sources of error are possible in ascribing the benefit to the drug when it is administered in this way—such as spontaneous improvement, desire on the patient's part to please the doctor, and the difficulty in assessing subjective symptoms such as dyspnoea, cough, and sputum. Some of these disadvantages are overcome by using the double-blind method, but difficulties still exist, such as the accurate assessment of subjective symptoms. Measurement of sputum volume was rejected from this trial as being impracticable because none of the patients were in hospital and many were working. Moreover, failure on the part of the patient to use a container every time sputum was produced could lead to misleading inaccuracy.

Summary

A total of 164 male chronic bronchitics in Aberdeen and Preston expectorating mucoid sputum took part in a double-blind controlled trial using methyl cysteine hydrochloride ("acdrile") and a placebo.

The response was assessed by the patient's general practitioner by the severity of the following symptoms and signs at the beginning and at the end of each week in a four-week period—dyspnoea, wheeze, cough, sputum, rales, and rhonchi. Those having methyl cysteine hydrochloride showed a greater reduction in cough and sputum compared with the controls, this difference for both cough and sputum being significant at the 5% level. Differences in response between the drug and control patients for the other symptoms were not significant.

This trial was made possible by the co-operation and interest of the general practitioners in Aberdeen and Preston, to whom our thanks are due. Our thanks are also due to Mr. R. Vaughan Hudson, who suggested and sponsored this trial. We also thank Berk Pharmaceuticals Ltd., London, for a generous supply of active and dummy tablets.

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Soon after the publication of the Younghusband Report the Association of General and Family Caseworkers, the Association of Psychiatric Social Workers, and the Institute of Almoners set up a Standing Joint Committee to consider the implications of this report for these three professional groups. This committee has now prepared a report, *The Professional Social Worker in Local Authority Health and Welfare Services*, and has sent a copy to all local authority health and welfare departments in England, Wales, and Northern Ireland. Copies are available (1s., post free) from 42 Bedford Square, London W.C.1.

EFFECT OF ORAL ALPHA-CHYMOTRYPSIN ON SPUTUM VISCOSITY

BY

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The use of crystallized trypsin when applied topically for the digestion of necrotic debris and liquefaction of thick viscid exudates has been reported on numerous occasions. After the good results obtained in thinning fluid by the intrapleural use of trypsin, the enzyme was used as an aerosol for the liquefaction of viscid bronchial secretions. Several papers (Roettig *et al.*, 1952; Limber *et al.*, 1952; Peck and Levin, 1952; Unger and Unger, 1953a, 1953b; Yates and Goodrich, 1953; Wilson and Stevenson, 1957) have been published showing that trypsin as an aerosol may decrease the viscosity of sputum. More recently, crystallized alpha-chymotrypsin, when administered intramuscularly, has been reported to be effective in respiratory conditions such as bronchial asthma, bronchitis, and sinusitis (Parsons, 1958; Teitel *et al.*, 1960; Taub, 1960).

Intramuscular injections are not always convenient and the availability of a tablet containing the proteolytic enzyme, specially formulated for oral administration and intestinal absorption, has many advantages over intramuscular administration. Several papers have been published on the effect of oral alpha-chymotrypsin ("chymoral") in the reduction of inflammation and oedema, and as a mucolytic agent in upper respiratory conditions (Teitel *et al.*, 1960; Taub, 1960; Billow, 1960). The proteolytic enzyme does not digest living tissue since both serum and viable cells contain specific enzyme inhibitors.

A common feature of chronic bronchitis is the distress caused by the expectoration of tenacious sputum, and an easily administered substance capable of producing sputum liquefaction would be a welcome addition to the drugs and antibiotics already in regular use.

The only available literature (Taub, 1960; Teitel *et al.*, 1960) reporting the mucolytic action of oral alpha-chymotrypsin makes no mention of a controlled investigation, and therefore a small-scale double-blind trial was carried out to assess the mucolytic activity of this compound. As chronic bronchitics are renowned to be influenced for good, at least temporarily, by any new preparation, it was decided to estimate progress by a measurement of the stickiness of the sputum, thus avoiding any subjective statements from the patient. It seemed a valid assumption that the stickiness of sputum could be expressed in terms of a viscosity measurement.

