Quality Standard for Antimicrobial Prophylaxis in Surgical Procedures


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Objective. The objectives of this quality standard are (1) to provide an implementation mechanism that will facilitate the reliable administration of prophylactic antimicrobial agents to patients undergoing operative procedures in which such a practice is judged to be beneficial and (2) to provide a guideline that will help local hospital committees formulate policies and set up mechanisms for their implementation. Although standards in the medical literature spell out recommendations for specific procedures, agents, schedules, and doses, other reports document that these standards frequently are not followed in practice.

Options. We have specified the procedures in which the administration of prophylactic antimicrobial agents has been shown to be beneficial, those in which this practice is widely thought to be beneficial but in which compelling evidence is lacking, and those in which this practice is controversial. We have examined the evidence regarding the optimal timing of drug administration, the optimal dose, and the optimal duration of prophylaxis.

Outcomes. The intended outcome is more uniform and reliable administration of prophylactic antibiotics in those circumstances where their value has been demonstrated or their use has been judged by the local practicing medical community to be desirable. The result should be a reduction in rates of postoperative wound infection in conjunction with a limitation on the quantities of antimicrobial agents used in circumstances where they are not likely to help.

Evidence. Many prospective, randomized, controlled trials comparing placebo with antibiotic and comparing one antibiotic with another have been conducted. In addition, some trials have compared the efficacy of different doses or methods of administration. Other papers have reported on the apparent efficacy of administration at different times and on actual practice in specific communities. Only a small group of relevant articles found through 1993 are cited herein. When authoritative reviews are available, these—rather than an exhaustive list of original references—are cited.

Values. We assumed that reducing rates of postoperative infection was valuable but that reducing the total amount of antimicrobial agents employed was also worthwhile. The cost of and morbidity attributable to postoperative wound infections should be weighed against the cost and potential morbidity associated with excessive use of antimicrobial agents.

Benefits, harms, and costs. More reliable administration of antimicrobial agents according to recognized guidelines should prevent some postoperative wound infections while lowering the total quantity of these drugs used. No harms are anticipated. The costs involved are those of the efforts needed on a local basis to design and implement the mechanism that supports uniform and reliable administration of prophylactic antibiotics.

Recommendations. All patients for whom prophylactic antimicrobial agents are recommended should receive them. The agents given should be appropriate in light of published guidelines. A short duration of prophylaxis (usually <24 hours) is recommended.

Validation. More than 50 experts in infectious diseases and 10 experts in surgical infectious diseases and surgical subspecialties reviewed the standard. In addition, the methods for its implementation were reviewed by the American Society of Hospital Pharmacists.

Sponsors. The Quality Standards Subcommittee of the Clinical Affairs Committee of the Infectious Diseases Society of America (IDSA) developed the standard. The subcommittee was composed of representatives of the IDSA (P.A.G. and J.E.M.), the Society for Hospital Epidemiology of America (R.P.W.), the Surgical Infection Society (E.P.D.), the Pediatric Infectious Diseases Society (P.J.K.), the Centers for Disease Control and Prevention (W.J.M.), the Obstetrics and Gynecology Infectious Diseases Society (R.L.S.), and the Association of Practitioners of Infection Control (T.L.B.). Funding was provided by the IDSA and the other cooperating organizations. The standard is endorsed by the IDSA.

Statement of Purpose

Our purpose is to standardize the use of prophylactic antimicrobial agents in association with surgical procedures and thus to reduce the incidence of wound infections and minimize the expenses and adverse reactions attributable to overuse of antibiotics.
Background Information

Wound infections are among the most common nosocomial infections among hospitalized surgical patients and are the second or third most common nosocomial infections among all hospitalized patients [1-3]. Surgical wound infections result in the administration of more antibiotics, an increase in the cost of care, and a prolongation of hospital stay [4]. Additional antibiotic use increases environmental pressure favoring the emergence of antimicrobial resistance. Extensive medical literature documents that the appropriate perioperative prophylactic use of antimicrobial agents can reduce the incidence of postoperative wound infections [5-11].

