Infective endocarditis

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Historical background

Lazerous Riverius recorded the first case of what is now known as infective endocarditis in 1723. He described a French magistrate with an irregular pulse, oedema, and congestion, who at autopsy had fleshy masses ‘the size of hazelnuts’ obstructing the aortic ostia. Fifty years later Morgani (1769) made the link between infection (fulminating gonorrhoea) and ‘whitish polypus concretions on the upper part of the aortic valve near its borders’.

The clinical picture of endocarditis was first described by Jean Baptiste Bouillard in 1835: ‘fever, an irregular pulse, cardiomegaly (by percussion) and a bellows murmur in the heart’. He gave the disease the name ‘ endocarditis’ or an inflammation of the inner membrane of the heart and fibrous tissues of the valve and was the first to use the term ‘vegetations’ for the valvular lesions.

Winge used the term ‘mycoses endocardi’ for the groups of micro-organisms that he saw when he examined vegetations under the microscope in 1870. In 1886 Wyssecokowitch cultured *Staphylococcus aureus* from an endocardial vegetation. Lenthartz in 1901 was the first to use blood cultures in the diagnosis of endocarditis. ‘Infective endocarditis’ was the term used by Thomas Horder in 1901 to describe the syndrome consisting of (i) the presence of valvular disease, (ii) the occurrence of systemic embolism, and (iii) the discovery of micro-organisms in the bloodstream.

Epidemiology

Infective endocarditis was universally fatal before the advent of antibiotic therapy. Since 1944 deaths from endocarditis have fallen by 80 per cent: about 200 deaths are recorded each year in the United Kingdom, which is probably an underestimate. The true incidence of the condition is unknown, but it is at least 25 cases per 1 000 000 of population. The incidence is greater in men, in those over 65 years of age, and in those with prosthetic heart valves. About 20 per cent of patients with infective endocarditis die and they account for about 0.1 per cent of the total deaths from diseases of the circulatory system (ICD codes 390–429).

Endocarditis does occur in children but is rare, especially in the first decade of life. In the older literature tetralogy of Fallot was the commonest cardiac problem associated with infective endocarditis, but nowadays cardiac surgery is the most likely predisposing cause.

Pathogenesis

Normal vascular endothelium is resistant to microbial infection and very few patients potentially at risk actually develop infective endocarditis. Since low-grade bacteraemia occurs frequently in everyone, a defence mechanism must exist that can eradicate microbes adherent to vegetations. Platelets play a pivotal role in the antimicrobial host defence mechanism and human platelets have been found to contain at least 10 different bactericidal proteins or ‘thrombocidins’.

Damage to the endothelial surface of the heart or blood vessels induces platelet and fibrin deposition, producing a sterile thrombotic vegetation; infective endocarditis is initiated by the binding of microbes, discharged into the general circulation from a peripheral site, to these vegetations. These microbes become encased in further depositions of platelets and fibrin and multiply.

The pathogenesis of infective endocarditis involves complex interactions between microbes and the host defence mechanisms, both circulating and at the site of endothelial damage. An essential step is the activation of the clotting system and the formation of a fibrin clot on the endothelial surface. Experimental evidence suggests that the main pathogens in infective endocarditis (streptococci and staphylococci) can bind to endothelial cells and induce functional changes within these cells, causing monocyte adhesion. The combination of damaged endothelial cells, bacteria, and endothelial-bound monocytes results in the induction of tissue factor-dependent procoagulant activity which initiates clot formation. Polymorphonuclear leucocytes that are recruited to the infected endothelial site subsequently may be involved in the disease progression: probably the contents of lysosomes released by the activated leucocytes cause softening and separation of valve tissue leading to its destruction.

In endocarditis the vegetations are found predominately on the left side of the heart (95 per cent). In a large autopsy series of more than 1000 cases reported over 50 years ago the mitral valve was involved in 86 per cent, the aortic in 55 per cent, the tricuspid in 20 per cent, and the pulmonary valve in only 1 per cent. The predominance of left-sided lesions led to the belief that the higher pressures and velocities encountered in the left side of the heart and the proximal aorta must impose a greater mechanical stress on the valves and endocardium, which in turn leads to local damage.

Endocarditis is classically associated with ‘jet lesions’, where blood flowing from a high pressure area through an orifice to an area of lower pressure produces a high velocity jet. Vegetations are usually found in the lower pressure area, for example on the atrial surface of the mitral valve in mitral regurgitation, or the ventricular surface of the aortic valve in aortic regurgitation. This particular deposition of vegetations has been explained on the basis of the Venturi effect.

Once a vegetation is established it determines the subsequent clinical picture by four basic processes: bacteraemia, local tissue destruction, embolization, and the formation of circulating immune complexes.

Clinical features

Early reports of infective endocarditis described a low-grade febrile illness caused by viridans streptococci from the patient’s mouth in those with chronic rheumatic heart disease. Night sweats, anorexia, and weight loss were followed by the development of splinter haemorrhages and Osler nodes, finger clubbing, and splenomegaly. The infection progressed relentlessly with increasing cachexia and the patient died from cardiac failure or a major embolic episode. The term ‘subacute bacterial endocarditis’ was used to describe this illness.

‘Acute or malignant endocarditis’ described an aggressive form of the disease usually caused by *S. aureus*, or other virulent bacteria.

During the past 50 years there has been a striking change in the pattern of endocarditis. The dramatic decrease in rheumatic fever in developed countries, the use of antibiotics, and the emergence of antibiotic-resistant organisms, together with surgical advances have all contributed to many clinical variants and modes of presentation.

The proportion of patients in developed countries with endocarditis with no known pre-existing cardiac lesion has risen to over 50 per cent. This change is related to both the decline in rheumatic heart disease and to the increase in extracardiac predisposing factors including intravenous narcotic abuse, haemodialysis, and the use of intravascular devices. Prosthetic heart valves are an important predisposing factor and cardiac surgery for complex congenital lesions has increased the lifespan of patients who would previously have died prematurely. The longevity of the populations in developed countries has resulted in an increasing age of patients with infective endocarditis. The mean age has risen from under 40 years before 1940 to between 60 and 70 years today.

Features of a bacteraemic illness

Discharge of the infecting agent into the circulation produces constant bacteraemia, which may present as pyrexia, rigors, malaise, anorexia, headache, confusion, arthralgia, and anaemia. However, some cases of endocarditis may present without fever, particularly in the elderly.

Features of tissue destruction

Endocarditis initially affects valve cusps, leaflets, or chordae tendineae. Tissue destruction results in valvular incompetence, cusp perforation, or rupture of the chordae producing an appropriate cardiac murmur that may change in character during the course of the illness. Large vegetations rarely obstruct a native valve, but mechanical obstruction of prosthetic valves is more common and clinically more difficult to detect. As the infective process progresses it may extend beyond the valve into the paravalvular structures. This is more common in native aortic valve endocarditis than in mitral valve infection. Aortic root abscess is a serious complication and a destructive lesion. When the abscess extends through the aortic wall into other tissues or cavities a fistula may be formed or pseudo-aneurysms produced. Involvement of the conducting tissue leads to heart block. Infection of a mechanical valve involves the sewing ring and may lead to valve dehiscence. Endocarditis involving an aortic mechanical valve is often localized to the junction between the sewing ring of the aortic valve and the aortic annulus: a large false aneurysm may develop in this area.

Features of systemic or pulmonary emboli

Fragments of an infected vegetation may be dislodged into the general or pulmonary circulation, depending on the site of the vegetation, producing the emboli that are reported in 20 to 40 per cent of cases; a higher incidence (50 per cent) has been reported in autopsy series. Emboli may lodge in any part of the

circulation and present as a cerebrovascular accident, arterial occlusion of a limb, myocardial infarction, sudden unilateral blindness, or infarction of the spleen or a kidney. In right-heart endocarditis, recurrent septic pulmonary emboli may be misinterpreted as ‘pneumonia’. Mycotic aneurysms arise from embolism of the vasa vasorum weakening the arterial wall: they have been reported in almost 3 per cent of clinical cases, but are found in up to 15 per cent of cases at autopsy. In the cerebral circulation such aneurysms may produce subarachnoid haemorrhage. The popliteal artery is a common site for mycotic aneurysms.

