During the period of observation 51 patients died as a result of hypertension, giving a mortality rate of 34%. The mortality for men alone was 44%. The height of the diastolic blood pressure had an important influence on the mortality rate.

A familial tendency has not appeared to prejudice a hypertensive patient's prospects, and the existence of a primary cause for the hypertension had only a slight adverse influence.

It is probable that the combination of obesity with hypertension appears favourable only on account of the misleading sphygmomanometer reading.

The progress or fate of these patients has been related to the main clinical features which presented at their first examination.

It is suggested that the stage reached by the disease can best be judged on the presence or absence of four features—namely, advanced retinal changes, albuminuria in excess of a trace, cardiac enlargement, and abnormality of the electrocardiogram.

If the present stage of the disease is recognized the rate of its advance can be estimated, and thus to a large extent the prognosis may be foreshadowed.

Even at the first examination it should generally be possible to classify the type of hypertensive disease as "benign" or "accelerated."

Sympathectomy is principally justified in patients with the accelerated form of hypertensive disease.

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PULMONARY EMPHYSEMA TREATED BY PNEUMOPERITONEUM

BY

R. D. C. BRACKENRIDGE, M.D., F.R.F.P.S.

Senior Medical Registrar, County Hospital, Whiston, Lancs

AND

A. THELWALL JONES, M.D., M.R.C.P., D.P.H.

Assistant Physician, United Liverpool Hospitals

Senior Consultant Physician, County Hospital, Whiston

Emphysema is a rather vague appellation given to patients suffering from dyspnoea, cough, and in some cases congestive cardiac failure. The term usually means the chronic hypertrophic vesicular emphysema with the "large lungs" described by Sir William Jenner.

A severe disability results from progressive dyspnoea, and all clinicians recognize the common clinical features of a life made wretched and too often hopeless. The breathless existence of the patient is prolonged to some extent by the control by antibiotics of episodes of acute pulmonary inflammation.

Emphysema occurs more commonly in men than in women, and this incidence seems pronounced enough to raise the suspicion of an occupational factor. There is no conclusive evidence on this point, but the inci-

dence does not seem to be higher in occupations where "blowing" is a feature. The effect of hard manual work is doubtful, but the importance of attacks of bronchitis and the effect of a chronic cough is recognized. Asthma is also recognized as an important predisposing factor, and bronchospasm in childhood may be followed by years of good health to be succeeded by the development of emphysema.

The essential pathological feature is a loss of elasticity in the lungs, which are voluminous but not truly distended. The lungs are pale, and the blood is supposedly pressed out of the capillaries. The alveolar walls are atrophied, bullae develop, and the intrapleural pressure is raised. Expiration is thus impaired, being largely a passive process produced by recoil of the elastic tissues of the lung. The changes result in an inability to ventilate the lungs, and the oxygen saturation of the arterial blood falls to 85%. The carbon dioxide in the blood and alveoli rises and the patient is unable to compensate by increasing the pulmonary ventilation. The inspired air tends to be drawn into avascular and dilated alveoli which form a large pathological dead space.

The clinical picture in the established case is one of misery. Dyspnoea is caused by the increased blood carbon dioxide and cyanosis is largely central. Polycythaemia is fairly common and clubbing of the fingers is sometimes present even in uncomplicated cases. The movement of the chest is poor and expansion often less than 1 in. (2.5 cm.); the antero-posterior diameter is widened and the shape sometimes "barrel"; the accessory muscles of respiration are fully employed; and hyperresonance obscures the hepatic and cardiac dullness. Air entry is poor, rhonchi and rales are widespread, and bronchospasm is often present.