Materials and Method

Patients known to be suffering from chronic bronchitis were picked at random, without regard to age or sex, from the clinic records and divided into two approximately equal groups. A four-weeks supply of two

tablets, A and B, was prepared by the manufacturer in labelled bottles. The identity of these tablets was not revealed to the investigators until after completion of the trial. Group 1, comprising 19 patients, was given tablet A (dummy), and group 2, consisting of 21 patients, received tablet B (alpha-chymotrypsin). Before each patient began the course of tablets he produced a sample of sputum, and thereafter took two tablets four times a day for four weeks. At weekly intervals he expectorated a sample of sputum for examination. Each of the five sputum specimens received from an individual patient during the trial was expectorated before breakfast and examined within two hours.

The Viscometer

A simple viscometer of the plate-and-spring type was used for making the weekly viscosity measurements. Most patients were capable of producing only very small amounts of sputum, and an initial difficulty was encountered in constructing an instrument able to deal with quantities of the order of 1 ml. Photographs of the instrument which finally suited this purpose are shown in Figs. 1 and 2. A round brass table (A) (11 cm. in diameter) was fixed to the spindle of a geared A.C. brush motor (B), the speed of which could be varied and accurately controlled by a variac (C). An aluminium disk (D) (3 cm. in diameter) was fixed 1 mm. above the brass table (A) along its axis and supported on a spindle (E) set between pivots. A pointer fixed to the spindle (E) measured the rotation of the aluminium disk on an engraved "perspex" scale with 0 to 60 divisions (F). Tension was applied to the spindle (E) by a hairspring (G). The complete aluminium disk assembly was fixed to a baseboard by two wing nuts and was easily removable for cleaning.

FIG. 1.—The lettering on the illustrations is explained in the text.

For each viscosity estimation a small sample of sputum was placed in the centre of the brass table; the aluminium disk was gently lowered into position and secured firmly by tightening the wing nuts. Any excess sputum which had extruded beyond the edge of the aluminium disk was carefully wiped away before the motor was started. The speed of the brass table was

FIG. 2

carefully controlled by the variac so that it made five revolutions a minute. After a few minutes' rotation the pointer became steady and the deflection was read from the perspex scale.

Results

The viscometer deflections given by the five specimens of sputum from the 19 patients receiving dummy tablets A in group 1 are recorded in Table I.

TABLE I.—Viscometer Readings of Sputum from Patients in Group 1 Receiving Tablet A

Patient No.	Viscometer Readings after Taking Tablet A				
	Initial Specimen	1st Week	2nd Week	3rd Week	4th Week
1	19	20	20	17	29
2	13	15	14	18	16
3	29	23	33	33	36
4	20	17	28	20	14
5	30	23	29	28	29
6	24	23	23	22	22
7	27	26	21	22	28
8	29	21	27	22	22
9	17	14	19	12	20
10	27	15	23	22	15
11	16	13	15	18	10
12	34	39	32	23	35
13	26	28	27	26	18
14	26	25	19	23	18
15	18	21	27	14	15
16	19	23	18	18	14
17	28	30	21	13	27
18	20	18	23	20	23
19	18	12	15	18	21

Table II records the results for the 21 patients in group 2 who received tablet B.

The results in these two tables can be arranged to show the mean viscosity reading for each weekly sample in the two groups and the percentage change in viscosity during the trial period. The mean viscosity and change (in parentheses) are shown in Table III.

TABLE II.—*Viscometer Readings of Sputum from Patients in Group 2 Receiving Tablet B*

Patient No.	Viscometer Readings after Taking Tablet B				
	Initial Specimen	1st Week	2nd Week	3rd Week	4th Week
1	20	26	16	8	5
2	27	22	12	11	10
3	23	24	9	16	14
4	29	25	15	12	0
5	14	17	11	10	7
6	24	7	2	4	7
7	26	27	17	18	15
8	23	20	13	12	10
9	27	9	7	8	7
10	24	20	19	12	10
11	20	20	14	12	4
12	26	8	0	4	3
13	26	16	12	15	4
14	18	13	12	10	6
15	30	22	19	12	4
16	21	20	17	15	10
17	18	20	15	16	10
18	17	20	17	10	5
19	27	23	20	19	12
20	30	30	22	9	10
21	35	29	26	6	7

