and make a plea for earlier diagnosis in the hopes of greater success with surgical treatment. The potential benefit of intra-arterial infusion of fluorouracil provides an additional reason for alertness.

REFERENCES

- Ariel, I. M., and Pack, G. T. (1967). *Cancer (Philad.)*, **20**, 793.
 Berman, C. (1951). *Primary Carcinoma of the Liver*. London.
 Borman, J. B., Harbott, A. J., and Morris, D. (1961). *Brit. J. Surg.*, **49**, 11.
 Brunschwig, A. (1963). *Cancer (Philad.)*, **16**, 277.
 Byron, R. L., Perez, F. M., Yonemoto, R. H., Bierman, H. R., Gildenhorn, H. L., and Kelly, K. H. (1961). *Surg. Gynec. Obstet.*, **112**, 689.
 Chan, K. T. (1967). *Ann. roy. Coll. Surg. Engl.*, **41**, 253.
 Clarkson, B., *et al.* (1962). *Cancer (Philad.)*, **15**, 472.
 Croft, P. B., and Wilkinson, M. (1965). *Brain*, **88**, 427.
 Elkington, S. G., McBrien, D. J., and Spencer, H. (1963). *Brit. med. J.*, **2**, 1501.
 Gorgun, B., and Watne, A. L. (1967). *Amer. J. Surg.*, **113**, 363.
 Lawrence, G. H., Grauman, D., Lasersohn, J., and Baker, J. W. (1966). *Amer. J. Surg.*, **112**, 200.
 Lawrence, W., jun. (1965). In *Progress in Clinical Cancer*, edited by I. M. Ariel, **1**, pp. 341–393. New York.
 Lee, F. I. (1966). *Gut*, **7**, 77.
 Lin, T.-Y. (1966). *Surg. Gynec. Obstet.*, **123**, 289.
 MacDonald, R. A. (1957). *Arch. intern. Med.*, **99**, 266.
 McWilliam, P. K. A. (1961). *Brit. J. Surg.*, **49**, 14.
 Nelson, R. S., Elizalde, R. de, and Howe, C. D. (1966). *Cancer (Philad.)*, **19**, 533.
 Nett, A. E., and Gilbert, J. A. L. (1966). *Canad. med. Ass. J.*, **95**, 45.
 Odman, P. (1958). *Acta radiol. (Stockh.)*, Suppl. No. 159.
 Odnorolov, N. I. (1964). In *Vascular Roentgenology*, edited by R. A. Schobinger and F. F. Ruzicka, p. 368. New York.
 Papac, R. J., and Calabresi, P. (1966). *J. Amer. med. Ass.*, **197**, 237.
 Patton, R. B., and Horn, R. C. (1964). *Cancer (Philad.)*, **17**, 757.
 Rochlin, D. B., and Smart, C. R. (1966). *Surg. Gynec. Obstet.*, **123**, 535.
 Schupbach, H. J., and Chappell, R. B. (1952). *Arch. intern. Med.*, **89**, 436.
 Schweizer, O., and Howland, W. S. (1960). *Surg. Gynec. Obstet.*, **110**, 61.
 Seldinger, S. I. (1953). *Acta radiol. (Stockh.)*, **39**, 368.
 Smith, R., and Sherlock, S. (1964). *Surgery of the Gall Bladder and Bile Ducts*, p. 220. London.
 Watkins, E., and Sullivan, R. D. (1964). *Surg. Gynec. Obstet.*, **118**, 3.
 Wilson, R. O., Love, J., Waken, J. K., and Gilrane, J. (1964). *Amer. J. Surg.*, **108**, 896.

Tetracycline-resistant Streptococci in South-west Essex : a Continuing Survey

M. H. ROBERTSON,* M.B., CH.B., M.C.PATH.

Brit. med. J., 1968, **3**, 349–350

Summary: Studies of beta-haemolytic streptococci isolated in material received from patients in South-west Essex for a further period of three years showed that the overall percentage of tetracycline resistance has remained almost stationary, varying from 28% in 1963 through 35% in 1965 to 27% in 1967.