Points in Diagnosis

Christie (1944) and others have stressed the importance of associated conditions. The diagnosis is not to be based on isolated symptoms and signs: it is established by the development of insidious dyspnoea on exertion which is not due to bronchospasm or left ventricular failure, together with some of the characteristic signs, and chronic bronchitis or asthma. The long duration and seasonal aggravation of the dyspnoea distinguishes it from cardiac dyspnoea, and there are no nocturnal attacks unless asthma is present. X-ray features are not diagnostic, but several abnormalities are common. Whitfield *et al.* (1951) found that the most constant radiological abnormalities were depression and flattening of the diaphragm, with poor respiratory excursion, the relative brilliance of the lung bases, and the translucency and area of the retrocardiac and antero-cardiac windows. The ribs are widely separated and transversely placed, and there is rotation and elongation of the heart shadow associated with prominent pulmonary arteries.

In many cases of emphysema associated with severe dyspnoea it is difficult to determine and assess the influence of myocardial failure. McMichael and Sharpey-Schafer (1944) showed that the cardiac output is normal or increased in cases of heart failure secondary to lung disease. Cardiac catheterization in cases of emphysema reveals that the right ventricular systolic pressures are normal but become raised with the development of cardiac failure. The pressure returns towards normal with recovery from failure, proving that the pulmonary hypertension cannot result solely from fixed anatomical changes in the vascular bed of the lungs (Mounsey *et al.*, 1952).

The clinical details of the cases under review are given later, but the electrocardiograms do not seem to help in diagnosing or in selecting cases. Seven cases had normal electrocardiograms, one case had cor pulmonale, and one had right axis deviation, and no difference was apparent

in the electrocardiograms taken before and after the institution of treatment by pneumoperitoneum. The criteria for the diagnosis of chronic cor pulmonale were taken from Katz (1946).

In 40 consecutive cases of emphysema admitted to the County Hospital, Whiston, the electrocardiograms were interpreted as follows: normal, 20; cor pulmonale, 2; right axis deviation, 6; left axis deviation, 6; myocardial insufficiency, 6.

The above brief review of the aetiology and diagnostic features of emphysema provides a basis for consideration of methods of treatment. A loss of lung elasticity is the basic disability, and this seems to be progressive and uninfluenced by treatment.

The correction of abnormalities in the nose and sinuses, postural drainage, and the control of infection by antibiotics are helpful. A cough can be reduced sometimes by sedatives; ephedrine relieves bronchospasm; and oxygen is a successful measure of therapy, especially in the presence of congestive failure, when the usual treatment is given. In spite of these measures numbers of severe cases are improved but little, and dyspnoea renders life so intolerable that any means of giving relief is to be welcomed.

Treatment

The treatment of pulmonary emphysema by pneumoperitoneum was introduced by Reich (1924) and used by Monaldi (1937) in the treatment of asthma. Sisti (1936), Piaggio-Blanco and Sayagues (1938), and Rubin and Gass (1948) have also reported on the use of pneumoperitoneum in asthma. New interest was aroused in the use of pneumoperitoneum in a preliminary report by Furman and Callaway (1950), who studied its effect on seven emphysematous patients, five of whom received impressive symptomatic relief.

The rationale of pneumoperitoneum is to increase the intra-abdominal pressure enough to cause elevation of the diaphragm during expiration and yet not to impede its contraction during inspiration. Increased excursion of the diaphragm is thus obtained, with consequent improvement in pulmonary ventilation.

Other better-known measures in use have a similar rationale—namely, breathing exercises and the use of an abdominal binder, advocated by Christie (1934), Gordon (1934), and Alexander and Kountz (1934); but with neither of these methods does the elevation of the diaphragm compare with that obtained in pneumoperitoneum.

Nine cases of severe pulmonary emphysema were selected for treatment by pneumoperitoneum and have been studied for varying periods.

The patients were selected because of their severe disability. As a preliminary, active bronchial infection was treated with antibiotics to which the organisms in the sputum were sensitive, after which the following control procedures were carried out: (a) the diaphragmatic excursion in full inspiration and expiration was measured radiologically; (b) the vital capacity was measured on a "British" Benedict spirometer, the readings being taken at three seconds and also with no time limit: the three-second reading was used by Furman and Callaway (1950) because, given enough time, an emphysematous subject can record quite a high vital capacity by prolonged muscular effort; (c) haemoglobin and red cell count; and (d) electrocardiogram.

