (or whole-body disinfection), antiseptics in obstetrics and gynaecology, management of burns, wound antiseptics and prevention and treatment of oral disease (plaque control, pre- and postoperative mouthwash, oral hygiene). When chlorhexidine is used orally, its bitter taste must be masked, and it can stain the teeth. Intravenous catheters coated with chlorhexidine and silver sulfadiazine are used to prevent catheter-associated bloodstream infections (171).

Chlorhexidine is most commonly formulated as a 4% aqueous solution in a detergent base; however, alcoholic preparations have been shown in numerous studies to have better antimicrobial activity than detergent-based formulations (172). Bactericidal concentrations destroy the bacterial cell membrane, causing cellular constituents to leak out of the cell and the cell contents to coagulate (169). The bactericidal activity of chlorhexidine gluconate against vegetative Gram-positive and Gram-negative bacteria is rapid. In addition, it has a persistent antimicrobial action that prevents regrowth of microorganisms for up to 6 hours. This effect is desirable when a sustained reduction in microbial flora reduces the risk for infection, such as during surgical procedures. Chlorhexidine has little activity against bacterial and fungal spores except at high temperatures. Mycobacteria are inhibited but are not killed by aqueous solutions. Yeasts and dermatophytes are usually susceptible, although the fungicidal action varies with the species (173). Chlorhexidine is effective against lipophilic viruses, such as HIV, influenza virus and herpes simplex virus types 1 and 2, but viruses like poliovirus, coxsackievirus and rotavirus are not inactivated (169). Blood and other organic material do not affect the antimicrobial activity of chlorhexidine significantly, in contrast to their effects on povidone-iodine (153). Organic and inorganic anions such as soaps are, however, incompatible with chlorhexidine, and its activity is reduced at extremely acidic or alkaline pH and in the presence of anionic- and nonionic-based moisturizers and detergents.

Microorganisms can contaminate chlorhexidine solutions, and resistant isolates have been identified (174). For example, Stickler and Thomas (175) found chlorhexidine-resistant *Proteus mirabilis* after extensive use of chlorhexidine over a long period to prepare patients for bladder catheterization. Resistance of vegetative bacteria to chlorhexidine was thought to be limited to certain Gram-negative bacilli such as *P. aeruginosa*, *Burkholderia (Pseudomonas) cepacia*, *P. mirabilis* and *S. marcescens*, but genes conferring resistance to various organic cations, including chlorhexidine, have been identified in *S. aureus* clinical isolates (176,177).

There are several other limitations to the use of chlorhexidine. When it is absorbed onto cotton and other fabrics, it usually resists removal by washing (169). Long-term experience with use of chlorhexidine has shown that the incidence of hypersensitivity and skin irritation is low, but severe allergic reactions including anaphylaxis have been reported (178,179). Although cytotoxicity has been observed in exposed fibroblasts, no deleterious effects on wound healing have been found in vivo. While there is no evidence that chlorhexidine gluconate is toxic if it is absorbed through the skin, ototoxicity is a concern when chlorhexidine is instilled into the middle ear during operations.

High concentrations of chlorhexidine and preparations containing other compounds, such as alcohols and surfactants, may also damage the eyes, and its use on such tissues is not recommended (180).

Iodophors: Iodophors have essentially replaced aqueous iodine and tincture as antiseptics. These are chemical complexes of iodine bound to a carrier such as polyvinylpyrrolidone (povidone) or ethoxylated nonionic detergents (poloxamers), which gradually release small amounts of free microbicidal iodine. The most commonly used iodophor is povidone–iodine. Preparations generally contain 1–10% povidone–iodine, equivalent to 0.1–1.0% available iodine. The active component appears to be free molecular iodine (181). A paradoxical effect of dilution on the activity of povidone–iodine has been observed: as the dilution increases, bactericidal activity increases to a maximum and then falls (182). Commercial povidone–iodine solutions at dilutions of 1:2 to 1:100 kill *S. aureus* and *Mycobacterium chelonae* more rapidly than do stock solutions (183). *S. aureus* can survive a 2-minute exposure to full-strength povidone–iodine solution but cannot survive a 15-second exposure to a 1:100 dilution of the iodophor. Thus, iodophors must be used at the dilution stated by the manufacturer.

The exact mechanism by which iodine destroys microorganisms is not known. It may react with the microorganisms' amino acids and fatty acids, destroying cell structures and enzymes (182). Depending on the concentration of free iodine and other factors, iodophors exhibit a broad range of microbicidal activity. Commercial preparations are bactericidal, mycobactericidal, fungicidal and virucidal but not sporicidal at the dilutions recommended for use. Prolonged contact is required to inactivate certain fungi and bacterial spores (157). Despite their bactericidal activity, povidone–iodine and poloxamer–iodine solutions can become contaminated with *B. (P.) cepacia* or *P. aeruginosa*, and contaminated solutions have caused outbreaks of pseudobacteraemia and peritonitis (184,185). *B. cepacia* was found to survive for up to 68 weeks in a povidone–iodine antiseptic solution (186). The most likely explanation for the survival of these microorganisms in iodophor solutions is that organic or inorganic material and biofilm provide mechanical protection.

