Aspects of Bacterial Endocarditis in the Johannesburg General Hospital

AN ANALYSIS OF 30 CASES

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SUMMARY

The records of 30 patients admitted to the Johannesburg Hospital with bacterial endocarditis were analysed. Sweating, although seldom volunteered by the patient, was the most common symptom and was present in 63%. Pyrexia was usually low grade and sometimes very intermittent, but was detected in all patients. In our experience, it is the single most important sign of bacterial endocarditis.

Staphylococcus albus was the only organism isolated from blood culture in 37% of patients. We believe that Staphylococcus albus is not infrequently responsible for bacterial endocarditis irrespective of whether previous cardiac surgery has been undertaken or not.

Since endocarditis occurs in edentulous patients, the extraction of healthy teeth in order to prevent recurrent attacks is not warranted.

A combination of antibiotics is usually required, but the infection can be controlled in most instances. Two (7%) of our patients died while still receiving antibiotic therapy. A further 2 died after cardiac surgery.


The classical description of bacterial endocarditis includes an abnormal heart, protracted fever, anaemia, systemic embolism, splenomegaly, clubbing of the fingers and positive blood cultures. However, not all of these features need be present,\(^1\)\(^2\) and we have been impressed by the atypical presentation of many cases of bacterial endocarditis. Pyrexia, often low grade, has usually been the single most important physical sign leading to the diagnosis. We believe that an awareness of this changing pattern of bacterial endocarditis is essential, if delayed diagnosis is to be avoided.

In this article the records of 30 patients with bacterial endocarditis are reviewed. An attempt is made to assess the nature and incidence of the presenting signs and symptoms. Laboratory investigations and the results of therapy are analysed and briefly discussed.

CLINICAL MATERIAL

All 30 patients, whose ages ranged from 11 to 62 years (Fig. 1), were examined by at least one of us between 1967 and 1971. Most of the patients were treated in the same Medical Unit and the series in no way reflects the total number of cases of bacterial endocarditis admitted to this Hospital. All subjects had a cardiac lesion and a pyrexia for which no other cause was detected. Blood cultures were taken with great care to avoid contamination. Where blood cultures were negative, the diagnosis was made on clinical criteria and the patient's response to therapy. With the exception of the erythrocyte sedimentation rate (Westergren) and examination of the urine, which were carried out by the attending house physician, all other investigations were performed at the South African Institute for Medical Research.

The underlying cardiac lesions are summarized in Fig. 2. The most common lesions were aortic and mitral regurgitation. Both patients with homograft aortic valves had some aortic regurgitation. All 3 patients

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who had had Starr-Edwards valves inserted, had associated regurgitant lesions, presumably through ring leaks.

The diagnosis of bacterial endocarditis was confirmed at necropsy in the 2 patients who died during treatment.

Symptoms

Sweating was the commonest symptom (Fig. 3) but it was unusual for the patient to be aware of pyrexia. Only 4 of the 19 patients with sweating had had a rigor. Thirteen (43%) complained of tiredness, weakness or of generally feeling unwell. Twelve (40%) had symptoms related to incipient or overt cardiac failure, such as increasing exertional dyspnoea, orthopnoea or ankle swelling. Six patients (20%) presented with symptoms compatible with emboli to the central nervous system. Of these, 3 developed a sudden severe headache, 2 were aware of some mental confusion, and I observed a facial paresis. In 4 patients, systemic emboli to other sites manifested as pain in a fingertip, an ankle, a heel and the left hypochondrium, respectively. One woman, who had previously had bacterial endocarditis, herself noticed splinter haemorrhages. Three patients were asymptomatic, and the diagnosis was suspected when pyrexia was detected at a routine outpatient examination.

Physical Findings and Laboratory Investigations

A pyrexia was invariably detected (Fig. 4.). However, this was frequently mild and less than 37.8°C. It had to be carefully sought and an abnormal spike would sometimes occur only on every second or third day, or at even longer intervals. Pyrexia was not detected for several days in a very breathless man until rectal temperatures were taken.

