

# The bowel, the genitourinary tract, and infective endocarditis

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**SUMMARY** Of 582 episodes of infective endocarditis 75 were attributable to organisms normally resident in the bowel and 12 others were associated with alimentary tract operations, investigations, or disease. The mean age of the 87 patients in this particular group was higher (59.7 years) than that of all the patients with infective endocarditis (51.4 years). As far as could be ascertained 41% had no pre-existing cardiac abnormality, and in a little under a half no predisposing event to initiate the illness was apparent. Where the portal of entry of the organism to the blood stream was evident it was slightly more often in the genitourinary than the alimentary tract.

Bowel organisms are no less important than those associated with the teeth in causing infective endocarditis. It is suggested that in all those patients with known cardiac abnormalities and possibly in those over the age of 60 with normal hearts antibiotic cover should be considered when they undergo genitourinary or alimentary tract surgery or instrumentation.

The prognosis of infective endocarditis has improved dramatically since the advent of antibiotic treatment<sup>1-13</sup> and more recently as a result of emergency valve replacement.<sup>3 5 8 9 12 13</sup> In the best centres the mortality rate is now apparently less<sup>8 14</sup> than the widely quoted figure of 30%.<sup>4 5 10 13-15</sup> Nevertheless, the prevalence of the disease is probably increasing and it remains a serious threat to life in all who suffer from it. Doubtless there will be further reductions in mortality with advances in cardiology, microbiology, and surgery, but the major effort must be in prevention. Those with rheumatic, congenital, or degenerative heart disease, with prosthetic valves<sup>6 7 9 12 16-19</sup> or who have undergone other cardiac surgery,<sup>4 7</sup> and those with a history of infective endocarditis<sup>4 12 16</sup> are at especial risk and should have antibiotic prophylaxis if they need dental treatment or investigatory or therapeutic procedures related to the alimentary, genitourinary, or respiratory tracts. In addition, the immunosuppressed, those addicted to alcohol, and those with diabetes<sup>3</sup> or malignant disease<sup>4</sup> are particularly vulnerable. Nevertheless, one tenth of patients with infective endocarditis have a pre-existing cardiac

abnormality which is not known to either them or their doctor,<sup>20</sup> and it is also becoming increasingly clear that a large proportion of patients with infective endocarditis have clinically normal hearts before the onset of their illness,<sup>6-9 13 16 20 21</sup> which are important factors that influence the application of any planned prophylactic regimen.

In a few patients with infective endocarditis the portal of entry of the causal organism is beyond dispute. In the vast majority, however, the mechanism or route by which the organism gains entry to the blood stream is unknown or unproved. Oral organisms are the most common, and dental surgery has been suspected for many years; although this is doubtless the cause in some patients, definite proof is lacking, and the proportion so attributable is probably small.<sup>22</sup> Other infections are thought to arise from the alimentary, genitourinary, or respiratory tracts or from the skin but again the evidence, though strong, is largely circumstantial. In fact the only group in which causation appears certain is in the right sided endocarditis of drug addicts.

A recent investigation conducted jointly by the Royal College of Physicians Research Unit and the British Cardiac Society and related especially to the dental prophylaxis of infective endocarditis has provided the largest series of patients yet studied.<sup>20 22</sup>

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This investigation concerned those patients in whom the causal organism's normal, but not exclusive, habitat was the alimentary tract and those in whom the illness followed some alimentary tract investigation, operation, or disease. Could infective endocarditis have been prevented in this not inconsiderable group?

### Methods

Members of the British Cardiac Society and fellows and members of the Royal College of Physicians in the United Kingdom were asked to complete a proforma in respect of all patients with infective endocarditis under their care during 1981 and 1982. The information requested included inter alia the causal organism, whether there was any known or unknown pre-existing cardiac abnormality, whether there had been any dental, other surgical, or investigative procedures or injury during the three months before the onset of illness, and if so whether antibiotic cover had been provided, and details of any other relevant factors.