TABLE III.—*Mean Viscosity Readings During Trial Period, with Percentage Change in Parentheses (Negative Sign Indicates Reduction in Viscosity)*

Group	Viscosity Readings				
	Initial Specimen	1st Week	2nd Week	3rd Week	4th Week
1	23.6	21.9	22.8	20.3	22.1
	(0)	(-7.2%)	(-3.4%)	(-13.9%)	(-6.3%)
2	24.0	19.9	14.5	12.0	7.6
	(0)	(-17%)	(-39.5%)	(-50%)	(-68.3%)

Discussion

The results of this investigation show that a marked reduction in viscosity or liquefaction occurred in patients receiving oral alpha-chymotrypsin. Recognizing that purulent sputum is less viscous than mucoid sputum, a record was made of the incidence of purulent specimens in each group. The number of purulent samples in group 2 differed only slightly from that in group 1: 57 mucopurulent specimens in group 1 (60%), and 70 in group 2 (67%). From this observation one may deduce that the reduced viscosity in group 2 patients is due to the direct mucolytic effect of the enzyme. No side-effects were observed and most of the patients in both groups described improvement in their symptoms and felt the tablets assisted them in expectorating sputum.

Summary

A small-scale double-blind trial using oral alpha-chymotrypsin is described.

The results indicate that oral alpha-chymotrypsin causes liquefaction of sputum as denoted by a reduction in its viscosity.

The Armour Pharmaceutical Company Ltd. supplied the tablets of alpha-chymotrypsin (chymoral).

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CONSERVATISM IN SURGICAL TREATMENT OF BRONCHIAL CARCINOMA

A REVIEW OF 826 PERSONAL OPERATIONS*

BY

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Every year we spend large sums on cancer research, and devoted workers labour to elucidate its problems. The object of this is presumably to prevent cancer; yet, within the limits of human fallibility, we know the cause of the commonest cancer afflicting the human body, and we do almost nothing about it. Why?

In 1950 cancer of the lung took second place to cancer of the breast. Now it exceeds it. In Great Britain it accounts for a quarter of all male deaths from cancer. It has increased 40 times in the past 30 years. It kills five times as many people as are killed annually on the roads, and we are beset by propaganda and punitive measures to enforce road safety, but hear little about the much greater menace of the two. Deaths from it increase by a steady 1,000 a year in the United Kingdom.

In the U.S.A. cancer of the lung caused 2,500 deaths in 1930, 18,000 in 1950, and over 30,000 in 1959. In New York State—where the statistics are particularly reliable—its incidence increased by 385% between 1930 and 1950, whereas that of other cancers fell.

A Major Health Problem

This pattern is confirmed in 16 other countries. The relationship between this appalling and increasing epidemic—which is surely one of the major international public health problems of the day—and cigarette smoking is not doubted by anyone who has troubled to read the formidable statistical, chemical, experimental, and pathological evidence now accumulated. It is surely by now familiar to everyone; but I will very briefly refer to some of the facts.

Seven years ago the American Cancer Society interviewed 200,000 men aged between 50 and 70. Since then 12,000 have died. Among the non-smokers there were 3.4 deaths per 100,000 from bronchial carcinoma; among cigarette smokers 78.6 deaths, with 28.9 deaths for pipe smokers and 11.4 among cigar smokers. These rates were directly related to the amount smoked: fewer than 10 a day, 51.4 per 100,000; 20 to 40, 143.9; and over 40, 217 per 100,000. The overall death-rate was 105% higher among smokers than among non-smokers, deaths from heart disease 115% higher and deaths from cancer of the lung 800% higher. A similar study of 200,000 subjects by the Veterans Administration yielded parallel results. In 1880 Americans smoked 16 cigarettes per head per annum; in 1959 the number was 3,700.

Doll and Hill's (1954, 1956) pioneer work—which among other things demonstrated that of every 11 men who smoke 20 cigarettes a day one will die of lung cancer—will certainly be familiar. In their survey of the smoking habits of British doctors they found a death

*Read in the Section of Cardiothoracic Surgery at the Annual Meeting of the British Medical Association, Auckland, New Zealand, 1961.