Seventeen patients had a sustained tachycardia. Clinical evidence of systemic emboli was common, and if splinter haemorrhages on the nails or petechiae elsewhere are included as signs of embolization, this was present in 20 (66%) patients. Splenomegaly was present in 18 (60%), but in 3 of these, all of whom had chronic tricuspid incompetence, the spleen had been palpable at least a year before the onset of the bacterial endocarditis. Twelve (40%) patients were admitted in congestive cardiac failure. In 6 of these cardiac failure had not been previously detected, whereas in another 4
their routine antifailure therapy had become inadequate. The remaining 2 had had long-standing cardiac failure, which was apparently not aggravated by the endocarditis. Clubbing of the fingers was uncommon and was seen in only 4 (13%) instances.

Although the erythrocyte sedimentation rate (Westergren) was the best indicator of ‘activity’, this exceeded 25 mm in the first hour in only 18 patients (60%). C-reactive and mucoprotein estimations were never abnormal in the absence of an elevated erythrocyte sedimentation rate. The haemoglobin was less than 12.5 g/100 ml in only 6 patients, the lowest level being 10.4 g/100 ml.

The results of urine microscopy, performed on a fresh centrifuged specimen, were recorded in 23 patients. only 5 of whom had haematuria. One of these had associated splinter haemorrhages and a pedal pulse disappeared in another. Microscopic pyuria was detected in 4 patients, but no abnormality was noted on repeated examination of the urine in the remaining 14.

Organisms

In 6 patients (20%), an organism was not isolated in spite of repeated attempts. Two of these had received prior antibiotic therapy before admission to hospital. The commonest organisms grown on blood culture were the Staphylococcus albus and Streptococcus viridans. The former was the only organism cultured in 11 patients, in 4 of whom it was found repeatedly, whereas in the remaining 7 patients, only one positive culture was obtained. All 5 patients in whom the Streptococcus viridans was the only organism isolated had numerous positive blood cultures. One patient had Staphylococcus aureus isolated repeatedly. Mixed infections were found in 7 patients, in 6 of whom Staphylococcus albus was one of the organisms cultured.

Dental Status

In order to assess the role of carious teeth as a possible portal of entry of the bacteria, the condition of the teeth was determined where possible. In the majority of instances, the dental status had been assessed at the time of the infection and a record made of recent dental procedures. In others, a questionnaire was sent in order to obtain this information. Adequate data were available in 26 patients (Fig. 5). Eight had healthy teeth whereas 14 had either had recent dental treatment or had caries. It is noteworthy that 4 patients were edentulous at the time of their infection.

Treatment and Response

Twenty-eight patients (93%) responded to therapy, and 2 died during the course of treatment. One, whom we have previously reported in detail, had a Streptococcus viridans isolated on blood culture and severe aortic stenosis supervened from large vegetations on that valve. The other died of a subarachnoid haemorrhage when the bacterial endocarditis was clinically cured. Staphylococcus albus had been cultured repeatedly and she had been treated with penicillin, cloxacillin and gentamicin. In only 9 of the 28 patients was a satisfactory response obtained with a single antibiotic agent, usually penicillin. Patients with negative blood cultures received penicillin, cloxacillin and gentamicin. The pyrexia of all the patients in this series returned to normal during the treatment.

Four of the 10 patients in whom cardiac failure first appeared during the endocarditis or who were aggravated by the infection, reverted to their former status following treatment. Six patients remained in cardiac failure and required valve replacement after completion of the full course of antibacterial therapy. One man, because of rupture of an aortic leaflet, required insertion of a homograft aortic valve during his course of treatment. Evidence of active infection was not detected in any patient at necropsy. Two patients died within 2 months of surgery, but in neither instance was there evidence of active bacterial endocarditis at necropsy.