### Results

Proformas in respect of 582 episodes of infective endocarditis occurring in 577 patients were received, five patients having had a second episode within the two year period. The age range of the patients was from 2 to 87 (mean age 51.4) years and there was a male preponderance (ratio 2:1).

Among the 582 episodes the evidence suggested that the alimentary or genitourinary tracts may have been responsible in 87 (15%). The causal organism was an unspiciated enterococcus in 17, *Streptococcus faecalis* in 14, *Streptococcus bovis* in 27 (Table 1), *Escherichia coli* and other Gram negative bacilli in 11, and *Streptococcus durans* or group D streptococci in six (Table 2). In addition there were 12 patients in whom the illness was temporally related to some alimentary tract disease or operation but in whom the dominant habitat of the causal organism was not the bowel (Table 3). Similarly details are given (but not otherwise considered here) of patients whose infective endocarditis was not caused by bowel organisms but whose illness was associated with genitourinary disease, investigation, or surgery (Table 3).

The twofold male preponderance in the group as a whole was the same in the 87 patients whose infective endocarditis may have arisen from the alimentary tract, but the mean age was higher in the latter (59.7 compared with 51.4 years). Ten of the 87 patients died, a slightly smaller proportion than that in the total 577 patients.

Of the 87 patients, 36 (41%) had, as far as could be ascertained, no pre-existing cardiac abnormality, a

proportion exactly the same as in the total 577 patients. The valves affected did not differ in the alimentary tract group from all those examined, the aortic valve being affected in 29 patients and the mitral valve in 23.

### Discussion

Table 1 shows that of the 17 cases due to unspiciated enterococci one was associated with gall bladder disease, one followed an appendicectomy and one a gastrointestinal infection, one had undergone a total pancreatectomy and was a diabetic and dependent on alcohol, and one had had a dental filling without antibiotic cover within the previous three months when his heart was thought to be normal. Three cases arose from the genitourinary tract: one after a transurethral prostatic resection, one after urethral dilatation, and one in association with a urinary tract infection. In another patient a lacerated hand was the portal of entry, but in the remaining eight patients there was no indication of how the organism gained entrance to the blood stream. These findings in respect of enterococcal infections are similar to those of other workers.<sup>21 23</sup> The fact that enterococci commonly colonise the anterior urethra, the vagina, and the cervix explains the cases arising from the genitourinary tract.

In the 14 *S faecalis* infections (Table 1) the causal factor was evident in all but two patients, one of whom had had a previous attack of infective endocarditis. Three infections followed an alimentary tract operation (hemicolectomy, haemorrhoidectomy, and surgery for a gangrenous femoral hernia). One case followed dental sepsis and one a Colles fracture and may have arisen from it or from the anaesthetic for its reduction. Five cases arose from the genitourinary tract (prostatectomy for carcinoma, cystoscopy, vaginal hysterectomy, insertion of a ring pessary, urinary tract infection), and one case developed during the thirty third week of pregnancy. Infective endocarditis during pregnancy has been reported,<sup>15 24</sup> and *S faecalis*, like unspiciated enterococci, often colonise the lower genitourinary tract and perineum. In 15 of the 27 cases due to *S bovis* (Table 1), however, there was no indication of why the infection developed except that one of the 15 patients had had a previous episode of infective endocarditis and one had a prosthetic mitral valve. Six cases were associated with alimentary tract disease or procedures (gastric polyp, tubocellular adenomata of colon, closure of colostomy, liver biopsy in a patient who probably had a carcinoma, and diverticular disease in two patients). In a further three patients dental sepsis was present, and one had had scaling within two months of the onset of illness with antibiotic cover. Of the remaining two patients, one was receiving prednisone for asthma

Table 1 Details of patients with infective endocarditis due to various bowel organisms