It was also intended to record the intrapleural pressures before and after treatment, but experience of this procedure on the first two patients, who were already orthopnoeic, was so alarming that it was abandoned. The above investigations were repeated at various intervals during treatment.

The pneumoperitoneum was induced with a Kjer-Petersen needle, the point of entry being roughly midway between the umbilicus and the anterior superior iliac spine, in either the right or left side: 400 c.cm. of air was given initially, and the volume was increased gradually twice a week until

800 to 1,000 c.cm. could be given without discomfort. Thereafter, refills were given at weekly or two-weekly intervals. When the pneumoperitoneum was established the final intra-abdominal pressure usually lay between 9 and 12 cm. of water.

Complications

Minor degrees of ascites occurred, and in one case existing inguinal herniae were aggravated. Abdominal discomfort was complained of by a few patients for the first 24 or 48 hours after a refill, and was usually caused by injecting too much air, but one patient (Case 6) had persistent abdominal pain, which led to the abandonment of treatment. The proper amount of air for the individual patient can soon be determined.

Free abdominal fluid was detected clinically during the course of treatment in four patients. This seemed to cause no inconvenience except for the splashing noise as the subject turned over in bed or stooped to tie his shoe-lace.

Other complications of pneumoperitoneum are listed by Banyai (1946), and include air embolism, mediastinal emphysema, subcutaneous emphysema, umbilical and scrotal pneumocele, aggravation of existing herniae, and accidental perforation of the intestine. The latter is extremely rare, and is an unlikely complication unless a loop of bowel is fixed to the anterior abdominal wall by adhesions.

Results

Of the nine patients treated by pneumoperitoneum, six have stated that they have obtained definite benefit. This was mainly shown by the disappearance of dyspnoea and an increase in the amount of exercise which could be taken. Three patients obtained no benefit after three months' treatment.

Vital Capacity.—The changes in vital capacity are recorded with the individual case histories. On the whole there is a significant increase during treatment, but not so striking as that reported by Furman and Callaway in their patients.

Diaphragmatic Excursion.—The range of movement of the diaphragm between inspiration and expiration was measured radiologically on a film taken by the double exposure technique (see Table).

Diaphragmatic Excursion

Case	Before Treatment		After Treatment	
	Right Side (cm.)	Left Side (cm.)	Right Side (cm.)	Left Side (cm.)
1	0.8	0.9	2.1	1.0
2	0.8	0.9	2.7	2.6
3	0.6	0.9	2.4	3.0
4	1.0	0.5	3.2	3.7
5	1.8	1.2	2.8	3.0
6	2.3	2.6	2.1	1.6
7	0.2	1.5	2.1	3.0
8	2.1	2.1	2.3	2.5
9	0.3	0.5	3.0	3.2

Haemoglobin and Red Blood Cells.—No significant alteration from the original levels of haemoglobin and the red-cell counts could be demonstrated in any case after treatment by pneumoperitoneum had been established.

Case Histories

Case 1.—A man aged 45 had had asthmatic attacks for 17 years. He developed pneumonia two years ago, which further aggravated his poor exercise tolerance. His convalescence was prolonged and he has remained very cyanosed since. Before beginning pneumoperitoneum treatment he rarely ventured out of his house. There has been no congestive cardiac failure. His blood pressure was 110/80 mm. Hg. A pneumoperitoneum was induced on October 24, 1951, and was maintained with fortnightly refills of air varying between 800 and 1,000 c.cm. There was evidence of a small amount of free abdominal fluid

about four months after treatment began, but this disappeared spontaneously in six weeks. His vital capacity before treatment was 2,300 c.cm. and at three seconds 1,300 c.cm. Seven months later the readings were 2,650 and 1,900 c.cm. respectively. Although still cyanosed, he could get about for walks in good weather, and maintained that he could not do without his refills.

