AHA Scientific Statement

Nonvalvular Cardiovascular Device–Related Infections

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More than a century ago, Osler took numerous syndrome descriptions of cardiac valvular infection that were incomplete and confusing and categorized them into the cardiovascular infections known as infective endocarditis. Because he was both a clinician and a pathologist, he was able to provide a meaningful outline of this complex disease. Technical advances have allowed us to better subcategorize infective endocarditis on the basis of microbiological etiology. More recently, the syndromes of infective endocarditis and endarteritis have been expanded to include infections involving a variety of cardiovascular prostheses and devices that are used to replace or assist damaged or dysfunctional tissues (Table 1). Taken together, infections of these novel intracardiac, arterial, and venous devices are frequently seen in medical centers throughout the developed world. In response, the American Heart Association's Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease wrote this review to assist and educate clinicians who care for an increasing number of patients with nonvalvular cardiovascular device–related infections. Because timely guidelines[1,2] exist that address the prevention and management of intravascular catheter–related infections, these device-related infections are not discussed in the present Statement.

This review is divided into two broad sections. The first section examines general principles for the evaluation and management of infection that apply to all nonvalvular cardiovascular devices. Despite the marked variability in composition, structure, function, and frequency of infection among the various types of nonvalvular cardiovascular devices reviewed in this article, there are several areas of commonality for infection of these devices. These include clinical manifestations, microbiology, pathogenesis, diagnosis, treatment, and prevention. The second section addresses each device and describes unique clinical features of infection. Each device is placed into one of 3 categories—intracardiac, arterial, or venous—for discussion.

General Principles

Clinical Manifestations

The specific signs and symptoms associated with an infection of a nonvalvular cardiovascular device depend on the location of the infected portion(s) of the device. Clinical manifestations of infected intravascular or endovascular portions of a device are similar to those seen in infective endocarditis or endarteritis.[3,4] Fever is present in most cases. Embolic events are also commonplace and involve either the pulmonary or systemic vasculature, according to the location of the infected device. Sepsis with shock and organ dysfunction is present in some acute presentations caused by virulent pathogens such as *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Subacute to chronic presentations are characteristic of infections produced by less aggressive microorganisms. Immune-mediated events are occasionally seen with chronic infections and include immune complex–mediated nephritis and vasculitis. These infections can present as bacteremia with fever and no other clinical findings. For devices that have infection involving percutaneous drivelines, there can be local pain, erythema, induration, warmth, and purulent drainage at the percutaneous exit site, often in association with bacteremia. For devices that are implanted subcutaneously, infection at the site can present with local findings of cellulitis or abscess formation, with or without bacteremia (Figure 1). Pseudoaneurysms develop in some cases of infection at vascular graft anastomosis sites and present as pulsatile masses. Occlusion of a graft may lead to distal manifestations of ischemia or necrosis.

Microbiology

Staphylococci account for the majority of device-related infections. Either coagulase-negative staphylococci or *S aureus* is the most common pathogen identified, according to the case series reported. Other types of skin flora produce infection less frequently. Distinguishing skin flora, particu-

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TABLE 1. Nonvalvular Cardiovascular Device–Related Infections

Type of Device	Incidence of Infection, %
Intracardiac	
Pacemakers (temporary and permanent)	0.13–19.9
Defibrillators	0.00–3.2
LVADs	25–70
Total artificial hearts	To be determined
Ventriculoatrial shunts	2.4–9.4
Pledgets	Rare
Patent ductus arteriosus occlusion devices (investigational in the United States: plugs, double umbrellas, buttons, discs, embolization coils)	Rare
Atrial septal defect and ventricular septal defect closure devices (Bard clamshell occluders, discs, buttons, double umbrellas)	Rare
Conduits	Rare
Patches	Rare
Arterial	
Peripheral vascular stents	Rare
Vascular grafts, including hemodialysis	1.0–6
Intra-aortic balloon pumps	≤5–26
Angioplasty/angiography-related bacteremias	<1*
Coronary artery stents	Rare
Patches	1.8
Venous	
Vena caval filters	Rare

*Closure device use ≤1.9%.

larly coagulase-negative staphylococci, as either pathogen or culture contaminant is a frequent diagnostic dilemma. Multiple sets of blood cultures should yield the pathogen if endovascular infection is present. Skin flora that grow in culture from percutaneous aspirates of fluid or abscess collection should be considered as pathogens. Recovery of skin flora at driveline transcutaneous exit sites or in open wounds in proximity to a device is more difficult to define as pathogen versus contaminant; a Gram's stain may be helpful. Other Gram-positive cocci, Gram-negative bacilli, and fungi, particularly *Candida* species, cause a minority of device-related infections. Multidrug resistance is common and reflects the nosocomial origin of many of these infections.

Pathogenesis

Three factors should be considered when addressing the pathogenesis of medical device–related infections: (1) pathogen virulence factors, (2) host response to the presence of an artificial device, and (3) the physical and chemical characteristics of the medical device. During the past decade, many published studies have detailed the complexities of the pathogenesis of medical device–related infections. These are a result of advances in molecular biology techniques that have facilitated the study of purported virulence determinants among both bacterial and fungal pathogens.

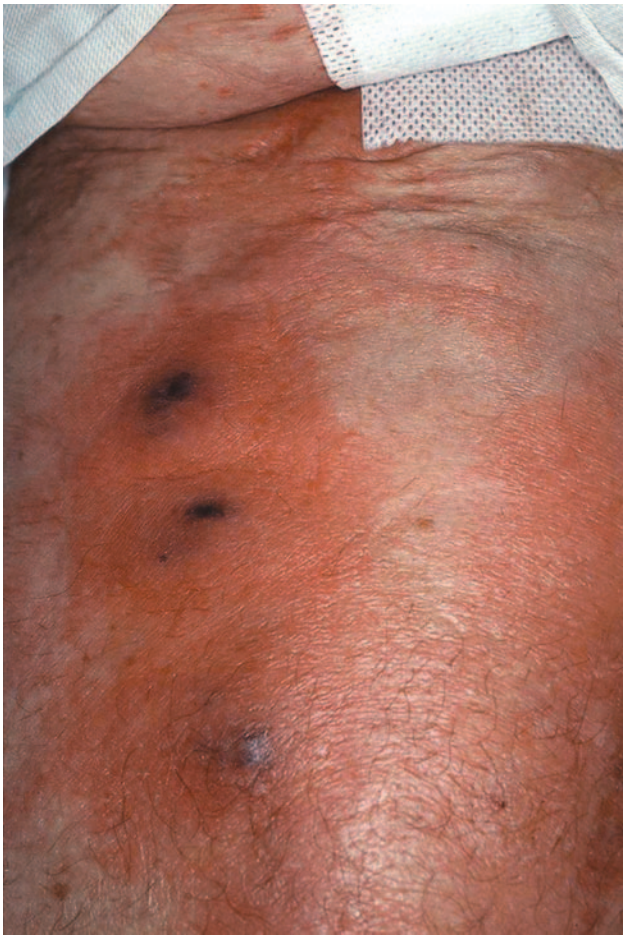

Figure 1. Vascular graft site infection in a hemodialysis patient due to methicillin-resistant *S aureus*. The patient suffered bacteremia in addition to focal skin and soft tissue changes at the graft site, including erythema, swelling, warmth, and pain.

Pathogen Virulence Factors

Two major areas of investigation of microbial virulence factors are (1) tissue and foreign body adherence molecules and (2) foreign body surface biofilm formation. There are several *S aureus* adhesins[5–9] that are operative in the binding of microorganisms to extracellular and host plasma proteins that coat the surface of indwelling medical devices. These host proteins are exposed in areas where endothelium has been denuded by contact with or attachment to indwelling devices. The adhesins, known as extracellular matrix-binding proteins or microbial surface components recognizing adhesive matrix molecules (MSCRAMM), have been studied in a number of in vitro adherence assays and in animal models of infection and have demonstrated their importance in microbial virulence. Much of the work has examined *S aureus* surface proteins, including fibronectin-binding protein A or B, clumping factor A or B, and collagen-binding protein. The only experimental model of cardiovascular infection that has been used to examine these putative virulence factors is the animal endocarditis model.[10] Findings derived from experimental endocarditis investigations may be applicable to cardiovascular device–related infections in humans.

