

interesting to consider its complications and to contrast them with those described for pulp abscess. The incidence of complications in the group of apical abscess was only 6.25%. In only 3 cases was bone infection met with and in none of these did major sequestration take place. All 3 were noted at the time of the patient's first attendance. In 1 case the first operation was inadequate to provide drainage, and in 1 case the patient's finger became stiff, probably owing to oedema, and a long course of mobilisation was necessary.

Subcutaneous Abscess.—In this group the complication-rate was 14.4%. In no case was this type of lesion complicated by bone infection. In 3 cases the first operation was inadequate and had to be repeated (only 1 of these was done in the clinic). In 3 cases the complication of delayed separation of slough was met with; this has already been discussed under pulp abscess. In 5 cases there was residual stiffness of the finger, probably due to failure to reduce oedema by splinting and elevation. In 1 case a premature incision had been made during the stage of cellulitis. Nine other complications were met with singly, and none was important apart from involvement of a tendon sheath (without fully developed tenosynovitis) in 1 case and involvement of an interphalangeal joint in another.

There is no particular interest in the complications met with in the other groups, and it is not proposed to enumerate them. It is, however, perhaps worth noting that no complication was met with in the treatment of *web abscesses* in this series, and between January, 1946 and April, 1951, 69 cases of this condition have been followed to complete healing without any complication.

Finally, in this series we have not encountered any example of a persistently tender scar in the cases which have been operated on in the clinic.

SUMMARY

A second report is presented of the methods and results of treatment in a special clinic for infections of the fingers and hand.

The principles of treatment are: rest in the diffuse stage of infection, control of infection with antibiotics, and drainage of abscesses through small incisions.

Since the first report (Pilcher et al. 1948) the duration of treatment has been reduced but delay in seeking treatment has not. In most categories delay in seeking treatment increases the length of treatment. Also complications are more common when treatment is delayed.

Pulp abscess and subcutaneous abscess have the highest incidence of complications.

Bone infection is the important complication of pulp abscess. Its incidence is clearly correlated with delay in starting treatment.

Apical abscess is differentiated from pulp abscess because of its better prognosis.

The hand clinic whose work I have reported is staffed by a team with frequent changes in membership. The following have worked in the clinic during the period covered by this report: Miss E. E. Davies, Messrs. J. F. Bolton Carter, A. R. C. Butson, K. Chitty, B. B. Milstein, N. C. Newton, D. E. H. Phillips, and A. G. Riddell. With them any credit for this work must be shared. The clinic is under the direction of Prof. R. S. Pilcher, to whom I am grateful for help and advice in the preparation of the report.

REFERENCES

- Bolton, H., Fowler, P. J., Jepson, R. P. (1949) *J. Bone Jt Surg.* **31B**, 499.
 Goodwin, M. A. (1950) *Brit. med. J.* **i**, 765.
 Jordan, I. (1951) *Brit. J. Surg.* **38**, 331.
 Harrison, S. H., Topley, E., Lennard-Jones, J. (1949) *Lancet*, **i**, 425.
 Jordon, J. B., Miniero, J. D., Scott, J. C. (1948) *J. Bone Jt Surg.* **30B**, 409.
 Rowden, T. G. (1951) *Lancet*, **i**, 196.
 Pilcher, R. S. (1951) *Brit. med. J.* **i**, 1378.
 — Dawson, R. L. G., Milstein, B. B., Riddell, A. G. (1948) *Lancet*, **i**, 777.
 Riddell, A. G. (1950) *Brit. J. Surg.* **37**, 317.

FACTORS INFLUENCING THE RATE OF HEALING OF GASTRIC ULCERS ADMISSION TO HOSPITAL, PHENOBARBITONE, AND ASCORBIC ACID

RICHARD DOLL

M.D. Lond., M.R.C.P.