Case 2.—A man aged 57 dated his incapacity to an attack of pneumonia seven years previously, since when he has suffered shortness of breath, sufficient to cause him to give up all work. His case notes show, however, that he had been subject to winter bronchitis for several years before that. Before treatment he was completely incapacitated, and even slight exertion in the house made him breathless. He has never had congestive cardiac failure. His blood pressure was 150/100 mm. Hg. A pneumoperitoneum was induced on October 24, 1951, and was maintained with refills of 800 c.cm. of air every fortnight. The vital capacity before treatment was 2,400 c.cm. and at three seconds 1,150 c.cm. During treatment the vital capacity has averaged 2,600 c.cm. and at three seconds 1,250 c.cm. Ascites developed about

FIG. 1.—Case 3. Diaphragmatic excursion before treatment.

FIG. 2.—Case 3. Diaphragmatic excursion during treatment with pneumoperitoneum.

five months after treatment began, but was negligible in amount and disappeared spontaneously. Improvement in exercise tolerance was remarkable in this patient, so much so that he developed intermittent claudication of the right leg two months after the beginning of treatment.

Case 3.—A man aged 65 had suffered from bronchitis for many years, and had severe pneumonia two years ago, after which congestive cardiac failure developed. Convalescence was prolonged, and he was

always extremely breathless, even at rest, and his ankles became swollen in the evenings. His blood pressure was 155/80 mm. Hg. An x-ray film confirmed the presence of gross emphysema. A pneumoperitoneum was induced on December 14, 1951, and was maintained with an average of 800 c.cm. of air every fortnight. The vital capacity before treatment was 1,900 c.cm. and 1,750 c.cm. at three seconds. During treatment the readings were 2,150 and 1,500 c.cm. respectively. This patient admitted to no improvement during treatment, and he continued to show signs of mild congestive cardiac failure. The pneumoperitoneum was abandoned four and a half months after it was begun.

Case 4.—A man aged 73 had suffered from chronic bronchitis and shortness of breath for 27 years. Since 1946 he has been an inmate of the chronic sick section, and could move only short distances with help. He was orthopnoeic and extremely cyanosed. An x-ray film of the chest confirmed the presence of gross pulmonary emphysema with practically no diaphragmatic movement. No episodes of congestive heart failure had been reported during his eight-year stay in hospital, but he was confined to bed most of the day. His blood pressure was 140/80 mm. Hg. A pneumoperitoneum was induced on December 14, 1951, and thereafter refills of 500 c.cm. of air were given once a week. The vital capacity before treatment was 1,500 c.cm. and with a time limit of three seconds 850 c.cm. The

readings two months later were 1,450 and 1,000 c.cm. respectively. There was no subjective or objective improvement in this case; he remained bedridden and very dyspnoeic, and, as the intra-abdominal pressure rose, bilateral inguinal herniae became aggravated, and treatment was abandoned after nine weeks.

Case 5.—A man aged 60 gave a 16-years history of shortness of breath and attacks of bronchitis. He contracted a severe suppurative pneumonia a year ago, which resulted in some fibrosis in the right upper lobe. Breathlessness became notably worse after this episode, but he could walk slowly for about half a mile. He has never had congestive cardiac failure. His blood pressure was 150/90 mm. Hg. A pneumoperitoneum was induced on January 14, 1952, and thereafter refills were continued every fortnight, the average volume of air given being 700 c.cm. A moderately large ascites developed ten weeks after the start of treatment but seemed to cause no discomfort. The fluid was turbid, containing polymorphonuclear cells, and a growth of a coagulase-negative staphylococcus was obtained. The fluid disappeared within a week after the patient was put to bed and given a course of penicillin. The vital capacity before treatment was 1,500 c.cm. and with a time limit of three seconds it was 1,250 c.cm. These figures became 1,950 and 1,500 c.cm. respectively two months after the start of treatment. Improvement in exercise tolerance was moderately good.

