SIMPLIFIED INTRAVENOUS OXYTOCIN-SENSITIVITY TEST

BY

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Amniotomy to induce labour has become a common practice in modern obstetrics, but failure of labour to commence within one or two days of the procedure is a serious problem. Foetal and maternal morbidity or mortality due to infection could be reduced by lowering the induction "failure" rate. In cases in which it could be forecast that labour was unlikely to follow amniotomy it would sometimes be preferable to perform caesarean section without the associated risks of prior amniotomy. The sensitivity of the uterus to a small dose of oxytocin offers a possible means of forecasting when surgical induction of labour is likely to be successful.

Smyth (1954) described an oxytocin-sensitivity test and gave results for a small number of cases. Later (Smyth, 1958a, 1958b) he reported a larger series. In his first report Smyth correlated the amount of intravenous oxytocin required to produce a uterine contraction with the subsequent time interval to the onset of spontaneous labour. In his later reports, however, he associated the sensitivity test result with the amniotomy-labour interval. Other authors have reported the use of the test in forecasting the spontaneous onset of labour (Müller, 1958; Göltner, 1959; Husslein and Baumgarten, 1960; Husslein *et al.*, 1960; Birmanac, 1960; McCarthy and Fugo, 1961). Schwarcz *et al.* (1960) used the test in 12 cases, relating the results to the ease of inducing labour with an intravenous oxytocin infusion. Apart from Smyth, only Husslein and his colleagues have studied the test in relationship to amniotomy.

A similar oxytocin-sensitivity test, using the nasal mucosa for absorption, has also been employed to forecast the success of amniotomy, intravenous oxytocin infusion, or nasal oxytocin in initiating labour (Hendricks, 1960; Baumgarten and Hofhansl, 1961a, 1961b). The latter authors correlated the intravenous test with the nasal response.

Smyth's original test employed a tokodynamometer and required two observers. Göltner (1959) concluded that palpation alone could not detect accurately the weak contractions produced in the test. Husslein and Baumgarten (1960) and Husslein *et al.* (1960), however, showed that simple palpation was satisfactory, and this was confirmed by Schwarcz *et al.* (1960) and by McCarthy and Fugo (1961). It is therefore possible for a single observer to perform the test, using one hand to palpate the uterus and the other to give the intravenous injection. Smyth, as do most of the other authors using this test, advocates a 15-minute period with the patient at rest in the dorsal position to allow uterine tone to fall, and the rate of spontaneous contractions can be noted. Husslein *et al.* (1960) suggested the test be repeated after 24 hours to eliminate errors from spontaneous contractions occurring during the test. In this series no preliminary rest phase was used and repeat tests were not carried out, the results being evaluated on a single observation. The test was thus not time-consuming and required no special apparatus.

Technique

The patient lay in the dorsal position in bed and the test was explained to allay any fear which might lead to increased uterine or abdominal tone. She was asked to report any symptoms occurring during the test. A 5-ml. syringe containing 0.05 international unit of synthetic oxytocin ("syntocinon") in 5 ml. of sterile water was used and the needle introduced into an antecubital vein.* The observer sat on the patient's right side facing towards her head, so that the intravenous injection rate could be controlled by the left hand while uterine tone was assessed by the right hand gently gripping the uterus below the umbilicus.

In only one case did the needle-prick lead to an increase in abdominal resistance or uterine tone, and in the absence of this the injection was begun at once. The solution was injected slowly and continuously at the rate of 1 ml. or 0.01 unit of oxytocin in one minute. The injection was stopped when the uterus contracted or when 5 ml. of solution (0.05 unit) had been injected. The test was recorded as "positive" if a contraction occurred during the five minutes of the injection. Braxton Hicks contractions occurred only three times in 154 tests and could be distinguished by the lack of maternal discomfort. High resting uterine tone interfered with palpation in only two patients, both of whom were post-mature. Hydramnios did not prevent contractions being detected. Labour appeared to be initiated by the test in one case. No ill effects that could be attributed to the procedure were noted during or after the tests.

