he rang me up and asked if he could show me how well he was. Certainly, eighteen months after my hopeless forecast, he looked as well as any man of his age in Europe and showed no sign of cancer. Fortunately he was pleased about it and did not threaten to sue me for £6,000 damages.

Fallacy of Statistics

Such experiences, indeed my whole experience, have left me with profound mistrust of statistics. I have not published mine since I was young and credulous; indeed, I do not know them now unless I ask my registrar to look them up for a particular purpose, and I do not pay any attention to those of others. Personal statistics, as I have said on many occasions, are at the bottom of all unsound teaching; they are either too good to be true or too true to be good.

Those who see statistics in the making are well aware how errors may creep in or be pushed in. Falsification may appear in many ways. The ailing may be transferred to another ward, another block, another hospital, there to die; they may develop complications and be entrusted to the care of a physician and disappear from the surgeon's series; the unsuccessful cases may be indexed under another diagnosis, or appear in the list of operations done by the assistant or the registrar. Quite apart from the temptation to dishonesty, there is, in the keeping and publishing of statistics, an almost insuperable temptation to the surgeon to depart from the only criterion of surgical rectitude—the best interests of the particular patient who is in the ward to-day and will be on the table to-morrow.

The surgeon who never does a severe operation has the fewest deaths, but he saves the fewest lives. The man who limits his operations on hypertension to a small group of young people who respond well to all tests has a wonderfully low death rate and high cure rate, but he passes by all those who need help most. The surgeon who closes up a high proportion of his cancer laparotomies as "inoperable" and reserves his resection for the early growths can show a fine record on paper; how will he himself show up before the recording angel? I personally suspect the man with huge figures and a negligible mortality of being a surgical spiv.

One gastric surgeon surprised the world some years ago by recording 500 gastrectomies for ulcer with 0.6% mortality. Fine! He then reached a total of 1,000 cases with a mortality of 0.6%. Grand! A little later he popped up with 2,000 with a mortality of 0.6%. Marvellous! He now has 3,000 with a mortality of 0.6%. Incredible; especially as the gastrectomies are all done under inhalation anaesthesia with open ether in a clinic where the science of anaesthesia is much where Morton left it. It is clear that to this man, a skilled surgeon, the figure of 0.6% is a symbol, a creed, a banner beneath which he goes into battle. It is his story, and he is going to stick to it. As for myself I shall leave him stuck. The only figures which I find statistically significant are those recorded anonymously and analysed impartially by someone with no personal interest in the verdict. Such are the many statistics published by Colonel Harnett on behalf of the British Empire Cancer Campaign, and Truscott's analysis of twenty years' records of cancer of the breast at the Middlesex Hospital.

I have said, in my Rutherford Morison lecture, that a man is brought into surgery by a love of his fellow men and a sincere wish to help them. As the years go by experience will increase that love and, if he uses it right, will make his power to help more effective. But he must leave it to others to judge in how far he has succeeded.

SEROLOGICAL CLASSIFICATION OF VIRIDANS STREPTOCOCCI FROM SUBACUTE BACTERIAL ENDOCARDITIS, TEETH, AND THROATS

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In a previous report on the treatment of 18 cases of subacute bacterial endocarditis with penicillin (Ward, Meanock, Selbie, and Simon, 1946) it was stated that the biochemical characters of 14 strains of streptococci isolated from these cases indicated that some were similar to *Streptococcus salivarius*, described by Andrewes and Horder (1906) as the most common organism of this type in the mouth and nasopharynx and of frequent occurrence in subacute bacterial endocarditis, while the others were similar to a number of strains isolated by Okell and Elliott (1935) from cases of subacute bacterial endocarditis and from blood cultures in cases of dental sepsis.

It thus appeared likely that our strains of streptococci were of a type often found in subacute bacterial endocarditis and of common occurrence in the region of the mouth. In our further investigation of streptococci from these sources it became evident that biochemical tests were of little value for the classification of the viridans streptococci because of the inconstancy of biochemical reactions within the defined species or groups, as originally pointed out by Andrewes and Horder (1906). We therefore decided that an attempt should be made to classify these streptococci by serological methods.

