to 0.05 unit or less of oxytocin was associated with labour occurring within 48 hours of amniotomy in 91% of cases, but if the test was positive to 0.03 unit or less the comparable figure was 100%. The test is particularly accurate when termination of pregnancy is contemplated more than one week before the expected date of delivery. It is in this group of cases that an indication of the likelihood of a rapid response to amniotomy would be of the greatest help in coming to a decision to perform amniotomy or elective caesarean section.

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REFERENCES

- Baumgarten, K., and Hofhansl, W. (1961a). *Geburtsh. u. Frauenheilk.*, **21**, 10.
 — (1961b). *Zbl. Gynäk.*, **83**, 154.
 Birmanac, D. (1960). *Med. Glas.*, **14**, 533.
 Caldeyro-Barcia, R. (1960). First International Congress of Endocrinology Symposium, Copenhagen, **2**, 41.
 Göltner, E. (1959). *Zbl. Gynäk.*, **81**, 113.
 Hendricks, C. H. (1960). *Amer. J. Obstet. Gynec.*, **79**, 789.
 Husslein, H., and Baumgarten, K. (1960). *Wien. klin. Wschr.*, **72**, 561.
 — and Hofhansl, W. (1960). *Zbl. Gynäk.*, **82**, 49.
 McCarthy, C. J., and Fugo, N. W. (1961). *Obstet. and Gynec.*, **17**, 531.
 Müller, H. A. (1958). *Arch. Gynäk.*, **191**, 65.
 Page, E. W. (1946). *Amer. J. Obstet. Gynec.*, **52**, 1014.
 Schwarcz, R., Fisch, L., and Schwarcz, R., jun. (1960). *Sem. méd. (B. Aires)*, **116**, 426.
 Smyth, C. N. (1954). International Congress on Gynaecology and Obstetrics, Geneva. Vol. *Exposition Scientifique*.
 — (1958a). *Triangle*, **3**, 150.
 — (1958b). *Lancet*, **1**, 237.

USE OF "CHYMORAL" IN MUCOVISCIDOSIS

BY

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There have recently been a number of reports on the use of the proteolytic enzymes trypsin and a close variant α -chymotrypsin as anti-inflammatory and mucolytic agents in the treatment of respiratory disease. Avakian (1961) has reviewed the oral administration of these enzymes from a pharmacological viewpoint. No conclusive clinical benefit in respiratory disease had been shown, however, until the recent trial of Bruce and Quinton (1962).

Present Investigation

On this account it was decided to investigate the effectiveness of such oral trypsin preparations in mucoviscidosis. "Chymoral," the oral preparation used, contains trypsin and chymotrypsin in the proportion of six to one, each tablet containing 50,000 units of proteolytic activity.

Twenty-two children aged 4 to 17 with proved mucoviscidosis were chosen. Pulmonary involvement varied from clinical and ventilatory normality to severe impairment both of clinical state and of ventilatory function. All the patients were ambulant. For the purpose of control they were divided into two groups of approximately similar composition as regards age, height, and clinical severity (see Tables I and II).

A series of tracings of forced expiration following a maximal inspiration was recorded on a Palmer multi-purpose recording spirometer at regular monthly intervals. The light aluminium bell moved 1 cm. for each 200-ml. increase in volume and the recording drum revolved at a speed of 2.5 cm. per second. The child, seated, expired through a mouthpiece of adjustable height. The mouthpiece was a Y-shaped metal tube, the stem and the two arms, which subtended a very acute angle, were all 2.5 cm. in calibre, as were the two tubes of thick "polythene" which led to the central core of the spirometer. A washable sleeve of polythene was used to cover the mouthpiece for each case. Standing height and weight were measured at each visit, and a brief clinical inquiry was made into cough, amount of sputum, and change, if any, of antibiotic; a clinical examination of the chest was also made. From the

maximum readings of at least eight tracings at each session consecutive monthly measurements of each child's forced vital capacity (F.V.C.) and one-second forced expiratory volume (F.E.V.₁) were made.

