

ASTHMA IN SCHOOL CHILDREN

by

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INTRODUCTION.

"Diseases of the lungs, especially asthma and bronchitis, are among the most common disorders in childhood". This statement is taken from "The Health of the School Child", the report of the Chief Medical Officer of the Ministry of Education for the years 1956 and 1957. The report notes that asthmatic boys and girls now form one of the largest groups of pupils in special schools for delicate children but no information is given regarding the prevalence of the condition although there is some suggestion that it may be increasing. More is indeed known about the prevalence of bronchiectasis, a much less common condition, which is undoubtedly decreasing.

The asthma clinic within the Birmingham school health service was started in November, 1953. The object was to provide special facilities for the care of asthmatic children which could not normally be provided by family doctor, school medical officer, general hospital or chest clinic. Care and supervision was planned to embrace all aspects of the asthmatic child's life and environment on the basis that asthma is a condition produced and maintained by the environment in an individual with an inherent liability to react abnormally to environmental factors which cause no disturbance in the majority of individuals.

The Local Authority agreed to provide the premises and equipment, the nursing staff, physiotherapy service and the assistance of the consultants in child psychiatry and oto-laryngology as required. The Regional Hospital Board agreed to provide the medical staff and such laboratory and radiological service as might be required. Originally, the medical staff consisted of

one consultant chest physician, but later, an assistant chest physician (S.H.M.O.) was added. The consultant chest physician was allowed the use of beds in a general pædiatric unit for children requiring admission. A full-time school health visitor was attached to the clinic in order to maintain close control of the home environment. Places in both residential and non-residential open-air schools were made available through the medical officer for special schools, although no special school was set aside for asthmatic children alone.

The information which has been accumulated about more than 500 of the children seen at this clinic during the first five years, investigated and treated and followed in most cases for considerable periods, will be presented. First, however, the results of a prevalence study carried out in relation to the routine school medical inspection will be presented. This study was designed to reveal the prevalence of asthma in children of each sex in various age groups during childhood. It was intended that this study would show something of the natural trends inherent in the condition of asthma as it occurs in children in this country.

When making provision for the care of patients suffering from any disease, the first step is to ascertain the extent and nature of the problem. In this country very little special provision has been made for children with asthma and very little official information is available regarding its prevalence. In Birmingham the asthma clinic was started first and the prevalence studied afterwards but other authorities may benefit from the information collected both with regard to the extent to which the condition occurs and also the experience which has been accumulated during the first

five or six years in Birmingham.

In addition to the prevalence study, the accumulated facts regarding the age and sex, the history of the ~~asthma~~ and associated conditions, the family circumstances and family history will be reported. Taken together these facts should give a guide to the natural history of asthma in children in Birmingham which can be compared with similar reports from other places.

Experience of the investigation of the causes underlying the asthmatic breathing will also be reported and compared with that of other workers so that some conclusions may be reached regarding the most satisfactory methods to employ in investigation and the interpretation to be drawn from the results. This leads naturally to a discussion of the causes thought to be operating in the case of the Birmingham children attending the asthma clinic and these will be discussed in relation to the experience and opinions of others who have studied the etiology of asthma, particularly in this country.

Finally the methods of treatment used in Birmingham will be reported and the results obtained so far, will be given. The results will include reports on several clinical therapeutic trials which have been undertaken and which, by following a pattern of objective assessment and statistical evaluation, have given reliable results. There is a clear need for information about the various forms of treatment available for asthma and the degree to which they may be expected to succeed in the asthmatic children in the cities of this country. Part of the delay in making adequate provision for the care of these children is due to uncertainty about what should be done and what success may be expected. It is hoped that by reporting the experience

obtained in Birmingham, guidance and encouragement may be given to others concerned with care of children suffering from asthma.

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very reliable figures for the prevalence of asthma in the year 1957-58 were obtained from a study of 10,000 children in Birmingham. The prevalence of asthma in this study was 1.57 per cent. Table I gives the results of the study. The children were not classified as asthmatic unless the asthma gave rise to difficulties in school. In some cases the asthma gave rise to difficulties in school but difficulties in school were more pronounced in some cases.

APPENDIX

Age	No. of children	Difficulties in school		No difficulties in school		Total
		No.	%	No.	%	
10	100	15	15.0	85	85.0	100
11	110	10	9.1	100	90.9	110
12	120	12	10.0	108	90.0	120
13	130	13	10.0	117	90.0	130
14	140	14	10.0	126	90.0	140
15	150	15	10.0	135	90.0	150
16	160	16	10.0	144	90.0	160
17	170	17	10.0	153	90.0	170
18	180	18	10.0	162	90.0	180
19	190	19	10.0	171	90.0	190
20	200	20	10.0	180	90.0	200
21	210	21	10.0	189	90.0	210
Total	5151	515	10.0	4636	90.0	5151
Total	10000	1570	15.7	8430	84.3	10000

THE PREVALENCE OF ASTHMA AMONG SCHOOL CHILDREN.

Mortality is no guide to the prevalence of asthma. In England and Wales nearly 3000 deaths occur each year - (Williams 1953) but only about 40 of these are in children. Asthma is, nevertheless, much more common in childhood than in adult life. Dees (1957) reviewed the reported prevalence studies of asthma in children and noted the scarcity of information on the subject. In Sweden Kraepelien (1954) carried out a survey in school children. He reported the figures for the whole country but these are probably artificially low and the more reliable figures are those reported for the years 1948-49 and 1949-50 when a deliberate attempt was made to find out the prevalence of asthma in elementary school children in Stockholm. This study covered 60,000 children and the overall prevalence of asthma was 1.37 per cent. Table I gives the figures in detail but unfortunately the children were not classified according to sex. Kraepelien noted that the asthma gave rise to difficulties in school in about one in three of the cases but difficulties in school were more noticeable in the younger children.

A S T H M A T I C S

TABLE I.

Class	No. of Pupils	Difficulties in School		No difficulties in school		Total	
		No.	%	No.	%	No.	%
I	11918	59	0.50	133	1.11	192	1.61
II	11688	58	0.50	104	0.89	162	1.39
III	9953	43	0.43	101	1.01	144	1.45
IV	8730	31	0.36	93	1.07	124	1.42
V	5131	20	0.39	56	1.09	76	1.48
VI	4022	21	0.52	42	1.04	63	1.57
VII	3262	14	0.43	27	0.83	41	1.26
VIII (Age 14)	2406	3	0.12	18	0.75	21	0.87
Special Classes	2953	-	-	-	-	-	-
TOTAL	60063	249	0.41	574	0.96	823	1.37

In Bergen, Eilertsen (1954) found a prevalence rate of 1.77% in 6032 children aged seven years.

In this country Williams (1951) discussed the social importance of asthma and quoted several investigations into its prevalence. More recently Williams (1958) gave figures for surveys carried out in the Vale of Glamorgan and in the Rhondda Fach in South Wales. Unfortunately the numbers of children in the population were too small to give reliable figures and those given for limited age groups are misleading. These figures are given in Table II.

TABLE II.

	<u>Male</u>		<u>Female</u>	
	Under 5	5 - 15	Under 5	5 - 15
Rhondda Fach	0.9%	1.5%	0.4%	0.8%
Vale of Glamorgan	0.3%	1.4%	0	2.6%

The diagnosis of cases in this study was made by trained health visitors working to an agreed definition. Any cases of doubt were referred to the physician. The definition used was "recurrent attacks of wheezing and dyspnoea coming on spontaneously and occurring within the last twelve months".

Douglas J.W.R. (1956) found a prevalence of 1.2% in children at the age of six years in a national sample in the United Kingdom and he found that there was a higher prevalence in children of professional people (1.9%) than in children of unskilled manual labourers (0.9%). Logan & Cushion (1959) found in general practice in England and Wales a prevalence of 1.23% in boys under fifteen years and of 0.64% in girls under fifteen years. The rate for both

sexes under fifteen was 0.94%.

Figures for the adult population from most parts of the world are roughly in agreement (Williams, 1951) and usually appear to be about 0.9%. Asthma as a cause of rejection for the Armed Forces at the age of eighteen years was 0.9% in the United Kingdom and 0.53% in the United States. Collins (1935) reported on records of 9000 families in eighteen States visited periodically for twelve months in the years 1928 - 1931. His figures are given in Table III.

PREVALENCE OF ASTHMA IN AGE GROUPS.
ANNUAL CASE RATE per cent.

TABLE III.

ASTHMA	All ages	0.419
	Under 5 years	0.330
	5 - 9 "	0.450
	10 - 14 "	0.310
	15 - 19 "	0.070
	20 - 24 "	0.190
	25 - 34 "	0.410
	45 - 54 "	0.600
	55 - 64 "	0.750
	65 and over	1.000

In order to estimate the prevalence of asthma in school children in Birmingham, an investigation was undertaken with the assistance of the school medical officers. School children are examined at routine medical inspections three times. The first occasion is usually in the first year after going to school. These children are five and six years of age. The second time is about five years later and these children are about ten or eleven, and the final inspection is before the usual school-leaving age and is carried out at ages of thirteen to fifteen. The school medical officers were asked to identify all children with asthma discovered at these inspections and make enquiry regarding

the presence or absence of asthma in all children who, because of sickness or for any other reason, were not seen at the medical inspection but were on the nominal roll of those due to be examined at that time. Care was also taken to find out which children in special schools who would normally have been seen at routine medical inspections suffered from asthma. The investigation covered the twelve months from September 1956 to October 1957.

It was felt necessary to make specific enquiry in the case of each child regarding the presence of asthma. The condition may give rise to no serious distress in children mildly affected and to no loss of school time. The less intelligent and the less anxious parents may ignore it and seek no medical assistance even in quite severe cases and the otherwise normal child has a very large reserve of respiratory function. In many cases, especially where other members of the family also suffer from asthma, remedies may be purchased direct from the chemist without taking the child to the doctor, or remedies prescribed for an adult may be occasionally used for the child.

For the purpose of investigation, "asthma" was defined simply as recurrent wheezing or dyspnoea not known to be of extra-pulmonary origin. At first sight this definition might appear to be too simple but from experience it was known that a mistake in a positive diagnosis of asthma in children of school age is extremely rare. Of over 500 cases referred to the asthma clinic by a large number of different medical practitioners, none was found to have been mistaken. Such confidence in the diagnosis would not be possible in children under five years or in adults. The diagnosis was checked personally in 173 of the cases reported during the survey, but in no case was there any doubt that it was correct.

The fact that the diagnosis was not mistaken in any of the cases seen does strongly suggest that the survey failed to reveal all the cases in the population and that an unknown number of mild cases were missed. It might, however, be considered that the value of the survey from a practical point of view was little affected thereby because these mild cases required no active treatment and the main purpose of the survey was to reveal the extent of the provision which is required for the special treatment of children in an urban area in England. It was, however, more disturbing to find that there was a variation between the figures reported from the different schools in the city which might have been due to a variation in reporting by the school medical officers who carried out the routine medical inspections. This also suggests that at least some of the school medical officers failed to discover and report on all the children with asthma in their area coming for medical inspection, but on the other hand Maunsell (1956) has noted that the nature of the soil in a particular place may have a bearing on the distribution of cases of asthma. She found that in districts of London around underground rivers and canals, her asthmatic patients seemed to live most frequently. Local variations within a city such as Birmingham are thus possible. The results of the Survey are given in Table IV.

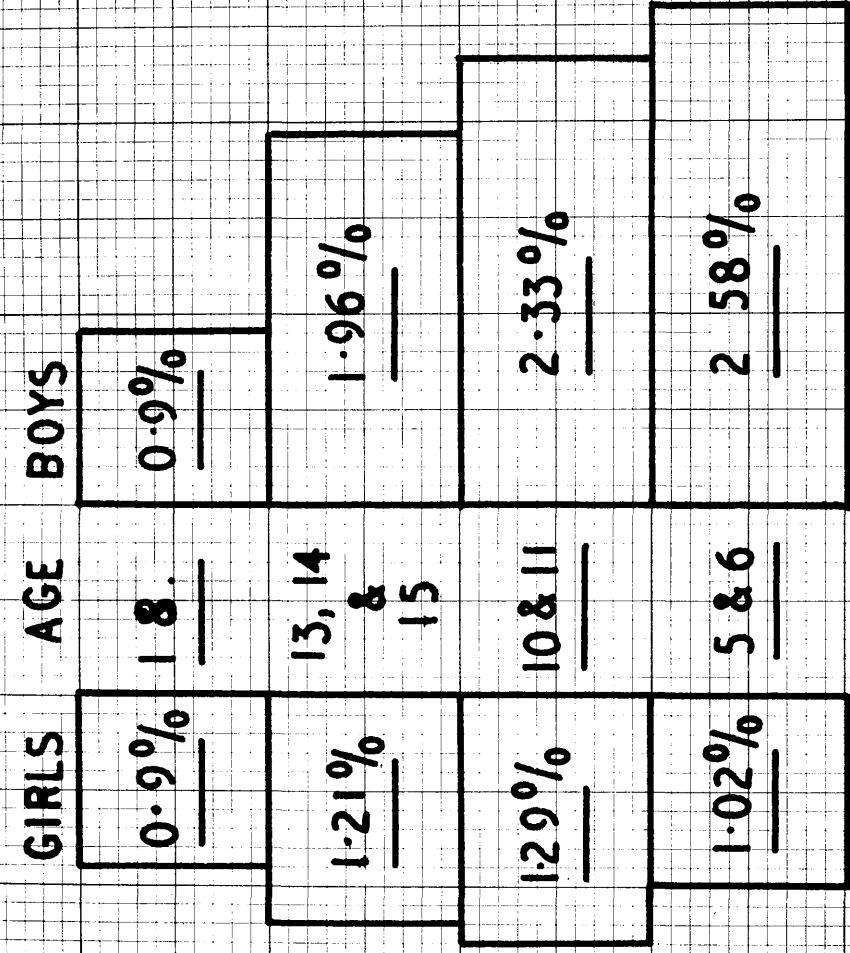
There was a fall in prevalence among boys between the ages of five and fifteen years. This is no doubt continued up to the age of eighteen years to reach about 0.9% as reported by National Service Medical Boards, although the figures given for University students (Williams 1958) are very much higher than this. Some of the milder cases do pass medical examination for the Forces and it is possible that asthmatics deliberately seek reserved occupations.

