The Society of Thoracic Surgeons Practice Guideline Series: Antibiotic Prophylaxis in Cardiac Surgery, Part I: Duration*

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I. Overview

Prophylactic intravenous antibiotics should be routinely administered to patients undergoing cardiac surgery. Although this is a well-accepted tenet of contemporary practice, the duration during which the antibiotics should be given is far from settled. As one may see from the studies discussed as follows, in the field of cardiac surgery there is wide variation in prophylactic antibiotic duration (PAD) across the United States as well as other countries.

In other surgical specialties, there seems to be little debate regarding PAD. However, in cardiac surgery there are several factors that contribute to the divergence of practice patterns: (1) The question of optimum duration has not been adequately explored with identical antibiotic regimens administered to groups differing only in the duration of prophylaxis; (2) surgical-site infections have been low during the years, implying that present practice is effective and need not be changed; and (3) there has been only a vaguely perceived downside to aggressive, prolonged prophylaxis.

However today there is mounting evidence of important disadvantages to prolonged prophylaxis. Emerging antibiotic resistance was once regarded as an ill-defined notion that received only passing notice [1, 2]. There is now considerable evidence that this problem is: (1) real, (2) clinically important, and (3) directly linked to the duration of prophylactic antibiotic administration. This fact alone is enough to prompt a reassessment of our practice, but in addition we now face the introduction of quality metrics linked to third party pay for performance initiatives [3]. In virtually all of these pay for performance programs, the duration of prophylactic antibiotics will be used as a quality metric. For example, one of the quality measures used in a demonstration project sponsored by the Center for Medicare and Medicaid Services specifies that prophylactic antibiotics in cardiac surgery should be administered for no more than 24 hours.

Organization and Scope of the Practice Guidelines

The principles of antibiotic prophylaxis are based on (1) the choice of the antimicrobial agent; (2) the timing of the first administered dose, and (3) the duration of the prophylactic regimen.

The Society of Thoracic Surgeons' guideline for antibiotic prophylaxis in cardiac surgery will consist of two parts. Because duration is the most controversial of the three principles previously listed, it will be addressed in the first guideline. Part 2 will focus on the choice of antibiotic agent and the timing of the first dose to be used in cardiac surgery.

Both guidelines will address the adult cardiac surgery population. In order to concentrate on the most appropriate and reasonably homogeneous population, the following patients are excluded from the analysis: patients with active preoperative infections, those undergoing cardiac transplantation, patients on immunosuppressive therapy, and those having aortic replacement surgery. Because of the paucity of published information regarding prophylaxis in off-pump cardiac surgery, this population will not be included.

The guidelines will cover the use of perioperative intravenous antibiotics used in prophylaxis. The use of topical agents such as nasal antimicrobial applications will not be considered. The writing committee fully recognizes the potential impact of mechanical aspects and medical management other than antibiotics, but factors such as glycemic control, use of internal mammary arteries, use of bone wax, and patient preparation techniques are beyond the scope of this guideline.

The spectrum of cardiac surgery has changed considerably in the past 2 decades. There is ample evidence that cardiac surgery patients of today are older and generally have higher risk factors with more pronounced comorbid conditions. Because of this well-recognized fact, only very few reports published more than 20 years ago will be used in the analysis.

The guidelines will consider surgical-site infections (SSI) as the primary outcome to be examined. Postoperative infectious complications not involving the surgical

*For the full text of the STS Guideline on Antibiotic Prophylaxis in Cardiac Surgery, as well as other titles in the STS Practice Guideline Series, visit http://www.sts.org/sections/aboutthesociety/practiceguidelines/ at the official STS website (www.sts.org).

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site, such as pneumonia, bacteremia, or urinary tract infection are not addressed. As seen as described as follows, many reports group both soft-tissue sternal infections and suppurative mediastinitis together as surgical-site infections. The writing committee has made a concerted effort to separate superficial soft-tissue infections from mediastinitis whenever possible.

Unique Aspects of Cardiac Surgery

There is general consensus that postoperative prophylactic antibiotics should be stopped within 24 hours of most major surgical procedures [4–9].