Iodophors are widely used for antiseptics of skin, mucous membranes and wounds. A 2.5% ophthalmic solution of povidone–iodine is more effective and less toxic than silver nitrate or erythromycin ointment when used as prophylaxis against neonatal conjunctivitis (ophthalmia neonatorum) (187). In some countries, povidone–iodine alcoholic solutions are used extensively for skin antiseptics before invasive procedures (188). Iodophors containing higher concentrations of free iodine can be used to disinfect medical equipment. However, iodophor solutions designed for use on the skin should not be used to disinfect hard surfaces because the concentrations of antiseptic solutions are usually too low for this purpose (157).

The risk of side-effects, such as staining, tissue irritation and resorption, is lower with use of iodophors than with aqueous iodine. Iodophores do not corrode metal surfaces (182); a body surface treated with iodine or iodophor solutions may absorb free iodine, however. Consequently, increased serum iodine (and iodide) levels have been found in patients, especially when large areas were treated for a long period. For this reason, hyperthyroidism and other disorders of thyroid function are contraindications for the use of iodine-containing preparations. Likewise, iodophors should not be applied to pregnant and nursing

women or to newborns and infants (181). Because severe local and systemic allergic reactions have been observed, iodophors and iodine should not be used in patients with allergies to these preparations (189). Iodophores have little if any residual effect; however, they may have residual bactericidal activity on the skin surface for a limited time, because free iodine diffuses into deep regions and also back to the skin surface (182). The antimicrobial efficacy of iodophors is reduced in the presence of organic material such as blood.

Triclosan and chloroxynol (para-chlorometaxynol): Triclosan (Irgasan DP-300, Irgacare MP) has been used for more than 30 years in a wide array of skin-care products, including handwashes, surgical scrubs and consumer products. A review of its effectiveness and safety in health-care settings has been published (190). A concentration of 1% has good activity against Gram-positive bacteria, including antibiotic-resistant strains, but is less active against Gram-negative organisms, mycobacteria and fungi. Limited data suggest that triclosan has a relatively broad antiviral spectrum, with high-level activity against enveloped viruses such as HIV-1, influenza A virus and herpes simplex virus type 1. The nonenveloped viruses proved more difficult to inactivate.

Clinical strains of bacteria resistant to triclosan have been identified, but the clinical significance remains unknown (191). Triclosan is added to many soaps, lotions, deodorants, toothpastes, mouth rinses, commonly used household fabrics, plastics and medical devices. The mechanisms of triclosan resistance may be similar to those involved in antimicrobial resistance (192), and some of these mechanisms may account for the observed cross-resistance of laboratory isolates to antimicrobial agents (193). Consequently, concern has been raised that widespread use of triclosan formulations in non-health-care settings and products might select for biocide resistance and even cross-resistance to antibiotics. Environmental surveys have not, however, demonstrated an association between triclosan use and antibiotic resistance (194).

Triclosan solutions have a sustained residual effect against resident and transient microbial flora, which is minimally affected by organic matter. No toxic, allergenic, mutagenic or carcinogenic potential has been identified in any study. Triclosan formulations can help control outbreaks of methicillin-resistant *S. aureus* when used for hand hygiene and as a bathing cleanser for patients (190), although some methicillin-resistant *S. aureus* isolates have reduced triclosan susceptibility. Triclosan formulations are less effective than 2–4% chlorhexidine gluconate when used as surgical scrub solutions, but properly formulated triclosan solutions can be used for hygienic hand washing.

para-Chlorometaxynol (chloroxynol, PCMX) is an antimicrobial agent used in hand-washing products, with properties similar to those of triclosan. It is available at concentrations of 0.5–3.75%. Nonionic surfactants can neutralize this compound.

Octenidine: Octenidine dihydrochloride is a novel bispyridine compound, which is an effective, safe antiseptic agent. The 0.1% commercial formulation compared favourably with other antiseptics with respect to antimicrobial activity and toxicological properties. It rapidly killed both Gram-positive and Gram-negative bacteria as well as fungi in vitro and in vivo (195,196). Octenidine is virucidal against HIV, hepatitis B virus and herpes simplex virus. Like chlorhexidine, it

has a marked residual effect. No toxicological problems were found when the 0.1% formulation was applied according to the manufacturer's recommendations. The colourless solution is a useful antiseptic for mucous membranes of the female and male genital tracts and the oral cavity, but its unpleasant taste limits its use orally (197). In a recent observational study, the 0.1% formulation was highly effective and well tolerated in the care of central venous catheter insertion sites (198), and the results of this study are supported by those of a randomized controlled clinical trial (199). Octenidine is not registered for use in the United States.

Table II.6.6 lists antimicrobial agents that are recommended for surgical skin preparation.