MEMBER, STATISTICAL RESEARCH UNIT, MEDICAL RESEARCH COUNCIL; ASSOCIATE PHYSICIAN, GASTRO-ENTEROLOGICAL DEPARTMENT, CENTRAL MIDDLESEX HOSPITAL, LONDON

FRANK PYGOTT

M.B. Lpool, D.P.H., D.M.R.E.

RADIOLOGIST, CENTRAL MIDDLESEX HOSPITAL, LONDON

DESPITE the extensive literature on the therapy of peptic ulcer, there is little detailed knowledge of the factors which influence the rate of healing of the ulcer crater. In their textbook on peptic ulcer Ivy et al. (1950) say: "There is no evidence showing that the strict Sippy regimen, or the continuous intragastric drip, is superior to less rigid regimens given under either hospitalization or ambulation in so far as the rate of filling in of the ulcer crater is concerned." Gill (1947) has even cast doubt on the value of any form of régime other than that necessary to gain the patient's confidence. With 1 exception, he found that 20 patients with chronic gastric ulcers treated only with daily injections of distilled water lost their pains as quickly as did a control series treated on orthodox lines. Moreover, healing of the ulcers, which was observed gastroscopically, took place in the usual time.

For these reasons we thought that a formal investigation into the factors influencing the rate of healing of peptic ulcers might be of therapeutic interest and might also provide a clue to aetiology. Gastric and duodenal ulcers are believed to have different causes, and they must therefore be studied separately. Since it is harder to assess the healing of duodenal ulcers, the investigation was confined to patients with gastric ulcers.

In view of Gill's (1947) observations the first object was to assess the value of hospital treatment. It was hardly practicable to insist that patients, many of whom were pain-free, should stay off work and in bed at home for several weeks; nor was it practicable to ensure that a very restricted diet was not exceeded when the patient was not under regular observation. We accordingly decided to compare the effects of a standard dietetic régime in bed in hospital with the effects of a convalescent diet taken when up and about at home. The use of a suitable experimental design made it possible to assess the effects of two subsidiary drug treatments at the same time, and phenobarbitone and ascorbic acid were chosen for inclusion in the initial trial.

METHOD

All new outpatients with uncomplicated and radiographically proven gastric ulcers were referred for consultation, and arrangements were made for their admission.

Some patients who had had ulcers diagnosed previously were also included in the early stages of the investigation; paucity of beds made it necessary to cut down the number of entrants, and the trial was later limited to patients whose ulcers were diagnosed for the first time.

Many patients were pain-free by the time of the consultation and were therefore not prepared to come into hospital. Those admitted were treated in a standard way for a week, during which the barium meal was repeated and gastroscopy was performed. At the end of the week the patient's clinical condition was assessed. Those in whom a benign gastric ulcer had not been confirmed in hospital by both radiography and gastroscopy and those whose clinical condition required some

specific treatment—e.g., operation—were excluded from the trial. The method of treatment of the remainder was then determined by opening one of a series of sealed envelopes which had been prepared independently by a colleague and which contained, in a random order, instructions to treat the patient by one or other of the prearranged methods.

Patients in series A were treated in bed in hospital for four weeks; for the first two weeks they were given a moderately strict orthodox diet (stage 2) and for the last two weeks a more liberal one (stage 3). They were then re-examined radiographically, discharged, recommended

to continue on a "convalescent" diet and advised to return to work as soon as they felt fit enough. The diets used were those recommended by Avery Jones (1949). Patients in series B were discharged immediately and were treated from the outset in the way series-A patients were treated after their month's stay in hospital.