In this communication it will be shown that when streptococci from cases of subacute bacterial endocarditis are tested with a number of antisera prepared by injecting rabbits with selected strains the reactions so obtained form a pattern on which a serological classification can be based. It will also be shown that streptococci from throat and teeth also react with these antisera to form a similar pattern, indicating a close relationship between the streptococci of subacute bacterial endocarditis and those commonly found in the region of the mouth. Some data are also presented on the relationship between streptococci isolated at different stages in several cases of subacute bacterial endocarditis.

Material and Methods

The investigation was based on 28 strains of streptococci isolated during the past three years at the Middlesex Hospital from 19 cases of subacute bacterial endocarditis and one case in which this condition was suspected, and two cultures of a strain of "streptococcus s.b.e." (Loewe, Plummer, Niven, and Sherman, 1946)—one from a case of subacute bacterial endocarditis and one of the same strain after passage through a rabbit—which were provided by Dr. Erna Altüre-Werber, of the Jewish Hospital, Brooklyn, N.Y. When the work was sufficiently advanced to show that these streptococci and similar streptococci from the throat, teeth, and other sources could be classified

serologically, an examination was made of three further collections of streptococci from cases of subacute bacterial endocarditis. The first of these, consisting of 39 strains from 30 cases, was supplied by Professor J. W. McLeod, of Leeds; the second, consisting of 14 strains from 13 cases at St. Bartholomew's Hospital, London, was supplied by Professor L. P. Garrod; and the third, consisting of 14 strains from 13 cases at St. Mary's Hospital, London, was supplied by Sir Alexander Fleming.

Streptococci from the throat and teeth were also investigated to see how far they could be correlated with the endocarditis strains. The 52 throat strains used were isolated from throat swabs taken by Dr. W. J. L. Sladen from 21 members of the Falkland Islands Dependencies Survey in November, 1947, immediately before the expedition sailed for the Antarctic. Of the 51 strains from teeth 15 were isolated from teeth extracted from four endocarditis cases under the care of Mr. J. W. Schofield and 36 were obtained during routine extractions in 18 cases under the care of Mr. A. L. Packham; 32 of the latter were isolated from the apices of extracted teeth and four from the blood stream of three patients immediately after extraction. Ten other strains of viridans streptococci were examined—three from specimens of sputum, four from abscesses, one from urine, and two from blood cultures in cases in which subacute bacterial endocarditis was suspected but not established.

After isolation and verification of the purity of the cultures the streptococci were transferred to tryptic digest broth with 10% horse blood, incubated overnight, and stored at 4° C. for periods up to six months.

Serological Tests

Preparation of Antisera.—The methods for producing antisera were essentially those used by Lancefield (1933). The immunizing antigen was prepared from 15 ml. of an 18-hour culture of streptococci in 1% glucose digest broth; the culture was centrifuged and the deposit of streptococci was resuspended in 15 ml. of normal saline. The antigen, which was kept at 4° C. when not in use, was injected intravenously into a rabbit in 1-ml. amounts daily for six days. The rabbit was then rested for eight days and given a second course of six daily injections with a fresh preparation of antigen followed by a rest period of eight days. This procedure was repeated until the serum developed enough antibody to give a satisfactory precipitin reaction with the homologous organism. The rabbit was then bled from the carotid artery or by cardiac puncture and the separated serum, with the addition of merthiolate to give a concentration of 1 in 15,000, was kept frozen in the refrigerator.

Untreated streptococci were at first used for immunization and produced good antisera in two rabbits, but several rabbits died with the lesions of bacterial endocarditis after one or two courses, so that subsequent antigens were treated either by heating at 60° C. for 30 minutes or by the addition of formalin to give a concentration of 0.2%. In some cases antisera giving a wider range of reactions were produced by the injection of antigen prepared from a strain after it had been grown for several subcultures in the presence of its homologous antiserum, a method that was used by Lancefield (1940) to produce variation in streptococci.

By these methods a total of 28 antisera were prepared against eight strains of streptococci isolated from cases of subacute bacterial endocarditis at the Middlesex Hospital, one strain of the American "streptococcus s.b.e."