TABLE IV.

PREVALENCE OF ASTHMA IN BIRMINGHAM
 SCHOOL CHILDREN 1956 - 57.

AGE	B O Y S			G I R L S			B O T H S E X E S		
	TOTAL NO.	WITH ASTHMA	%	TOTAL NO.	WITH ASTHMA	%	TOTAL NO.	WITH ASTHMA	%
5 and 6	8785	227	2.58	7993	82	1.02	16,778	309	1.84
10 and 11	8635	202	2.33	7924	101	1.29	16,559	303	1.83
13, 14, 15	7719	152	1.96	8217	100	1.21	15,936	252	1.58
T O T A L	25,139	581	2.31	24,134	283	1.17	49,273	864	1.76

FIG. 1



This fall in prevalence in boys is, however, quite clear and must be due to recovery as the prevalence never again reaches such high levels in later life. The fall cannot be accounted for by death as death is very rare in childhood. Since over 80% of school children seen at the asthma clinic had already begun to suffer from asthma by the age of six in both sexes, it would not seem likely that the children who still had asthma at the age of fifteen years were predominantly new cases. Indeed it is known that the earlier the age of onset of the asthma, the more severe the course tends to be and the more persistent the condition. It appears likely that during the ten years from the age of five to fifteen years about 10% of the girls recover and are replaced by fresh cases, whereas about 40% of the boys recover and are only replaced to the extent of one case in four by new cases.

Figure I illustrates the difference in prevalence between the sexes as it occurs in school children decreasing with adolescence, disappearing in early adult life.

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CLINICAL FINDINGS IN OVER 500 CASES OF
ASTHMA AMONG SCHOOL CHILDREN

During the five years from November, 1953 to December, 1958 five hundred and thirty new cases of asthma were seen at the asthma clinic of the Birmingham school health service. All of them were seen and examined initially by the consultant physician and in most cases a full history was taken, usually supplemented by one or more visits to the home by the health visitor. Nearly all the children were fully investigated and had skin tests done to common inhalants and foods. At least one chest radiograph was done in each case, mainly to exclude other possible causes of dyspnoea.

It is proposed to give an account of the clinical findings in these cases, many of whom continued to attend the clinic for years, and to give an account of the methods of treatment applied with some critical evaluation of the results obtained.

AGE AND SEX DISTRIBUTION

As has already been shown, asthma is much more common in boys than in girls. This was reflected in the sex ratio of 2.7 to 1 in favour of the boys. Table V shows the age and sex distribution.

It will be noted that although the total numbers of boys and girls are different, the relative numbers at each age are very much the same. The children were, in fact, quite evenly distributed throughout the ten years of school life.

Bray (1934) found that there was nearly a three-to-one preponderance of males among asthmatic children although this excess of males disappeared in

TABLE V.

ASTHMA CLINIC CASES

AGE WHEN FIRST SEEN

<u>BOYS</u>			<u>GIRLS</u>		
AGE	NO.	% AGE	AGE	NO.	% AGE
5 +	40	10.26	5 +	11	7.63
6 +	65	16.67	6 +	28	19.44
7 +	41	10.51	7 +	20	13.89
8 +	32	8.20	8 +	17	11.80
9 +	35	8.97	9 +	7	4.86
10 +	38	9.74	10 +	13	9.03
11 +	43	11.03	11 +	14	9.73
12 +	96	24.62	12 +	34	23.62
ALL	390	100.00	ALL	144	100.00

number of years

more or less frequently

later life. Amongst 1390 cases arising in the first decade, the percentage incidence per year was given as follows :-

First year	22 $\frac{1}{4}$ %
Second "	17%
Third "	13 $\frac{1}{2}$ %
Fourth "	10 $\frac{3}{4}$ %
Fifth "	10 $\frac{1}{2}$ %
Sixth "	8 $\frac{1}{2}$ %
Seventh "	6 $\frac{1}{4}$ %
Eighth "	5 $\frac{1}{2}$ %
Ninth "	4 $\frac{1}{4}$ %
Tenth "	1 $\frac{3}{4}$ %

From these figures it is evident that Bray was reporting cases of a very different age distribution to the Birmingham series now being studied. "Recent Advances in Allergy" by Bray, which was last published in the 3rd edition in 1938, is almost the only British text-book of relatively recent publication which deals with asthma in children to any great extent so that much of the information available must be derived from Bray's series of cases. These cases appear to be mainly of children in the first five years of life, unlike the present series of children who were from five to fifteen years of age.

AGE OF ONSET OF THE ASTHMA AND COURSE OF THE DISEASE

A high proportion of cases of asthma commence in childhood, although it is not uncommon to see an adult who initially admits to having asthma for only a few years but on closer questioning gives a history of asthma in childhood which cleared up for a number of years only to recur later. This is not to say that asthma does not frequently arise in adult life in people who have not had it before. In children the onset of asthma is most

commonly found to be during the first six years of life.

Bray (1934) stated that one third of all cases of asthma have their onset in the first decade. In a pædiatric practice Glaser (1956) found 43% of 276 cases commenced during the first two years of life, and 87% had commenced before the age of seven years. Williams (1958) reported the age of onset in 200 cases at all ages. His findings are illustrated in Figure 2.

Fuller (1952) reported that 84% of his patients began to have symptoms before the age of seven years. Table VI shows the age of onset in his cases.

The findings with regard to age of onset in the children attending the Birmingham Clinic are in agreement with those of Glaser and Fuller. There would seem to be no geographical or sex difference in the age of onset. Table VII shows the figures in detail and Figure 3 illustrates the parallel behaviour of the sexes in this respect.

The majority of the children when first seen were not obviously improving or deteriorating but rather more were showing some improvement than those showing deterioration so that there was a definite impression to gradual tendency to improve. About 10% of the children had such severe asthma that they were seldom free of symptoms and only rarely able to remain more than a few days at school at a time without illness. About a third of the cases were mild and although they often had some wheezing at night or in the early morning and often became wheezy after exercise or as a result of emotional upset, they were not disabled and hardly ever lost school time or became confined to bed because of their asthma. The mild cases were perhaps the most easily defined group due to their excellent school attendance and they

FIG. 2.

AGE OF ONSET OF ASTHMA IN 100 MALES
AND 100 FEMALES

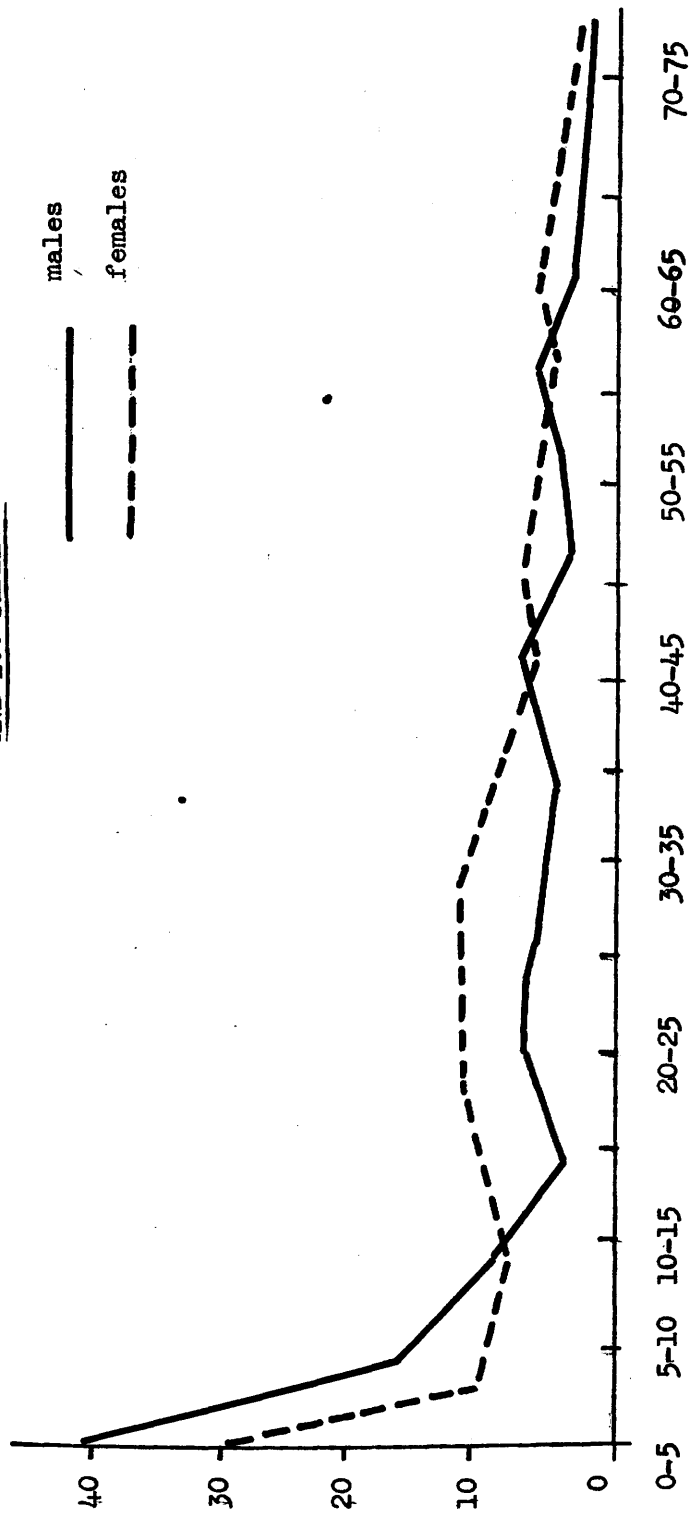


TABLE VI

AGE IN YEARS

	-1	-2	-3	-4	-5	-6	-7	-8	-9	-10	-11	-12	-13	-14	-15	-16	TOTAL
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

TABLE VII.

AGE AT ONSET

BOYS

GIRLS

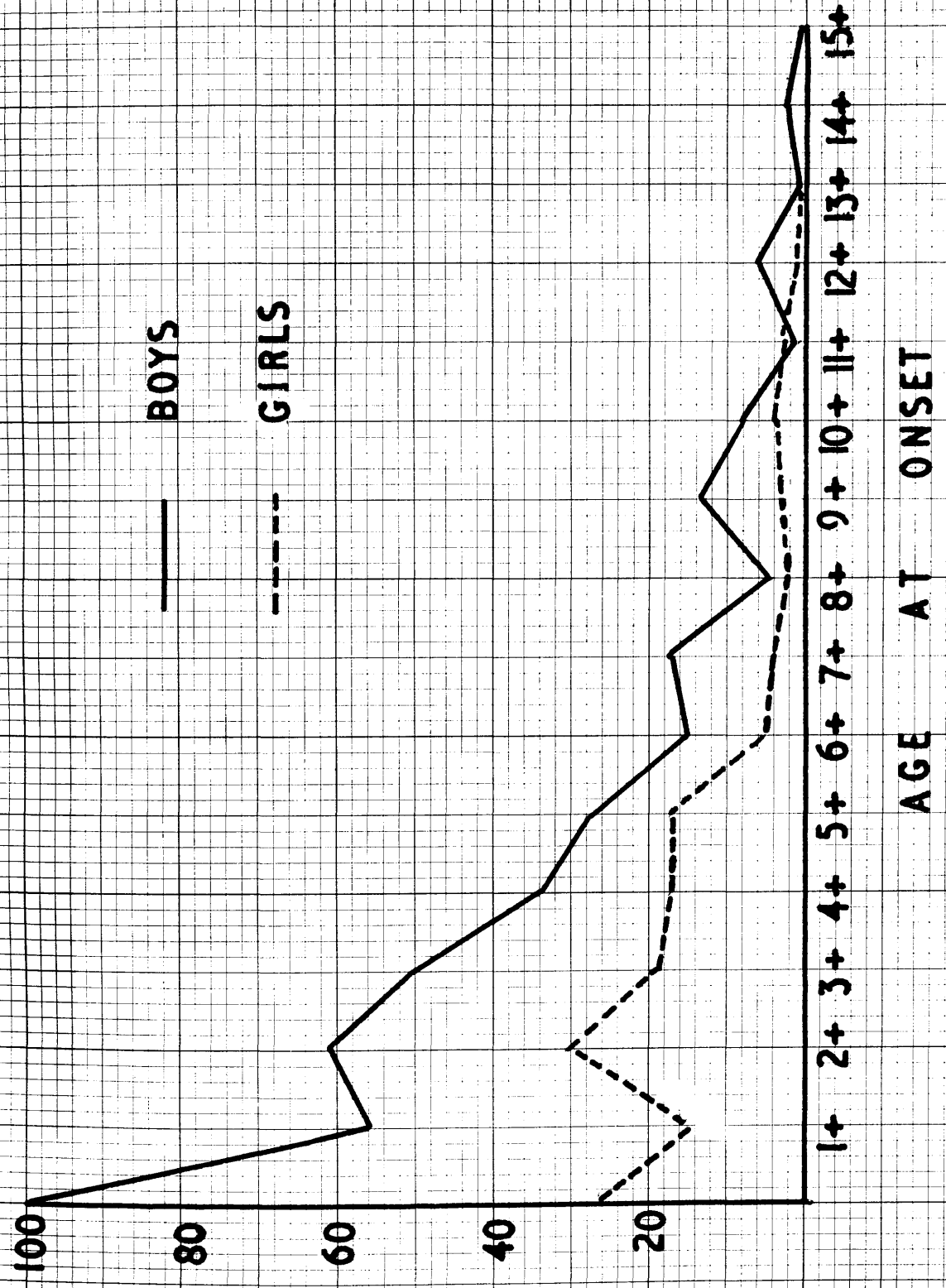
AGE	NO.	% AGE	AGE	NO.	% AGE
0 - 1	95	24.49	0 - 1	28	19.06
1 - 2	55	14.18	1 - 2	15	10.20
2 - 3	61	15.72	2 - 3	31	21.10
3 - 4	51	13.15	3 - 4	19	12.92
4 - 5	33	8.50	4 - 5	17	11.56
5 - 6	28	7.21	5 - 6	17	11.56
6 +	65	16.75	6 +	20	13.60
ALL	388	100.	ALL	147	100.