The test was performed on patients when a decision to carry out amniotomy had been made, and the results were not used to influence the decision in this series. A total of 154 tests were performed on 144 patients. The few repeat tests were done when the obstetrician in charge postponed amniotomy until a later date. The postponement was always for some reason other than the result of the oxytocin-sensitivity test. Most of the inductions were done within two hours of the test, and only those cases in which amniotomy was carried out within six hours of the test are analysed.

Results

One hundred and six patients had amniotomy performed within six hours of a sensitivity test, but one of these was delivered by caesarean section on account of foetal asphyxia within two hours of amniotomy, before labour had commenced. Therefore 105 cases are available for analysis. Ninety-eight of these went into labour following amniotomy and seven had caesarean section performed without labour having started. Six of these were in the negative test group. The one patient with a positive test response had 24½ hours "trial of induction" before caesarean section was carried out. She was included in the 24-hour analysis but excluded from the 48-hour analysis, and the others were treated similarly. These patients were included in amniotomy-labour calculations, using the amniotomy-caesarean section time as an alternative.

The Chart shows graphically the percentage in labour up to 36 hours after amniotomy, and Table I shows

*The test solution was made up by adding 0.25 unit of oxytocin in 1 ml. of water to 25-ml. vials of sterile water with 0.1% chlorocresol from which 1 ml. of water had previously been withdrawn. By this means solution for several tests could be prepared at once.

the number in the positive and negative groups who were in labour within 24 and 48 hours.

The Chart shows that 53.4% of positive patients had started labour within five hours, compared with 24% of negative patients. Within 24 hours 76.8% of the patients in the positive group had started labour compared with

Percentage of patients in labour up to 36 hours after amniotomy.

TABLE I.—Oxytocin-sensitivity Test Followed by Amniotomy. Number of Patients in Labour Within 24 and 48 Hours

Dose of Oxytocin (International Units)	Cases	Labour Within	
		24 Hours	48 Hours
<i>Positive Test</i>			
(a) Up to 0.01 ..	2	2 (100%)	2 (100%)
(b) 0.011 to 0.02	4	3 (75%)	4 (100%)
(c) 0.021 „ 0.03	17	15 (88.2%)	17 (100%)
(d) 0.031 „ 0.04	21	13 (62%)	17 of 20* (85%)
(e) 0.041 „ 0.05	12	10 (83.3%)	10 (83.3%)
Total ..	56	43 (76.8%)	50 of 55* (90.9%)
<i>Negative Test</i>			
	49	27 of 48* (56.3%)	35 of 46* (76.1%)

* The discrepancies in totals arise from cases in which caesarean section was performed, without labour commencing, in less than the specified 24- or 48-hour period.

56.3% of the negative group, while at 48 hours 90.9% of the positive group had started in labour compared with 76.1% of the negative group. If only patients with a positive result up to 0.03 unit of oxytocin are considered, 87% of these were in labour within 24 hours and 100% had started within 48 hours. The longest amniotomy-labour interval in this group was 30 hours 40 minutes. The numbers in labour at 24 and 48 hours in the positive and negative test groups are significantly different at the 5% level ($\chi^2=4.9$ and 4.12 respectively).

Table II shows the same test groups and gives the mean times from amniotomy to the onset of labour, or to the time of caesarean section if done before labour commenced. It also shows the mean length of labour in each group. Six of the seven patients who did not go into labour were in the negative test group, in which the mean amniotomy-labour interval is therefore probably under-represented in relation to the positive group.

The mean amniotomy-labour interval in the positive group was 13 hours 15 minutes, while in the negative group it was 41 hours 22 minutes. In the negative test group two patients were undelivered a week after amniotomy. If these are excluded the mean time to labour falls to 28 hours 1 minute. Cases positive to 0.03 unit or less of oxytocin gave a mean time to labour of

8 hours 24 minutes, and those from 0.031 to 0.05 unit gave a mean time of 16 hours 37 minutes.

