AN INVESTIGATION INTO THE COMPARATIVE EFFICACY OF CERTAIN INHALANTS IN THE TREATMENT OF ASTHMA

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An investigation has been carried out at the Asthma Clinic, St. David's Hospital, Cardiff, into the efficacy of various inhalants commonly used in the treatment of asthma. This was prompted by the desire to have statistical information upon which to base advice to doctors and patients rather than to rely on the more prevalent but less scientific clinical impressions. The inhalants used and their costs are as follows :

	Hospital Price per fl. oz.	Retail Price per fl. oz.
	s. d.	s. d.
"Riddobron"	11 5	17 0
"Brovon"	8 0	13 6
"Neo-epinine" No. 2	9 6	15 9
Neb. adrenal. et atrop. co. (*N.F.*)	1 1½	3 6
A control mixture of water and glycerin 15%		

An indication of the cost to the hospital services is given by the fact that the cost of inhalants for one year was £260 for two Cardiff hospitals.

Method

Nineteen patients were selected to take part in the investigation; their asthma had been fairly constant. All except two had previously used inhalers. The investigation began on October 3, 1950.

The solutions to be tested were supplied in small bottles, identified by letters, A, B, C, D, E, F, G, H, and I. The bottling and labelling were performed by the pharmacist at St. David's Hospital, and he alone knew the key to the contents of the bottles. The key was:

Riddobron	A and F
Neo-epinine No. 2	B and G
Brovon	C and H
Neb. adrenal. et atrop. co.	D and I
Control	E

The arrangement of the experiment initially was that each patient should use the five inhalants A, B, C, D, and E for one weekly period each. The patients were divided into five groups, and each group was given a different inhalant for the first weekly period. For the next four periods each group was issued with the inhalants next in alphabetical order. Thus one group was issued with the inhalants in the order A, B, C, D, and E; another in the order B, C, D, E, and A, and so on. This procedure was adopted to minimize external influences, such as the weather, on the testing conditions for any one inhalant.

After the first five periods, when all the inhalants had been used by each patient, the patients were reissued with the inhalants (except the control), but in different orders and under new labels. For this part of the investigation the patients were divided into two groups, one group using the inhalants in the order G, I, F, and H, and the other in the reverse order. The patients were not informed that the same inhalants were being used. By this means a direct comparison, in successive weeks, of all the inhalants except the control was possible. During the first five weeks a control mixture was used, but in 16 out of 17 cases it was regarded as giving incomplete or no relief, and in some cases had to be given up. Its use was therefore discontinued, for the object of the investigation was to examine the comparative, and not the absolute, values of the inhalants.

Patients were normally seen at weekly intervals, and at each visit were given a supply of different inhalant and a card upon which to record the number of times the inhalant was used during each 12 hours for the period, any other treatment found necessary, and any untoward happenings which might have affected them. Patients were instructed that if they were unable to attend in one week they should continue using the inhalant issued and attend the next week. They were asked to discontinue using any particular inhalant only if attacks were quite uncontrolled by it or if it was too unpleasant to use.

At each visit the patient's assessment of the relief obtained from the inhalant just used ("good," "incomplete," or "no relief") and the incidence of side-effects were recorded. Inquiries were made regarding any alteration in his health or normal routine and its effect on his asthma.

The patient's comparison of the inhalant with the previous one used was recorded as "better," "worse," or "same." In making the comparison the criteria used were the speed of action, the frequency of use, the degree of relief, the side-effects experienced, and the amount of other symptomatic treatment required; all these factors were taken into account by the patient. Alterations in asthmatic states were also considered. If, for example, a patient's asthma was worse during one period and an inhalant had to be used more often than that in the next period, he might still prefer the former, making due allowance for his condition.

The survey began with 18 patients, and one joined during the third week of the survey. Not all were able to complete the full course of inhalants; 12 used all the inhalants, one used eight, one used seven (although issued with eight), one used six, three used five, and one used four. Table I shows the number of periods each inhalant was used and the number of patients who used each inhalant for two periods, under different labels. Thus six patients used riddobron as A and 13 used it once as A and later as F.