ONSET BEFORE THE AGE OF SIX

in 83.25% - Boys

In 86.40% - Girls

FIG. 2



were studied to see if there was any age or sex difference in the distribution. Table VIII shows these cases, of which there were 205 in all, divided into the age groups used in the prevalence study.

TABLE VIII.

	Age 5 - 7 years			Age 10 - 12 years			Age 13 - 16 years		
	Total	Mild	%	Total	Mild	%	Total	Mild	%
Boys	59	18	30.5	53	18	33.9	31	8	25.8
Girls	25	9	36.0	26	11	42.3	11	5	45.4
Both sexes	84	27	32.1	79	29	36.7	42	13	30.9

These findings indicate a rather higher proportion of mild cases among the girls than the boys at all ages. The percentage of mild cases does not appear to change greatly during the period. From this evidence there is nothing to indicate that more boys recover as they get older because there are more mild cases among the boys, nor would it appear that those who do spontaneously recover are essentially the mild cases because in that case one would expect the proportion of severe cases to increase with increasing age. There is, however, a possibility that the mild cases do, in fact, tend to recover, but their places are taken by more severe cases becoming mild as they get older.

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FAMILY SIZE AND CIRCUMSTANCES

There is a widespread belief that asthma is commoner among only children and among children of middle class families. Most of the children attending the Birmingham Clinic came from comfortable working-class homes, a high proportion living in municipal houses. There appeared to be no real difference in relation to income group but possibly this was due to the fact that most were in the same group. Douglas (1956) in a personal communication stated that he had found a prevalence of asthma of 1.9% in the children of professional people and of only 0.9% in the children of unskilled manual workers. Williams (1951) noted a much higher prevalence of asthma among University students in Wales than among National Service recruits.

As far as family size is concerned, no evidence was found among the Birmingham cases of a particularly high proportion of only children. Table IX shows the family size in 518 of the cases compared with the number of children in primary family units as estimated for Birmingham using the 1% sample of the 1951 census.

TABLE IX

FAMILY SIZE IN CHILDREN WITH ASTHMA.

<u>Family Size</u>	<u>No. of Patients</u>	<u>% Age of Patients.</u>
Only child	76	14.67
2 children	171	33.02
3 "	124	23.94
4 "	67	12.93
5 "	36	6.95
6 "	22	4.25
7 "	10	1.93
8 or more children	12	2.31
All sizes	518	100.00

CHILDREN IN PRIMARY FAMILY UNITS, -1951-BIRMINGHAM

<u>Family Size</u>	<u>No. of Units</u>	<u>Percentage</u>
One child	86,500	46.6
2	58,200	31.3
3	24,400	13.1
4-5	12,000	6.4
6-8	3,800	2.0
9 or more	400	0.2
all sizes	185,300	

This comparison suggests that the asthmatic children came from families containing substantially more children than would be expected from the census figures. Certainly there is no unduly high proportion of asthmatic only children but the census figures relate to a higher proportion of uncompleted families with one child only than is likely with the families of school children. No more comparable figure could be obtained.

Williams (1956) has shown that responsibility, success, good food, good homes with low physical demands have no ill effects on asthma, in fact these appear to be the most desirable attainments for the asthmatic.

In the professional and technical occupations the prognosis for the asthmatic is best both for working capacity and for life. Crowded conditions both at home and at work may give rise to increased infection with resultant increase in incapacity and in death. In children crowded and unsatisfactory homes may necessitate removal to a residential school. Williams states that he has for years urged asthmatic children to work hard at school to develop mental capacities to compensate for their physical disabilities.

FAMILY HISTORY

A definite family history of allergic disease, particularly of asthma, eczema, hay fever, migraine and food allergy, was given in 63.7% of 529 cases. This is in keeping with most findings but could undoubtedly have been increased by questioning other members of the family as well as the patient's mother. Bray (1930) reported a very careful study of the family history in 200 consecutive cases of asthma in children up to the age of 12 years. He considered in all 4,152 relatives of the children, an average of over 20 per case, and enquired particularly about asthma, hay fever, eczema, urticaria and migraine. A positive family history was obtained in 68.5% of his cases which was unilateral in 51.5% and bilateral in 17%. He went further to study the method of inheritance but could find no strict relationship to a Mendelian pattern. He was, however, able to demonstrate that transmission through an unaffected mother was more common than through an unaffected father and that inheritance of allergic manifestations is twice as frequent through the female as through the male and twice as many offspring are likely to be affected when the female transmits. Bray also found that children with a bilateral family history tended to develop allergic disease earlier than those with a unilateral family history.

There is a tendency, apparently, to inherit one particular form of allergic condition. Thus, among families attending the clinic, several members frequently had the same condition. In one family, the father suffered from asthma only, the mother from hay fever only, all three children

from hay fever and two of them from asthma as well. No doubt exposure to potent allergens may determine the onset of disease. Inhalent allergens are usually associated with allergic rhinitis, hay fever and asthma but occasionally with other conditions. Indeed, Hardwicke et al (1959) have reported pollenosis in relation to recurrent nephrosis.

As Schwartz (1952) said, "Practically everyone engaged in the study of asthma has noticed that the disease occurs to a major degree in certain families". He reviewed the literature on allergic disease and on allergy in general, together with the literature on the subject of heredity in asthma with great care and clarity. He listed the main papers and their findings from 1868 up to 1948. None of the studies were conclusive and none showed clearly the method of inheritance of the condition. Schwartz himself studied the hereditary background of three groups, namely Group A.191 asthma probands, Group B.200 matched controls, and Group C.50 probands with baker's asthma.

The asthmatic cases in Group A were thought to consist of 74 definitely allergic cases and 117 where no evidence of allergy was found. All the cases of baker's asthma in Group C were allergic to flour.

The incidence of asthma, rhinitis and Besnier's Prurigo was significantly greater in the relatives of Group A than of Group B, and a study of deceased relatives showed a much higher incidence of asthma in Group A than in Group B. The statistical conclusions from his work were as follows :-

- (a) Asthma is an inherited disease;
- (b) Genetic relationship exists between asthma and vasomotor rhinitis;
- (c) Besnier's Prurigo and hay fever also appear to be genetically related to asthma;

- (d) It is possible but not very likely that urticaria and Quinke's Oedema (giant urticaria) in females may, in certain instances, be genetically related to asthma;
- (e) "Eczema" (contact dermatitis) migraine, psoriasis, gastro-intestinal allergy, ichthyosis and epilepsy are genetically unrelated to asthma.

Asthma, he says, must be presumed to be a genetic entity. Baker's asthma is due to an inherited predisposition to asthma in general. An inherited predisposition to asthma, vasomotor rhinitis or hay fever does not affect the period of sensitisation to flour (14.3 years average in this study).

The fact of an inherited predisposition to asthma as a disease as well as a predisposition to develop allergic sensitivity, although not new and already suggested by others (Coca and Cooke, 1923; Vallery Radot et al, 1956, and Hurst 1943) had never before been based on statistical evidence.

Concerning the mode of inheritance Schwartz believes that there is a predominant likelihood of dominant heredity with failing manifestation. The degree of manifestation of the asthma gene being about 40%. Thus, if one parent has asthma and one is healthy, 50% of the children will be carriers of the gene but only 40% of these, or 20% of the total, will acquire manifest disease. Of these 20% about 13% will develop asthma and the rest (7%) vasomotor rhinitis, Besnier's Prurigo or hay fever.

If both parents have asthma 75 to 100% of the children will be carriers of the gene and 30 to 40% will have manifest disease - as asthma in 20 to 25% and as vasomotor rhinitis, Besnier's Prurigo or hay fever in the remaining 10 to 15%. No other work on this subject really compares with that of Schwartz which certainly must be considered to be the most complete and authoritative so far produced. There is, however, some criticism which may be made. The control group chosen by Schwartz excluded probands with allergic disease.

This is not really satisfactory since it produced a highly artificial group. An unselected group from the general population would include probands with a history of allergic disease in some form in at least 10% and possibly much more. There is undoubtedly still further work required on this subject and an extremely careful genetic study of mental illness and allergic disease now being carried out by Dr. Denis Leigh and others at the Maudsley Hospital, London, should yield important results.

* * * * *

Age in years	No. of cases
Up to 6 months	36
6 to 12 months	12
12 to 18 months	
18 to 24 months	
24 to 30 months	
30 to 36 months	
36 to 42 months	
42 to 48 months	
48 to 54 months	
54 to 60 months	
60 to 66 months	
66 to 72 months	
72 to 78 months	
78 to 84 months	
84 to 90 months	
90 to 96 months	
96 to 102 months	
TOTAL	176

... of the study ... in all cases ... and in some cases the ... attempts to make in the clinic to differentiate between the various types

ASSOCIATED ALLERGIC DISEASES

Eczema is by far the commonest associated condition and usually preceded the asthma, but occasionally the asthma and eczema commenced simultaneously, usually in infancy. When the disease occurred simultaneously, the asthma was frequently severe. Eczema was present or had been present, in 170 cases or 32% of the 530 asthmatic children. Thirty-one of the 170 cases (18%) were suffering from mild asthma which did not lead, as a rule, to loss of schooling, whereas over 30% of the 530 cases were mild. The sex distribution of the eczema cases was similar to asthma cases. There were 117 boys and 53 girls with eczema.

The age of onset was generally earlier than with asthma and is shown in Table X.

ONSET OF ECZEMA

TABLE X.

Age of Onset	No. of Cases
Up to 6 months	86
6 to 12 months	32
1 year to 2 years	7
2 years to 3 years	6
After 3 years	4
Not known	35
TOTAL -	170

In 143 cases the eczema preceded the asthma, in 21 cases the conditions began simultaneously and in 6 cases the eczema came on after the asthma. No attempt is made in the clinic to differentiate between the various types of eczema named in dermatological text books and Besniers Prurigo is taken to be

the same condition as infantile eczema. The precipitating factor initially giving rise to infantile eczema may well be, in most cases, allergy to ingested foreign protein in a young child given such foreign protein at an age when only human protein in breast milk should be given. Grulee and Sanford (1936) have shown that eczema is seven times as common in infants fed on cow's milk as in those who are wholly breast-fed. Glaser and Johnstone (1953) were able to demonstrate the possibility of prophylaxis by avoidance of foreign animal protein in the diet of babies born into families with an allergic history.

There is, however, little doubt that the persistent eczema, usually confined to the flexures, seen in asthmatic children of school age, has only occasionally a relationship to food allergy. The condition is confined to the soft thin areas of skin and trauma from clothing and from scratching appears to play an important part in its persistence. Of 170 cases in the clinic, only 25 gave a definite history that any food made the condition worse. Of the 25 cases, 18 had a positive skin reaction to one or more common food, and 8 had no such positive skin reaction. Of the 170 cases of eczema, 118 (69.41%) gave no positive skin reactions to any common food.

In spite of the absence of a definite indication of relationship between the flexural eczema in school children and food allergy, there is a very frequent alternation between asthma and eczema in the same child. Thus, when the asthma is troublesome, the eczema is less and when the asthma is better, the eczema becomes worse. It has been noted that successful treatment of asthma may give rise to exacerbation of the eczema. When the asthma improves,

the appetite improves, and when the asthma is bad, the child may eat very little for days. It is tempting to postulate that foods do have some effect on the skin condition, not in minute quantity but only when taken liberally. The degree of food allergy may be slight but still present clinically, although insufficient to give any positive skin test or positive clinical test except in such quantities as are usually eaten by a healthy hungry child.

The relationship between eczema and asthma has been demonstrated by the long-term follow-up of infantile eczema cases reported by Purdy (1953) from Edinburgh, and by Finn (1955) from Dundee. Purdy sent an enquiry to all the patients who first attended the Royal Infirmary in Edinburgh in the years 1931 to 1937. The youngest was thus 14 years of age at the time of the enquiry. Sixty per cent answered the enquiry and the results are given in Table XI.

TABLE XI.

	Total	Asthma	Wheezy	Hay Fever	Besniers Frurigo	Migraine
Male	62	25 (40.3%)	7. (11.1%)	24 (38.7%)	18 (29%)	7 (11.1%)
Female	31	12 (38.7%)	3 (9.3%)	15 (48.4%)	5 (16.3%)	0 (0)
TOTAL	93	37 (39.8%)	10 (10.7%)	39 (41.9%)	23 (24.7%)	7 (7.5%)

Approximately half of the cases of infantile eczema went on to develop asthma and a quarter still had flexural eczema ("Besniers Frurigo") in later childhood. No doubt if this group were followed on for a further twenty years, the incidence of hay fever and of migraine would increase as these conditions are late in onset compared with eczema and asthma, frequently not

arising until adult life is reached. Finn's figures from Dundee were almost identical with those of Purdy, although the numbers were smaller and the follow-up less complete.

