Prophylactic Antibiotics and Prevention of Surgical Site Infections

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KEYWORDS

• Surgical site infection • Prophylactic antibiotics • Perioperative infection control

KEY POINTS

- Surgical site infections (SSIs) are the most common type of healthcare-associated infection in the United States, affecting more than 500,000 patients annually. Studies suggest that 40% to 60% of these infections may be preventable.
- Patients diagnosed with SSI face a 2 to 11 times increase in mortality along with prolonged hospital stays, treatment-associated risks, and potential long-term sequelae.
- Nationwide efforts to improve SSI rates include monitoring compliance with preventive guidelines via the Surgical Care Improvement Program (SCIP) along with reporting of risk-adjusted infection rates via the National Healthcare Safety Network (NHSN) and the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP).
- Preoperative prophylaxis with appropriately selected procedure-specific antibiotics administered 1 hour before skin incision is a mainstay of SSI prevention; excess prophylactic antibiotic use either through poor selection or continuation postoperatively is a major driver of increased multidrug-resistant organism isolates.
- Adjunctive measures, such as surgical safety checklists, minimally invasive surgical techniques, and maintenance of perioperative homeostasis, can help further reduce the burden of SSI.

INTRODUCTION

Healthcare-associated infections (HAIs) present a significant source of preventable morbidity and mortality. More than 30% of all HAIs are represented by surgical site infections (SSIs), making them the most common subtype.[1,2] Between 1.9% and

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2.7% of all surgical patients, more than 500,000 per year, are diagnosed with an SSI leading to an estimated 8000 annual deaths.[3–6]

Studies suggest that 40% to 60% of these infections are preventable.[7] Despite this, many hospitals have yet to implement evidence-based best practices.[3,8] This article reviews the impact of SSIs, describes their measurement and reporting, and most importantly provides perioperative strategies for their prevention with a focus on the appropriate use of prophylactic antibiotics.

SURGICAL SITE INFECTION METRICS

Clinical and Social Costs

SSIs represent a significant clinical and financial burden. Those diagnosed with an SSI face a 2 to 11 times increase in mortality.[9,10] Although most survive their infection, prolonged hospital stays and secondary risks associated with treatment are common.[11] Even when patients recover, many find their overall quality of life is significantly impacted over the long term.[12] In addition to these clinical concerns, associated costs can range from $400 for superficial SSI to upward of $30,000 for organ/space SSIs leading to system-wide excess costs of more than $7 billion per year.[13,14]

Scope of the Problem

- 500,000 SSIs per year
- 8000 annual deaths
- 40%–60% preventable
- $7 billion in excess cost

Tracking Surgical Site Infections: Outcomes

The impact of SSIs and their preventability have spurred national efforts to measure and reduce their incidence. The Centers for Disease Control and Prevention (CDC) has made hospital infections a priority, establishing the National Nosocomial Infections Surveillance system in the 1970s to monitor US acute care hospital infection rates.[15] This system, known today as the National Healthcare Safety Network (NHSN), is still the most widely used HAI tracking mechanism. More than 12,000 medical facilities including acute-care hospitals, long-term acute-care hospitals, and ambulatory surgery centers report SSIs and other HAIs to the NHSN.[16]

More recently, the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) and the Veterans Affairs Surgical Quality Improvement Program that preceded it have also made strides in SSI tracking at participating acute-care hospitals nationwide.

Tracking Surgical Site Infections: Process Measures

Initiated by the Centers for Medicare and Medicaid Services and the CDC, the Surgical Care Improvement Project (SCIP) is a multistakeholder partnership to reduce surgical complications including SSI. Since 2005, several process metrics around SSI have been developed, implemented, and revised with hospital performance being publically reported and sometimes tied to reimbursement (**Table 1**). Despite their widespread use, adherence to SCIP measures has not been convincingly linked to a reduction in SSI rates.[7]