A number of studies[6,7] suggest that binding to fibrinogen is critical in the pathogenesis of catheter-induced experimental

endocarditis in rats. Other work[5] suggests that binding of staphylococci to collagen is advantageous. There are temporal aspects of binding; fibrin(ogen) binding early in the infection process seems to be important with *S aureus*. Fibronectin binding may be more important later, when bound fibrin degradation occurs because of plasmin.[9] Other investigations[7,8] that used recombinant techniques demonstrated that fibronectin binding was also important in virulence in the animal endocarditis model. In a rat model of experimental endocarditis examining the role of fibronectin binding in virulence, conflicting results were seen. In one investigation, fibronectin binding by *S aureus* seemed important,[8] whereas in another, it did not.[9] There has been limited investigation of the role of collagen-binding protein.[4]

Another area of interest in microbial pathogenesis of cardiovascular medical device infections is biofilm formation.[11–13] Biofilm, consisting of infecting microorganisms and extracellular matrix, forms on the surface of an indwelling medical device and serves as a protected environment for microorganisms. It is believed that mature biofilm formation is predominantly responsible for the inability of the host immune response and antimicrobial therapy to clear device-related infections. Because of this protected environment, device removal to achieve cure of infection is usually required.

Staphylococcus epidermidis[13] has received the most investigative attention among the variety of microorganisms that can produce biofilm-related medical device infections. The polysaccharide intercellular adhesin that is responsible for cellular aggregation and biofilm formation has been characterized, and the gene cluster (*ica*) that contains all genes required for polysaccharide intercellular adhesin production has been described.[14,15] Notably, similar genes that are present in other coagulase-negative staphylococci and in *S aureus* are responsible for the production of the polysaccharide intercellular adhesin and biofilm.[14]

Host Response to Medical Devices

Many of the critical host elements that affect the risk for device infection, including the endothelium, white blood cells, platelets, and microorganisms within the bloodstream, react to the specific quality of blood flow to which they are exposed. Normal cardiovascular flow is regularly pulsatile and dynamic. Each region of the cardiovascular system has a characteristic normal shear stress (the frictional force due to the flowing blood in contact with the wall) and circumferential strain (the distending force of the intraluminal pressure). Normal flow at physiological shear rates is antistimulatory to the endothelium[16,17]; the endothelial cells align and flatten with the flow, and apoptotic and inflammatory mediators are suppressed.

Many of the devices discussed in detail in this Statement, including electrophysiological devices, left ventricular assist devices (LVADs), ventriculoatrial shunts, total artificial hearts, stents, grafts, and balloon pumps, create or reside within sites of very abnormal cardiovascular blood flow. The flow changes may augment the infective potential of the devices and impede response to therapy. Some important characteristics of abnormal flow are abnormally high or low shear stress and increased gradient in shear, alterations in circumferential strain, and abnormal boundary surfaces. Examples of abnormal flow conditions and devices often associated with them are turbulence caused by tricuspid regurgitation due to a pacemaker lead[18,19] that interferes with valve closure, high shear caused by a LVAD valve, and abnormal circumferential strain produced by vascular grafts.

Turbulence is not a prominent component of normal cardiovascular flow. It occurs alongside high-velocity jets, such as along the edges of jets of tricuspid regurgitation or prosthetic valve hinges. Some turbulence may occur at arterial branch points, creating characteristic zones where flow becomes disorganized, with low velocities and random fluctuations in flow. Low shear stresses in turbulent regions increase the reactivity of the endothelial cells and circulating platelets and have been closely associated with regional progression of atherosclerosis and thrombosis. Platelets and microorganisms caught in the turbulent zones are exposed to adverse shear conditions. These conditions strongly promote regional endothelial activation, increase platelet aggregation, and provide opportunities for platelet and microbial adherence.[16,20] The spatial and temporal disorganization in a turbulent zone thwarts any compensatory endothelial realignment that the cardiovascular system would normally invoke to minimize the adverse effects of abnormal flow.

High shear stress, beyond the 14 dyne/cm^2 that is the normal upper limit for the arterial tree, occurs with luminal stenosis. The high shear at vascular stenotic sites, including those due to constriction from grafts or intraluminal devices, affects neutrophil and monocyte adherence and phagocytosis[21,22] without impeding, and possibly increasing, microbial adherence.[23] These deleterious effects on endothelial cells, platelets,[24] and cell-mediated immunity may have important etiologic roles with regard to establishment and maintenance of device infection.

All devices present an artificial surface to the blood. Neutrophil and monocyte function has also been shown to be adversely affected by contact with some prosthetic surfaces,[21] and antibiotic penetration into areas of medical devices may be diminished. The abnormal material properties of some vascular grafts, which change the circumferential strain experienced by the endothelium within the grafts, may similarly increase endothelial activation and platelet and microbial adherence.[25] In addition, T-cell function may be influenced by the presence of some of these devices.[26] Endothelialization of an implanted device is a key factor in the prevention of subsequent infection. In animal studies of explanted devices, endothelialization has been noted to occur as early as 1 month after implantation and to be complete by 3 months.[27] The "healing response" to device implantation in humans has been much less studied, but in a recent report of human cases involving explanted devices, similar results were found.[28] The development of a nonthrombotic fibroelastic pseudointima was apparent in these cases by 2.7 months and was not affected by the site of implantation.

Physical and Chemical Characteristics of Medical Devices

Many authorities believe that the occurrence of infection is related to the ability of red blood cells, platelets, and

fibrinogen to adhere to prosthetic material. Fibrinogen is one factor that promotes "sticking" to a prosthetic device. It is a highly hydrated macromolecule and precedes platelet attachment to biomaterial. Biomaterials with lower critical surface tension, including Teflon and other fluorocarbon polymers, do not attract platelets. The biomaterials with higher critical surface tension, such as Dacron polyethamine, attract platelets and fibrinogen, both of which aggressively bind to these materials. Clumps of fibrinogen and platelets attract white blood cells, and a surface-bound mass develops around the biomaterial.

Diagnosis

Laboratory, radiological, and echocardiographic procedures are helpful in making a diagnosis of cardiovascular device–related infection. In untreated patients with bacteremia, blood cultures are usually positive. Culture of purulent drainage from a percutaneous driveline exit site or from a subcutaneous pocket or other site identifies a specific pathogen. Gram's stain of the drainage material is useful in demonstrating neutrophils and infecting bacteria.

Despite collection of clinical specimens for microbiological examination, stains and cultures fail to demonstrate a pathogen in some patients with nonvalvular cardiovascular device–related infections. These culture-negative cases, much like those seen with infective endocarditis, are often due to recent antibiotic administration, which may diminish the sensitivity of subsequent microbiological studies. Unlike infective endocarditis, fastidious and uncommon microorganisms that do not grow or stain positive by routinely used laboratory methods have not been identified as pathogens in nonvalvular device-related infections. These groups of rare pathogens that are now being identified as causes of culture-negative endocarditis by technical advances in the laboratory[29] have not accounted for culture-negative nonvalvular infections.

Role of Imaging

All imaging modalities (Table 2) discussed in the following section are useful only as aids in diagnosis and treatment. Findings from these studies have to be interpreted for the individual patient and with the results of other diagnostic testing to assist the clinician in forming a diagnosis of device-related infection.

Plain radiographic films play a minor and indirect role in diagnosing infections of nonvalvular implanted cardiovascular devices but can provide important information when used judiciously. Infections may be related to misplacement or displacement of devices. For example, a port catheter in the superior vena cava or high right atrium, as intended, is less likely to thrombose and develop an infection than is a catheter that is displaced into the internal jugular vein or is left with its tip in the less capacious subclavian vein.

Computed tomographic (CT) scanning can give similar information. The advantage of CT scanning is that it is less operator dependent than ultrasonographic scanning, in both acquisition and interpretation of images. Furthermore, particularly with newer multislice units, images can be obtained very rapidly, often obviating the need for breath holding and limiting the degree to which patient cooperation is necessary. Even relatively large areas, such as vascular grafts and stent-grafts, can be quickly and accurately imaged. On the negative side, contrast injection may be necessary, and this is a concern in patients with compromised renal function. Also, stents cause metallic artifacts so that visualization within the stented lumen is limited. Devices such as wires, catheters, and stent-grafts (with Nitinol stents [Nitinol Devices and Components], as opposed to stainless steel alloys) do not produce such artifacts.