However, results of studies on the general surgical population do not directly apply to cardiac surgery. The most obvious reason is the fact that cardiopulmonary bypass is used in cardiac surgery. The pump itself is associated with a broad array of adverse physiologic sequelae that predispose cardiac surgery patients to infectious complications. Cardiopulmonary bypass is known to compromise humoral immunologic defenses, reduce phagocytosis, and activate white blood cells, all of which impair the ability to neutralize infectious organisms. The often-used systemic hypothermia is associated with increased SSI [7, 9, 10] and the degradation of clotting factors predisposes postoperative bleeding, which is also recognized as a risk factor for postoperative infection [11].

The length of a surgical procedure is also generally correlated with the risk of postoperative infection [7, 12]. Cardiac surgical procedures routinely require 3 to 4 hours for completion, thereby placing patients at increased infectious risk. In addition, cardiac surgery patients invariably leave the operating room with indwelling chest catheters that have the potential to serve as external routes for bacterial entry.

Probably the most compelling, unique aspect of cardiac surgery is the specter of suppurative mediastinitis. Postoperative mediastinitis carries a very high hospital mortality [13–15] and is also associated with reduced long-term survival [13]. This complication invariably involves an additional operation, a prolonged hospitalization, a significant toll in clinical resources, and dramatically increased costs. Anyone who has provided care for a patient with mediastinitis also knows well the emotional cost not only for the patient but also for the family, the nursing staff, and the surgeons. Truly one of the most devastating infections in all of surgery, this dreaded complication influences the perioperative management strategy of virtually all cardiothoracic surgeons.

The Central Issue

All surgeons, regardless of specialty, want to minimize the possibility of postoperative infection. Because of the adverse sequelae of the pump and the high cost of mediastinitis, cardiac surgeons rightly consider their patients to be at particularly high risk. It is therefore logical and appropriate to be exceptionally aggressive in minimizing this risk.

One approach has been to adopt a policy in which the duration of antibiotic prophylaxis lasts several postoperative days. A common approach involves the use of antibiotics until all chest tubes and central intravenous lines are removed [6, 16, 17].

The downside to this approach is the fact that prolonged administration of antibiotics carries the certainty of increased cost, the prospect of drug toxicity, and the distinct possibility of creating an environment favorable to the development of resistant bacterial strains. Superinfection, particularly with Clostridium difficile, is associated with prolonged cephalosporin administration [18, 19] and must also be taken into account. Of these, the issue of bacterial resistance is the most compelling consideration.

The central issue then involves the balance between the risk of SSI and the risk of developing resistant bacterial organisms. Several questions must be addressed in order to objectively analyze this central issue:

1. Does the duration of antibiotic prophylaxis influence the probability of developing antibiotic-resistant bacteria?
2. If so, at what postoperative time does this become clinically significant?
3. Does the duration of antibiotic prophylaxis influence the incidence of SSI?
4. If so, at what postoperative time does this become clinically significant?

II. Antimicrobial Resistance

In the context of cardiac surgery, antimicrobial resistance essentially refers to the development of cephalosporin-resistant enterobacteriaceae and vancomycin-resistant enterococci [16, 20]. The threat of resistant staphylococci is related to vancomycin-resistant enterococci and may be associated with significant infectious complications [20].

In the last 2 decades, the incidence of antimicrobial-resistant organisms has increased considerably [20, 21]. The Centers for Disease Control and Prevention reports that intensive care unit vancomycin-resistant enterococci has increased in the United States from 0.3% in 1989 to greater than 25% in 1999 [2, 22]. Although several factors, including patient age [20], may play a role in the development of antimicrobial resistance, there is universal agreement that excessive antibiotic usage is one of the most important causes [8, 16, 20, 21, 23–26].

The clinical sequelae of resistant organisms are quite serious. Patients infected with antibiotic-resistant bacteria experience higher mortality, prolonged hospitalization, and increased health care costs compared with those infected with nonresistant organisms [21, 27]. In spite of the documented increase in antibiotic resistance and the recognition of clinical consequences, there is a distinct tendency to consider the problem to be only a minor inconvenience [1, 2]. Further evidence for this lies in the fact that a literature search of the two major United States cardiothoracic surgery journals failed to find any articles addressing antibiotic resistance in the last 2 decades.