Table 1
SCIP inpatient quality measures

ID#	Measure Name
SCIP-Inf-1	Prophylactic antibiotic received within 1 h before surgical incision
SCIP-Inf-2	Appropriate prophylactic antibiotic selection for surgical patients
SCIP-Inf-3	Prophylactic antibiotics discontinued within 24 (48 for cardiac surgery) h after surgery end time
SCIP-Inf-4	Cardiac surgery patients with controlled postoperative blood glucose
SCIP-Inf-6	Surgery patients with appropriate hair removal
SCIP-Inf-9	Urinary catheter removal on postoperative day 1 or 2
SCIP-Inf-10	Surgery patients with perioperative temperature management

Adapted from Surgical Care Improvement Project Core Measure Set Effective for Discharges January 1, 2014. Surgical Care Improvement Project. The Joint Commission. Available at: http://www.jointcommission.org/assets/1/6/SCIP-Measures-012014.pdf. Accessed June 1, 2014.

Classifying Wounds

Critical to SSI tracking is risk adjusting for the level of wound contamination. The clean, clean-contaminated, contaminated, and dirty or infected wound classifications provided by the CDC in **Box 1** are currently in widest use.[17]

Box 1
Criteria for classifying surgical wounds

Clean

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

Operative wounds where 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

Open, fresh, accidental wounds. In addition, operations with major breaks in sterile technique (eg, open cardiac massage) or gross spillage from the gastrointestinal tract, and incisions in which acute, nonpurulent inflammation is encountered including necrotic tissue without evidence of purulent drainage (eg, dry gangrene) are included in this category.

Dirty or Infected

Includes old traumatic wounds with retained 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.

Adapted from April 2013 CDC/NHSN protocol corrections, clarification, and additions. Available at: http://www.cdc.gov/nhsn/PDFs/pscManual/9pscSSIcurrent.pdf. Accessed May 30, 2014.

Classifying Surgical Site Infections

The CDC defines an SSI as an infection related to an operative procedure that occurs within 30 or 90 days postoperatively depending on the procedure.[17] NSQIP and Veterans Affairs Surgical Quality Improvement Program definitions are largely based on the CDC model.[18] SSIs are further classified by the CDC based on their anatomic involvement relative to the surgical wound as in **Fig. 1** and **Box 2**.[19]

SURGICAL SITE INFECTION PREVENTION STRATEGIES: PREOPERATIVE

Antibiotic Prophylaxis

Appropriately selected antibiotic prophylaxis can protect patients from postoperative infection by reducing the bacterial load present within the surgical site at the time of operation.[20] In addition to specific risks to patients, however, the increasing burden of fungal and antibiotic-resistant organisms highlights the importance of evidence-based practice and antibiotic stewardship.[21,22]

Antibiotic Selection

Evidence-based guidelines should direct antibiotic selection guided by the organisms most commonly linked to SSI following the operative procedure. Selection based on local antibiograms may supersede the national recommendations listed (**Table 2**).

Timing

In addition to appropriate selection, timing of antibiotic administration and redosing play important roles (**Table 3**). Preoperative dosing within 1 hour or less of incision is an important factor in prophylactic efficacy in addition to appropriate antibiotic