(No. 2) and one (No. 30) from a suspected case of subacute bacterial endocarditis. Twenty antisera were used for classification, comprising two (Nos. 2 and 3) produced by the injection of untreated streptococci, two (Nos. 1 and 16) produced by the injection of streptococci treated with formalin, and 16 prepared against four streptococci (Nos. 5, 8, 10, and 30). Each of these four streptococci was used to produce four antisera—two by the injection of heat-treated and formalized organisms and two by the same procedures after growth of the streptococcus in its own antiserum. In the classification of our streptococci shown in Table I the

TABLE I.—Classification of Streptococci from Subacute Bacterial Endocarditis, Throats, Teeth, and Other Sources by Precipitin Reactions with Antisera

Group	No. of Strains	Reactions with Antisera							
		5	30	8	3	16	2	1	10
I	32	6	+	+	+	—	—	—	—
	12	+	+	10	1	—	—	—	—
	14	+	+	6	2	—	—	—	—
Ia	41	17	+	+	+	—	2	5	13
	15	+	+	2	5	—	1	5	13
	9	+	+	+	4	—	1	4	7
II	28	20	—	—	—	+	+	+	—
	2	—	—	—	—	+	1	—	—
	6	—	—	—	—	1	3	+	—
IIa	55	29	15	7	4	+	+	+	21
	15	11	10	4	1	+	7	—	3
	11	8	3	3	1	4	6	+	4
	13	6	—	—	—	—	—	—	+
III	25	5	—	+	1	—	—	1	+
	7	—	+	—	—	—	—	—	—

The streptococci are classified into five groups each containing three series of strains, in each of which the reactions with the appropriate antisera are indicated thus: + = all strains positive; — = all strains negative; numeral = number of strains positive.

reactions indicated as positive under antisera Nos. 5, 8, 10, and 30 represent positive reactions with any or all of the four antisera prepared against each streptococcus.

Preparation of Extracts of Streptococci.—The method used for the preparation of extracts of streptococci for precipitin tests was the formamide method described by Fuller (1938) for the extraction of polysaccharides and destruction of protein substances.

Precipitin Tests.—The method used for the precipitin test followed that of Lancefield (1933), 0.1 ml. of streptococcal extract being layered above 0.1 ml. of antiserum in a 4 by 0.5-cm. tube. In positive reactions a precipitate at the interface usually formed within 10 minutes, but in some cases there was a delay of up to 30 minutes when the final reading was made. A diffuse flocculation was sometimes observed, but this type of reaction was ignored, as it could not be reproduced and was therefore obviously not specific.

Biochemical Tests

In the fermentation tests the test reagents were purified and used at a concentration of 1% in 1/5 strength infusion broth to which was added 1% bactopectone, 0.5% NaCl, 2% horse serum, and phenol red as indicator. The results were finally read after incubation for three days at 37° C. Starch-splitting was tested by a plate method following that described by Andrewes (1930) and Hodgson, Heggie, and Sutherland (1943). Bile resistance was tested by the method of Belenky and Popowa (1929) on 5% blood agar with 40% bile prepared from "difco" dried ox bile.

Results of Serological Tests

Positive precipitin reactions to our antisera have been obtained with 181 of the 209 strains of streptococci examined. These positive reactions are tabulated in Table I, where it will be seen that the streptococci are classified according to their reactions with groups of antisera. In

the first group of streptococci are 32 strains which react only with members of the first group of four antisera. In Group Ia are 41 strains reacting mainly with the same four antisera but having side-reactions with other antisera but not No. 16. Group II consists of 28 strains which react only with members of the second group of three antisera; while in Group IIa are 55 strains which react mainly with the same three antisera but have side-reactions with other sera. In Group III are 25 strains which react with antisera 30 and 10, only eight strains having side-reactions with other antisera.

The results obtained with all the streptococci are shown in Table II, which also includes details of the classification

TABLE II.—*Serological Classification of Streptococci from Various Sources*

	No. of Strains	Group					Lancefield				No Reaction
		I	Ia	II	IIa	III	A	D	G	K	
Endocarditis											
Middlesex Hospital..	27	5	8	4	3	5	0	2	0	0	0
Leeds	39	10	7	4	5	7	0	2	0	0	4
St. Mary's Hospital	14	1	3	1	0	2	1	1	1	1	3
St. Barts. Hospital	14	1	1	5	4	1	0	0	0	1	1
"Streptococcus s.b.e."	2			1	1						
Total endocarditis	96	17	19	15	13	15	1	5	1	2	8
Teeth	51	7	12	8	19	3	0	0	0	0	2
Throats	52	7	9	4	19	6	0	3	0	0	4
Total teeth and throats	103	14	21	12	38	9	0	3	0	0	6
Other sources ..	10	1	1	1	4	1	0	0	0	0	2
All streptococci	209	32	41	28	55	25	1	8	1	2	16