It is clear that antibiotic resistance is a progressive problem with serious clinical implications. It is less clear that the problem is directly linked to prolonged use of prophylactic antibiotics in cardiac surgery. Harbarth and colleagues [16] specifically explored this relationship in an observational study of 2,641 patients undergoing coronary artery bypass grafting (CABG). His group found that antibiotic prophylaxis for more than 48 hours increased antimicrobial resistance. Specifically, patients receiving greater than 48 hours of antibiotics had a 1.6 times higher probability of harboring resistant organisms compared with those having a regimen of less than 48 hours. The criteria for selecting which patients to undergo culture were not mentioned. Only 41% of patients were cultured, and the site from which the culture was taken was not specified.

Several general studies have suggested some correlation between the prolonged use of postoperative antimicrobial prophylaxis and the development of resistance [24, 26, 28]. Unfortunately these reports are not controlled for specific postoperative time and there is a wide variation in the antibiotics used. Nevertheless there is universal agreement that the longer the duration of an antibiotic regimen, the greater the probability of developing resistant microorganisms [2, 9, 11, 12, 16, 20, 23–26, 28].

The implications for cardiac surgery are not straightforward. Other than the Harbarth and colleagues study [16], there is no evidence directly linking duration of prophylactic antibiotics in cardiac surgery to antibiotic resistance. There is no scientific evidence that prophylactic antibiotics used for less than 48 hours after cardiac surgery are associated with the development of antibiotic resistance. We believe that there are no studies specifically addressing the issue of resistance in the first 24 hours after cardiac surgery.

However, the fact that the issue has not been specifically studied is not a license to disregard the problem. The position of cardiac surgeons seems to be precisely stated in a well-respected surgical text endorsed by the American College of Surgeons [11]: "Complications of antibiotic prophylaxis are few. Although data linking prophylaxis to the development of resistant organisms are meager, resistant microbes have been developed in every other situation in which antibiotics are utilized, and it is reasonable to expect that prophylaxis in any ecosystem will have the same result, particularly if selection of patients is poor, if prophylaxis lasts too long, or if too many late-generation agents are used."

CONCLUSION. The duration of a prophylactic antibiotic regimen is directly related to the probability of developing resistant microorganisms.

OPTIMAL PRACTICE. The duration of a prophylactic antibiotic regimen is limited to the shortest amount of time required to effectively minimize the probability of postoperative infection (class IIa, level B).

III. Surgical Site Infection

Recent studies show that the incidence of deep sternal infections associated with cardiac surgery ranges between 0.25% and 4% [13, 17, 29–31]. The Society of Thoracic Surgeons National Cardiac Surgery Database reported an incidence of 0.4% in 2002 [31]. Superficial sternal wound infections are seen in approximately 2% to 6% of patients after cardiac surgery [30–33]. It should be emphasized that even superficial infections are associated with prolonged patient care, increased costs, and reduced patient satisfaction [30].

Table 1. Single-Dose Studies

					Single-Dose		Multiple-Dose			
Author	Country	Date	Number	RCT	Agent	Surgical Site Infections (%)[a]	Agent	Surgical Site Infections (%)[a]	Duration	Significant Difference in SSI
Bucknell and colleagues [43]	Australia	2000	353	No	Cephazolin	1.0	Cephazolin	0.7	48 Hours	No
Saginur and colleagues [38]	Canada	2000	3027	Yes	Teicoplanin	2.0	Cefazolin	1.2	48 Hours	Yes
Salminen and colleagues [37]	Finland	1999	200	No	Ceftriaxone	4	Vancomycin	5	48 Hours	No
Kriaras and colleagues [36]	Italy	1997	1009	Yes	Cefuroxime	0.6	Amoxycillin	1.0	4 Days	No
Nooyen and colleagues [42]	Netherlands	1994	844	Yes	Cefuroxime	1.9	Cefuroxime	0.9	72 Hours	No
Sisto and colleagues [39]	Finland	1994	551	Yes	Ceftriaxone	2.9	Cefuroxime	2.9	48 Hours	No
Hall and colleagues [40]	Australia	1993	1031	No	Ceftriaxone	2.7	Flucloxacillin gentamycin	1.6	48 Hours	No
Beam and colleagues [41]	United States	1984	94	Yes	Ceftriaxone	4.1	Cefazolin	2.2	48 Hours	No

[a] Surgical site infections refers to the incidence of sternal infections, including mediastinitis and superficial sternal wound infections.