After the third or fourth monthly measurement, when it was hoped a baseline had been obtained, each child was put on one tablet four times a day of either chymoral or a dummy blank prepared by the same firm, so that one group of children received chymoral and the control group the dummy tablets. Administration of the tablets was continued for the next three months, while the monthly forced expiratory tracings were continued. At the end of this time all the tablets were stopped, and the final tracings were taken one month later. During the course of the investigation the children remained so far as possible on constant treatment in respect of antibiotics and dose of pancreatin. No adjuvant treatment such as breathing exercises was given.

The maximum value for the three preliminary control estimations in respect of both F.E.V.₁% and F.V.C. was then compared in each case with the maximum value obtained during the trial and with the final value approximately one month after the end of the trial. Maximum values have been used with regard to F.E.V.₁% and F.V.C., as errors in their recording are not random; less than maximum values are associated with errors usually of technique or of lack of concentration or understanding on the child's part.

The results are shown in Tables I and II.

Conclusion

The results show that there is no significant difference between the two series, and that so far as pulmonary ventilation is concerned chymoral in a dose of one tablet six-hourly has had no effect over a period of three months.

This correlated with a clinical lack of improvement as regards exercise tolerance, sputum quantity, and physical signs in the chest. In the three months following the end of the trial three deaths occurred—two in the group who had had chymoral and one in the control group.

TABLE I.—*Forced Vital Capacity*

Case No.	Sex	Ht. (cm.)	Age	Max. Control	Max. Trial	% Change	End Control
<i>Group on Dummy Tablets</i>							
1	F	148	12	1,920 (66%)	2,000	+4.2	1,920
2	F	166	16	3,400 (87%)	3,200	-5.9	3,060
3	F	137	10	1,450 (63%)	1,520	+4.8	1,600
4	M	131	8	1,120 (53%)	900	-19.6	1,040
5	M	164	14	1,960 (49%)	1,940	-1	2,000
6	M	142	11	1,840 (71%)	1,980	+7.6	2,000
7	M	107	5	540 (<50%*)	420	-22.2	540
8	F	97	4	400 (50%*)	440	+10	380
9	M	133	10	1,660 (76%)	1,780	+7.2	1,700
10	M	118	8	740 (44%)	620	-16.2	—
11	F	112	5	1,260 (85%*)	1,240	-1.6	1,220
Mean		141	9½	1,470	1,460	-0.7	

<i>Group on Chymoral Tablets</i>							
12	M	150	13	2,950 (100%)	3,060	+3.7	2,880
13	M	185	16	4,980 (96%)	4,600	-7.8	4,540
14	F	133	10	2,060 (100%)	2,100	+1.9	2,060
15	M	126	9	1,740 (92%)	1,840	+5.2	1,660
16	M	152	13	1,660 (62%)	1,880	+13.2	1,700
17	F	135	10	1,140 (52%)	1,040	-8.8	840
18	M	111	6	340 (<50%*)	300	-11.8	360
19	F	108	6	530 (<50%*)	560	+5.6	320
20	M	123	8	1,180 (66%)	1,320	+11.9	1,140
21	M	113	6	1,070 (67%)	1,050	-1.9	1,100
22	M	178	17	4,660 (94%)	4,700	+0.8	4,460
Mean		138	10½	2,030	2,040	+0.5	1,920

Values of F.V.C. estimated in terms of percentage of normal mean values for particular height and sex (Strang, 1959) are included in parentheses alongside each maximum control reading.

* Very approximate figures as no standard available.

