SENSITIVITY TO FIVE ANTIBIOTICS OF STRAINS OF STAPH. PYOGENES ISOLATED FROM OUT-PATIENTS

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Few factors limit the usefulness of an established antibiotic so much as the development of resistance to it by bacteria originally sensitive. For penicillin this has happened with *Staphylococcus pyogenes*, and recent reports suggest that more than half the strains of this organism isolated from patients in hospital wards are likely to be resistant. This proportion, while undoubtedly reflecting a real increase in penicillin-resistant strains, also represents the results of cross-infection while in hospital, and so gives little indication of the incidence of resistance amongst the general population. For this latter figure, strains recovered from hospital out-patients provide a fairer sample, and this paper records the sensitivity of 200 such strains of *Staph. pyogenes* to penicillin, and to streptomycin, aureomycin, chloramphenicol, and terramycin.

Sources of *Staphylococci*.—Swabs were taken from patients with staphylococcal infections of the skin and subcutaneous tissues who were attending the casualty department between January and April, 1952. Whenever possible swabs were taken at the first attendance or when a lesion was opened. Swabs taken from patients attending other out-patient departments such as the skin, or ear, nose, and throat department were not included in this series, but no attempt was made to exclude patients who had received antibiotics in the past.

Methods of Isolation and of Testing Sensitivity

All the swabs were sown direct on to horse-blood-agar plates from which two cups had been cut with a cork-borer. After inoculation the cups were filled with penicillin, 10 units per ml., and streptomycin, 100 µg. per ml. respectively. Staphylococci which coagulated plasma in a tube were described as *Staph. pyogenes*; those which were inhibited by the antibiotics to approximately the same extent as the Oxford H staphylococcus were regarded as sensitive. Penicillinase production was noted from the primary plate by the method of Waterworth (1948). Staphylococci were stored on agar slopes until tube dilution-sensitivity tests were carried out.

For these tests stock solutions of the calcium salt of crystalline penicillin G, streptomycin calcium chloride complex, chloramphenicol, and crystalline terramycin hydrochloride were prepared in sterile distilled water and stored at 4° C. The following concentrations were used: penicillin, 1,000 units per ml.; streptomycin, 10,000 µg. per ml.; chloramphenicol and terramycin, 1,000 µg. per ml. The solutions of penicillin, streptomycin, and chloramphenicol were replaced monthly, and the terramycin solution weekly. A solution of aureomycin hydrochloride, 1,000 µg. per ml., was prepared immediately before use.

For testing, series of twofold dilutions of each of the five antibiotics in 0.5 ml. of meat extract broth were prepared. For the inoculum a 24-hour meat extract broth

culture of each staphylococcus was diluted 1 in 100 in broth and 0.5 ml. was added to each tube. All tubes were incubated at 37° C. for 18 hours, and the end-point was determined by inspection as the lowest concentration of antibiotic preventing visible growth.

Penicillin-sensitive strains were not titrated below a concentration of 0.25 unit per ml., or resistant ones above 128 units per ml.

Results

Table I shows the sensitivity of the 200 strains tested to penicillin. Of these, 168 strains were inhibited by 0.25 unit per ml., and had been judged to be sensitive to penicillin when isolated. The remaining 32 strains had been thought on isolation to be resistant, and had produced penicillinase.

TABLE I.—Sensitivity to Penicillin of 200 Strains of *Staph. pyogenes*

Minimum Inhibitory Concentration Units per ml.	No. of Strains
>128	6
128	2
64	3
32	7
16	6
8	2
4	4
2	2
1	0
0.5	0
0.25	168

Total No. of resistant strains, 32 (16%)

None of the staphylococci tested appeared markedly resistant to streptomycin, aureomycin, chloramphenicol, or terramycin. Their sensitivity to these antibiotics is shown in Table II.

TABLE II.—Sensitivity of 200 Strains of *Staph. pyogenes* to Streptomycin, Aureomycin, Chloramphenicol, and Terramycin

Minimum Inhibitory Concentration (µg. per ml.)	Streptomycin No. of Strains	Aureomycin No. of Strains	Chloramphenicol No. of Strains	Terramycin No. of Strains
64	0	0	0	0
32	23	0	10	0
16	125	0	150	0
8	47	0	36	0
4	5	0	4	5
2	0	8	0	87
1	0	59	0	104
0.5	0	108	0	4
0.25	0	25	0	0
0.125	0	0	0	0

There were no resistant strains.

Discussion

In testing the sensitivity of organisms to antibiotics the size of the inoculum used in each test may considerably affect the result. In this investigation the inoculum used was large, and the minimum inhibitory concentrations were higher than those which might be obtained by a method using a smaller inoculum. A large inoculum was used in the belief that it may more nearly represent the conditions in which the antibiotic is required to act in the body (Spink, 1951).

Penicillin.—Of the strains tested 16% were resistant to penicillin, as compared with 6.5% of staphylococci collected from similar patients in the same department three years before (Griffiths, Jones, Shooter, and Heady, 1949).

Streptomycin.—Staphylococci are known to become resistant to this drug, and numerous workers have reported resistant strains from hospital in-patients. The prevalence of such resistant strains among out-patients presumably depends on the freedom with which streptomycin is used, and our finding of no highly resistant strains is similar to that of Rountree, Barbour, and Thomson (1951), and of Barber and Whitehead (1949). There are few indications for the use of streptomycin in staphylococcal infections, and it was included as a matter of theoretical interest.