Table II.6.6 – Antimicrobial agents recommended for surgical skin preparation

Solution	Comment
60–90% isopropanol	Not for use on mucous membranes
7.5–10% povidine–iodine	Can be used on mucous membranes
2–4% chlorhexidine	Not for use on eyes, ears, mucous membranes
Iodine, 3% preparation	Not for use on mucous membranes; can cause skin irritation if left for a long time
<i>para</i> -Chlorometaxylenol (PCMX)	Not for use on newborn babies; penetrates skin

Adapted from reference (206)

Special cases for decontamination

Vaginal and uterine surgery: Endometritis and wound infection are common significant postoperative complications of vaginal surgery, with reported infection rates varying between 5% and > 50%. The best-recognized risk factors for post-caesarean endometritis involve the introduction of large quantities of bacteria from the vagina and cervix into the uterine cavity. Therefore, reducing bacterial contamination of the vagina and cervix by vaginal swabbing with povidone–iodine solution before caesarean section is a reasonable approach. In one study, this led to a significant decline in the rate of postoperative endometritis (200); however, a randomized controlled trial failed to demonstrate an effect (201). Vaginal decontamination may be particularly useful in indigent patients or in settings where the bioburden of the vagina might be high.

Digestive-tract surgery: Selective decontamination of the digestive tract has been recommended for decades to decrease the rates of postoperative pneumonia and, to a lesser extent, surgical site infections (202). These effects should, however, be balanced against the cost, workload and risk for the emergence of multiresistant pathogens. Several recent trials indicate that a mouth rinse with chlorhexidine had a similar effect to selective decontamination of the digestive tract in patients undergoing cardiac surgery (203–205).

Antibiotic prophylaxis

Before the late 1960s, most ‘prophylactic’ antibiotics were administered after the end of a surgical procedure and were therefore found to be ineffective. Patients who received antibiotics had a higher rate of infection than patients who did not, probably because they were administered ineffectively and given only when the surgeon recognized an increased risk (207). Classic experiments in animals by John Burke demonstrated the sequence of events that occur in a surgical incision before infection and the importance of administering the antibiotic before wound contamination occurs (208,209). Subsequent placebo-controlled trials in humans showed a significant reduction in surgical site infections when antibiotics were used preoperatively. One prospective trial indicated that starting antibiotics before the immediate preoperative period was not beneficial (210), and a large retrospective examination of the time of antibiotic administration showed an increase in surgical site infection rates when antibiotics were given more than 2 hours before incision or after the incision (211). Initially, prophylactic antibiotics were given when the patients were called to the operating room, but subsequent studies showed that intravenous administration immediately before (average, 20 minutes) anaesthesia induction achieved better serum and tissue levels both at the beginning and at the end of the operation (212 and J. DiPiro, personal communication). DiPiro found that cefazolin given on average 17 minutes (7–29) before incision achieved an average tissue level of 76 mg/l, while cefoxitin given 22 minutes (13–45) before incision achieved an average tissue level of 24 mg/l. The interval between being called to the operating room and the start of most operations is highly variable, and this unpredictable interval leads to an extended delay between delivery of antibiotics and skin incision. Consequently, the tissue levels of antibiotic are often less than ideal at the start of the operation. A recent review of total joint arthroplasty operations in the Netherlands confirmed the importance of preoperative administration of prophylactic antibiotics and showed that the lowest infection rate was associated with administration within 30 minutes of incision (213,214). Vancomycin is one of the few antibiotics that require adjustments in timing; commencement of infusion should be timed such that completion is achieved within an hour of incision (215,216).

There is widespread agreement and good evidence to support the use of prophylactic antibiotics before all gastrointestinal (including appendicitis), oropharyngeal, vascular (including abdominal and leg), open-heart and obstetric and gynaecological procedures, orthopaedic prosthesis placement, spinal operations, craniotomy and even some ‘clean’ procedures (217,218). The typical reductions in infection rates seen in early placebo-controlled trials of prophylaxis are shown in Table II.6.7. While there is some controversy about the use of prophylactic antibiotics for designated ‘clean’ operations, it is well accepted for open-heart operations, joint replacement, vascular prostheses and craniotomy in which the absolute number of infections is low but the consequence of any infection is severe (Table II.6.8). The reduction in infection rate is similar for other ‘clean’ procedures (219–222), but the absolute number of infections prevented is lower when the underlying infection rate is lower (220,223). If the number of administrations of routine prophylaxis needed to prevent one infection is high, the morbidity of the infection should be high, or the cost, both financial and medical, of the prophylaxis should be low.

Table II.6.7 – Typical rates of infection and reduction with prophylaxis in placebo-controlled trials

Operation (reference)	Prophylaxis (%)	Placebo (%)	Number needed to treat to avoid one surgical-site infection
Colon (224–227)	4–12	24–48	3–5
Other (mixed) gastrointestinal tract (228–231)	4–6	15–29	4–9
Vascular (232,233)	1–4	7–17	10–17
Cardiac (234,235)	3–9	44–49	2–3
Hysterectomy (236)	1–16	18–38	3–6
Craniotomy (237–239)	0.5–3	4–12	9–29
Spinal (240)	2.2	5.9	27
Total joint replacement (241,242)	0.5–1	2–9	12–100
Breast and hernia (221)	3.5	5.2	58

Table II.6.8 – Preoperative Wound Classification of the Centers for Disease Control and Prevention (United States)

Clean Wounds: An uninfected operative wound in which no inflammation is encountered and the respiratory, alimentary, genital, or uninfected urinary tracts are not entered. In addition, clean wounds are primarily closed and, if necessary, drained with closed drainage. Operative incisional wounds that follow nonpenetrating (blunt) trauma should be included in this category if they meet the criteria.
Clean-Contaminated Wounds: Operative wounds in which the respiratory, alimentary, genital, or urinary tracts are entered under controlled conditions and without unusual contamination. Specifically, operations involving the biliary tract, appendix, vagina, and oropharynx are included in this category provided no evidence of infection or major break in technique is encountered.
Contaminated Wounds: Includes open, fresh, accidental wounds. In addition, operations with major breaks in sterile technique (e.g., open cardiac massage) or gross spillage from the gastrointestinal tract, and incisions in which acute, nonpurulent inflammation is encountered are included in this category.
Dirty or Infected Wounds: Includes old traumatic wounds with retained or devitalized tissue and those that involve existing clinical infection or perforated viscera. This definition suggests that the organisms causing postoperative infection were present in the operative field before the operation.