of streptococci from different sources. It will be seen that we have succeeded in classifying all 27 strains from cases of subacute bacterial endocarditis at the Middlesex Hospital and 61 of the remaining 69 endocarditis strains. The 79 endocarditis strains in our serological groups are fairly evenly distributed in the five groups, but there is a preponderance of Group I streptococci in the Leeds collection and of Group II and IIa in the strains from St. Bartholomew's Hospital. The 17 endocarditis streptococci which do not fall into our classification consist of nine strains reacting with Lancefield group antisera and eight with which we have failed to obtain any reaction with the antisera at our disposal.

It is also shown in Table II that 94 of the 103 strains of streptococci from teeth and throats have been classified with our antisera. There is no difference in distribution within the five groups between the strains from these two sources, in spite of the fact that only streptococci showing α -haemolysis on blood agar were selected from cultures of teeth, whereas the streptococci from throats included 13 strains producing no change in blood agar. The distribution of the streptococci from teeth and throats in the five groups, unlike that of the endocarditis strains, is uneven, in that 38 strains, or over one-third, are found in Group IIa and only nine, or about one-tenth, in Group III. The proportion of streptococci from teeth and throats not falling within our classification is even smaller than in the case of the endocarditis strains, there being only nine such strains, three of which react with Lancefield Group D antiserum.

Of the 10 streptococci examined from other sources, four belong to Group IIa, four are distributed among the four other groups, and two do not react with any of the antisera at our disposal.

Regarding the relationship of the streptococci falling within our serological classification to streptococci of the

Lancefield groups, we have found cross-reactions with only one streptococcus, No. 30, a strain which was not associated with subacute bacterial endocarditis. This streptococcus is heat-resistant, ferments mannitol, and reacts with Lancefield Group D antiserum, but it also reacts with five of our antisera, Nos. 5, 30, 8, 3, and 10 (Table I), and is thus a typical member of our Group Ia. Three of the antisera prepared against this streptococcus react with only a few streptococci and not with any of our Lancefield Group D streptococci, but the other antiserum, prepared after growing the streptococcus in its own antiserum, reacts with about half our strains and also with five of our eight Lancefield Group D streptococci.

Results of Biochemical Tests

The results of some of the biochemical tests on the streptococci falling into our classification are shown in Table III. All strains ferment dextrose and sucrose. Only

TABLE III.—*Biochemical Reactions*

	Percentage of Strains Giving Positive Reactions in Group					No Reaction
	I	Ia	II	IIa	III	
Fermentation of:						
Lactose	71	79	90	71	76	70
Inulin	16	7	4	7	16	14
Raffinose	37	38	36	49	44	42
Salicin	62	57	14	34	52	42
Trehalose	81	74	32	45	60	42
Splitting of starch ..	25	36	7	29	52	35
Growth on 40% bile blood agar ..	46	45	4	18	54	42
No. of strains in each group ..	32	41	28	55	25	16

one strain, No. 30, which has already been mentioned, ferments mannitol. Fermentation of sorbitol, resistance to a temperature of 60° C. for 30 minutes, growth at 45° C., or growth in 6.5% of sodium chloride are found in only a few strains, which are evenly distributed in the five serological groups. All except three strains produce clot and acid in litmus milk and clot in milk to which 0.1% methylene blue has been added, although it has been stated by Sherman and his co-workers that all known streptococci seem to be inhibited by this concentration of methylene blue except the members of the lactic and enteric groups (Sherman, 1937; Sherman, Stark, and Mauer, 1937).

The results in Table III show some correlation between the biochemical reactions and the serological classification of our streptococci. In Groups I and Ia a relatively high proportion of the strains ferment salicin and trehalose, whereas comparatively few strains in Group II ferment these substances. In Group II also there are only two strains that split starch and only one capable of growing on 40% bile blood agar, whereas a moderate proportion of the strains in the other groups respond to these tests. In Group IIa the proportion of positive reactions is intermediate between those in Group II and Groups I and Ia, thus showing a correlation with the serological characterization of Group IIa by its side-reactions with the antisera determining Groups I and Ia. In Group III there is a moderate proportion of positive reactions to all the tests shown in Table III, with a higher proportion of strains capable of splitting starch than in the other groups. The streptococci not reacting with any antisera do not show any marked difference from the other groups.