TABLE I.—*Number of (weekly) Periods Each Inhalant Used*

	Riddobron	Neo-epinine No. 2	Brovon	N.F. Mixture	Control
No. of patients using inhalant for 2 periods ..	13	15	12	15	0
No. of patients using inhalant for 1 period ..	6	4	7	4	17
Total periods used ..	32	34	31	34	17

Results: (1) Comparative Assessment of the Inhalants

The inhalants, except the control, were all used on successive weeks and a direct comparison was made possible.

Table II shows which pairs of inhalants were used on successive weeks by each patient and the preference of the patient. The Table is not chronologically arranged and does not show the order in which the inhalants were used. The paired names at the top indicate the inhalants compared, and the names in the columns underneath which of the inhalants were preferred; the letter O indicates that the patient had no preference and thought them equally good or bad. The total at the foot of each column shows the number of times each pair of inhalants was compared. Thus in the comparison of riddobron and neo-epinine No. 2, which was made 16 times, riddobron was preferred on four occasions, neo-epinine No. 2 on 11 occasions, and on one occasion no preference was made.

TABLE II.—*Results of Comparing Inhalants on Successive Weeks*

Case No.	Ridd./Neo-ep.	Neo-ep./Bro.	Bro./N.F.	Ridd./Bro.	Ridd./N.F.	Neo-ep./N.F.	Ridd./Cont.	N.F./Cont.
1	Neo-ep.	Bro.	Bro.	Bro.	N.F.	O	—	N.F.
2	,,	—	,,	,,	O	O	O	,,
3	,,	O	,,	Ridd.	Ridd.	Neo-ep.	Ridd.	—
4	—	Neo-ep.	N.F.	Bro.	N.F.	,,	,,	N.F.
5	Neo-ep.	—	Bro.	Ridd.	Ridd.	O	,,	,,
6	Ridd.	Bro.	,,	,,	N.F.	Neo-ep.	—	Cont.
7	O	,,	—	O	Ridd.	N.F.	Ridd.	N.F.
8	Neo-ep.	Neo-ep.	O	Bro.	O	,,	,,	—
9	,,	—	N.F.	Ridd.	N.F.	,,	,,	N.F.
10	Ridd.	Bro.	Bro.	Bro.	O	Neo-ep.	—	Cont.
11	Neo-ep.	,,	—	,,	Ridd.	,,	Ridd.	N.F.
12	—	Neo-ep.	N.F.	Ridd.	,,	,,	,,	,,
13	—	O	O	—	O	O	,,	,,
14	Ridd.	Neo-ep.	—	—	—	N.F.	,,	,,
15	Neo-ep.	O	—	—	—	O	—	—
16	,,	Bro.	N.F.	—	—	—	Ridd.	—
17	Ridd.	Neo-ep.	,,	—	—	—	,,	—
18	Neo-ep.	O	—	—	—	—	,,	N.F.
19	,,	Neo-ep.	N.F.	—	—	—	—	—
Total ..	4 Ridd. 11 Neo-ep. 1 O	6 Bro. 6 Neo-ep. 4 O	6 Bro. 6 N.F. 2 O	5 Ridd. 6 Bro. 1 O	5 Ridd. 4 N.F. 4 O	4 N.F. 6 Neo-ep. 5 O	13 Ridd. 1 O	2 Cont. 11 N.F.
	16	16	14	12	13	15	14	13

Abbreviations indicate which inhalant of each pair was preferred: O indicates no preference. Ridd. = Riddobron. Neo-ep. = Neo-epinine No. 2. Bro. = Brovon. N.F. = Neb. adrenal. et atrop. co. (*N.F.*). Cont. = Control, water and glycerin 15%. — = No comparison made.

