Endocarditis
Diagnosis and Management
Endocarditis
Infection remains the number one killer worldwide. Nevertheless, it is the expectation that bacterial infections can be eliminated with antibiotics. Unfortunately, there remain infections due to bacteria that are difficult to detect and difficult to reach, because of minimal blood supply, with even the most potent of antibiotics. One of the diseases in this category is infections that initiate on the inner lining of a vital organ, the heart. These infections are referred to as endocarditis since they involve the endocardium, the inner lining of the heart and valves. The initial site of infection is generally in areas exposed to mechanical trauma or prosthetic device. Unfortunately the damage to the heart if not treated can be fatal and often survival requires surgical replacement of one of the valves. Despite the tremendous array of antibiotics and the marked increase in potency of these drugs to eradicate bacterial infection, the efficacy of treating the relatively avascular lining of the heart or its valvular apparatus often eludes the desired effect. This is further complicated by the changing substrate for bacterial endocarditis, namely, artificial valves and devices and the increasing number of individuals who are imuno-suppressed because of drug use, human immuno deficiency virus infections or other debilitating conditions. Endocarditis due to bacteria and other agents remains a continuing threat as well as a challenge in terms of diagnosis, management and treatment.

Drs Chan and Embil have brought together the expertise of pathologists, infectious disease experts, cardiologists, pharmacologists and surgeons to provide a comprehensive approach to the problem of endocarditis. The book is organized to include a chapter on the pertinent pathology followed by population studies. The diagnostic section is extensive, comprehensive and very clearly written so that both medical and paramedical personnel can appreciate the armamentarium and its application. The management section is broad based to include treatment of the acute and chronic forms as well as potential sequelae that may occur. Echocardiography has become a major tool in the management of endocarditis and transesophageal echocardiography is now essential in the diagnosis and management of suspected prosthetic valve endocarditis. The role of echocardiography is critically assessed in several chapters dealing with specific clinical situations. The chapters reflect the authors’ first-hand experience in dealing with endocarditis. The book in essence brings together the most current and evidence-based approaches as practiced by a group of experts who are intimately involved in the management of this disease.

In a world in which longevity is sought by all and lifespan has doubled just in the past century, it is expected that bacterial infections will not rob us of this expanding lifespan. The fact that they can and do in today’s world of modern technology and ever revolving therapies remains a sobering thought. This book is an example of the thoughtful analysis that is required if we are to prevail in our long battle with serious infections such as endocarditis. It is a gem for the student, the teacher and the practitioner.

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Despite advances in medical and surgical treatments, infective endocarditis continues to be an important clinical problem. It has an in-hospital mortality of 10–20%, and many patients will require valve surgery during long-term follow-up. The diagnosis is difficult since it is based on a constellation of findings and none of the clinical findings alone is pathognomonic. Unequivocal diagnosis is often made only at surgery or autopsy.

Our aim is to provide an up-to-date approach to the diagnosis and management of endocarditis based on a critical analysis of recent studies. The book is structured in a format that is easy to follow, clinically relevant, and evidence-based. Key points are listed at the end of each chapter for quick review. It is divided into three sections. The first section provides a comprehensive review of the basic principles underlying the management of endocarditis. In addition to chapters on etiologic agents and pathologic findings, the changing epidemiology and the vexing issue of antibiotic prophylaxis are discussed. The second section presents the clinical principles underlying the diagnosis and treatment approaches, both medical and surgical. The role of transthoracic and transesophageal echocardiography is discussed in detail, particularly in relation to false-positive and false-negative test results. The third section focuses on difficult clinical scenarios frequently encountered in patients with this disease, including culture-negative endocarditis, prosthetic valve endocarditis, natural history and management of perivalvular abscess, systemic embolism, and etiologies and treatments of neurologic events. The practical clinical approach of this section is underscored by the inclusion of an illustrative case in each of the clinical chapters in the book.

We sincerely hope that this book will serve as an important source of clinical information on diagnosis and management of endocarditis that is useful to all practitioners involved in the care of these critically ill patients.

We would like to thank all the authors for their thoughtful and erudite contributions covering the protean facets of this challenging disease. We are indebted to our colleagues, past and present, for their support and inspiration. Finally, we would like to express our sincere appreciation to our families for their understanding, patience and encouragement without which this text would not have become a reality.

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Case Study

Alfred Reinhart was born in 1907 with a brilliant mind. He contracted rheumatic fever at age 13 and was hospitalized at Peter Bent Brigham Hospital in Boston. Despite losing a year of school, he excelled in his studies. He was admitted to Harvard College at age 17 and subsequently to Harvard Medical School in 1928 at age 21. Rheumatic fever left him with severe aortic insufficiency and for about 10 years he had 0 diastolic blood pressure. His own onset of endocarditis, caused by *Streptococcus viridans*, was recognized by him in May 1931, many months before the diagnosis was accepted by his treating physicians. He faced this “incurable” disease with dignity and went on to provide a vivid and detailed chronicle of his symptoms.