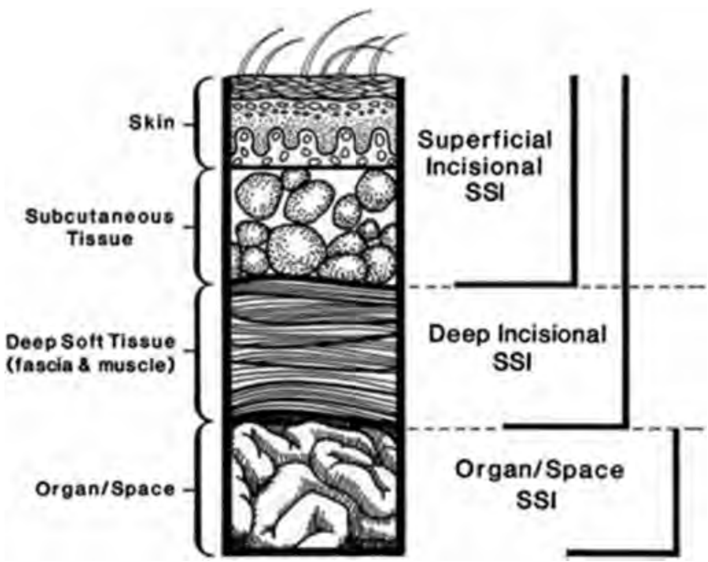

Fig. 1. Anatomic SSI classifications. (*From* Horan TC, Gaynes RP, Martone WJ, et al. CDC definitions of nosocomial surgical site infections, 1992: a modification of CDC definitions of surgical wound infections. Infect Control Hosp Epidemiol 1992;13(10):607.)

Box 2
Criteria for defining a SSI

Superficial incisional SSI

Infection occurs within 30 days after the operation and infection involves only skin or subcutaneous tissue of the incision and at least one of the following:

- Purulent drainage, with or without laboratory confirmation, from the superficial incision.
- Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision.
- At least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness, or heat and superficial incision is deliberately opened by surgeon, unless incision is culture-negative.
- Diagnosis of superficial incisional SSI by the surgeon or attending physician.

Deep incisional SSI

Infection occurs within 30 days after the operation if no implant is left in place or within 1 year if implant is in place and the infection seems to be related to the operation and infection involves deep soft tissues (eg, fascial and muscle layers) of the incision and at least one of the following:

- Purulent drainage from the deep incision but not from the organ/space component of the surgical site.
- A deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms: fever (>38°C), localized pain, or tenderness, unless site is culture-negative.
- An abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination.
- Diagnosis of a deep incisional SSI by a surgeon or attending physician.

Organ/space SSI

Infection occurs within 30 days after the operation if no implant is left in place or within 1 year if implant is in place and the infection seems to be related to the operation and infection involves any part of the anatomy (eg, organs or spaces), other than the incision, which was opened or manipulated during an operation and at least one of the following:

- Purulent drainage from a drain that is placed through a stab wound into the organ/space.
- Organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space.
- An abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation, or by histopathologic or radiologic examination.
- Diagnosis of an organ/space SSI by a surgeon or attending physician.

From Horan TC, Gaynes RP, Martone WJ, et al. CDC definitions of nosocomial surgical site infections, 1992: a modification of CDC definitions of surgical wound infections. Infect Control Hosp Epidemiol 1992;13(10):607.

selection.[23,24] Administration within 120 minutes of incision is acceptable for vancomycin and fluoroquinolones requiring prolonged infusion times. Redosing should be based on antibiotic half-life or extensive blood loss.[23,25] Redose for blood loss greater than 1500 mL or procedures greater than two half-lives long.

Table 2
Antibiotic prophylaxis recommendations

Type of Procedure	Recommended Agents	Alternatives for β-Lactam Allergy
Cardiac/coronary artery bypass	Cefazolin, cefuroxime	Clindamycin, vancomycin
Cardiac device insertion procedures (eg, pacemaker implantation)	Cefazolin, cefuroxime	Clindamycin, vancomycin
Ventricular-assist devices	Cefazolin, cefuroxime	Clindamycin, vancomycin
Thoracic procedures including lobectomy, pneumonectomy, lung resection, and thoracotomy	Cefazolin, ampicillin-sulbactam	Clindamycin, vancomycin
Gastroduodenal procedures involving entry into lumen of gastrointestinal tract (bariatric, pancreaticoduodenectomy)	Cefazolin	Clindamycin or vancomycin + aminoglycoside or aztreonam or fluoroquinolone
Procedures without entry into gastrointestinal tract (antireflux, highly selective vagotomy) for high-risk patients	Cefazolin	Clindamycin or vancomycin + aminoglycoside or aztreonam or fluoroquinolone
Biliary tract, open procedure	Cefazolin, cefoxitin, cefotetan, ceftriaxone, ampicillin-sulbactam	Clindamycin or vancomycin + aminoglycoside or aztreonam or fluoroquinolone Metronidazole + aminoglycoside or fluoroquinolone
Elective laparoscopic procedure in low-risk patients	None	None
Elective laparoscopic procedure in high-risk patients	Cefazolin, cefoxitin, cefotetan, ceftriaxone, ampicillin-sulbactam	Clindamycin or vancomycin + aminoglycoside or aztreonam or fluoroquinolone Metronidazole + aminoglycoside or fluoroquinolone

