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PROLONGED ANTIBIOTIC TREATMENT OF SEVERE BRONCHIECTASIS

A REPORT BY A SUBCOMMITTEE* OF THE ANTIBIOTICS CLINICAL TRIALS (NON-TUBERCULOUS) COMMITTEE OF THE MEDICAL RESEARCH COUNCIL

Experience with penicillin and later with other antibiotics has shown that these drugs are effective in the treatment of many acute respiratory infections. The management of chronic bronchial infections, particularly in patients with bronchiectasis, has proved more difficult. Although an initial response may be obtained in individual patients, especially during acute episodes, cessation of treatment is usually followed by an early relapse and the re-establishment of infection.

The therapeutic trial reported in detail below was designed to study the effect of prolonged antibiotic therapy in severe cases of bronchiectasis characterized by abundant purulent or mucopurulent sputum. Since the study was concerned with long-term therapy, patients were treated entirely at home unless some intercurrent infection necessitated admission to hospital. Patients were accepted only if they were able to attend regularly at a special out-patient clinic. As will be seen, the criteria of severity were stringent, and it was surprising how few patients satisfied them.

Since the patient assesses his illness in terms of general health, the amount and character of sputum, and his ability to work and enjoy a full life, the observations recorded at each attendance were designed to evaluate these criteria. Because of the normal fluctuation in the symptoms of this disease with the change of season, patients were observed over a consecutive period of 52 weeks whilst they received the appropriate drug under a uniform scheme.

The difficulties inherent in a trial of this character will be appreciated, not least of them being the subjective improvement which might be expected when more intense interest is shown. This difficulty was met by introducing a control medicament, lactose, and making the trial a " blind " one in which neither the clinician nor the patient knew which drug was being given. The nature of the trial was explained to the patients beforehand, and all were volunteers. The results of the study, which have been analysed in the various tables, are an attempt to obtain an objective assessment of a number of symptoms and signs common to most patients with infected bronchiectasis.

Plan of Trial

The trial was conducted on out-patients at seven centres—Chester, Edinburgh, Glasgow, Leeds, Liverpool, Newcastle, and Sheffield. Patients had to be between 15 and 55 years of age and to have had symptoms for at least three months. It was required that the bronchogram should show frank bronchiectasis affecting at least two lung segments. Before admission to the trial the patient had to be observed on four visits at weekly intervals, on each occasion bringing a 24-hour specimen of sputum; the total quantity of the four specimens, which had to be either purulent or mucopurulent, had to be at least 150 ml., and the last had to measure at least 25 ml. Patients with tuberculosis were excluded. Patients who had been receiving antibiotics or sulphonamides could be admitted only after a period of at least a month without such treatment.

During the pre-treatment period of four weeks observations were made on cough, haemoptysis, dyspnoea, and disability, as well as on sputum measurement. A postero-anterior film of the chest was taken. On the fourth visit the weight, haemoglobin, red-cell count, and degree of clubbing were recorded and the patient's general condition was assessed. If he satisfied the criteria for admission he was allocated at random, according to a centrally held list, to one of the three treatment groups—penicillin, oxytetracycline, or lactose. The drugs were provided in 0.25-g. capsules which were indistinguishable, and the supply for each patient was issued in bottles which were identified only by the patient's allocation number. As the allocation and supply of drugs was controlled centrally neither the patient nor his physician was aware of the treatment given. The patients were instructed to take two capsules four times a day on two days a week—for example, on Wednesday and Saturday—making a total dose of 2 g. each day or 4 g. a week.

Treatment was continued for a year, and during this time regular visits were made to the out-patient department, at first weekly for a month and thereafter at four-weekly intervals. On each attendance the patient brought a 24-hour specimen of sputum, and observations on the severity of cough, dyspnoea, haemoptysis, and disability were made as on the pre-treatment visits. At the completion of one year's treatment additional observations were made on clubbing, weight, general assessment of progress, and the patient's own assessment of his response to treatment. During the year's treatment it was provided that any acute episode might be treated according to the discretion of the clinician, including, if necessary, penicillin by injection or other antibiotics. All such additional treatment was to be recorded. Provision was made for the routine reporting of any presumed toxic reactions to treatment. In all groups treatment by postural drainage was conducted in accordance with the practice of the physicians in clinical charge of individual patients.

