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Antibiotic susceptibility of streptococci and related genera causing endocarditis: analysis of UK reference laboratory referrals, January 1996 to March 2000

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A combination of penicillin and gentamicin is recommended for streptococcal endocarditis by both the Endocarditis Working Party of the British Society for Antimicrobial Chemotherapy and the American Heart Association, with vancomycin replacing penicillin for those who are allergic to penicillin.^{1,2} The Public Health Laboratory Service's Antibiotic Resistance Monitoring and Reference Laboratory and Streptococcus and Diphtheria Reference Unit routinely test bacteria referred from cases of endocarditis from a wide range of hospitals, representing about 15% of all UK isolates from endocarditis. We retrospectively analysed the species distribution and antimicrobial susceptibility of streptococci and related bacteria from patients with endocarditis received over 4.25 years; enterococci have been reviewed previously.³

Methods and results

Isolates from confirmed cases of endocarditis referred between January 1996 and March 2000 were identified from the reference laboratory's database, which provides antibiotic susceptibility as minimum inhibitory concentrations of each antibiotic for each isolate. Isolates were categorised as susceptible or resistant using published criteria.⁴

Data were available for 607 non-duplicate isolates, comprising 26 genera or species, referred from 168 UK hospitals (table). Most (86%) of the isolates were "viridans" group streptococci, which are documented as the commonest agents of endocarditis.⁵ Five species accounted for over two thirds of the isolates. Among these, 13% of *Streptococcus oralis* isolates, 14.5% of *S sanguis*, and 5.5% of *S gordonii* had reduced penicillin susceptibility (minimum inhibitory concentrations greater than 0.125 mg/l), whereas all *S bovis* type I and *S mutans* isolates were susceptible. Other species and

genera comprised fewer than 20 isolates each, precluding meaningful calculation of percentage resistance. None the less, it was notable that both isolates of *Abiotrophia defectiva* and six of 15 isolates of *A adjacens* had reduced susceptibility to penicillin. All isolates of *S pneumoniae* and Lancefield groups A, B, C, and G streptococci were susceptible to penicillin.

Overall, 88.8% of the isolates were susceptible to penicillin (minimum inhibitory concentrations \leq 0.125 mg/l), and minimum inhibitory concentrations of 0.25 mg/l were seen for another 4.4%. Minimum inhibitory concentrations of 4-8 mg/l were seen for only seven isolates (1.2%). All of the isolates were susceptible to vancomycin and teicoplanin (minimum inhibitory concentrations 0.5 to 2 mg/l) and none had high level resistance (minimum inhibitory concentration greater than 2000 mg/l) to gentamicin.

Comment

Although the clinical data available to our reference laboratory are sometimes limited and there is a potential for submission bias, we believe that our analysis is the most comprehensive possible for streptococcal endocarditis. The data confirm the dominance of "viridans" streptococci and indicate that whereas a few (1.2%) have substantial penicillin resistance, most remain fully susceptible. Some guidelines advocate that endocarditis of a native valve caused by streptococci that are susceptible to penicillin should be treated for two weeks with penicillin plus gentamicin, provided patients lack thromboembolic disease and cardiac risk factors, have small vegetations, and respond clinically within the first week.¹ In patients not fulfilling these criteria or with infection of a prosthetic valve, four weeks of penicillin plus gentamicin is recommended. Treatment for at least four weeks is also advocated for

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Identification of 607 isolates from cases of endocarditis and their susceptibility to penicillin