Streptococci in Relapses of Subacute Bacterial Endocarditis

The properties of streptococci isolated at different times from 11 cases of subacute bacterial endocarditis are shown

TABLE IV.—*Properties of Streptococci Isolated at Different Times in Cases of Subacute Bacterial Endocarditis*

Cases	Days After First Isolation (0 = First Isolation)	Sero-logical Group	Biochemical Reactions						
			Lactose	Inulin	Raffinose	Salicin	Trehalose	Starch	Bile
Middlesex Hospital									
A (363)*	0	III	+	+	+	—	+	+	+
	2	III	+	+	+	—	+	+	+
B (295)	0	II	+	—	+	—	—	—	—
	40	II	+	—	+	—	—	—	—
C	0	Ia	+	—	—	+	+	—	+
	77	I	+	—	—	+	+	—	+
D (289)	0	I	+	—	—	+	+	—	+
	65	Ia	+	+	+	+	+	+	+
		I	+	+	+	+	+	+	+
	823	Ia	+	—	+	+	+	+	+
		Ia	+	—	+	+	+	—	+
		Ia	+	—	+	+	+	—	+
St. Bartholomew's Hospital									
E	0	IIa	—	—	—	—	—	—	—
	334	II	—	—	—	—	—	—	—
St. Mary's Hospital									
F	0	I	—	—	—	—	+	—	—
	246	Ia	—	—	—	+	+	—	—
Leeds									
G	0	I	—	—	—	+	+	—	+
	41	I	+	—	—	+	+	—	+
H	0	Ia	—	—	+	+	+	+	+
	45	I	+	—	—	+	+	+	+
I	0	IIa	—	—	—	—	—	—	—
	87	IIa	—	—	—	—	—	—	—
J	0	I	+	—	—	—	+	—	+
	40	I	+	—	—	—	+	—	+
	61	I	+	+	—	+	+	—	+
	77	IIa	—	—	—	+	—	—	—
	122	III	+	—	—	+	+	—	+
K	0	I	—	—	—	—	—	—	—
	194	D	+	—	—	+	+	—	+
	250	D	+	—	—	+	+	—	—

* Reference to case No. in communication of Ward, Meanock, Selbie, and Simon (1946).

in Table IV. In all these cases, with the exception of Case A, the second strain has been isolated during a relapse after treatment with penicillin. In eight cases only two strains have been examined, and in four of these cases both strains are of the same serological group, while in the other four cases the two strains are closely related, one belonging to a group and the other to the corresponding subgroup. In Case D the primary strain, the relapse strain, and four strains isolated at necropsy more than two years later—three from vegetative lesions in the heart and one from the spleen—all belong to Group I or its subgroup, Group Ia. In Case J the primary strain and the first two strains isolated during relapse are all of Group I, but the two later strains belong to Groups IIa and III, although all five strains react with our antiserum 5.

In all the nine cases of relapse that have been mentioned the serological properties of the streptococcus first isolated after penicillin treatment are so similar to those of the initial strain that it would seem that recrudescence of the original infection is a much more frequent cause of relapse than reinfection with another streptococcus. That reinfection does occur, however, is well shown by Case K, in which the second infecting organism is a Lancefield Group D streptococcus presumably derived from an abscess in the buttock from which a *Streptococcus faecalis* was isolated.

The biochemical properties of these streptococci, also shown in Table IV, largely confirm the serological findings. Of the nine cases in which there is a close serological relationship between original and relapse strains, six show identical biochemical reactions or a difference in only one test and two show only two differences, both in the direction of negative to positive, while only in Case H are there more than two differences or differences in both directions.