The devastating sequelae of mediastinitis are well recognized by all cardiothoracic surgeons. The in-hospital mortality associated with mediastinitis ranges from 7% to 20% [5, 14, 15], and the mortality in patients with superficial sternotomy infections may be in excess of 5% [30]. In addition to the high hospital mortality from mediastinitis, there is a residual increase in long-term mortality in those having had mediastinitis [5, 32].

Overview of Studies

Most studies purport to show that the duration of antibiotic prophylaxis does not significantly influence the incidence of SSI. There is a common thread of logic among these studies that because the duration does not influence SSI, then short durations should be chosen over longer ones.

Unfortunately even the randomized studies almost invariably are poorly controlled to specifically examine the issue of duration. In those reports specifically addressing PAD, there are often confounding factors such as the use of different antibiotics in each arm of the study. These factors may obscure the results and make it difficult to draw meaningful conclusions about PAD.

Single-Dose Studies

In other surgical specialties, there is evidence that a single dose of prophylactic antibiotic is sufficient to optimally reduce SSI [4, 7–9, 34–36]. This has led to several investigations involving the use of a single prophylactic dose in cardiac surgery.

Table 1 shows the most salient features of important single-dose reports published in the last 20 years.

The studies by Salminen and colleagues [37], Saginur and colleagues [38], Sisto and colleagues [39], Hall and colleagues [40], Beam and colleagues [41] and Kriaras and colleagues [36] all involve at least one antibiotic in the multiple-dose arm that was different from the antibiotic used in the single-dose arm. This fact alone disallows a meaningful comparison based solely on PAD. With this type of study design, one simply cannot determine whether the specific antibiotic, the duration, or both account for the observed SSI incidence.

In the Netherlands prospective randomized trial by Nooyen and colleagues [42], the population was restricted to "uncomplicated" procedures. Prolonged postoperative ventilation, use of an intraaortic balloon pump, an operation of greater than 6 hours, and "severe noninfectious complications" were criteria for exclusion. As acknowledged by the authors, the analysis of SSI was underpowered. The sternal wound was examined on the postoperative day 7, but not thereafter. This is a significant design flaw, because sternal infections are well-known to become manifest after discharge [33] and more than 2 weeks postoperatively [12, 16].

It is worthwhile to consider the fact that mediastinitis occurred in 2 patients in the single-dose group and none of the patients in the multiple-dose group. In the patients with mediastinitis, there existed a 7% to 20% risk of death, the certainty of another major operation, an additional 1 to 2 weeks hospitalization, a significantly reduced long-term survival, and additional medical costs of at least $20,000. The cost of the additional 3 days of prophylaxis is less than $20, a negligible risk of drug toxicity, and a remote chance of developing resistant strains. One certainly cannot say with authority that additional prophylaxis would have prevented the cases of mediastinitis, but weighing the relative risks of each prophylactic option does illustrate the undeniable clinical nature of the problem.

In the Australian prospective nonrandomized trial by Bucknell and colleagues [43], patients considered to be "at high risk from methicillin-resistant Staphylococcus aureus" received teicoplanin and timentin prophylaxis. Twenty-six percent of the single dose group received teicoplanin and timentin compared with only 8.6% of the multiple-dose group. The study, consisting of only 353 patients, was underpowered. In addition, teicoplanin has poor sternal penetration and a relatively slow onset of action, thereby making it a suboptimal prophylactic agent.

Randomized Studies

In addition to the randomized studies dealing with single-dose prophylaxis, there are several prospective randomized studies dealing generally with other PAD intervals.

