The value of tracheostomy was assessed for each patient in relation to the subsequent progress of the underlying disease, to complications of the tracheostomy, and to mortality. Three grades of value were distinguished: (1) the patient would have died had tracheostomy not been performed—211 (54%); (2) the tracheostomy was of definite value to the patient and contributed materially to recovery, even if death eventually occurred as a result of the underlying disease—105 (27%); and (3) tracheostomy was of no value in that the patient died as a result of a complication of that procedure, or the complication was a closely related cause of death, or, more usually, tracheostomy was carried out on an already moribund patient—73 (19%).

This rather arbitrary grading of tracheostomies emphasizes the value of the operation and justifies, in part, the present enthusiasm for it. However, it should be remembered that almost half the complications were infective in origin and one-quarter were due to loss of a patent airway through the tracheostomy tube. In addition, many of the complications occurred in the first 48 hours after tracheostomy. It is probable, therefore, that complications could be significantly reduced by a barrier-nursing technique in a specialized unit such as an intensive therapy or respiration unit. Because of the particularly high complication rate in children the use of nasal endotracheal tubes might be considered as an acceptable alternative to tracheostomy.

Summary

In order to assess the type and incidence of complications after tracheostomy a retrospective survey was made of every tracheostomy carried out in the United Oxford Hospitals over the 10-year period 1 January 1950 to 31 December 1959. A total of 389 tracheostomies were performed on 383 patients, and 252 complications occurred after 192 of the operations—an incidence of 49.3%; 13 deaths were directly due to the complications—a mortality rate of 3.4%.

In spite of the high complication rate the value of tracheostomy outweighs the risks of these complications, the majority of which are due to infection and to loss of a patent airway.

I am grateful to Sir Robert Macintosh, Nuffield Professor of Anaesthesia, the Radcliffe Infirmary, Oxford, for helpful advice while carrying out this survey and for permission to publish these results. I also wish to thank Professor W. W. Mushin, the Welsh National School of Medicine, for his assistance with the presentation of the data.

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Beta-haemolytic Streptococci in South-west Essex, with Particular Reference to Tetracycline Resistance

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The beta-haemolytic streptococcus has not shown the same ability to produce antibiotic- or chemotherapeutic-resistant variants as *Staphylococcus aureus*. In the past, however, it has shown a capacity to produce variants resistant to sulphonamide, notably in a plastic surgery unit where sulphonamide powder had been used prophylactically (Francis, 1942), and in naval establishments where a few types, after becoming resistant to sulphonamide, became predominant in populations receiving prophylactic sulphadiazine (U.S. Navy Epidemiology Unit, Number 22, 1945; Damrosch, 1946). None of these strains had lost their pathogenicity. Sulphonamide-resistant group A streptococci have been described in a civilian population in New York State (Johnson and Hartman, 1947).

The advent of penicillin reduced the importance of such strains, and indeed seemed almost to banish the beta-haemolytic streptococcus from Britain for many years. A survey of the antibiotic sensitivities of pathogenic organisms isolated in a large English hospital from 1951 to 1956 does not mention the beta-haemolytic streptococcus, presumably because the numbers isolated were too small (Giles and Shuttleworth, 1958), and this was my experience during the same period in Eastern Scotland. From November 1957 to April 1959 1,002 strains were isolated in the laboratories of the Northern Ireland Hospital Authority Laboratory Service (Mitchell, 1962) and 2,647 strains were isolated during eight periods of one week from 1952 to 1956 by the Public Health Laboratory Service in England and Wales. These isolations numbered from 569 to 213 a week (Report, 1957). During this period, however, the streptococcus was still producing small outbreaks of infection in hospitals, but only 22 epidemics of more than four cases were reported to the Public Health Laboratory Service during the period 1955 to 1958 (Williams *et al.*, 1960). Those authors also give a list of references to these small outbreaks.

The administration of antibiotics, particularly of tetracycline, in the prophylaxis of rheumatic fever in penicillin-allergic subjects has been advocated (Hodes, 1959), and long-term therapy with tetracycline for chronic bronchitis is effective just now (Murdoch *et al.*, 1959; Francis *et al.*, 1964). This widespread use of tetracycline for respiratory infections and a noticeable increase in the numbers of beta-haemolytic streptococci being isolated, many of which were tetracycline-resistant *in vitro*, prompted the present communication.

Tetracycline-resistant streptococci have been reported from many parts of the world, notably in a special burns unit in England where a chlortetracycline-resistant group A streptococcus was observed to arise during the course of treatment (Lowbury and Cason, 1954), and, again in the same unit, an atypical anaerobic form, designated AN, associated with tetracycline-resistance, was described (Lowbury and Hurst, 1956). Of more serious import were an outbreak of pharyngitis in New Orleans due to a tetracycline-resistant variant (Mogabgab and Pelon, 1958) and a report of tetracycline failure in the treatment of streptococcal pharyngitis due to tetracycline-resistance in New York (Stillerman *et al.*, 1960). The presence

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of tetracycline-resistant group A beta-haemolytic streptococci was reported in the general population of Seattle (Kuharic *et al.*, 1960), in New York (McCormack *et al.*, 1962), and in Victoria, Australia (Lane, 1962). Their presence in widely separated areas of Great Britain was also recognized at this time (Parker *et al.*, 1962).

