TREATMENT OF BOILS WITH ERYTHROMYCIN AND WITH ANTIBIOTIC E 129

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The well-known propensity of strains of *Staphylococcus aureus* to develop resistance to the effects of bactericidal and bacteriostatic drugs has been a major factor in the search for newer antibiotics. E 129, one of the most recently produced of these, has already been described and tested in the laboratory (Garrod and Waterworth, 1956). The present study records the results of a clinical investigation of this alternative therapeutic agent. Its purpose was to compare the efficacy of E 129 in the treatment of a relatively "standard" clinical infection—a furuncle—with that of an established antistaphylococcal antibiotic, erythromycin, to which E 129 is related. In addition to judging therapeutic effect by clinical criteria, laboratory studies were carried out to determine the effect on the staphylococcus itself, and in particular on its sensitivity to each of the antibiotics used in treatment.

Methods

Patients were a consecutive series, 210 in all, who attended the out-patient department of St. Bartholomew's Hospital for the treatment of boils. The period of study occupied the year from February, 1957, to February, 1958. No patients under 16 were treated in this series, largely because of the difficulty presented for children by the ingestion of the large quantity of E 129 tablets (12 daily) during their treatment. The ages ranged from 16 to 67 years, with a mean of 27. There was a slight preponderance of males—3:2.

Several criteria were used to decide whether the patient was suitable for inclusion in this series: (1) the lesion must have been fresh, (2) no treatment of the patient with antibiotics in the preceding six months, and (3) no secondary space infections (such as may be seen on the hand).

Classification of Boils.—(1) Localized infection of diameter under 1 cm., and with no surrounding reaction. (2) Localized infection, larger than above, with minimal adjacent reaction. (Neither of these two groups had any systemic symptoms or signs.) (3) Local infection of diameter over 2.5 cm., with marked surrounding cellulitis, moderate regional lymphadenopathy, some tissue destruction, occasional mild fever. (4) Large area of local infection, with marked peripheral cellulitis, regional lymphadenopathy, and systemic signs—for example, fever, fatigue. The first part of the study included patients with boils of all four types, but the main series included boils of the last-named two groups only.

Therapy.—All patients received local applications of mercury perchloride, 0.1% aqueous solution. In approximate consecutive rotation, therapy was conducted in successive patients with (*a*) local application alone; (*b*) erythromycin 250 mg. four times daily per os for seven days; (*c*) E 129, 750 mg. four times daily per os for seven days. The larger dose of E 129 was decided on for three reasons: as obtainable at the time of the investigation, this substance included a substantial amount of impurities; it is believed to be less readily absorbed than erythromycin; and *in vitro* it has about one-half of the activity of the latter against *Staph. aureus*. Eleven patients on placebo therapy whose condition was deteriorating rapidly were removed from the series and given treatment as indicated.

Observations.—Swabs were taken from the boil of each patient before the beginning of therapy, and on the second, fourth, and seventh days of treatment. Further cultures were taken until the area healed. In addition a clinical assessment of each case was made on the above days until healing was complete. Further examinations were made in the third and sixth weeks after therapy.

Results

General Observations

In the treatment of boils categorized as 1 and 2 no substantial difference was noted in the results obtained with either placebo or antibiotic routines. This prompted us, therefore, to limit our further patients to those who had boils of group 3 or 4—a total of 165 patients.

A comparison of results obtained in the treatment of boils of less than four days' duration with those of longer than four days demonstrated that the latter tended to be of greater severity (22% in contrast to 12% classed as group 4), with a prolonged healing-time (30% required over two weeks), and a higher incidence both of necessary surgical drainage (22% in contrast to 9%) and of fresh outbreaks (40% in contrast to 17%). Cultures became negative over a slightly longer period.

A consideration of the mean duration of boils prior to treatment in each of the three therapeutic groups showed these values to be almost the same. Hence for the purposes of the remainder of the results the boils of varying duration are discussed together.

