

approximately twice the diameter measured on the arteriogram film. It is convenient to have two or three prostheses of slightly different dimensions prepared before operation. One of them is usually found to be of the correct size. Should it prove too long it is easy to unpick some of the seam and trim it to the required length.

4. *Sterilization*.—The completed tubes are sterilized by boiling or autoclaving before operation. The latter is preferable. It is important to avoid folds or wrinkles in the cloth. The completed prostheses are smoothed with an electric iron before autoclaving. This is particularly helpful in keeping the folds at the stomata turned conveniently backwards so that suturing is facilitated when the time comes. Glass rods or small test-tubes are inserted inside the prostheses to prevent wrinkling during autoclaving.

Discussion

The advantages of these cloth prostheses over homografts are obvious. They are far more easily obtained and there is no anxiety about their sterility. They have, however, limitations. They cannot be used across the line of flexion of a joint, or certainly not if the joint is to be acutely flexed in the immediate post-operative period, for if this is done the tube is folded, the lumen obstructed, and thrombosis follows. This was the result when a prosthesis was inserted in a dog from the aorta to the femoral artery and the hip-joint flexed. Perhaps if flexion was avoided by splintage or other means until a firm collagenous wall had formed success might be obtained. Until this point is elucidated further we have avoided using a prosthesis below or across the inguinal ligament in patients, relying still upon homografts for this region.

A point of technical interest became evident when the aortograms were examined. When the classical Carrel everting suture was used a definite constriction was always produced at the anastomosis. This did not occur when a simple over-and-over running suture was used without eversion of the inner surfaces. The latter type of suture also has the advantage of greater speed and ease of execution.

The idea of using seamless tubes soon comes to mind when considering prostheses, and through the kindness of Messrs. Ethicon Sutures we have had some of these for preliminary trial. Certain disadvantages came to light which were not at first obvious. A turnover at the ends is desirable, and this necessarily produces some constriction, which is undesirable in the smaller-lumen tubes. Also, where branches are involved they are less adaptable for use compared with the prostheses made to measure. However, there is no doubt that with further trial still better prostheses will be evolved.

Summary

Experimental studies using "orlon" cloth prostheses to replace arteries of dogs are described.

The prostheses can be inserted end-to-end, end-to-side, or side-to-side into the arterial tree of the host. Branching prostheses may also be used.

Their clinical use in the treatment of arterial disease is reported.

Technical points in preparing the prostheses are outlined.

Advantages and disadvantages of prostheses compared with homografts are discussed.

We are grateful to many colleagues who have helped with this work. Professor Sir James Paterson Ross has given advice and encouragement, and Professor E. C. Amoroso has given us hospitality and facilities at the Royal Veterinary College for the animal studies. Dr. Hugh Cleland has helped with some of the operations. Miss D. Aitken has given skilled technical help, particularly in preparing the prostheses.

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SENSITIVITY TO FIVE ANTIBIOTICS OF A FURTHER 200 STRAINS OF STAPH. PYOGENES ISOLATED FROM OUT-PATIENTS

BY

E. G. REES, M.B., M.R.C.P.

R. A. SHOOTER, M.D.

(From the Department of Bacteriology, St. Bartholomew's Hospital)

AND

G. D. H. SHAW, M.B., B.S.

Surgical Registrar in Charge of the Casualty Department, St. Bartholomew's Hospital

Three years ago a report was made from this laboratory of the sensitivity to five antibiotics of strains of *Staphylococcus pyogenes* isolated from out-patients (Birnstingl, Shooter, and Hunt, 1952). It was found that, although the majority of staphylococci isolated from in-patients at that time were resistant to penicillin, resistant staphylococci were isolated from only 32 of 200 out-patient infections. No strains were resistant to streptomycin, chlortetracycline, oxytetracycline, or to chloramphenicol. In view of the continued prevalence of penicillin-resistant staphylococci in hospital wards, and the increasing number of strains found to be resistant to the later antibiotics, we have again examined 200 strains of *Staph. pyogenes* isolated from out-patient infections to see if resistant staphylococci are responsible for more of these infections than was the case three years ago.

Sources of Staphylococci

Swabs were taken from patients with acute infections of the skin and subcutaneous tissues attending the casualty department between October, 1954, and March, 1955. Whenever possible, swabs were taken on the first attendance, or, if this was not possible, when a lesion was opened. Swabs taken from patients attending other out-patient departments of this hospital, such as the skin and ear-nose-and-throat departments, were not included in the series, and care was also taken to exclude patients attending other hospitals, or who had recently been discharged from hospital wards.

Methods of Isolation and of Testing Sensitivity

All the swabs were sown direct on to two horse-blood-agar plates from which cups had been cut with a cork-borer. After inoculation these cups were filled with penicillin 10 units/ml., streptomycin 250 µg./ml., oxytetracycline 50 µg./ml., chloramphenicol 250 µg./ml., and erythromycin 100 µg./ml. respectively. Staphylococci which coagulated plasma in a tube were regarded as *Staph. pyogenes*: those which were inhibited by antibiotics to approximately the same degree as the Oxford H staphylococcus were described as sensitive.

Dilution sensitivity tests were carried out for all the antibiotics used with the exception of penicillin. For these tests stock solutions of streptomycin calcium chloride complex (1,000 µg./ml.), oxytetracycline (100 µg./ml.), chloramphenicol (1,000 µg./ml.), and erythromycin (100 µg./ml.) were prepared in distilled water and stored at -8° C. The solutions of streptomycin and chloramphenicol were replaced every two months; solutions of oxytetracycline and erythromycin were made up weekly. For testing, series of two-fold dilutions of each of the four antibiotics in nutrient agar plates were prepared immediately before use, each plate

containing 14 ml. of nutrient agar and 1 ml. of a solution of antibiotic of such strength as to give the required concentration when uniformly diffused in the medium. Each plate was divided by diamond marking into 12 approximately equal sectors of just over 5 square cm. An 18-hour nutrient broth culture of each staphylococcus was used as the inoculum, a 1-mm. loopful of the undiluted culture being spread over each sector. (For streptomycin, tests were also made using this inoculum diluted 300 times.) The plates were incubated at 37° C. for 18 hours, and the end-point was determined by inspection of the surface of the medium.