TABLE III.—*Effectiveness of Inhalants*

	No. Periods Used	Relief			No. Times Discontinued
		Good	Incomplete	No Relief	
Riddobron	32	21	9	2	2
Neo-epinine No. 2 ..	34	24	9	1	1
Brovon	31	21	8	2	3
N.F. mixture	34	20	11	3	2
Control	17	1	5	11	4
Total	148	87	42	19	12

(2) Relief Obtained from the Inhalants

Table III shows the number of periods of one week each inhalant was used, the relief obtained, and the number of periods in which each inhalant had to be discontinued. In ascertaining the degree of relief the patient's impressions were used, as no satisfactory objective criteria could be found. Thus the time elapsing before relief is felt can vary from immediately to five minutes in different persons, all of whom may call the relief obtained from the inhalant good. Each inhalant was used about the same number of times, except the control, which was abandoned after the first five weeks.

It will be seen that inhalants were discontinued on 12 occasions, on each occasion due to insufficient relief being given, except one which was discontinued because of unpleasant side-effects. One patient discontinued riddobron, neo-epinine No. 2, brovon, and the neb. adrenal. et atrop. co., the latter on two occasions. He was a chronic asthmatic who had severe asthma. Riddobron was discontinued on another occasion by a patient who had a severe cold which worsened her asthma. She reverted to her usual brovon, but had to use that frequently. Brovon was discontinued on another occasion by a patient who suffered an exacerbation of his asthma during the period. On another occasion it was discontinued by a patient whose asthma was not worse than usual but who noted unpleasant effects. The control mixture was discontinued on four occasions. Three of the patients had their usual asthma on these occasions; the fourth had an exacerbation due to a superadded chest infection.

(3) Side-effects of the Inhalants

Table IV shows the side-effects obtained with these inhalants and the frequency with which they occurred. It will be seen that the control mixture gave rise to unpleasant side-effects on very few occasions. The other inhalants were used for 131 periods, for 79 periods with side-effects. The commonest side-effects seen were dryness, oral and pharyngeal irritation, unpleasant taste, and cough. Less common side-effects were nausea, palpitation, sneezing, headaches, and chest pain.

TABLE IV.—*Side-effects of Inhalants*

Inhalant	Total Periods Used	Periods Used with Side-effects	Dryness	Irritation	Taste	Cough	Nausea	Palpitation	Sneezing	Headache	Chest Pain
Riddobron ..	32	14	6	4	3	3	1	1	1	1	—
Neo-epinine No. 2	34	25	12	7	8	4	1	2	4	—	—
Brovon ..	31	20	8	10	7	5	3	—	1	1	1
N.F. mixture ..	34	20	7	10	10	4	—	2	1	—	—
Control ..	17	7	3	2	1	3	—	1	—	—	—
Totals ..	148	86	36	33	29	19	5	6	7	2	1

Table V shows the incidence of side-effects reported with each inhalant and the total number of side-effects reported with each inhalant. Thus, for example, riddobron was used for 14 periods when side-effects were recorded. In nine of these periods only one side-effect was reported, and in only one period were three side-effects recorded.

TABLE V.—*Showing Incidence of Side-effects with Each Inhalant*

	Riddobron	Neo-ep. No. 2	Brovon	N.F. Mixture	Control
No. periods used with side-effects	14	25	20	20	7
No. periods used with:					
1 side-effect	9	16	11	11	3
2 side-effects	4	5	4	4	2
3 ,, ,, ...	1	4	3	5	1
4 ,, ,, ...	—	—	2	—	—
Total side-effects	20	38	36	34	10

Table VI shows the number of periods the different inhalants were used without any side-effects being recorded and the degree of relief obtained during these periods. Thus, for example, it will be seen that riddobron was used for 32 periods; no side-effects were recorded in 18 periods: of these 18 periods good relief was obtained in 13, incomplete relief in four, and no relief in one.

TABLE VI.—*Effectiveness of Inhalants Used Without Side-effects*

	Total Periods Used	Total Periods Used with No Side-effects	Relief		
			Good	Incomplete	No Relief
Riddobron	32	18	13	4	1
Neo-epinine No. 2 ..	34	9	6	2	1
Brovon	31	11	7	2	2
N.F mixture ..	34	14	8	4	2
Control	17	10	1	2	7

(4) Comparison of Assessments of Inhalants

As a test of the patients' reliability and consistency in the assessment of the relief obtained from the inhalants, their assessments of the same inhalants used under different letters have been examined. The results are shown in Table VII.