Case 6.—A man aged 54 had remained well up to six years ago, when attacks of bronchitis and asthma developed. These attacks became more frequent, and after an attack of pneumonia one year ago his dyspnoea was much worse. For some time before admission to hospital he had been severely incapacitated and confined to his home. He was cyanosed and orthopnoeic, and an x-ray film of his chest revealed gross emphysema. It was evident that the severity of his dyspnoea was due in part to bronchospasm. There was no history suggestive of congestive heart failure. His blood pressure was 120/70 mm. Hg. A pneumoperitoneum was induced on January 14, 1952, and after it was established refills averaging 700 c.cm. were given once a fortnight. The vital capacity before treatment was 2,000 c.cm., and at three seconds 1,150 c.cm. Two months later, during treatment, the figures had not changed appreciably, being 1,850 and 1,100 c.cm. respectively. There seemed to be much improvement in exercise tolerance during the initial stages of treatment in hospital, but after discharge the attacks of asthma returned and he relapsed into his previous dyspnoeic condition. After persisting with the pneumoperitoneum for three months it was considered that there was going to be no improvement, and treatment was discontinued.

Case 7.—A man aged 47 had been troubled with shortness of breath and asthmatic attacks for the past 17 years. He was admitted to hospital two years ago, having sustained a spontaneous pneumothorax on the right side, presumably due to rupture of an emphysematous bulla. His exercise tolerance had become very poor during the past four years,

FIG. 3.—Case 4. Diaphragmatic excursion before treatment.

FIG. 4.—Case 4. Diaphragmatic excursion during treatment with pneumoperitoneum.

and he could walk only a few yards without becoming breathless. An x-ray film of the chest showed the typical features of emphysema. There has been no congestive cardiac failure. His blood pressure was 140/90 mm. Hg. A pneumoperitoneum was induced on January 14, 1952, and subsequent refills have amounted to 900 c.cm. a fortnight. A small amount of free peritoneal fluid was detected ten weeks after the start of treatment, but this disappeared spontaneously two weeks later. The vital capacity before treatment was 1,900 c.cm. and with a time limit of three seconds 1,030 c.cm. These figures had improved two months later to 2,100 and 1,300 c.cm. respectively. The improvement in general well-being and exercise tolerance was most gratifying. He can walk about outside with less dyspnoea than previously and he also sleeps more comfortably owing to improved breathing.

Case 8.—A man aged 52 was admitted to hospital in April, 1952, because of severe breathlessness and cough. He gave a history of having had chest trouble for 20 years, including frequent attacks of bronchitis, and hay-fever. His breathlessness was such that he was able to climb a flight of stairs at home only once a day, and even that amount of exertion disabled him for fifteen minutes. There was no history suggestive of congestive cardiac failure. His blood pressure was 160/80 mm. Hg. An x-ray film of his chest confirmed the presence of marked pulmonary emphysema. The vital capacity was 1,750 c.cm., and the reading with a three-seconds limit was the same. After induction of a pneumoperitoneum on April 21, 1952, refills were carried out twice a week while in hospital and then fortnightly after discharge, an average of 700 c.cm. of air being given. The vital capacity during treatment became 1,900 c.cm. and with a time limit of three seconds 1,500 c.cm. Symptomatic improvement was good; he was able to take much more exercise than before admission to hospital, and his exercise tolerance continued to improve.

Case 9.—A man aged 46 first noticed that he was becoming breathless on exertion when he was 22. He continued to work at a cotton mill, but his cough and dyspnoea became worse and he had to give up all work in 1941. He

has had pneumonia three times, the worst attack being in 1936. Before treatment he could walk about half a mile very slowly and with a great deal of effort. He does not give a history suggestive of congestive cardiac failure. His blood pressure was 130/90 mm. Hg. An x-ray film of the chest confirmed the presence of pulmonary emphysema with very little diaphragmatic movement. A pneumoperitoneum was induced on April 29, 1952, and while in hospital refills were given twice

FIG. 5.—Case 9. Diaphragmatic excursion before treatment.

FIG. 6.—Case 9. Diaphragmatic excursion during treatment with pneumoperitoneum.

weekly until it was established. An average of 800 c.cm. of air was given once every two weeks as an out-patient. The vital capacity before treatment was 1,450 c.cm., and with a time limit of three seconds 880 c.cm. Seven weeks after the start of treatment the readings had become 1,950 and 1,200 c.cm. respectively. He has improved tremendously; his exercise tolerance is better than previously and he can walk longer distances without becoming so breathless.