Angiography has little role in diagnosing infections. Cardiac catheterization may, however, offer therapeutic options that decrease the risk of infection. It may be useful in confirming and correcting malpositioned lines or wires. Percutaneous stripping of thrombus from catheters with a

TABLE 2. Imaging for Nonvalvular Cardiovascular Device–Related Infections

Manifestation of Infection	Initial Imaging Modality
Endocarditis	TEE
Pacemakers (temporary and permanent)	
Defibrillators	
LVADs	
Ventriculoatrial shunts	
Pledgets	
Patent ductus arteriosus occlusion devices	
Atrial septal defect closure devices	
Conduits	
Patches	
Pericarditis	TTE or TEE
Coronary artery stents	
Pledgets	
Perivasculitis	CT or MRI
Peripheral vascular stents	
Vascular grafts, including hemodialysis	
Angioplasty/angiography-related bacteremias	
Coronary artery stents	
Patches	
Aneurysm or pseudoaneurysm	Angiography
Pledgets	
Coronary artery stents	
Patches	
Angioplasty/angiography-related bacteremias	
Vascular grafts, including hemodialysis	
Infected thrombosis	Ultrasound
Vena caval filter	
Vascular grafts, including hemodialysis	
Pocket site infections	Ultrasound
Pacemakers (permanent)	
Defibrillators	
LVADs	
Total artificial hearts	

Imaging with a complementary modality may be required in addition to the initial evaluation.

snare has been widely used to restore function. It may also decrease the risk of infection, although this has not been well investigated. Angiographic dye-related renal toxicity is another concern.

Ultrasound may be helpful in several ways; however, its efficacy is dependent on the proficiency of the technician. It can identify abnormal fluid collections around a device. By demonstrating septations or inhomogeneity of the fluid in such collections, it can provide clues as to whether or not the fluid is likely to be infected. Ultrasound is also very useful in guiding aspiration, for both diagnosis and treatment of fluid collections. Ultrasound can detect pseudoaneurysm formation. The addition of Doppler flow studies provides physiological information that can give indirect evidence of infection—eg, slowed or turbulent flow through a graft due to thrombus formation.

Transthoracic and transesophageal echocardiography have proven useful in visualizing abnormalities such as valvular vegetations, pericardial effusion, abnormal position of a device such as a pacemaker wire, or thrombus on or related to a device.

Magnetic resonance imaging (MRI) does not have a major role. Its use is contraindicated in patients with electrophysiological cardiac devices. Current information should be obtained from an institution's MRI safety committee when considering MRI use in patients with other types of cardiovascular devices. Metallic implants such as stents produce artifacts that significantly degrade image quality. It may be a more sensitive technique than CT scanning in evaluating subtle perigraft inflammatory changes.

Radionuclide studies can be valuable in difficult cases in determining whether there is a focal infection or which area is infected. Both Tc99m-labeled white blood cells and gallium can be used. The advantage of the Tc99m white blood cell scan is that results are available within a few hours of white blood cell injection. Gallium scans require 1 to 2 days after nuclide injection before scan results are interpretable.

Antimicrobial Therapy—General Principles

Initial antimicrobial treatment of nonvalvular cardiovascular device–related infections should incorporate certain goals. These goals represent the consensus opinion of the authors and are not based on data obtained from prospectively conducted clinical trials. Antimicrobial therapy should be directed against an identified pathogen and guided by the in vitro antimicrobial susceptibility testing results for the isolate. In some cases, however, because of negative cultures or an inability to collect cultures, no pathogen is recovered, and empiric broad-spectrum therapy should be selected to treat many potential nosocomial and skin-colonizing organisms. Therapy should be bactericidal (for bacterial infections) and should be administered parenterally in patients with known or suspected bacteremia. Removal of the medical device, if feasible, is preferable. Without prompt removal, risk of morbidity and mortality may increase. The duration of antimicrobial therapy should be individualized for each patient. If there is associated bacteremia, particularly if due to *S aureus*, then a minimum of 14 days of antimicrobial treatment is necessary after removal of the device and the first negative blood culture. Other experts suggest 4 weeks of antimicrobial therapy after the device is removed for patients with *S aureus* bacteremia (SAB) due to an infected cardiovascular device or if vegetations are present. If bacteremia is due to staphylococcal endocarditis of a LVAD valve, 6 weeks of antimicrobial therapy is suggested, with a regimen similar to that suggested for prosthetic cardiac valve infection.[30]

A regimen including vancomycin is recommended as initial empiric therapy because staphylococci are frequently identified as pathogens, and methicillin resistance is common among these strains. Alternative antimicrobial regimens are limited for patients who do not respond to or who cannot tolerate vancomycin. Two newer agents, linezolid and the combination of quinupristin/dalfopristin, offer treatment options for methicillin-resistant staphylococcal infections and infections due to vancomycin-resistant enterococci. Both agents should be used only when vancomycin is not a treatment option, such as in the case of vancomycin-resistant enterococci infection or patient history of true vancomycin allergy.

Local administration of antibiotics at the device infection site has been used. In the case of vascular graft infection, antibiotic-bonded prosthetic grafts have been implanted for in situ revascularization after resection of infected aortic prosthetic grafts.

Long-term suppressive therapy is a useful treatment option for selected patients with cardiovascular device–related infection in whom surgical removal of a device is not possible. These patients should be stable from a cardiovascular standpoint, have responded to antimicrobial therapy, and not be candidates for surgical removal of the indwelling device. Two recently published case series[31,32] discuss the use of long-term (lifelong) suppressive antimicrobial therapy in patients with cardiovascular device–related infection. Five patients who had undergone abdominal aortic aneurysm repair developed proven or suspected graft infection.[31] Because of severe concomitant medical conditions, none of the 5 patients were considered appropriate surgical candidates for graft replacement. All 5 were infected with Gram-positive cocci and received long-term suppressive antibiotics after initial treatment with a course of parenteral therapy. The patients were followed up for a median period of 32 months (range, 30 to 72 months) on chronic suppressive oral antibiotic therapy with no clinical evidence of graft site infection and reportedly tolerated therapy.

Members of the Infectious Diseases Society of America's Emerging Infections Network were queried in January 2000 to contribute data for patients who received chronic suppressive antimicrobial therapy for cardiovascular device–related infection.[32] Data for 51 patients were provided. Vascular graft infections were present in 30 cases (58.8%). Five patients had pacemaker-related infections, 3 had central venous catheter infections, and 1 had an infected venous filter. The remaining 12 patients (23.5%) had infected prosthetic cardiac valves; in 3 of these, aortic grafts were also present. Sixty-three percent of infections were due to Gram-positive cocci.

Duration of antimicrobial therapy ranged from 3 to 120 months; duration was 1 year or longer in 51% of cases. Three patients (7.3%) suffered relapse of infection, with one of

these relapses due to *P aeruginosa* that had become resistant during ciprofloxacin monotherapy. Adverse drug events were described in 3 (6.52%) of 46 cases for which information was provided.

Prevention

Because of the proclivity for indwelling medical devices to become infected and the general requirement for device removal when they are infected, prevention of infection is a primary goal. Prevention interventions include primary and secondary prophylaxis, antimicrobial impregnation of devices, appropriate infection-control measures, and careful surgical technique for device implantation. Primary or preimplantation antimicrobial prophylaxis is modeled after that used to prevent surgical site infection. In contrast to that used to prevent surgical site infections, primary prophylaxis for the prevention of device-related infection has not been examined in prospective randomized trials. This is due, in large part, to the infrequency of infection. Nevertheless, primary prophylaxis is routinely given to patients who undergo placement of electrophysiological cardiac devices (pacemakers, cardioverter-defibrillators), ventricular assist devices, total artificial hearts, ventriculoatrial shunts, cardiac pledgets, vascular grafts, and arterial patches. One dose of antibiotic, usually cefazolin, is administered to prevent methicillin-susceptible staphylococcal infection of the cardiovascular device. A single dose of vancomycin should be considered for use only in patients who are unable to tolerate beta-lactam antibiotics or for patients known to be colonized or infected with methicillin-resistant staphylococci. Therapeutic antibiotic concentrations should be present in tissue from initiation to completion of device placement to achieve optimal prophylactic efficacy. This requires that prophylactic antibiotics be intravenously administered ≈1 hour before onset of the procedure. Additional doses of antibiotic may be required intraoperatively for prolonged procedures. Repeat dosing during the operative period for the commonly used antibiotics cefazolin, cefamandole, cefuroxime, and vancomycin should be at 6, 2, 4, and 8 hours, respectively.[33] Most experts believe that primary prophylaxis for surgical site infection should be stopped once the wound is closed or within 24 hours of wound closure.[34–36]

Secondary prophylaxis, defined in this Statement as prophylaxis that is given in the setting of certain dental, respiratory, gastrointestinal, genitourologic, or other invasive procedures in patients with indwelling devices, is largely unstudied. At present, there is no convincing evidence that microorganisms associated with these procedures cause infection of nonvalvular vascular devices at any time after implantation. These infections are most often caused by staphylococci, Gram-negative bacteria, or other microorganisms in association with implantation of the device or resulting from wound or other active infections. Accordingly, this committee does not recommend antibiotic prophylaxis after device placement for patients who undergo dental, respiratory, gastrointestinal, or genitourologic procedures. Secondary prophylaxis is recommended for patients when they undergo incision and drainage of infection at other sites or replacement of an infected device (Table 3). For patients in whom device implantation has not achieved the desired result of complete obliteration of intracardiac or intravascular shunting (residual leaks), currently published American Heart Association guidelines[37] for secondary prophylaxis for congenital cardiac lesions remain applicable. This would include the patient with an atrial septal defect who would not require prophylaxis ordinarily, but because of inadequate treatment with an occlusion device, is left with a residual leak and requires continued secondary prophylaxis.