Hay fever is relatively uncommon in children up to the age of 15 years and it is more uncommon before the age of 5 years. There were only 20 cases of Hay Fever among 520 children with asthma. The age of onset is shown in Table XII.

AGE OF ONSET OF HAY FEVER

TABLE XII.

Age of Onset	No. of Cases
18 months	2
2 years	1
3 "	2
4 "	2
6 "	3
7 "	3
8 "	2
9 "	2
10 "	2
11 "	1
TOTAL -	20

The late age of onset may be due to the intermittent exposure to the specific allergen which is seasonal and varies widely from one season to another as Hyde (1959) has shown. Allergic rhinitis, not due to grass pollen, occurs but is seldom severe in children. There is, however, quite frequently a rhinitis which is probably allergic, accompanying asthma in children. The most useful diagnostic point appears to be the itchiness of the nose which accompanies the condition and gives rise to the characteristic movements of the child called by some the "allergic salute", in which the nose is rubbed with

the back of the hand and forefinger.

Transient urticaria is common in all children but persistent urticaria was not encountered. Migraine was also rare and gastro-intestinal allergic symptoms were of little clinical importance although not infrequent.

* * * * *

Frequently, however, the attacks are associated with other allergic symptoms or occur after the onset of an infection and particularly those precipitated by infections were called allergic or pneumonia. There is no doubt that wheezing and dyspnea may be a direct effect of asthma, may arise in infants and young children as bronchitis but some of these will go on to develop typical asthma will not. By the time school age has been reached, an asthmatic child is referred to a special clinic, there is very little chance of cure. The child may have attacks only during winter and not during summer, as in a boy of nine years of age. Physical and laboratory examinations were negative and the attacks could not be precipitated by any means and even two attacks several years. A thorough examination, including electrocardiography, revealed no abnormality until on one visit the boy was found to have an attack of par

PHYSICAL EXAMINATION

The most important feature of the clinical examination is the taking of a full history of the patient's asthma, other illnesses and family background. Particular attention must be paid to the nature and periodicity of the attacks in relation to precipitating causes, season variation, weather, upper respiratory infection and emotional upset. The first duty of the physician is to confirm the diagnosis of asthma. This is seldom difficult although a very long list might be made of the possible causes of attacks of dyspnoea in childhood. Frequently, however, the diagnosis has not been made with certainty for some months or years after the onset of the condition and recurrent attacks, particularly those precipitated by infection were called acute bronchitis or pneumonia. There is no doubt that wheezing and dyspnoea, indistinguishable from an attack of asthma, may arise in infants and young children from true bronchitis but some of these will go on to develop typical asthma and others will not. By the time school age has been reached, and when a child is referred to a special clinic, there is very little chance of a mistake in diagnosis. Only in one case did serious doubts arise. The history was of attacks of dyspnoea coming on only during exertion and not noticeably accompanied by wheezing, in a boy of nine years of age. Physical and radiological examination was negative and the attacks could not be precipitated by making the boy run up and down two flights of stairs several times. Cardiological examination, including electro-cardiography, revealed no abnormality until on one visit the boy was found to have an attack of paroxysmal tachycardia which came on in the out-patient department. It was

concluded that attacks of paroxymaltachycardia had been mistaken for asthma. However, during the succeeding year the boy did develop unmistakable true asthma. In none of 530 children referred to the asthma clinic was the diagnosis mistaken.

Radiological examination was carried out in all cases to exclude other causes of dyspnoea. In the majority the radiological appearances were normal but in some an obvious deformity of the chest wall, best seen in the lateral film, was found. The anterior-posterior diameter of the chest was increased and the ribs more horizontal than normal. Occasional cases were found to have pulmonary shadows. These usually cleared spontaneously within a week and were associated with the more severe attacks of asthma. Physical examination never revealed any signs which would have led to the diagnosis of this condition. It seems likely that the shadows are produced by temporary blockage of a segmental bronchus. In no case was a complete collapse of a whole lobe or lung noted but this does occur.

Physical examination revealed the general condition of each child, the height and weight, presence or absence of thoracic deformity and of abnormal physical signs on examination of the chest. The presence of sibilant ronchi at any one time in a case of asthma is fortuitous and adds little to the knowledge of the condition. Less characteristic physical signs, such as coarse ronchi and crepitations are not infrequently heard. Variability is a characteristic of the condition so that a single physical examination may be of little value in making a definite diagnosis of asthma. Bray (1934) stressed the increasing persistence of dyspnoea in asthmatics with increasing

age. He found persistent dyspnoea to be present in about 20% of patients in the first and second decades and in nearly 70% of patients in the fifth and sixth decades.

In relatively mild cases of asthma no adverse effect was found on the general condition and growth of the child but in severe cases, particularly where symptoms were persistent, growth was impaired and the child small and considerably under normal weight. One of the most dependable indices of improvement in a severe case of asthma is a marked gain in weight.

Deformity of the chest was found in 70 children out of 495 in whom this was particularly sought. The deformity is clearly established and fixed by the age of five years in most cases. It is related to the severity of the asthma, particularly in infancy. Table XIII shows the relationship found between the severity and the presence of deformity in 495 cases. The cases with deformity contained only 2.6% of all the mild cases but 37% of all the severe cases.

TABLE XIII.

SEVERITY	WITH DEFORMITY	WITHOUT DEFORMITY	TOTAL
Mild	4 (5.71%)	148 (34.82%)	152
Moderate	26 (37.15%)	209 (49.18%)	235
Severe	40 (57.14%)	68 (16.0%)	108
TOTAL	70 (100%)	425 (100.0%)	495

The presence of a deformity of the thoracic cage should not be taken to indicate the presence of true destructive emphysema with breaking up of the

alveolar walls and permanent destruction of lung function. Bates (1952) studied the pulmonary function of 13 asthmatic children and found that abnormalities of function could be revealed in the absence of any physical signs of bronchospasm. The majority showed no significant impairment of carbon monoxide uptake even in the presence of poor mixing efficiency and a low vital capacity. The difference between the asthmatic lung and the emphysematous lung is essentially that in asthma there is normal perfusion, whereas in emphysema this is not so.

Williams & Leopold (1958) reported their findings on post-mortem study of large lung sections from 25 persons who had died as a result of status asthmaticus. They found plugging of the medium and small bronchi with mucus but they found that the cellular reaction did not extend to the terminal bronchiole in uncomplicated cases and in only two of the cases was there any evidence of destructive emphysema. They expressed the opinion that emphysema was only likely to occur if there had been episodes of infective bronchiolitis.

Dekker & Groen (1957) studied the mechanism of production of wheezing, and demonstrated that the sound could be produced in the larger bronchi and trachea by rapid and turbulent flow of air and can be reproduced at will by people who have learned the technique. They found radiologically that tracheal narrowing was present during wheezing both in normal subjects taught to wheeze and in patients with asthma. The narrowing of the large air passages and wheeze could be produced in post-mortem specimens of lung made to "breathe" artificially in conditions where the expiratory pressure

was high. Thus it would appear that the high expiratory pressure in asthma tends to cause constriction of the major bronchi and trachea and causes the wheezing. The rigidity of the trachea and bronchial tree has probably been over-estimated in the past and the assumption that the wheezing arose from the smaller bronchi which are partly blocked by mucus and by spasm may well be mistaken. It is also clear from this work that wheeziness can be produced independently of these obstructions in the smaller bronchi, and indeed can be easily produced at will by some subjects.

There is an obvious relationship between emotional influences and wheezing revealed by this work.

* * * * *

SKIN TESTS

The use of skin tests in the investigation of asthma and other conditions is confined to the last 50 years and it is, therefore, a relatively new clinical method about which quite a lot of disagreement still exists. A recent annotation in the Lancet (1955) discussed this continued controversy. The method possibly owes its origin to Blackley (1873) who found that pollen introduced into the conjunctiva or broken skin of persons with hay fever produced a local reaction. Noon & Freeman (1911) made practical use of the conjunctival test which has again been used recently by Loveless (1958) as a measure of the degree of hypersensitivity to pollen in patients about to receive "single-visit" repository immunisation. Cooke (1911) used the intradermal injection technique. Others extended the scope and use of the tests. To-day extracts of almost anything may be obtained commercially for intradermal, scratch or prick testing. These extracts are very reliable and give repeatable results when properly used.

There are two main methods of doing the tests, namely the intradermal injection and the scratch or prick method. In the former, a tiny injection of about 0.01 cc is made into the skin, while in the latter a scratch or prick is made through a drop of solution. The strength of solutions for intradermal tests is about 1 in 5000 and for prick testing about 1 in 50. When testing with allergens such as foods or pollens which may, in sensitive subjects, give a very marked reaction, only the prick method is safe. The routine method used in the children reported was the prick test. Children have thin and vascular skin, as a rule, and good reactions to the

prick tests can almost always be obtained.

The tests chosen were those to all common materials giving rise to dust in ordinary houses, common pollens, common moulds, common foods and the danders from domestic animals. It was considered that allergy to uncommon inhalants or foods would be likely to give rise to a train of events easily recognised by the patient and that any skin test then used would merely be for confirmation of the history. Allergy to inhalants so common as to be unrecognisable as a cause of the symptoms might, however, be indicated by a series of routine skin tests. The tests in routine use are as follows :-

House Dust	Cladosporium
Mixed Feathers	Alternaria
Horse Hair	Aspergillus
Cotton Flock	Dry Rot
Wool Flock	Penicillium
Kapok	Egg
Cat Fur	Milk
Dog Fur	Fish
Grass Pollen	Wheat
Tree Pollen	Oats
Shrub Pollen	Orange

The solutions of moulds and pollens are in groups. The extracts are obtained from Messrs. Bencards Ltd. Occasional use is made of solutions prepared from individual grasses, moulds and other plants. It should be noted that plants with insect-borne pollen have little importance in relation to asthma, but common wind-borne pollens like those of the grasses are of great importance. Even in a city such as Birmingham grass pollen is plentiful and in London the pollen of the plane trees is of particular local importance. It has been found that extracts obtained from several manufacturers give similar results in the same individual provided the site

used and the technique are the same. Even pure horse dander antigen prepared by Stanworth (1958) gave no more reliable results than the commercial product.

Although the standard text books on Allergy, such as Bray (1934), Vaughan and Black (1948) and Glaser (1956) all describe the technique and interpretation of skin testing in similar terms, there is still much criticism of the method, not all of which seems well informed. No doubt the practice of selling sets of skin testing material by means of salesmen visiting doctors and persuading them that the treatment of asthma can usually be successful by giving a course of injections of a solution made up from all the things to which the patient gives a positive skin test, is partly responsible. In certain centres chemists employ technicians to do skin tests and supply solutions for injection without any medical supervision at all. It is little wonder that the disappointment of both the patient and the doctor in the results of treatment based on such methods has brought skin testing into disrepute as a scientific method of investigation.

Apparently careful and reliable work demonstrating the unreliable results of skin testing such as that reported by Ogilvie (1954) may be completely invalidated, as pointed out by Bruce Pearson (1954), by lack of knowledge of the technique and failure to guard against fallacies in the results obtained. Recently, with the advent of the inhalation test (Citron, Frankland and Sinclair (1958)), the skin test has been heavily criticised (Lancet, 1955). Inhalation testing seems at first to be likely to yield more accurate information but it has not been used in clinical practice for long enough as yet to be fully evaluated. Only one allergen can be tested

at a time and each test is time-consuming and potentially dangerous. In children particularly violent reactions may occur and the method is considered to be too dangerous for use in the Birmingham school health asthma clinic. Perhaps the most disturbing feature of the inhalation test is the possibility of delayed reactions after the patient has gone home and is no longer under immediate medical supervision.

The assumption in inhalation testing is that the test being made on the shock organ avoids the false positive and false negative results which occur commonly in skin testing. This assumption is, however, dangerous since the strength of the inhalation test may bear little relation to normal clinical conditions and other factors besides the allergen may determine the occurrence of the attack of asthma. Psychological influences and non-specific atmospheric pollution are only two such influences which are well recognised. To neglect the skin tests in the investigation of asthma is to lose the benefit of a simple safe method of investigation which in many cases, but not in all, yields to the experienced physician information of value. They do not provide an easy short-cut to the discovery of the cause of asthma in clinical practice and they yield to the inexperienced, misleading, disappointing and even dangerous information. They always provide some information and positive results mean something, although in many cases this will have no bearing at all upon the clinical condition. Without the careful clinical history which is the most important part of the investigation, skin reactions are of no value, but taken together with the history they may be of great value. Bray (1934) summarises the position as follows :-

"A positive ~~skin~~ reaction obtained according to the principles out-

lined may be interpreted as indicating :-

- (a) the specific cause of the disease, a reaction of great utility for eliminative or desensitisation measures;
- (b) a definite sensitivity but not necessarily the etiology of the condition in question, a reaction of value from the prophylactic standpoint;--
- (c) a latent sensitivity that has not yet matured, which may be due to an absence or insufficient contact with the allergen. 25% of the apparently normal brothers and sisters of allergic children gave positive skin reactions;
- (d) a specific sensitivity in a person who has lost or never developed sensitivity clinically; positive skin reactions may still be given even after successful desensitisation measures have been carried out;
- (e) temporary pseudo or non-specific reactions as well as traumatic must be excluded.