Three randomized studies from the 1980s examined PAD. In 1983, Hillis and colleagues [44] randomized 160 CABG patients to receive either a 48-hour course of kanamycin and cephalothin or the same regimen followed by 3 days of oral cephalexin. There was no difference in SSI between the groups. Geroulanos and colleagues [45] compared a 2-day course of cefuroxime against a 4-day course of cefazolin in 569 randomized patients undergoing cardiac surgery in Switzerland. There was no statistically significant difference between infectious complications in the two groups. In 1988, Jewell and colleagues [46] randomized 200 CABG patients into a group receiving 48 hours of intravenous cephalothin or a group receiving 3 days of oral cephalexin, finding no difference in infectious outcomes.

In a 1997 randomized study from Switzerland, Niederhauser and colleagues [47] examined a high-risk group of 53 cardiac surgery patients. All patients received 24 hours of cefazolin prophylaxis. The study population received an additional 2 days of ticarcillin and clavulanate and also vancomycin until removal of the intraaortic balloon pump. In this very select population there was no advantage to providing more than the 24 hours of cefazolin.

In 2002, Finkelstein and colleagues [48] reported on a group of patients undergoing cardiac surgery in an Israeli hospital with a high prevalence of methicillin-resistant staphylococcal infections. Patients were randomly assigned to receive 24 hours of vancomycin or 24 hours of cefazolin. There was no significant difference in the outcomes of the groups. This study is most notable for the 1.6% rate of major sternal complications seen in the cefazolin group, indicating that the 24-hour cefazolin regimen produced very acceptable infection rates in this high-risk population.

Once again however, it is difficult to draw conclusions regarding PAD, primarily because of the differing antibiotic regimens used in these trials.

Nonrandomized Studies

In 2000, Harbarth and colleagues [16] published an observational study of 2,641 patients undergoing CABG or valve surgery or both in Boston. Patients were divided into two groups depending on PAD. The short prophylaxis group received antibiotics for less than 48 hours, and the prolonged prophylaxis group received antibiotics for greater than 48 hours. Antibiotics consisted of "principally cefazolin 1 g; in some cases vancomycin 1 g, ceftriaxone 1 g, or a combination of these agents" [16]. Surgeons were encouraged to administer prophylactic antibiotics for no more than 48 hours, but 1,139 (43%) of the 2,641 patients received more than 48 hours of prophylactic antibiotics.

There was no statistically significant difference in SSI between the groups in both an unadjusted and a risk-adjusted anaylsis. SSI were seen in 8.7% of the short PAD group and in 8.8% of the long PAD group. The incidence of mediastinitis was not reported. There was no mention of a difference in mortality or length of stay in the two groups.

The authors conclude that the maximum clinical benefit of prophylaxis is realized by 48 hours, and the administration of antibiotics for more than 48 hours is ineffective in further reducing SSI. Their statement could be defended if the choice of antibiotics had been identical in the two groups, but the differing antibiotic regimen does not allow one to isolate duration as the only difference in the groups. Furthermore the choice of continuing antibiotics for more than 48 hours could well have been influenced by the surgeon's judgment that the patient was at high risk for SSI. If that were the case then the prolonged PAD group would be at higher infectious risk than the short PAD group. Because PAD was not controlled, it is not possible to rule out biased patient selection in the two groups.

Multicenter Reviews and Meta-Analyses

In 1991, Ariano and Zhanel [12] published an extensive review of antimicrobial prophylaxis in CABG surgery. In this review he noted many of the problems associated with published reports. Inconsistency in definitions, in-