**DISCUSSION**

Recent reviews of bacterial endocarditis have emphasized the tendency towards an increasing age of patients affected. Several factors to account for this have been considered, most important of which are the decreasing incidence of rheumatic fever, and the older age of the general population. The patients in our series were relatively young and the peak incidence occurred in the age range 21-30 years (Fig. 1) with only 4 (13%) patients over the age of 50 years. This discrepancy can partly be explained by the fact that rheumatic heart disease remains common in South Africa.
Mitral valve disease has usually been the most common cardiac lesion predisposing to the development of bacterial endocarditis, and no significance should be attached to the equal number of patients with mitral and aortic valve involvement in our small series. It is noteworthy, however, that as many as 6 patients had the billowing posterior mitral leaflet syndrome, and the importance of this entity in relation to bacterial endocarditis will be the subject of a further communication.

The most important sign of bacterial endocarditis in our patients was a pyrexia, and this was detected in all. It must be emphasized, however, that in many instances it was a low grade and was not present every day. In 1 patient, who was dyspnoeic at rest, pyrexia was detected only when rectal temperatures were recorded. The invariable finding of a pyrexia in bacterial endocarditis has not, in our view, received sufficient emphasis. Vogler et al. accepted its absence in 4.1% of cases and Pankey in 4.8%. Although Friedberg stressed the importance of fever of more than a week's duration as a sign of bacterial endocarditis in any patient with a cardiac lesion, he and colleagues also stated that a temperature above 37°C is sufficient to warrant careful exclusion of bacterial endocarditis. Our patients were a pyrexia, and this was detected in 93% of the patients of Shinebourne et al. whereas Pankey found haematuria in 46% with subacute and in 78% with acute bacterial endocarditis. Although haematuria is an important diagnostic feature, we cannot agree with Shinebourne and co-workers that its absence makes the diagnosis of bacterial endocarditis unlikely.

Microscopic haematuria was a relatively uncommon finding (5 of 23 patients). In contrast, it was present in 93% of the patients of Shinebourne et al. whereas Pankey found haematuria in 46% with subacute and in 78% with acute bacterial endocarditis. Although haematuria is an important diagnostic feature, we cannot agree with Shinebourne and co-workers that its absence makes the diagnosis of bacterial endocarditis unlikely.

Only 20% of our patients were anaemic and in 40% the erythrocyte sedimentation rate was normal. Although others found these parameters abnormal in a much greater percentage of patients, our observations confirm that neither anaemia, nor a raised erythrocyte sedimentation rate is essential for the diagnosis.

This study illustrates the changing pattern of causative organisms in bacterial endocarditis. The culture of a Staphylococcus albus in 17 of the 30 patients (57%) is extremely high. In 8 of them (27%), this organism was cultured repeatedly. Staphylococcus albus was found in only 1 of the 61 patients with a positive blood culture in the series of Shinebourne et al. and in 23 of 186 episodes of bacterial endocarditis, in 7 of whom a single culture only was positive, by Pankey. Contrary to the experience of Cherubin and Neu who related an increased incidence of Staphylococcus epidermidis (albus) endocarditis to infection occurring after cardiac surgery, 15 of our 17 patients in whom this organism was isolated had not had previous cardiac surgery.

A major problem lies in assessing the significance of a single positive blood culture of Staphylococcus albus, frequently only obtained after prolonged incubation. In one such patient of ours, an identical organism was cultured repeatedly from the urine as well. Although Staphylococcus albus is one of the most common contaminants of bacterial cultures, its isolation from a specimen cannot automatically be regarded as evidence of contamination.

Another significant finding in this series was the relatively low incidence of Streptococcus viridans. This organism was cultured in 8 patients (27%), in 3 of whom another organism (Staphylococcus albus and Streptococcus pneumoniae in 1) was also isolated. Other reports have shown an incidence of Streptococcus viridans infection ranging from 28% to 65%. One reason for the relatively low incidence of Streptococcus viridans endocarditis is almost certainly the common usage of long-term penicillin as prophylaxis against rheumatic activity. Such therapy also has the disadvantage of changing the mouth flora and leaving organisms resistant to penicillin.