TABLE 3. Antibiotic Prophylaxis Recommendations for Use With Placement of Nonvalvular Cardiovascular Devices

Primary prophylaxis

- Modeled after that used to prevent surgical site infection.
- Because of the low incidence of infection for many of the devices, evidence-based data have not been collected that prove efficacy.
- Routinely used for placement of electrophysiological cardiac devices, ventricular assist devices, total artificial hearts, ventriculoatrial shunts, cardiac suture line pledgets, vascular grafts, and arterial patches.

Secondary prophylaxis

- Antibiotic prophylaxis is not routinely recommended after device placement for patients who undergo dental, respiratory, gastrointestinal or genitourinary procedures.
- It is recommended for patients with these devices if they undergo incision and drainage of infection at other sites (eg, abscess) or replacement of an infected device.
- It is recommended for patients with residual leak after device placement for attempted closure of the leak associated with patent ductus arteriosus, atrial septal defect, or ventricular septal defect.

Patients who are severely immunocompromised as a result of underlying disease or immunosuppressive treatment have increased risk of infection. However, immunosuppression is not an independent risk factor for nonvalvular device infections. Immunocompromised hosts who have a nonvalvular cardiovascular device should receive primary and secondary antibiotic prophylaxis as advocated for immunocompetent hosts.

Antimicrobial impregnation of medical device surfaces has been studied[38] as an infection-prevention technique for central venous catheters. Several agents have been used for impregnation and have been shown to reduce infection risk. Impregnated vascular grafts have also been evaluated and are commercially available.

There are numerous issues that pertain to intraoperative reduction of infection risk and apply to all types of surgical procedures, including those that are used for medical device placement. Infection-control measures include sterilization of equipment, surgical attire, and drapes; asepsis; and careful surgical technique.[39]

Specific Devices—Intracardiac

Pacemakers and Implantable Cardioverter-Defibrillators

Worldwide, there are estimated to be 3.25 million patients with functioning pacemakers.[40] Initial cases of pacemaker endocarditis were described in the early 1970s.[41,42] Pacemaker infection has been reported to occur in 0.13%[43] to 19.9%[44] of patients. Most infections occur in the pacemaker generator pocket. Pacemaker endocarditis is less common and

is reported to account for ≈10% of the pacemaker-associated infections.[45]

Implantable cardioverter-defibrillators (ICDs) have been in use for more than 20 years.[46] As a result of technical advances, most ICD leads are now implanted transvenously, obviating the need for epicardial leads placed via thoracotomy. In addition to the obvious benefits of avoiding thoracotomy, the use of transvenous leads has resulted in an overall decline in the risk of ICD infection. Published infection rates[47,48] for ICDs implanted in the decade of the 1990s range from 0% to 0.8%. One retrospective analysis[49] indicates that the infection rate for prepectoral ICD implantations may be lower than that associated with abdominal implantation. Of the 959 patients, who had a mean follow-up time of 35 months, infection rates for patients who underwent pectoral versus abdominal approaches were 0.5% (2 of 375 patients) and 3.2% (19 of 584 patients), respectively ($P=0.03$). The 6-fold difference in infection rates could be due, in part, to the practice of implanting pectoral ICDs as a 1-stage procedure, rather than the 2-stage procedure that is used for abdominal implantation.

In pacemaker/ICD infective endocarditis, vegetation formation is not limited to the tricuspid valve and can be found anywhere along the course of the electrode, including the endocardium of the right atrium or right ventricle. Septic pulmonary emboli or empyema can complicate pacemaker/ICD endocardial infection.

Several sources for infection of the pacemaker/ICD pocket and electrode have been postulated. One possible source is contamination of the pocket at the time of device implantation. Pocket site infection can also complicate cutaneous erosion of the generator or the defibrillator. Microorganisms from the pacemaker/ICD pocket can spread along the electrode to the endocardium and the electrode tip. Additional possible sources of pacemaker/ICD infection include hematogenous seeding of the endovascular electrode during transient bacteremia related to a pacemaker/ICD pocket infection or to an unrelated site of infection. The most common predisposing condition for pacemaker/ICD endocarditis is pacemaker/ICD pocket infection, and the most common pathogens of pacemaker/ICD endocarditis are skin flora, including staphylococci and corynebacteria. Hematogenous seeding from a distant focus of infection may account for late-onset infection due to *S aureus*[50] and other less commonly identified pacemaker/ICD endocarditis pathogens, including viridans group streptococci, enterococci, Gram-negative bacilli, and fungi, including *Aspergillus* and *Candida* species.

The diagnosis should be suspected in patients with pacemakers/ICDs and unexplained fever. The Duke criteria used for the diagnosis of infective endocarditis can be used in cases of suspected pacemaker/ICD endocarditis. The diagnosis is confirmed by positive blood cultures and an echocardiogram that demonstrates vegetations on the pacemaker/ICD lead (Figure 2). Transesophageal echocardiography (TEE) has been found to be more sensitive in detecting pacemaker/ICD-related endocarditis than transthoracic echocardiography (TTE). TEE has a reported sensitivity of >95% in pacemaker/ICD endocarditis, versus <30% for TTE.[40,51–53]

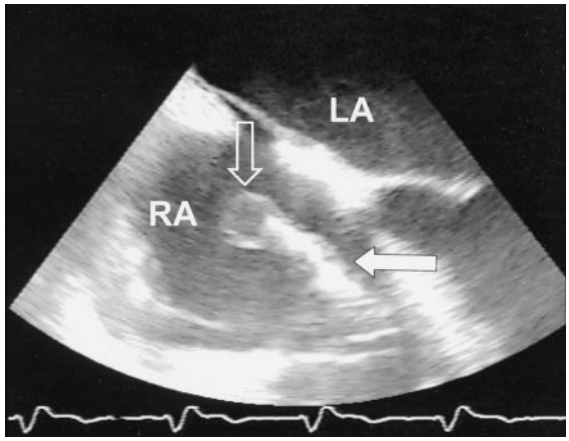

Figure 2. Transesophageal echocardiographic view of the left atrium (LA) and right atrium (RA). A pacemaker lead (filled arrow) is seen as it crosses the tricuspid valve. The lead is thickened by infective material, and there is a round mobile vegetation (open arrow) attached to its right atrial portion.

In one group[50] of patients with pacemakers (29 patients) or ICDs (4 patients) who had SAB, pacemaker/ICD infection was confirmed in 45% (15 of 33 patients). Nine of 12 patients (75%) with early SAB (ie, SAB occurring within 1 year of implantation) and 6 of 21 patients (29%) with late SAB had confirmed pacemaker/ICD infection. The pacemaker/ICD became infected in 60% from hematogenous seeding from a distant or unknown source. No focal evidence of generator pocket infection was noted in 9 (60%) of 15 patients; nevertheless, pocket cultures grew *S aureus* in 5 of these 9 patients. For the 18 patients studied with both TTE and TEE, 6 had vegetations detected by TEE only, and 2 others had vegetations detected by both TTE and TEE. This study supports the diagnostic superiority of TEE for pacemaker/ICD endocarditis, although the number of patients examined was small.

There are no prospective studies that compare cure rates for antibiotic treatment alone versus antibiotic therapy combined with pacemaker/ICD system removal. However, the high rate of uncontrolled or relapsing bacteremia, even after prolonged medical therapy, makes removal of the entire pacemaker/ICD system optimal. In one recent retrospective case analysis[40] that included patients with an infected pacemaker or ICD, infection relapse was strongly associated with failure to completely remove all hardware. This case series included 123 patients, 119 (97%) of whom had transvenously implanted leads. Only 1 (0.86%) of 117 patients who underwent removal of their entire system had infection relapse. In contrast, 3 of 6 (50%, $P=0.003$) without complete hardware removal suffered relapse. The only patient who had hardware removal and still had infection relapse had a new generator implanted in an old pocket site. All other patients had new devices placed at different sites at a later date.