Organism	No (%) of isolates	No of hospitals	No of isolates with indicated penicillin minimum inhibitory concentrations (mg/l)							
			≤0.06	0.125	0.25	0.5	1	2	4	8
<i>Streptococcus oralis</i> *	145 (23.9)	78	98	28	9	3	3		3	1
<i>Streptococcus sanguis</i> *	110 (18.1)	69	82	12	5	6	5			
<i>Streptococcus gordonii</i> *	55 (9.1)	41	50	2	2				1	
<i>Streptococcus bovis</i> type I*	54 (8.9)	39	53	1						
<i>Streptococcus mutans</i> *	51 (8.4)	39	50	1						
<i>Streptococcus mitis</i> *	28 (4.6)	24	18	3	1	1	2	2		1
Lancefield Group B	22 (3.6)	20	22							
Lancefield Group G	19 (3.1)	19	19							
<i>Streptococcus galloyticus</i> *†	17 (2.8)	16	17							
<i>Streptococcus vestibularis</i>	17 (2.8)	15	10	1	1	1	4			
<i>Streptococcus parasanguis</i> *	16 (2.6)	15	5	5	4	1		1		
<i>Abiotrophia adjacens</i>	15 (2.5)	15	6	3	4	1				1
<i>Streptococcus anginosus</i>	15 (2.5)	15	13	2						
<i>Gemella morbillorum</i>	10 (1.6)	10	9	1						
<i>Streptococcus salivarius</i>	7 (1.2)	6	5	1				1		
<i>Streptococcus pneumoniae</i>	7 (1.2)	5	7							
<i>Streptococcus intermedius</i>	5 (0.8)	5	5							
<i>Gemella haemolyans</i>	4 (0.7)	4	3			1				
Lancefield Group A	3 (0.5)	3	3							
<i>Abiotrophia defectiva</i>	2 (0.3)	2			1	1				
Lancefield Group C	2 (0.3)	2	2							
<i>Streptococcus constellatus</i>	1 (0.2)	1	1							
Lactococcus spp	1 (0.2)	1				1				
<i>Streptococcus sobrinus</i> *	1 (0.2)	1	1							
All isolates	607 (100)	168	479 (78.9%)	60 (9.9%)	27 (4.4%)	16 (2.6%)	14 (2.3%)	4 (0.7%)	4 (0.7%)	3 (0.5%)

*Species included with "viridans" group of streptococci.

†Previously known as *S bovis* type II.

patients with streptococci with reduced susceptibility to penicillin: the British Society for Antimicrobial Chemotherapy advocates penicillin plus gentamicin for four weeks when the minimum inhibitory concentration of penicillin exceeds 0.1 mg/l; the American Heart Association advocates penicillin for at least four weeks, with gentamicin for the first two weeks if the minimum inhibitory concentration of penicillin is 0.25 mg/l or for at least four weeks if it exceeds this value.

Although reduced susceptibility to penicillin was noted in about 11% of our isolates, with 1.2% substantially resistant, none showed resistance to vancomycin or high level resistance to gentamicin, which would abolish synergy in combined treatments. Although reduced susceptibility to penicillin has implications for the duration of treatment, penicillin and gentamicin remain appropriate for most patients, with vancomycin and gentamicin a universally active alternative for those who are allergic to penicillin or who have more resistant isolates.

Contributors: APJ conceived the idea for the project, collected and analysed the data, and drafted the paper; he will act as guarantor for the paper. MW performed the antibiotic susceptibility tests. KB and AE speciated the bacterial isolates. DJ assisted in collection and collation of the data. DML and RCG contributed to discussions.

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One hundred years ago Longevity in Spain

If any one is ambitious to achieve the honour of centenarianism he might, if any trust is to be put in statistics, do worse than go and live in Asturias. The list of voters drawn up for the recent elections showed that there is a remarkable number of persons who have attained to a patriarchal length of days in that province of Spain. Each of the electoral districts of Langreo, Morcin, Grado, Villaviciosa, and Carreno has one centenarian; Siero and Oviedo have each two; Salas has electors aged respectively 101, 103, and 104; Cangas de Tineo has still more venerable triplets of

101, 105, and 106; Boal has two aged 101 and 102; Franeo one of 107; Valdes two of 105 and 107; Pitona two of 102 and 104; while Parres holds the record with three fine relics of antiquity, aged respectively 103, 105, and 107. This single province therefore rejoices in no fewer than 28 centenarians in a total population of 600,000. The fact speaks well for the excellence of the climate of Asturias and for the vital stamina and healthiness of life of its inhabitants.

(*BMJ* 1901;i:418)