TABLE II.—*Forced Expiratory Volume*

Case No.	{ Max. Control		{ Max. Trial		Change in F.E.V. ₁ %	{ End Control	
	F.E.V. ₁	F.E.V. ₁ %	F.E.V. ₁	F.E.V. ₁ %		F.E.V. ₁	F.E.V. ₁ %
	<i>Group on Dummy Tablets</i>						
1	1,560	89	1,540	77	-12	1,480	77
2	2,740	83	2,680	84	+1	2,720	89
3	1,200	83	1,240	83	0	1,260	79
4	920	82	580	64	-18	720	69
5	860	46	900	46	0	720	36
6	1,340	75	1,470	74	-1	1,560	78
7	480	89	380	90	+1	380	67
8	400	(100)*	440	(100)*	(0)	380	(100)*
9	1,400	84	1,420	80	-4	1,420	84
10	660	91	520	84	-7	440	85
11	1,200	95	1,120	91	-4	1,120	92
Mean		83		79	-4		78
<i>Group on Chymoral Tablets</i>							
12	2,400	84	2,480	81	-3	2,360	82
13	2,900	61	2,560	57	-4	2,220	49
14	1,760	86	1,720	87	+1	1,740	84
15	1,100	64	1,120	66	+2	1,060	64
16	920	55	960	51	-4	820	48
17	880	77	620	66	-11	580	80
18	300	88	260	87	-1	240	62
19	520	98	390	70	-28	230	72
20	1,040	88	1,100	86	-2	960	84
21	800	83	800	77	-6	760	69
22	3,360	79	3,400	75	-4	3,160	71
Mean		78		73	-5		70

Mean F.E.V.₁% in boys, 84.6%; mean F.E.V.₁% in girls, 88.6% (Strang, 1959).

* F.E.V.₁% is not a valid figure at this girl's age and height.

Summary

Eleven children with varying degrees of ventilatory deficiency due to mucoviscidosis were given chymoral tablets, containing trypsin and α -chymotrypsin, over a period of three months in half the adult dosage—that is, one tablet six-hourly. Comparing them with a control group of 11 children with mucoviscidosis of approximately similar clinical severity who were given dummy tablets, no significant changes were noted in two standard parameters of ventilatory function—namely, forced vital capacity and one-second forced expiratory volume expressed as a percentage of forced vital

capacity. This was associated with no subjective change in the clinical findings in the two groups.

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REFERENCES

- Avakian, S. (1961). *New Engl. J. Med.*, **264**, 764.
Bruce, R. A., and Quinton, K. C. (1962). *Brit. med. J.*, **1**, 282.
Strang, L. B. (1959). *Thorax*, **14**, 305.

Medical Memoranda

Occurrence of Adenovirus Type 21 in Great Britain

The adenoviruses most frequently causing human infections in Great Britain belonged, until recently, to types 1–8 and 14. Types 3, 4, 7, and 14 were mainly associated with outbreaks of respiratory disease among recruits or schoolchildren; type 8 with outbreaks of epidemic keratoconjunctivitis among shipyard workers; and types 1, 2, 5, and 6 with sporadic infection in children.

In 1961 Zhdanov and Dreizin reported the isolation in 1957–8 of a new adenovirus type from young adults with upper respiratory infections. This strain was designated type 19 by these workers, but was subsequently found (personal communication from Dr. R. Huebner) to be identical with type 21, previously isolated by Bell *et al.* (1960) from a case of trachoma in Saudi Arabia. The same virus type was found by van der Veen and Dijkman (1962) to be causing outbreaks of respiratory infection among military recruits in Holland in 1960–1, and it has been isolated in India by Kurian *et al.* (1962) from outbreaks of respiratory disease among military recruits during the winter of 1961–2. Until 1962 its isolation had not been reported in Great Britain. Since February, 1962, however, this virus type has been isolated with some frequency in different parts of the country from patients of all ages suffering from a variety of respiratory syndromes. It has also been found in the stools of apparently normal children.

In order to estimate the presence of this serotype in previous years a serological survey was carried out with sera from comparable groups obtained before and after the first isolation of this virus. Because of the importance of adenoviruses among military personnel sera obtained in 1960 from R.A.F. recruits were also examined. A later comparable group could not be studied because recruits were not available.

MATERIALS EXAMINED

Adenovirus strains were isolated in various public health laboratories from specimens obtained from cases of respiratory infection or from stools of normal children under 5 years of age examined in the course of an enterovirus survey. These strains were sent for identification to the Virus Reference Laboratory, where neutralization tests were done with rabbit antisera prepared with the prototype adenoviruses, including type 21 (kindly supplied by Dr. J. van der Veen). Sera sent to the laboratory for the routine estimation of anti-streptolysin titres were collected over a period of several weeks from November, 1961, until January, 1962 (406 samples) and from April until June, 1962 (196 samples).