Comparison of the Results of Placebo and Antibiotic Therapy

The results are stated in the Table. The evolution of the boil process continued in 42% of the placebo-treated group for over four days, in contrast to the course in patients of the antibiotic group, in which only 2% were observed to progress after therapy was started. In 24% of the former group the boil was not controlled even after one week.

Comparison of the Results of the Treatment of Boils Using Placebo, Erythromycin, and E 129

	Form of Therapy Employed		
	Placebo	Erythromycin	E 129
No. of cases	55	55	55
Duration of boil (average in days)	4 (3–10)	4·2 (2–7)	4 (2–7)
Progression of boil during therapy:			
1–2 days	10 (18%)	26 (47%)	31 (56%)
3–4 ,,	23 (42%)	27 (50%)	23 (42%)
5–7 ,,	10 (18%)	2 (4%)	1 (2%)
8–21 ,,	12 (22%)	0	0
Duration of healing:			
4–7 days	5 (9%)	16 (29%)	24 (44%)
8–14 ,,	27 (50%)	29 (53%)	29 (53%)
15–21 ,,	9 (16%)	8 (14%)	1 (2%)
22–28 ,,	9 (16%)	2 (4%)	1 (2%)
29–42 ,,	5 (9%)	0	0
Degree of final tissue damage:			
Grade 1	10 (18%)	39 (71%)	45 (82%)
,, 2	18 (32%)	13 (23%)	10 (18%)
,, 3	27 (50%)	3 (6%)	0
Last positive culture:			
Within 4 days	20 (36%)	26 (47%)	29 (53%)
5–7 days	21 (36%)	16 (29%)	18 (32%)
8–14 ,,	10 (18%)	7 (12%)	6 (11%)
15–21 ,,	2 (4%)	1 (2%)	1 (2%)
Over 21 days	2 (4%)	0 (5 sterile throughout)	0 (1 sterile throughout)
New lesions during therapy	14 (25%)	5 (9%)	5 (9%)
,, ,, after ,,	5 (9%)	8 (14%)	5 (9%)
Drainage required	11 (20%)	8 (14%)	3 (6%)

Healing-time was less than a week in only 9% of the placebo group, while 25% required over three weeks for healing.

Of those having no antibiotic therapy, 50% suffered marked local necrosis, with subsequent scarring after the infection; in contrast to this only a small number of antibiotic-treated patients showed this complication.

Eventual surgical drainage of the boil area was required in 20% of the first group, while an even greater number (34%) developed fresh lesions within the observation period of six weeks. It is interesting that antibiotic therapy in the other group did not appear to influence the tendency of some patients to recurrent furunculosis.

Various systemic complications were observed in the placebo-treated group; these included fever in 36% of cases, usually lasting about three days.

Although most of the untreated boils showed only a slightly slower rate of disappearance of positive cultures, 8% of the tests still yielded a positive result even after 14 days.

Clinical Comparison of the Results of Treatment with Erythromycin and E 129

Both antibiotics showed approximately the same ability to arrest the progress of the boil—about 50% controlled within two days, and only 2% uncontrolled after four days. The development of the boil appeared to be halted slightly more rapidly with E 129.

The boils treated with E 129 healed more rapidly than those given erythromycin; 44% healed within the first week, in contrast to only 29% of those in the latter group. It can be shown, using the χ^2 test for a trend (Armitage, 1955), that the difference in rates of healing is statistically significant at the 5% level ($\chi_0^2=5.7$; $0.01<P<0.05$).

Tissue damage was not marked in either of the two groups—over 80% of the E 129 group and 72% of the erythromycin group could be placed in stage 1, although three patients in the latter group did show sufficient damage to be classified as grade 3.

Surgical drainage was necessary in slightly more (8) of the erythromycin group, while the incidence of fresh lesions was about equal.

Diarrhoea associated with the presence of *Candida* in the stools followed erythromycin therapy in four patients. No such complication was observed with E 129.

