Incidence, Mortality and Prevention of Infective Endocarditis

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Since 1933 the number of deaths in England and Wales, certified as due to infective endocarditis (IE), has fallen by about four-fifths\[1,2\]. In the pre-antibiotic era the incidence of the disease was the same as the number of deaths because IE was then uniformly fatal. Since curative treatment became available, reported series from the UK\[3-11\] and from abroad\[12-14\], have shown considerable differences in mortality and, as the disease is not notifiable, the incidence is unknown. Oakley\[15\] has suggested that it is probably in excess of 1,500 new cases annually in the UK but Smith et al.\[9\] report it to be only 16 per million of the population each year in South-East Scotland, which is about two-thirds of Oakley’s estimate. Certainly IE is still the cause of over 200 deaths each year in England and Wales\[2\] and of a severe and dangerous illness in those who recover.

The purpose of this article is to consider the findings in a recent study of 582 episodes of IE by the British Cardiac Society and the Royal College of Physicians Research Unit and to examine such other relevant evidence as is available in order to ascertain the current incidence of and mortality from the disease and to identify any possible measures by which they might be reduced.

Method

The Survey

All members of the British Cardiac Society were asked, verbally and by letter, to complete a proforma in respect of each patient with IE under their care in 1981 and 1982 and to persuade the physicians in their hospital to participate in the investigation. A similar request was made to all Fellows and Members of the College through its Regional Advisers. Microbiologists reporting cases to the Communicable Disease Surveillance Centre were asked to encourage the clinician in charge to submit a proforma in respect of any such patients about whom details had not already been supplied. The survey was given wide and repeated publicity in the British Heart Journal, the British Medical Journal and The Lancet; cardiologists and physicians were reminded of the project on all suitable occasions. The proforma asked for the patient’s full name, age, sex and hospital number, the name of the consultant in charge and the hospital where the patient was treated, the causal organism and the outcome. It also required details of any dental, surgical or investigative procedure, injury or other circumstances that might have caused the illness, and the nature of any pre-existing cardiac abnormality and whether or not its presence was known to the patient or his or her doctor or dentist prior to the illness. Any areas of uncertainty were clarified by further correspondence or other contact.

Official Statistics

The Registrar-General’s and Office of Population Censuses and Surveys’ (OPCS) Annual Mortality Statistics for England and Wales were used to obtain the total population and the number, age and sex of those certified as dying from IE during each of the 50 years 1933-83.

Other Reported Series

All major series of cases of IE reported during the past half-century were studied to obtain evidence regarding total incidence of the disease and changing trends in its mortality, pathogenesis and microbiology.

Results

From the Survey

Proformas in respect of 582 episodes of IE occurring in 577 patients were received, five patients having a second episode within the two-year period. The age range was
2-87 (mean age 51.4 years); 32 patients were under 20 and all but six of them had congenital heart disease; 163 were over 65 years of age. There was a male preponderance (ratio 2:1). In all, 137 had pre-existing rheumatic heart disease, 108 congenital heart disease and 145 other cardiac abnormalities, chiefly mitral valve prolapse and calcific aortic valve disease. Of these 390 patients, 97 had had valve replacement and 38 had suffered previous attacks of IE; 183 patients were not thought to have had any previous cardiac abnormality.

The aortic valve was the site most frequently affected (148 patients) and after that the mitral valve (122 patients) and congenital heart lesions (54 patients). In 27 patients both aortic and mitral valves were involved.