A negative skin reaction may be interpreted as indicating :-

- (a) a true absence of sensitivity;
- (b) a very early stage in the development of sensitivity, where sufficient has not yet been acquired to react with the allergen when applied locally;
- (c) unreliability of the extracts employed;
- (d) a false result occurring in a patient who clinically demonstrates sensitivity to the particular factor. This happens following a severe allergic reaction, after therapy, after freedom from contact and after administration of Adrenalin (or antihistamine or steroid drugs).

Skin reactions have been used in the most careful scientific work, such as that of Squire (1949) and of Stanworth (1953). Two types of skin reaction occur. The immediate reaction appearing within about ten minutes is associated with asthma, hay fever, eczema and urticaria. The delayed

reaction, usually appearing after 48 hours, is of the tuberculin type and is associated with bacterial allergy and contact dermatitis. These two types of reaction probably do not indicate completely separate types of allergy, but the mechanism of the reactions is different depending upon the carriage of the antibody. The immediate type is associated with antibody circulating in the plasma, whereas in the delayed type the antibody appears to be carried by cellular elements (Pepys 1953). Squire (1954-55) discusses these different types of hypersensitivity. In the immediate type the sensitivity can be passively transferred to another subject by injection of serum from the hypersensitive subject into an area of skin. The recipient's skin can then be found to give a positive reaction to the allergen in the area of the injected serum (Prausnitz and Kustner, 1921).

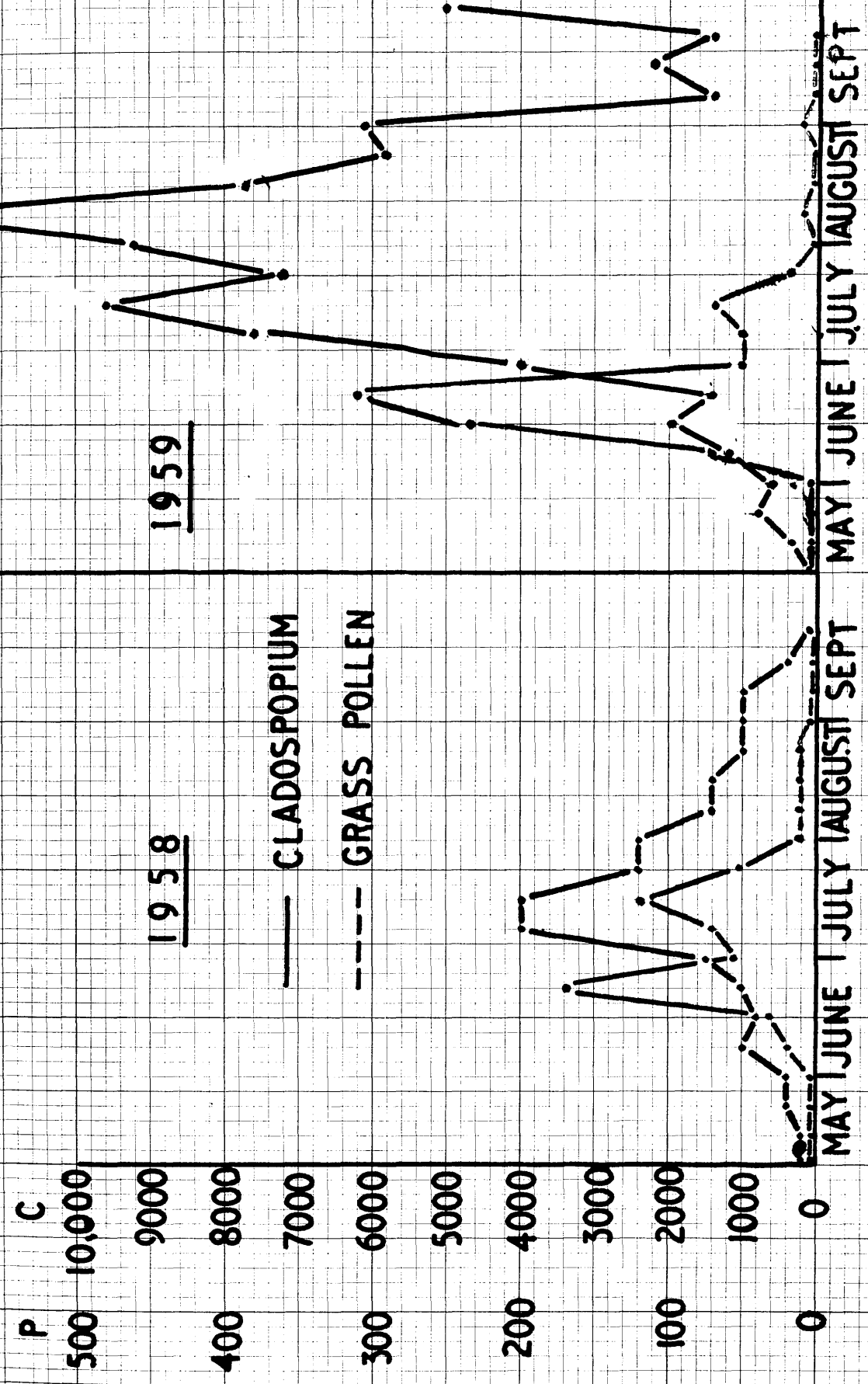
In Vitro methods of studying plasma antibodies are in the earliest stage of development and Akroyd (1949, 1954) demonstrated platelet agglutination in vitro in sedormid purpura and more recently precipitin reactions have been shown by several workers, mainly in fungal allergy, using the gel. plate technique developed by Ouchterlony (1949). These methods have only begun to be applied to clinical work. Among the first clinically significant studies of this nature is that of Pepys (1959) in relation to pulmonary aspergillosis. This technique has also been used in studying auto-immunity in Hashimoto's disease, (Doniagh^h, Roitt & Hudson, 1959). None of these methods have, as yet, been applied in the cases reported here from the Birmingham asthma clinic.

In presenting the relationship between the results of skin tests and the clinical findings revealed by the history and by observation, it is

essential to discuss clearly recognisable syndromes. Pollinosis, by its seasonal character which is usually typical and can be checked by means of aerobiological studies and by comparison with other well-known cases of the condition, is particularly suitable. When the physician suffers from hay fever, the syndrome can hardly be mistaken. Weekly pollen and mould counts have been received during 1958 and 1959 from Mr. H. A. Hyde at the Asthma and Allergy Research Unit, St. David's Hospital, Cardiff, and from Miss Elizabeth Hamilton at the Wright Fleming Institute, St. Mary's Hospital, London, Figure 5. Both these workers have reported their work in the literature (Hyde H.A., (1952, 1956, 1959. Hyde H.A. & Adams K.F., 1958, Hamilton E.D., 1959). Both used the automatic volumetric spore trap (Hirst, 1952).

Table XIV shows that 259 children were found to have positive skin reactions to grass pollen, but of these only 13 had clinical pollinosis. It also shows that the larger the skin reaction the more likely it is to be associated with clinical symptoms (Figure 6). None of the 94 children with small (+) reactions had symptoms of pollinosis, but even with the largest reactions (++++) less than half had clinical symptoms. This is not to say that positive skin reactions to grass pollen in children have no significance and are not worth noting. They are of value as confirmatory evidence of true hay fever and it is very rare to find a patient with true clinical allergy but a negative skin reaction. None such were encountered in the series. It is not even true to say that the positive reaction in patients without corresponding symptoms has no significance. Frankland (1958) found that girls employed in the collection of pollen for the preparation of pollen vaccines and

FIG. 5



Weekly Average Grass Pollen and Cladosporium Spore Counts from the Wright-Fleming Institute, London.

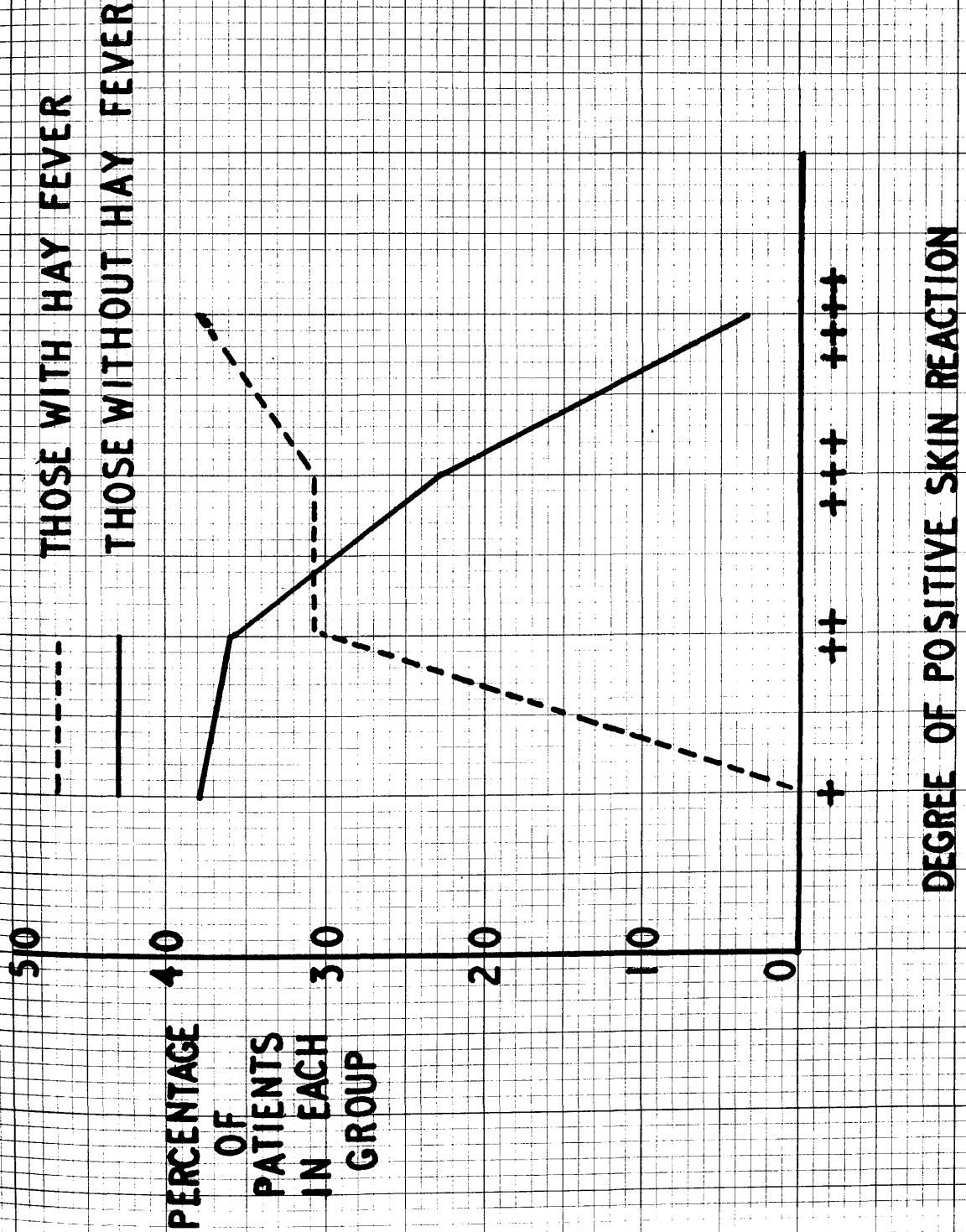
TABLE XIV.

SKIN REACTION TO GRASS POLLEN IN RELATION
TO HAY FEVER SYMPTOMS

DEGREE OF SKIN REACTION	PATIENTS WITH SYMPTOMS	PATIENTS WITHOUT SYMPTOMS	TOTAL
++++	5	7	12
***	4	56	60
++	4	89	93
+	0	94	94
TOTAL	13	246	259

HAY FEVER SYMPTOMS IN RELATION TO SKIN REACTION

FIG. 6



THOSE WITH HAY FEVER

THOSE WITHOUT HAY FEVER

PERCENTAGE
OF
PATIENTS
IN EACH
GROUP

DEGREE OF POSITIVE SKIN REACTION

therefore heavily exposed to inhalation of the pollen, were liable to develop symptoms of pollinosis after several seasons' exposure. By skin testing these girls prior to employment it was found that those who gave a positive skin test later developed pollinosis and those who gave a negative skin test did not do so. Thus a child with a positive skin test to grass pollen but no history of clinical disease may develop hay fever in later life, depending upon the extent of exposure to the allergen and the susceptibility of the individual. Although the chance of developing symptoms depends upon heredity, exposure and local conditions in the shock organ there may well be other factors such as endocrine disturbances of which we know nothing, which also play a part.

Food allergy is another clearly recognisable clinical condition when confined to simple repeatable attacks associated with vomiting, urticaria, eczema or asthma. In children of school age it is not common and not usually serious. Only 81 cases were found. Table XV shows the relationship between these cases and the skin reaction to the food which caused the symptoms. In this case the position is probably in one respect opposite to that in pollinosis. The period when food allergy is commonest is in infancy when the infant is subjected to ingestion of foreign protein at a time when its natural food is human milk and its gastro-intestinal tract is not fully equipped to deal with anything else (Glaser, 1956 and Lancet, 1955).

In older children with a mature digestive system, the exposure to food allergens may well have ceased since the child can digest food and avoid absorbing it in such a form as to be allergenic. Foreign protein molecules are broken down before entering the blood-stream. The older child is often able to eat foods which formerly caused an upset and the skin reactions also

TABLE XV.

RELATIONSHIP BETWEEN SKIN REACTIONS TO
COMMON FOODS AND CLINICAL FOOD ALLERGY

SKIN REACTION	POSITIVE	NEGATIVE	TOTAL
+ + + +	8	0	8
+ + +	12	2	14
+ +	8	4	12
+	29	27	56
-	24	416	440
TOTAL	81	449	530

TABLE XVI.