The mortality rate in patients with pacemaker/ICD endocarditis treated with antibiotics alone ranges from 31% to 66%. In contrast, the mortality rate in patients who had combined antibiotics and electrode removal was only 18% (range, 13% to 33%) in one literature review.[54] Another series also reported failure to remove an infected indwelling intra-

vascular device to be associated with increased all-cause mortality.[50] Patients whose infected pacemaker or ICD was not removed had an almost 3-fold (47.6% versus 16.7%) increased risk of dying. The relatively small number (n=32) of patients included in this analysis probably prevented the finding of a statistical association, although a trend ($P=0.13$) was seen.

Chamis et al[50] recommend removal of the pacemaker/ICD system in patients with SAB in specific circumstances: (1) if there is clinical or echocardiographic evidence of pacemaker/ICD infection, (2) if there is no other source identified for SAB, or (3) if there is relapsing SAB after a course of appropriate antibiotic therapy.

Lead removal may be technically difficult as a result of neoendothelialization and fibrocollagenous sheath formation that develops along the electrode. A prolonged length of time that the pacemaker/ICD is in place has been associated with greater difficulty of lead removal and complications during attempts at removal. Several different techniques for electrode extraction have been described.[55] One option involves the use of a "locking stylet" that is introduced onto the lead and affixed close to the distal end of the electrode to apply traction directly to the tip. If this is not successful, then a telescoping sheath can be advanced over the lead to disrupt fibrous attachments of the lead to vein or cardiac tissue, and the lead can be freed by countertraction. A laser sheath also has been used to photoablate the fibrous attachments instead of using mechanical force. In a recent review,[55] these approaches completely extracted 81% to 93% of leads. Major complications, such as tamponade, occurred in 0% to 3.3%, and death occurred in 0% to 0.8%, usually as a result of tamponade. In some patients, the electrodes can only be removed by cardiotomy, which carries additional risks. Minimally invasive video-assisted pacemaker lead removal under thoracoscopic vision has also been reported to be successful.[56]

New embolization without clinical sequelae has been reported during intravascular extraction in 30% of 33 patients with vegetations <10 mm.[52] Surgical extraction is favored by some for patients with larger vegetations; however, 2 deaths from septic complications occurred in 10 patients after surgical lead extraction.[52] Others have found no evidence that endovascular removal of larger vegetations is deleterious.[57]

Device reimplantation should be at a new site when the patient is no longer bacteremic. Once the pacemaker/ICD system is removed, need for reimplantation should be reassessed. With regard to pacemakers, 13% to 52% of patients may no longer require pacing support.[40,54,55]

Although antibiotics are frequently used as primary prophylaxis of pacemaker implantation, there are no large randomized, controlled trials to support this practice. A recent meta-analysis[58] reviewed 7 published prospective studies. Each study enrolled 100 to 500 patients who received either no antibiotic or an antistaphylococcal beta-lactam drug for 1 to 5 days perioperatively. These studies included 2023 patients with lengths of follow-up ranging from 1 to 48 months, although most patients were not monitored for >1 year. The incidence of infectious disease end points in control groups ranged from 0% to 12%. The meta-analysis found a consistent protective effect of antibiotic prophylaxis ($P=0.0046$; OR 0.256; 95% CI 0.1 to 0.656).

Whether the prophylactic administration of preplacement antibiotics reduces ICD infection risk is unproved. Nevertheless, antibiotic prophylaxis is commonly administered before ICD placement for at least 3 reasons. First, the pathogenesis of pacemaker-related infections is thought to be similar to that of ICD-related infections, and antibiotic prophylaxis for pacemaker implantation may decrease infection risk.[58] Second, infection of an ICD can have devastating septic complications,[59,60] and all efforts should be made to prevent it. Third, infection and fear of ICD shocks are 2 key factors that prompt patients to refuse continued use of ICDs. Despite antiarrhythmic medical therapy, survival expectation is severely limited for some patients[61] without the device.

Left Ventricular Assist Devices

Infection is a frequent complication of LVAD use, and the risk increases with the duration of use. In a current case series,[62] 85% of LVAD infections occurred when the device was left in place for >2 weeks. The incidence of infection has been highly variable among different surveys[63–75] and has been reported to range between 13% and 80%. The wide variability in infection risk is, in part, due to different types of infections that have been included under the category of LVAD-related infections. Some studies have included patients with surgical site infections, postoperative pneumonia, central venous catheter–related sepsis, and nosocomial urinary tract infections, in addition to infection of the LVAD.

The most current study of LVAD-related infections included 36 LVADs placed in 35 patients[76] between October 1996 and May 1999. The mean duration of LVAD use was 73 days and ranged from 2 to 262 days. Surgical site infections occurred in 16 patients (6.2 infections per 1000 LVAD days). Nine of the infections were deep-tissue or organ/space (device) infections, and these deep infections were statistically ($P=0.02$) associated with the postoperative requirement for hemodialysis. Because a variety of nosocomial pathogens have caused LVAD-related infections, patients in this survey received some combination of 5 antimicrobial agents (vancomycin, ciprofloxacin, rifampin, fluconazole, and a beta-lactam or monobactam) as standard perioperative prophylaxis for device placement for at least 48 to 72 hours.

Infections of LVADs can present as 3 different syndromes. Driveline infection, which is the most common type of LVAD infection, presents with local inflammatory changes and drainage at the cutaneous exit site. The second syndrome is infection of the LVAD pocket site, which causes local inflammatory changes. The third and least frequently seen infection of LVADs is endocarditis due to infection involving the valves and/or the internal (blood-contacting) lining of the device. Like patients with native or prosthetic valve infections, patients with LVAD-related endocarditis manifest systemic findings that include fever, bacteremia, embolic phenomena, and valvular incompetence. The 3 infection presentations are not mutually exclusive and patients can have mixed infections involving more than one part of the device.

Recent evidence suggests that there may be additional mechanisms involved in the pathogenesis of LVAD-associated infections. The LVAD induces iatrogenic immunodeficiency that may predispose to infection.[24,77–82] The device induces an aberrant state of T-cell activation that leads to programmed cell death among CD4-bearing T cells. This results in progressive defects in cellular immunity that may predispose to certain types of infection, including fungal infections. In one case-control analysis[24] the risk of developing disseminated candidiasis was markedly increased (28% versus 3%; $P=0.003$) in LVAD recipients as compared with control patients who received medical management and no LVAD placement. Moreover, the LVAD recipients had cutaneous anergy to intradermally injected recall antigens and lower T-cell proliferative responses than control patients did after activation via the T-cell receptor complex.[77,78] T cells from LVAD recipients had higher surface expression of CD95 and a higher rate of spontaneous apoptosis than did those of control patients.[81,82] CD4 T-cell death increased >3-fold ($P<0.05$) in LVAD recipients compared with only 1.2-fold in controls.[82]

Because of both increased T-cell activation and a diminution of Th1 cytokine-producing CD4 T cells in LVAD recipients, these patients develop B-cell hyperactivity and dysregulated immunoglobulin synthesis by unopposed Th2 cytokines and increased CD40 ligand–CD40 interaction.[80] This may result in the excessive production of a variety of antibodies, including those directed against human leukocyte antigen and phospholipid-related antigens, including panel-reactive antibodies. Detection of these antibodies has been associated with an increased risk of antibody-mediated allograft (cardiac) rejection and has prolonged the waiting time for LVAD recipients to find suitable transplant donors. The use of intravenous gamma-globulin and cyclophosphamide has reduced anti–human leukocyte antigen alloreactivity, shortened transplantation waiting periods, and reduced post-transplantation rejection episodes.[77]

Data from several investigations[73,83–84] suggest that LVAD infection, including persistent bacteremia or fungemia, is not a contraindication to cardiac transplantation. This is an extremely important observation because of the concern that immunosuppressives used for transplantation may exacerbate ongoing or recent infections related to the LVAD. Furthermore, it appears that transplantation is life saving for some patients with aggressive and uncontrollable LVAD infections.

Total Artificial Heart

The total artificial heart perhaps has been the most publicized cardiovascular device. The development of the Jarvik-7 artificial heart was much heralded more than 2 decades ago, but preliminary use of the device was complicated by numerous infectious and noninfectious events.[85–87] Because of this and other factors, interest turned to ventricular assist devices. Nevertheless, less-heralded research activity has continued in the development of a total artificial heart. In January 2001, the US Food and Drug Administration granted permission to Abiomed to begin human trials with the AbioCor artificial heart. This device, which has several advances compared with the Jarvik-7 heart, has been implanted in 10 patients to date (March 10, 2003). The entire device, except for an external battery that is worn on a patient's belt and a lead from it to an electrical inductor coil, is totally implanted. Noteworthy is the fact that none of the initial 7 patients has reportedly suffered an infection related to the device[88]; no data on infection occurrence are available for the remaining 3 patients. Blood-clotting problems and strokes have been more common complications of the current device in use. Clinical trials with the AbioCor artificial heart continue.