Few studies have examined the ideal dose of prophylactic antibiotics. A study of morbidly obese patients showed a two-thirds reduction in surgical site infection rates when the dose of cefazolin was increased from 1 g to 2 g (243). Early trials involving patients undergoing cardiac surgery demonstrated a correlation between risk for infection and absence of antibiotic in the serum at the end of the operation (244) and low levels of antibiotics at the time of cannulation (245). In a study of prophylaxis in patients undergoing colectomy, the strongest association with avoidance of surgical site infection was the level of drug in the serum at the end of the operation (246). Repeated administration of the drug at one to two half-lives or use of a drug with a long half-life during lengthy operations also reduced infection rates (247,248). Thus, the most

important aspect in the timing and dosing of prophylactic antibiotics is achieving effective levels throughout the time that the incision is open.

Early trials of antibiotic prophylaxis usually involved a three-dose regimen, with the first and last dose separated by 12 hours. Within a short time, many placebo-controlled trials demonstrated the efficacy of a single preoperative dose of prophylactic antibiotic. Nevertheless, the practice of continuing prophylactic antibiotics postoperatively, often for days, is widespread. For example, there is no evidence to support the common practice of using prophylactic antibiotics until all central lines and drains have been removed. Many trials in which shorter duration of prophylaxis was compared with longer failed to show any benefit of longer duration (249–251). Other studies show that more resistant bacteria are recovered from patients who receive prophylaxis for a long time (252). An expert panel assembled by the United States Center for Medicare and Medicaid Services recommended that prophylactic antibiotics be initiated during the 60 minutes before incision and stopped within 24 hours of the end of the operation (14).

Many different antibiotics have been shown to reduce the incidence of surgical site infections. The primary consideration is that the antibiotic used is active against the spectrum of bacteria commonly encountered during the procedure and recovered from surgical site infections. There is general agreement that the antibiotic agents used for prophylaxis should be different from those usually chosen for first-line treatment of established infections, although this supposition has never been studied systematically. A number of societies and organizations, including the Surgical Infection Society (218), the Infectious Diseases Society of America (217), the American Society of Hospital Pharmacists (253), Johns Hopkins University (254), the *Medical Letter* (255) and the Scottish Intercollegiate Guidelines Network (256), have published well-researched guidelines and recommendations for surgical antibiotic prophylaxis.

Table II.6.9 gives recommendations published by various professional societies and organizations. Usually, a single first-generation cephalosporin for operations not expected to encounter anaerobes or a single second-generation cephalosporin with anaerobic activity for anaerobic operations based on local susceptibility patterns is sufficient. For clean operations on the skin and subcutaneous tissues that do not involve any portion of the gastrointestinal tract, a semi-synthetic penicillin resistant to penicillinases, such as oxacillin or cloxacillin, is probably effective, although there are limited published data to support this recommendation. Administration of antibiotics that are active against enteric anaerobes for procedures involving the lower gastrointestinal tract should be considered routine. Procedures on the upper gastrointestinal tract should involve use of antibiotics with activity against Gram-positive cocci and common Gram-negative organisms but which are not active against anaerobes. Procedures that do not enter any portion of the intestinal or genitourinary tract are sufficiently covered with antibiotics that are primarily active against Gram-positive cocci.

Table II.6.9 – Current recommendations of agents for surgical prophylaxis

Procedure	Agents
Colectomy	Cefotetan, cefoxitin, cefazolin plus metronidazole, ampicillin/sulbactam or ertapenem; metronidazole combined with an aminoglycoside, a quinolone or trimethoprim/sulfamethoxazole, or clindamycin combined with an aminoglycoside, a quinolone, aztreonam or trimethoprim/sulfamethoxazole ^a
Other gastrointestinal surgery	Cefotetan, cefoxitin, cefazolin or cefuroxime ^b
Hysterectomy	Cefotetan, cefoxitin, cefazolin or cefuroxime, cefazolin plus metronidazole ^c
Vascular and cardiac surgery	Cefazolin or cefuroxime, penicillinase-resistant penicillins such as oxacillin and cloxacillin, or vancomycin or clindamycin
Total joint replacement	Cefazolin or cefuroxime or a penicillinase-resistant penicillin

Not all agents listed have been tested in prospective placebo-controlled trials, but most are widely used and fulfill the criterion of being active against the usual pathogens encountered in these settings.