TABLE VII.—*Comparison of Inhalants Used Under Different Letters*

Inhalant	No. Patients Who Used Inhalant Twice	No. Patients Giving Different Assessment	Reason for Difference	
			No Apparent Reason	Exacerbation of Asthma
Riddobron A and F	13	3	1	2
Neo-epinine No. 2 B and G ..	15	5	1	4
Brovon C and H ..	12	6	3	3
N.F. mixture D and I	15	3	1	2
Totals ..	55	17	6	11

Thus riddobron was used twice (as A and F) by 13 patients. Three gave a different assessment when they used it a second time. With one patient there was no apparent reason for the difference. The other two had an exacerbation of their asthma when they gave a different assessment.

In connexion with the variation in assessment it is interesting to study the patients' assessment of their usual inhalants when they were used as unknown inhalants. Most patients had one usual inhalant, and two used two inhalants regularly. They all regarded their usual inhalants as being of great value and capable of affording good relief.

Six patients customarily used riddobron, and during the experiment five of them used it twice as A and F. Three of the five patients assessed the relief as good on both occasions. Two of the five assessed the relief as good on one occasion and incomplete on another during an exacerbation of the asthma. One patient used it once only, and assessed the relief as good.

Eleven patients customarily used brovon, and during the experiment eight of them used it twice as C and H. Three of the eight patients assessed the relief as good on both occasions. Five of the eight assessed the relief as incomplete on one occasion and good on another. On three of the "incomplete" occasions there was a worsening of the asthma; on one there was no apparent reason, and on the last the patient actually discontinued using the inhalant as C because of lack of relief and reverted to his own brovon. When he used brovon as H he gave it a good assessment. The remaining 3 of the 11 patients used brovon as C. One found the relief good, another incomplete (for no apparent reason), and the third discontinued the inhalant owing to lack of relief and reverted to his own brovon.

(5) Study of Frequency of Use of Inhalants

Patients recorded on a card the number of times they had recourse to each inhalant during every 12-hour period—9 a.m. to 9 p.m. and 9 p.m. to 9 a.m. In some cases no record was submitted for the 12 hours in which the clinic was visited and the inhalant changed. Because of this the index "the average number of times used per 12-hour period in each week" was calculated (*a*) for day periods, and (*b*) for night periods.

The patients were unaware that inhalants A and F, B and G, C and H, and D and I were the same, so that the records giving the number of times F was used may be regarded as replications of records of A. Similarly, G records are replications of B, H of C, and I of D.

Four average values were therefore provided by each patient in regard to each inhalant—namely, the average number of times inhalant A was used per 12-hour *day* period, and also per 12-hour *night* period; and replications of these two averages when the same inhalant (F) was, unknown to the patient, used. Excluded from the primary tabulation of these averages (Table VIII) were all instances

TABLE VIII.—*The Average Number of Times Each Inhalant was Used per 12-hour Period (Over a Week), Together with the Total Times per 48-hour Period*