Emboli are characteristic of *S. aureus* infections and large emboli are a feature in HACEK (see below) and fungal endocarditis. Emboli usually occur before or within the first few days after starting antimicrobial therapy. The risk of emboli decreases with time during appropriate antimicrobial treatment. There is no significant difference between mitral valve and aortic valve vegetations with respect to embolization. Vegetation size does not predict systemic embolization, but large vegetations (greater than 10 mm) are associated with a poor outcome overall.

Features of circulating immune complexes

The infected vegetation contains antigens that trigger an immune response. The length of the illness seems to determine the extent of this response; chronic antigenaemia stimulates generalized hypergammaglobulinaemia, so that after several weeks of infection a variety of autoantibodies can be detected. Immune complex deposition may cause many of the extracardiac manifestations of infective endocarditis, but these classic signs are relatively uncommon and are often absent in individual patients.

Splinter haemorrhages

These are found in the nail bed of the fingers, less commonly the toes, and are linear in form (Fig. 1 and Plate 1).

Osler nodes

These transient painful erythematous nodules are found at the ends of fingers and toes and the thenar and hypothenar eminences. An alternative explanation is that Osler nodes are due to minute infected emboli.

Janeway lesions

These irregular painless erythematous macules are found in roughly the same distribution as Osler nodes. They tend to blanche with pressure.

Vasculitic rash

Immunoglobulin and complement deposits are found in the walls of skin capillaries (Fig. 2 and Plate 2). Vasculitis may account for some of the neurological findings in infective endocarditis.

Roth spots

Boat-shaped haemorrhages in the retina are often called Roth spots, but true Roth spots are white retinal exudates that may be surrounded by haemorrhage. They consist of perivascular collections of lymphocytes.

Splenomegaly

Clinical splenomegaly is now less common than reported in the earlier literature. CT scanning of the abdomen shows the spleen to be enlarged in at least 50 per cent of cases and often demonstrates splenic infarcts.

Nephritis

Immune complexes can cause glomerulonephritis, with immunofluoresence demonstrating deposition of immunoglobulins and complement in irregular granular deposits in the glomerular basement membrane and mesangium. Proteinuria, haematuria, and cellular urinary casts may be present.

Arthralgia

The joint manifestations of infective endocarditis may result from immune complex deposition in the synovial membrane.

Other features

Up to 30 per cent of patients with endocarditis present with neurological symptoms; these are most common in staphylococcal infection, in which one-third present with the clinical features of meningitis. Headaches, confusion, and toxic psychosis can be present as well as encephalomyelitis. Cerebral embolism, which may produce a stroke as a result of cerebral infarction, is more characteristic of viridans streptococcal and enterococcal endocarditis. Mycotic aneurysms may rupture causing subarachnoid or intracerebral bleeding. Septic embolism may result in the formation of a cerebral abscess. It is not certain whether some of these neurological manifestations arise from repeated small emboli or from a vasculitic process within the cerebral circulation resulting from immune complex deposition. The cerebrospinal fluid can show an increase in white cells, but is usually sterile on culture, although very occasionally positive in staphylococcal infection.

Immune-mediated glomerulonephritis has been regarded as the typical lesion of infective endocarditis, but this assumption was based on small series pre-dating modern treatment regimens. More recent work indicates that the commonest renal histological finding is infarction, usually septic. Glomerulonephritis is usually vasculitic. Acute postinfective glomerulonephritis and membranoproliferative glomerulonephritis are less common. Circulatory compromise can cause severe renal impairment as a result of acute tubular necrosis or (very rarely) renal cortical necrosis.

Finger clubbing is one of the classic features of infective endocarditis, usually seen after 1 or 2 months of the illness. It is seldom seen now, but remains a useful sign since it rarely occurs in conditions with which infective endocarditis is confused.

Specific types of endocarditis

Prosthetic valve endocarditis

Patients with prosthetic heart valves have a small but constant risk of infective endocarditis, estimated at 0.2 to 1.4 events per 100 patient years. The incidence of prosthetic valve endocarditis is about 3 per cent in the first postoperative year, with the highest risk during the first 3 months. Prosthetic valve endocarditis is five times more common with aortic than mitral prostheses, and may involve mechanical, xenograft, and homograft valves.

Prosthetic valve endocarditis has been classified as early or late according to its temporal relationship to the time of surgery. Early prosthetic valve endocarditis accounts for 30 per cent of cases and usually occurs within 60 days of open heart surgery. It is caused either by contamination of the prosthetic valve at implantation or by perioperative bacteraemia. The commonest organisms are usually coagulase-negative staphylococci.

Late prosthetic valve endocarditis accounts for 70 per cent of cases and usually occurs 60 days or more after surgery. The pathogens are usually those seen in native valve endocarditis with a preponderance of viridans streptococci and staphylococci, but with a higher incidence of other organisms. Some patients with late prosthetic valve endocarditis will have acquired the infection at the time of surgery, but a bacteraemia is usually the principal cause.

Bacteraemia in a patient with a prosthetic valve must always be taken seriously, but it may not always be the result of endocarditis. The clinical picture of prosthetic valve endocarditis is usually fever, malaise, and weakness, but the more classic signs are usually absent. The condition is often insidious and difficult to diagnose clinically. A new murmur may appear and heart failure and embolic phenomena result in a high mortality (20 to 50 per cent). Infection in a mechanical valve is located in the sewing ring; the infection can spread into the host tissues producing annular abscesses, paravalvular leak, and prosthetic dehiscence. Myocardial abscesses can develop as a consequence of an annular abscess with xenograft or homograft valves. Infection usually involves the valve leaflets, resulting in destruction or perforation and consequent valvular incompetence. The infection involves the valve annulus less commonly than with a mechanical prosthesis. Vegetations may cause obstruction with all forms of prosthetic valve.

The diagnosis of prosthetic valve endocarditis requires a high index of clinical suspicion, blood cultures, and transoesophageal echocardiography. This technique is far superior to the transthoracic approach for finding vegetations and identifying periprosthetic spread of the infection. Vegetations are more difficult to identify in patients with mechanical valves than those with bioprostheses.

Right-sided endocarditis

Right-sided infective endocarditis accounts for only 5 per cent of cases overall, but centres that treat large numbers of intravenous drug users will have a higher incidence. The clinical picture differs significantly from left-sided disease. It is usually associated with intravenous drug addiction or indwelling intravascular

devices, and in the former is found particularly in a younger population. *S. aureus* is the commonest pathogen and the tricuspid valve is more commonly affected that the pulmonary. Fever is almost always present and a cardiac murmur is found in 80 per cent of cases. Right-sided endocarditis is associated with septic pulmonary emboli, and the resultant pulmonary infarcts may cavitate. Symptoms include cough, haemoptysis, and pleuritic chest pain, while a chest radiograph shows pulmonary infiltrates often misdiagnosed as 'patches of pneumonia' (Fig. 3). Renal involvement has been described in over half the cases; most commonly abscess formation or diffuse pyelonephritis. Myocarditis is more common in right-sided involvement than left. Peripheral stigmas of infective endocarditis, splenomegaly, and central nervous system involvement are rare, being described in 5 per cent or less of cases. Death is most commonly due to sepsis, rarely to heart failure.

Endocarditis in intravenous drug users

Endocarditis is a serious complication of intravenous drug abuse. The right side of the heart is affected most commonly, but the left may also be involved in a substantial number of patients (37 per cent), and both right and left side in a minority (7 per cent). On the right side the tricuspid valve is affected in 80 per cent of cases, while the mitral and aortic valves are equally infected in left-sided disease. A history of previous heart disease is only found in some 25 per cent of cases. *S. aureus* is responsible for 40 per cent of all cases. Gram-negative bacilli are the next most frequent, with *Pseudomonas aeruginosa* and *Serratia marcescens* accounting for the majority of these. Candida can cause endocarditis in intravenous drug users and polymicrobial endocarditis accounts for 5 per cent of cases.