Ear, wound, and skin infections retain a high incidence of resistant strains, while sputa are still a relatively minor source of such organisms. Organisms isolated from throat swabs have an incidence of resistance closest to the mean.

Introduction

Tetracycline-resistant beta-haemolytic streptococci of Lancefield's groups A, B, and G have been recorded in the general population from many parts of the world since 1960 and in this area of South-west Essex since 1963 (Robertson, 1965). These organisms probably became important in the United Kingdom in 1961, a little later than in the United States (Dadswell, 1967a).

Dadswell published an eight-year summary of their isolation from patients in an ear, nose, and throat hospital and pointed out the rapid rise in incidence in the years 1961 and 1962; he also expressed the view that any further rise is likely to be slow.

The present communication deals with the incidence of such strains isolated in two general hospitals and from general-practice patients over the period 1963–7 and continues a series previously reported (Robertson, 1965).

The sources of material and the methods used are identical, but the population covered has risen by approximately 20,000. Sensitivity was estimated by means of paper discs (Oxoid) containing 10 µg. of tetracycline, 10 µg. of erythromycin, 10 µg.

of chloramphenicol, or 1.5 units of penicillin on blood agar plates incubated overnight. Organisms were recorded as resistant if they grew right up to these discs. Minimal inhibitory concentrations (M.I.C.) were estimated as previously reported and bactericidal levels were obtained by plating out the tubes showing no growth and recording the lowest concentration of tetracycline from which there was no growth.

Results

Of 2,249 strains of beta-haemolytic streptococci isolated over the five-year period 715 (31.8%) were tetracycline-resistant. The Table shows their sources and the numbers isolated from each site. Percentages are recorded where the isolations exceed or closely approximate to 50.

A breakdown of isolations from material examined in the last three-year period, sent by general practitioners (528 strains) and from inpatients (525 strains), outpatients (367 strains), and nurses (100 strains), showed the percentages of resistant strains to be 35.3% from the general-practitioner specimens, 33.5% from inpatients, 29% from outpatients, and 16% from the nurses. These figures show a slight fall in the percentages from general practice and nurses and a slight rise in the percentages from both inpatients and outpatients, compared with the years 1963 and 1964.

Lancefield-grouping of 123 strains from the last three years showed 51% to belong to group A, 5% to B, 12% to C, 7% to D, 10% to G, and 13% to none of these groups. The figures are expressed to the nearest whole number. They show a fall in the proportion of group A strains, but the numbers involved are too small to be significant.

Antibiotic sensitivity results are as follows for the second period of the survey. All strains were fully sensitive to penicillin, with the exception of nine which all proved to belong to Lancefield's group D. These nine strains produced small zones around the penicillin discs. Other strains which were obviously

* Consultant Bacteriologist, St. Margaret's Hospital, Epping, and Princess Alexandra Hospital, Harlow, Essex.

Sources of Isolation of Beta-haemolytic Streptococci and Number of Tetracycline-resistant Strains

	1963			1964			1965			1966			1967			5-year Period		
	Total	T.R.		Total	T.R.		Total	T.R.		Total	T.R.		Total	T.R.		Total	T.R.	
		No.	%		No.	%		No.	%		No.	%		No.	%		No.	%
Throat	159	39	24.5	176	55	31	252	89	35	258	78	30	235	57	24	1,080	318	29.5
Sputum	78	15	19	77	10	13	44	12	27	59	12	20	74	19	26	332	68	20
Ear	21	14	—	27	20	—	38	18	—	29	19	—	35	14	—	150	85	57
Nose and sinuses ..	7	4	—	12	5	—	18	8	—	11	6	—	10	5	—	58	28	48
Wounds and skin infections ..	36	17	—	63	27	43	59	26	44	57	27	47	89	27	30	304	124	41
Perineum	5	—	—	8	6	—	2	1	—	5	3	—	7	2	—	27	12	—
Vulva	19	3	—	27	9	—	60	16	27	57	17	30	56	16	28	219	61	28
Miscellaneous ..	9	2	—	5	2	—	21	5	—	22	5	—	22	5	—	79	19	24
Total	334	91	28	395	134	34	494	175	35	498	167	33.5	528	145	27	2,249	715	31.8

resistant and grew on MacConkey agar were not included in the series, being regarded as enterococci. Of 1,311 strains tested against chloramphenicol four showed reduced zones but were not completely resistant. These were isolated from the sputum of inpatients in three cases and from an inpatient's bedsores in the fourth. Of 1,437 tested against erythromycin three gave reduced zones but were not completely resistant. All three were from general practice throat swabs, and in only one case was Lancefield grouping attempted. It did not belong to groups A, B, C, D, or G.