The portal of entry of the causal organism, where known, is summarised in Table 1. Streptococci were responsible in 367 patients, staphylococci in 116, a Gram-negative bacterium in 15 and Coxella burnetii in 9. Blood cultures were negative in 53 patients and in the remainder IE was caused by a vairity of organisms. Factors rendering patients especially susceptible to IE are shown in Table 2. Table 3 shows the age, mortality and infecting organism in the 84 patients with prosthetic valve endocarditis.

| Table 1. Portal of entry for causal organism. |
|-----------------------------------------------|
| Possibly dental | 108 |
| Gastrointestinal tract | 24 |
| Genito-urinary tract | 25 |
| Respiratory tract | 17 |
| Skin | 16 |
| i.v. drug abusers | 9 |
| Fractures | 4 |
| Pregnancy and parturition | 3 |
| Nosocomial infections resulting from procedures involving access to the bloodstream | 27 |
| No portal of entry apparent | 349 |
| Total | 582 |

| Table 2. Factors causing increased risk of IE. |
|-----------------------------------------------|
| Prosthetic valves | 84 |
| Other cardiac surgery | 13 |
| Previous IE | 38* |
| i.v. drug abusers | 9 |
| Diabetes mellitus | 8 |
| Alcoholism | 4 |
| Immunosuppression | 9 |
| Renal failure and haemodialysis | 8 |

*Includes 9 of the 84 who had undergone valve replacement

Of the 577 patients, 83 (14.4 per cent) died, of whom 32 were female. The mean age of those dying (59.3 years) was greater than those who recovered (50.0 years). Of those with staphylococcal infections, 31 per cent died, as compared with 12 per cent in whom bowel organisms were responsible and 6 per cent who succumbed to other streptococcal infections.

Emergency valve replacement was required in 36 patients. The diagnosis of IE was not made until operation in 4 patients and autopsy in 5.

From Official Mortality Statistics

The total population of England and Wales and the mortality from IE each year over the period 1933-83 as reported in the Registrar-General’s and OPCS Annual Mortality Statistics is shown in Fig. 1, the age of those dying in Fig. 2 and their sex in Fig. 3.

From Other Reported Series

Table 4 shows the period covered by other major reported series, the number of patients included, the sex ratio, mortality and causal organism. It also includes the proportion considered to have had previously normal hearts and the number with prosthetic valves.

Discussion

It was hoped that the joint survey by the British Cardiac Society and the Royal College of Physicians Research Unit would provide information regarding the incidence of the disease, but notification fell very far short of expectations and it was clear that ascertainment was low. The total number of proformas received was only slightly in excess of the known mortality; none was received from the Republic of Ireland and none from a number of large hospitals in the UK, while patients reported to the Communicable Disease Surveillance Centre included
many for whom no proformas were forthcoming. Moreover, the low mortality in the 577 patients (14.4 per cent) suggested under-reporting.

If the mortality among those suffering IE was accurately known it would be simple to calculate the incidence from the total population figures. Thus if Hayward's[7] and Oakley's[15] estimate of 30 per cent was correct, an incidence of 1,116 cases in England and Wales in 1983 could be assumed, leaving only the undiagnosed and incorrectly certified deaths excluded. However, Table 4 shows a wide range of mortality (19-46 per cent) in the other reported series [3-14]. Some of this discrepancy is explained by the evolution of treatment over the years, particularly in antibiotic therapy and emergency valve replacement, and some reflects the special interest and expertise of the authors. However, it also indicates that none of the series can be accepted as a representative sample. Smith et al.[9], whose series is probably less biased and nearer total ascertainment than any other, suggest an annual incidence of 16 per million of the population but their mortality was 46 per cent.

The only way, therefore, to ascertain the incidence of the disease would be to have it made notifiable. This again would exclude undiagnosed cases and there would inevitably be some diagnosed cases which were not notified. It is also doubtful whether the information obtained would be of sufficient value to justify the work and expense entailed in collecting it. The number of undiagnosed cases may be substantial, for it is a disease notoriously difficult to recognise, as is shown by patients undiagnosed until operation or autopsy in this and other series[9,10,15]. Moreover, the traditional purpose of notification, which never gives reliable absolute numbers, is to enable local public health doctors to take early action to prevent spread of disease.

Another possible source of information about incidence is the Hospital In-Patient Enquiry. This, however, relates only to a 10 per cent sample of in-patients in National Health Service hospitals and is therefore unlikely to provide accurate data.