Case No	Sex	Age (yr)	Previous cardiac abnormality	Valve affected	Portal of entry or other causal factor	Outcome
<i>Unspiciated enterococci</i>						
6	M	75	None	Aortic	TUR	Died
24	M	61	Congenital aortic stenosis and previous AVR	Aortic	None	Died
36	M	61	Rheumatic heart disease	Mitral	Gastrointestinal infection 3 weeks before onset	
37	M	38	None	NS	Diabetic. Alcoholic. Had had total pancreatectomy	
39	M	61	Rheumatic heart disease	NS	None	
59	M	18	None	Aortic	Dental filling within 3 months without antibiotic cover	
85	M	62	Previous AVR for aortic stenosis	Aortic	None	Died
103	M	60	Previous AVR for aortic stenosis	Aortic	Lacerated thumb	
106	M	44	Bicuspid aortic valve	Aortic	None	
126	F	71	Known cardiac abnormality nature uncertain	NS	Urinary tract infection	
127	F	46	None	Aortic	None	
243	M	76	Rheumatic heart disease	Mitral	Urethral dilatation	
245	F	29	Rheumatic heart disease	Aortic	Appendectomy	
331	M	71	None	NS	None	
345	M	63	None	Aortic	Gall bladder disease	
413	F	58	None	NS	None	
440	F	80	None	NS	None	
<i>Streptococcus faecalis</i>						
13	M	60	None	Aortic	Right hemicolectomy for angiodysplasia	Died
18	F	58	Previous IE	Mitral	Previous IE	
87	F	27	VSD	VSD	33 weeks' pregnant	
146	F	73	None	Mitral	8 weeks after Colles fracture	Died
157	F	47	Rheumatic heart disease	NS	After operation for haemorrhoids	
204	M	68	None	Mitral and aortic	None	Died
217	F	73	Aortic stenosis	Aortic	After operation for gangrenous femoral hernia	
221	M	71	Known murmur	Aortic	None	
309	F	NS	None	NS	After vaginal hysterectomy	
320	M	77	Known mitral incompetence	Mitral	Urinary tract infection	
435	F	79	None	NS	After insertion of a ring pessary	
437	M	66	Had had MVR	Mitral	After cystoscopy	
481	M	71	Mitral valve prolapse	Mitral	After prostatectomy for carcinoma of prostate	
506	M	59	Degenerative heart disease	Aortic	Dental sepsis	
<i>Streptococcus bovis</i>						
16	F	61	Congenital heart disease	Congenital defect	Dental sepsis	
21	F	NS	Rheumatic heart disease	NS	None	
57	M	34	Aortic incompetence	Aortic and mitral	None	
105	F	54	None	NS	Dental sepsis	
112	M	42	Rheumatic heart disease	NS	None	
116	M	43	None	Mitral	Alcoholism	
150	M	44	None	NS	Dental sepsis	
171	M	62	Rheumatic heart disease	NS	None	
175	M	77	Mitral incompetence	Mitral	Gastric polyp, dental caries	
182	M	38	Bicuspid aortic valve	Aortic	None	
233	F	46	Rheumatic heart disease, previous MVR	Mitral	None	
240	M	55	None	NS	None	
259	M	68	Mitral incompetence	Mitral	None	Died
273	M	63	None	Aortic	Scaling 5-8 weeks previously without antibiotic cover	
327	M	61	None	Aortic	None	
337	M	71	Myocardial infarction (1973)	NS	Closure of colostomy	
389	F	76	Aortic sclerosis	Aortic	None	
418	F	61	Mitral incompetence	Mitral	None	
447	M	72	None	Mitral	None	
452	F	69	None	NS	Diverticulitis	
461	M	61	None	NS	Liver biopsy, probably carcinoma	Died
474	F	61	None	NS	Prednisone for asthma	
480	M	60	None	NS	Diverticular disease	
490	M	48	None	NS	Two tubocellular adenomata of colon	
493	F	63	None	Aortic	None	
538	M	77	Rheumatic heart disease, IE (1981)	NS	None	
545	F	80	Rheumatic heart disease	Mitral	None	Died

TUR, transurethral resection; AVR, aortic valve replacement; VSD, ventricular septal defect; NS, not stated; IE, infective endocarditis; MVR, mitral valve replacement.