*The members of the subcommittee were: Dr. J. G. Scadding (chairman), Professor J. W. Crofton, Drs. T. Anderson, A. C. C. Hughes, J. Knowelden, A. G. Ogilvie, W. S. Sutton, M. Telling, K. Zinneman, and C. S. Darke (secretary).
The present report was prepared for the subcommittee by Dr. C. S. Darke and Dr. J. Knowelden.

Initial Comparability of Treatment Groups

Between January, 1953, and March, 1954, 122 patients were admitted to the trial. Of these, 38 were allocated to penicillin, 44 to oxytetracycline, and 40 to lactose. The age and sex distribution of the groups were comparable. In each the male patients formed a majority, 58% of the penicillin group, 70% of the oxytetracycline, and 60% of the lactose. The average ages of the patients in these treatment groups were 34.3, 32.3, and 32.6 years respectively, and rather more than 50% of those allocated to each treatment were in the 15–34 year age group. No patient had had symptoms for less than two years, the average duration being about 20 years for each group.

Table I compares various characteristics of the three treatment groups such as their past medical history, and shows that in most respects they were alike initially. The largest

TABLE I

	Penicillin	Oxytetracycline	Lactose
Season in which treatment started			
Season:			
Jan.–March	14	19	17
April–June	9	13	11
July–Sept.	10	7	7
Oct.–Dec.	5	5	5
Total	38	44	40
Age at Onset			
Under 5 years	18	19	16
5–14 ,,	12	13	8
15 and over	8	12	16
Total	38	44	40
Bronchogram			
Average No. of segments involved	9·5	8·2	9·4
Type (No. of patients):			
Cylindrical	6	11	17
Cystic	9	7	7
Combined	23	26	16
Collapse (No. of patients):			
None	17	14	18
Partial	16	22	13
Complete	5	8	9
History of Respiratory Illnesses, etc.			
No. of patients with history:			
Asthma	5	4	3
Bronchitis	29	27	27
Bronchopneumonia	18	19	12
Lobar pneumonia	11	16	20
Pleurisy	14	11	21
Empyema	2	1	2
Haemoptysis: Streaks	20	19	17
Haemoptysis: Clots	2 (31)	6 (30)	5 (28)
Haemoptysis: Frank	9	5	6
Clubbing: Slight	11	14	11
Clubbing: Moderate	7 (23)	1 (28)	7 (20)
Clubbing: Gross	5	3	2
Average weight in lb. (kg.)	125·4 (56·9)	125·1 (56·7)	120·1 (54·5)

number of patients were admitted in the months of January to March, as the winter months of both years, 1953 and 1954, contributed to the total number. Nearly half the patients in each group had the first symptoms of their disease earlier than the fifth birthday. On the average the bronchograms showed eight to nine segments involved, principally with both cystic and cylindrical types. About 40% showed no collapse in any segment, while complete collapse of at least one segment was present in about 20%. Few patients had had asthma or empyema, but nearly 70% had had bronchitis, while pneumonia and pleurisy were common. About three-quarters had some degree of haemoptysis, but principally streaks only. About a half showed some degree of clubbing.

Results

Deaths.—During the year's treatment three patients died, one in each treatment group. The patient given penicillin, a woman aged 54, completed 42 weeks' treatment, defaulted, and on inquiry was found to have died in another hospital six weeks later. No necropsy was performed and the cause of death was given as coronary artery disease, the pulmonary condition being unmentioned. A boy aged 15 had shown signs of slight improvement when last seen after eight weeks' treatment with oxytetracycline. He died suddenly while waiting in a bus queue a week later, and the cause of death confirmed by necropsy was cor pulmonale. The fatality in the lactose group occurred in a man aged 26, who had attended only two weeks from the start of treatment. He became suddenly ill and died of " pneumonia " in a few days. He had not been admitted to hospital and there was no necropsy.