Since early reports of this effect, research has focused on the delineation of the specific surgical procedures in which antimicrobial prophylaxis is beneficial, the optimal agents, and the optimal timing and duration of administration of those agents. It is widely agreed that antimicrobial prophylaxis is beneficial in operations entailing entry of the gastrointestinal tract, with the consequent exposure of the surgical wound to endogenous intestinal bacteria. A single exception is elective surgery on the stomach for duodenal ulcer disease; in this situation the highly acidic environment results in a very low endogenous bacterial density, and thus rates of postoperative infection are low. Antimicrobial prophylaxis is recommended for high-risk gastroduodenal surgical procedures. These high-risk procedures include operations for cancer, gastric ulcer, bleeding, obstruction (including pyloric stenosis), and perforation as well as surgery involving patients who have received effective acid-reducing therapy, whether medical (H2 blockers, proton pump inhibitors) or surgical [5-11]. Prophylaxis is also recommended for gastric operations when the patient is morbidly obese [5-11]. The biliary tract is normally sterile, with only a low rate of colonization when elective operations for stone-related disease are undertaken in young patients; accordingly, antimicrobial prophylaxis in biliary surgery has been recommended only for high-risk patients-defined as those who are >60 years old or who have had common duct stones, bile duct obstruction, recent acute cholecystitis, or prior operations on the biliary tract [5-11].

For elective surgical procedures on the colon, rates of infection are high when antimicrobial prophylaxis is not used [11-13], and such prophylaxis is not controversial. For most other types of surgical procedures, parenteral administration is standard when prophylaxis is opted for. However, for colon procedures, oral (luminal) and/or parenteral administration may be used. Studies have demonstrated the efficacy of either route, but the benefit of the two combined has not been firmly established [13]. The most common practice in the United States is oral antibiotic administration along with mechanical bowel cleansing the evening before the operation and parenteral antibiotic administration in the operating room just before incision [13, 14].

Other procedures that do not require entry into the gastrointestinal tract but that are associated with a high rate of infection (e.g., lower-extremity vascular procedures, hysterectomy, and primary cesarean section), with devastating consequences of infection (e.g., joint replacement or other prosthetic hardware placement, cardiac procedures, and aortic vascular grafting), or with both (craniotomy) have been widely accepted as indications for antimicrobial prophylaxis [5-11]. Whether the benefits outweigh the risks has been questioned for “clean,” low-risk procedures such as hernia repair, breast operations, and skin surgery [15-24]. It may be that the benefits exceed the risks in these procedures when a risk index or some other information indicates an increased probability of postoperative wound infection [10, 25, 26]. The advantages of prophylaxis are especially evident when the risk of infection is high.

Urologic and gynecologic procedures that involve the intestinal tract are covered by the guidelines listed above for general surgical procedures. Like hysterectomies, gynecologic procedures entailing entry of the vagina probably all merit prophylaxis. Urologic procedures that do not involve entry into the intestine and that do involve patients with sterile urine are clean operations. If the urine is infected, it is preferable to sterilize it before beginning an elective procedure on the genitourinary tract [11]. If that is not possible, then antimicrobial therapy targeting the responsible pathogens should be initiated before the procedure and continued until the urinary tract infection has resolved.

The selection of an antimicrobial agent can be confusing. Literally dozens of agents have been reported to be effective in reducing rates of wound infection following most procedures. Hundreds of articles on trials of antimicrobial prophylaxis in surgical procedures have been published in the past decade. In general terms, the agent chosen should be effective against the pathogens most often recovered from infections occurring after that specific procedure and against the endogenous flora of the region of the body being operated upon. In practical terms, the most common recommendation is the use of cefazolin for operations that do not involve the distal ileum, appendix, or colon [5-11]. Operations on the latter sites require the use of an agent-or combination of agents-with activity against both aerobic and facultative enteric bacteria and against the obligate anaerobes of the colon, including Bacteroides fragilis [13]. Cefotetan or cefoxitin is recommended. Newer, “advanced-generation” agents have not been proved to be more effective than cefazolin, cefoxitin, or cefotetan for prophylactic purposes [11]. While Enterococcus species are frequently present in the endogenous bowel flora, no reports have described a greater reduction in surgical-site infections for antimicrobial regimens with specific activity against the enterococci than for regimens lacking such activity. Regimens active against enterococci (ampicillin, amoxicillin, or vancomycin combined with gentamicin) are, however, recommended for prophy-
laxis of endocarditis when a patient with certain cardiac lesions undergoes genitourinary or gastrointestinal tract procedures [27].