The skin is the commonest site from which pathogens enter the bloodstream via needles. Gram-negative bacilli are rarely recovered from needles or the drug itself and it has been suggested that these organisms come from tap water, sinks, or lavatory pans.

The clinical picture of drug-associated endocarditis depends on which side of the heart is affected. Right-sided disease is associated with fever, a murmur of tricuspid incompetence, and pulmonary infiltrates on the chest radiography. Left-sided disease behaves like that seen in cases not associated with intravenous drugs, with a high incidence of heart failure, arterial embolism, central nervous system involvement, and peripheral stigmas.

The overall mortality depends on when the patient presents: it is high if they present late and reflects, among other things, the difficulty in dealing with addicts because of their poor compliance and reluctance to discontinue their drug habit. The principles of management are similar to those for patients who do not abuse drugs. The duration of intravenous antibiotics should be at least 4 weeks, but it is usually impossible to do this in practice; while in right-sided endocarditis simple removal of the valve without replacement appears to be the best strategy.

The diagnosis of infective endocarditis

Laboratory diagnosis

Blood culture

This is the most important laboratory investigation in the diagnosis of endocarditis. Isolation of the pathogen enables an effective antibiotic treatment regimen to be devised. Blood cultures should be taken before antibiotics are given; if they have already been given, cultures should still be done, and if possible the giving of further antibiotics delayed for a few days. However, previous antibiotics may render the blood sterile for some time and the chances of recovering the pathogen, particularly when it is a viridans streptococcus, are very low. Much mystique has been attached to the number and timing of blood cultures in cases of suspected endocarditis. What is known is that the bacteraemia is usually constant and that whenever the blood is obtained for culture, and however many sets are taken, in most cases all bottles will grow the pathogen. There are of course rare exceptions when only a small proportion of bottles cultured are positive, and this is one reason why it is conventional to take two or three sets. Another reason for several cultures is to assess the relevance of the common skin contaminants, particularly the coagulase-negative staphylococci but also *Corynebacterium* spp., which can cause endocarditis.

In most laboratories blood culture systems are automated, with continuous monitoring which flags up growth for further investigation. Most cultures become positive within 48 h and after this the chances of isolating the pathogen recede, with the exception of fastidious organisms of the HACEK group (see below) that may take much longer to recover from the blood. In most laboratories blood cultures are incubated for 5 to 7 days, but this may not be long enough for the rare fastidious slow grower. The onus is on the clinical microbiologist or clinician to request prolonged incubation of blood cultures from patients in whom endocarditis is strongly suspected on clinical grounds and echocardiography who have not had previous antibiotics and whose blood cultures are sterile after a week's incubation.

Blood tests

In infective endocarditis an elevated erythrocyte sedimentation rate and C-reactive protein are almost invariable and these inflammatory markers are used most commonly to monitor the activity of the disease. A normochromic normocytic anaemia is often present and a polymorphonuclear leucocytosis is found in the majority of cases. Hypergammaglobulinaemia and a low serum complement may be present, together with a false-positive rheumatoid factor. Circulating immune complexes may be detected.

Dipstick testing of the urine may reveal the presence of proteinuria or haematuria, indicating renal involvement. When haematuria is present the pellet of a centrifuged specimen of urine should be resuspended and examined microscopically for the presence of red cell casts, which clinch the diagnosis of glomerulonephritis in this context.

Serology

Serum antibodies are used to diagnose *Coxiella burnetii* (Q fever), bartonella, and chlamydia endocarditis and should be done in any patient with convincing evidence of endocarditis and negative blood cultures. Candida antibodies are of no diagnostic value.

Echocardiography

In suspected cases of endocarditis echocardiography should be performed as soon as possible and interpreted by an experienced cardiologist. Its principal role is to detect vegetations. Echocardiography is not sufficiently sensitive to allow the clinician to exclude the diagnosis confidently on the basis of a negative result. The sensitivity depends on the size of the vegetations and the time course of the disease. Echocardiography can resolve vegetations as small as 1 to 2 mm, but it is more difficult with prosthetic than native valves, and more difficult with mechanical than biological prostheses.

Vegetations appear as thick, ragged, non-uniform echoes oscillating on or around a cardiac valve or in the path of a regurgitant jet. They do not usually restrict leaflet mobility and exhibit valve-dependent motion. On native valves vegetations are usually attached to the ventricular side of the aortic valve and the atrial side of the mitral and tricuspid valves.

Two-dimensional echocardiography should be employed initially in all cases of suspected endocarditis (Fig. 4). Transoesophageal echocardiography has improved the rate of diagnosis of infective endocarditis over that of transthoracic echocardiography, particularly in the presence of a prosthetic valve. Transoesophageal echocardiography has made it easier to recognize many complications of prosthetic valve endocarditis, such as abscesses, fistulas, and paravalvular leak (Fig. 5). In addition to vegetations, echocardiography may demonstrate indirect signs of valvular integrity, such as excessive systolic expansion of the left atrium in mitral incompetence or fluttering of the anterior leaflet of the mitral valve in aortic incompetence. Ventricular size and contractility are both easily assessed. The diagnosis of right-sided endocarditis has been greatly facilitated by echocardiography, particularly transoesophageal echocardiography. Vegetations, which in general tend to be larger on the right side, can be demonstrated in 80 to 100 per cent of cases.

Vegetations need to be differentiated from other conditions that produce echo density on cardiac valves, including calcification, myxomatous degeneration, and atrial myxoma. Echocardiography does not provide direct information on blood flow, but Doppler echocardiography complements the technique and adds significantly to the diagnosis of valvular function. It is able to diagnose valvular regurgitation with great accuracy.

Criteria for the diagnosis of infective endocarditis

In 1994 Durack and his colleagues introduced criteria for the diagnosis of infective endocarditis that have been accepted as ‘the Duke Criteria’ (Table 1). These include two major criteria (typical blood culture and positive echocardiogram) and six minor criteria (predisposition, fever, vascular

phenomena, immunological phenomena, suggestive echocardiogram, and suggestive microbiological findings). Application of these criteria is used to define three diagnostic categories: definite, possible, or rejected cases of infective endocarditis.

Modifications of the Duke Criteria to increase their sensitivity have been suggested by others. These include the following additional minor criteria: the presence of newly diagnosed clubbing, splenomegaly, splinter haemorrhages and petechias, a high erythrocyte sedimentation rate or a high C- reactive protein, and the presence of central non-feeding lines, peripheral lines, and microscopic haematuria.

Microbiology

While almost any micro-organism can cause infective endocarditis, particularly when this involves a prosthetic valve, certain species do so much more commonly than others and the predominant species involved in the infection have not changed significantly in their incidence in the past three decades. Overall, viridans streptococci and staphylococci account for about two-thirds of all cases. However, endocarditis cannot be considered as a microbiologically homogeneous entity as the incidence of any specific organism depends: (i) on the patient—whether an intravenous drug user or not; (ii) on the valve—whether native or prosthetic; if native whether previously abnormal or not, and if prosthetic whether mechanical or a bioprosthesis, and whether the infection was acquired early or late; and (iii) where (and how) the infection was acquired—whether in the community or (and increasingly these days) in hospital, usually via an infected intravascular device. The more common species encountered will be considered individually.

Streptococci

The genus *Streptococcus* includes species of differing virulence and pathogenicity as well as differing normal habitat in man. It has undergone numerous taxonomic revisions over the past decade or more and the previous dependence on haemolytic activity on blood agar and serological reactions has been superseded in many cases by molecular and chemotaxonomic approaches. Examples of such taxonomic change include the assignment of the faecal streptococci to the genus *Enterococcus*, of *Streptococcus morbillorum* to *Gemella morbillorum*, and of the nutritionally dependent streptococci previously known as *Streptococcus adjacens* and *Streptococcus defectivus* to the genus *Abiotrophia.* There are many other examples, but taxonomic change is of limited interest to clinicians and has no bearing on the management of infection.