The mean length of labour in the positive and negative groups was closely similar, being 9 hours 29 minutes and 10 hours 8 minutes respectively.

The data were examined to determine whether other factors were influencing the results, as it was found that

TABLE II.—Oxytocin-sensitivity Test Followed by Amniotomy. Mean Times from Amniotomy to Onset of Labour

Group as in Table I	Cases	Mean Time to Labour*	Mean Length of Labour
<i>Positive Test</i>			
a	2	2 hr. 10 min.	2 hr. 52 min.
b	4	12 .. 52 ..	7 .. 31 ..
c	17	8 .. 5 ..	8 .. 52 ..
d	21	17 .. 32 ..	10 .. 44 ..
e	12	15 .. 2 ..	10 .. 51 ..
Total	56	13 hr. 15 min.	9 hr. 29 min.
<i>Negative Test</i>			
	49	41 hr. 22 min.	10 hr. 8 min.

* The time given in this and subsequent tables is the time from amniotomy to the onset of labour or to the time when caesarean section was performed in the seven cases that did not go into labour. Six of these cases were in the negative test group, the other in group d.

a few patients giving negative tests were in labour less than an hour after amniotomy, whereas others with positive tests had an induction-labour interval of 24 hours or more. The results were considered in relation to four factors: (1) the length of gestation, (2) parity, (3) age, and (4) mode of amniotomy. No attempt was made to correlate the results with "ripeness" of the cervix, because this was recorded by different observers who might vary in their assessment.

1. Variations with Length of Gestation

The cases were divided into three groups: those in whom test and induction were performed (a) eight or more days before the estimated date of delivery (*pre-term*); (b) between seven days before and seven days after term (*term*); and (c) eight or more days past term (*post-term*). The numbers of positive and negative tests obtained were similar in each chronological group. Table III shows the results in the three groups in terms of percentage in labour 24 and 48 hours after amniotomy and mean time to labour (or to caesarean section).

The pre-term group shows the most striking differences. Of 14 patients with positive tests 13 (93%) had started labour within 4 hours 35 minutes, the remaining patient, who was induced 30 days before term, was delivered by caesarean section 24½ hours after amniotomy because of severe pre-eclampsia, when she had not started labour. There were 12 patients with a negative test in the

TABLE III.—Effect of Length of Gestation on Oxytocin Sensitivity

TABLE IX: Effect of Length of Gestation on Delivery Time				
Group	Cases	Labour Within		Mean Time to Labour
		24 Hours	48 Hours	
Positive Test				
Pre-term ..	14	13 (93%)	13 of 13* (100%)	3 hr. 23 min.
Term ..	23	18 (78.3%)	20 (87%)	15 „ 8 „
Post-term ..	19	12 (63.2%)	17 (89.5%)	18 „ 14 „
Negative Test				
Pre-term ..	12	2 (16.7%)	4 of 11* (36.4%)	107 hr. 21 min.
Term ..	20	12 of 19* (63.2%)	16 of 18* (89%)	20 „ 36 „
Post-term ..	17	13 (76.5%)	15 (88.2%)	19 „ 19 „

* The discrepancies in totals arise from cases in which caesarean section was performed, without labour commencing, in less than the specified 24- or 48-hour period.

pre-term group. Only two of these started labour within 24 hours and another two in the succeeding 24 hours. Four were eventually delivered by caesarean section because of failure to go into labour, approximately 42, 49, 74, and 165 hours after amniotomy. To stress the unreliability of amniotomy in a pre-term patient with a negative sensitivity test the amniotomy-labour intervals in the other eight patients are recorded, being 5, 9, 41, 45, 72, 72, 201, and 511 hours approximately. The mean time to labour or delivery was 3 hours 23 minutes in the positive group and 107 hours 21 minutes in the negative group.