Studies of animals have demonstrated that antimicrobial drugs are most effective for preventing postoperative infection when they are administered before the operation begins. In nearly all recent clinical trials, the administration of prophylactic agents has been initiated within 120 minutes before incision. Recent reports have confirmed the importance of this timing [20, 21, 28]. Indeed, pharmacokinetic data indicate the desirability of administration as close to the time of incision as is practical e.g., at anesthesia induction [29, 30]. If a drug with a short half-life is given 120 minutes before incision, its levels may be very low during most of the procedure. Postoperative initiation of antimicrobial “prophylaxis” is still relatively common in practice [28, 31-33] but is not recommended, nor is the administration of the first dose after incision desirable. (Cesarean section is a specific exception, as discussed below.)

The necessary duration of antimicrobial prophylaxis is not clear. In the earliest clinical trials, the duration was 12 hours. Reports of trials employing longer durations have continued to appear periodically, and considerably longer durations are common in clinical practice [28, 31-33], although their benefit has not been proved. While a single report suggests greater efficacy of a longer course of prophylaxis in certain high-risk patients undergoing peripheral vascular procedures [34], most of the published data support a short duration [11, 21, 35].

The Standard

Throughout this standard, the strength of each recommendation and the quality of the evidence supporting it are given in bold type; these ratings are defined in tables 1 and 2, respectively, of “Purpose of Quality Standards for Infectious Diseases” on page 421 of this issue [36] and are adapted from McGowan et al. [37].

Procedures

Parenteral antimicrobial prophylaxis should be administered for the following surgical procedures: procedures that entail entry into the oropharynx (A, I); abdominal and lower-extremity vascular procedures (A, I); craniotomy (A, I); orthopedic procedures with hardware insertion (A, I); cardiac procedures with median sternotomy (A, I); hysterectomy (A, I); primary cesarean section or other cesarean sections involving prolonged rupture of membranes (A, I); and procedures that include the implantation of permanent prosthetic materials” (B, III).

Parenteral antimicrobial prophylaxis is optional for the following procedures: breast and hernia procedures* (B, I); other “clean” procedures in which the clinical setting indicates an increased risk of infection (B, III); ordinarily clean procedures in which contamination takes place” (C, III); and low-risk gastric and biliary procedures** (B, III).

“Minimally invasive” procedures (C, III). No available data indicate how these recommendations should be applied to so-called minimally invasive procedures, such as laparoscopic cholecystectomy and laparoscopically assisted bowel resection. Pending further data, it seems safest to apply the standards that would be used for the same procedure done through a traditional incision.

Open urologic procedures (B, III). Open urologic procedures that involve the bowel are covered by the guidelines that have been developed largely for general surgical procedures. The literature for transurethral procedures is large and controversial. It seems prudent to eradicate bacteriuria before undertaking any urinary-tract procedure when clinical circumstances permit. Beyond that, local guidelines for implementation of the standard should reflect local practice.

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* "High-risk" patients, defined as patients undergoing gastric procedures for cancer; gastric ulcer; bleeding or obstruction; morbidly obese patients; or patients with iatrogenic or natural suppression of gastric acid secretion.

† “High-risk” patients, defined as those >60 years old; those with recent symptoms of acute inflammation; common duct stones, or jaundice; or those who have previously undergone biliary surgery.

‡ Oral prophylaxis with neomycin plus erythromycin or another proven regimen, administered for 18 hours preoperatively, is sufficient for scheduled colon operations in which the bowel can be effectively cleansed. When cleansing is impossible because of obstruction or another emergency condition or when the surgeon wants to provide extra prophylactic protection to a high-risk patient, parenteral antimicrobial agents may also be administered. An agent effective against Entrobacteriaceae and organisms of the B. fragi-

lis group should be used.