Aureomycin, Chloramphenicol, and Terramycin.—Naturally occurring strains of staphylococci resistant to these

drugs must be rare, and no such strains were found. This was supported by previous unpublished work by one of us (R. A. S.) in which an examination of 501 strains of *Staph. pyogenes* collected prior to 1950 failed also to show any strains resistant to aureomycin. Reports in the American literature suggest that resistant strains are becoming common among hospital patients in the United States. We have isolated strains resistant to aureomycin and strains resistant to chloramphenicol from patients in hospital. It is presumably only a matter of time before these organisms appear amongst the general population.

In view of the recent suggestion (Banks, 1952) that chloramphenicol is the drug of choice for treating penicillin-resistant staphylococcal infections, it is of some interest that the usual minimum inhibitory concentration of this drug for the organism in our series of strains was 32 times greater than that of aureomycin and 16 times that of terramycin.

Summary

Two hundred strains of *Staph. pyogenes* isolated from out-patients with staphylococcal infections of the skin and subcutaneous tissues have been tested for their sensitivity to penicillin, streptomycin, aureomycin, chloramphenicol, and terramycin.

Of the strains tested 16% were resistant to penicillin. No strains markedly resistant to the other antibiotics were found.

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THE ADOLESCENT FEEBLE-MINDED IN LAW AND PRACTICE

BY

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While there is general agreement that revision of the mental deficiency code is overdue, opinions differ on whether its future scope should be enlarged or be restricted among the subnormal. It is hoped that this account of a specialized practice will be conducive to a reorientation of views on the needs and prognoses of high-grade aments, encourage the allocation of suitable facilities for them, and indicate how both law and practice might better serve their interests and those of society.

Of the 1% of the population liable in certain circumstances to certification as mentally defective, about a fourth are so subnormal that they are a handicap, if not an intolerable burden, to the afflicted families. It is relevant, however, that the incidence of severe defect is equal throughout society and that its victims tend to assume, in both medical practice and popular belief, an importance out of all proportion to their social signifi-

cance. On the other hand, the implications of feeble-mindedness tend to be underrated, although high-grade aments constitute a formidable social problem. They comprise three-fourths of the potentially certifiable, and their incidence is greatest in the "submerged tenth"; but, unlike idiots and imbeciles, the majority become useful citizens if they are properly trained; neglected, they fail to realize their mental and social potentials, and many remain in the "social problem group" and contribute to its degradation.

Until the Mental Deficiency Act, 1913, became effective feeble-minded adults had no legal recognition and educational provision for feeble-minded children was merely permissive. The Mental Deficiency Act, however, imposed statutory duties on local authorities to "ascertain" the mentally defective "subjects to be dealt with" and to provide for their care and control. Unfortunately, however, the ascertainment of defectives remains quite inadequate, and even to-day only 50,000 beds (mostly taken by low-grade cases) are provided in England and Wales for aments of all classes and types.

The Manor Hospital

The Manor Hospital practice originated in the L.C.C.'s decision to develop its hospital services with regard for the very different needs of high-grade, as distinct from low-grade, aments and the suitability of its institutions for the concentration of facilities appropriate for one or other type of case. Thus in 1922 the Manor became a training colony for aments (mostly of high grade), but since the State assumed control in 1948 low-grade aments have been admitted in increasing numbers.

Among 1,470 cases on the books females rather outnumber males; 10% are children and 40% are incapable of socially useful improvement because of the severity of their disabilities. Training facilities include a school where young people between 10 and 20 years of age acquire, among other things, the rudiments of the three Rs; older inmates learn a variety of crafts and domestic arts in other departments; speech and occupational therapists cater for appropriate cases; Scout and Guide activities form part of the training regimen, and welfare officers place and supervise patients in wage-earning employment in the Epsom district. The general care of patients is vested in the medical and nursing staff, and psychologists function in an advisory capacity. Thus The Manor, although a hospital, has much in common with a large co-educational boarding school.

Some of the results achieved are shown in the table.

Unfavourable home circumstances are conspicuous in the case histories of high-grade patients under care at The Manor. Typical records include reference to some combination of parental cruelty, desertion, neglect, domestic discord, remarriage, sexual irregularities, and crime. "Social

	1951	1950	1949	1948	1947
On the books	1,473	1,471	1,451	1,437	1,390
On "daily service" ..	175	216	226	211	164
Advanced to licence ..	19	22	29	18	27
Failed "to make good" ..	38	69	49	52	26
On licence, both "local" and "distant"	218	216	223	236	270
Recommended discharges ..	29	29	20	35	30
Failed "to make good" ..	29	25	30	23	69

"Daily service" cases reside in hospital and go out to work in the Epsom district: they earn £2-£4 weekly, some a trifle less, and others much more. Those chosen for "local" licence reside with their employers or in lodgings, and are selected for this form of community trial either because they happen to be friendless or because their home circumstances are deemed unlikely to be propitious to their social habilitation; "distant" licence cases are placed in the care of parents, relatives, or employers further afield. Almost all licensed cases are fully self-supporting and many earn standard wages, which in some instances amount to £7-£8 weekly. "Teen-agers" rarely succeed unless their home conditions are exceptionally favourable, and, as a rule, patients on community trial need repeated tests, over a period of years, before they achieve tolerable social competence. Indeed, final discharge is rarely recommended until full adult status is attained.