Defaulters.—Four patients defaulted, two on oxytetracycline and two on lactose, before six months' treatment had been completed.

Unable to Continue Treatment.—Two patients complained that they could not take the treatment allocated, one being given penicillin and the other oxytetracycline. The former had a history of duodenal ulcer and stopped treatment after only 12 capsules of penicillin, which he said caused severe burning pain. The other complained of vomiting one hour after taking the capsules and stopped treatment after 16 weeks.

Change in Diagnosis.—One patient aged 15 originally allocated to lactose continued to receive treatment for 44 weeks and was then taken out of the trial and treated with oxytetracycline for an intercurrent illness. She improved temporarily, but died three months later (more than 12 months after starting treatment in the trial), and at necropsy was found to have fibrocystic disease of the pancreas.

All the 10 patients listed above—two from the penicillin group and four each from the oxytetracycline and lactose groups—were excluded from the remaining analysis, which is therefore confined to 112 patients (36 on penicillin, 40 on oxytetracycline, and 36 on lactose).

In addition to the four defaulters excluded from the remaining analysis, one penicillin patient defaulted at the 36th week of treatment, and one on oxytetracycline was taken off the trial at the 44th week suffering from an intercurrent illness. The observations on these two patients up to these dates have been included in the analysis. Sulphonamides or antibiotics, other than the trial capsules, were administered for a pulmonary condition to six patients in the penicillin group, to three in the oxytetracycline group, and to five in the lactose group. Nearly all this additional treatment was given by general practitioners, and since these patients remained in the trial they have been included in the analysis.

In the analysis of the observations made routinely on each visit, the four pre-treatment readings have been taken as one group. The observations in the treatment period have also been amalgamated in four groups of four consecutive readings each : (*a*) weeks 1, 2, 3, and 4 ; (*b*) weeks 8, 12, 16, and 20 ; (*c*) weeks 24, 28, 32, and 36 ; and (*d*) weeks 40, 44, 48, and 52 from the start of treatment.

Sputum

At each visit the patient brought in a flask specially provided a specimen of *all* sputum coughed up in the previous 24 hours (8 a.m. to 8 a.m.). The odour was noted, and recorded as " foul " or " not foul." The flask was then kept for 72 hours, by which time separation into layers of mucus and pus had usually taken place. The total volume, and that of each fraction, were then recorded. In some specimens separation was incomplete. These have been excluded from the averages of total volumes. Table II shows the average weekly volumes in the pre-treatment and treatment periods for each treatment group, and in the second part expresses the volumes at different parts of the treatment period as percentages of the average of the four pre-treatment readings.

Initially the average 24-hour specimen had a total volume of 96.7 ml. in the penicillin group, 76.7 ml. in the oxytetra-

TABLE II.—*Average 24-Hour Sputum Measured (a) by Volume in ml. and (b) as Percentage of Pre-treatment Volume*

		Pre-treatment (Weeks 1–4)	Treatment Period (Weeks from Start) 1–4	8–20	24–36	40–52
Volume in ml.:						
Penicillin	Mucus	53	49	38	39	43
	Pus	44	36	34	29	29
	Total	97	85	72	67	72
Oxytetracycline	Mucus	40	31	23	26	31
	Pus	37	20	18	18	18
	Total	77	51	41	44	49
Lactose	Mucus	57	50	48	49	46
	Pus	47	43	39	34	34
	Total	104	93	87	83	80
% of pre-treatment volume:						
Penicillin	Mucus	100	93	71	73	81
	Pus	100	84	78	66	67
	Total	100	89	74	70	74
Oxytetracycline	Mucus	100	77	58	66	77
	Pus	100	54	49	48	50
	Total	100	66	54	57	64
Lactose	Mucus	100	88	85	85	81
	Pus	100	90	83	72	71
	Total	100	89	84	79	76

cycline group, and 104.4 ml. in the lactose group. In each the mucus fraction was about 55% of the total. In the penicillin group the total volume fell to 89% of its original level in weeks 1–4 after starting treatment, to 74% in weeks 8–20, to 70% in weeks 24–36, and was again 74% in the final weeks (40–52). The oxytetracycline group experienced a greater relative decline in total volume, and this was seen early in treatment, the proportions in the successive periods being 66, 54, 57, and 64% of the initial level. The corresponding proportions in the lactose group, 89, 84, 79, and 76% show less change from the initial level than the other treatment groups, especially in the earlier part of the trial. In the oxytetracycline group in particular the greatest change took place in the pus fraction of the sputum, which rapidly reached and stayed at about 50% of its original volume, but, unlike the other two groups, there was little evidence of further improvement beyond the 8–20 weeks after starting treatment.