Within both series the patients were divided into sub-groups of four, each member of which was allocated at random one of four drug régimes:

- (1) ascorbic acid 50 mg. t.d.s. and phenobarbitone gr. 1/2 t.d.s.;
- (2) ascorbic acid 50 mg. t.d.s. and an inert tablet t.d.s.;

TABLE I—CASE SUMMARIES, TREATMENT, AND RESULTS

Case no.	Sex	Age (yr.)	History		Size of ulcer niche (sq. mm.)				Symptoms (for scale see text)			
			Length of history	Previous hospital treatment	At start of treatment	1 month later		3 months later		At start of treatment	1 month later	3 months later
						Size	% change	Size	% change			
<i>Treatment inpatient, phenobarbitone, and ascorbic acid:</i>												
1	F	40	5 yr.	—	87	31	-64	13	-85	+	1	0
23	M	38	6 mos.	—	34	34	0	483	+1321	+	2	2
39	M	55	2 1/2 yr.	—	53	15	-72	5	-91	+	2	1
59	M	26	18 mos.	—	105	107	+2	63	-40	—	2	1
77	M	63	4 mos.	—	152	63	-59	13	-91	+	1	0
96	M	53	20 yr.	—	16	6	-63	28	+75	—	0	0
116	M	58	2 yr.	—	52	47	-10	84	+62	+	1	2
122	M	25	1 yr.	—	13	6	-54	0	-100	—	0	1
<i>Treatment inpatient and phenobarbitone; no ascorbic acid:</i>												
15	M	40	3 mos.	—	119	21	-82	24	-80	+	1	1
48	F	72	3 yr.	—	30	0	-100	0	-100	+	1	0
69	M	53	10 yr.	+	18	6	-67	37	+106	+	1	2
72	F	63	38 yr.	—	13	4	-69	0	-100	+	1	1
91	M	67	10 yr.	—	26	0	-100	0	-100	—	0	0
110	M	68	6 mos.	—	90	30	-67	0	-100	+	0	0
132	M	53	4 mos.	—	214	59	-72	14	-93	+	2	1
138	M	27	18 mos.	—	10	8	-20	0	-100	—	0	0
<i>Treatment inpatient and ascorbic acid; no phenobarbitone:</i>												
7	F	39	4 yr.	+	23	4	-83	5	-78	+	1	2
21	F	45	17 yr.	—	7	11	+57	9	+29	+	1	2
54	M	54	15 yr.	—	170	28	-84	0	-100	+	2	0
62	M	46	10 yr.	+	89	38	-57	59	-34	+	2	2
89	F	57	6 wk.	—	92	26	-72	0	-100	+	0	0
94	M	46	14 yr.	—	51	0	-100	5	-90	—	0	1
109	M	59	11 mos.	—	15	0	-100	37	+147	+	0	2
121	F	58	3 wk.	—	137	22	-84	0	-100	+	0	2
<i>Treatment inpatient; no phenobarbitone or ascorbic acid:</i>												
10	M	54	6 yr.	+	22	25	+14	22	0	—	0	1
30	M	71	18 mos.	+	276	31	-89	46	-83	+	1	1
37	M	50	18 yr.	+	34	0	-100	0	-100	+	0	0
53	M	60	25 yr.	+	275	222	-19	23	-92	+	2	2
80	M	66	10 yr.	+	140	81	-42	26	-81	+	2	0
103	F	66	15 yr.	+	27	4	-85	0	-100	+	0	0
105	M	66	18 yr.	—	17	2	-88	0	-100	—	0	0
154	M	53	20 yr.	—	89	39	-56	48	-46	+	2	2
<i>Treatment outpatient, phenobarbitone, and ascorbic acid:</i>												
29	M	37	4 yr.	+	154	70	-55	63	-59	+	2	2
36	F	68	7 mos.	—	347	192	-45	75	-78	+	2	2
55	F	52	2 yr.	—	20	26	+30	31	+55	+	1	2
84	F	35	6 yr.	—	41	14	-66	29	-29	+	1	1
99	M	51	2 mos.	—	57	21	-63	15	-74	—	1	2
107	M	52	6 wk.	—	161	161	0	396	+146	+	2	2
123	M	46	18 mos.	+	15	0	-100	26	+73	+	2	2
134	M	42	3 yr.	—	28	13	-54	0	-100	—	1	0
<i>Treatment outpatient and phenobarbitone; no ascorbic acid:</i>												
12	F	47	1 yr.	—	37	23	-38	4	-89	+	1	2
19	M	51	12 yr.	+	16	12	-25	28	+75	+	1	1
49	M	64	5 yr.	—	2	0	-100	0	-100	+	1	1
68	M	52	7 yr.	—	17	20	+18	10	-41	+	2	0
70	M	37	7 yr.	+	8	10	+25	10	+25	+	1	1
97	M	38	4 mos.	—	14	14	0	4	-71	—	1	1
108	M	51	7 wk.	—	20	3	-85	5	-75	—	2	2
129	M	44	10 yr.	—	89	27	-70	6	-93	+	2	2
<i>Treatment outpatient and ascorbic acid; no phenobarbitone:</i>												
3	M	64	4 yr.	+	9	37	+311	103	+1044	+	2	2
27	M	47	7 yr.	+	68	67	-1	93	+37	—	0	1
34	F	63	5 yr.	+	20	27	+35	64	+220	+	2	2
56	F	45	12 yr.	+	10	8	-20	7	-30	—	2	2
88	M	60	4 mos.	—	15	3	-80	0	-100	+	0	0
102	F	72	2 yr.	—	5	0	-100	0	-100	+	1	1
125	F	49	19 mos.	—	19	21	+11	32	+68	+	1	2
142	F	63	7 yr.	—	20	56	+180	49	+145	+	2	2
<i>Treatment outpatient; no phenobarbitone or ascorbic acid:</i>												
16	M	52	28 yr.	+	54	72	+33	46	-15	+	1	1
20	M	52	20 yr.	—	15	13	-13	3	-80	—	0	0
38	F	61	10 mos.	—	25	10	-60	7	-72	—	0	0
51	M	43	19 mos.	—	16	1	-94	0	-100	+	1	0
76	M	43	20 yr.	+	90	81	-10	67	-26	+	2	1
92	M	53	29 yr.	—	10	9	-10	8	-20	+	0	0
120	M	33	8 yr.	—	15	19	+27	18	+20	—	0	2
153	F	76	4 mos.	—	95	41	-57	32	-66	+	0	0