Appendectomy for uncomplicated appendicitis	Cefoxitin, cefotetan, cefazolin + metronidazole	Clindamycin + aminoglycoside or aztreonam or fluoroquinolone Metronidazole + aminoglycoside or fluoroquinolone
Small bowel surgery in nonobstructed patients	Cefazolin	Clindamycin + aminoglycoside or aztreonam or fluoroquinolone
Small bowel surgery in obstructed patients	Cefazolin + metronidazole, cefoxitin, cefotetan	Metronidazole + aminoglycoside or fluoroquinolone
Hernia repair (hernioplasty and herniorrhaphy)	Cefazolin	Clindamycin, vancomycin
Colorectal surgery	Cefazolin + metronidazole, cefoxitin, cefotetan, ampicillin-sulbactam Ceftriaxone + metronidazole Ertapenem	Clindamycin + aminoglycoside or aztreonam or fluoroquinolone Metronidazole + aminoglycoside or fluoroquinolone
Clean-contaminated cancer surgery	Cefazolin + metronidazole, cefuroxime + metronidazole, ampicillin-sulbactam	Clindamycin
Vascular surgery	Cefazolin	Clindamycin, vancomycin
Heart, lung, or heart-lung transplantation	Cefazolin	Clindamycin, vancomycin
Liver transplantation	Piperacillin-tazobactam, cefotaxime + ampicillin	Clindamycin or vancomycin + aminoglycoside or aztreonam or fluoroquinolone
Pancreas and pancreas-kidney transplantation	Cefazolin, fluconazole (for patients at high risk of fungal infection, such as those with enteric drainage of the pancreas)	Clindamycin or vancomycin + aminoglycoside or aztreonam or fluoroquinolone
Plastic surgery: clean with risk factors or clean-contaminated	Cefazolin, ampicillin-sulbactam	Clindamycin, vancomycin

Adapted from Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis insurgery. Am J Health Syst Pharm 2013;70:195–283.

Table 3
Antibiotic dosing guidelines

Antimicrobial	Recommended Adult Dose	Half-Life (h) in Adults with Normal Renal Function	Recommended Redosing Interval
Ampicillin-sulbactam	3 g (ampicillin 2 g/ sulbactam 1 g)	0.8–1.3	2
Ampicillin	2 g	1–1.9	2
Aztreonam	2 g	1.3–2.4	4
Cefazolin	2 g, 3 g for pts weighing ≥120 kg	1.2–2.2	4
Cefuroxime	1.5 g	1–2	4
Cefotaxime	1 g	0.9–1.7	3
Cefoxitin	2 g	0.7–1.1	2
Cefotetan	2 g	2.8–4.6	6
Ceftriaxone	2 g	5.4–10.9	NA
Ciprofloxacin	400 mg	3–7	NA
Clindamycin	900 mg	2–4	6
Ertapenem	1 g	3–5	NA
Fluconazole	400 mg	30	NA
Gentamicin	5 mg/kg based on dosing weight (single dose)	2–3	NA
Levofloxacin	500 mg	6–8	NA
Metronidazole	500 mg	6–8	NA
Moxifloxacin	400 mg	8–15	NA
Piperacillin-tazobactam	3.375 g	0.7–1.2	2
Vancomycin	15 mg/kg	4–8	NA
Erythromycin base	1 g	0.8–3	NA
Metronidazole	1 g	6–10	NA
Neomycin	1 g	2–3 (3% absorbed under normal gastrointestinal conditions)	NA

Redosing in the operating room is recommended at an interval of approximately two times the half-life of the agent in patients with normal renal function. Recommended redosing intervals marked as "not applicable" (NA) are based on typical case length; for unusually long procedures, redosing may be needed.