In the pre-treatment period the proportion of specimens recorded as "foul" was 29% in the penicillin, 23% in the oxytetracycline, and 37% in the lactose group. In each group these proportions fell during the year, the foul specimens forming 8, 6, and 15% of those submitted in the final four visits. This fall was gradual in the penicillin and lactose groups, but immediate in the oxytetracycline group, where in the first four weeks of treatment only 6% of specimens were foul, compared with 24% in the penicillin group and 32% in the lactose group.

Cough

At each visit the cough was graded, according to the patient's statement, as 0="none" 1="morning only"; 2="more than 1 and less than 3"; and 3="night and day." Table III shows the proportions of readings in each period falling into these four grades. The initial distribution of grades in the three groups was not closely alike, but in each during treatment there was a subjective improvement in this symptom with a reduction in the proportion with grade 3 and slight increase in the proportion with no cough. The grading was difficult to apply, but "night and day" cough, a great disturbance to the patient, was considered to be better defined than grades 1 and 2. In the penicillin group the initial proportion of 40% with this most severe grade fell to about 20% during treatment. In the oxytetracycline group the initial proportion of 34% fell more strikingly to about 10%, while in the lactose group there was relatively less change from an initial proportion of 37% to about 25%.

TABLE III.—*Percentage of Patients Exhibiting Cough of Grade 0 to 3**

	Grade	Pre-treatment (Weeks 1–4)	Treatment Period (Weeks from Start) 1–4	8–20	24–36	40–52
Penicillin (36 patients)	0	6	6	8	6	9
	1	8	17	33	40	30
	2	46	45	37	34	38
	3	40	32	22	20	24
Oxytetracycline (40 patients)	0	0	0	4	4	3
	1	4	18	36	38	31
	2	62	63	51	47	56
	3	34	19	9	12	11
Lactose (36 patients)	0	0	0	0	3	3
	1	14	21	22	27	32
	2	49	55	56	46	36
	3	37	24	23	24	29

* For definitions of grades see text.

Haemoptysis

The occurrence of episodes of haemoptysis since the previous visit was recorded as "none," "streaks," "clots," or "frank." At some time in the treatment period 25 (69%) of the 36 patients on penicillin reported one or more episodes of haemoptysis compared with 16 (40%) of the 40 patients on oxytetracycline and 22 (61%) of the 36 on lactose (Table IV). In each treatment group the majority of these episodes were streaks, and frank haemoptysis was rare. About half the patients treated with penicillin who reported haemoptysis had only one episode during the year. Single episodes formed the majority of those reported by the oxytetracycline group, while repeated episodes were the commonest among lactose-treated patients.

TABLE IV.—*Haemoptysis—Number of Patients with Haemoptysis in Treatment Period*

	Penicillin	Oxytetracycline	Lactose
One episode only	12	12	4
Two or more episodes	13	4	18
No haemoptysis	11	24	14
Total	36	40	36

Dyspnoea

Dyspnoea at the time of each examination was recorded in five grades (Table V): (1) patient does not become more breathless than other men/women of his/her own age and build at work or walking, and on climbing hills and stairs; (2) patient is able to walk with normal men/women of his/her own age and build on the level but is unable to keep up on hills or stairs; (3) patient is unable to keep up with normal men/women on the level, but is able to walk a mile or more at his/her own speed; (4) patient is unable to walk more than about 50 yards on the level without a rest; and (5) patient is breathless on talking or undressing, or unable to leave his/her house because of breathlessness. Initially about a quarter of each group were in grade 1, about the same in grade 2, about 40% in grade 3, and a small proportion in grade 4. No patient was initially so breathless as grade 5, and on only one occasion subsequently did a patient on penicillin have this degree of dyspnoea. In each treatment group there was some improvement with a shift down the scale of grading, but no clear difference emerged between the treatments. Table V summarizes this pattern by showing the proportion of patients in grades 1 and 2 combined and in grades 3, 4, and 5 combined in each of the four consecutive readings.