The present communication deals with the frequency of isolation of beta-haemolytic streptococci and their resistance to tetracycline in an area of South-west Essex during 1963 and 1964. A similar study in the Bristol area carried out during part of this period with very similar results has been reported (Mitchell and Baber, 1965). This laboratory serves a population of approximately 140,000.

Materials and Methods

All streptococci showing beta-haemolysis on aerobic horse-blood agar plates isolated during 1963 and 1964 are surveyed. It has not been the practice to incubate cultures from throat swabs or sputa anaerobically as a routine, although all wound swabs and pus specimens are so treated. The number of isolations from throats and sputa is therefore a little smaller than would have been obtained had this routine been carried out.

Only one isolation of streptococci per patient was counted unless the history made it very probable that two infections had occurred. The number of occasions on which this took place was very small.

Lancefield grouping was performed by the acid-extraction method described by Cruickshank (1962). Sensitivity tests were carried out by the dry disk method with Mast disks or Sentest tablets, and the estimation of minimal inhibitory concentrations (M.I.C.) of tetracycline and penicillin was carried out in doubling dilutions of the drugs in 0.1% glucose broth containing 10% horse serum. The inoculum was one drop of an overnight culture of the organism in the same broth. The tubes were incubated overnight and the reading was taken as the concentration of drug in the first tube where growth was inhibited.

Results

Of 729 strains of beta-haemolytic streptococci isolated during the two-year period, 228 (31%) were resistant to tetracycline; the Table shows their sources and the numbers from each site. Percentage figures are given where the total number of isolations exceeds or closely approaches 50.

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

Source	1963			1964			Two-year Period		
	Total	Tetracycline-resistant		Total	Tetracycline-resistant		Total	Tetracycline-resistant	
		No.	%		No.	%		No.	%
Throat ..	159	39	24·5	176	55	31	335	94	28
Sputum ..	78	15	19	77	10	13	155	25	16
Ear	21	14	—	27	20	—	48	34	70
Nose and sinuses ..	7	4	—	12	5	—	19	9	—
Wounds, skin infections ..	36	17	—	63	27	43	99	44	44
Perineum ..	5	—	—	8	6	—	13	6	—
Vulva	19	3	—	27	9	—	46	12	26
Miscellaneous	9	2	—	5	2	—	14	4	—
Total ..	334	94	28	395	134	34	729	228	31

A similar breakdown of isolations from material sent by general practitioners (197 strains) and from ward patients (289 strains), out-patients (199 strains), and nurses (44 strains) showed the practitioner material to contain 41.5% resistant strains, the ward patients 31%, the out-patients 23%, and the nurses 20.5%.

Lancefield grouping of 50 unselected strains showed that 80% belonged to group A, 12% to group G, 4% to group B, and 2% to group D. The remaining 2% were ungroupable. Of a small unselected sample of the tetracycline-resistant strains 75% were of group A, 10% of group B, 5% each of group G, group D, and ungroupable strains.

Antibiotic-sensitivity results are as follows. All strains were tested against penicillin and chloramphenicol, no resistant variants being found. Of 353 strains tested against erythromycin four were resistant.

The M.I.C. of tetracycline to 15 group A strains showing tetracycline resistance varied from 32 to 512 μg./ml., while the highest M.I.C. of penicillin to the same strains was 0.018 μg./ml.

The usual M.I.C. of tetracycline for sensitive strains is 0.25 μg./ml. and of penicillin 0.015 μg./ml. (Barber and Garrod, 1963). The resistance to tetracycline is of a high degree, and the sensitivity of group A strains to penicillin is unimpaired. Group B and group G strains also showed a high resistance to tetracycline, M.I.C.s ranging from 2 to 64 μg./ml. being found.

Discussion

The beta-haemolytic streptococcus, apparently suppressed for a considerable period in this country, is being more frequently isolated again, and there is therefore a risk of a rise in incidence of rheumatic fever and other conditions associated with haemolytic streptococcal infection. Figures to show the increase of streptococcal disease in recent years are difficult to produce, but general practitioners and paediatricians confirm the impression that there is an increase. Calculations made from population figures at the 1955 census, ignoring qualitative differences in the populations, show that isolations in the area served by this laboratory are now five and a half times what would be expected from Mitchell's (1962) isolations for Northern Ireland in 1958 and 1959 and four to ten times the expected number for England and Wales in 1952 and 1956 (Report, 1957). This increased incidence of streptococcal infections may be partly due to the use of tetracycline for respiratory-tract and ear infections as a safe, easily administered broad-spectrum antibiotic without confirmation that the causative organism is sensitive to the drug, or that, once the patient has recovered, it has been eliminated from the site of infection. It has now been clearly established that, in Southern England, one-third of haemolytic streptococci are resistant to tetracycline.