Table 2 Details of patients with infective endocarditis due to *E coli*, gram negative bacilli, *S durans*, and group D streptococci

Case No	Sex	Age (yr)	Previous cardiac abnormality	Organism	Valve affected	Portal of entry or other causal factor
<i>E coli</i> and Gram negative bacilli						
68	F	59	None	Coliform	NS	Nephrectomy for pyelonephritis
79	F	NS	AVR (1972)	<i>B fragilis</i>	Aortic	None
266	M	50	Myocardial infarction	<i>E coli</i>	Mitral	TUR
322	F	65	Rheumatic heart disease	<i>E coli</i>	NS	None
409	F	64	Rheumatic heart disease	<i>E coli</i>	NS	Urinary tract infection
462	M	68	Ischaemic heart disease	<i>E coli</i>	NS	None
470	M	62	None	<i>E coli</i>	NS	Diabetes; carcinoma of bladder
495	M	27	Bicuspid aortic valve	Gram negative bacillus	Aortic	None
534	F	NS	Rheumatic heart disease	<i>E coli</i>	NS	Urinary tract infection
552	M	32	Congenital heart disease; pacemaker	<i>E coli</i>	Pacemaker	None
553	M	33	Marfan's syndrome; AVR	<i>E coli</i>	Aortic	None
<i>S durans</i> and group D streptococci						
32	M	22	Known enlarged heart	Group D streptococcus	Aortic	None
60	M	72	None	Group D streptococcus	NS	None
96	M	72	AVR for aortic stenosis	Group D streptococcus	Aortic	None
307	M	58	Rheumatic heart disease	<i>S durans</i>	Aortic and mitral	None
509	M	76	Rheumatic heart disease	<i>S durans</i>	NS	None
569	F	59	None	Group D streptococcus	NS	Nerve conduction studies for peroneal muscular atrophy

NS, not stated; AVR, aortic valve replacement; TUR, transurethral resection.

Table 3 Details of patients with infective endocarditis apparently related to the alimentary tract or the genitourinary tract

Case No	Sex	Age (yr)	Previous cardiac abnormality	Organism*	Valve affected	Portal of entry or other causal factor
<i>Alimentary tract</i>						
114	F	73	None	$\alpha$ haemolytic streptococcus	Aortic	Cryptogenic cirrhosis; monilial angular stomatitis
119	M	79	Ischaemic heart disease	$\alpha$ haemolytic streptococcus	NS	Bilateral inguinal herniotomy
192	M	66	Rheumatic heart disease	$\alpha$ haemolytic streptococcus	Mitral	Dilatation of oesophageal stricture
195	M	65	None	Coagulase negative staphylococcus	NS	Right inguinal herniotomy
380	M	27	Congenital heart disease	Group B streptococcus	Congenital lesion	Down's syndrome; bleeding haemorrhoids
381	F	57	Rheumatic heart disease	$\alpha$ haemolytic streptococcus	Aortic	Gall bladder disease
434	F	63	Previous MVR and TVR	Negative	Tricuspid and mitral	Gastroscopy; dental sepsis
457	M	71	None	$\alpha$ haemolytic streptococcus	Mitral	Gastroscopy
473	M	86	None	<i>S mutans</i>	Aortic	Cholecystectomy for empyema of gall bladder
485	M	60	None	<i>S sanguis</i>	Mitral	Surgery for rectal carcinoma
512	M	78	Mitral incompetence	<i>S mutans</i>	Mitral	Carcinoma of rectum
578	M	52	None	Group B streptococcus	NS	Liver failure
<i>Genitourinary tract</i>						
1	M	75	Rheumatic heart disease	<i>S viridans</i>	NS	Urinary tract infection
41	M	74	None	Negative	Aortic	Within one month of retropubic prostatectomy
131	M	57	Infective endocarditis and valve replacement (1973)	<i>Staphylococcus aureus</i>	NS	Urethral dilatation; urinary tract infection
144	F	37	None	<i>S viridans</i>	Mitral	Followed parturition
199	M	55	Aortic valve replacement (1973)	Negative	Aortic	Urinary tract infection
209	F	71	None	Proteus sp	Mitral	Pyelonephritis; diabetes mellitus; proteus sp in urine
210	F	38	None	<i>S viridans</i>	Aortic	22 weeks pregnant
292	F	72	None	<i>Staph aureus</i>	NS	Within one month of repair of vaginal prolapse; diabetes; myxoedema
334	M	36	None	<i>S sanguis</i>	Aortic and mitral	Renal calculus and colic; ?Marfan's syndrome
431	M	65	Bicuspid aortic valve (not known)	<i>Pseudomonas aeruginosa</i>	Aortic	Urinary tract infection
433	M	68	Calcific aortic stenosis	<i>Staphylococcus albus</i>	Aortic	Followed transurethral prostatic resection; rheumatoid arthritis
522	F	63	Aortic and mitral valve replacements for rheumatic heart disease (1981)	<i>S viridans</i>	Aortic and mitral	Carcinoma of cervix; dilatation and curettage and radiotherapy