Patient	Inhaler AF			Inhaler BG			Inhaler CH			Inhaler DI			Total	Total + Estimated Missing Numbers
	Day	Night	Total	Day	Night	Total	Day	Night	Total	Day	Night	Total		
1	11·429	6·571	30·858	9·429	7·571	32·428	8·286	6·429	25·715	8·143	6·571	31·428	120·429	4·715
2	0·143	0·429	0·572	0·143	0·429	2·858	—	—	0*	—	—	—	4·715	
3	1·286	3·143	7·429	1·286	3·286	9·572	4·500	5·000	11·929	1·714	3·143	9·857	38·787	22·821
4			6·820*	0·286	1·143	5·144	0·143	1·571	3·000	1·714	4·143	7·857	16·001	
5	8·429	4·286	24·715	7·571	4·000	23·428	5·571	3·714	21·856	7·143	4·143	23·572	93·571	
6	1·857	5·429	13·143	1·429	3·714	14·000	2·714	5·286	14·000	3·286	5·429	16·429	57·572	
7	0·143	0·286	1·858	0·857	0·143	1·715	0·333	1·000	3·190	0·429	0·143	2·143	8·906	
8	3·714	4·429	13·143	3·714	3·000	12·714	2·714	3·571	13·571	3·143	6·286	17·572	57·000	
9	7·857	1·571	20·999	8·000	1·000	20·857	6·857	1·000	18·286	7·511	1·143	20·142	80·284	
10	6·429	3·571	33·143	8·143	6·143	8·714	4·429	3·429	12·001	1·857	1·714	10·428	76·287	99·569
11			26·007*	7·714	3·571	20·715			23·472*			4·571	24·805*	25·285
12	0·286	1·143	3·000	0·571	1·714	5·285	0·143	1·286	1·858	0·429	1·000	2·286	9·572	
13	6·571	6·286	23·857	6·143	6·714	3·142	3·000	3·714	19·428	7·857	6·857	1·572	20·999	84·855
14	0·571	1·143	2·143	0·571	0·857	4·000	2·143	0·857	3·714	1·857	2·000	0·714	4·571	12·285
15	1·750	2·250	4·715	1·286	2·857	20·571			2·678*	0·714	0·286	0·714	1·714	13·715
						1·857								1o·393
Totals ..	50·465	40·537	179·575	57·143	46·142	7·286	40·833	36·857	174·698	46·000	43·429	194·374	699·264	
Totals + estimated missing numbers			212·402			201·572								783·046

* Average times used per patient as estimated from missing plot technique (Kendall, 1946).

in which all four averages were not available for any specified inhalant. For example, patient No. 2 used inhalant C but not H, and was therefore excluded from the tabulated values of CH. Although some adjustment of this became necessary in the course of the analysis, a dash in the Table indicates that the patient was given the inhalant but had no occasion to use it during the week. In the result, 13 sets of four values were available for inhalant AF, 15 for BG, 12 for CH, and 14 for DI—a total of 54 sets of four averages for the four inhalants.

Combining the average values for each set of four gives the average number of times each inhalant was used by each patient during a 48-hour period. From these values the means for each inhalant per 48-hour period per patient were:

Inhalant	Average No. of Times Used per 48-hour Period
Riddobron	13·8
Neo-epinine No. 2	13·4
Brovon	12·4
Neb. adrenal. et atrop. co.	12·1

Whilst it is true that these differences between the inhalants are not large, they seemed sufficiently so to warrant a study of their statistical significance by an analysis of variance.

The total "sum of the squares" (of the deviations of the 216 individual readings from the grand mean of all readings) was 1962.115, with 215 degrees of freedom (Table IX).

TABLE IX

	D. of F.	Sum of Squares	Mean Square	F. Value	
				Calculated	Theoretical 1% Level
Between plots	53	1422·481	26·839	8·1	1·7
Within plots	162	539·634	3·331		
Total	215	1962·115			

It was convenient for this purpose to denote a set of four readings by one patient using one inhalant as a "plot," and since there were 54 such plots this gave 53 degrees of freedom between plots with sum of squares 1422.481, leaving 162 degrees of freedom within plots with sum of squares = 539.634. The variance ratio (F) 26.839/3.331 = 8.1 was significant, indicating that there was much greater variation between plots than within plots.

The usual procedure would next be to split up the sum of the squares *between* plots into the amount due to variation between patients, the amount due to variation between inhalants, and the amount arising from interaction of the two, giving in fact:

	Degrees of Freedom
Between patients	14
,, inhalants	3
Patients × inhalant interaction	42
	59

Here, however, the matter was complicated by the fact (noted above) that instances where all four readings were not available for any plot had been excluded. If differences between patients exist—as in fact will later be demonstrated—the missing values would not affect the inhalant totals equally. For this problem it seemed accurate enough to estimate the six missing plot values by the technique suggested by Kendall (1946) and to reduce the degrees of freedom for "patients × inhalant interaction" to 42 − 6 = 36 (see Table X).