Distribution of Serological Groups in Teeth and Throats

In cases in which more than one streptococcus has been examined from the teeth of one patient it has been usual to find streptococci of different serological groups. Thus, of 11 strains isolated from seven extracted teeth from a case of subacute bacterial endocarditis (Case C, Table IV) nine are distributed in all our five groups and two are the only strains from teeth in our collection that do not react with any of the antisera at our disposal. The four strains that we have isolated from the blood stream immediately after the extraction of teeth are also a representative series, two from one patient being of Groups I and Ia and two from two patients being of Groups II and IIa. Our findings are similar to the 48 streptococci isolated from the throat in the 17 cases in which more than one streptococcus has been examined. In only one of these instances is one serological type alone represented, and in only two are there only streptococci of a group and its corresponding subgroup.

The limited data so far available thus show that there is no tendency for the streptococci of the teeth or throat in a single person to belong to one serological group.

Endocarditis Streptococci in Relation to Response to Penicillin Treatment

In Table V is shown the relationship between the response to treatment with penicillin and the sensitivity to penicillin and serological group of the streptococci isolated before

TABLE V.—*Relationship of Result of Penicillin Treatment of 59 Cases of Subacute Bacterial Endocarditis to Penicillin Sensitivity and Serological Group of Streptococcus Isolated Before Treatment. Streptococci Reacting with Lancefield Group Antisera Are Not Included*

Serological Group of Streptococci	Response of Case to Penicillin Treatment	No. of Strains with Coefficient of Penicillin Resistance* of					Totals in Serological Groups	
		0.25-0.75	1	1.3-2	4-6	33, 50	Bad Response	All Cases
I ..	{ Good Bad	3 1	1 0	0 0	0 2	1 0	3	8
Ia ..	{ Good Bad	3 0	0 2	2 3	4 2	0 0	5	14
II ..	{ Good Bad	0 0	2 1	3 1	2 1	0 1	4	13
IIa ..	{ Good Bad	1 0	4 0	0 1	2 0	0 0	1	8
III ..	{ Good Bad	3 0	2 0	3 0	2 1	0 0	1	11
None ..	{ Good Bad	2 0	1 1	1 0	0 0	0 0	1	5
Totals in sensitivity groups	{ Bad response All cases	16 1	2 12	5 14	6 15	2 1	15	59

* Penicillin resistance *in vitro* expressed as multiple of resistance of standard Oxford staphylococcus.

penicillin treatment in the 59 cases in which the necessary information is available. Response to treatment is assessed as bad when the patient died without control of the infection. This table has been examined by Mr. T. E. Cowan, F.C.I.S., F.R.S.S., records officer, Middlesex Hospital, who states: "I agree that the main point brought out is that in total the proportion of bad responses to penicillin treatment increases with resistance of the infecting organism to penicillin. The regularity of the arithmetical progression is sufficient to justify this view. I do not think it can be taken that the classification according to the serological group of the infecting streptococci shows a correlation between the serological group and the response to infection; the numbers examined are too small to be statistically significant."

Discussion

The difficulties presented by the complex antigenic structure of the viridans streptococci have hitherto prevented an

adequate classification of these organisms by serological methods. The situation is well exemplified by the observations of Gordon (1922), who found that 16 strains of *Str. salivarius* represented at least 12 different types, whereas 125 of 131 strains of *Str. pyogenes* were of the same serological type. We also have found that the viridans streptococci are a heterogeneous group of organisms, but we have succeeded in making a serological classification by using antisera with a wide range of action and basing our classification on the reactions obtained with groups of these antisera.

In this way we have been able to classify 181 (92%) of the 197 strains of our collection that do not belong to the Lancefield groups into five groups containing 32, 41, 28, 55, and 25 strains respectively. This represents a higher degree of success than that attained by Solowey (1942), who, with a similar collection of 205 strains of viridans streptococci, classified 136 strains (66%) into 14 groups, 11 of which contained only one to five strains each. It is noteworthy that Solowey's three main groups, comprising 77, 23, and 13 strains, were based on reactions with groups of seven, five, and two antisera respectively, whereas the other smaller groups were determined by reactions with single antisera.

It would thus seem in the present state of our knowledge that these streptococci are amenable to classification only by studying their reactions to groups of antisera with a wide range of action. It would also appear necessary to prepare bacterial extracts for the precipitin test by the formamide method of Fuller (1938), which in our experience provides a much more efficient antigen than the acid extraction method of Lancefield (1933), which was used by Solowey (1942).