Viridans streptococci

For many years it has been conventional to refer to a group of streptococci that produce greening (α-haemolysis) on blood agar as viridans streptococci, indeed many still refer (inaccurately) to a microbe ‘Streptococcus viridans’. While most of these streptococci are virtually specific to the normal oropharyngeal flora and are rarely encountered at other sites, some are not found in the oropharynx at all,

for example *S. bovis*, and others are found at many sites including the oropharynx, for example the milleri group of streptococci. The viridans streptococci are the commonest cause of community-acquired native valve endocarditis and community-acquired late-onset prosthetic endocarditis. The commonest species of the viridans streptococci that are specific to the oropharynx are *S. sanguis*, *S. oralis*, and *S. mutans*, but there are others. Dextran formation may be a virulence factor in these streptococci. Contrary to popular belief they do not require a dental extraction to enter the bloodstream and cause frequent bacteraemias after chewing, tooth brushing, and so on. They are organisms of low virulence and thus usually only infect previously abnormal heart valves. Whereas *S. oralis* and *S. sanguis* are occasionally isolated from blood cultures of patients who do not have endocarditis, the isolation of *S. mutans* from the blood is virtually synonymous with endocarditis.

Streptococcus bovis

This streptococcus, which may appear 'viridans' on blood agar, is part of the normal intestinal flora but may initially be mistaken for an oral streptococcus. In common with the enterococci it bears the Lancefield group D antigen and thus can also be mistaken for *Enterococcus faecalis*, though it is sensitive to penicillin whereas the latter is resistant. There is a significant association between *S. bovis* bacteraemia (and hence endocarditis) and colonic pathology, and any patient with *S. bovis* endocarditis thus warrants appropriate investigation for this. *S. bovis* endocarditis is much less common than that caused by oral streptococci.

Pyogenic streptococci

These organisms, often referred to as β-haemolytic streptococci, cause endocarditis less frequently than the viridans streptococci, but are more aggressive microbes and are likely to affect (and often rapidly destroy) a previously normal valve. The commonest pyogenic streptococcus to cause endocarditis is the Lancefield group B β-haemolytic streptococcus (**GBS**) sometimes referred to as *S. agalactiae*. This organism is found as normal flora in the genital and gastrointestinal tracts. As with *S. aureus*, any patient with community-acquired GBS bacteraemia should be assumed to have infection in bone, joint, or on a heart valve until proved otherwise. Groups C and G β-haemolytic streptococci occasionally cause endocarditis and group A even more rarely. The milleri group of streptococci are best regarded as pyogenic streptococci. These streptococci form part of the normal flora of all mucous membranes and occasionally cause endocarditis, though much more often abscesses at many different sites. The milleri group consists of three species, *S. constellatus*, *S. intermedius*, and *S. anginosus*. Interestingly these streptococci can bear the Lancefield antigens A, C, G, or F (or none); all group F streptococci are milleri but not all milleri are group F.

Streptococcus pneumoniae (pneumococcus)

Pneumococcal endocarditis accounted for about 10 per cent of cases of endocarditis in the preantibiotic era, but is now rarely seen, although it is sometimes diagnosed at autopsy of patients with fatal pneumococcal infection.

The pneumococcus is a virulent pathogen and attacks normal heart valves. Patients with endocarditis generally have pneumonia and sometimes meningitis, the organism originating in the upper respiratory tract.

Enterococci

Enterococci form part of the normal gastrointestinal flora. They are more virulent than viridans streptococci and more resistant to antibiotics. The past decade has seen an increase in enterococcal endocarditis, particularly in the elderly, but this infection is still much less common than that caused by viridans streptococci. While there are many species of enterococci, those causing endocarditis are usually *E. faecalis* and occasionally *E. faecium*. Most cases are community acquired but the infection can be acquired in hospital, sometimes as a result of urological instrumentation. Any patient admitted from the community with *E. faecalis* in the blood should be investigated for endocarditis.

Staphylococci

Staphylococci now account for about a third of cases of community-acquired endocarditis and are the commonest cause of hospital-acquired endocarditis. Most of these staphylococci are *S. aureus*, but an increasing proportion is now due to coagulase-negative staphylococci. All staphylococci are skin organisms and patients become infected from their own skin flora, or in the case of methicillin-resistant *S. aureus* (**MRSA**) from that of others by cross-infection.

Staphylococcus aureus

S. aureus is an important and aggressive pathogen in community-acquired native valve endocarditis. Sometimes a trivial skin lesion can be identified as the source of the organism, but there is often no obvious lesion. *S. aureus*, and increasingly now MRSA, is the commonest cause of hospital-acquired endocarditis. Prosthetic valves can become infected with *S. aureus* both early as result of sternal wound sepsis and late as with native valves. *S. aureus* is the commonest pathogen causing endocarditis in intravenous drug users.

Coagulase-negative staphylococci

Although still regarded by many as pathogens of prosthetic rather than native valves, coagulase-negative staphylococci also cause native valve infection and this has become more common, or certainly more commonly recognized, in the last two decades. The infecting species is most often *S. epidermidis* (*sensu stricto*) but in many reports the designation *S. epidermidis* tends to be used for any unspeciated coagulase-negative staphylococcus. Many other species have been reported in native valve endocarditis including *S. lugdunensis*, *S. simulans*, *S. warneri*, *S. capitis*, *S. caprae*, and *S. sciuri*. Coagulase-negative staphylococci are normal skin flora and different species vary in their distribution throughout the body. As in community-acquired *S. aureus* endocarditis, there is sometimes a presumptive predisposing skin lesion. Most patients have a pre-existing cardiac abnormality. Many of these staphylococci can be as virulent as *S .aureus* and actually share some of the same virulence factors.

Other organisms

A wide variety of organisms account for the small percentage of cases of endocarditis that are not caused by streptococci, staphylococci, or enterococci. Only a few warrant a specific mention here.

HACEK group

These are fastidious slow-growing species that are oropharyngeal commensals and have a predilection for heart valves, such that their presence in blood cultures is virtually synonymous with this infection. The group consists of *Haemophilus aphrophilus/paraphrophilus*, *Actinobacillus actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella kingae*. *A. actinomycetmecomitans* in particular seems more likely to infect prosthetic than native valves. The large vegetations thought to be characteristic of HACEK organisms in native valve infection may be the result of diagnostic delay and prolonged illness rather than any inherent property of the microbes *per se*.

Organisms that cannot be cultured by routine techniques

Endocarditis is a rare (and late) sequel of acute *Coxiella burnetii* (Q fever) infection. Most infections occur in middle-aged men with pre-existing valve disease. The reservoir of the organism is usually sheep or cattle, but the source and mode of transmission in many human cases is unknown. The diagnosis is usually made serologically, although *C. burnetii* can be recovered from the blood and excised valves by special techniques. The disease is almost certainly underdiagnosed and some cases are labelled ‘culture negative’ endocarditis.

Bartonella quintana endocarditis was first recognized in 1995 in homeless alcoholic patients; *Bartonella henselae* infection may be associated with cat or cat flea contact and other species of bartonella have also been described causing endocarditis. Bartonella infection is usually diagnosed by serology, although these bacteria can also be recovered from the blood and excised valves by special culture techniques and their presence detected by polymerase chain reaction (PCR). False-positive serology for *Chlamydia* spp. has been reported with bartonella infections, but *Chlamydia* spp.—and particularly *C. psittaci*—can also cause endocarditis (very rarely); it is possible that some cases attributed to chlamydia in the past on the basis of serology may have been caused by bartonella.

Fungi

Fungal endocarditis is very rare and more likely to occur on prosthetic than native valves, except in intravenous drug users. Most infections are acquired in hospital, when infection at intravascular access sites and broad-spectrum antibiotics predispose to candida infections. *Candida* spp., usually *C. albicans*, are the commonest fungi, but *Aspergillus* spp. and more exotic genera have also been reported. Blood cultures are only likely to be positive with *Candida* spp., and then often only intermittently; for other fungi the diagnosis must be made by serology and culture of the fungus from the excised valve or detection on valve histology.