Adapted from Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis insurgery. Am J Health Syst Pharm 2013;70:195–283.

Mechanical Bowel Preparation

Preventing SSI after colorectal surgery is especially challenging given the significant bacterial colonization of the large intestine. Reducing this burden using oral antibiotics and bowel preparations designed to evacuate the large bowel has been the subject of controversy. A recent Cochrane review along with a propensity-matched cohort of 2000 patients did show improvement in SSI rates in patients receiving intravenous (IV) and oral antibiotics along with a mechanical bowel preparation over patients receiving IV antibiotics alone; effect size, however, was small and studies evaluating specific regimens with respect to one another are challenged by heterogeneity and sample size concerns.[26,27] Both Cochrane and Agency for Healthcare Research and Quality reviews of oral mechanical bowel preparation versus enema or no preparation including more than 5000 patients showed no significant outcome differences.[28,29]

ADDITIONAL PREOPERATIVE SURGICAL SITE INFECTION PREVENTION STRATEGIES

Surgical Safety Checklists

Checklist use has been associated with improved compliance with antibiotic administration guidelines and significantly lower SSI rates in several global trials.[30,31] However, implementation factors loom large. Buy-in from front-line providers is critical, because large-scale mandatory implementation without extensive training likely mitigates impact.[32]

Skin Decontamination

Preoperative patient-applied chlorhexidine scrubs may decrease SSI rates as compared with no bathing; however, a significant benefit over bathing with regular soap has not been demonstrated.[33] The costs associated with specialized scrubs make it wise to limit their use to procedures associated with the highest risks associated with SSI, such as colorectal surgery, cardiac surgery, or orthopedic surgery for prostheses.[34,35]

Preoperative skin preparation with chlorhexidine-alcohol has shown benefit over povidine-iodine solutions. A prospective, randomized trial including 849 patients with clean-contaminated wounds showed significant decreases in superficial (4.2% vs 8.6%) and deep SSIs (1% vs 3%) with preoperative cleansing using chlorhexidine-alcohol versus povidone-iodine.[36]

Nasal decontamination with mupirocin has been shown to decrease SSI rates in several randomized controlled trials for colonized cardiac surgery patients. Routine decontamination of all patients has not been conclusively shown to be effective and should not be used because of concerns around promoting resistance.[37]

Hair Removal

Hair removal is a common preoperative practice; however, a meta-analysis of 11 randomized controlled trials reveals little evidence to support hair removal as strategy for SSI prophylaxis. If hair is removed, however, electric clippers should be used; razors have been linked to increased SSI rates.[38]

Surgical Scrubs

Modern “dry scrub” alcohol rubs are equivalent to traditional aqueous surgical scrubs when used as directed. Chlorhexidine scrubs are more effective and long-lasting than iodine in decreasing bacterial counts; however, it is unclear if this impacts SSI rates.[39]

INTRAOPERATIVE CONSIDERATIONS

Irrigation

Several studies over the past three decades have evaluated wound and intracavity irrigation with regard to SSI rates. The secular effects of increased evidence-based antibiotic prophylaxis make studies difficult to interpret; however, there seems to be little evidence in support of irrigation to prevent SSI in current practice.[40]

Laparoscopy

Laparoscopy is generally associated with decreased SSI rates in virtually all procedures in which it is a viable technique.[41–44] In light of this, some authors have suggested that minimally invasive surgery should be viewed as an important component in the SSI reduction toolbox.[45,46]

Incision and Closure

The use of electrocautery has no discernable impact on SSI rates relative to traditional scalpels for skin incision.[47] In two recent meta-analyses, however, triclosan-coated sutures significantly decreased SSI in abdominal surgery, but not breast or cardiac surgery.[48,49] As with other high-cost prevention strategies with marginal benefit, it is important to limit use to the highest-risk procedures if at all.