** Many authorities believe that these procedures do not require antimicrobial prophylaxis. Certain clinical factors increase the risk of postoperative infection and may increase the motivation to administer prophylactic agents [12]. These factors include an American Society of Anesthesiologists preoperative assessment of 3, 4, or 5 (28); the diagnosis of three or more major preoperative conditions [27]; and the expectation that an operation will last longer than 2 hours [27] or longer than the 75th percentile for that procedure [28]. (See specific references for details.) An undesirable local rate of wound infection may also increase the benefits conferred by antimicrobial prophylaxis.
Procedures involving newborns (C, III). It is common practice among pediatric surgeons to administer broad-spectrum antimicrobial prophylaxis for most operative procedures involving infants <30 days old. No specific data address the necessity for or effectiveness of this practice.

Choice of Antimicrobial Agents

Many antimicrobial agents have been demonstrated to be effective for perioperative prophylaxis. The drug chosen should be active against the pathogens most commonly associated with wound infections following the specific procedure and against the pathogens endogenous to the region of the body being operated upon. For procedures involving the distal ileum, colon, or appendix, the drugs used should always be active against both the Enterobacteriaceae and the common enteric anaerobic species, especially the B. fragilis group [5-11, 31]. Although infections following gynecologic operations (especially hysterectomy) often involve anaerobic bacteria, combinations including drugs specific for anaerobes have not been shown to be superior to cefazolin alone [5, 11, 38-41]. An acceptable option is to use cefotetan or cefoxitin for operations involving the distal ileum, appendix, or colon and to use cefazolin for all other procedures (A, I).

Vancomycin can be given instead of cefazolin to patients who are allergic to cephalosporins or in settings where infections with methicillin-resistant Staphylococcus aureus (MRSA) are prevalent. Since vancomycin provides no activity against facultative gram-negative bacilli, which may be involved in settings such as upper gastrointestinal surgery, lower-extremity vascular surgery, or hysterectomy, another agent with gram-negative activity should be added to the regimen under these circumstances. If vancomycin is being given because of concern over MRSA, cefazolin can be administered in addition. If allergy to cephalosporins is the concern, aztreonam or an aminoglycoside can be administered with vancomycin. An aminoglycoside can be combined with either clindamycin or metronidazole, or aztreonam can be combined with clindamycin to substitute for cefoxitin or cefotetan for the treatment of allergic patients undergoing a colonic procedure. Aztreonam should not be used in a two-drug combination with metronidazole because this combination lacks activity against gram-positive cocci and may permit a higher rate of infection caused by S. aureus [42]. If this combination is used, an agent with activity against gram-positive cocci must also be included. Unfortunately, data on the efficacy of these alternative regimens are not available (C, III).

Dose

Few reports have focused on the appropriate dose for antimicrobial prophylaxis [43]. The prophylactic dose should never be smaller than the standard therapeutic dose of a drug. In light of the short duration of administration recommended for prophylaxis and the safety profile of most prophylactic antimicrobial agents, it is reasonable to use a dose on the high side of the usual therapeutic range (e.g., 1-2 g of cefazolin, cefotaxin, or cefotetan for adults and 30-40 mg/kg for children) (C, III).

Timing

The goals in prophylaxis are to achieve inhibitory antimicrobial levels at incision and to maintain adequate levels for the duration of the procedure. Agents used for parenteral perioperative prophylaxis should be administered intravenously during the interval beginning 60 minutes before incision [30]. Administration up to the time of incision—or as close as possible to that time—is preferred (A, I) [29].

For cesarean section, antimicrobial prophylaxis should be delayed until the umbilical cord is clamped and then should be initiated immediately (A, I) [5, 9, 38].

Duration

The optimal duration of perioperative antimicrobial prophylaxis is not known. Many reports document effective prophylaxis with a single dose of drug (B, II). It is likely that no further benefit is conferred by the administration of additional doses after the patient has left the operating room. Thus, pending further data, postoperative administration is not recommended (C, III). Antimicrobial prophylaxis should certainly be discontinued within 24 hours of the operative procedure (B, III). The optimal duration of prophylaxis for cardiac operations is still being debated, and many investigators believe that longer durations are needed (C, III) [44]. However, the continuation of prophylaxis until all catheters and drains have been removed is not appropriate.

