the ulcers themselves? We maintain that the average rates of healing have significance, not least so because both the aggregated results from numerous cases in Table I and the less numerous ones in Tables I and II correspond closely to our clinical impression accumulated in treating leg ulcers over many years.

The need for further investigation on the subject of leg ulcers is clamant, and representatives from all branches of medicine must co-operate in this. Many problems remain, but Anning (1954) has stated that venous thrombosis is the commonest cause of failure of the muscle pump leading to leg ulceration, and it occurred in 74.85% of the patients in his series. 27.6% of the women in Anning's series suffered from post-partum thrombosis, and it was hoped that the advent of antibiotics and improved maternity care might cause leg ulcers from this factor to become a thing of the past.

A. M. Giles (1960, personal communication) states that the incidence of true deep venous thrombosis in post-partum cases is very much less than in pre-antibiotic times, but there are coming to the fore resistant organisms which may result in a return of the original incidence of this complaint. Therefore we cannot afford to be complacent. We hope that the introduction of this technique will act as a stimulus to further research in the treatment of leg ulcers and that its first fruits, our advocacy of a reversion to simple methods of treatment, may lead to more efficient but less expensive therapy and to a great reduction in unnecessary suffering.

Summary

A series of 271 cases of leg ulcers was submitted to area measurement and the speed of healing calculated in sq. mm. per day while various medicaments were being exhibited.

Eusol produced the fastest regression rate, and it was concluded that simple applications and procedures are best in treating leg ulcers.

It is a pleasure to acknowledge the assistance of the ward sisters and nursing staff. Dr. Alex. Berrie, of Glasgow University, advised on the statistics. Messrs. Glaxo Laboratories and Messrs. Upjohn of America forwarded generous supplies of triiodothyronine and of gelfoam respectively.

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London County Council has issued a small booklet, *Notes for Guidance of Child Guidance Clinics*, by J. Wilson Wheeler (Children's Officer), W. F. Houghton (Education Officer), and J. A. Scott (Medical Officer of Health and Principal School Medical Officer). The main services are discussed under the three headings of: (1) special education for children remaining in their homes; (2) provision for placing children away from their homes; and (3) recommendations made to the juvenile courts. The booklet includes the names, addresses, and telephone numbers of the district care organizers, the area children's officers, and the divisional medical officers in the London boroughs.

TABLE FOR ASCERTAINING WHETHER DIFFERENCES BETWEEN PERCENTAGES ARE STATISTICALLY SIGNIFICANT AT THE 1% LEVEL

BY

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In a previous paper (Garside, 1958) a table was given to ascertain whether differences between percentages are significant at the 5% level. The accompanying table can be used to find whether such differences are significant at the 1% level. The method of use of the present table is identical with that of the previous table.

Yates's Correction for Continuity

It has been asked whether Yates's correction for continuity (see Hill, 1955) can be incorporated when using the previous table. This correction can be used with both tables. It is never wrong to use the correction, but its effect becomes small as the numbers involved become large. It should, however, be used if Pa or (100 - Pa), whichever is smaller, multiplied by Nb or (N - Nb), whichever is smaller, is less than 1,000. If this product is less than 500, then, as stated in the previous paper, a more accurate method of finding significance should be used (see Fisher and Yates, 1948). At first sight, 1,000 and 500 seem very large, but they are percentages and correspond to actual frequencies of only 10 and 5 respectively. Pa, Nb, and N are defined in the previous paper.

To apply Yates's correction using either table, the difference tested—that is, that between Pa and Pab/b—should be reduced by 100/2Nb. If this corrected difference (Dc) equals or exceeds the corresponding percentage tabulated in the previous table, the difference is significant at the 5% level, and if Dc equals or exceeds the corresponding percentage in the present table then the difference is significant at the 1% level. In using the tables 1/Nb has to be found anyway, so the correction is simple to apply.

It can easily be shown that Dc—that is, |Pa - Pab/b| - 100/2Nb—divided by its standard error—that is, $\sqrt{Pa(100 - Pa)(1/Nb - 1/N)}$ —equals the square root of chi squared corrected for continuity—that is,

$$\frac{N(|AD - BC| - 1/2N)^2}{(A + B)(A + C)(B + D)(C + D)}$$

where A, B, C, and D are the cell frequencies in a fourfold table. Thus using the tables with the correction gives precisely the same results as using the corrected chi-squared test. An example will illustrate this and make the procedure clear.