Bacteriological Findings

Coagulase-positive staphylococci were found in the initial culture from 159 of the 165 patients: the few negative cultures are attributable to the fact that the lesion was sometimes still closed when the first swab was taken. Although 37 (23.3%) of these strains were resistant to penicillin and 3 (1.1%) to tetracycline, they were uniformly sensitive to both erythromycin and E 129, the respective minimum inhibitory concentrations almost invariably found, using the method of Garrod and Waterworth (1956), being 0.12 and 0.25 μg./ml.: no strain differed from this figure by more than one (doubled) dilution.

Negative cultures were obtained after about the same time in both groups—within four days in 47% of the erythromycin group and 53% of the E 129 group. All strains of coagulase-positive staphylococci recovered from the original boil after the seven-days period of treatment (8 in the erythromycin group and 7 in the E 129), and those from fresh lesions developing during or after treatment (13 and 10 respectively) were retested and found to have undergone no change in sensitivity to either antibiotic.

Discussion

The apparent lack of effect that antibiotics had on less severe boils is in keeping with our knowledge of the adequacy of the body's natural defences against such infections. In the treatment of more severe infections it is clear that the use of antibiotics promotes more rapid recovery with fewer sequelae such as post-necrotic scarring, although the better results appear to depend not so much on the rapid elimination of the infecting organisms as on limitation of their destructive activity.

By each of the criteria used the effect of E 129 was slightly superior to that of erythromycin, and by one of these—the rate of healing—the difference has a statistical significance. Against this advantage has to be set the fact that a larger dose of E 129 was given. Reasons for adopting this dose have been stated, and, allowing for the impurity of the E 129 and its less complete absorption, the effective doses of the two antibiotics must have been approximately equivalent. It would be unwise, however, to base any final conclusion about the relative merits of these two antibiotics on these findings.

It was thought possible that a difference between them might be found in another direction. Staphylococci acquire resistance to erythromycin rather readily and to E 129 less so (Garrod and Waterworth, 1956). It has been a common practice to restrict the use of erythromycin severely for fear of breeding resistant strains, and it would not have been surprising if in some of these patients with persisting or recurrent infections increased resistance to the antibiotic had been found. In fact, no instance of increased bacterial resistance to either antibiotic was seen in the whole series. Whether this is to be credited to strict limitation of the treatment to seven days, or whether the nature of the lesion is unfavourable to change in bacterial resistance, is uncertain. It is nevertheless encouraging to know that this form of staphylococcal infection can be treated in this way apparently without serious risk of producing such a change.

Summary

Patients with severe boils were treated with erythromycin (1 g. daily) and E 129 (3 g. daily) each for one week, or by the local application of mercury perchloride only. There were 55 patients in each group.

As judged by each of four criteria, patients in both antibiotic-treated groups recovered more rapidly and more satisfactorily than the controls. Slight differences between the treated groups were in favour of E 129.

All strains of staphylococci found in these patients were normally sensitive to both antibiotics, and none cultivated again after seven days' treatment had acquired resistance to either of them.

The advice of Dr. R. M. B. MacKenna and Professor L. P. Garrod on the clinical and bacteriological aspects respectively of this work is gratefully acknowledged. Mr. M. P. Curwen kindly made the statistical calculation referred to in "Results." Antibiotic E 129 was kindly supplied by Glaxo Laboratories Limited.

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EFFECT OF ABDOMINAL OPERATIONS ON TOTAL LUNG CAPACITY AND ITS SUBDIVISIONS

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Although serious pulmonary complications of an inflammatory nature are becoming less frequent after abdominal operations, atelectasis and bronchitis still occur. One of the main factors is the interference with the mechanical efficiency of the lungs. The effect of laparotomy on vital capacity has been extensively studied (Churchill and McNeil, 1927; Powers, 1928; Overholt, 1930; Anscombe, 1957) and reductions of up to 80% of the preoperative figure may occur after an upper abdominal operation.

Other effects on pulmonary function have not been examined in such detail. Beecher (1933) measured the