TABLE II—COMPARISON BETWEEN PATIENTS IN EACH TREATMENT GROUP BEFORE TREATMENT WAS STARTED

Characteristics of patients before treatment	No. of patients in each group					
	Main treatment		Pheno-barbitone		Ascorbic acid	
	A	B	+	-	+	-
Sex:						
M	24	21	25	20	19	26
F	8	11	7	12	13	6
Age:						
Under 35 yr. .. .	3	1	3	1	2	2
35- .. .	4	8	9	3	6	6
45- .. .	9	14	10	13	11	12
55- .. .	9	6	6	9	11	4
65+ .. .	7	3	4	6	2	8
Length of history:						
Under 1 yr. .. .	8	8	10	6	9	7
1- .. .	8	9	11	6	12	5
5- .. .	7	11	9	9	8	10
15+ .. .	9	4	2	11	3	10
Previous hospital treatment:						
Yes	9	10	5	14	8	11
No	23	22	27	18	24	21
Presence of symptoms on admission:						
Yes	24	23	23	24	24	23
No	8	9	9	8	8	9
Size of ulcer crater:						
Under 15 sq. mm. .. .	4	7	6	5	5	6
15- .. .	11	16	13	14	12	15
50- .. .	8	6	6	8	8	6
100+ .. .	9	3	7	5	7	5

(3) an inert tablet t.d.s. and phenobarbitone gr. $\frac{1}{2}$ t.d.s. ;

(4) two inert tablets t.d.s.

The drugs were, in each case, given daily for three months.

Alkaline powders (1 drachm of equal quantities of calcium and magnesium tribasic phosphate) were given to patients in both series, to be taken at the patient's discretion as necessary for the relief of pain.