TUR, transurethral resection; MVR, mitral valve replacement; TVR, tricuspid valve replacement; NS, not stated.

\* $\alpha$  haemolytic streptococcus was previously known as *S viridans*.

and the other was dependent on alcohol.

Table 2 shows the 11 *E coli* and other Gram negative infections. In five cases the organism appeared to come from the urinary tract, while in the remaining six there was no indication of how it gained entrance to the blood stream. *E coli* and other Gram negative bacilli are of course often responsible for urinary tract infection. Of the six cases due to group D streptococci or *S durans* (Table 2), one followed nerve conduction studies, but in the other five the portal of entry was not known, although one of the five had a prosthetic valve.

By definition all patients shown in Table 3 had some alimentary tract disorder or had undergone an operation or investigation: liver disease (two), gall bladder disease (two), rectal carcinoma (two), herniotomy (two), haemorrhoids (one), and dilatation of an oesophageal stricture (one). In eight of the 12 cases the organism was of the *Streptococcus viridans* group, in two a group B streptococcus (considered by some to be a bowel organism), in one a coagulase negative staphylococcus, and in one the culture was negative. Of the 75 cases of infective endocarditis due to organisms normally present in the bowel, there were therefore 12 that appeared to arise from the alimentary tract and 15 from the genitourinary tract, while in 40 the portal of entry was not known.

In addition to dental procedures many investigations, diseases, and operations of the alimentary tract are known to be associated with transient symptomless bacteraemia.

Bacteraemia has been reported after upper gastrointestinal endoscopy<sup>25</sup> and after endoscopic retrograde cholangiopancreatography,<sup>26</sup> but in none of these cases did infective endocarditis develop. In two of the patients (cases 434 and 457), however, infective endocarditis followed gastroscopy. Case 434 had prosthetic mitral and tricuspid valves and dental sepsis; case 457 had no pre-existing cardiac abnormality but the causal organism was an  $\alpha$  haemolytic streptococcus (previously termed *S viridans*). Gastroscopy may be associated with considerable mucosal trauma. Buchman and Bergland reported positive blood cultures after sigmoidoscopy in 13 of 100 patients but thought that most, if not all, were due to contaminants.<sup>27</sup> Le Frock and his colleagues<sup>28</sup> and Weinstein,<sup>29</sup> however, found transient symptomless bacteraemia in 9.5% of 200 patients after sigmoidoscopy, but this was not confirmed by Engeling and his co-workers.<sup>30</sup> Moreover, blood cultures after colonoscopy with or without biopsy have been negative<sup>31</sup> unless associated with colonic carcinoma,<sup>32</sup> itself well known to be associated with infective endocarditis.<sup>33</sup> Two of our 90 patients had rectal carcinoma (cases 485 and 512).

Transient symptomless bacteraemia has been

reported after a barium enema<sup>29 34</sup> and even after a normal bowel action. Bacteraemia<sup>35 36</sup> but not infective endocarditis has been reported after percutaneous liver biopsy and after transrectal prostatic biopsy.<sup>37</sup> One of the patient's symptoms of infective endocarditis began after liver biopsy (case 461), but he probably had carcinomatosis.