TABLE V.—*Percentage of Patients Exhibiting Dyspnoea of Grades 1 and 2, or 3, 4, and 5*

	Grade	Pre-treatment (Weeks 1–4)	Treatment Period (Weeks from Start) 1–4	8–20	24–36	40–52
Penicillin	1 and 2	50	51	65	68	61
	3+	50	49	35	32	39
Oxytetracycline	1 and 2	58	62	73	75	71
	3+	42	37	27	25	28
Lactose	1 and 2	59	62	65	65	68
	3+	41	38	35	35	32

Disability Since Last Visit

At each visit episodes of known fever, the number of days confined to bed, and the number of days off work due to a respiratory illness since the previous attendance were recorded (Table VI). During treatment the penicillin

TABLE VI.—*Disability as Measured by (a) Episodes of Known Fever, (b) Days Confined to Bed, and (c) Days Off Work*

	Pre-treatment (Weeks 1–4)	Treatment Period (Weeks from Start)			
		1–4	8–20	24–36	40–52
Episodes of known fever:					
Penicillin (36 patients) ..	3	1	4	7	13
Oxytetracycline (40 patients)	4	5	6	9	8
Lactose (36 patients) ..	1	1	6	12	17
Days confined to bed:					
Penicillin ..	16	6	89	107	179
Oxytetracycline	14	7	20	57	34
Lactose ..	3	5	88	153	200
Days off work and proportion of time off work:					
Penicillin ..	246 (24%)	240 (24%)	813 (20%)	818 (20%)	796 (21%)
Oxytetracycline	273 (24%)	247 (23%)	619 (14%)	605 (14%)	793 (19%)
Lactose ..	241 (24%)	224 (22%)	1,033 (26%)	1,021 (25%)	981 (25%)

group reported 25 episodes, the oxytetracycline group 28, and the lactose group 36. The total number of days confined to bed were 381 for the penicillin, 118 for the oxytetracycline, and 446 for the lactose group. On the average, therefore, the patients in the three groups spent 2.95, 0.84, and 3.45% respectively of the treatment year confined to bed. The total days off work were 2,667 for those given penicillin, 2,264 for those given oxytetracycline, and 3,259 for those given lactose—that is, they spent 20.7, 16.1, and 25.0% respectively of the year off work. Much of this time off work was contributed by patients who were not at work for the whole of their time in the trial. If these are excluded the total days off work become 477, 804, and 1,069 for penicillin, oxytetracycline, and lactose groups respectively, with corresponding proportions of 3.7, 5.7, and 8.2% of the total time.

This result gives a less favourable picture for oxytetracycline, as fewer patients were excluded from this group because they did not work at any time in the year than from the two other treatment groups. However, this difference may be due to the oxytetracycline-treated patients not previously at work having a better chance of improving sufficiently to take up a job during the year. This is suggested by the fact that there were eight patients in the penicillin group, nine in the oxytetracycline group, and eight in the lactose group who did not work at all in the pre-treatment period. Subsequently five oxytetracycline-treated patients returned to work at some time in the year compared with only two in each of the other treatment groups.

Final Assessment

At the final visit, apart from the routine measurements, records were made of the weight, the degree of clubbing, and of the patient's and the physician's assessments of response to treatment. In each treatment group more patients gained than lost weight over the year, the corresponding average gain per patient being 0.76 lb. (348 g.) for penicillin, 3.38 lb. (1,533 g.) for oxytetracycline, and 0.63 lb. (286 g.) for lactose. Estimates of the degree of clubbing changed very little in any group.