The following is his description of extrasystoles, which troubled him greatly [1]:

The extrasystole has always affected me as if it were a cannon ball, shot point blank at my brain. The sensation is that of a terrific explosion, occurring within the narrow and limited confines of a calcified skull, which refuses to yield to the compressive force. It is like an irresistible force against an immovable object. Most of the time I am helpless before it and simply wait patiently in terror until the ordeal has passed.

Reinhart was convinced he had endocarditis when he noticed petechiae on his wrist [1]:

At any rate, at approximately one-quarter to twelve that night, I remember distinctly getting up from my chair and from the table, where my books lay, and taking off my suit coat. No sooner had I removed the left arm of my coat, than there was on the ventral aspect of my left wrist a sight which I never shall forget until I die. There greeted my eyes about fifteen or twenty bright red, slightly raised, hemorrhagic spots about 1 millimeter in diameter which did not fade on pressure and which stood defiant, as if they were challenging the very gods of Olympus. I had never seen such a sight before, I have never seen such a sight since, and I hope I shall never see such a sight again. I took one glance at the pretty little collection of spots and turned to my sister-in-law, who was standing nearby, and calmly said, “I shall be dead within six months.”

He died of endocarditis in October 1931, after suffering complications including splenic infarcts, retroperitoneal hemorrhage, embolic stroke, subarachnoid hemorrhage, and pulmonary edema.

The case of Alfred Reinhart illustrates many of the protean manifestations of endocarditis, vividly described by a keen observer with medical knowledge. Despite major advances in the diagnosis and treatment of endocarditis since Reinhart’s death, endocarditis remains an elusive diagnosis, and the complications which afflicted Reinhart are still observed today.

Historical Perspectives

Historical perspectives are fraught with interpretation and bias. For this author, particular points of interest include recollections and reminiscence from almost 50 years of medical learning and practice, as an observer to both the science and the management of endocarditis and the personal triumphs and failures in the care of patients with endocarditis. Although these biases will be apparent in this review, my goal is to
provide my perspective on what many regard as the most fascinating of infectious diseases.

Several authors attribute the initial description to clinicians and pathologists in the 17th and 18th centuries who described the clinical course and autopsies in patients who in retrospect almost certainly had bacterial endocarditis. This includes Rivierins in 1646, Lancisi in 1707, Glynn in 1749, Morgagni in 1769, and Baillie in 1793 [2]. Baillie clearly differentiated rheumatic endocarditis from what we now know as bacterial endocarditis [3]. Corvisart in 1806 described the “warty” lesions on heart valves and some of these appear, in retrospect, to have been bacterial vegetations [4].

Over the next 75 years, however, rheumatic endocarditis and bacterial endocarditis were not clearly differentiated clinically or pathologically. In 1852 Kirkes was the first to describe emboli arising from heart valves in cerebral, renal, splenic and other arteries [5]. Subsequently Virchow and Beckmann each described embolic phenomena and showed that they contained elements which appeared to be bacteria [6,7]. Specifically, Heiberg described chains of cocci in vegetation [8].

In 1859 Quinquaud used the term “chronic” to describe a patient and this allowed subacute bacterial endocarditis to be differentiated from acute [9]. Cayley in 1877 first used the term “infective endocarditis” and this replaced the earlier term “ulcerative endocarditis” [10]. A major advance occurred when Osler in his Gulstonian Lecture in 1885 reported on the clinical course and outcome of 209 cases [11]. He first identified the tendency of bacteria to localize on “diseased valves.” He also was the first to mention the importance of bacterial culture.

Meanwhile in Paris, Jaccoud had described endocarditis, and subsequently in France it is often referred to as “Jaccoud’s disease” [12]. The long duration of the illness and its subacute presentation was emphasized by both Osler and Jaccoud [11,12].

Numerous other individuals have made important contributions. At the end of the 19th century, the clinical course of endocarditis and its microbial etiology were described fully [11–15]. Thayer and Blumer recovered gonococci in the bloodstream of a patient with endocarditis in 1895 and subsequently reviewed a 100 cases of gonococcal endocarditis [13]. Lenhartz introduced material from a vegetative lesion into the urethra of a male patient and produced classical gonococcal urethritis [14]. Schott-
heart failure, 3 from cerebral emboli, and 2 from renal failure. An additional 10% died between one and three years, primarily of heart failure. The risk of reinfection/year was about 2%.