Blood culture negative endocarditis

The possibility that the illness is not endocarditis should always be entertained when blood cultures are repeatedly negative. However, in 5 to 10 per cent of definite cases of endocarditis the blood cultures will be negative. The commonest explanation for this is previous antibiotics. In a few cases the pathogen will be recovered from another site, including the excised valve, excised emboli, or specifically in right-sided endocarditis, respiratory specimens. Other causes of negative blood cultures are infection with organisms that cannot be grown by conventional blood culture methods and infections that are diagnosed by serology such as *C. burnetii*, *Bartonella* spp., and *Chlamydia* spp.

Treatment

Initial therapy

In those patients who have been chronically unwell for many weeks, antibiotic treatment can be deferred until the blood cultures are positive and the pathogen known. In patients who are acutely ill, antibiotic treatment should be started after taking blood cultures, using a broad-spectrum combination that can be adjusted when the pathogen is known. However, in many who are acutely ill with native valve infection, endocarditis is often not suspected initially—there may be no obvious signs of this—and the antibiotics are started for 'septicaemia'. There are many possible combinations for acutely ill patients, but intravenous vancomycin and gentamicin will encompass most possible pathogens. When methicillin-resistant staphylococci (whether *S. aureus* or coagulase-negative staphylococci) are likely pathogens, vancomycin or teicoplanin are an essential component of any combination.

Definitive therapy

There are various national guidelines for the treatment of specific organisms. It is important to realize that very few are based on clinical trials that show efficacy of any particular regimen. It is possible to conduct such trials in endocarditis caused by viridans streptococci, but well nigh impossible in cases caused by virulent organisms such as staphylococci as the patients are seldom comparable, with many needing surgery after varying periods of antibiotic treatment. It is conventional to estimate the minimum inhibitory concentration (**MIC**) of the antibiotic for the pathogen, though in practice routine disc sensitivity tests are quite satisfactory in many cases. Although it is widely believed that prosthetic endocarditis requires a longer duration of antibiotic treatment than native valve infection, there are few data to support this. Recommendations for the commonest causative organisms will be given.

Penicillin-sensitive streptococci (MIC & 0.1 mg/l)

It was shown 30 years ago that native valve endocarditis caused by sensitive streptococci could be treated effectively with 2 weeks of intravenous penicillin and an aminoglycoside (originally streptomycin but now gentamicin). The purpose of the aminoglycoside is to achieve synergy, so a full therapeutic dose is not given. This regimen is seldom used in practice in the United Kingdom.

Patients allergic to penicillins should be given vancomycin or teicoplanin and gentamicin.

Streptococci with reduced sensitivity to penicillin (MIC > 0.1 mg/l)

The regimens given above should be continued for 4 weeks

Enterococci

Enterococci are rather more sensitive to amoxicillin and ampicillin than penicillin and thus these agents are recommended rather than penicillin. Many enterococci are still relatively sensitive to gentamicin and this drug is given with amoxicillin (for synergy, not a full therapeutic dose) for 4 weeks. Patients allergic to penicillin should be given vancomycin and gentamicin. Some enterococci are now resistant to high levels of gentamicin and for such strains gentamicin should not be given. Some gentamicin-resistant strains are sensitive to streptomycin and, if so, this can be used instead of gentamicin. If not, high-dose amoxicillin should be given for 4 to 6 weeks. Unfortunately some enterococci (usually *E. faecium*) are resistant to amoxicillin, gentamicin, and vancomycin and for them expert help should be obtained.

Staphylococci

The same antibiotic regimens should be used whether the staphylococcus is *S. aureus* or a coagulase-negative strain—it is the antibiotic sensitivity that matters not the infecting species. Strains that are sensitive to penicillin should be treated with this, those that are penicillin resistant but methicillin sensitive should be treated with flucloxacillin, and methicillin-resistant strains with vancomycin. There is no evidence that the addition of gentamicin (for gentamicin-sensitive strains) to the β-lactam antibiotic improves cure rates, but it may result in more rapid defervescence and clearance of bacteraemia.

Practical treatment recommendations are shown in Tables 2 and 3.

Monitoring of treatment

Serum bactericidal titres against the infecting organism are no longer recommended. There was always great variation in the monitoring methods used for these tests and in the interpretation of their results. At best they could only predict bacteriological not clinical cure and bacteriological failure is very rare. The most useful laboratory test for monitoring the response to treatment (which is usually obvious clinically) is serial C-reactive protein estimation. This is of much more use than the erythrocyte sedimentation rate, which is much slower to fall.

Prevention and prophylaxis

While antibiotic prophylaxis in ‘at-risk patients’ is accepted as reasonable, there are many uncertainties about its value and data confirming its effectiveness are lacking. The rationale for antibiotic prophylaxis depends on indirect data from *in vitro* studies, experimental animal models, and clinical bacteraemia studies. Despite this uncertainty, all authorities continue to recommend antibiotic prophylaxis to cover certain procedures associated with a predictable and

significant bacteraemia in patients known to be at risk, but accept that prophylaxis may fail, even with the recommended regimens, and that adverse reactions to the antibiotics are important even if relatively uncommon.

An international consensus group has recently undertaken a comparative analysis of the published national guidelines, which in the main are quite similar, though the antibiotic regimen for a given procedure may vary according to the perceived cardiac risk. Controversial areas include fibreoptic bronchoscopy, colonoscopy, vaginal hysterectomy, and vaginal delivery. Based on their analysis the consensus group have proposed universal guidelines for cardiac (Tables 4 and 5) and procedural (Table 6) risks. Prophylactic regimen are shown in Table 7.

Surgical treatment of infective endocarditis

Surgery will be required in about 30 per cent of cases during the acute phase (first 4 months) of endocarditis and 20 to 40 per cent of cases thereafter (Fig. 6 and Plate 3). Since surgery may be required at any time during an episode of endocarditis, it is essential to involve a cardiac surgeon in the overall management from the outset: in practical terms this means transferring the patient to a centre with cardiac surgery wherever possible. Even so, surgery for endocarditis carries a risk of 10 to 25 per cent mortality, and up to 25 per cent of patients develop a paravalvular leak requiring a further operation. The main predictive factors for mortality associated with surgery are prosthetic valve endocarditis, infections due to staphylococci or candida, perioperative shock, or late referral. The timing of surgery is all important and demands experience and clinical judgement, which is best achieved by a team approach with cardiologists, cardiac surgeons, and microbiologists.

The main indications for surgery are haemodynamic instability and persistent infection. In such cases surgery should never be delayed, even if only hours or days of antibiotic treatment have been given. The primary goals of the surgeon are to remove all infected material and to reconstruct the heart and/or restore valvular function at the lowest operative risk. An understanding of the surgical anatomy of infective endocarditis is a precondition for surgical success, which means the involvement of an experienced surgical team. Wherever possible surgeons now strive to preserve the native valve, either by removal of the vegetation(s) or valve repair. In prosthetic valve endocarditis removal of all foreign material is mandatory.

There are two unresolved issues with regard to the surgical treatment of endocarditis. The first concerns the timing of surgery in patients who have had a cerebrovascular accident either as a result of an embolic stroke or from haemorrhage due to a ruptured mycotic aneurysm. As a general rule, if haemorrhage is detected by CT scanning, delay of at least 1 week is suggested; if there is no haemorrhage, surgery can be undertaken within 72 h.

The second issue concerns the duration of antibiotic treatment postoperatively. If the excised valve is sterile it is doubtful whether further antibiotics are of any benefit. If the pathogen is isolated from the excised valve, antibiotics should be

given for a further 2 weeks. If debridement is incomplete, whatever antibiotics are given may fail.

Further reading

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Baine RJI *et al*. (1988). Impact of a policy of collaborative management on mortality and morbidity from infective endocarditis. *International Journal of Cardiology* **19**, 47–54. [This paper demonstrates the benefit of a 'team approach' to the management of infective endocarditis.]

Birmingham GD, Rahko PS, Ballantyne R (1992). Improved detection in infective endocarditis with transoesophageal echocardiogram. *American Heart Journal* **123**, 774–821. [This paper describes the benefits of using the transoesophageal approach to echocardiography in the diagnosis of infective vegetations.]