We have shown that viridans streptococci isolated from cases of subacute bacterial endocarditis have a distribution in our serological groups similar to that found in streptococci from teeth and normal throats. The same observation has been made by Solowey (1942) on the basis of her serological classification, and we agree with her that no distinction can be made between the viridans streptococci derived from these different sources. It would, however, appear from our results that streptococci of Group IIa, the largest group in streptococci from teeth and throats, have less tendency to produce subacute bacterial endocarditis than the streptococci of the other four groups. These observations nevertheless give further support to the view we have previously expressed in common with others that the viridans streptococci of subacute bacterial endocarditis come from the region of the mouth (Ward, Meanock, Selbie, and Simon, 1946). In the earlier communication we noted the association between dental sepsis and the initiation of the symptoms of subacute bacterial endocarditis, and here we have not only confirmed the finding of Okell and Elliott (1935) that viridans streptococci may escape into the blood stream during dental extraction but have also found that these streptococci belong to the same serological groups as those of subacute bacterial endocarditis.

It is not, however, generally agreed that the great majority of the streptococci of subacute bacterial endocarditis are derived from the region of the mouth. It has recently been reported from America that about one-third of the streptococci isolated from cases of subacute bacterial endocarditis belong to a hitherto undescribed group of the viridans type, usually referred to as "streptococcus s.b.e.," which is not a normal inhabitant of the human mouth and has been given the name of "*Streptococcus sanguis*" (Loewe, Plummer, Niven, and Sherman, 1946; White and Niven, 1946).

The two strains of "streptococcus s.b.e." that we have examined have few of the biochemical properties ascribed to this group by the American authors, but in this respect are very similar to other streptococci of Groups II and IIa to which they belong in our classification. On the other hand, our findings with an antiserum we have produced with one of our strains of "streptococcus s.b.e." (No. 2), which reacts with about 27% of our endocarditis strains, are similar to those of Schneierson (1948), who, working with American strains from cases of subacute bacterial endocarditis, found that 23% of a total of 34 strains gave a positive precipitin reaction with an antiserum prepared against a strain of "streptococcus s.b.e." Washburn, White, and Niven (1946) have described two serological types of "streptococcus s.b.e.," but have also found cross-reactions with other types of viridans streptococci.

It would thus seem that further clarification is necessary before it is possible to assign the position of "streptococcus s.b.e." in relation to the other viridans streptococci. This is a question of some importance, because this group of streptococci is regarded as being somewhat more resistant to penicillin than the other viridans streptococci. In our experience, however, there appears to be no significant correlation between the serological characters of the streptococci of subacute bacterial endocarditis and penicillin sensitivity or response of the case to penicillin treatment (Table V) except for the streptococci of Lancefield Group D, which are highly resistant to penicillin.

Another question that has recently been raised concerns the position of *Str. salivarius*, which was originally described by Andrewes and Horder (1906) as the most common streptococcus in the human throat and of frequent occurrence in subacute bacterial endocarditis. Sherman, Niven, and Smiley (1943) have now assigned this name to a streptococcus which is found in the human throat but has never been isolated from cases of subacute bacterial endocarditis and is identified by the production of large mucoid colonies on sucrose agar. We have confirmed that streptococci of this type are present in small numbers in a high proportion of normal throats, and that they form a homologous group in both their biochemical and their serological characters. They form a distinct group of streptococci, differing widely from all the streptococci that we have isolated from cases of subacute bacterial endocarditis and from the streptococci that are encountered in cultures obtained from teeth and throat by the usual routine methods. We are, however, of the view that, although *Str. salivarius* is an ill-defined species, its definition should remain sufficiently wide to include streptococci of the type originally observed by Andrewes and Horder (1906) and not be restricted to streptococci not usually met with either in the examination of throat swabs by routine bacteriological methods or in cases of subacute bacterial endocarditis.

Our finding that streptococci isolated during relapses after penicillin treatment in subacute bacterial endocarditis are usually similar to the strains isolated before treatment is of some clinical importance in that it indicates that relapses are generally due to a recrudescence of the original infection and not to reinfection. It would seem, therefore, that relapses after penicillin therapy are usually due to inadequate treatment. That the dosage of penicillin in many cases may have been inadequate in relation to the resistance of the infecting organism is indicated by the findings in Table V, in which a bad response to penicillin treatment is correlated in 11 of 29 cases with a coefficient of resistance of 1.3 to 6 and in only three of 28 cases with a coefficient of resistance of 1 or less. It can therefore be expected that a

general increase in dosage from half a million units of penicillin a day for 28 days to two million units a day for six weeks, as recently recommended by Christie (1949), will improve the results of penicillin treatment.