Maintenance of Homeostasis

In addition to the obvious importance of maintaining stable hemodynamics throughout the perioperative period, goal-directed intraoperative hemodynamic control significantly decreases SSI rates.[50]

Maintenance of normothermia is also critical. Even mild intraoperative hypothermia is associated with more than two times the risk of SSI in two randomized studies.[51,52]

Adequate oxygenation is a basic tenet of perioperative management; supraphysiologic oxygenation, however, may have a role to play in certain procedures. High fraction of inspired oxygen may be beneficial in high-SSI-risk procedures, such as colorectal surgery; it is unclear how to balance this against concerns over the potential toxicity associated with prolonged hyperoxygenation.[53,54] Accordingly, CDC recommends maintaining a fraction of inspired oxygen of 50% intraoperatively and in the immediate postoperative period for selected procedures.

Local Antibiotics

Some studies have shown a benefit to the local application of antibiotics in selected procedures, such as impregnated cement in orthopedic surgery and antibiotic irrigation in breast augmentation.[55] Recent in vitro data suggest that soaking synthetic mesh in an antibiotic solution increases bacterial clearance after contamination.[56] There is not yet convincing clinical evidence to support local or topical antibiotic use in general, however, and certainly not in lieu of IV antibiotics when indicated.

POSTOPERATIVE CONSIDERATIONS

Antibiotic Prophylaxis

The routine use of postoperative antibiotics for infection prophylaxis beyond 24 hours has not been shown to decrease SSI rates in general surgery.[57] In light of adverse effects including antibiotic-associated diarrhea and the development of multidrug-resistant organisms, postoperative antibiotic prophylaxis should not be used in patients without evidence of infection or significant contamination intraoperatively.[25] A growing awareness of antibiotic overuse has led to the development of SCIP measures, listed in **Table 1**, to combat the practice.

Blood Transfusion

The relationship between blood transfusion and SSI is complicated. Although several studies show a strong positive correlation, it is unclear whether allogeneic blood is causative or merely indicates increased infection risk. Nevertheless, there is currently no evidence to support withholding blood products as a strategy to reduce SSI.[58–60]

Glucose Control

Poorly controlled diabetes and stress-induced hyperglycemia (>200 mg/dL) are recognized risk factors for SSI. Careful management of perioperative blood sugar, especially in patients with diabetes, can reduce postoperative infections. There is no convincing evidence, however, that strict glycemic control beyond usual care (<200 mg/dL) is protective against SSI.[61]

Wound Management

For clean wounds, although silver-impregnated dressings may provide some benefit in high-risk cases, postoperative dressings likely have little role to play in SSI prevention.[62] A recent Cochrane review showed no appreciable difference between various wound dressings and wounds open to air, although interpretation of these results was limited by small studies and heterogeneity.[63]

A randomized controlled clinical trial has shown a benefit to daily probing of contaminated wounds, however, with reductions in SSI rates, pain, and length of stay in the intervention group.[64]

SUMMARY

SSIs are the most common type of HAI in the United States, affecting more than 500,000 patients annually.[4] Patients diagnosed with SSI, some 40% to 60% of which may be preventable, face a 2 to 11 times increase in mortality along with prolonged hospital stays, treatment-associated risks, and potential long-term sequelae.[7,9,10,12]

The widespread impact of SSI has led to nationwide efforts to improve infection rates by monitoring compliance with preventive guidelines via the SCIP along with reporting of risk-adjusted infection rates via the NHSN and the ACS-NSQIP.

Preoperative prophylaxis with appropriately selected procedure-specific antibiotics administered 1 hour before skin incision is a mainstay of SSI prevention.[23] Excess prophylactic antibiotic use either through poor selection or continuation postoperatively is a major driver of increased multidrug-resistant organism isolates.[21,22]

Adjunctive measures, such as surgical safety checklists, minimally invasive surgical techniques, and maintenance of perioperative homeostasis, can help further reduce the burden of SSI.[30,31,42,44,48]

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