^a The recommendations for metronidazole and clindamycin combined with various Gram-negative agents as listed above have had limited or no testing but represent logical choices on the basis of antibiotic susceptibility patterns and known colonic flora. In addition, they have all been used successfully in the treatment of infections originating in the colon.

^b Procedures of the stomach and pancreatic and biliary systems are managed with any of these agents. Distal ileal and appendix operations are more appropriately managed with the agents listed for colectomy.

^c Early studies showed no difference between agents with (cefotetan, cefoxitin) and without (cefazolin, cefuroxime) anaerobic activity. More recent trials demonstrate better results with agents active against anaerobes.

β -Lactam allergies are often cited as a contraindication for antibiotic prophylaxis. Many patients who are reported to be allergic on their medical record do not, however, have a true antibiotic allergy but have experienced nonsevere adverse reactions, such as *Candida* overgrowth or gastrointestinal upset. Before choosing an alternative prophylactic agent for a patient with a history of 'allergy', the nature of the previous reaction should be confirmed. Patients who have had immediate, anaphylactic type reactions should not receive an antibiotic to which they are allergic. For operations in which the risk is primarily from skin organisms, vancomycin or teicoplanin is a common choice for patients allergic to β -lactam. If local susceptibility patterns are favourable, clindamycin can be used. Some experts recommend that in hospitals with a high rate of methicillin-resistant *S. aureus*, a glycopeptide should be used prospectively for procedures involving a risk for infection with skin organisms. There is, however, no agreement about the level of methicillin-resistant *S. aureus* that would justify this approach. The only prospective trial performed to address this question showed no reduction in surgical site infections with the prophylactic vancomycin and an excess number of infections due to methicillin-sensitive *S. aureus* (257). There have been no controlled trials of antibiotic prophylaxis for colon operations with agents appropriate for patients allergic to β -lactam. Logic suggests that a combination of clindamycin or metronidazole with either an aminoglycoside or a fluoroquinolone, or even trimethoprim and sulfamethoxazole or a combination of clindamycin with aztreonam, should be effective.

Prophylaxis for caesarean section: Caesarean section, one of the most commonly performed operations, carries a significant risk for postoperative infection. Infectious complications have been estimated to occur in 7–20% of such patients (258). Griffiths et al. (259) reported an overall surgical site infection incidence of 9.9% in a case–control study. A Cochrane review concluded that the two-third reduction in wound infections and the three-fourths reduction in endometritis justify recommendation of prophylactic antibiotics in both elective and non-elective caesarean section (260). First-generation cephalosporins are the most commonly used agents. Debate about the optimal timing of administration of prophylactic antibiotics continues. Concern about neonatal exposure to antibiotics and the effect on neonatal sepsis have led to delays in administering antibiotics until after the umbilical cord has been clamped. Thigpen et al. (261) found in a recent randomized clinical trial that there was no difference in maternal infectious complications, including neonatal sepsis and admissions to an intensive care unit, whether antibiotics were given before skin incision or at cord clamping. Sullivan et al. (258) reported that administration of antibiotics before skin incision resulted in a decrease in infectious complications when compared with administration at the time of cord clamping. The WHO guidelines *Managing complications in pregnancy and childbirth* (262) recommend a single dose of prophylactic antibiotics after the cord is clamped and cut. It may, however, be more effective to administer prophylactic antibiotics during the hour before incision rather than waiting until the umbilical cord is clamped, as there is no clear evidence for harm to the newborn of administration of antibiotic before incision. Clearly, there is controversy on this question, and either practice is acceptable and more effective for preventing post-caesarean infection than placebo.

Prophylaxis in children: Very few trials of surgical antibiotic prophylaxis have been done in paediatric populations, but the issue has been reviewed by the American Academy of Pediatrics (263), which concluded that the basic biological principles of prophylaxis are unlikely to be different in paediatric patients and adults. They recommend that the same basic principles be followed but that the doses be adjusted according to standard dosing principles for paediatric patients.

Subacute bacterial endocarditis prophylaxis in patients undergoing surgical procedures: Guidelines for subacute bacterial endocarditis prophylaxis are available for patients who are at risk for endocarditis and undergoing an operation. The American Heart Association recently released a new guideline, which has been endorsed by the Infectious Diseases Society of America and the Pediatric Infectious Diseases Society (264). Endocarditis prophylaxis is not recommended for patients undergoing surgical procedures, including endoscopy, except for those with prosthetic valves or previous infectious endocarditis, cardiac transplant recipients who have cardiac valvulopathy or the following examples of congenital heart disease: unrepaired cyanotic congenital heart disease (including patients with palliative shunts and conduits), congenital heart defects completely repaired with prosthetic materials only during the first 6 months after the procedure, and repaired congenital heart disease with residual defects at or adjacent to the site of a prosthetic patch or prosthesis. The guidelines state that “no published data demonstrate a conclusive link between procedures of the gastrointestinal or genitourinary tract and the development of infectious