RELATIONSHIP BETWEEN FOOD ALLERGY AND SKIN REACTIONS IN ECZEMA		
++++	Skin Reactors	6
+++	" "	2
++	" "	3
+	" "	6
Negative		8
TOTAL NO. WITH HISTORY OF FOOD ALLERGY		25

TABLE XVII.

RELATIONSHIP BETWEEN POSITIVE SKIN REACTIONS TO COMMON FOODS AND ECZEMA			
DEGREE OF REACTION	NO. WITH ECZEMA	NO. WITHOUT ECZEMA	TOTAL
+	25	31	56
++	11	1	12
+++	9	5	14
++++	7	1	8
TOTAL	52	38	90

tend to decrease and disappear, although they may persist after the clinical symptoms have gone.

Table XVI shows 25 cases of eczema in whom an exacerbation of the eczema could be caused by ingestion of a food. Even in these, eight had negative skin reactions and in most the offending food had less effect than it had had some years previously. Table XVII shows that skin reactions done routinely in the clinic using extracts of common food, were positive in 90 cases but of these only 52 had eczema. Again as in the case of pollen tests, the chance of having a related clinical syndrome was greatest when the skin reaction was strongest. Of 170 children with eczema, 52 gave positive skin reactions to common foods.

It can be concluded that skin tests are simple, safe and easily done in an out-patient clinic. Testing materials are easily obtained commercially and are reliable. The results are repeatable but their relationship to clinical disease is highly unreliable both as a guide to etiology and to treatment. In spite of this, the method does give some information which may be of value to the experienced physician in conjunction with other findings. There is as yet no comparable method of investigation at present available which will give more accurate information more easily and safely so that skin testing should continue to be used.

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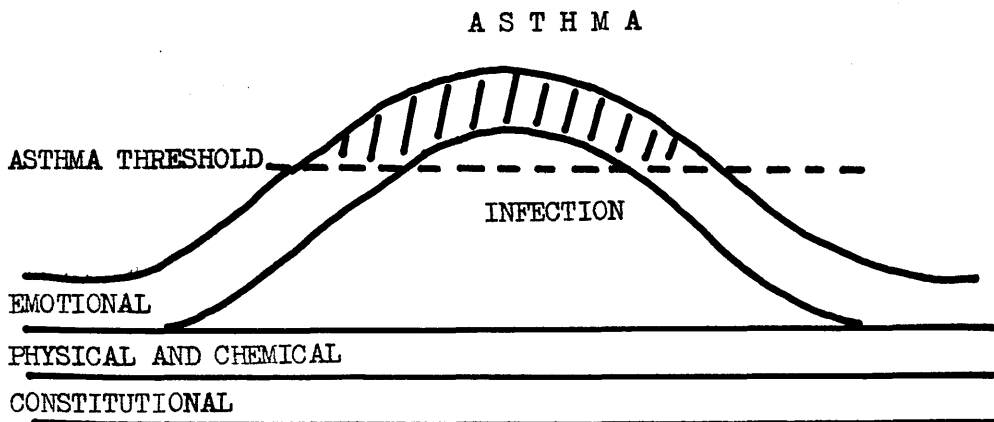
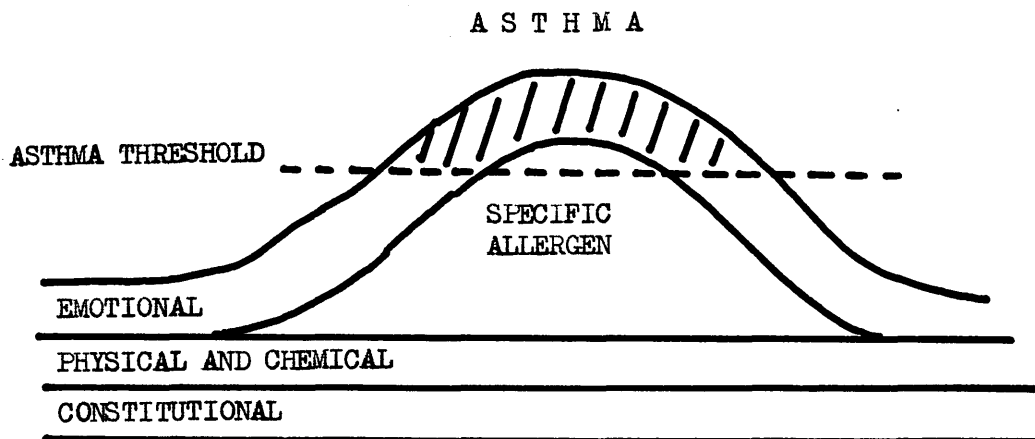
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DISCUSSION OF THE CAUSES OF ASTHMA IN SCHOOL CHILDREN.

Much vital information about the etiology of asthma may remain yet to be discovered. Thus there is scope for disagreement and for vague generalisation wherever the subject is discussed. Some cases are clearly caused by a single allergen, some by more than one. Pollen asthma is probably the commonest clear-cut allergic asthma but even this is frequently accompanied by asthma outside the pollen season due to other causes. In children it is not uncommon to meet with cases where the attacks are caused by infection and do not arise otherwise. In other cases emotional factors appear to be the only precipitating causes. There is no general agreement about the basic cause of asthma but it seems unlikely that either infection or emotion could produce asthma in an otherwise normal subject. The basic abnormality may be a state of allergic hypersensitivity insufficient alone to cause clinical asthma without the addition of another factor. Hurst (1943) in a paper on "Asthma in Childhood", written near the end of his life, during which he had suffered for many years with asthma, considered it to be - "the reaction of an over-excitabile bronchial system". He was of the opinion that the over-excitability of the bronchial system was an inherited condition and the other factors allergic, infective and psychological, merely precipitating in action. To some extent this is borne out by the work of Schwartz (1952), although not entirely, when he showed that a tendency to asthma as a disease is inherited as well as a tendency to develop allergy.

Wright (1955) explains the accepted concept of the etiology of the asthmatic attack diagrammatically :-

FIGURE 7. .



As Williams (1959) points out, many authors have noted the frequency with which naso-respiratory infection precedes the first attack of asthma. Such infections often precede each attack in children no matter what other causes also operate. Williams describes a study carried out with Lewis - Fanning, in which they found that of 487 consecutive asthmatics of all ages attending Williams' clinic, 51 per cent gave a history of bronchitis, 15 per

cent a history of pneumonia, and 22 per cent of "other respiratory infections" preceding the onset of asthma while in matched controls who were attending the accident department of the same hospital only 13 per cent gave a history of bronchitis, 8 per cent a history of pneumonia and 10 per cent a history of "other respiratory infections".

It has been the experience in Birmingham, however, that at least half the children attending the asthma clinic get attacks when they get colds and that in many cases an initial diagnosis of pneumonia or of bronchitis preceded the diagnosis of asthma but was either mistaken initially, or the doctor decided not to alarm the parents by making a diagnosis of asthma during the first attack in the hope, perhaps, that further attacks might not occur.

Chobot et al. (1951) found infection to play a part in 87% of 400 children and to be the sole cause in 30%. It is doubtful whether it is really justifiable to regard infection as the sole cause in any case and it may only appear to be so as a result of the inadequacy of our knowledge and methods of investigation. No real evidence of bacterial allergy causing asthma has been found in the Birmingham series and skin reactions to common bacterial groups have failed to give any direct positive reactions. Williams (1959) notes that the question is still open to doubt. Vallery-Radot, Halpern, Blamontier, Biozzi and Binacerraf (1956) have suggested that infection plays its part by determining the organ to be affected by allergic disease and determining the site of the antigen-antibody reaction.

There is no doubt that the "popular" aspect of the etiology of asthma is, at present, the psychological. This is readily disclosed in the history and indeed many mothers of asthmatic children seem pre-occupied with this aspect

to the exclusion of all else. It is respectable to have "nervous asthma" perhaps because it is considered to have a good prognosis and it neither casts a slur on the heredity nor gives rise to an obligation in respect of treatment. While the importance of emotion in the etiology of asthma must be recognised, it is possible that it may give rise to complacency on the part of both parents and practitioners, especially in an illness which is seldom fatal in childhood. Much discussion of the psychosomatic aspect of asthma in children is based on limited experience, often accompanied by lack of knowledge of allergic disease and its investigation. Such papers as that of Batten (1959) based on a single case, incompletely investigated, serve only to obscure the knowledge we have, while adding nothing to it.

A very much more thoughtful paper on the psychosomatic aspect of asthma is that of Crocket (1959) based on a thousand cases in which he recognises the significance of three main factors in the etiology - emotional, infective and allergic. A painstaking attempt is made to apply statistical analysis to this subject and to express the significance of each factor in relation to age and sex. The Table XVIII gives Crocket's results. A five-point scale is used in which 1 signifies no relevance and 5 the maximum relevance of the factor :

TABLE XVIII

	Psychological factor.		Infective factor.		Allergic factor.	
	Average Value		Average Value		Average Value	
Age	Males	Females	Males	Females	Males	Females
0 - 5	2.36	2.00	1.81	1.77	3.19	2.77
6 - 10	2.71	2.97	2.24	2.35	2.97	3.03
11 - 20	2.46	2.93	2.37	2.29	3.18	2.89
21 - 30	3.00	3.11	2.25	2.20	3.46	3.11
31 - 40	3.06	3.29	2.20	2.35	3.38	2.88
41 - 50	2.61	3.24	2.47	2.76	3.19	2.98
51 - 60	2.62	3.04	3.13	2.61	2.63	2.91
61 +	2.67	3.32	2.78	2.79	1.78	2.95
All ages	2.68	3.08	2.32	2.38	3.145	2.962
Standard Deviation	1.01	0.91	0.89	0.94	0.994	0.953

This elaborate mathematical method of assessing the significance of the investigation of 1000 cases depends in the end upon the physician's opinion and its mathematical accuracy is more apparent than real. Even such careful work as that of Dekker and Groen (1956) using provocation tests with spirometric control of both allergic and psychological factors, fails to achieve the absolute accuracy in assessing the significance of each factor which it appeared to promise. Wilken - Jensen (1951) reported the psychosomatic investigation of 45 asthmatic children. In the discussion on this paper Dr. Z. Erickson - Lühr stated, "There is a certain danger in placing too strong an emphasis on the importance of psychic factors in allergic disease. It can easily make us forget that an accurate analysis of the purely somatic factors must still form the basis of all treatment in these diseases."

B. Stokvis (1959) discussed the subject of the psychosomatic aspects of allergic disease with great care and gave 296 references to the literature on the subject. Much, however, was written about the psychological aspects of phthisis until the discovery of effective chemotherapeutic treatment for tuberculosis caused this aspect of the disease to be largely forgotten. Any chronic condition where the treatment is unsatisfactory does tend to engage interest from a psychological point of view, perhaps out of proportion to the importance of this aspect in the etiology. There is no doubt that investigations have found psychic disturbances in allergic children (Clarke, 1950, Dees, 1945, Miller et al, 1948). These have mainly been disturbances of the child-parent relationships. Stokvis (1959) found no evidence of specificity with respect to personality structure in either psychosomatic patients in general or in persons with allergic diseases in particular. He concludes that although emotional influences play a part in many cases either in the conditioning or in the outward manifestation of allergic disease or in both, not every case of allergy can, as such, be considered a psychosomatic affection.

In order to eliminate personal bias as far as possible and obtain an accurate estimate of the factors in the etiology of asthma, Williams et al (1958) studied 482 consecutive cases in Cardiff. Each case was subjected to examination by a physician interested in allergy, a psychiatrist, an otolaryngologist and, in the case of children, by a paediatrician. Their conclusions are summarised below :-

	% age in which more than one factor was present	% age in which only one factor was present	TOTAL
Allergic factor	60.8	3.3	64
Infective "	76.8	11.3	88
Psuchological factor	69.0	1.2	70.2

From this assessment all three factors were roughly of equal importance and cases with single etiology rare. The combination of factors was as follows :-

Allergic, infective and psychological	-	38.2%
Infective and psychological	-	23.4%
Allergic and infective	-	15.2%
Infective only	-	11.3%
Allergic and psychological	-	7.4%
Allergic only	-	3.3%
Psychological only	-	1.2%

The numbers of children in the study were small but it is of interest to see the relative importance of the factors in various age groups :-

TABLE XX

<u>Dominant Type</u>	0-4	5-14	15-24	25-34	35-44	45 +	all
Allergic	15%	24%	72%	48%	26%	10%	29%
Infective	38%	36%	18%	30%	52%	71%	41%
Psychological	46%	40%	10%	23%	20%	18%	30%

A purely personal attempt to classify the basic causes of asthma in 400 consecutive children attending the asthma clinic in Birmingham was made. Much more importance was ascribed to allergic causes which were through to be present in 71% of the cases.

ETIOLOGY OF ASTHMA IN 407 BIRMINGHAM SCHOOL CHILDREN

<u>Etiology</u>	<u>Number</u>	<u>% Age</u>
House Dusts	221	54.3
Pollen	20	4.9
House dusts + Pollen	29	7.1
Foods	4	1.0
House Dusts + Foods	1	0.25
Mould allergy	3	0.75
Home Dusts + Mould	7	1.7
Home Dust + Pollen + Mould	4	1.0
Non-allergic causes	67	16.5
Etiology unknown	51	12.5
	TOTAL: 407	100

There may be another factor of great importance, particularly in the cities of the United Kingdom, where dampness is so often allied to atmospheric pollution. This factor is the non-specific pulmonary irritation which may account for the extraordinary prevalence of chronic bronchitis in this country (Committee on Air Pollution - Interim Report, 1953). Middtun (1959) reported a series of 33 cases of asthma arising in workers in an aluminium-producing factory in Northern Norway. These workers had been carefully chosen so as to avoid men with personal or family histories of asthma and the only factor which appeared to cause their asthma was inhalation of highly irritating fluoride gas which occurred in concentrations of up to five parts per million in the air of the factory. The condition appeared to have arisen from this non-specific irritation of the lungs without any evidence of allergic hypersensitivity. Atmospheric pollution appears to cause asthma in some subjects, chronic bronchitis in others and no obvious ill-effects in most people. An attempt to associate allergy with chronic bronchitis in adults, however, gave negative results (Smith & Sumner, 1957).