Results

For *Staph. pyogenes*, resistance to penicillin is dependent on the production of penicillinase, and as this can be detected in primary culture no further examination was thought necessary. Of the 200 strains isolated, 43 produced penicillinase and were resistant. Sensitivity to the

Sensitivity of 200 Strains of *Staph. pyogenes* to Streptomycin, Oxytetracycline, Chloramphenicol, and Erythromycin

Minimum Inhibitory Concentration (µg. per ml.)	Streptomycin		Oxytetracycline	Chloramphenicol	Erythromycin
	Undiluted Inoculum	1 in 300 Inoculum			
> 64	1	—	—	—	—
64	1	—	—	1	—
32	26	—	—	1	—
16	87	—	—	186	—
8	67	1	—	12	—
4	17	4	—	—	—
2	1	103	38	—	—
1	—	90	119	—	13
0.5	—	2	42	—	187
0.25	—	—	1	—	—

other antibiotics is shown in the Table. With one exception strains found sensitive by the dilution method had already been so described on primary isolation.

We have deliberately used a heavy inoculum when testing sensitivity, partly to enable a comparison to be made with previous work, and partly in the belief that the results obtained may be more applicable to conditions in the body (Spink, 1951). In a small pilot experiment involving 12 strains it was found that for oxytetracycline, chloramphenicol, and erythromycin, the difference between an inoculum of undiluted culture or a 1 in 300 dilution of undiluted culture amounted to only one serial dilution of the antibiotic. For streptomycin the difference was greater, and the results are accordingly reported as those obtained with undiluted culture or its 1 in 300 dilution.

Discussion

Penicillin.—In the three years since the last survey much penicillin has been prescribed in general practice, and many members of the public have entered and left hospital wards. A considerable number of this last group of patients must have taken with them to the outer world penicillin-resistant hospital staphylococci, and it is gratifying and perhaps a little surprising that we have isolated only 43 resistant strains (21.5%), as compared with 16% three years ago. The spread of resistant staphylococci within hospitals has been so rapid that it might be thought that there is some special feature of the hospital environment which encourages them in preference to sensitive strains. Perhaps in the outer world sensitive staphylococci are better able to hold their own, and a 21.5% rate represents a state of equilibrium.

Streptomycin.—With the use of a heavy inoculum two of our strains were relatively resistant to streptomycin, but that this represents the selection of a few resistant variants is suggested by the finding that all the strains were sensitive when tested with a dilute inoculum. There are few indications for the use of streptomycin in the treatment of staphylococcal infections, and it was included as a matter of theoretical interest.

Other Antibiotics.—Resistance to oxytetracycline, chloramphenicol, erythromycin (and streptomycin) is the result of

exposure of staphylococci to these drugs, and resistance, once acquired, is permanent. This type of resistance is becoming an additional characteristic of hospital staphylococci, and its occurrence is related to the frequency with which the newer antibiotics are prescribed. That we have found only one staphylococcus to be resistant to chloramphenicol and none to be resistant to the other antibiotics presumably reflects the relatively restricted use of antibiotics in general practice, and the dilution among the general public of resistant hospital strains.

If *in vitro* sensitivity tests can be taken as a guide to the likely outcome of treatment—and for most infections and drugs there is general agreement that they can—our findings would suggest that some 80% of staphylococcal infections originating outside hospital will respond to treatment with penicillin, and almost all to treatment with oxytetracycline, chloramphenicol, and erythromycin.

Summary

Two hundred strains of *Staph. pyogenes* isolated from out-patients with acute staphylococcal infections of the skin and subcutaneous tissues have been tested for their sensitivity to penicillin, streptomycin, oxytetracycline, chloramphenicol, and erythromycin. Of the strains tested, 21.5% were resistant to penicillin. One strain was resistant to chloramphenicol, and none to the other antibiotics.

Comparison of these results with those of a similar investigation carried out three years ago has shown that there has been a slight increase in the proportion of strains resistant to penicillin, but virtually no increase in strains resistant to the other antibiotics.

We are indebted to Professor L. P. Garrod for advice, and to Miss M. Rhodes for technical assistance.

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TREATMENT OF THE PREMENSTRUAL SYNDROME VALUE OF ETHISTERONE, MEPHENESIN, AND A PLACEBO COMPARED

BY

G. I. M. SWYER, D.M., D.Phil., M.R.C.P.

Consultant Endocrinologist, Department of Obstetrics,
University College Hospital

In a recent penetrating contribution on the premenstrual syndrome Greene and Dalton (1953) reached the conclusion that the wide variety of distressing symptoms from which many women suffer during the final week or so of the menstrual cycle, and occasionally at other points of the cycle, are probably due to water-retention. This, in turn, they felt was very likely the result of an abnormal elevation of the oestradiol/progesterone ratio. Claims for the beneficial results of treatment aimed either at dehydration or at correcting the alleged hormonal disturbance have, they point out, been made by a number of writers. They themselves found treatment by a progestogen to be almost invariably successful, in mild cases relief usually being obtained by the oral administration of ethisterone in a dosage of 25 mg. twice daily during the second half of the menstrual cycle. Still more effective was the intramuscular injection of progesterone, 25 mg. on alternate days during