Suppose the following data relate to two factors or symptoms:

	Yes	No	Total
Yes	3	10	13
No	9	2	11
Total	12	12	24

Then Pa = 50%, N = 24, Nb = 13, and N - Nb = 11. Pa multiplied by (N - Nb) equals 550, and therefore Yates's correction should be applied. Now Pab/b

Table of D Significant at 1% Level—Percentages

Pa= or n=	0.5 99.5	1.0 99.0	1.5 98.5	2.0 98.0	3 97	4 96	5 95	6 94	7 93	8 92	9 91	10 90	12 88	14 86	16 84	18 82	20 80	25 75	30 70	35 65	40 60	45 55	50% 50%
0.100	5.75	8.11	9.91	11.5	13.9	16.0	17.8	19.4	20.8	22.1	23.4	24.5	26.5	28.3	29.9	31.3	32.6	35.3	37.4	38.9	40.0	40.6	40.8
0.095	5.60	7.90	9.66	11.2	13.6	15.6	17.4	18.9	20.3	21.6	22.8	23.9	25.8	27.6	29.2	30.6	31.8	34.4	36.4	37.9	38.9	39.5	39.7
0.090	5.46	7.69	9.40	10.9	13.2	15.2	16.9	18.4	19.8	21.0	22.2	23.2	25.2	26.9	28.4	29.7	31.0	33.5	35.5	36.9	37.9	38.5	38.7
0.085	5.30	7.48	9.13	10.6	12.9	14.8	16.4	17.9	19.2	20.4	21.5	22.6	24.5	26.1	27.6	28.9	30.1	32.6	34.5	35.9	36.8	37.4	37.6
0.080	5.14	7.25	8.86	10.2	12.5	14.3	15.9	17.4	18.6	19.8	20.9	21.9	23.7	25.3	26.8	28.0	29.2	31.6	33.4	34.8	35.7	36.3	36.5
0.075	4.98	7.02	8.58	9.88	12.1	13.9	15.4	16.8	18.0	19.2	20.2	21.2	23.0	24.5	25.9	27.2	28.3	30.6	32.4	33.7	34.6	35.1	35.3
0.070	4.81	6.79	8.29	9.55	11.7	13.4	14.9	16.2	17.4	18.5	19.6	20.5	22.2	23.7	25.0	26.2	27.3	29.6	31.3	32.6	33.4	34.0	34.1
0.065	4.64	6.54	7.99	9.20	11.3	12.9	14.4	15.6	16.8	17.9	18.8	19.8	21.4	22.8	24.1	25.3	26.3	28.5	30.1	31.4	32.2	32.7	32.9
0.060	4.46	6.28	7.67	8.84	10.8	12.4	13.8	15.0	16.1	17.2	18.1	19.0	20.6	21.9	23.2	24.3	25.3	27.4	29.0	30.1	31.0	31.4	31.6
0.055	4.27	6.02	7.35	8.46	10.4	11.9	13.2	14.4	15.5	16.4	17.3	18.2	19.7	21.0	22.2	23.3	24.2	26.2	27.7	28.9	29.6	30.1	30.3
0.050	4.07	5.74	7.01	8.07	9.83	11.3	12.6	13.7	14.7	15.7	16.5	17.3	18.8	20.0	21.2	22.2	23.1	25.0	26.4	27.5	28.3	28.7	28.8
0.045	3.86	5.44	6.65	7.65	9.33	10.8	12.0	13.0	14.0	14.9	15.7	16.4	17.8	18.9	20.1	21.0	21.9	23.7	25.1	26.1	26.8	27.2	27.4