In the pre-term group statistical analysis of the numbers in labour at 24 and 48 hours shows highly significant differences ($\chi^2=12.4$, $P<0.001$; and $\chi^2=8.8$, $P<0.005$ respectively).

In the term group 18 of 23 (78.3%) patients with positive results were in labour within 24 hours of amniotomy compared with 12 of 19 (63.2%) with negative tests. In this group and the post-term group the numbers in labour 24 hours after amniotomy were not significantly different and were virtually the same at 48 hours for positive or negative results (88% approximately). The mean amniotomy-labour intervals were thus significantly different only in the pre-term group.

2. Variations with Parity

Seventy-six patients were parous and 29 primigravid. The results related to parity are shown in Table IV. In the primigravid positive group 14 of 15 (93.3%) were in labour within 24 hours, compared with 9 of 13 (69.2%) in the negative group, and at 48 hours the figures are 93.3% and 90.2% respectively. Of the parous patients with a positive test 29 of 41 (70.7%) were in labour within 24 hours of amniotomy, compared with 18 of 35 (51.4%) with a negative test. These differences are not statistically significant at the 5% level.

TABLE IV.—Relationship Between Sensitivity Test and Parity

Group	Cases	Labour Within	
		24 Hours	48 Hours
Positive Test			
Primigravidae ..	15	14 (93.3%)	14 (93.3%)
Multiparae ..	41	29 (70.7%)	36 of 40* (88%)
Negative Test			
Primigravidae ..	14	9 of 13* (69.2%)	12 of 13* (90.2%)
Multiparae ..	35	18 (51.4%)	23 of 35* (69.7%)

* The discrepancies in totals arise from cases in which caesarean section was performed, without labour commencing, in less than the specified 24- or 48-hour period.

3. Variations with Age

The relationship of the test results with the mother's age is shown in Table V, and, although it appears that response to amniotomy was better and more rapid in

TABLE V.—Results of Sensitivity Test Grouped According to Age

Age	Labour Within		Mean Time to Labour
	24 Hours	48 Hours	
Positive Test			
35 or over ..	8 of 11	11 of 11	11 hr. 4 min.
Under 35 ..	35 of 45	39 of 44*	13 „ 47 „
Negative Test			
35 or over ..	7 of 11	10 of 11	20 hr. 47 min.
Under 35 ..	20 of 37*	25 of 35*	45 „ 31 „

* The discrepancies in totals arise from cases in which caesarean section was performed, without labour commencing, in less than the specified 24- or 48-hour period.

those aged 35 or over, the differences are not statistically significant.

4. Variations with Method of Amniotomy

All sensitivity tests, but only 52 of the amniotomies, were performed personally. In these 52, rupture of the forewaters was performed in 40 cases and hindwater rupture in 12. Of the 53 who had amniotomies carried out by others forewater rupture was performed in only 11 cases; hindwater rupture was not employed particularly in difficult cases—for example, patients with a "high head"—but merely because it was the preference of individual operators.

Table VI shows the results subdivided according to the method of amniotomy. It is seen that the efficiency of the sensitivity test in forecasting the onset of labour after amniotomy is uninfluenced by the method of amniotomy, although clearly forewater rupture is more efficient than hindwater rupture in inducing labour. After a positive test the mean forewater amniotomy-labour interval was 7 hours 21 minutes, whereas the mean hindwater amniotomy-labour interval was 20 hours 4 minutes.

TABLE VI.—Results of Oxytocin-sensitivity Test and Variable Effect from Method of Amniotomy

Group	Cases	Labour Within		Mean Time to Labour
		24 Hours	48 Hours	
Positive Test				
Forewater amniotomy	30	26 (86.7%)	30 (100%)	7 hr. 21 min.
Hindwater " "	26	17 (65.4%)	20 of 25* (80%)	20 " 4 "
Negative Test				
Forewater amniotomy	21	15 (71.4%)	18 (85.7%)	23 hr. 11 min.
Hindwater " "	28	12 of 27* (44.4%)	17 of 25* (68%)	55 " 3 "

* The discrepancies in totals arise from cases in which caesarean section was performed, without labour commencing, in less than the specified 24- or 48-hour period.