Cohen PS, Maguire JH, Weinstein L (1980). Infective endocarditis caused by Gram-negative bacteria: a review of the literature 1945–1977. *Progress in Cardiovascular Diseases* **22**, 205–41. [Even after 20 years this is still one of the best reviews of this particular aspect of endocarditis.]

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Gutschik E and The Endocarditis Working Group of the International Society of Chemotherapy (1998). Microbiological recommendations for the diagnosis and follow-up of infective endocarditis. *Clinical Microbiology and Infection***4**, 3S10–3S16. [A comprehensive review of investigations currently available for the diagnosis of infective endocarditis.]

Hoen B *et al*.(1995). Infective endocarditis in patients with negative blood cultures: analysis of 88 cases from a one year nationwide survey in France. *Clinical Infectious Diseases* **20**, 501–6. [An excellent review of the problems involved in culture-negative endocarditis. How the problem might be tackled.]

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Medline (Ovid) Searches of IVDA and endocarditis

Ovid Technologies, Inc. Email Service

Search for: from 15 [limit 14 to review articles] keep 3-5,7,11-12,15,17,20-21,24,29,31,46-47,54
Citations: 1-16

<1>
Unique Identifier
12092473
Medline Identifier
22087846
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Infective endocarditis in intravenous drug abusers and HIV-1 infected patients. [Review] [123 refs] Source
Infectious Disease Clinics of North America. 16(2):273-95, vii-viii, 2002 Jun.
Abstract
Infective endocarditis (IE) is one of the most severe complications of parenteral drug abuse. The incidence of IE in intravenous drug abusers (IVDAs) is 2% to 5% per year, being responsible for 5% to 20% of hospital admissions and 5% to 10% of the overall death rate. IVDAs often develop recurrent IE. The prevalence of HIV infection among IVDAs with IE ranges between 30% and 70% in urban areas in developed countries. The incidence of IE in IVDAs is currently decreasing in some geographical areas, probably due to changes in drug administration habits undertaken by addicts in order to avoid HIV transmission. Overall, Staphylococcus aureus is the most common etiological agent, being in most geographical areas sensitive to methicillin (MSSA). The remainder of cases is caused by streptococcoci, enterococci, GNR, Candida spp, and other less common organisms. Polymicrobial infection occurs in 2% to 5% of cases. The tricuspid valve is the most frequently affected (60% to 70%), follo wed by the mitral and aortic valves (20% to 30%); pulmonic valve infection is rare (< 1%). More than one valve is infected in 5% to 10% of cases. HIV-positive IVDAs have a higher ratio of right-sided IE and S. aureus IE than HIV-negative IVDAs. Response to antibiotic therapy is similar among HIV-infected or non-HIV-infected IVDAs. Drug addicts with non-complicated MSSA right-sided IE can be treated successfully with an i.v. short-course regimen of nafcillin or cloxacillin for 2 weeks, with or without addition of an aminoglycoside during the first 3 to 7 days. Surgery in HIV-infected IVDAs with IE does not worsen the prognosis. The prognosis of right-sided endocarditis is generally good; overall mortality is less

than 5%, and with surgery less than 2%. In contrast, the prognosis of left-sided IE is less favorable; mortality is 20% to 30%, and even with surgery is 15% to 25%. IE caused by GNB or fungi has the worst prognosis. Mortality between HIV-infected or non-HIV-infected IVDAs with IE is similar. However, among HIV-infected IVDAs, mortality is significantly higher in those who are most severely immunosuppressed, with CD4+ cell count < 200/microL or with AIDS criteria. Finally, IE in HIV-infected patients who are not drug abusers is rare. [References: 123]

<2>
Unique Identifier
12426917
Medline Identifier
22314283
Authors
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Institution
Department of Cardiology, Marshfield Clinic, 1000 N Oak Ave, Marshfield, WI 54449, USA. takt@mfldclin.edu Title
An update on the epidemiology, pathogenesis and management of infective endocarditis with emphasis on Staphylococcus aureus. [Review] [51 refs] Source
WMJ. 101(7):24-33, 2002.
Abstract
The incidence of infective endocarditis (IE) is thought to be around 4/100,000 person years in the general population, and 15/100,000 over the age of 50 years. The risk of acquiring IE is higher among patients with valvular heart disease (e.g., rheumatic valves, bicuspid aortic valves, myxomatous degeneration, etc.), congenital heart disease (e.g., coarctation, patent ductus arteriosus, ventricular septal defect, etc.), prosthetic cardiac valves, and among intravenous drug abusers. Staphylococcus aureus is one of the most common infective agents of IE, and most commonly originates from nosocomial sources, e.g., intravenous and arterial catheters, pacemaker leads, and prosthetic valves. Endocarditis caused by S aureus has a mortality rate of approximately 20% to 40%. In up to 40% of patients, IE caused by S aureus is associated with embolic complications. The risk of death increases with the development of complications. The epidemiology and microbiology of S aureus are chan ging rapidly, and resistance to antibiotics, especially methicillin, is becoming more widespread. In this review we will focus on the epidemiology, microbiology, and pathogenesis of S aureus IE, and also summarize the current guidelines for diagnosis, treatment, and prophylaxis of this clinical condition. [References: 51]

<3>
Unique Identifier
12356347

Medline Identifier
22244082
Authors
Seghatol F. Grinberg I.
Institution
Northwestern Memorial Hospital, Chicago Illinois 60611, USA. f-seghatol@northwestern.edu Title
Left-sided endocarditis in intravenous drug users: a case report and review of the literature. [Review] [16 refs] Source
Echocardiography. 19(6):509-11, 2002 Aug.
Abstract
We report a case of staphylococcus endocarditis of the mitral and aortic valves in an intravenous drug user (IVDU) complicated by abscess of the aortic root and aorto-left atrial fistula. Interestingly, the tricuspid valve was free of vegetation. Infective endocarditis in IVDUs more commonly involves right-sided valves; left-sided endocarditis is rare, indicates severe disease, or is a postmortem finding. This case illustrates the need for considering left-sided valve endocarditis in IVDU with septicemia, even if the tricuspid valve shows no evidence of vegetation. [References: 16]

<4>
Unique Identifier
11118386
Medline Identifier
20568853
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Fungal endocarditis: evidence in the world literature, 1965-1995. [Review] [34 refs] Source
Clinical Infectious Diseases. 32(1):50-62, 2001 Jan.
Local Messages
Held at BMA Library
Abstract
We analyzed 270 cases of fungal endocarditis (FE) that occurred over 30 years. Vascular lines, non-cardiac surgery, immunocompromise and injection drug abuse are increasing risk factors. Delayed or mistaken diagnosis (82% of patients), long duration of symptoms before hospitalization (mean +/- standard deviation, 32+/-39 days) and extracardiac manifestations were characteristic. From 1988 onwards, 72% of patients were diagnosed preoperatively, compared with 43% before 1988 (P=.0001). The fungi most commonly isolated were Candida albicans (24% of patients), non-albicans species of Candida (24%), Apergillus species (24%), and Histoplasma species (6%); recently-emerged fungi

accounted for 25% of cases. The mortality rate was 72%. Survival rates were better among patients who received combined surgical-antifungal treatment, were infected with Candida, and had univalvular involvement. Improvement in the survival rate (from <20% before 1974 to 41% currently) coincided with the in troduction of echocardiography and with improved diagnostic acumen. Fungal endocarditis recurs in 30% of survivors. It is recommended that fungal endocarditis be diagnosed early through heightened diagnostic acumen; that patients be treated with combined lipid-based amphotericin B and early surgery; and that patients be followed up for > or =4 years while on prophylactic antifungal therapy. [References: 34]