All the patients were kept under observation for three months; patients in series B were seen twice in the first month, but otherwise all outpatients were seen monthly, unless their clinical condition required more frequent supervision. Barium examinations were repeated four weeks, eight weeks, and twelve weeks after the initial inpatient barium meal. As far as possible the radiographic examinations were made by the same radiologist, and the radiographs were taken in such a way as to show as large as possible the niche produced by the ulcer.

Progress was assessed subjectively by the patient's description of his symptoms and objectively by measuring the size of the niche. The subjective assessment was recorded on a three-point scale according to the severity of the symptoms during the period of observation: 0, pain-free; 1, occasional pain or minor dyspeptic symptoms; 2, daily pain for as long as a week. Symptoms during the initial week of investigation, before the

TABLE III—RELATION BETWEEN PROGNOSIS AND CERTAIN SELECTED CHARACTERISTICS OF PATIENTS

Rank correlation between % reduction in size of ulcer crater and:	S/S.E.(S)	Probability of getting as high a value of S, purely by chance
Sex	0.37	0.70 <P < 0.80
Age	1.34	0.10 <P < 0.20
Length of history .. .	1.47	0.10 <P < 0.20
Previous hospital diagnosis .. .	1.21	0.20 <P < 0.30
Presence of symptoms on admission	0.17	0.80 <P < 0.90
Size of ulcer crater before treatment	0.24	0.80 <P < 0.90

start of specific treatment, were ignored. The size of the niche was measured by outlining it in pencil on the radiograph, covering the radiograph with transparent graph paper, and counting, under a magnifying-glass, the number of squares 1 mm. in diameter included within the pencilled outline. Ulcers were considered to be healed when the radiologist reported that no niche was detectable; the finding of convergent folds, or an irregularity in the gastric outline, without a niche, was taken to indicate scarring. It is realised that gastroscopy would have shown incomplete epithelisation in many so-called healed cases, but repeated gastroscopies were not considered justifiable, and, since the same criteria were used uniformly throughout the investigation, the inaccuracy was not material. The extent of healing in a given period was determined by expressing the reduction in size of the niche as a percentage of its initial size.

With this form of experimental design it is possible to assess the effects of three forms of treatment on the same group of patients. The results obtained in series A can be compared directly with the results obtained in series B, for both series are comparable in that a quarter of the patients in each received phenobarbitone, a quarter received ascorbic acid, a quarter received both, and a quarter received neither. Similarly, the patients who received phenobarbitone can be compared with those who did not, and the patients who received ascorbic acid can be compared with those who did not.

RESULTS

The number of patients included in the investigation was 64. Details of the cases, methods of treatment, and results are shown in table I.

The investigation was not planned to ensure that any one type of ulcer was equally represented in all the treatment groups because it was not known with certainty that any specific type healed more or less rapidly than

TABLE IV—RESULTS OF TREATMENT ASSESSED BY CHANGES IN SIZE OF ULCER CRATER (COMPARISON BETWEEN PATIENTS IN SERIES A AND B)

Treatment group	No. of cases with crater			
	Healed	$\frac{2}{3}$ or more healed	Less than $\frac{2}{3}$ healed	Larger
	<i>One month after start of treatment:</i>			
A	5	13	11	3
B	3	4	16	9
	<i>Three months after start of treatment:</i>			
A	12	10	4	6
B	5	8	8	11

any other. Consequently it is necessary to determine what differences there were between the patients in each group before treatment was begun, and to test whether the differences could produce different rates of healing for the different groups. The constitution of each of the treatment groups as regards sex, age, length of history, hospital treatment before the investigation, presence of symptoms on admission, and initial size of the ulcer niche is shown in table II.

From table II it is clear that there were some differences between the groups, and this was to be expected in view of the random method of allocation of treatments. More patients in series A than in series B were aged 55 or over, and more had moderate or large ulcers—i.e., craters with measured cross-sections of more than 50 sq. mm. More of the patients who received phenobarbitone than of those who did not were men, more gave a history of less than five years, and less had had any previous hospital treatment. Less of the patients who received ascorbic acid than of those who did not were men, and more gave a history of symptoms for less than five years.