For the purpose of splitting up the variation *within* plots (which is unaffected by the inclusion of the six estimated total plot values) it should be noted that there were three degrees of freedom within any one plot—namely,

Between replications	1
Within replications:	
Between night and day	1
Error	1

making for the 54 such plots together, the 54 × 3 = 162 degrees of freedom shown above. The analysis is shown in Table X.

Discussion of Analysis of Variance

All sources of variation examined in Table X are significant at the 1% level when tested against the residual variance (column 5), but the striking feature is the size of the

TABLE X.—*Analysis of Variance*

Source of Variation	D. of F.	Sum of Squares	Mean Square	Tested Against Residual Variance	Tested Against Interactions
Between plots:					
Between patients	14	1309·710	93·6	175·2*	
Between inhalants	3	12·162	4·1	7·6*	1·5 N.S.
Patients × inhalant interaction	36	100·609	2·8	5·2*	1·0
	53	1422·481			
Within plots:					
Between replications	54	158·903	2·9	5·5*	
Within replications:					
Between day and night	1	19·919	19·9	37·3*	3·2 N.S.
(Day − Night) × plots interaction	53	332·002	6·3	11·7*	1·0
Residual	54	28·810	0·534	1·0	
	162	539·634			
Total	215	1962·115			

* = Significant at 1% level. N.S. = Not significant.

mean square deviation between patients, giving a variance ratio of 93.6 + 0.534 = 175.2 (F = 2.43). Thus there are great variations between the members of this group of patients as regards frequency of use of these inhalants which are not assignable to differences between inhalants, to differences between repeated use of the same inhalant (replications), or to differential usage during day and night. The significance of the mean square for interaction between patients and inhalants (2.8/0.534 = 5.2) indicates, as would be expected, that the effect of any specified inhalant is not always the same but depends on the patient by whom it is used.

The fact that the comparison of the mean square deviation for inhalants with the *residual* is significant (4.1/0.534 = 7.6) merely means that if a very much larger number of observations had been obtained *from these same 15 patients* there would have been real differences between the frequency of use of the four inhalants. But since, as shown above, inhalant effects vary from patient to patient, the problem to be solved is: although there are differences between the effects of inhalants among these 15 patients, is there any evidence that these differences would appear amongst the general population of asthmatic patients? The appropriate test is to compare the mean square deviation for inhalants not against the residual but against the mean square for interaction between patients and inhalants (4.1/2.8 = 1.5) (column 6 of Table X). This variance ratio is not significant even at the 5% level, and the conclusion must be that there is no evidence from these data that real differences would exist between the frequency of use of these four inhalants amongst the general population of asthmatic patients.

That great caution is needed in the interpretation of these differences between the frequency of use of the inhalants is further stressed by the fact that there is significant variation between the responses of these patients to the same inhalants on different occasions (replications).

It may also be noted that these 15 patients show significant variation in the frequency of day compared with night use, but again not to the degree that would justify the assumption that similar variation is present in the whole population.

The main conclusion from the analysis of variance is that, although some slight difference is apparent in the average frequency with which these 15 patients had recourse to the four inhalants, there is no evidence from the material

analysed to justify an assumption that similar real differences in the frequency of their use would occur in the general population of asthmatic patients. The effect of any one inhalant was found to vary greatly from patient to patient and on different occasions for the same patients.

Summary and Conclusions

An experiment was designed to compare the need for recourse to four inhalants—riddobron, brovon, neo-epinine No. 2, and neb. adrenal. et atrop. co. (*N.F.*)—and their effect on a series of asthmatic patients.

No outstanding degree of preference was expressed for any one inhalant, and only the control inhalant was specifically commented upon adversely (see Table II).

The proportion of the total weekly periods used, which resulted in "good relief," "incomplete relief," and "no relief," were similar for all inhalants (except the control inhalant) (see Table III).