<5>
Unique Identifier
11269786
Medline Identifier
21166336
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Title
Isolated pulmonic valve endocarditis caused by group B streprococcus (Streptococcus agalactiae)--a case report and literature review. [Review] [30 refs]
Source
Angiology. 52(3):211-5, 2001 Mar.
Local Messages
Held at BMA Library
Abstract
The pulmonic valve is the least commonly involved valve in infective endocarditis. Pulmonic valve endocarditis is usually associated with tricuspid valve endocarditis, and isolated pulmonic valve endocarditis is exceedingly rare. The predisposing factors for developing pulmonic valve endocarditis include a congenitally anomalous pulmonic valve, intravenous drug abuse, and the presence of indwelling intravenous or flow-directed pulmonary artery catheters. More cases of group B streptococcus endocarditis are being reported. The risk factors for group B streptococcus endocarditis include diabetes mellitus, cancer, alcoholism, malnutrition, immunocompromised status, intravenous drug abuse, postpartum and postabortion states, and underlying valvular disease. The vegetations of this type of endocarditis are usually large and have a higher tendency to result in embolism. The presentation of group B streptococcus endocarditis is usually acute and may result in rapid valve destructi on if not treated promptly. A case of isolated pulmonic valve endocarditis caused by group B streptococcus, Streptococcus agalactiae, is presented that was diagnosed with multiplane transesophageal echocardiography in a 40-year old, alcoholic,

malnourished man, who was successfully treated with intravenous penicillin G. The literature on the isolated pulmonic valve endocarditis caused by group B streptococcus is reviewed. [References: 30]

<6>
Unique Identifier
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Medline Identifier
20568853
Authors
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Institution
Faculty of Medicine and Health Sciences, United Arab Emirates University, Al Ain, United Arab Emirates. michael.ellis@uaeu.ac.ae Title
Fungal endocarditis: evidence in the world literature, 1965-1995. [Review] [34 refs] Source
Clinical Infectious Diseases. 32(1):50-62, 2001 Jan.
Local Messages
Held at BMA Library
Abstract
We analyzed 270 cases of fungal endocarditis (FE) that occurred over 30 years. Vascular lines, non-cardiac surgery, immunocompromise and injection drug abuse are increasing risk factors. Delayed or mistaken diagnosis (82% of patients), long duration of symptoms before hospitalization (mean +/- standard deviation, 32+/-39 days) and extracardiac manifestations were characteristic. From 1988 onwards, 72% of patients were diagnosed preoperatively, compared with 43% before 1988 (P=.0001). The fungi most commonly isolated were Candida albicans (24% of patients), non-albicans species of Candida (24%), Apergillus species (24%), and Histoplasma species (6%); recently-emerged fungi accounted for 25% of cases. The mortality rate was 72%. Survival rates were better among patients who received combined surgical-antifungal treatment, were infected with Candida, and had univalvular involvement. Improvement in the survival rate (from <20% before 1974 to 41% currently) coincided with the in troduction of echocardiography and with improved diagnostic acumen. Fungal endocarditis recurs in 30% of survivors. It is recommended that fungal endocarditis be diagnosed early through heightened diagnostic acumen; that patients be treated with combined lipid-based amphotericin B and early surgery; and that patients be followed up for > or =4 years while on prophylactic antifungal therapy. [References: 34]

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20417133
Authors
Ferguson E. Reardon MJ. Letsou GV.
Institution
Department of Surgery, Baylor College of Medicine, Houston, Texas, USA.
Title
The surgical management of bacterial valvular endocarditis. [Review] [18 refs]
Source
Current Opinion in Cardiology. 15(2):82-5, 2000 Mar.
Abstract
Bacterial endocarditis is an important cause of cardiac valvular problems. The diagnosis of bacterial endocarditis can be difficult, and, often, an aggressive clinical evaluation including serial blood cultures is necessary. The pathophysiology of endocarditis is changing with the rise of intravenous drug use; staphylococci are an increasingly common cause. Endocarditis often warrants surgical intervention. Operations for bacterial endocarditis range from valve repair to valve replacement to homograft replacement. The operations are technically challenging, but new methods of myocardial protection have markedly improved the surgical outcomes. Valve excision is an option for intravenous drug users with tricuspid valve endocarditis. Surgical management of endocarditis is a technically challenging but rewarding procedure that should be offered to appropriate patients. [References: 18]

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9753530
Medline Identifier
98426291
Authors
McLean L. Sharma S. Maycher B.
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Departments of Internal Medicine and Radiology, University of Manitoba, Winnipeg, Canada.
Title
Mycotic pulmonary arterial aneurysms in an intravenous drug user. [Review] [13 refs] Source
Canadian Respiratory Journal. 5(4):307-11, 1998 Jul-Aug.
Abstract
A case of mycotic pulmonary artery aneurysm (PAA) in an intravenous drug user in whom resolution occurred with conservative therapy is described. The natural history of PAA is not well described in the literature. Although PAA is potentially fatal, resolution may occur in patients who do not have hemoptysis. Clinical presentation, diagnosis and management of PAA are reviewed. [References: 13]

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Unique Identifier
9360059
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Fundacion del Centro de Estudios Infectologicos (FUNCEI), Buenos Aires, Argentina. funcei@cei.com.ar Title
Recognition, management and prophylaxis of endocarditis. [Review] [144 refs]
Source
Drugs. 54(5):730-44, 1997 Nov.
Local Messages
Held at BMA Library, but some gaps (check catalogue) Abstract
Infective endocarditis (IE) remains a disease with high morbidity and mortality. In recent years, a higher frequency of IE has been observed in the elderly, in intravenous drug users and in patients with prosthetic valves. The diverse manifestations of this disease demand a high degree of suspicion from the practitioner, in order to make an early diagnosis. Advances in and increasing use of echocardiography (especially transoesophageal) allow us to identify valvular changes earlier and more precisely. The use of the new Duke's diagnostic criteria, based on clinical manifestations and microbiological and echocardiographic findings, facilitates the diagnosis and categorisation of IE. An increase in staphylococci and other problem pathogens, such as penicillin-resistant streptococci, enterococci resistant to beta-lactams, aminoglycosides and methicillin-resistant staphylococci has been observed. Important changes have also taken place in the management of IE. There is a clear trend towards the use of shorter treatment courses, oral and once-daily regimens and outpatient programmes, all of which aim to reduce costs and provide patients with improved quality of life. Antibiotic prophylaxis for the prevention of IE is still controversial. In the past few years more rational regimens have been used, and indications are now more precise. In spite of all this, however, few cases are prevented and patient compliance to the prophylaxis regimens remains low. [References: 144]

<10>
Unique Identifier
9130133
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Title
Infectious endocarditis and sudden unexpected death: incidence and morphology of lesions in intravenous addicts and non-drug abusers. [Review] [13 refs]
Source
Journal of Heart Valve Disease. 6(2):198-203, 1997 Mar.
Abstract
BACKGROUND: Intravenous drug (IVD) use is a wellknown risk factor for infectious endocarditis (IE), but there are few morphologic and epidemiologic data comparing IVD-related and non-IVD-related IE in cases of sudden death. MATERIAL AND RESULTS: Between 1992 and 1994, acute IE was diagnosed in 13 IVD users at the Office of the Chief Medical Examiner in Maryland, indicating a yearly incidence of IE-related sudden unexpected deaths of 12 per 100,000. Eleven (85%) cases of acute IE occurred on apparently previously normal valves, and there was one unicuspid valve and one infected porcine prosthesis. There were three right-sided (tricuspid) lesions (23%), nine left-sided lesions (69%), and one multivalvular lesion (8%). During the same period, there were five cases of healed IE in IVD abusers, three of which involved the tricuspid valve. The prevalence of incidental healed lesions in autopsies of IVD users was 0.2%. The healed tricuspid lesions consisted of smooth-edged defects in the valve leaflet without perforations characteristic of mitral or aortic IE. The mean age of the deceased with healed lesions was 45 +/- 6 years versus 34 +/- 10 years for those with acute endocarditis (p = 0.03). During the same time period, there were six cases of acute IE among non-drug users, indicating a yearly incidence of sudden unexpected death of 0.04 per 100,000. Acute IE occurred on congenitally malformed (n = 5) or prosthetic (n = 1) valves. There were two cases of incidental healed IE (mitral and aortic valves), indicating a prevalence of 0.02%. CONCLUSION: IVD users are 300 times more likely to die suddenly with IE than non-IVD users, and healed lesions are 25 times more common. Healed IE of the tricuspid valve is associated with IVD abuse, and has a characteristic gross appearance that differs from healed left-sided IE. [References: 13]