Cardiac Suture Line Pledget Infections

Infection of the left ventricular suture line after ventriculotomy is an uncommon but noteworthy complication because it can present as 3 different syndromes: (1) chest wall or epigastric involvement with infection, (2) bronchopulmonary infection, or (3) endocardial infection. Symptoms appeared, on average, 16 months from the time of surgery among patients in one investigation.[89] Chest wall or epigastric involvement can cause chronic draining sinuses, subcutaneous masses, or pain with or without an associated friction rub. Extension of infection to involve the bronchopulmonary system can cause recurrent hemoptysis, bronchiectasis with cough and purulent sputum production, and pneumonia with empyema. Infection of the cardiac suture line with extension to the endocardium can cause bacteremia. Bacteremia can be the sole manifestation of suture line infection or can be associated with other findings suggestive of infective endocarditis, pulmonary infection, or chest wall process.

In an extensive review of cardiac suture line infections[89] that included 25 cases, 24 (96%) had associated infection of pledgets used at the cardiac suture line. Pseudoaneurysms of the left ventricle that were contiguous with the suture line were identified in 15 cases. Staphylococci accounted for the majority of infections. Antibiotic therapy with surgical debridement of infected cardiac suture line sutures and pledgets was required for cure. Six patients (24%) died as a result of infection.

Because onset of symptoms after cardiac surgery is often remote, and in most cases, a well-healed, normal-appearing sternotomy site is present, a diagnosis of cardiac suture line infection may not be considered. Thus, delays in appropriate treatment or complications associated with ill-advised invasive diagnostic or surgical procedures contributed to this relatively high mortality rate. Surgical exploration is often required to secure the correct diagnosis. In some cases, the diagnosis is not made until postmortem examination.

Ventriculoatrial Shunt Infections

Because ventriculoatrial cerebrospinal fluid (CSF) shunts involve prosthetic implants, they are at risk of colonization with microorganisms, and infections in patients with these devices are common. The lack of effective phagocytosis and killing within the CSF, the tendency for bacteria to adhere to foreign implants, and biofilm production from such organisms, such as coagulase-negative staphylococci, lead to pathogen persistence on the ends of the CSF shunts and the circulation of microorganisms within the CSF.[90,91]

The underlying mechanisms of CSF shunt infections include wound or skin breakdown, retrograde infection from

the distal end of the shunt, and hematogenous seeding or colonization of the shunt at the time of insertion.

Complications of vascular CSF shunts include endocarditis and shunt nephritis. Meningitis is rare, and, if present, is more often associated with lumboperitoneal than ventriculoatrial shunts.

At least two thirds of all shunt infections are caused by a *Staphylococcus* species. Externalized devices may have a somewhat higher incidence of Gram-negative bacterial infection. Both aerobic and anaerobic diphtheroids have been commonly associated with shunt infections in recent years. This may be due to an increased recognition of these microorganisms as potential pathogens, rather than contaminants, and to improved microbiological culture techniques. *Propionibacterium acnes*, an anaerobic diphtheroid, is often isolated from CSF and CSF shunts and should not be dismissed as a contaminant, particularly when recovered from multiple CSF cultures obtained from a patient. The encapsulated pathogens frequently associated with meningitis, such as *Streptococcus pneumoniae* and *Haemophilus influenzae* type b, are rarely recovered from CSF shunt infections. Fungal shunt infections, such as with a *Candida* species, are rare and, when seen, are usually recovered from patients with immunocompromised host defenses (such as in patients with leukemia) or are related to prolonged antibiotic use, parenteral hyperalimentation, diabetes mellitus, or corticosteroid use.

Blood cultures should be obtained in patients suspected of having an infection, particularly with ventriculoatrial shunt infections, because the blood may be more frequently positive than cultures of the CSF. CSF or other material collected before beginning antimicrobial therapy should be obtained using strict antiseptic protocols. The CSF and any other material, such as abscess material, should be collected and transported in a container designed for preservation of anaerobic bacteria, such as *P acnes*. The microbiology laboratory should be consulted so that it is aware that an anaerobic organism, such as *P acnes*, is suspected; such cultures of CSF should be incubated for at least 14 days. Surgical removal of the colonized shunt hardware, externalization of the shunt on the distal end, and the use of a ventriculostomy should be considered as important as the use of antimicrobial therapy. Placement of a new shunt should be done only after total resolution of the infection.

The antibiotic therapy should be designed with the infecting pathogen and complications in mind. There are 2 essential principles in choosing antibiotics: bactericidal activity of the antibiotic and the ability to penetrate the CSF spaces. Intraventricular administration of antibiotics may be necessary when the infection is unresponsive or resistant to systemic antibiotics or when the antibiotic of choice is not bactericidal. The total duration of antimicrobial treatment may vary from 4 to 8 weeks after removal of the shunt according to the severity of the infection and should continue for a few weeks after insertion of a new CSF shunt.

Devices for Patent Ductus Arteriosus, Atrial Septal Defect, and Ventricular Septal Defect Occlusion

During the past 2 decades, the nonsurgical treatment of congenital heart defects with therapeutic cardiac catheterization has become increasingly accepted as a management option. In particular, device placements for patent ductus arteriosus, arteriovenous fistulae, and, more recently, secundum atrial septal defect have become widespread.[92–94] Therapeutic catheterization for selected ventricular septal defects also is gaining acceptance.[95]

In general, complications from use of approved devices for these purposes are exceedingly rare, and infectious complications are even less frequent.[92,96–98] An animal model has demonstrated the risk of infection after coil occlusion of patent ductus arteriosus.[99] All case reports of infection have required surgery for device removal as part of the treatment program. The treatment is the same regardless of type of device infection. There have been no reported fatalities.

Specific Devices—Arterial

Peripheral Vascular Stents

The use of endovascular stents has increased dramatically over the past decade. Stents are deployed in >50% of cases during percutaneous angioplasty procedures for the treatment of sequelae of atherosclerosis. It has been estimated that >400 000 patients each year in the United States undergo stent placement.[100] Stent infection, however, is rare; one medical center estimated an incidence between 1993 and 2000 of <1 in 10 000 cases.[100] When they occur, however, stent infections can cause severe complications,[101] including pseudo- and mycotic aneurysms, abscess formation, arterial necrosis, septic emboli, refractory sepsis, need for amputation, and death.

Most endovascular stent infections occur early (≤4 weeks) after stent placement.[102] *S aureus* has been identified as a pathogen[101,102] in the large majority of cases and is recovered from blood and operative specimen cultures. CT scanning and angiography have been useful in suggesting a diagnosis of endovascular stent infection by showing fluid and inflammatory reaction around the stent.

Excision with extra-anatomic revascularization for infected stents is the treatment of choice and is combined with parenteral antibiotic therapy. For patients with serious underlying medical and/or surgical conditions in whom surgical intervention is not feasible, long-term suppressive antibiotic treatment has been used after initial induction therapy of several weeks' duration to prevent infection relapse.[102]

Primary prophylaxis for stent placement is not routinely advocated because the overall infection risk is extremely low. Although not yet analyzed statistically, there are purported risk factors for endovascular stent infection, and a consideration for the administration of primary prophylaxis seems reasonable if these risk factors are present. Purported risk factors[102,103] include prolonged use of an indwelling catheter or sheath or reuse of the same sheath after 24 hours (eg, during administration and follow-up of thrombolytic therapy), local hematoma formation, multiple interventions on the same or adjacent sites, prolonged procedural time, and use of the same femoral artery for vascular access within 1 week of a prior catheterization.

Secondary prophylaxis is unnecessary because arterial wall incorporation of the stent appears protective in animal infection model work.[104,105] In addition, dental, respiratory, gas-

trointestinal, or genitourinary procedures have not been implicated as causes of bacteremia that have accounted for stent infections.