Six (20%) of our patients had persistently negative blood cultures. In other series, this figure has ranged from 12 to 26%, and Friedberg et al. have emphasized the dangers of delaying treatment because of failure to obtain an organism. The explanation for the absence of a positive culture in a patient with bacterial endocarditis is not always apparent, but failure to provide specialized growth requirements or prior use of antibiotics are sometimes relevant factors.

The causal relationship between oral sepsis or dental extraction to bacterial endocarditis is generally recognized. Dental clearance to prevent Streptococcus viridans endocarditis, irrespective of the state of the patient's teeth, has been advocated. Hillson stated that bacterial endocarditis frequently occurs without a history of recent dental procedure and that streptococcal endocarditis is exceedingly rare in edentulous patients. However, there is accumulating evidence to suggest that removal of healthy teeth is not justified. Although Croxson et al. found a relapse rate of bacterial endocarditis in 6 (14%) of 42 patients who retained their teeth, 10% of their original series of 75 patients with Streptococcus viridans endocarditis were edentulous. Simon and Goodwin have also recently reported 3 cases of Streptococcus viridans endocarditis in edentulous patients and emphasized the problems associated with full dentures. In our series, 4 patients were edentulous. Although none of these were shown to have Streptococcus viridans endocarditis—in 3 a Staphylococcus albus was the organism responsible and blood cultures were sterile in the fourth—the possibility remains that the portal of entry of the offending organism was through abrasions of the oral mucosa. We agree entirely with recently expressed sentiments that the extraction of healthy teeth is not justified as a measure to prevent recurrent bacterial endocarditis.
The frequent use of a combination of antibiotics has become necessary, because of the number of organisms which are now resistant, or partially resistant, to penicillin. Where blood cultures are negative, it is invariably our policy to add gentamicin in order to provide cover against Gram-negative organisms. All the patients in this series became apyrexial, although 2 died while still receiving antibiotic therapy. A further 2 died following cardiac surgery.

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REFERENCES

FIRST DISCUSSION PERIOD

Chairman: PROFESSOR M. S. GOTSMAN

Subject: BACTERIAL ENDOCARDITIS

Professor Gotsman: May we start off with the first question by Dr Stewart of Johannesburg: ‘What are the criteria for the duration of therapy when subacute bacterial endocarditis is diagnosed and suspected?’

Professor Barlow: I would not have thought that I could give a definite answer to that. If you have a Streptococcus viridans infection in a patient with, say, a small ventricular septal defect, who has never been in hospital before and this patient then presents with bacterial endocarditis, such an organism is likely to be extremely sensitive indeed to penicillin. The patient will become apyrexial probably in 4-5 days and treatment of such a patient will be for 3 weeks, not more than 4 weeks. On the other hand, there are patients whom we start treating with penicillin therapy, adding cloxacillin and gentamicin, thus attaining a period of apyrexia for a few days, but when pyrexia again develops, we often withdraw the penicillin and cloxacillin, adding cephalosporin to the gentamicin. This treatment may have to continue from 10 to 14 days before the patient becomes completely apyrexial. We would then continue this therapy for at least 14 days after the patient has become apyrexial.

Professor Gotsman: The next question is from Dr Saner of Johannesburg: ‘Can Professor Barlow outline his regimen of therapy; he mentioned combined therapy if the organism is sensitive. Does this mean that he employs simultaneously penicillin, cloxacillin and gentamicin, or does he use these antibiotics serially? In other words, is this combined treatment started initially, or does he introduce each antibiotic serially?’

Professor Barlow: If we do not know the type of organism, we start with penicillin and if the patient does not respond in 6 or 7 days, we add cloxacillin and gentamicin (gentamicin to cover possible Gram-negative organisms). If the patient does not respond to this regimen, we usually withdraw the penicillin and cloxacillin, but continue the gentamicin for possible Gram-negative organisms and also add cephalosporin.

Professor Gotsman: A question from Professor Powell of Durban: ‘What dose of penicillin do you use? If given intravenously, do you give it intermittently or by continuous intravenous drip?’

Professor Barlow: We used to use about 100 million units of penicillin per day, but it was considered inadvisable in this dosage because of superinfection, so that we now use about 10 million units per day. At present penicillin is