<11>
Unique Identifier
8838184
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96435298
Authors
Sandre RM. Shafran SD.
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Title

Infective endocarditis: review of 135 cases over 9 years. [Review] [25 refs]
Source
Clinical Infectious Diseases. 22(2):276-86, 1996 Feb.
Local Messages
Held at BMA Library
Abstract
One hundred thirty-five cases of infective endocarditis in adults at the University of Alberta Hospital from 1985 to 1993 were reviewed and the von Reyn and Duke criteria were compared. There were 80 cases of native valve endocarditis, 15 cases of endocarditis in intravenous drug users, 7 cases of early prosthetic valve endocarditis, and 33 cases of late prosthetic valve endocarditis. Valve replacement or repair was performed in 33% of all cases. The overall mortality was 19%. The mortality among patients treated surgically was significantly lower than that among those treated medically (9% vs. 24%, respectively; P = .037). However, when patients who were too medically unstable for surgery or who refused surgery were excluded, the mortality among the medically treated group decreased to 15%, which was not significantly different from that among the surgically treated group. The 33 patients transferred from other hospitals were infected with similar pathogens; however, the r
ate of surgical intervention among these patients was much higher than that among other patients (64% vs. 24%, respectively; P < .0001), and the mortality was slightly lower (12.1% vs. 21.6%, respectively; P = .31). The 54 surgical and autopsy-proven cases were classified by the von Reyn and the Duke criteria without knowledge of the operative and autopsy results: 15% of these cases were rejected by the von Reyn criteria, and none were rejected by the Duke criteria. [References: 25]

<12>
Unique Identifier
7671931
Medline Identifier
95401992
Authors
Bille J.
Institution
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Title
Medical treatment of staphylococcal infective endocarditis. [Review] [16 refs]
Source
European Heart Journal. 16 Suppl B:80-3, 1995 Apr.
Local Messages
Held at BMA Library, but some gaps (check catalogue)
Abstract
Staphylococcal infective endocarditis is a severe event requiring aggressive therapy. Antibiotic regimen depends mainly on (1) the species of Staphylococcus

(Staphylococcus aureus versus coagulase-negative staphylococci) and its resistance pattern (resistance to penicillin, to methicillin, to multiple classes of antibiotics); (2) the type of infected valve (native versus prosthetic); (3) the site of infection (left side versus right side endocarditis); (4) some underlying conditions of the host, in particular the presence or not of intravenous drug abuse. Based on in vitro susceptibility results, animal models and clinical trials, the following regimens are currently recommended. For native valve endocarditis, penicillin G 20 million units per day i.v. for 4-6 weeks for penicillin-susceptible strains; a penicillinase-resistant penicillin (oxacillin) 2 g i.v. q 4 h for 4-6 weeks plus an aminoglycoside (gentamicin) 1.0 mg.kg-1 i.v. q 8 h for 1 week, for penicillin-resistant,
methicillin-susceptible strains; for methicillin resistant strains, vancomycin 30 mg.kg.day-1 i.v. in 2-4 doses for 4-6 weeks with the addition or not of rifampin 600-900 mg.day-1 orally. For a prosthetic valve endocarditis, a three-drug regimen (oxacillin or vancomycin, plus gentamicin and rifampin) and a longer duration (6 weeks or more) are generally recommended. Shorter (2 weeks) treatment could be delivered to uncomplicated cases of right-sided endocarditis. In view of an increased resistance to classic drugs and suboptimal efficacy of some of them, new therapeutic modalities should be looked at, in particular for endocarditis cases due to methicillin-resistant strains. [References: 16]

<13>
Unique Identifier
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Title
Infective endocarditis: prevention, diagnosis and management. [Review] [16 refs]
Source
European Journal of Emergency Medicine. 1(2):104-9, 1994 Jun.
Abstract
Infective endocarditis remains an important problem and the means of prevention are still insufficient. The causal bacteria have changed very little, but the incidence of nosocomial infections and endocarditis complicating intravenous drug abuse are increasing. The distinction between subacute and acute clinical presentations remains appropriate. Cardiac and neurological complications are frequent and carry a high risk of mortality. The diagnosis is obtained by the integration of clinical data and the results of blood cultures. Echocardiography is extremely useful for detecting vegetations, and for assessing the haemodynamic consequences and specific cardiac complications. Risk stratification can be

obtained by correct integration of multiple parameters. The causal agent should be identified before the initiation of antimicrobial therapy. Surgery is frequently required, and should be performed rapidly when indicated. [References: 16]

<14>
Unique Identifier
2268967
Medline Identifier
91098793
Authors
Keys TF.
Institution
Department of Infectious Diseases, Cleveland Clinic Foundation, Ohio 44195.
Title
Diagnosis and management of infective endocarditis. [Review] [17 refs]
Source
Cleveland Clinic Journal of Medicine. 57(6):558-62, 1990 Sep.
Abstract
Advances in chemotherapy and surgery have significantly improved the outcome of infective endocarditis, but the disease remains a therapeutic challenge with an overall mortality of 20%. More cases of infective endocarditis seen today are associated with prosthetic heart valves, intravenous drug abuse, or complications of medical and surgical technology. Prosthetic valve endocarditis occurs in 1% to 4% of patients with prosthetic valves. Echocardiography is not a precise diagnostic test for endocarditis, but it helps detect a variety of cardiac lesions, including valvular incompetence, annular ring abscesses, and sometimes vegetations. Serum bactericidal titers are predictive of neither cure nor treatment failure. The principal indication for urgent surgical intervention is acute valvular dysfunction. Other considerations for surgery include evidence of myocardial invasion, infection by antibiotic-resistant organisms, and large vegetations. For patients at risk of infective endocarditis, antibiotic prophylaxis during invasive procedures is an accepted practice. [References: 17]

<15>
Unique Identifier
2201527
Medline Identifier
90353228
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Roberts R. Slovis CM.
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Emory University School of Medicine, Atlanta, Georgia.
Title

Endocarditis in intravenous drug abusers. [Review] [106 refs]
Source
Emergency Medicine Clinics of North America. 8(3):665-81, 1990 Aug.
Abstract
IE due to parenteral drug use is an ever-increasing problem for physicians working in the ED. IE may present with a multitude of signs and symptoms of variable severity. Patients may complain of only vague symptoms consistent with a viral syndrome, or they may present with a neurologic or cardiovascular catastrophe. ED physicians must have a high degree of suspicion for IE whenever they evaluate a patient who could possibly be abusing drugs. [References: 106]

<16>
Unique Identifier
3518020
Medline Identifier
86207596
Authors
Gallagher PG. Watanakunakorn C.
Title
Group B streptococcal endocarditis: report of seven cases and review of the literature, 1962-1985. [Review] [108 refs]
Source
Reviews of Infectious Diseases. 8(2):175-88, 1986 Mar-Apr.
Local Messages
Held at BMA Library, but some gaps (check catalogue)
Abstract
Infective endocarditis is an uncommon manifestation of group B streptococcal disease. Seven cases of group B streptococcal endocarditis are reported herein. Another fifty-five cases published in the literature since 1962 are reviewed: the male to female ratio was 1.4:1. The average age was 53.8 years, and 45% of patients were 60 years of age or older. Two cases of nonsocomial endocarditis and two cases of polymicrobial endocarditis were identified. There were five cases of prosthetic valve endocarditis. Mitral and aortic valvular involvement were present in 48% and 29% of cases, respectively. Underlying heart disease was found in more than half of the cases. Rheumatic heart disease was the commonest underlying cardiac condition. Noncardiac underlying conditions included diabetes mellitus, alcoholism, pregnancy, intravenous drug abuse, and genitourinary disease. Onset was varied as was initial presentation of the disease. Large arterial thrombi were common. Overall mortality was 43.5%. Penicillin is the treatment of choice for group B streptococcal endocarditis. However, based on in vitro and in vivo studies as well as case reports, some authors feel that the combination of penicillin and an aminoglycoside is a superior regimen. Cephalothin or vancomycin are alternatives for patients who are allergic to penicillin. [References: 108]