There is no valid evidence as to whether the incidence is increasing, decreasing or remaining static[7,12,13,15]. The number of cases reported by Public Health Laboratory Service and hospital microbiologists to the Communicable Disease Surveillance Centre showed an increase from 298 in 1975 to 488 in 1980 but this probably reflects improved reporting rather than higher incidence.

The mortality from IE, however, has fallen dramatically since curative treatment became possible, despite an increase in the total population of England and Wales of over nine million during the past half-century (Fig. 1). In 1933 there were 1,256 such deaths in England and Wales and mortality remained at, or slightly below, this level until antibiotics became available some ten years later,
Fig. 2. Annual deaths from infective endocarditis by age group, England and Wales, 1933–83.

Fig. 3. Annual deaths from infective endocarditis by sex, England and Wales, 1933–83.
when deaths from IE were rapidly reduced to 498 in 1948 and 339 in 1953. They remained at about that level for a decade until the benefits of emergency valve replacement became evident and the number of deaths fell to 282 in 1968, but for the past decade they have fluctuated between 189 (1979) and 249 (1974) [1,2]. This failure to reduce further the number of deaths is due to the relatively new phenomenon of IE in i.v.-drug abusers (Tables 1 and 2[8,10,11-15,16-18]), in those with prosthetic valves (Tables 2, 3 and 4[8-11,14,16,19,20]) and the increased number of old people in the population who develop IE on previously normal heart valves and have a poorer chance of survival than younger subjects (Fig. 2[4,5,8-14,16]).

The benefits of emergency valve replacement are not wholly attributable to rescuing those in danger from heart failure but also encompass the eradication of a deeply entrenched nidus of infection and protection of the kidneys from embolic and other damage.

Apart from antibiotic therapy and valve replacement, the better dental state of the population and antibiotic prophylaxis to cover dental and surgical procedures and investigations have doubtless helped to reduce mortality, and the diminution in rheumatic heart disease has greatly reduced one group at special risk.

The age and sex of those dying from IE have changed significantly during the past 50 years[1,2]. In the pre-antibiotic era about 20 per cent of the deaths occurred in patients under 20 years of age, but during the past 25 years the number has been above 5 per cent in only one year and in 1983 only one of the 225 deaths was in this age group. On the other hand, deaths in the “over 65s” have risen from about 8 per cent 50 years ago to one half of the total during the past decade (Fig. 2). Before antibiotics there were more female than male deaths but since treatment became available the reverse has been the case (Fig. 3). The diminution in rheumatic heart disease, more common in the female, and the increase, especially in the male, of congenital bicuspid aortic valves and their sequel, calcific aortic valve disease, doubtless explain much of this change[4,5,8-14,16]. The Registrar-General’s and OPCS Mortality Statistics do not show such a high male preponderance as that reported by some authors[5,12,14], another indication that they are describing selected groups.

Prosthetic valve endocarditis carries a high mortality, 45 per cent in early cases and 23.8 per cent in late cases in this series in which 84 of the 577 patients (15 per cent) had this type of endocarditis (Table 3). The Communicable Disease Surveillance Centre found a lower frequency of endocarditis in those with prosthetic valves (128 cases (5.3 per cent) in 2,432 episodes) but this may reflect failure to mention such a valve on the laboratory forms[20]. Wilson et al.[21] reported a higher mortality (86 per cent in early and 40 per cent in late cases) and 0.98 per cent of the 4,706 who had prosthetic valves inserted at the Mayo Clinic developed prosthetic valve endocarditis during the period 1963-74. Masur and Johnson[19] described 48 cases at the New York Hospital-Cornell Medical Centre during the period 1962-78 during which 1,282 patients had prosthetic valves implanted. The mortality rate in early cases was 75 per cent and in late 66 per cent. All writers have reported an increased proportion of staphylococcal infections, particularly in early cases[8-11,14,20,22] and due to Coxiella burnetii in those occurring later. In this series 33 of 84 cases were caused by staphylococci. Of the 33, all the early cases and 10 of the 25 later cases were caused by coagulase negative species, which accords with the findings of Masur and Johnson[19] and the Communicable Disease Surveillance Centre[20].