Discussion

After several months' experience of this particular treatment it was possible to select more accurately the type of case that would derive benefit from it, and exclude those showing certain features now known to be contraindications. The latter may be best illustrated by the three cases which showed no improvement. Case 3 had signs of congestive cardiac failure for two years before treatment was instituted; this was not gross, and was manifest by congestion of the veins in the neck, some swelling of the ankles after exercise, and a little engorgement of the liver. Case 4, practically bedridden for six years in the chronic ward because of exertional dyspnoea and considered to have myocardial failure, made no response to treatment. We believe that any benefit which pneumoperitoneum might have is not enough to overcome the effects of established failure of the myocardium.

A feature of Case 6 was the frequent attacks of severe asthma. Despite the favourable reports on the treatment of asthma by pneumoperitoneum made by others, we found that it had not the slightest effect; in fact, the violent muscular efforts during an attack of asthma seemed to cause considerable pain in the abdominal muscles, which were already stretched by the pneumoperitoneum. We would exclude those cases, therefore, in which asthma is a marked feature.

The emphysematous subject is particularly liable to attacks of bronchitis, which have the effects of almost complete disablement. Several patients under treatment with pneumoperitoneum developed bronchitis during the winter months, and we found that any good effect of the treatment was nullified until the infection was controlled and the sputum again became scanty. Some of the fluctuations in the vital capacity might be explained by the presence or absence of bronchitis at the time the records were made.

On the other hand, it is necessary to examine why there was no great increase in the vital capacity in our patients despite the fact that the diaphragmatic excursion had been improved.

Banyai (1946) found that in a group of tuberculous patients undergoing pneumoperitoneum treatment the vital capacity showed an average decrease of 14.7%, while Furman and Callaway reported a dramatic increase in vital capacity in their emphysematous patients—two, indeed, having double their pre-treatment values.

Meakins and Christie (1934) pointed out that, whereas the normal functional residual air amounted to 35–40% of the total lung volume, in severe emphysema the figures might reach 70 to 80%. And, since the vital capacity is also reduced, the resting tidal air and vital capacity may approach equality.

We think that in those of our cases in which the exercise tolerance improved and yet was not reflected in a greatly increased vital capacity the effect of the improved function of the diaphragm was to decrease the residual air in proportion to the total lung volume, thus allowing improved aeration.

Antispasmodics such as ephedrine and aminophylline were found to be a valuable adjunct to pneumoperitoneum in cases in which there was a tendency to bronchospasm. In patients who are not subject to such attacks ephedrine is probably of little value, since Whitfield *et al.* (1950) showed that this drug produced no alteration in the subdivisions of lung volume in emphysematous subjects without bronchospasm.

Finally, the psychological effects of a new form of treatment on patients who have been incapacitated for years must be remembered. There is no doubt that the enthusiasm of the operator is often reflected in the patient, at least during the first few weeks, and certainly many of the glowing testimonials from some of our patients could be attributed to this. After due allowance has been made for this, however, we believe that there has been a genuine

improvement in most of the cases treated by pneumoperitoneum, which warrants its use in a larger series of patients.

A pneumoperitoneum may be continued indefinitely, refills being given at weekly or, more usually, fortnightly intervals, although in Reich's experience the high position of the diaphragm was maintained for long periods after the pneumoperitoneum was discontinued. This he attributed to the fact that during treatment the patient performed an unconscious respiratory exercise, relaxing the diaphragm and contracting its antagonists, the abdominal muscles, and continued to do so without the aid of a pneumoperitoneum.

Summary

A brief review of pulmonary emphysema and methods of accepted treatment is given.

The progressive nature of the disease and the misery which is the lot of those severely affected warrant exploration of all new avenues of treatment.

Nine severe cases of pulmonary emphysema treated by pneumoperitoneum are presented, with results encouraging enough to justify further study. The rationale of pneumoperitoneum is to increase the intra-abdominal pressure sufficiently to cause elevation of the diaphragm during expiration, and yet not to impede its contraction during inspiration. Increased excursion of the diaphragm is thus obtained, with consequent improvement in pulmonary ventilation.