Comparison with Rapid-injection Technique

In 20 patients the test was also performed as detailed by Smyth (1958a) in addition to using the method described here. In Smyth's technique 1 ml. of oxytocin solution of the same strength is injected rapidly at one-minute intervals to a maximum of 5 ml. The total maximum dose employed is therefore the same, as is the amount injected at any minute after beginning the test. The interval between performing the two tests on each patient was one hour. The test employed first was selected at random, 9 of the 20 being tested by Smyth's method first. In 14 cases both tests were negative. In two cases one test alone gave a positive result, both responses being recorded as weak, one being by each method. Four patients gave a positive response to each test; the results are shown in Table VII.

TABLE VII.—Comparison Between Two Methods of Performing an Oxytocin-sensitivity Test in 20 Cases

Smyth's Method	Present Series Method
Positive 0.03 unit	Positive 0.04 unit
" 0.012 "	" 0.02 "
" 0.032 "	" 0.04 "
" 0.042 "	" 0.02 "
Weak positive 0.028 unit	Negative
Negative	Weak positive 0.05 unit
" (14 patients)	Negative (14 patients)

Subsequent Oxytocin Infusions

Oxytocin was given by intravenous infusion in seven cases when amniotomy had not led to labour. Three had a positive sensitivity test, and infusion led to labour in two of these patients within a short time. Of four

patients with a negative test, only one was stimulated into labour by the infusion. The results in these seven cases are shown in Table VIII, but no conclusions can be drawn from them.

TABLE VIII.—*Oxytocin Infusions Following Amniotomy*
(7 Cases)

Sensitivity Test	Amniotomy- Infusion Interval	Infusion to Labour if Successful	Labour After Failed Infusion
Positive (0.04 unit)	24 hours	3 hours	—
" (0.038 ")	48 "	2 "	—
" (0.032 ")	48 "	—	40 hours later
Negative	48 and 144 hours	—	C.S. 7 days after amniotomy
"	48 hours	—	30 hours later
"	48 "	—	21 days "
"	68 "	1 hour	—

Discussion

From these results the oxytocin-sensitivity test appears to be of value in eliminating unsuccessful surgical induction of labour, thus reducing the intrauterine infection rate. It seems that the test is not influenced by the age or parity of the patient. This agrees with the findings of Müller (1958) and Göltner (1959).

In this series the stage of gestation strongly influenced the accuracy of the sensitivity test. In those patients eight or more days before the estimated date of delivery with a positive test, 93% were in labour within 24 hours of amniotomy, compared with 16.7% of those with a negative test. The test therefore is of particular use in deciding whether to carry out amniotomy between 34 and 39 weeks' gestation, by giving an accurate forecast of its effect. This situation is likely to arise in cases of pre-eclampsia and severe rhesus iso-immunization. In these cases the foetus is already at risk, and a trial of surgical induction with little chance of success will increase the foetal hazards.

For example, one patient with severe pre-eclampsia had a positive test at 36½ weeks' gestation. Amniotomy was carried out and within three hours she had a normal delivery of a child of 2 lb. 9 oz. (1,160 g.). In contrast, a case of severe rhesus iso-immunization with a negative test had an amniotomy nine days before her estimated date of delivery, and 165½ hours later caesarean section had to be carried out. Labour had not started, and *Proteus vulgaris* was cultured from the vagina. The foetus thus ran the double risk of erythroblastosis and intrauterine infection. The test suggested that labour would not rapidly follow amniotomy, and elective caesarean section would have been preferable.