It is well known that infantile eczema is frequently a generalised condition in infancy and precipitated by food allergy. In later childhood the food allergy has usually disappeared and yet the eczema persists in the flexures as Besnier's Prurigo. It seems reasonable to assume that the principal factor responsible for the flexural eczema is the irritation of the clothing and of scratching on sites where the skin is thin and is exposed to movement. Should this be so, the persistence of asthma throughout life in many cases where no obvious allergic mechanism can be demonstrated, may be due to non-specific irritation of a bronchial mucosa which has been initially rendered abnormal by allergy but which, were it not for the irritation, or for chronic infection, would have returned to normal. Possibly there is some point when a state is reached which is irreversible and the so-called "intrinsic asthma" is reached. In support of this theory it has been noticed personally that during the pollen season in June and July, a subject not actually aware of nasal abnormality but nevertheless subject to hay fever, may have a much lowered threshold of reactivity to irritants in the air. Thus a fit of sneezing may occur due to some mild irritant which fails to cause normal subjects to sneeze and would not cause the pollen-sensitive subject to sneeze outside the pollen season. Careful examination of such a person will show a mildly abnormal mucous membrane in the nose even when he is unaware of any abnormality. It is sometimes difficult to explain on any other basis but the reduction of atmospheric irritation, the marked improvement in relatively mild cases of asthma when these children are taken from their homes in the city to a residential school or convalescent home just outside the city boundary. This does not occur in the more severe cases but in those in whom

it does occur, the experiment may be repeated many times with return of asthma in the city and recovery just outside it.

Should there be any truth in the above hypothesis it follows that anti-allergic treatment should be used at as early a stage in the treatment of asthma as possible to obtain success, and that the greater success in the treatment of hay-fever due to pollen allergy may be at least partly due to its later onset. Williams et al (1958) found that only 7% of pollen asthmatics began to have symptoms before the age of five years, compared with 40% in all asthmatics. The campaign for clean air may have as much importance to the asthmatic as it has to the chronic bronchitic.

Finally, two more speculative aspects of the etiology remain to be discussed. The first concerns the exceptionally well marked sex difference in the prevalence of asthma which has already been shown to exist in childhood. Environmental factors would seem to be quite unable to explain this for in Britain children are subjected to no environmental difference on account of sex such as might be expected, for instance, in a Moslem country. The reason for the sex difference must, therefore, be intrinsic and the most likely explanation seems to be a hormonal difference which is abolished slowly as puberty occurs and adult life approaches. Indeed this hormonal difference may even be reversed in later life. Either the adrenal or the pituitary gland would seem the most likely source of this effect but at present no evidence is available which suggests the nature of this difference. The growth spurt does, however, take place later in boys (Tanner, 1955). Estimation of hormonal activity is at present difficult and uncertain, and Loraine (1958)

in his book entitled, - "The Clinical Application of Hormone Assay", says that at the time of writing there was no assay method for cortico steroids in urine which was entirely satisfactory. In relation to this possibility of hormonal disturbance in allergic subjects there is the disordered metabolism of sodium shown by Hughes, McDowall and Soliman (1956); Hughes and McDowall (1958) and further reported on by Buxton and McDowall (1959) at the Fourth European Congress of Allergy. These workers have shown that in allergic states sodium is deficient in the skin and bronchi and there seems to be an inability to retain sodium in the tissues. Further study of these phenomena and of the adrenal function of asthmatic children may be fruitful.

The second speculative aspect is that discussed by Glaser (1957) in his chapter on the prophylaxis of allergic disease. The basis of his opinion is that the development of one allergic disease in an individual with an inherited tendency to allergic hypersensitivity will entail an increased likelihood of developing a second allergic disease. Thus children from allergic families who develop infantile eczema may be more likely to develop asthma subsequently than those who do not develop infantile eczema. As Grulee and Sanford (1936) have shown, infantile eczema is seven times as common in infants fed on cows milk than in those wholly breast-fed. Glaser and Johnstone (1953) report the results of attempting to prevent allergic disease by withholding cows milk during the first six months of life. They were apparently unable to have the infants in their experimental group breast-fed but had to use food substitutes of low allergic potency, (Glaser, 1953). Their experimental group consisted of 96 infants who were kept off cows milk for the first six months of life. The controls were a group of 65 children, siblings of the experimental group

and a selected matched group of 175 children from allergic families. Up to six years of age the incidence of major allergic disease in the experimental group was 14.6% and in the siblings 64.6%, while in the unrelated controls it was 52.0%. There did thus appear to be a significant success resulting from this experiment. It seems reasonable that it should be so since the natural food of infants for the first six months of life at least, is human milk and their digestive system is not developed to deal with a more complex environment. The modern tendency to abandon breast-feeding and to substitute cows milk preparations, vitamin supplements and early mixed feeding has gone a long way to improve nutrition in babies, but the cost may be an increase in allergic disease. As the Lancet (1954) says, it is most unlikely that mothers can be persuaded to abandon cows milk in favour of soya bean milk for infant feeding. This, however, is not the real point for a return to breast feeding and an abandonment of largely unnecessary vitamin supplements, and early mixed feeding could certainly be achieved if paediatric opinion were convinced of the necessity and it was taught to medical students, nurses and health visitors. Such measures would, however, require a convincing proof of Glasers hypothesis and a generation of medical re-education to bring about. A careful follow-up study of a sufficiently large sample of the infant population containing infants fed exclusively on breast milk for the first six months of life would be of great interest and allow of a re-assessment of modern teaching and practice in infant feeding not only in relation to allergic disease but in a very much larger field of interest.

* * * *

THE TREATMENT OF ASTHMA IN SCHOOL CHILDREN

In discussing the treatment of asthma in children, three main aspects will be considered. All three require consideration in each case. They are palliative treatment, non-specific treatment and specific treatment. Where the results of curative treatment are as uncertain as they are in asthma, the physician has a clear duty, not only to use every available method to attain a cure but at the same time to provide as much symptomatic relief as can be obtained.

Palliative Treatment

It has been quite frequently found that children attending the asthma clinic for the first time have never had any effective form of palliative treatment at all, even when the condition has been present for several years. This applies to relatively mild cases but these are just the cases where almost complete relief of symptoms can be obtained by simple safe palliative treatment. The most widely used drug is Ephedrine, the active principle of the herb Ma Huang (*Ephedra Vulgaris*) known to Chinese physicians for about 5000 years. Ephedrine was first isolated by Yamanashi in 1885 and obtained in the form of the pure alkaloid by Nagai in 1887, who gave it its name. It was prepared synthetically by Furneaux in 1904. It first became widely used for asthma in Japan in 1917, and was introduced to the Western world by Chen and Schmidt in 1923. Chemically it is quite closely related to Adrenaline and it has a similar sympathomimetic action. It relieves bronchospasm but has certain side effects, such as increasing the heart rate, causing faintness, tremor, and in children it quite frequently causes vomiting.

For this reason it is often combined with other substances in a tablet such as "Franol" (Beyer Ltd.) which contains small amounts of ephedrine with aminophylline and phenobarbitone. One rather strange effect of ephedrine, frequent in children, is sleepiness. The opposite effect is more common in adults. Aminophylline is perhaps of more value by mouth in children than in adults usually combined with ephedrine as described. It is of great value in status asthmaticus given intravenously but this is rarely required in children. It can also be given in the form of a suppository but this is of limited application.

Adrenaline is the active principle of the adrenal medulla and was first isolated in pure crystalline form by Takamene and Aldrich in 1901. It has subsequently been widely used for the relief of asthma given by injection in a 1 in 1000 solution or as an inhalation in a 1 in 100 solution. There is probably some advantage in the compound spray which also contains atropine and papaverine. Isoprenaline tends to have a more prolonged action than adrenaline. Sub-lingual tablets can be useful in severe asthma when the spray is ineffective due to the intensity of bronchospasm but usually in these circumstances an injection of 0.25 to 0.5 cc. of Adrenaline 1 in 1000 is preferable.

The most important thing is to find the palliative which will give effective relief in each case without unpleasant side effects, to teach the mother to use it rationally and to dispel fears of habit-forming and other harmful effects which seem to be widely spread and often lead to unnecessary withholding of treatment and consequent suffering.

The latest development in the field of palliative therapy is the introduction of the steroids but extract of suprarenal cortex was used by Finiman (1933) with some success in four cases of asthma and in 1936 Wilmar and Miller reported the treatment of 72 patients with cortical extract, obtaining improvement in 42%. With the production of Cortisone or Compound E by Merck & Co., New York, in 1943, and the synthesis of cortisone and hydrocortisone in 1950, the widespread clinical use of these compounds became possible. The isolation of pure adrenocorticotrophic hormone (ACTH) was first accomplished in 1943 by Li, Evans & Simpson and by Sayers White & Long. Prednisone and prednisolone are derived from cortisone and hydrocortisone and are roughly five times as active in all clinically important effects and have some advantage in a reduced ability to cause salt and water retention. The latest compounds with even greater activity are triamcinolone which is only about 20% more active than prednisolone and dexamethasone which is approximately five times as active (Stresmann.1959). Cope (1959) discusses the principles of modern steroid therapy and summarises the present position regarding the clinical use of these compounds.

The Medical Research Council conducted a controlled trial of cortisone in chronic asthma (M.R.C.1956). This trial, although carefully conducted, did not yield such valuable results as the controlled trials conducted by the Tuberculosis Research Unit of the Medical Research Council. The conclusions were that patients were subjectively and objectively improved during the first two months of treatment but that cortisone treatment was hardly sufficient to make a significant contribution to improved capacity for work and cannot by any standard be regarded as dramatic or as great as that shown in patients with

status asthmaticus. It was further concluded that the early improvement was not maintained and by the end of six months when the Cortisone-treated group showed no significant advantage over the control group. These findings, while true for a proportion of adult cases, are certainly not true for children, nor are they true for all, or even the majority of adults (Phear, Bell & Page, 1960). No doubt the trial delayed the use of steroid therapy for asthma and led to extra caution in its use but clinical experience has resulted in a better appreciation of this form of therapy which is not in accord with the main conclusions of the trial. Perhaps one of the most important ill-effects of the Medical Research Council trial of cortisone in chronic asthma and in status asthmaticus has been to encourage physicians to use steroid therapy in an unsatisfactory manner. It is common still to give very large initial doses and to rapidly reduce these and use repeated short courses of treatment rather than to introduce a small daily dose and continue this over very long periods. The latter regime is much better and loss of effect over several months has not been experienced. The papers of Savidge and Brockbank (1954) also had the effect of suggesting that cortisone was of little value and might even lead to death from status asthmaticus. Better results with ACTH gel were reported by Gay and Murgatroyd (1954) and by Davies and Williams (1955). Hill and Swinburn (1954) reported a death due to an anaphylactic reaction to corticotrophin and nearly all modern steroid therapy is by means of the synthetic oral preparations. Herxheimer (1955) in a letter to the British Medical Journal expressed disagreement with the leading article in the same Journal on 22nd. January 1955, which expressed the

same gloomy view of steroid therapy as Savidge and Brockbank (1955). Even as late as 1957 the British Medical Journal of February 9th more or less dismissed cortisone as of little value in asthma on the basis of the M.R.C. Trial and one or two papers based on small numbers of cases.

A much more satisfactory clinical evaluation of the place of long-term steroid therapy in bronchial asthma was published by Arnoldsson (1958) as a supplement to the Acta Allergologica. He reported very good results of a long continued therapy using small dosage, with much improvement in working capacity and no loss of effect. Peptic ulcer and osteo-porosis were the most serious complications encountered. No deaths could be attributed to the treatment directly or indirectly. Hypertensive patients did not suffer any serious increase in blood pressure. Repeated radiographic examinations were carried out and peptic ulcer was found in 21 (14.6%) of 144 patients which corresponded to an incidence of 5.3% of new peptic ulcers for each year of treatment. This, he thought, might be related to the level of dosage. He did not interrupt his treatment but used an ulcer diet and antacids with good results. Radiographic appearances of osteo-porosis were observed in 19.5% of the patients on long-term steroid therapy compared with 10.9% of the controls and three of the patients on steroid therapy had spontaneous vertebral fractures. This osteo-porosis was found mainly in women of post-menopausal age. Arnoldsson also investigated the adreno-cortical function in 39 asthmatic patients and concluded that they were normal in this respect. He then investigated adreno-cortical function in 126 patients who had received long-term cortico-steroid therapy and concluded that even after prolonged steroid

therapy at low dosage levels the adrenal cortex responds adequately to stressful stimuli and that the majority of the patients had normal adrenocortical activity. The "withdrawal syndrome" was not observed. This careful work gave a very different picture of cortico-steroid therapy compared with the early British reports already mentioned and indicated that the best results can be obtained by the use of small dosage over a very long period and that the risks although present, are not such as to preclude the use of this treatment in a serious and distressing complaint. Such conclusions are in keeping with clinical experience in the Birmingham clinic and that of Kennedy and Thursby-Pelham (1956).