endocarditis. Moreover, no studies exist to demonstrate that the administration of antimicrobial prophylaxis prevents infectious endocarditis in association with procedures performed on the gastrointestinal or genitourinary tract.... For patients with the conditions listed above who have an established gastrointestinal or genitourinary tract infection, or for those who receive antibiotic therapy to prevent wound infection or sepsis associated with a gastrointestinal or genitourinary tract procedure, it may be reasonable that the antibiotic regimen include an agent active against enterococci, such as penicillin, ampicillin, piperacillin, or vancomycin; however, no published studies demonstrate that such therapy would prevent enterococcal infectious endocarditis. Amoxicillin or ampicillin is the preferred agent for enterococcal prophylaxis for these patients. Vancomycin may be administered to patients who do not tolerate ampicillin. If infection is caused by a known or suspected strain of resistant *Enterococcus*, consultation with an infectious diseases expert is recommended.” For patients with the conditions listed above “who undergo a surgical procedure that involves infected skin, skin structure, or musculoskeletal tissue, it is reasonable that the therapeutic regimen administered for treatment of the infection contain an agent active against staphylococci and β -hemolytic streptococci, such as an antistaphylococcal penicillin or a cephalosporin. Vancomycin or clindamycin may be administered to patients unable to tolerate a β -lactam or who are known or suspected to have an infection caused by a methicillin-resistant strain of staphylococcus.... Prophylaxis at the time of cardiac surgery should be directed primarily against staphylococci and should be of short duration.... The choice of an antibiotic should be influenced by the antibiotic susceptibility patterns at each hospital.”

Minimizing contamination in the operating room

In addition to the risks that the patient, the operation and the team bring to the procedure, the environment of the operating room can also pose a risk to patients. Effective, appropriate planning and forethought in the construction of an operating room minimize such risks. Regular maintenance and cleaning of surgical suites are essential.

Disinfection of surfaces: The surfaces in operating rooms should be kept clean by the use of water, detergent and wiping. As surfaces are considered ‘non-critical’ according to Spaulding’s classification system (265), keeping them clean should be enough for safety. Use of disinfectants, either in a cleaning solution or vaporized into the air, has not proven to make a difference in the rates of surgical site infections and can pose risks to health-care workers (266).

Surgical attire: The use of masks that cover the mouth and nose, hair-coverings such as caps, sterile surgical robes and impermeable sterile gloves is standard for surgical teams. Some correspond to basic principles of aseptic technique and their use is based on laboratory or microbiological studies or rationale, but scientific evidence of their impact in preventing surgical site infections is not available or has been disputed.

The use of masks to cover the mouth and nose is standard practice. The purpose is to prevent contamination of the patient’s tissues with microorganisms from the upper respiratory tract of the surgical team and also to prevent

exposure of the mouth and nose of operating room staff from splashes of blood or other fluids from patients during a procedure. Use of masks significantly reduces contamination of the surgical site (267,268), but the association between mask use and surgical infections is less clear. Tunevall (269) randomly assigned 115 weeks of wearing masks or no mask during 3967 surgical operations in the period 1984–1985 and reported 184 surgical site infections (4.6%). When the randomization of weeks was assessed, no differences between groups were observed in terms of age, type of surgery, elective or not elective or clean or not clean, and no difference in rates was documented whether masks were used or not. Few studies have investigated whether the type of mask affects the rate of infections, and no clear conclusions can be drawn because of low power due to the small numbers of persons studied (270). There is evidence that the use of masks protects from splashes of blood or other fluids from patients during surgery, but its role in preventing the transmission of microorganisms is not clear (271–273).

Sterile robes are used to prevent bacteria on the skin of surgeons from coming into contact with the patient's tissues and also to prevent blood and fluids from patients from coming into contact with the skin of the surgical team. Some fabrics are less permeable than others to fluids, moisture or bacteria. The use of different fabrics did not make a difference in contamination in experimental studies that did not involve actual surgery (274). No difference in the rates of surgical site infections by *S. epidermidis*, *S. aureus* or other agents was observed in randomized controlled trials of patients undergoing cardiac surgery by surgeons wearing surgical attire made of disposable materials or reusable cotton fabric (275–277).

The use of sterile gloves for surgery is standard practice; however, 8–15% of surgical gloves are torn or punctured during procedures (278–280). No difference in surgical site infections rates was observed when gloves were damaged or not during surgery, and the use of two pairs of gloves (double gloving) did not decrease the rates (281,282). When double gloving was used, the outer glove had more perforations than the inner glove, and the hands of the surgical team were less contaminated with blood or other body fluids. In a study of cerebrospinal fluid shunt surgery, the use of double gloves was associated with a 50% reduction in infections of the shunt as compared with use of single gloves (283).

The use of shoecovers for transit in the operating room or during surgery is a frequent practice, although the relation between contamination of the floor of the operating room and the rate of surgical site infections has not been established. In a systematic review of studies published between 1950 and 2003, it was found that the dispersion of microorganisms from the floor to the air was low and that there was no association between the dispersion and contamination of the surgical wound or the rate of surgical site infections (284).

Guaranteeing the sterility of surgical instruments: sterility indicators

Sterilization is the process by which an item is purged of all microorganisms and spores. The use of sterile materials for surgery is considered standard practice internationally. Microorganisms have different degrees of resistance to sterilization methods depending on their type, capacity to form spores, sensitivity to heat, chemicals and disinfectants, and the composition and thickness of the bacterial cell wall or viral envelope. Microbial agents can be organized by their resistance to sterilization procedures: medium-sized viruses tend to be the least resistant to destruction, while bacterial spores tend to be the most resistant. Any

process that kills bacterial spores is considered to be able to eliminate all other infectious agents, and elimination of bacterial spores is a satisfactory indicator that sterilization has been achieved. Processes that kill *M. tuberculosis* but neither bacterial spores nor prions are considered to achieve 'high-level disinfection'. (The destruction of prions requires special procedures and is not described in this document.)