TABLE V—RESULTS OF TREATMENT ASSESSED SUBJECTIVELY BY PATIENTS' SYMPTOMS (COMPARISON BETWEEN PATIENTS IN SERIES A AND B)

Treatment group	No. of cases with symptoms (for scale see text)		
	0	1	2
A B	13 6	<i>First month :</i> 10 14	
	13 8	<i>Second and third months :</i> 9 9	
A B	13 8	9 9	10 15

The effect of each of the characteristics considered can be tested separately by the method of rank correlation (Kendall 1948). For example, if the results for each patient are listed in order according to the extent of healing secured in a month, it can be determined whether there is any tendency for the results in patients of one sex to be aggregated towards one end of the list, or whether the male and female cases are evenly distributed throughout. Since eight different combinations of treatment were used (inpatient, phenobarbitone and ascorbic acid; inpatient, phenobarbitone but no ascorbic acid; &c.) it might have been necessary to test the effect of each characteristic within each treatment subgroup separately and to sum the results. It will, however, be shown that the giving of phenobarbitone and ascorbic acid made little or no difference; hence these treatments can be ignored. Correlations were therefore calculated independently only for patients in series A and B. The results are set out in table III.

It is not justifiable to conclude from table III that the characteristics considered are completely unrelated to the rate of healing of gastric ulcers in general. The series

TABLE VI—EFFECTS OF TREATMENT ON SUBSEQUENT HEALING OF ULCERS (COMPARISON BETWEEN PATIENTS IN SERIES A AND B)

Treatment in first month	Change in size of ulcer crater in second and third months. No. of cases with crater			
	Healed	$\frac{2}{3}$ or more healed	Less than $\frac{2}{3}$ healed	Larger
A	9	5	4	9
B	3	4	13	9

1. Patients whose ulcers were completely healed after one month's treatment are excluded from the table.
2. The number of ulcers which healed completely in the second and third months (12) is not equal to the difference between the numbers which were healed at the end of the third and of the first months respectively, shown in table IV—i.e., 17-8—because 3 of the ulcers which were healed after a month broke down again in the next two months.

is small, and a larger series might well reveal a significant correlation between, for example, the rate of healing and the length of history. It is, however, reasonable to conclude that the differences noted between the patients in the different treatment groups are unlikely to have materially affected the results, and the groups may be considered comparable from the point of view of assessing the effects of the different treatments.

Hospital Treatment

Table IV shows the extent of healing achieved by patients in series A and B after one month's and three months' treatment. Table V shows the patients' subjective assessment of their symptoms. Both tables IV and V indicate that patients in series A did better than patients in series B. If the numbers of patients in the two series who showed more and less than two-thirds healing are compared, the differences are statistically significant both one and three months after the beginning of treatment

(one month, $X^2=7.94$, $n=1$, $P<0.01$; three months, $X^2=5.11$, $n=1$, $0.02<P<0.05$). The division at two-thirds healing is admittedly somewhat arbitrary, and it may be suggested that, if some other dividing line had been chosen, the differences might not appear so definite. The procedure is, however, justified by the results obtained by the more detailed statistical test of rank correlation, which has been referred to above. This test, which does not depend on any arbitrary grouping, confirms that there is a significant difference between the results obtained in the two series—a marked one after one month ($S/S.E.(S)=2.78$; $P<0.01$) and a less marked one after three months ($S/S.E.(S)=2.52$, $0.01<P<0.02$). On the other hand, the figures in table V, indicating the patients' subjective assessments of their symptoms, do not show a statistically significant difference between the series. They do, however, suggest a tendency in the same direction—i.e., for better results to be obtained with inpatient treatment. The failure to

TABLE VII—EXTENT OF HEALING IN SECOND AND THIRD MONTHS IN RELATION TO EXTENT OF HEALING IN FIRST MONTH

Extent of healing in first month	Progress in second and third months. No. of cases showing		
	Complete healing	Partial or no healing	Deterioration
$\frac{2}{3}$ or more ..	9	3	5
Less than $\frac{2}{3}$..	3	15	9
Deterioration ..	0	8	4

Patients whose ulcers were completely healed after one month are excluded from the table.

demonstrate a significant difference may reasonably be attributed to the coarseness of the method of assessment.