Most of the patients thought they had improved during the year—78% of those given penicillin, 78% of the oxytetracycline group, and 61% of the lactose group. Nearly all the remainder considered they had not changed, only four patients—three given penicillin and one given oxytetracycline—saying they were worse at the end of the year. The physician's assessments were more conservative, recording 42% of the penicillin, 60% of the oxytetracycline, and 28% of the lactose group as improved, though much of the improvement was attributed to regular postural drainage. Only two patients, both given penicillin, were worse at the end of the year in the physician's opinion.

Drug Toxicity

No serious toxic symptoms were observed in any patient. Apart from the two patients who were unable to continue treatment—one on penicillin complaining of burning abdominal pain, the other on oxytetracycline who vomited one hour after taking the capsules—toxic symptoms were reported by five patients on penicillin, eight on oxytetracycline, and four on lactose, nearly all in the first few weeks of treatment. Diarrhoea was the commonest symptom, recorded by 10 patients—three on penicillin, five on oxytetracycline, and two on lactose—while anorexia, nausea, vomiting, flatulence, or epigastric discomfort formed the next group in order of frequency. The only other recorded symptoms were swelling of the foot accompanied by a rash which lasted a week and developed eight weeks after starting penicillin treatment, paraesthesiae of both hands lasting a few weeks 16 weeks after starting oxytetracycline, and joint pain the day after taking lactose capsules, experienced in the early weeks of therapy.

Discussion

It has been shown in trials previously reported that treatment of bronchiectasis with antibiotics, particularly chloramphenicol, can achieve some success in eliminating infection and in reducing the amount and purulence of the sputum. Franklin and Garrod (1953) reported that chloramphenicol was effective in eliminating *Haemophilus influenzae* from the sputum of bronchiectatic children, and in certain instances the drug was used for periods up to five months. Previously Mulder *et al.* (1952) had described comparable results in adult patients, and clinical studies by Wynn-Williams and Moyes (1951) and Harris *et al.* (1952) had also proved satisfactory. More recently Helm, May, and Livingstone (1954, 1956) have shown that there is a place for long-term antibiotic treatment in advanced cases, although only a proportion of these will respond well. Unfortunately the occurrence of blood dyscrasias following long-term chloramphenicol therapy made it necessary to exclude this drug in the present trial.

In the investigation reported here an attempt has been made to assess, by a controlled blind trial, the value of certain long-term antibiotic regimes to the patient with severe bronchiectasis. The symptoms of cough, expectoration, and haemoptyses are interrelated and reflect the state of the bronchial tree. From this standpoint it is clear that oxytetracycline was more effective than was oral penicillin. The lessening of general disability was much more pronounced than that observed in the other two groups. In particular, the reduction by nearly half of the purulent fraction of the sputum was achieved on the average within two weeks, and this change was maintained over the whole year. In the lactose group there was some improvement, but of a degree which could be expected to follow more regular postural drainage. The penicillin group fared a little better, but some of these changes probably reflected the general benefit observed in the lactose group. In all groups there was some indication that the symptoms fluctuated with climatic changes.

During the period of treatment the patients receiving oxytetracycline suffered less severe interference with their lives. The number of days on which patients in this group were confined to bed was less than half the total for those receiving penicillin and only a little over a quarter that for the lactose group. The number of days off work was also substantially less in the oxytetracycline group. On the whole the results by the different methods of assessment are consistent in indicating a definite benefit from the oxytetracycline regime and a probable, but lesser, benefit from oral penicillin. Nevertheless, even in the oxytetracycline group the effect was not dramatic. It is possible that

improvement was limited more by the irreversible changes of bronchitis and emphysema than by failure of the drug to eliminate particular infecting organisms.

It is significant that no serious toxic effect was recorded and that only two patients were unable to continue the trial. It may be concluded that the oxytetracycline regime used is both beneficial in severe cases of bronchiectasis and also safe. It is, however, expensive. A year's treatment on the lines indicated would cost, at the time of writing, at least £60 per patient for oxytetracycline. In regard to the overall problem, it is clear that the response obtained and expense entailed do not justify the widespread use of long-term oxytetracycline therapy in most patients with bronchiectasis. For the relatively few advanced cases it does offer a measure of relief not apparently attainable by oral penicillin in the doses used. The characteristic symptoms of bronchiectasis can be modified and the natural history of the disease influenced whilst oxytetracycline therapy is maintained, but there is no indication that such improvement as may be achieved is permanent, and relapse is almost certain after treatment is stopped.