0.040	3.64	5.13	6.27	7.22	8.79	10.1	11.3	12.3	13.2	14.0	14.8	15.5	16.8	17.9	18.9	19.8	20.7	22.4	23.7	24.6	25.3	25.7	25.8
0.035	3.40	4.80	5.86	6.75	8.23	9.45	10.6	11.5	12.3	13.1	13.8	14.5	15.7	16.8	17.7	18.6	19.3	20.9	22.1	23.0	23.7	24.0	24.1
0.030	3.15	4.44	5.43	6.25	7.62	8.75	9.73	10.6	11.4	12.2	12.8	13.4	14.5	15.5	16.4	17.2	17.9	19.4	20.5	21.3	21.9	22.2	22.4
0.025	2.88	4.06	4.96	5.71	6.95	7.99	8.88	9.68	10.4	11.1	11.7	12.3	13.3	14.2	15.0	15.7	16.3	17.7	18.7	19.5	20.0	20.3	20.4
0.020	2.57	3.63	4.43	5.10	6.22	7.14	7.94	8.66	9.30	9.89	10.5	11.0	11.9	12.7	13.4	14.0	14.6	15.8	16.7	17.4	17.9	18.2	18.3
0.015	2.23	3.14	3.84	4.42	5.39	6.19	6.88	7.50	8.05	8.56	9.03	9.47	10.3	11.0	11.6	12.2	12.7	13.7	14.5	15.1	15.5	15.7	15.8
0.010	1.82	2.57	3.14	3.61	4.40	5.05	5.62	6.12	6.58	6.99	7.38	7.73	8.38	8.94	9.45	9.90	10.4	11.2	11.9	12.3	12.7	12.9	12.9
0.008	1.63	2.30	2.81	3.23	3.94	4.52	5.03	5.48	5.88	6.26	6.60	6.92	7.49	8.00	8.45	8.86	9.22	9.98	10.6	11.0	11.3	11.5	11.6
0.006	1.41	1.99	2.43	2.80	3.41	3.91	4.35	4.74	5.10	5.42	5.71	5.99	6.49	6.93	7.32	7.67	7.99	8.64	9.15	9.52	9.78	9.93	9.98
0.004	1.15	1.63	1.99	2.29	2.78	3.20	3.56	3.87	4.16	4.42	4.67	4.89	5.30	5.66	5.98	6.26	6.52	7.06	7.47	7.78	7.99	8.11	8.15
0.002	0.813	1.15	1.41	1.62	1.97	2.26	2.52	2.74	2.94	3.13	3.30	3.46	3.75	4.00	4.23	4.43	4.61	4.99	5.28	5.50	5.65	5.74	5.76
0.001	0.575	0.811	0.991	1.15	1.39	1.60	1.78	1.94	2.08	2.21	2.34	2.45	2.65	2.83	2.99	3.13	3.26	3.53	3.74	3.89	4.00	4.06	4.08
0.0005	0.407	0.574	0.701	0.807	0.983	1.13	1.26	1.37	1.47	1.57	1.65	1.73	1.88	2.00	2.12	2.22	2.31	2.50	2.64	2.75	2.83	2.87	2.88
0.0001	0.182	0.257	0.314	0.361	0.440	0.505	0.562	0.612	0.658	0.699	0.738	0.773	0.838	0.894	0.945	0.990	1.04	1.12	1.19	1.23	1.27	1.29	1.29
0.00001	0.058	0.082	0.100	0.115	0.139	0.160	0.178	0.194	0.208	0.221	0.234	0.245	0.265	0.283	0.299	0.313	0.326	0.353	0.374	0.389	0.400	0.406	0.408
0.000001	0.019	0.026	0.032	0.037	0.044	0.051	0.057	0.062	0.066	0.070	0.074	0.078	0.084	0.090	0.095	0.099	0.104	0.112	0.119	0.123	0.127	0.129	0.129