In the classification system of Spaulding et al. (265), devices that enter normally sterile tissue, body cavities or the vascular system should be sterile. Articles that come into contact with intact mucous membranes and that do not ordinarily penetrate sterile tissue are classified as 'semicritical' and should receive at least high-level disinfection. Although the categories of disinfection may be oversimplified in this system, it is currently the most useful means of categorizing instrument decontamination.

Achieving sterility, particularly for reusable surgical instruments, requires a sequence of cleaning and mechanical removal of gross contamination, inspection and assembly, packaging, sterilization, storage, transport and delivery to the operating room, and certification of the sterilization process. Cleaning is the mechanical or chemical removal of any residual matter, organic or inorganic, from an item with water, detergents and mechanical means. Cleaning decreases the microbial load but does not destroy microorganisms. It can be achieved manually or with automatic equipment. Residual organic matter interferes with the efficacy of sterilization and disinfection by preventing contact of the microbicidal agent with the surface of the instrument or prolonging the time of exposure required to achieve destruction of microorganisms (285–287). Because of the significant reduction in microbial load due to cleaning, it has also been called 'decontamination', especially when chemical agents are used. Inspection consists of direct visualization of cleaned instruments, usually through a magnifying glass, to detect residual matter (including oils or lubricants) that can interfere with sterilization. Packaging of instruments and tray assembly must allow the sterilizing agent to reach every item and effectively kill all microorganisms. For successful tray packaging, the tray must not be overloaded. The packaging should also allow handling of the tray after sterilization without contaminating the items on it. Each sterilizing agent and method has its own requirements for tray packaging to ensure successful sterilization (288). The packaging system should be permeable to the sterilizing agent but resistant to traction and manipulation.

Sterilization is the exposure of instruments, devices and other materials to a sterilizing agent. All remaining microorganisms and spores should be eliminated by use of this agent. A wide variety of methods is available for sterilization, and Table II.6.10 lists the advantages and limitations of those most frequently used. The choice of method should be based on the characteristics of the instruments and devices, the need for proper cleaning and packaging, the time required for exposure and sterilization, the temperature and pressure achieved, the humidity and its potential to damage devices or items, the existence of a vacuum and circulation of the agent within the sterilization chamber (288). These relations are shown for the most frequent methods of sterilization in Table II.6.11.

Table II.6.10 – Advantages and limitations of methods for sterilizing articles in health-care settings

<i>Method</i>	<i>Advantages</i>	<i>Limitations</i>
Heat (steam sterilization)	Short exposure Effective for prions Not toxic for humans or the environment Easy certification Low cost Widely available Easy to operate	Not compatible with thermolabile items Does not eliminate pyrogens Cannot be used for oils or powders
Heat (dry air)	Not corrosive Deep penetration Not toxic for humans or the environment Easy to operate Widely available	Long exposure Not compatible with thermolabile items Hard to certify High cost Efficacy against prions not known
Ethylene oxide	Compatible with thermolabile items Penetrates certain plastics Easy to operate	Long exposure Not effective for prions Toxic for humans and the environment
Hydrogen peroxide plasma	Compatible with thermolabile items Short exposure Not toxic for humans or the environment Easy to operate	Not all materials are compatible Not effective for prions Does not reach the centre of long lumens effectively
Liquid peracetic acid in automatic equipment	Short exposure Easy to operate Not toxic for the environment	Useful only for materials that can be immersed In existing equipment, few containers can be processed Not effective for prions Processed items must be used immediately
Formaldehyde	Compatible with thermolabile items Short exposure Easy certification	Not all materials are compatible Not effective for prions

Table II.6.11 – Standardized conditions for sterilization with saturated steam, dry heat and ethylene oxide

Time after temperature and pressure are reached	Temperature (°C)	Pressure (atm)
<u>Saturated steam</u>		
15 min	121	1.5
10 min	126	2.0
3 min	134	2.9
<u>Dry heat</u>		
60 min	170	
120 min	160	
150 min	150	
180 min	140	
Overnight	121	
<u>Ethylene oxide</u>		
5 h	35	
2.5 h	55	

Storage, transport and delivery are the processes by which the instruments and devices are maintained until their use in the operating room. Means of preserving the integrity and impermeability of the packaging by keeping the sterilized materials in appropriate storage (ideally in closed, dust-free shelves and in a dry environment) must be available.