There were slight differences between the average number of times each inhalant was used per twelve-hour period in each week, but the evidence was not strong enough to justify the conclusion that similar differences would exist amongst the general asthmatic population.

The use of all the inhalants (except the control mixture) was discontinued an approximately equivalent number of times, for various reasons.

Measured objectively by the frequency of use, there was significant variation between the responses of patients to the same inhalants on different occasions; this was reflected in the subjective assessments of the same inhalant at different times and the usual inhalant when used as an unknown.

Each inhalant was given a poor assessment by a proportion of patients.

There was no difference of statistical significance between the inhalants as regards the incidence of side-effects (Tables IV and V). The side-effects most commonly noted during the investigation were dryness of the mouth, oro-pharyngeal irritation, unpleasant taste, and cough. Table VI shows that pleasantness is not incompatible with effectiveness.

It would seem from this investigation that, of the four inhalants specified, not one is outstanding, whether judged subjectively according to patients' opinion or objectively according to recorded frequency of recourse to it. Also, it became apparent that, although some asthmatic patients strongly affirmed their preference for one particular inhalant, that was not solely on account of any intrinsic value the inhalant may possess. The opinion may not be so favourable if the inhalant is first tested at an inauspicious time. The cheapness of the neb. adrenal. et atrop. co. is not accompanied by a corresponding feebleness of action.

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ASTHMA IN CHILDHOOD

A SURVEY OF THE WORK OF AN ASTHMA CLINIC IN HAMPSHIRE

BY

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Over a period of many years I have been increasingly impressed by the number of patients presenting at the Royal Hampshire County Hospital with clear physical signs of the effects of asthma, which no systematic or continued attempt had been made to prevent. I was therefore prompted to initiate a special clinic for asthma and other allergic diseases, with the purpose of the systematic investigation and continued management of asthmatic children. After consultation with colleagues and with the county medical officer of health, the clinic was begun early in 1947.

One advantage of an asthma clinic is the progressive increase in the number of patients who attend from year to year: the mere presence of such a special clinic in an area brings to medical treatment sufferers who might otherwise be content to continue without treatment until their health was irrecoverably damaged. In this clinic we have now investigated, treated, and followed up 209 children of school age and under. This preliminary report shows something of the pattern of the natural history of asthma, as affected by treatment, in a predominantly agricultural but partly urban area in Southern England. Adults suffering from allergic conditions are also investigated and treated in the clinic, but are not here considered.

Age and Sex Incidence

The grouping of patients according to their age at the onset of asthmatic symptoms is shown in the accompanying Table. It will be seen that in 84% these symptoms appeared in the first seven years of life.

Age at Onset of Symptoms of Asthma

	Age in Years															Total
	-1	-2	-3	-4	-5	-6	-7	-8	-9	-10	-11	-12	-13	-14	-15	-16	
Boys	24	15	29	19	10	15	9	4	1	6	5	2	0	1	1	1	142
Girls	11	6	15	7	8	4	4	3	2	2	2	2	1	0	0	0	67
Total	35	21	44	26	18	19	13	7	3	8	7	4	1	1	1	1	209

Boys are affected more often than girls, in the proportion of 2:1 (142:67). Coke and Coke (1939), in 3,000 adult and child asthmatics, found only 8% more males than females, but they report that boys are affected more often than girls and show that the approach to equality in the overall figures derives from a preponderance of women between puberty and the menopause over men of the same age period. The Table shows the age of onset to be similar in boys and girls.

A definite history that a close relative had suffered from an allergic condition was obtained in 49% of our cases, a figure similar to that reported by Coke and Coke (1939) and Williams and Williams (1949).

Degree of Disability

Figures showing the average loss of school time are in course of collection, but their accumulation must necessarily be slow; on the one hand, not all the school time lost by asthmatic children is lost by reason of asthma, and, on the other hand, long periods of absence from school at a time antecedent to the diagnosis of asthma may be ascribed to some other cause. How great a handicap the