It would appear from a rapid examination of the above data that tetracycline-resistant beta-haemolytic streptococci are more commonly seen in general practice than in hospital and among hospital staff, but the findings are considerably weighted. Only one-quarter of the strains came from general practice, and these contained nearly all those from ear infections (34 out of 47), the source with the highest incidence of resistant streptococci. In contrast, only a few strains came from sputa from general-practitioner sources (4 out of 155), and sputa had the lowest proportion of resistant strains. Many patients were treated with tetracycline before arriving in hospital, and this probably caused an increase in the number of resistant strains in the material from hospital sources. There is a tendency for practitioners to send material for investigation only from cases that have not responded to their treatment, thus probably increasing the number of resistant strains in the general-practice specimens.

It is obvious, therefore, that no useful purpose can be served by trying to describe "hospital" or "G.P." strains of streptococci; what is important is to consider the lesions in which these organisms are occurring and the factors probably responsible for their appearance. It could be said that, since much of the material reaching this laboratory comes from sources possibly treated with tetracycline, the findings are valueless for

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ascertaining the incidence of resistant variants. This is not so, as an organism which is not eradicated by an antibiotic and becomes resistant is a source of resistant descendants in the community.

Points which stand out in the present investigation are: (1) haemolytic streptococci causing ear infections are very likely to be resistant to tetracycline (70%); (2) haemolytic streptococci causing skin infections, wound infections, and abscesses have a 44% chance of being resistant; (3) sputa, in spite of the prevalence of long-term tetracycline therapy, have a low incidence of resistant streptococci; and (4) throat swabs, although showing a lower incidence of resistant strains compared with, say, wound swabs, were the commonest source of streptococci, and their incidence of resistant variants was closest to the mean.

Tetracycline is inferior to penicillin in eradicating streptococci from the throat (Stillerman *et al.*, 1960), and would appear to be less effective in eradicating them from other sites, such as wounds and abscesses. It is a bacteriostatic drug, while penicillin is bactericidal.

The facts indicate that tetracycline is unsuitable for use in beta-haemolytic streptococcal infections without bacteriological control, and that penicillin is the drug of choice. It could be argued that in the presence of a mixed infection including penicillinase-producing staphylococci the streptococci may be protected by the staphylococcal penicillinase. A cure rate of 95% in five days has been claimed in cases of acute otitis media when using oral phenethicillin or intramuscular benzylpenicillin. The usual cause of failure was the presence of a penicillin-resistant staphylococcus, but phenethicillin cured some such infections, and in only one case of failure was a beta-haemolytic streptococcus isolated after treatment (Morrison, 1961).

When patients are allergic to penicillin there are cogent reasons for using erythromycin.

Injections of benzylpenicillin give the highest blood levels of the drug, and, weight for weight, this form of penicillin is the most effective against sensitive organisms. Injections may prove inconvenient in general practice or when the patient is a child, but oral phenoxymethylpenicillin and phenethicillin are almost as effective against haemolytic streptococci (Garrod, 1960), and are more active than propicillin or phenbenicillin (Bond *et al.*, 1963).

The relative absence (16%) of tetracycline-resistant streptococci from sputa is probably a reflection of the general recognition that penicillin is the drug of choice for pneumonia. Nearly all the sputa examined came from ward patients or out-patients who, under long-term supervision by the physicians, were likely to have been treated with penicillin, so preventing the production of tetracycline-resistant variants. The "long-term tetracycline" patient seems to be such an obvious source of tetracycline-resistant streptococci in the community that a survey of such persons while on no other antibiotic might reveal these organisms in the throat. The proportion of tetracycline-resistant strains in the general population is rising; no survey previous to 1963, however, has been reported from this country. It was 20% in Seattle (Kuharic *et al.*, 1960), 19% in New York (McCormack *et al.*, 1962), 19% in Australia (Lane, 1962), and 32% in Bristol (Mitchell and Baber, 1965).

Summary

The incidence of beta-haemolytic streptococcal infections in South-west Essex is considerable and is probably rising. Thirty-one per cent. of the infections are due to tetracycline-resistant strains, and these have not lost their virulence. Resistant strains have not been frequently noted in sputa, but it is possible that the "long-term tetracycline" patient is a source of these strains in the community. It is fruitless to speak of "hospital" or "G.P." streptococci, as resistant strains are being produced in both types of practice and the proportion of such strains in the population in general is rising. Penicillin is the drug of choice for beta-haemolytic streptococcal infections, and oral penicillin is preferable to tetracycline if injections are inconvenient.

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