Huge advances have occurred in the diagnosis and management of bacterial endocarditis during the past 40 years and this history is documented within the remaining chapters in this book. The important of enterococcal, staphylococcal, and fastidious Gram-negative rod endocarditis have all been recognized, and strategies for early diagnosis and treatment are now routine in most centers. The Duke criteria for diagnosis and its continued modification has made the diagnosis more precise [25]. The diagnosis and management of prosthetic valve infections have also become an important part of the overall management of endocarditis. The appropriate timing for surgical interventions has also become more evidence based.

The role of echocardiography has markedly changed the management of bacterial endocarditis and given us a tool that has enabled more sensitive and specific diagnosis to occur. Today it is difficult to envision management of endocarditis without access to this technology. In particular, transesophageal echocardiography has become routine for excluding this diagnosis in patients with bacteremia, particularly with staphylococci [26].

Recent advances have enabled the diagnosis of very fastidious microorganisms, including *Coxiella burnetii*, Bartonella sp., and others to now occur with both serologic and cultural tests [27]. Infective endocarditis of unknown etiology is now less common due to continued improvements in microbial diagnosis particularly with the advent of nucleic technologies.

The prevention of endocarditis remains controversial and largely expert consensus-based rather than based on solid scientific evidence. Our current dilemmas in this regard are well reviewed in a subsequent chapter.

Infective endocarditis remains a fascinating illness and continues to intrigue us as clinicians and as individuals attempting to understand the complex biologic processes of host and microbe interactions. Certainly there will be more to learn about this disease. However, we have reached the point in 2006 where we can usually precisely diagnose the infection, localize it to a site on the endocardium, treat it with an established effective regimen, manage complications including surgical interventions with a low mortality, and expect a favorable outcome in over 90% of patients. This is remarkable progress over the past six decades since the advent of penicillin.

Only the future will identify further landmark events that will be highlighted by individuals recording their memories of this disease. In the meantime, as physicians seeing patients with a wide variety of symptoms, we must continue to remember the lessons learned, obtain blood cultures before antimicrobial therapy is instituted and be aware of the many, many presentations of this fascinating illness.

**Key Points**

1. There have been major advances in the diagnosis and treatment of endocarditis over the past 60 years.
2. The advent of antibiotics has dramatically improved the prognosis of patients with endocarditis.
3. Endocarditis remains an elusive diagnosis because of its many disguises.
4. Early diagnosis and prompt antibiotic therapy are the most effective way to minimize mortality and morbidity.

**References**

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Case Study

A young man presented to hospital with acutely painful legs. He had chronic osteomyelitis and took chronic oral antibiotics. Leg ischemia was diagnosed and surgical thrombectomy yielded large pale thrombi from both leg arteries. Due to the suspicion of a potential cardiac source, an echocardiogram was performed, which demonstrated aortic and mitral vegetations with valve destruction and an aorto-right atrial fistula. Surgical replacement of the aortic and mitral valves was performed and the intracardiac fistula was closed. The excised leg thrombi and the valve vegetations all grew Aspergillus (Figure 2.10). Antifungal medications were administered. Postoperatively the individual continued to be septic with recurrent strokes and died a few weeks after surgery.

At autopsy the fistula between the aorta and right atrium was still infected (Figure 2.14). The tricuspid valve had new fungal vegetations. The strokes were due to embolic cerebral infarctions, as the intracardiac fungal vegetation had massively re-occurred at the aortic valve prosthesis site partially immobilized the valve discs and parts of the vegetation had embolized to the brain (Figure 2.18).

Infective endocarditis (IE) has many clinical manifestations, not just limited to the heart. Pathology is important in the diagnosis of endocarditis and assessment of valvular and perivalvular complications.

Introduction

Infective endocarditis (IE) may give rise to numerous extracardiac, cardiac, and valvular findings, including infected thrombi (vegetations), sequelae of local tissue destruction, and systemic manifestations including vasculitis, emboli, and ischemic events. This is an appropriate term as the causal organisms may be bacterial, fungal, rickettsial, or even viral or mycoplasmal. Traditionally a distinction between acute and subacute IE was made depending upon the severity and rate of disease progression. This reflected an organism’s virulence and the presence of underlying cardiac disease. With antimicrobial treatment these clinical divisions have little pathologic significance, and it is preferable to think in terms of active, healing, and healed IE [1,2]. The disease is now probably best described by its anatomical location and the organism involved.

Infective endocarditis may arise in normal hearts with normal valves, or more commonly in patients with abnormal cardiac anatomy [2,3]. The most common preexisting cardiac valvular lesions are left-sided ones, including aortic stenosis (especially the congenitally bicuspid aortic valve), aortic insufficiency, and mitral insufficiency [4–6]. Valves damaged by rheumatic fever continue to be the most common type of predisposing cardiac valvular abnormality in developing countries. However, in developed countries degenerative or age-related diseases, including mitral valve prolapse, degenerative