There are, however, cases in which relapse cannot be ascribed to undue resistance of the infecting streptococcus to penicillin, and it may be that the causal organisms are so protected by dense vegetative lesions that they are inaccessible to the action of penicillin. It is now accepted that in conditions where the sources of infection are accessible the chances of a recrudescence of the infection can be greatly reduced by the removal of infected and avascular tissue after infection has been brought under control by penicillin (Hudson, Meanock, McIntosh, and Selbie, 1946). It is thus possible that surgery may yet provide a solution to the problem of persistent relapses after penicillin therapy in subacute bacterial endocarditis by evolving methods for the removal of the infected vegetations and the reconstruction of damaged valves.

Summary

Streptococci of the viridans type from cases of subacute bacterial endocarditis and from normal throats and extracted teeth have been differentiated into five serological groups.

The distribution in the five serological groups of the streptococci from subacute bacterial endocarditis is similar to that of the streptococci from throats and teeth, indicating that the streptococci of subacute bacterial endocarditis are derived from the region of the mouth.

Streptococci isolated during relapses after penicillin treatment in subacute bacterial endocarditis are usually similar in their serological and biochemical characters to the streptococci isolated before treatment, indicating that relapses are generally due to a recrudescence of the original infection and not to reinfection by another streptococcus.

The relationships of "streptococcus s.b.e." and *Str. salivarius*, as described by Sherman and his co-workers, to other members of the viridans group of streptococci are discussed.

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TREATMENT OF EARLY SYPHILIS WITH PENICILLIN COMBINED WITH NEOARSPHENAMINE AND BISMUTH

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Since the introduction of penicillin for the treatment of syphilis routine standard courses of treatment have been in use in the Army for the treatment of early cases. In 1944 the first scheme of treatment to be used consisted of 2,400,000 units of penicillin in aqueous solution given intramuscularly in 60 divided doses, each of 40,000 units. In 1946 it became obvious from a scrutiny of the records of patients so treated that there was a failure rate of 8% in the first six months (Marshall, 1946).

In consequence, a course which consisted of 4,000,000 units of penicillin in aqueous solution given intramuscularly in divided doses over a period of 12½ days was introduced at certain military hospitals. Also, in view of the fact that Eagle and his co-workers (1946) showed that there was a synergistic action between penicillin and arsenic in the treatment of rabbit syphilis, a standard scheme was introduced at certain other scheduled hospitals in the United Kingdom, consisting of 2,400,000 units of penicillin together with ten daily injections of 0.06 g. of "mapharside." In addition, at one military hospital in the United Kingdom a series of cases of early syphilis was treated by means of a somewhat similar course with the addition of 1 g. of bismuth (Willcox, 1946).

The cumulative relapse rates following treatment by means of the above four schedules were calculated by James, Mackay, and Wright (1948) in a series of 281 cases, using a formula evolved by the Honorary Consultant in Statistics to the Army. By this means it was found that the cumulative relapse rates at twelve months in the case of patients treated with 2,400,000 units of penicillin were 14% for sero-negative primary syphilis, 13% for sero-positive primary syphilis, and 17.5% for secondary syphilis. The results of the other courses of treatment were essentially much the same.

In 1946 reports from the United States had shown that penicillin K was less effective than penicillin G in the treatment of rabbit syphilis, and that commercial penicillin had tended to contain increasing amounts of penicillin K. The Subcommittee on Venereology of the Army Medical and Personnel Research Panel therefore adopted a scheme of treatment by which a total of 4,000,000 units of penicillin was given over a period of ten days, combined with a course of neoarsphenamine and bismuth (Eames, 1948); the addition of the latter conformed to the original suggestion of Harrison (1945). This schedule is the one considered here.

Treatment, Surveillance, and Sources of Material

The treatment was carried out as follows. During an initial period in hospital a course of 4,000,000 units of commercial penicillin (50,000 units in aqueous solution intramuscularly at three-hourly intervals over a period of ten days) was given. On the second, fifth, and ninth days