Smyth (1958a) recommended amniotomy with a positive test response to 0.03 unit of oxytocin or less, all of 36 cases recorded by him being in labour or delivered within 24 hours of induction. Using the same criteria, Husslein and Baumgarten (1960) found 108 of 164 cases (65.8%) in labour in the same interval, and in the present

series 20 of 23 (87%) had started in labour. Table IX shows the results of amniotomy following a positive sensitivity test to 0.03 unit or less of oxytocin. It is seen that 48 hours after amniotomy 100% of the present series and 97% of Husslein and Baumgarten's (1960) cases were in labour or delivered after a positive test to 0.03 unit. Husslein, in fact, suggested that amniotomy should be carried out only on patients with a positive test to 0.01 unit of oxytocin. This, however, would mean the virtual abandonment of surgical induction; only 2 of the present series of 105 cases would have been recommended for amniotomy.

Some authors (Smyth, 1954; Göltner, 1959; McCarthy and Fugo, 1961) have suggested that a positive sensitivity test indicates imminent labour. Table IX shows their results for spontaneous labour following a positive oxytocin test up to 0.03 unit, for comparison with those treated by amniotomy. Within 24 hours of a positive test and without amniotomy about 15% were in labour, and within 48 hours about 27% had started labour. If pregnancy is to be terminated within a short time amniotomy is therefore required. If only those with a positive test to 0.01 unit or less of oxytocin are considered, 73 of 76 patients in the amniotomy series (Smyth, 1958b; Husslein and Baumgarten, 1960; present series) were in labour within 24 hours, whereas in the non-amniotomy series (Göltner, 1959; Birmanac, 1960; McCarthy and Fugo, 1961) approximately 58 of 122 patients were in labour within the same period (Smyth's cases are not included as his data were insufficient). It thus appears that, even with evidence of high oxytocin sensitivity, less than 50% of patients can be expected to commence labour in a short period without amniotomy.

In the present series 17 of 36 women (48%) showed no response to 0.05 unit of oxytocin eight or more days past the estimated date of delivery. The weight and appearance of the infants born to these women suggested that they were "post-mature." The test thus seems to be of little use in confirming suspected post-maturity. This is in agreement with the findings of Müller (1958), Göltner (1959). Husslein *et al.* (1960) state that the test helps in deciding if term has been passed, but they do not support this by figures. It is possible that increased uterine tone past term masks slight contractions induced by the test and false-negative results are obtained. In this group of cases the use of a tokometer might give more accuracy.

The physiological basis for the test is not certain. An oxytocin-inhibiting enzyme which inactivated oxytocin on incubation *in vitro* within a few minutes has been shown in human and animal plasma by Page (1946) and others. Page found that oxytocinase activity rose steadily to term, with no fall until after delivery. Caldeyro-Barcia (1960) also reported no fall in oxytocinase activity prior to or during labour. One must assume, therefore, that increased natural oxytocin secretion from the pituitary gland occurs at the time of labour. Shortly before this time, it may be postulated, injected synthetic oxytocin raises the plasma oxytocin level to a critical value in relation to the oxytocinase level, and a uterine contraction results.

Summary

A simplified oxytocin-sensitivity test is described which can be performed by one person without special equipment in under 10 minutes. A positive response

TABLE IX.—*Results with a Positive Test Up to 0.03 Unit*

Author	Cases	Labour Within		Amniotomy
		24 Hours	48 Hours	
Smyth (1958b) ..	36	100%	100%	Yes
Husslein and Baum- garten (1960) ..	164	65.8%	97%	"
Present series ..	23	87%	100%	"
Göltner (1959)* ..	173	10.9%	22%	No
McCarthy and Fugo (1961)* ..	118	12.7%	30.5%	"
Birmanac (1960) ..	19	0%	0%	"
Smyth (1954) ..	10	100% (positive to 0.02 unit)	—	"

* These results are approximate, being deduced from diagrams and text.

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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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.