Patients in series A were discharged from hospital after a month's treatment and were treated as outpatients for two more months in the way patients in series B had been treated from the outset. The extent of healing achieved during the second and third months, in those patients incompletely healed after a month, is shown in table VI. More patients in series A than in series B achieved a further two-thirds' healing in this period ($X^2=4.58$, $n=1$, $0.02<P<0.05$). The rank correlation test, however, does not confirm the statistical significance of the difference ($S/S.E.(S)=1.43$, $0.10<P<0.20$), and the suggestion that a course of inpatient hospital treatment continues to exert a beneficial effect on the rate of healing of a gastric ulcer after the patient has been discharged should therefore be regarded as non-proven.

The rate of healing in the second and third months was, to some extent, related to the rate in the first month (table VII). The relationship was not close, but complete healing seemed unlikely to be obtained in three months

TABLE VIII—RESULTS OF TREATMENT ASSESSED BY CHANGES IN SIZE OF ULCER CRATER (COMPARISON BETWEEN PATIENTS TREATED WITH AND WITHOUT PHENOBARBITONE AND WITH AND WITHOUT ASCORBIC ACID)

Treatment group	No. of cases with crater			
	Healed	$\frac{2}{3}$ or more healed	Less than $\frac{2}{3}$ healed	Larger
<i>One month after start of treatment :</i>				
Phenobarbitone ..	4	8	16	4
No phenobarbitone ..	4	9	11	8
Ascorbic acid ..	4	6	15	7
No ascorbic acid ..	4	11	12	5
<i>Three months after start of treatment :</i>				
Phenobarbitone ..	8	11	7	9
No phenobarbitone ..	9	7	8	8
Ascorbic acid ..	7	7	5	13
No ascorbic acid ..	10	11	7	4

TABLE IX—RESULTS OF TREATMENT ASSESSED SUBJECTIVELY BY PATIENTS' SYMPTOMS (COMPARISON BETWEEN PATIENTS TREATED WITH AND WITHOUT PHENOBARBITONE AND WITH AND WITHOUT ASCORBIC ACID)

Treatment group	No. of cases with symptoms (for scale see text)		
	0	1	2
		<i>First month :</i>	
Phenobarbitone ..	5	16	11
No phenobarbitone ..	14	8	10
Ascorbic acid ..	8	11	13
No ascorbic acid ..	11	13	8
		<i>Second and third months :</i>	
Phenobarbitone ..	9	11	12
No phenobarbitone ..	12	7	13
Ascorbic acid ..	7	8	17
No ascorbic acid ..	14	10	8

unless the ulcer had healed to a third of its size in one month.

Phenobarbitone and Ascorbic Acid

The results of treatment with phenobarbitone and ascorbic acid are set out in tables VIII and IX. Inspection of the tables is sufficient to indicate that neither drug exerted any beneficial effect on the rate of healing of the ulcers or on the patients' symptoms.

DISCUSSION

In the investigation special care was taken to ensure that the patients had equal confidence in all the treatments tested. All the patients were examined and treated throughout by one doctor, and all were given what were superficially the same medicaments by mouth. This appeared to have the desired effect. Inpatient treatment with rest in bed and a "gastric" diet is seen to have produced better results than ambulant treatment with advice to diet according to a prescribed sheet. Whether this was due to the rest in bed or to the diet, which could be more strictly enforced in hospital, is not known. It has been suggested that even the modern gastric diet, so much more liberal than the old "slop" diets, is more restricted than is really necessary, and perhaps rest in bed was the essential therapeutic factor. Possibly the psychological effect of withdrawing the patients from their home surroundings was also beneficial.

