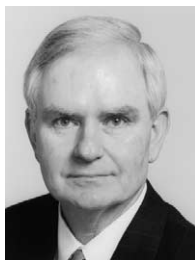




Preface

Infective endocarditis



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Infective endocarditis (IE) has been the subject of more or less continuous study since the 1880s. Substantial knowledge has accumulated over this period, derived from a variety of approaches and methods of investigation. We may think of this progress as occurring in a sequence of overlapping eras, which I have summarized as follows:

- The Oslerian era, 1880–1920
- The Blood Culture era, 1890–
- The Case Studies era, 1900–
- The Treatment era, 1944–
- The Pathogenesis era, 1970–
- The Advanced Diagnostics era, 1975–
- The Informatics era, 2000–

To introduce the present issue of the *Infectious Disease Clinics of North America*, I will comment briefly on how each of these “eras” has contributed to our present understanding of IE, setting the context for the chapters that follow.

The Oslerian era, 1880–1920

Scientific progress in the field of IE during this period was based predominantly upon personal, anecdotal experience. The doyen of all such observers was William Osler. His deep grasp of the essential concepts of

pathology, coupled with meticulous personal clinical observations in the hospital and the autopsy room, allowed him to single-handedly develop an early understanding of IE over a period of only a few years. Osler presented the first major synthesis of his unmatched knowledge of endocarditis in magisterial tones by way of the Gulstonian Lectures of 1885 [1], in which he went so far as to say that

“...the etiological, clinical, and anatomical characters of the disease have been fairly well ascertained, and that we have got about as far towards a full knowledge of the affection as the ordinary means at our disposal will permit...”

In 1885, this statement was perhaps an overreach, even for Osler!

The Blood Culture era, 1890–

Louis Pasteur himself was the first, or at least among the first, to propose that human blood should be cultured to recover pathogenic bacteria. Some of his students attempted such cultures, with mixed results initially. In the early 1900s, however, blood culture was established as the primary laboratory test for diagnosis of IE. By 1905 Thomas Horder was routinely culturing the blood of his endocarditis patients in London. In 1910 Libman and Celler [2] reported on their experience with over 3,000 blood cultures, commenting that for IE “the absolute diagnosis must, for the present, rest on the cultural study of the blood.” Nearly a century later blood culture retains its pre-eminent role in diagnosis of IE. This is clearly emphasized in the monograph by Towns and Reller in Chapter 6, which also offers up-to-date guidelines for best practices in the laboratory diagnosis of IE.

The Case Studies era, 1906–

After the Gulstonian Lectures, others began to collect their own observations on endocarditis, resulting in notable early examples of personal series such as 150 cases reported by Thomas Horder from London in 1909 [3]. Ten cases of chronic infectious endocarditis were published by Osler himself in the same year, 25 years after his Gulstonian Lectures [4]. A stream of publications describing small and large “case series” has continued to flow ever since.

These clinical studies have provided many useful insights, such as the important distinction between rheumatic and bacterial endocarditis, the existence of “bacteria-free” (blood culture negative) cases, and the relationship of dental, urologic, and obstetric interventions to bacteremia and IE, with implications for prophylaxis. Today researchers continue to gain important information from case series, as illustrated by Petti and Fowler in Chapter 9. Their extensive collection of cases of staphylococcal bacteremia has yielded many useful clinical insights. In Chapter 2 Miró and colleagues use

various case series to describe and compare the characteristics of IE in parenteral drug abusers and HIV-infected subjects. For the future productive investigation of IE, however, researchers must progress beyond traditional clinical case studies to harness the power of medical bioinformatics (see below and Chapter 1).

The Treatment era, 1944–

There have been only two truly revolutionary events in the treatment of IE. The first was the introduction of antibiotic therapy. Initial results with penicillin, reported by Chester Keefer in 1943, were disappointing due to inadequate dose and duration of penicillin therapy. Within five years of this report, the basis of successful antibiotic therapy for IE had been established and mortality had decreased from 100% to about 30%. This was success indeed. For the first time cures could be achieved, the annual number of deaths from IE fell, and it seemed possible that the problem of IE could be solved. This ideal has not been achieved, but progress continues. In Chapter 10 Hoen describes management strategies for difficult-to-treat gram-positive bacterial species that can cause IE. Paradoxically, while there are now more antibiotics than ever before, the ever-increasing problem of antibiotic resistance among pathogenic bacteria limits the options for treatment of IE. In Chapter 13 Sexton and Spelman describe strategies to reduce morbidity and improve outcomes in IE patients through expert management of major complications.