There is a considerable population at especial risk of IE (Table 2). Prosthetic valve implantation is the major hazard but other writers have found a similar susceptibility in those who have had a previous attack of IE[13,14,23-25], in i.v.-drug abusers[8,10-15,16,24], diabetics[5,10,11,13,24,25], those suffering from malignancy[5,11-13,15,25] or leukaemia[11,13], alcoholics[5,10,24,25], the immunosuppressed[15,23-25] and those on renal dialysis[8,14,24].
Table 1 shows the portal of entry of the causal organism in the 582 episodes of IE included in the British Cardiac Society/Royal College of Physicians Research Unit survey. In 349 no portal of entry was apparent, while in the remaining 233 a variety of explanations appeared likely; 108 were possibly dental in origin, while 109 arose from the gastrointestinal tract, the genito-urinary tract, the respiratory tract, or the skin, or from nosocomial infection resulting from procedures involving access to the blood-stream. Smaller numbers were attributable to narcotic addiction, fractures and pregnancy or parturition. Other writers have reported similar findings[5,9,11-15,16,23-27].

The success of efforts to reduce the incidence of and mortality from IE is greatly prejudiced by the fact that in three-fifths of the patients there is no hint as to how the causal organism gained access to the blood-stream. Since Horder’s[28] classic paper three-quarters of a century ago, dental sepsis and dental procedures have been thought frequently responsible. Gates and Christie[3] thought the teeth were the culprit in nearly one-quarter of their 442 patients and it has long been considered necessary to give antibiotic prophylaxis to anyone with known rheumatic or congenital heart disease to cover any dental procedure they may undergo. This has not proved as satisfactory as was hoped. Thousands and thousands of dental procedures are carried out every day under widely differing circumstances and the fact that the patient has a cardiac lesion may be easily forgotten or not known, or the antibiotic may be incorrectly administered or correctly administered and ineffectual[25,29]. Recent reports[5,6,10,13,14,30] have indicated that a dental source for the infection is less frequent than hitherto and the British Cardiac Society/Royal College of Physicians Research Unit survey[25] showed only 11.7 per cent of 544 episodes of IE possibly due to dental procedures and 7.1 per cent possibly due to dental sepsis but of these patients 42.5 per cent were not known to have any pre-existing heart disease. They recommended prophylactic antibiotic cover for all those with known cardiac disease as suggested by the British Society for Antimicrobial Chemotherapy[31], but stressed the importance of encouraging people to seek better routine dental care.

It is even more unrealistic to hope to prevent episodes of IE of gastrointestinal, genito-urinary, respiratory or dermal origin or those associated with fractures, pregnancy and parturition. Cases so caused are very few, especially when considered in the light of the enormous number of surgical and investigative procedures carried out on the gastrointestinal, genito-urinary and respiratory tracts, the common infections, tumours and other lesions in these organs and the very frequent breaches of the skin surface which most people experience, all of which could act as the portal of entry.

Added to these difficulties is the increasingly recognised fact that in about one-third of cases of IE the infection appears to attack previously normal hearts. The scope for effective prophylaxis is therefore limited but the susceptibility of those with rheumatic or congenital cardiac abnormalities, calcific aortic stenosis, prosthetic valves, previous other cardiac surgery, previous attacks of IE, who are immunosuppressed or on dialysis, who are diabetics or addicted to drugs or alcohol, should be kept constantly in mind and for these groups antibiotic prophylaxis, as suggested by the British Society for Antimicrobial Chemotherapy, should be considered whenever they are at risk.

Acknowledgements

We are greatly indebted to Fellows and Members of the College and to members of the British Cardiac Society for their co-operation and help in this project.

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