Certification is the method by which sterilization is ascertained and confirmed. It requires a number of procedures to verify that the process has been successful. The physical parameters of sterilization, such as temperature, pressure and length of exposure to the sterilizing agent, must be measured for every sterilization cycle and load. For automatic equipment, this is frequently measured and documented by the equipment itself. Manual equipment should be operated by trained personnel, and calibrated thermometers, barometers, clocks and load sensors should be used. Biological indicators contain a known load of the most resistant microorganism killed by the sterilizing method. Spores of *Geobacillus stearothermophilus* for saturated hot steam, hydrogen peroxide plasma and formaldehyde and *Bacillus subtilis* var *niger* for dry heat and ethylene oxide are usually used. After the process has finished, the viability of the microorganisms is assessed. If there is no microbial activity, the process is considered successful. The frequency of use of biological indicators has not been standardized; however, it should be used on every load of implantable materials, at least once a week for other materials, and always after sterilizing equipment has been repaired. The results of these biological indicators may be available within hours or days, depending on the type of indicator, but rarely immediately or by visual inspection by the operating team at the time of surgery. Chemical indicators must be used routinely to monitor the performance of the equipment and sterilization. Existing chemical indicators are made of thermochromic ink which changes colour when exposed to the sterilizing agent. Most sterilization

indicators turn from beige to black once sterilization is finished. Different types of indicators react to different processes and serve different purposes:

- Processing indicators, such as indicator tape, are placed outside each package to show whether the materials within were processed. Used chemical indicators should be discarded before packaging, and a new indicator should be used for each package.
- Parametric indicators are used inside each package to demonstrate that sterilization was effective.
- A special use of chemical indicators is the Bowie-Dick test for pre-vacuum sterilizing methods (such as some steam autoclaves), which allows confirmation of the effectiveness of the vacuum pump in the sterilization chamber (288). The Bowie-Dick test should be performed daily when autoclaves of this type are used.

Maintaining records of sterilization also appears to be useful, by allowing tracking of machinery and maintenance, verification of the sterility of surgical equipment and quality control.

There are numerous methods for controlling contamination and reducing infectious complications of surgical care. A system as complex as surgery requires the coordination of many individuals to ensure that appropriate procedures and processes are in place to guarantee the cleanliness of the operating room and the sterility of the instruments and equipment used during surgery. Measures known to reduce infection must also be implemented in a timely fashion. Policies for systematically minimizing the risks for infection can make a tremendous difference in the outcome of surgical care, save numerous lives and prevent much morbidity.

Recommendations

Highly recommended:

- Prophylactic antibiotics should be used routinely in all clean-contaminated surgical cases and considered for use in any clean surgical case. When antibiotics are given prophylactically to prevent infection, they should be administered within 1 hour of incision at a dose and with an antimicrobial spectrum that is effective against the pathogens likely to contaminate the procedure. Before skin incision, the team should confirm that prophylactic antibiotics were given within the past 60 minutes. (When vancomycin is used, infusion should be completed within 1 hour of skin incision.)
- Every facility should have a routine sterilization process that includes means for verifying the sterility of all surgical instruments, devices and materials. Indicators should be used to determine sterility and checked before equipment is introduced onto the sterile field. Before induction of anaesthesia, the nurse or other person responsible for preparing the surgical trays should confirm the sterility of the instruments by evaluating the sterility indicators and should communicate any problems to the surgeon and anaesthesia professional.

- Redosing with prophylactic antibiotics should be considered if the surgical procedure lasts more than 4 hours or if there is evidence of excessive intraoperative bleeding. (When vancomycin is used as the prophylactic agent, there is no need for redosing in operations lasting less than 10 hours.)
- Antibiotics used for prophylaxis should be discontinued within 24 hours of the procedure.
- Hair should not be removed unless it will interfere with the operation. If hair is removed, it should be clipped less than 2 hours before the operation. Shaving is not recommended as it increases the risk for surgical site infection.
- Surgical patients should receive oxygen throughout the perioperative period according to individual requirements.
- Measures to maintain core normothermia should be taken throughout the perioperative period.
- The skin of all surgical patients should be prepared with an appropriate antiseptic agent before surgery. The antimicrobial agent should be selected on the basis of its ability to decrease the microbial count of the skin rapidly and its persistent efficacy throughout the operation.
- Surgical hand antisepsis should be assured with an antimicrobial soap. The hands and forearms should be scrubbed for 2–5 minutes. If the hands are physically clean, an alcohol-based hand antiseptic agent can be used for antisepsis.
- The operating team should cover their hair and wear sterile gowns and sterile gloves during the operation.

Recommended:

- ‘On call’ orders for administration of antibiotic prophylaxis should be discouraged.
- If hair is to be removed, the use of depilatories is discouraged.
- Tobacco use should be stopped at least 30 days before elective surgery if possible.
- Surgical patients should take a preoperative shower with antiseptic soap.
- Prior infections should be eliminated before a scheduled operation.
- The operating team should wear masks during the operation.
- Surgical drapes that are effective when wet should be used as part of the sterile barrier.
- Sterile dressing should be maintained over the surgical wound for 24–48 hours.
- Active surveillance for surgical site infections should be conducted prospectively by trained infection control practitioners.
- Information on the surgical site infection rate should be provided to surgeons and appropriate administrators.

Suggested:

- A high fraction of inspired oxygen (80%) should be administered throughout the operation, and supplemental oxygen should be administered for at least 2 hours postoperatively.
- Positive pressure ventilation should be maintained in the operating room.
- The operating room should be cleaned thoroughly after ‘dirty’ or ‘infected’ cases and at the end of each operating day.
- Standardized infection control policies should be implemented.
- Surgical teams should be educated about infection prevention and control at least annually.

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