The second revolutionary event in therapy for IE was the introduction of intracardiac surgery in the 1960s. Surgery enabled physicians to save the lives of individuals with unusual, difficult-to-treat forms of IE such as early postoperative prosthetic valve endocarditis and IE due to antibiotic-resistant organisms, including fungal IE. Valve replacement surgery reduced long-term morbidity, late deaths from heart failure, and other complications of IE. While surgery has not reduced overall death rates to the same extent as antimicrobial therapy, it is clearly of central importance in the management of 30% to 40% of patients with IE. In Chapter 11 Olaison and Petterson describe the role of modern cardiovascular surgery with special emphasis on indications for surgical intervention. In Chapter 12 Karchmer and Longworth present their approach to the management of post-surgical infections of prosthetic heart valves and other implanted devices—all major, life-threatening complications that are difficult to manage and that jeopardize the success of surgery in some unfortunate patients.

The Pathogenesis era, 1970–

As early as the 1880s some important concepts in pathogenesis that were based upon experimental findings in animal models of IE were reported in

Europe and the United States. For many years following these reports there was relatively little progress in the laboratory study of pathogenesis, with the exception of the work of Rodbard on the influence of blood flow and turbulence on sites of endocardial infection. In the 1970s a resurgence of experimental studies occurred, beginning with classical experimental animal pathology, encompassing many later studies of the effects of antibiotics for treatment and prevention of IE in animals, and progressing more recently to utilization of molecular techniques to answer fundamental questions of pathogenesis. In Chapter 3 Moreillon, Que, and Bayer provide an elegant discussion of the latest understanding of the pathogenesis of endocarditis caused by gram-positive cocci.

The Advanced Diagnostics era, 1975–

After blood culture, advances in the diagnosis of IE have been evolutionary rather than revolutionary, but there has been progress in many areas. Of these, the most important has been the application of ultrasound for intracardiac imaging. Echocardiography has become an essential tool in modern diagnosis of IE and is one of only two major criteria recognized for the clinical diagnosis of IE. Incorporation of specifically defined echocardiographic findings was the key to developing the Duke criteria for improved clinical diagnosis of IE. In Chapter 4 Sachdev, Peterson, and Jollis bring us up to date on the applications of modern imaging for the diagnosis of endocarditis. Another advance in diagnostic methods is the refinement of histologic evaluation of valves and other tissue specimens, as described by Lepidi, Durack, and Raoult in Chapter 5. New or improved methods for detection of intracellular and difficult-to-culture pathogens that cause IE are described by Houpijian and Raoult in Chapter 7. Finally, molecular methods, although not yet in routine use, show promise for the diagnosis of certain forms of IE in the future, as discussed by Lisby, Gutschik, and Durack in Chapter 8.

The Informatics era, 2000–

The next series of advances in IE is likely to come through harnessing the power of information technology. The usefulness of the traditional “case series”—even quite large ones, say 100 to 150 patients—has already become quite limited. We now need one or two large global databases that will eventually comprise thousands of cases of IE. This is the only way we will be able to gain a better understanding of rare causes, special complications, and unusual associations. Only in this way will we be able to attack the issues of timing and choice of surgical and other interventions, problems that do not lend themselves easily to solutions by prospective randomized trials.

Fortunately, the process has recently begun. Members of the International Society for Cardiovascular Infectious Diseases (ISCVID) have formed

a major consortium, the International Collaboration on Endocarditis (ICE), which already comprises contributors at 15 sites in 8 countries. The collation of several existing databases has provided approximately 2500 retrospective cases, while the prospective arm has accumulated more than 500 cases to date. In Chapter 1 Cabell and Abruytn provide an update on this important development. There are many challenges to overcome, including the need for meticulous quality control of the data and scrupulous avoidance of multiple potential varieties of bias. There are logistical difficulties of the project as well, including collection of echocardiograms from many sites, storage and transportation of pathogenic microorganisms, and so forth. This kind of project is the way forward, however, and I believe that the ICE initiative and similar informatics-based approaches will soon be seen as the most important contemporary contribution to the study of IE.

At the beginning of the third millennium, the central challenge posed by IE lies in its continuing high mortality. We understand pathogenesis and we have effective antimicrobials, yet the overall death rate associated with IE remains much the same as forty years ago. This edition of *Infectious Disease Clinics of North America* is dedicated to the eventual success of ongoing efforts to reduce the mortality of IE. With that goal in mind, this monograph is intended to present the latest scientific information on some evolving aspects of IE together with guidelines for best practices in the diagnosis and management of this challenging disease.

References

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