Table 2. Guideline Recommendations for Cardiothoracic Surgery

Guideline	Recommendation	Comment
Sanford Guide [6]	Cefazolin as a single dose or for 1–2 days	Single injection just before surgery probably just as effective as multiple doses. For prosthetic heart valves, customary to stop prophylaxis either after removal of retrosternal drainage catheters or just a second dose after coming off bypass.
Surgical Infection Prevention Project [5]	Cefazolin or cefuroxime for $<$ 24 hours	The consensus of the workgroup is that administration of prophylaxis for $<$ 24 hours is acceptable and that there is no evidence that providing antimicrobials for longer periods will reduce surgical site infection rates. Pending a systematic review of the literature by its Committee on Evidence-Based Medicine, the Society of Thoracic Surgeons currently recommends that antimicrobial prophylaxis be continued for 24–48 hours.
ACC/AHA 2004 Guideline Update for Coronary Artery Bypass Surgery [56]	Cephalosporin class of antimicrobials	Data suggest that a 1-day course of intravenous antimicrobials is as efficacious as the traditional 48-hour (or longer) regimen.
American Society of Health-System Pharmacists Commission on Therapeutics [4]	Cefazolin for up to 72 hours	The duration is based on consensus of the expert panel because the data do not delineate the optimal duration of prophylaxis. Prophylaxis for 24 hours or less may be appropriate for cardiothoracic procedures.
Centers for Disease Control and Prevention [7]	No specific recommendation for cardiac surgery	
Surgical Infection Society [8]	Cefazolin for 48 hours	Although recent trends in other settings favor only intraoperative coverage, the data are not yet conclusive for patients undergoing cardiac operations.
Infectious Diseases Society of America [55]	No specific recommendation for cardiac surgery	The optimal duration of prophylaxis for cardiac operations is still being debated, and many investigators believe that longer durations are needed.

appropriate length of follow-up (both too short and too long), and the wide variation in independent variables contributed to the difficulty in evaluating the literature. After a critical analysis of major trials, the authors recommended the use of cefazolin for the first 2 postoperative days.

Kreter and Woods [49] recently reported a meta-analysis of clinical trials in cardiothoracic surgery. The article was published in 2000 and covered trials from the previous 30 years. As anticipated, the analysis demonstrated a clear benefit for the use of prophylactic antibiotics, with a five-fold reduction in SSI when prophylaxis was used. The issue of PAD was examined, but firm recommendations were not offered. The authors did conclude that there was no clinical advantage associated with administration of prophylactic antibiotics for more than 48 hours.

Kriaras and colleagues [50] sought to specifically study the optimal duration of prophylactic antibiotics in cardiovascular surgery. In this analysis the authors focused on four prospective, randomized controlled trials between 1980 and 1995. A meta-analysis of the trials included seven prophylactic regimens used in 2,970 cardiovascular surgery patients. The authors conclude that "if a cephalosporin is administered properly at the induction of anesthesia, a low infection rate occurs that cannot be lowered by longer duration of antimicrobial administration" [50]. One should note that this conclusion was drawn from four trials, three of which took place in the 1980s. The experience involved seven prophylaxis protocols, five different antibiotics, and antibiotic durations of 1, 2, and 4 days in addition to a single-dose arm. The inability to effectively control for this wide array of variables makes it difficult to accept the conclusions drawn by the authors.

Existing Guidelines

Table 2 lists some important contemporary guidelines along with recommendations and comments taken directly from the guidelines. As one can see at a glance, the guidelines have inconsistent recommendations. None of the guidelines specifically recommend single-dose prophylaxis, although the Sanford Guide [6] notes that it is "probably just as effective" as multiple doses. Several guidelines suggest the appropriateness of less than 24 hours duration, but each stops short of making a firm recommendation to that effect.

Bringing the Information Together

There are numerous reasons for the difficulty in reconciling issues associated with prophylactic antibiotic duration in cardiac surgery. There are very few randomized, controlled studies, and there are no studies which are both randomized and well-controlled for PAD. Few trials focus specifically on PAD. Of the few that do, the 24-hour to 48-hour interval is not covered. Even with the existence of ample practice guidelines, definitions are often not consistent between reports. Importantly, risk stratification techniques are seldom used. It is well-recognized that all cardiac surgery patients do not carry the same risk of infectious complications, but in spite of several risk-adjustment algorithms [51–54], stratification is seldom used.

Does this mean that the issue is too ill-defined to draw conclusions? Some authorities believe this is the case. The practice guideline of the American Society of Health-System Pharmacists [4] states: "the duration of antibiotic prophylaxis in cardiac surgery is based on consensus of the expert panel because the data do not delineate the optimal duration of prophylaxis." Others [43] have recently stated: "there is no consensus about the type of antibiotic prophylaxis, whether a single agent or a combination should be used, or the duration of administration."