The M.I.C. of tetracycline to 20 group A tetracycline-resistant strains ranged from 2 to 128 $\mu\text{g./ml.}$, only one strain having a level of 2 $\mu\text{g./ml.}$ Bactericidal levels were measured for 12 of these strains, and ranged from 8 to over 256 $\mu\text{g./ml.}$ Group B and C strains also showed M.I.C.s ranging from 2 to 128 $\mu\text{g./ml.}$

Discussion

The prevalence of tetracycline-resistant beta-haemolytic streptococci in the general population is roughly 32%, and this figure does not appear to be rising. In fact examination of the yearly percentages isolated in this survey may show that a peak had been passed in 1965 and the figures now to be actually on the decline. The 1967 figure is below that for 1963. It will be of interest to note whether this decline continues. The reason for this levelling off is not easy to assess. It may be due to changed prescribing habits of doctors, to the use of penicillins instead of tetracycline, or we may be observing a natural wave of prevalence of infection due to particular strains of streptococci. The second explanation is unlikely unless organisms of different Lancefield groups are behaving in similar fashion.

Erythromycin-resistant beta-haemolytic streptococci are very rare but have been recorded four times, isolated from patients treated with the drug (Lowbury and Hurst, 1959) or with lincomycin (Kohn *et al.*, 1968). These all had M.I.C.s of

100 $\mu\text{g./ml.}$ or over, while the average sensitivity of beta-haemolytic streptococci to erythromycin is 0.005 to 0.1 $\mu\text{g./ml.}$ (Griffith and Black, 1963). Four strains were reported in the previous part of this survey. They have also been discovered among the unhospitalized contacts of a child with acute respiratory infection (Sanders *et al.*, 1968).

Haemolytic streptococci isolated from infected ears have shown a high incidence of tetracycline resistance. It was 70% in this area in the period 1963–4, and, though over the five-year period the figure falls to 57%, this site still yields the highest proportion of resistant strains. Dadswell (1967b) recorded an incidence of 41% in a series of patients with acute otitis media.

Nose and sinus infections also have a high rate (48%) and wound and skin infections remain high at 41%. Sputa still have a low incidence (20%), and throat swabs, with 29.5%, remain closest to the mean figure.

Perineal and vulval isolations together have an incidence of 22.8%. This is of interest, as at least one minor hospital outbreak of tetracycline-resistant streptococcal infections has been traced to anal carriage of these organisms (McKee *et al.*, 1966).

Thanks are due to all those general practitioners and consultants in the Epping and Harlow areas who sent specimens used in this survey and to Mr. M. G. Howe, Mr. P. Allen, and Mrs. S. Vince for efficient technical assistance.

REFERENCES

- Dadswell, J. V. (1967a). *J. clin. Path.*, **20**, 641.
- Dadswell, J. V. (1967b). *Lancet*, **1**, 243.
- Griffith, R. S., and Black, H. R. (1963). *Curr. ther. Res.*, **5**, 57.
- Kohn, J., Hewitt, J. H., and Fraser, C. A. M. (1968). *Brit. med. J.*, **1**, 703.
- Lowbury, E. J. L., and Hurst, L. (1959). *J. clin. Path.*, **12**, 163.
- McKee, W. M., Di Caprio, J. M., Roberts, C. E., and Sherris, J. C. (1966). *Lancet*, **2**, 1007.
- Robertson, M. H. (1965). *Brit. med. J.*, **2**, 569.
- Sanders, E., Foster, M. T., and Scott, D. (1968). *New Engl. J. Med.*, **278**, 538.