There have been many reports linking *S bovis* endocarditis with carcinoma of the colon<sup>38-40</sup> and other colonic disorders,<sup>41-43</sup> and in some the endocarditis has presented before any symptoms of the colonic lesion have been evident.<sup>39</sup> Although 27 of the 75 patients with endocarditis caused by bowel organisms had *S bovis* infections, only six had any abnormality of the alimentary tract.

Disease of the biliary tract is often associated with bacteraemia, and there have been reports of infective endocarditis arising from it particularly when surgical intervention is necessary.<sup>15 16 44</sup> Gall bladder disease (case 345) and cholecystectomy (case 473) were the only examples among the 87 patients.

There have been excellent studies of enterococcal,<sup>21 23</sup> *E coli*,<sup>45</sup> and group D streptococcus endocarditis,<sup>23 46</sup> each of which has reflected the frequency with which the infection stems from the genitourinary tract. They also indicate the now well known fact that while *S bovis* infections respond well to penicillin those due to unspiciated enterococci and *S faecalis* require treatment with an aminoglycoside in combination with penicillin. The nomenclature and classification of the organisms confuse the issue as does the now well known difficulty of differentiating between *S bovis* and *S faecalis*.<sup>9</sup>

Transient symptomless bacteraemia obviously follows alimentary and genitourinary surgical and investigative procedures not infrequently and may also occur under physiological conditions. Only an extremely small proportion of such bacteraemias progress to infective endocarditis, and among the factors influencing this development are the magnitude of the bacteraemia, the virulence of the organism, and the susceptibility of the host. The presence of a prosthetic valve, a previous episode of infective endocarditis, and a rheumatic, congenital, or degenerative cardiac abnormality play an important part, but depression of defence mechanisms by age, malignancy, alcohol dependence, diabetes, immunosuppression, hepatic or renal failure, or other serious illness are frequent contributory influences. Even so, in nearly half the 75 patients, in whom infective endocarditis was due to organisms normally resident in the gut, there was no explanation of why the bacteraemia occurred.

With regard to the prophylaxis of infective endocarditis due to bowel organisms, it is clear that such infections occur in older patients and derive

from the genitourinary tract slightly more often than from the alimentary tract. Furthermore, only 16% of cases of infective endocarditis are due to bowel organisms, and nearly half of these are unexplained; in the face of the enormous number of operations and investigatory procedures involving the alimentary and genitourinary tracts the risk of infective endocarditis arising therefrom must be very small indeed. Nevertheless, despite the minimal danger of such procedures infective endocarditis remains an appreciable cause of morbidity and mortality, and measures for its prevention are important. Certainly, the present findings indicate that all those with known cardiac abnormalities should be given antibiotic cover for all surgical, alimentary, and genitourinary procedures and for gastroscopy. Furthermore, in view of the high proportion of older patients with normal hearts contracting infective endocarditis those in this age group should be considered for similar prophylaxis. The measures suggested by the British Society for Antimicrobial Chemotherapy<sup>47</sup> may be appropriate, but in each patient there will be differing circumstances to be taken into account. The case for antibiotic cover is certainly as strong as that for dental procedures. In the 582 episodes of infective endocarditis, of the 329 with "*S. viridans*" infections or with negative blood cultures, only 38 (12%) of those known to have a cardiac abnormality had had a dental procedure within three months of the onset of illness, and eight of the 38 had had antibiotic prophylaxis which failed. In comparison, of the 87 patients in whom infective endocarditis was caused by bowel organisms or followed some alimentary tract investigation or operation, 15 (17%) had a known cardiac abnormality, and only two received antibiotic prophylaxis at the relevant time, which failed. Nevertheless, it must be acknowledged that had prophylaxis such as we suggest been given to those of the 87 patients in whom it would have been considered appropriate at most the infective endocarditis would have been prevented in only about a fifth. Many were particularly vulnerable on account of age and other serious illness.

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