Repeated Doses During the Surgical Procedure

The need to administer additional doses of a prophylactic antimicrobial agent during an operative procedure of long duration has not been clearly defined. A number of references, however, document a reduced rate of effectiveness of antimicrobial prophylaxis in lengthy procedures [45-47] and when levels of drug in serum or tissue are low during a procedure [48, 49]. Current information indicates that additional intraoperative doses of an antimicrobial agent should be given at intervals of one or two times the half-life of the drug\footnote{Representative half-lives (with normal renal function) of the antimicrobial agents usually recommended for prophylaxis are as follows: cefazolin, 1.8 hours; vancomycin, 3-9 hours; cefotaxin, 40-60 minutes; cefotetan, 3-4.6 hours; aztreonam, 1-6.2 hours; aminoglycosides, 2 hours; clindamycin, 2-4.3 hours; and metronidazole, 8 hours.} so that adequate levels are maintained throughout the operation (C, III).
Implementation

The standard should be implemented by incorporating the administration of perioperative prophylactic antimicrobial drugs into the routine procedures executed in the operating room by either the anesthesiologist or the circulating nurse. For example, a standard check-off box on the medical record forms could be routinely completed by either of these individuals or by the nurse in the preoperative holding area. The dose, route, and exact time of administration of a parenteral agent-or the surgeon’s specific instruction not to give such an agent-would be noted. For cases in which no parenteral antimicrobial agent was administered, the form would be checked to indicate that oral antimicrobial drugs had previously been given for a scheduled colon procedure, that the surgeon had determined that prophylaxis was not indicated, or that the patient was receiving therapeutic antibiotics at the time of the procedure.

It might be helpful to develop preprinted standing orders for antimicrobial prophylaxis from each surgical division for all operations in its specialty in which prophylaxis is deemed appropriate. The forms should be developed by a joint committee of surgeons, anesthesiologists, and nurses, with participation of the hospital’s operating room, pharmacy and therapeutics, and infection control committees, and should include recommendations about the usual drug choices (including a reminder about the need for anaerobic coverage in cases involving the colon). Provision should be made for administering antimicrobial agents other than those usually chosen, and the reason for such a choice should be delineated. Standard antimicrobial choices can be listed with their usual doses and half-lives, and the form can include the recommendation that an additional dose be administered if the duration of the operation exceeds approximately twice the half-life of the drug being used. The form should record the time of antimicrobial administration and the time of incision. The operating room should stock the usual prophylactic drugs listed on the standard form, and the standard drug in the standard dose should be provided to the anesthesiologist along with the anesthetic agents. The presence of a satellite pharmacy in the operating-room area may be helpful in this respect.

Alternative programs that accomplish the same goals may be developed and instituted on the local level. In fact, levels of compliance and implementation will probably be highest with locally developed procedures. A sample form should be developed as a model by the Quality Standards Subcommittee of the IDSA and should be modified by local institutions as needed. The quality assurance committee of the individual hospital should conduct periodic surveys to determine that initial doses are being administered before incision and that additional doses are being given during the operation if necessary.

The guidelines should encourage the administration of prophylactic antibiotics for a total of <24 hours; to this end, a standard prophylaxis order could specify automatic discontinuation of prophylaxis at the time determined by the individual hospital committee developing the local guidelines. The quality assurance committee of the hospital should be encouraged to conduct periodic surveys of the records of surgical patients to determine whether prophylaxis has indeed been discontinued within 24 hours. If the incidence of prophylactic drug administration after 24 hours is high, a program should be developed to reduce long-term antibiotic use.

Compliance with the principles of prophylactic antibiotic administration should be reviewed at least annually by the hospital’s infection control or quality assurance committee or by another designated body within the hospital. Data on prophylactic antibiotic use should be summarized by type of procedure, surgeon (coded anonymously), and service. Summary data should be reported periodically to the appropriate committees and persons, including the operating room, quality assurance, and pharmacy and therapeutics committees and the chiefs of surgical services. The surgical chiefs should have access to data regarding individual surgeons. If the results are not satisfactory, the chief should take corrective action. The implementation and continued monitoring of this standard would be an ideal quality-assurance project. If the infection control committee is monitoring postoperative wound infections, their occurrence can be studied in relation to the appropriate use of prophylactic antimicrobial agents.

References