Summary

In a controlled trial at seven centres 122 patients with bronchiectasis were allocated at random to one of three treatments—38 to penicillin, 44 to oxytetracycline, and 40 to lactose. The drugs were provided as indistinguishable 0.25-g. capsules, two of which were given four times a day on two days each week for a period of a year. Regular visits were paid to the out-patient departments throughout this period, at which measurements were made of the volume of a 24-hour sputum specimen and of the severity of cough, dyspnoea, haemoptysis, and disability since the previous visit.

The three treatment groups were similar in their age distribution, the history of previous respiratory illnesses, and the extent of involvement as determined by a recent bronchogram. During the year's observations three deaths occurred—one in each treatment group. Two patients—one on penicillin and one on oxytetracycline—could not tolerate the capsules and stopped treatment. Four patients—two on oxytetracycline and two on lactose—defaulted before six months' treatment had been completed. One patient given lactose who died subsequent to the year's observation was found to have had fibrocystic disease of the pancreas and was excluded from the analysis.

The records of the remaining 112 patients, 36 on penicillin, 40 on oxytetracycline, and 36 on lactose, were examined to compare the response to the treatments. Each group showed a reduction in sputum volume, greater for the pus than for the mucus fraction, during the year. The reduction in the oxytetracycline group was rapid, and for pus to about half the pre-treatment level. The reduction in the penicillin and lactose groups was slower, and to about 70% of the original level in each. There was some reduction in each treatment group in the severity of cough and dyspnoea and in the number of episodes of haemoptysis, with a slight advantage shown by those taking oxytetracycline. A more pronounced effect in the oxytetracycline group was observed in the reduction of disability expressed by the number of days off work, in the episodes of fever, and in the number of days confined to bed. No serious toxic effects were observed in any group. Although in general oxytetracycline was beneficial and was more effective than oral penicillin, the limited effect of long-term therapy, having regard to its cost, would not justify its widespread use in most patients with bronchiectasis.

Those taking part in the trial were: Chester: Dr. A. C. C. Hughes (clinician). Edinburgh: Professor J. W. Crofton and Dr. A. R. Somner (clinicians). Glasgow: Drs. T. Anderson, A. W. Lees, and G. Allan (clinicians); Dr. J. B. Landsman (bacteriologist). Leeds: Drs. M. Telling and G. N. Chandler (clinicians). Liverpool: Drs. W. S. Sutton and G. Penrhyn Jones (clinicians); Dr. F. Whitwell (pathologist). Newcastle: Dr. A. G. Ogilvie (clinician). Sheffield: Drs. C. S. Darke and J. E. Middleton (clinicians); Drs. E. H. Gillespie and J. E. M. Whitehead (bacteriologists).

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ADULT CHRONIC BRONCHITIS—THE INFECTIVE FACTOR AND ITS TREATMENT

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The pathogenesis of chronic bronchitis involves several factors, one of which is believed to be infection (May, 1953a, 1953b; Oswald and Medvei, 1955).

During 1955 in the City of Leeds (population 508,000) 67 persons died of pulmonary tuberculosis, 270 from carcinoma of the lung, and 463 from the effects of bronchitis. The actual incidence of bronchitis in the population is difficult to determine, but Goodman *et al.* (1953) have shown that chronic respiratory disease is an important cause of disability, and accounts for more unemployment than any other physical condition. Similarly, Stuart-Harris (1954) reported finding cough and sputum in 55% of men aged 50–60 in an industrial population, whilst Higgins *et al.* (1956) estimated that 10% of non-miners in the mining community they investigated had bronchitis. Stocks (1947) has drawn attention to the inverse relationship that exists between hours of sunshine and deaths from bronchitis.

It is therefore of some importance to assess critically the value of any treatment of this common disease, particularly in relation to the control of the infective element.