=23.1% and $100/2Nb=3.8$. Therefore $Dc=50-23.1-3.8=23.1$. To find the corresponding percentage in the table, $n=1/Nb-1/N$ is calculated; this equals 0.035. The percentage corresponding to $Pa=50\%$ and $n=0.035$ in the present table is 24.1, which exceeds Dc . Therefore the difference is not significant at the 1% level, and the chances are less than 99 in 100 that the two factors are related. The corresponding percentage in the 5% table is 18.4, which is less than Dc , and therefore the chances are greater than 95 in 100 that the factors are related. Chi squared (corrected) from these data equals 6.04, which is significant at the 5% level but not at the 1% level.

Had the correction not been applied, an uncorrected D of 26.9—that is, $50-23.1$ —would have been obtained which is greater than 24.1, and thus the erroneous conclusion would have been drawn that the difference was significant at the 1% level. A similar error would be made if uncorrected chi squared were calculated; this equals 8.22, which is significant at the 1% level.

The data in the above example have been chosen so that both Pa and n are equal to tabulated values of these variables. But in practice, of course, the actual value of Pa and n will not usually coincide with the tabulated values. In this case the procedure outlined in the previous paper (Garside, 1958) must be adopted.

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Preliminary Communications

Preliminary Clinical Assessment of Betamethasone

Betamethasone ("betnelan"; 16 β -methyl-9 α -fluoro-prednisolone) is closely related chemically to dexamethasone (16 α -methyl-9 α -fluoro-prednisolone), but the altered configuration of the methyl group at carbon atom 16 might be expected to alter the metabolism of the hormone and to modify side-effects. Betamethasone is therefore an essentially new substance meriting independent assessment. Investigation of the drug was further encouraged by the prospect that its cost would be low in comparison with other recently introduced compounds.

The clinical evaluation of a new corticosteroid should be based upon the following criteria: (1) its potency and effective dosage ratio in comparison with other steroids; (2) the presence or absence of recognized side-effects usual with other steroids; (3) the incidence of any side-effects peculiar to the new steroid; and (4) the cost of effective therapy.

With these criteria in mind 46 patients have been treated with betamethasone since the onset of the trial eight months ago. Sixteen of them have received simultaneous chrysotherapy: these are not considered here, but will be the subject of a separate communication. Of the remainder, 23 have been studied in sufficient detail to warrant the following report.

SCHEME OF TRIAL

Selection of Cases.—Most of the patients were suffering from typical rheumatoid arthritis. In addition, one case each of disseminated lupus erythematosus, ankylosing spondylitis, and spasmodic asthma have been included. Many of these cases had been maintained on other steroids prior to betamethasone. Case selection has followed the usual criteria for steroid therapy—namely, (1) progressive disease unrelieved by other methods of treatment; (2) preservation of essential function and prevention of deformity; and (3) the absence of definite contraindications. In this series a higher proportion of elderly patients than is usual was purposefully included, since we feel that, provided certain routine precautions are taken, there may be greater scope for steroid therapy in geriatric cases than is usually accepted. It is in these patients that functional and social disability may be out of all proportion to the severity of the disease.

Method.—The following factors were considered. (1) The patient's subjective response, especially in answer to specific questions regarding duration of morning stiffness and pain and disturbed sleep. (2) The number of joints actively inflamed at the time of examination—any two of the usual criteria of inflammation being accepted. (3) Measurement of grip, using a sphygmomanometer cuff inflated to 30 mm. Hg. (4) The erythrocyte sedimentation rate. Patients were specifically questioned regarding likely side-effects, notably dyspepsia. Careful observations were made for gain in weight, moon facies, oedema, glycosuria, hirsuties, purpura, hypertension, and osteoporosis.

RESULTS

This investigation is continuing, but results to date can be summarized as follows:

Comparison Between Betamethasone and Dexamethasone.—Of the seven patients in this group four received identical doses of the two steroids. Two of these patients responded equally, while two preferred dexamethasone. In the other three patients betamethasone was the more effective steroid even when given in a slightly lower dosage. Side-effects were infrequent with both steroids, although facial mooning appeared to be more prominent with betamethasone; indigestion was negligible with both.

Comparison Between Betamethasone and Prednisolone.—The antirheumatic activity of dexamethasone is said to be about seven times as great as that of prednisolone, although this ratio may vary in individual patients. A similar variation of individual response was noted in this series. The accompanying table illustrates this point. Dyspepsia, which had troubled six patients in this group, was notably reduced

Case No.	Dose Required to Produce Equal Subjective Response		Ratio	Objective Response at this Ratio
	Prednisolone	Betamethasone		
1	10 mg.	1 mg.	10:1	Equal
3	15 "	3 "	5:1	Betamethasone slightly superior
4	10 "	1 "	10:1	Equal
6	12.5 "	2 "	6:1	Betamethasone slightly superior
7	12.5 "	1 "	12:1	Betamethasone superior
8	7.5 "	1.5 "	5:1	Betamethasone superior
11	15 "	2 "	7:1	Equal
15	12.5 "	2 "	6:1	Prednisolone superior
16	7.5 "	0.5 "	15:1	Betamethasone much superior