The rate of healing after discharge from hospital was little, if at all, greater than that in the control group of patients treated as outpatients throughout. Such advantage as did accrue may, perhaps, be attributed to the fact that some of the series-A patients continued to stay away from work for a period of "convalescence" (lasting one to three weeks) after discharge from hospital; in contrast all the control patients—apart from the few who continued to have incapacitating pain—were working.

The practical conclusion to be drawn is that those gastric-ulcer patients whose condition merits admission to hospital should be kept in hospital until healing is complete—that is, if it is believed that the patient's prognosis is improved by securing healing of the ulcer. Healing may, however, continue with ambulant treatment, should it be impossible to keep the patient in hospital.

The proportion of ulcers which healed completely in the present series is small; no more than 8 out of 64 were healed after a month's treatment, and even after three months the total was only 17. These figures cannot, however, be compared with many other series, because the most favourable ulcers, those which had healed between diagnosis in outpatients and the initial examination after admission, have been excluded.

The disparity between the relief of the patients' symptoms and the extent of healing of the ulcer is of interest. A certain parallelism exists, but it is notable that some patients had no symptoms while their ulcers

increased in size, and others continued to have pain while healing was proceeding actively. Such observations underline the need for using an objective method (as well as the subjective one) in assessing the effects of a new treatment for gastric ulcers.

SUMMARY AND CONCLUSIONS

A trial was undertaken to assess the factors influencing the rate of healing of gastric ulcers. Inpatient treatment on a regulated gastric diet was compared with outpatient treatment and advice to follow the diet on a prescribed sheet; the effect of added phenobarbitone and ascorbic acid was also determined.

Inpatient treatment led to a significantly quicker rate of healing, as judged by measurements of the ulcer crater in the radiograph, and seemed to be more effective in relieving symptoms. It is not known whether the therapeutic factor was rest in bed or the supervised diet.

After discharge from hospital, healing usually continued, but the evidence that a course of inpatient treatment exerted any beneficial effect on the subsequent rate of healing is not conclusive. Unless the ulcer had healed to a third of its size in one month it was unlikely to heal completely in three.

The giving of phenobarbitone and ascorbic acid did not increase the rate of healing.

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REFERENCES

- Gill, A. M. (1947) *Lancet*, i, 291.
 Ivy, A. C., Grossman, M. I., Bachrach, W. H. (1950) *Peptic Ulcer*. London; p. 914.
 Jones, F. A. (1949) *Brit. med. J.* ii, 1463.
 Kendall, M. G. (1948) *Rank Correlation Methods*. London; p. 37.

THE SIZE OF FOLLICLES IN NON-TOXIC GOITRE

SELWYN TAYLOR*

M.A., M.Ch. Oxf, F.R.C.S.

LECTURER IN SURGERY, POSTGRADUATE MEDICAL SCHOOL OF LONDON, HAMMERSMITH HOSPITAL, LONDON

NON-TOXIC goitre is common in London, and a careful observer will not take long in finding numerous examples if he looks about him in any of the city's thoroughfares. It seems unlikely that a lack of iodine is primarily responsible, since the Londoner has traditionally included fish in his diet. Latterly, strict rationing of meat for some ten years has probably increased the consumption of iodine-containing sea food by people of all income levels.

In an attempt to follow the metabolism of iodine in this type of goitre, patients were given a tracer dose of radioactive iodine, and after thyroidectomy sections of the removed glands were placed in contact with photographic film. The resulting autoradiograms showed a patchy distribution of the isotope, intense blackening being confined to a few discrete areas not necessarily correlated with nodules, and the remainder of the gland showing little evidence of iodine uptake (figs. 1-3). This is in sharp contrast to the iodine uptake seen in normal thyroid, where the autoradiogram presents blackening scattered throughout the entire gland (fig. 4).

When a histological survey was made of these discrete areas of iodine uptake, it was at once apparent that they showed certain characteristics which distinguished them from the rest of the gland. The follicles

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