The writing committee considers this degree of nihilism unwarranted. It appears possible to draw several well-reasoned conclusions from the evidence as follows:

1. Chest Tubes and Antibiotic Prophylaxis

Some centers continue antibiotic prophylaxis until chest tubes are removed [16]. The writing committee found no scientific evidence that this practice provides enhanced protection against infectious complications. To the contrary, there is uniform agreement that this policy should not be followed [4, 24, 55].

CONCLUSION. The duration of antibiotic prophylaxis should not be dependent on indwelling catheters of any type.

OPTIMAL PRACTICE. Decisions regarding the continuation of antibiotic prophylaxis are not guided by the presence of indwelling catheters (class IIa, level C).

2. Single-Dose Prophylaxis

In the DiPiro and colleagues [34] review of single-dose antibiotics in surgery the authors concluded that "for open heart operations or those in which prosthetic materials are implanted, the value of single-dose regimens has not been established." The 1993 guideline of the Surgical Infection Society [8] states: "although recent trends in other settings favor only intraoperative coverage, the data are not yet conclusive for patients undergoing cardiac operations." After careful examination of the evidence, the writing committee is in agreement with these statements.

CONCLUSION. Single dose antibiotic prophylaxis may be effective in cardiac surgery, but there are inconclusive data to confirm this effectiveness. There is insufficient evidence to recommend routine use of single-dose prophylaxis in cardiac surgery.

OPTIMAL PRACTICE. Single-dose prophylaxis is used in circumstances the surgeon considers optimal for patient care (class IIa, level B).

3. Prophylaxis for 48 Hours

There is no scientific evidence that prophylactic antibiotics used for less than 48 hours after cardiac surgery are associated with development of antibiotic resistance.

There is minimal information regarding the development of resistance in the period immediately beyond 48 hours, but there is no doubt that resistance increases as the duration of the antibiotic regimen increases.

CONCLUSION. Antibiotic prophylaxis of as great as 48-hours duration is unlikely to produce antibiotic resistance.

Three randomized studies report acceptable infectious outcomes using a 48-hour period of prophylaxis [44–46]. It is noteworthy that with the exception of the Sisto and colleagues [39] report, all the 48-hour regimens associated with single-dose trials produced clinically acceptable infectious rates (see Table 1). In a detailed review of major trials [12], antibiotic prophylaxis was recommended for the first 2 postoperative days. The Surgical Infection Society [8] recommends prophylaxis for 48 hours.

CONCLUSION. Antibiotic prophylaxis of 48 hours duration is clinically effective in minimizing infectious complications in cardiac surgery.

The meta-analysis by Kreter and Woods [49] and the recent study by Harbarth and colleagues [16] concluded that there was no clinical advantage associated with administration of prophylactic antibiotics for more than 48 hours.

CONCLUSION. Antibiotic prophylaxis of 48 hours duration may be as effective as prophylaxis administered for longer than 48 hours.

In the review by Ariano and Zhanel [12], the authors conclude: "there are not enough data at this time to recommend less than 2 days of antimicrobial prophylaxis for this type of surgery." The writing committee is in agreement with this statement.

Summary Conclusions

There is evidence indicating that antibiotic prophylaxis of 48-hours duration is effective. There is some evidence that single-dose prophylaxis or 24-hour prophylaxis may be as effective as 48-hour prophylaxis, but additional studies are necessary before confirming the effectiveness of prophylaxis lasting less than 48 hours. There is no evidence that prophylaxis administered for longer than 48 hours is more effective than a 48-hour regimen.

OPTIMAL PRACTICE. Postoperative prophylactic antibiotics are given for 48 hours or less (class IIa, level B).

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Appendix

Classification of Recommendations

Class I	Conditions for which there is evidence or general agreement, or both, that a given procedure is useful and effective
Class II	Conditions for which there is conflicting evidence or a divergence of opinion, or both, about the usefulness and efficacy of a procedure
	II.a. Weight of evidence favors usefulness and efficacy
	II.b. Usefulness and efficacy is less well established by evidence
Class III	Conditions for which there is evidence or general agreement, or both, that the procedure is not useful and effective
Level of Evidence	
Level A	Data derived from multiple, randomized clinical trials
Level B	Data derived from a single, randomized trial or from nonrandomized trials
Level C	Consensus expert opinion