Prosthetic Vascular Grafts

Infection of a vascular graft is a potentially limb- and life-threatening complication. Infection complicating homograft use was first reported 4 decades ago and has occurred more recently with the engraftment of prosthetic devices. The long-term (≥5 years) incidence of prosthetic vascular graft infection is between 1% and 6%.[106] Infection risk varies with the location of the prosthetic graft. The risk of infection for aortic grafts limited to the abdomen is 1% or less; the incidence rates for aortofemoral and infrainguinal grafts that originate in the groin are 1.5% to 2% and up to 6%, respectively.[107–110]

Infection is thought to occur in the intraoperative or perioperative setting in the majority of infections. Because of this, infection presentation within 2 months of prosthetic graft placement is commonplace.[109] The virulence of the infecting organism may also impact timing of infection presentation. In particular, bacteria, such as coagulase-negative staphylococci, may contaminate the graft in the perioperative period and may not cause symptoms of infection for 6 months or longer after graft placement.[110]

Several risk factors have been identified for vascular graft infection and include groin incisions, emergent surgery, history of multiple invasive interventions before or after graft placement, and contiguous infection in the graft area. Immunologic and other disorders of the host are also considered risk factors for graft infection and include diabetes mellitus, chronic renal disease, obesity, and immunocompromised conditions that predispose to disseminated fungal infections.[107]

The clinical presentation of prosthetic graft infection can vary from a classic picture to a nonspecific complex of signs and symptoms that may leave the correct diagnosis in question until the time of surgical exploration. Infections that involve an extremity, such as the femoral component of an aortic prosthetic graft, tend to present with focal inflammatory changes suggestive of infection. In contrast, infection of intracavitary graft locations may present with nonspecific findings and be more difficult to diagnose.[111] This difficulty is only magnified when infection presentation occurs years after graft placement. Gastrointestinal bleeding due to aortoenteric fistula formation or erosion is seen in a minority of patients with aortic graft infection, and its occurrence dictates an evaluation for graft infection.

Radiological and nuclear medicine procedures have been extremely helpful in supporting a diagnosis of intracavitary graft infection. Much of the experience has included CT scanning in patients with possible aortic graft infections. Reported sensitivity and specificity of this diagnostic modality have been 94% and 85%, respectively.[108] MRI also has good sensitivity (85%) and specificity (100%). The specificity of indium white blood cell and gallium scanning appears lower than that reported for CT scanning or MRI.

Management of vascular graft infections has become complex and varies, to some degree, according to the expertise of the local vascular surgeons. Bunt[112] has outlined 4 tenets that are central to surgical management of graft infections and include: (1) excision of the graft as a foreign body that can potentiate infection; (2) wide and complete debridement of devitalized, infected tissue to provide a clean wound in which healing may occur; (3) maintain or establish vascular flow to the distal bed; and (4) institute intensive and prolonged antibiotic coverage to reduce sepsis and prevent secondary graft infection. Individual medical centers have recognized these 4 principles and have adopted a variety of treatment approaches to vascular graft infection[106–108,112–118] that go beyond the scope of discussion for this document.

Hemodialysis Prosthetic Vascular Grafts

Graft infections used for vascular access in hemodialysis patients deserve additional comment. These patients are unique in their increased risk of vascular graft infection for several reasons, which include an immunocompromised state, repetitive needle puncture at the graft site for hemodialysis access, and an increased carriage of *S aureus*.

Data from the initial report[113–119] of a national surveillance system created by the Centers for Disease Control and Prevention to monitor infection in outpatient hemodialysis patients demonstrate the proclivity for vascular access site infection. The overall vascular access site infection rate was 3.2 per 100 patient-months. This rate was based on infections of synthetic grafts, native arteriovenous fistulas, and cuffed and noncuffed catheters. The infection rate of 1.36 for synthetic arteriovascular grafts was higher than for native arteriovenous fistulas (0.56) and less than that for cuffed (8.42) and noncuffed (11.98) catheters. Among pathogens causing access-related bacteremias in patients with fistulas or grafts, 53% were *S aureus*, and 20.3% were coagulase-negative staphylococci.

As with other types of vascular graft infections, management issues are complex, with the prevailing concerns of availability of new graft sites if an infected graft has to be removed for attempted infection cure. Also, old, nonfunctioning hemodialysis arteriovenous grafts can harbor potential pathogens that may, at some later date, produce septic complications.[120] Treatment algorithms have been devised to assist in management of these treatment conundrums.[121]

The recovery of several different multidrug-resistant Gram-positive cocci, including methicillin-resistant *S aureus*, vancomycin-resistant enterococci, linezolid-resistant *S aureus*, and *S aureus* with reduced susceptibility to vancomycin from chronic hemodialysis patients, makes treatment even more difficult.[122] Because of the repetitive exposure to antibiotics and clinical environments conducive to cross-transmission of multidrug-resistant bacteria, chronic hemodialysis patients have been among the first and most heavily impacted patient populations by these microorganisms. Perhaps the worst-case scenario is the recovery of *S aureus* that is fully resistant to vancomycin. That has just recently been described[123] in a patient who had undergone chronic hemodialysis, had an infected arteriovenous hemodialysis graft due to methicillin-resistant *S aureus*, and later developed an exit site infection of a temporary hemodialysis catheter caused by vancomycin-resistant *S aureus*.

Intra-Aortic Balloon Counterpulsation Catheters

The intra-aortic balloon pump, the most commonly employed mechanical cardiac support device, is utilized in medically refractory unstable angina,[124] cardiogenic shock,[125–127] or preoperative hemodynamic instability.[128] For nearly 20 years after its introduction into clinical practice, surgical insertion and removal were required. The development of a percutaneous technique in 1980[129] led to a rapid method for insertion of this device, usually under fluoroscopic guidance, albeit with a higher associated vascular complication rate.[130]

Infection resulting solely from intra-aortic balloon therapy is an uncommon complication. Local wound infections have been reported to occur in up to 5% of patients and bacteremia in up to 2.2%.[131–133] Most cases of bacteremia appear to be related to spread from a colonized or infected insertion site. In many series, local wound infections necessitate drainage, debridement, irrigation, and antibiotics.[134,135]

Several factors have been implicated in the genesis of intra-aortic balloon pump–related infections. Improper preparation and contamination of the femoral area, especially in obese patients, may lead to a higher incidence of infection, particularly with surgical insertions. The setting of the intra-aortic balloon procedure also influences the risk of infectious complications. In one series, the highest incidence of infection occurred with insertions performed in the coronary care unit or surgical intensive care unit (26% of patients with infections), particularly if the insertion was performed on an emergency basis. In the same series, the lowest incidence occurred with insertions performed in the operating room or cardiac catheterization laboratory (12% and 17% of patients with infections, respectively).[135] This discrepancy may be due particularly to the sterility of the setting as well as to the clinical acuity of the patient. It should be noted that patients undergoing intra-aortic balloon support usually have 2 or more intravascular monitoring lines in addition to the balloon pump. The presence of these lines is an additional factor in the frequency of fever and bacteremia.[136]

As expected, duration of cardiac support with the intra-aortic balloon pump is directly related to the rate of infection.[133] The rate of local wound infection did not increase with the increasing duration of balloon pumping in one study; however, the frequency of fever and bacteremia did.[134] The route of intra-aortic balloon insertion is also related to the incidence of infection. Most series, which compared surgical versus percutaneous techniques, reported a higher incidence of infection associated with the surgical procedure.[137] Finally, in one series, *Pseudomonas cepacia* bacteremia was associated with a contaminated water reservoir in the intra-aortic balloon pump.[138]

Diagnosis of intra-aortic balloon pump–related sepsis is usually speculative unless the organism detected in the blood is also detected at the wound site or tip of the balloon catheter. Treatment consists of appropriate antibiotics and local wound care in addition to removal of the intra-aortic balloon pump if feasible. Prevention of intra-aortic balloon pump–related infection is enhanced by meticulous insertion technique whenever possible. Routine use of antibiotic prophylaxis is not commonly practiced.

Coronary Angiography and Percutaneous Coronary Artery Intervention

In the past 5 decades, there has been a continuous growth in the performance of both diagnostic coronary angiography and coronary angioplasty procedures. It was estimated that by the end of 2002, ≈900 000 percutaneous coronary interventional procedures were performed annually worldwide, and stents were used in 80% to 85% of procedures. This section addresses infections associated with both performing angiography and the devices implanted during the procedure. It is particularly noteworthy that although percutaneous revascularization has been extended to older patients with more complex coronary anatomy and comorbid disease, the overall incidence of infection-related complications of the procedure remains exceedingly low. In fact, phlebitis, fever, local infection, and bacteremia occur in <1% of all procedures.[139] Furthermore, in a large series of patients undergoing cardiac catheterization between 1991 and 1998, bacteremia occurred in 0.11% at a median of 1.7 days after the procedure.[140] In a similar series of 4217 patients undergoing coronary angioplasty procedures, angioplasty-related bacteremia occurred in 0.64% of patients, and septic complications (femoral artery mycotic aneurysm, septic arthritis, and septic thrombosis) occurred in 0.24%.[141]

Fever occurs rarely and is usually transient. It may represent a pyrogen reaction, allergy to contrast agents, or systemic reaction to local phlebitis or infection. Bacterial endocarditis as a complication of cardiac catheterization is exceedingly rare, and antibiotic prophylaxis is not routinely used.