The vital capacity was increased in seven cases and the excursion of the diaphragm, measured radiologically, was improved in all cases. No improvement was evident in two cases with a history of congestive cardiac failure and in one case with asthma.

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In his preface to the annual statistical report of the Middlesex Hospital for 1952, Colonel the Honourable J. J. Astor, chairman of the board of governors, points out that, while in the past the main function of the report was to persuade the public to subscribe to the hospital's funds, its present task "is to say whether public money, assigned by Parliament for the upkeep of their hospitals, has been used to the best advantage." During the year under review there were 633,000 out-patient attendances at the hospital and its constituent institutions, compared with 582,000 in 1951. The physiotherapy clinic accounted for 219,000, of whom 10,000 were new patients; 117,000 attended the rheumatism clinic, and 40,000 attended for radiotherapy. In-patients numbered 14,800, a slight increase on the previous year. Good progress is reported in converting Latimer House, acquired in 1951 to serve as an institute of clinical research and experimental medicine, and the institute will be in action later this year.

SENSITIVITY STUDIES ON SHIGELLA SONNEI

BY

G. B. FORBES, M.D.

Pathologist, Kent and Canterbury Hospital

This report concerns a study of the antibacterial activity of streptomycin, chloramphenicol, aureomycin, and terramycin against *Shigella sonnei*, together with observations on the suitability of these antibiotics for the treatment and control of Sonne dysentery.

Seventeen representative strains of *Sh. sonnei* were collected from separate outbreaks and isolated cases of Sonne dysentery which occurred in East Kent and Hertfordshire. The identity of the strains was confirmed by biochemical tests and agglutination to titre with specific typing serum. In addition the strains were grouped according to their bacteriophage reactions (Hammarström, 1947) and fermentative behaviour towards xylose (Bojlen, 1934) to ensure that the collection included a variety of types. Dr. Mayr-Harting, of Bristol, kindly performed the bacteriophage tests, and found that most strains belonged to phage type 3, a type commonly encountered in this country (Cooper and Mayr-Harting, 1951); five other phage types were represented (Table I). One of the strains fermented xylose; the others were xylose-negative and gave the usual biochemical reactions of strains isolated in this country (Carter, 1937).

TABLE I.—Xylose Fermentation and Bacteriophage Reactions

Strain	Xylose Fermentation	Phage Type
1, 2, 4, 7, 8, 9, 10, 11, 14, 15, 16, 17	—	3
3	—	85
5	—	32
6	—	66
12	—	23
13	+	? 17b

In-vitro Experiments

I. Tube Sensitivity Tests

Method.—Graded concentrations of each antibiotic were prepared in nutrient broth and tubed in 1-ml. amounts; 0.02 ml. of 1:100 dilution of an overnight broth culture of each strain was added to the appropriate set of tubes, which were then incubated at 37° C. The lowest concentrations of antibiotic required for growth suppression as judged by complete absence of turbidity and bacterial deposit were noted after 12, 18, 24, 36, and 42 hours' incubation.

Results.—The results of these tests, expressed as the average sensitivity of the 17 strains to each antibiotic, are given in Table II. It will be seen that the end-points increased progressively with prolongation of the incubation period beyond 12 hours. With the more stable antibiotics (streptomycin, chloramphenicol, and terramycin) the inhibiting concentrations rose slightly, to give readings at 42 hours approximately twice as high as those obtained at 12 hours.

TABLE II.—Mean Sensitivity of 17 Strains After Varying Periods of Incubation

Antibiotic	Hours' Incubation				
	12	18	24	36	42
Streptomycin	4.94*	6.23	7.29	7.76	8.47
Chloramphenicol ..	5.52	7.41	7.88	8.47	8.58
Aureomycin	1.01	2.00	4.00	7.53	9.06
Terramycin	2.06	2.94	3.76	3.88	4.35

* Minimal inhibiting concentration in µg./ml.