Pyrogen reactions result from the introduction of foreign protein, endotoxin, or other antigenically active substances into the blood.[142] A typical reaction consists of rigors with subsequent development of fever and may follow intravascular injection or angiography by intervals ranging from 1 to 60 minutes. Rigors can be severe, and temperatures in excess of 102°F may be seen. Interestingly, clinical manifestations often respond to small doses of intravenous morphine. Catheterization should be promptly discontinued with the development of such reactions until the source of the pyrogenic material is found. Fortunately, the incidence of pyrogen reactions has been substantially reduced in recent years with the increased use of disposable catheters, stopcocks, and other equipment. However, careful cleaning and preparation of catheters and instruments with the appropriate sterilization techniques are all that is required to minimize the occurrence of these reactions.

Several factors have been implicated in the genesis of diagnostic and interventional catheterization-related infection. Access site location has played a role in the past. Brachial artery access has been associated with a 10-fold higher incidence of infectious complications. This was due to a brachial cutdown approach, which is used today in <10% of patients who undergo interventional catheterization.[139] Certainly, contamination of the sterile field by the patient or operator is exceedingly rare but can occur.[143,144] Repeat puncture of the ipsilateral femoral artery and leaving indwelling femoral artery sheaths for several days after the procedure have been associated with an increased incidence of infec-

tion.[145] Indwelling sheaths are usually connected to a pressurized heparin solution, which also increases the risk of local infection and/or bacteremia.[144] In one study, older age and recent congestive heart failure were independent predictors of postprocedural bacteremia.[140] An increased risk of infection with the use of any of a variety of interventional devices, including atherectomy devices, lasers, thermal devices, and angioplasty devices, has not been demonstrated.

Treatment of catheterization-related infection consists of antibiotic therapy and local wound care. Although most of the infections are due to staphylococci, Gram-negative bacilli were detected in the blood of 68% of bacteremic patients in one study.[140] Therefore, patients in whom sepsis develops after these procedures should be initially treated with empiric antibiotics that are effective against multidrug-resistant Gram-positive cocci and Gram-negative bacilli. CT scanning or angiography should be considered for patients with persistent sepsis, septic emboli, and abdominal flank pain. Infected access site aneurysms may require resection or ligation because of the propensity of these aneurysms to rupture.[143]

Prevention strategies consist of use of meticulous sterile technique, avoidance of access through endovascular grafts where possible, and avoidance of femoral artery access ipsilateral to a prosthetic hip. The use of reused or sterilized catheters should be minimized. Contralateral puncture of the femoral artery for repeat procedures, particularly if a closure device has been recently used, should be performed, and the use of indwelling catheters after the procedure minimized wherever possible.

Coronary Artery Stents

Infections specifically related to the use of intracoronary stents, although also exceedingly rare, are associated with significant morbidity and mortality.[146] In addition to contamination of the stent at the time of delivery, transient bacteremia from various causes such as skin flora via access site hematomas, pseudoaneurysms, and delayed bleeding is theorized to result in infection at the site of stent deployment. Endothelialization of the stent struts may be important in the prevention of stent infections.

To date, there are 5 reported cases of intracoronary stent infection.[147–151] The incubation period ranged between 4 days and 4 weeks, and the responsible organism was either *S aureus* (n=3) or *P aeruginosa* (n=2).[146] Associated findings consisted of local abscess formation, suppurative pancarditis, and pericardial empyema. Mortality was high, with death occurring in 3 of the 5 patients.

The optimal management strategy and timing of surgical intervention for patients with infected coronary stents are unknown. Despite the usual practice of debridement and removal of the foreign body, this approach may not be necessary and can be problematic. After removal of the intracoronary stent and resection of the coronary artery segment, it is unclear whether coronary artery bypass grafting should be performed in the same setting. The incidence of late aneurysmal transformation after intracoronary stent infections is not known but has been shown to occur after treatment of infected stents in peripheral vessels.[100] Because aneurysms can develop in the absence of symptoms and their occurrence is difficult to predict, imaging studies should be done serially.

Vascular Closure Devices

Hemostasis of the femoral artery puncture site after catheterization has been achieved by 3 methods: manual compression, compression devices, and percutaneous arterial closure devices. Five hemostatic puncture closure devices have been approved by the US Food and Drug Administration for use in this country[152] and have gained rapid acceptance over the past few years. These devices are favored over manual compression or compression devices because they decrease the time to hemostasis and to ambulation and are more comfortable for patients. This has led to an earlier hospital discharge. The available vascular closure devices vary in complexity and in design, with material placed intravascularly with some devices and extravascularly in others. The enthusiastic acceptance of these devices has been tempered by a growing number of reports that indicate that (1) infectious complications are more common with hemostatic puncture closure devices than with manual compression and (2) infectious complications are more severe, more difficult to treat, and may require surgical intervention for attempted cure of infection.[152–158] The pathogen most often isolated in these infections is *S aureus,* and methicillin resistance among the strains has been described. The risk may be highest among diabetic patients, and the prophylactic use of a broad-spectrum antibiotic is generally used with device placement in these patients. It is also advocated by some when a prosthetic graft is used for vascular access and placement of a closure device.

Dacron Carotid Patches

Reports describing synthetic carotid patch infection are scarce. Two case series[159,160] describe 10 patients with Dacron graft closure of carotid endarterectomy who subsequently developed patch infections. The incidence of infection was calculated in one of the case series to be 0.5% of 1258 carotid endarterectomies and 1.8% of 340 synthetic carotid patches placed. Primary prophylaxis had been used perioperatively among these patients on an arbitrary basis.

Patients developed local (cervical) evidence of infection, and in 7 of the 10 cases, the diagnosis was made within 2 months of patch placement. Viridans group streptococci and staphylococcal species were identified as pathogens in 5 and 4 cases, respectively; in one case, no organism was isolated. It is noteworthy that all 5 infections due to viridans group streptococci occurred acutely (≤32 days) after carotid patch placement and appeared to represent surgical site infections.

Surgical intervention was required in each case, and the Dacron patch was removed in 8 cases.[159] No standard antibiotic regimen or duration was used, and none of the 10 patients suffered relapsing infection.

Specific Device—Venous

Vena Caval Filters

Vena caval filters have been in use for almost 3 decades, and 10 filters have been available commercially in the United States. Although a variety of noninfectious complications

have been described[161] with both temporary and permanent filters, infection of these devices is extremely rare. Proven[162,163] and suspected[32,164] vena caval filter infections have been described in only 5 cases. Staphylococcal species accounted for all 5 infections, and 4 of the infected patients developed bacteremia. Two cases were complicated by lumbar spondylodiscitis. Apparent cure of infection was achieved in 3 cases after device removal.[162,163] Of the remaining 2 cases, 1 patient died of sepsis likely related to vena caval device infection,[164] and the other survived infection without device removal because long-term suppressive antibiotic therapy was administered.[32]

In at least one case,[165] a temporary vena caval filter was used to prevent septic pulmonary embolism. In that case, a patient had septic thrombophlebitis of a femoral vein and was to undergo surgical thrombectomy. A temporary caval filter was placed preoperatively and left in place for 4 days after surgery; an infected thrombus was captured in the filter.

Conclusions

The development of medical devices has greatly enhanced our ability to care for patients with cardiovascular diseases. The use of these devices has not only extended the life span of patients, but also has improved quality of life. For some patients, the benefits of device availability are not fully realized because of complicating device infection. Moreover, these infections are often severe and, in some cases, life threatening. Cure of infection may be difficult to achieve if removal of the infected device is not a treatment option. Thus, future developments should be directed at designing nonvalvular, cardiovascular devices that are more resistant to infection and identifying antimicrobial agents that have enhanced activity in clearing infection from these indwelling medical devices. Methyl-silicone surface layers that are under development may minimize the accumulation of platelets, fibrinogen, and white blood cells, thereby reducing the mass of debris that is an excellent substrate for growth of microorganisms on biomaterials. Another exciting aspect of infection prevention is the expected future availability of staphylococcal vaccines, which would make preoperative use of active or passive immunization feasible. Cardiovascular device infections will continue to present critical clinical challenges that demand vigilance and attention to changing materials, design, and patient characteristics for best outcomes.

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