The possible use of very small quantities of cortico-steroids to obtain a local action on the bronchial tree was an attractive one as it would eliminate the dangers attendant upon systemic therapy. The paper of Herxheimer and McAllen (1956) on the treatment of hay fever with hydrocortisone snuff suggested that considerable success might be obtained. This was followed by other papers such as those of Morris-Owen and Truelove (1958) and of Helm and Hinworth (1958) and of Herxheimer, McAllen and Williams (1958) which all suggested that this treatment was successful. Unfortunately, however, these results have not been substantiated in clinical practice and a careful controlled trial with objective assessment of results carried out in the Birmingham clinic (Smith, J. Morrison, 1958) failed to demonstrate a significant beneficial effect from the use of this type of therapy.

In this trial the treatment consisted of the inhalation of 5 mgm. of hydrocortisone supplied as the soluble hemisuccinate in solution. Treatment

was allocated according to a set of random numbers supplied by the statistician (Dr. Ian Sutherland) and the results were plotted on a sequential diagram designed to show whether 50% more individuals benefitted from the hydrocortisone than did so from the placebo. Allowing for a 15% benefit from the placebo, 65% of the cases treated with hydrocortisone would have to show benefit in order to satisfy the criteria on which the chart was based. In practice 16% of the cases receiving the placebo showed improvement, but only 26% of those receiving hydrocortisone inhalations improved; thus the treatment failed to satisfy the criteria set by the trial. It was felt that the design of the trial and the methods of assessment were important in relation to all trials of treatment in patients suffering from asthma. An attempt to obtain objective evidence of improvement was made by using a respiratory function test - in this case the forced expiratory volume in three-quarters of a second, together with a simple daily symptom record card which indicated merely whether the patient was quite well, wheezy but able to go to school, unable to go to school or confined to bed. Such a record had been in general use in the Clinic for two years prior to the trial and the patients were accustomed to them. The cards also contained a record of the number of antispasmodic tablets used or the number of times an adrenaline inhalation was required. Any definite evidence of improvement was sought, no matter how small, the degree of improvement was not considered to be important.

There seems to be a need for objective study of methods of treatment in asthma, not only new methods but also methods which have been in use for many years but without any general agreement as to their efficacy. Using a

similar pattern, trials have been carried out with glycyrrhetic acid and with hypnosis and the value of house dust hyposensitisation is now being assessed in a similar way. The main ingredients of the method are random allocation of treatment without the knowledge of either the patient or the physician, statistical assessment by sequential analysis and objective criteria for judging whether the patient has or has not shown definite improvement.

Systemic steroid treatment has been used with the greatest caution among the children attending the Birmingham clinic and the indications have either been failure to provide adequate relief for severe cases after 1 - 5 years of treatment or the need to give some adequate relief to severely affected children concurrently with their specific treatment to enable them to attend the clinic at all. The total experience amounts to 21 cases. The same treatment was given in all irrespective of age - Prednisolone 5 mgm.daily. This dose, from experience, does not interfere with growth (Metre and Pemberton, 1959) and as yet no side effects of any kind have occurred. All children receiving prednisolone are tuberculin negative and the tuberculin tests are repeated at three monthly intervals so that prophylactic anti-tuberculous chemotherapy could be given in the event of infection with the tubercle bacillus occurring. There are three exceptions to this. All of them have had B.C.G. vaccination, two before starting prednisolone and one after. No experience was available to indicate whether the steroid therapy might make B.C.G. vaccination dangerous, perhaps giving rise to generalised spread of the attenuated tubercle bacillus and as yet no deliberate policy can be formulated

with regard to B.C.G. vaccination in these children. Since only about 10% of children reaching the age of 13 years in Birmingham have become tuberculin positive and even this low figure is still falling, the risk of tuberculosis is not great.

Of the 21 children, 12 had eczema as well as asthma and indeed, in one case the steroid treatment was initiated by a dermatologist. In 6 cases the prednisolone was commenced at the same time as hyposensitisation, whereas in 14 cases more than a year of treatment had already been given before the decision was made to start prednisolone. In the remaining case only five months treatment had been given at the clinic, but the child had already spent four years in a residential open-air school. Of the others, six had previously been in residential open-air schools and five had spent periods in Switzerland. In 20 out of the 21 cases, the asthma had clearly a predominantly allergic background and in 16 out of the 21 cases hyposensitisation was carried on together with the prednisolone.

There is a very great danger of abuse of steroid treatment in asthma. To give such treatment without full investigation and prior or concurrent specific treatment to the limit of modern knowledge is unethical and unsound, but there can be no doubt that the temptation to do so must be great because of the tedious and difficult nature of the specific treatment available and the relatively poor results often obtained. The special clinic willing to undertake such treatment and staffed and equipped to do so must, in these circumstances, be of the greatest value. In all of the 21 cases prednisolone has been of obvious benefit which has been considerable in 18 of them and less marked but, none the less definite, in 3.

The importance of palliative treatment in severe asthma in childhood should never be discounted and excessive suffering for both child and parents should not be allowed to continue. This was dramatically demonstrated by the suicide of a mother who attended the clinic for several months with one of her children with severe asthma, who failed to respond to out-patient treatment. He subsequently went to a residential open-air school where he has improved greatly. No doubt other factors contributed to this poor woman's suicide but the suspicion remains that her child's distressing condition had an important bearing on it. In these circumstances it cannot but be a matter for regret that his admission to the residential school could not be secured earlier, or that steroid treatment was not given pending his admission.

In contrast to the success of the cortico-steroids in asthma, the anti-histamine drugs have been disappointing. They are of great value in other allergic conditions, notably urticaria and hay fever, and are often useful in preventing or treating reactions during hyposensitisation. Occasionally the sedative effect of an anti-histamine such as promethazine hydrochloride may be useful at night. Although new members of this group are still being added, the review of Frankland (1953) serves as an adequate guide and the newer text books of allergy, such as Glaser (1957) devote only a few pages to these drugs. The work of W.E.Brocklehurst and others at the National Institute of Medical Research, Mill Hill, London, some of which was reported at the Third International Congress of Allergology in Paris in 1958, probably gives the clue to the failure of the anti-histamines. Other mediators besides histamine are concerned in the allergic reaction of which a slow reacting substance is of importance. Some of the conclusions reached by Brocklehurst are that in all cases in which histamine causes an increase in

capillary permeability, this effect will probably be prolonged by plasma kinins and globulin permeability factors. In human asthma, the bronchospasm can be accounted for by histamine and SRS-A (a slow reacting substance). Whilst the oedema of connective tissue and increased glandular activity may be caused in part by plasma kinins, it is unlikely that 5 hydroxytryptamine is important either in asthma or skin reactions in man.

Glycyrrhetic acid and its isomers extracted from liquorice root have some anti-inflammatory effect and are non-toxic. The effect is related to that of cortisone and the substances can be used locally as well as systemically. No real effect has been demonstrated in asthma but the very fact of the lack of toxicity makes this an attractive field. A small trial has been carried out in the Birmingham Clinic. No clinically useful effect was demonstrated with the preparations available. Colin-Jones (1957) mentions some experience with glycyrrhetic acid but as yet no really encouraging effects of these preparations have been reported.

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... accepted ... as if ...
... of all ages, and particularly children, of ...

NON-SPECIFIC TREATMENT

It is owing to the uncertain results of specific treatment that non-specific treatment in asthma is of importance, but all the measures which will be considered under this heading should be recognised for what they are and not regarded as really satisfactory by themselves no matter how useful they may be in practice.

ANTIBIOTICS.

Since infection plays a significant role in precipitating attacks of asthma in children, it is important to combine antibiotic treatment, usually with penicillin, and antispasmodic treatment during acute attacks. The younger the child, the greater is the need to use penicillin during the acute attacks and the more likely the patient is to respond. As children get older, particularly after they pass nine years of age, they become less susceptible to acute upper respiratory infections. Even in the absence of purulent sputum, antibiotics may be of value. Severe anaphal⁷actic reactions to penicillin have not been encountered in the Birmingham children. Wayne (1958) states that the people who get drug reactions characterised by anaphal⁴actic shock, by asthma or urticaria are predominantly allergic individuals. It seems doubtful if this is really true and certainly this statement should not be accepted without satisfactory evidence as it would tend to deprive asthmatics of all ages, and particularly children, of such valuable drugs as penicillin through fear of provoking severe allergic drug reactions. In a large (unpublished) series of acute allergic reactions occurring in the course

of anti-tuberculous treatment, very few subjects had any previous history of allergic disease and many patients with a previous history of allergic disease failed to develop drug allergy in the course of long continued triple drug treatment in spite of the fact that it is very common, occurring in more than 12% of all patients so treated. Lewis-Faning and Davies (1959) give an account of a controlled trial of continuous oral penicillin therapy in asthmatic children during five winter months. They experienced no serious side-effects but they did not find this continuous therapy materially improved the children or reduced the number of their attacks compared with the controls. A further study of tetracycline treatment given in the same way is to be undertaken. In spite of the negative results obtained with continuous penicillin, the value of penicillin in the treatment of the acute attack of asthma should not be discounted.

TONSILLECTOMY.

The removal of tonsils and adenoids for the relief of asthma in children is still very widely practised although from time to time over many years reports have been published showing poor results from this procedure. Peshkin (1927) in 100 children found only one improved and Bullen (1931) found that no improvement occurred and that allergic manifestations were at least as likely to develop in children who had been subjected to tonsillectomy as in those who had not. McCorkle, Hodges, Badger, Dingle and Jordon (1955) studied the effect of tonsillectomy on the ratio of respiratory infection encountered in children and concluded that it had no effect at all. In this country Fry (1957) in a

paper entitled, "Are all T's and A's really necessary?" showed that there was an undiminished number of tonsillectomies being carried out among primary school children in England and Wales in spite of evidence that the procedure was often of little or no value. He has found that in his general practice there is a natural tendency for children to "grow out" of their common respiratory infections after the age of 7 - 8 years. He himself referred only 5% of the children in his practice for tonsillectomy over a 10 year period compared with the national average of $33\frac{1}{3}\%$, but in spite of this, had not apparently given rise to harmful effects to the children in the practice.

The experience of tonsillectomy among the children attending the asthma clinic in Birmingham has been disappointing. The results are given in Table XXII, together with similar results reported by Fisher (1946) from Manchester. The operation is now rarely recommended.

TONSILLECTOMY FOR ASTHMA.

TABLE XXII.

<u>Good Effect</u>	<u>Bad Effect</u>	<u>No Effect</u>	<u>Total</u>	
10	17	62	89	Birmingham
12	9	36	57	Manchester

BREATHING EXERCISES.

There are two small books on breathing exercises for asthmatics both of which are excellent. "The asthmatic child", by G.F. Walker (1950) is specifically designed for children and "Physical Exercises for Asthma", published by the Asthma Research Council (1949) is designed for all ages. Within the Birmingham School Health Service there are facilities for physiotherapy by fully trained physiotherapists at a number of the school clinics. The exercises used

are those recommended by the Asthma Research Council. Facilities for physiotherapy also exist in all the open-air schools, both residential and non-residential. Thus a high proportion of the children attending the asthma clinic receive active tuition in breathing exercises. There is no doubt that it is a very useful practice to teach all children to make the best possible use of their respiratory function and although breathing is a natural function, few people are able to make the best use of their ability without tuition and practice. Where there is a condition, such as asthma, which tends to give chronic or recurrent attacks of impaired respiration, it is desirable to obtain the best reserve of respiratory capacity possible. There are some advantages also in that the patient may gain in confidence in relation to breathing. On the other side, however, is the fact that further attendances at clinics will be required during school time and in Birmingham it is always urged that the child be taught to do the exercises and thereafter to continue them at home. The limitations of breathing exercises should be recognised. They are not applicable to the seriously ill child who is seldom able to attend school. They cannot be expected to correct thoracic deformities which have arisen in infancy and they have no true curative effect on the illness. Van Ufford (1956) sets out the purpose of physical therapy as -

- (a) the prevention or correction of changes in position and deformities;
- (b) the improvement of the type of breathing;
- (c) to increase the power of endurance, while retaining the correct breathing technique during movements;
- (d) relaxation therapy.

Livingstone and Gillespie (1935) reported that 52 patients out of 75 treated with breathing exercises only for a year had improved compared with 36 out of 50

patients who were treated by removal of allergens, hygiene and injections. All were allowed to use the usual palliatives. In spite of the good results obtained with exercises alone they conclude that specific treatment should be used as well.

OPEN-AIR SCHOOLS AND CONVALESCENT HOMES.

Birmingham is particularly fortunate in having several residential and non-residential open-air schools. The need for them is, of course, considerable in such a large industrial centre. The non-residential open-air schools should provide special facilities for delicate children, including asthmatics, and should enable them to benefit from the educational facilities more than would be possible otherwise. Unfortunately they fail to some extent in relation to the asthmatic children. The quality of the teaching does not appear to be sufficiently high and as Williams (1959) states - it is of the greatest importance to these children to make the best of their education. The practice in these schools is to have the children attend half an hour before the normal school time and to give them breakfast. This does not suit the asthmatic as it means a bus journey during the busiest hour and often when his chest has not recovered from the early morning exacerbation which is so common.

The residential school on the other hand, has many advantages and a large number of the children with moderate and mild asthma of non-seasonal type obtain great relief at these schools even when they are just outside the city boundary. There is a marked tendency for relapse to occur during holidays at home and on leaving these schools. Ideally all specific and non-specific treatment should be

carried on while the children are at these schools but this has not been possible, partly because they are scattered between four different schools and partly because the teaching staff do not appreciate the need to continue treatment in children who, while in the residential school, are not always troubled by their asthma. The best results are obtained in children from poor and crowded homes whose asthma is largely of infective etiology and who have a marked tendency to natural recovery in late childhood.

The British Red Cross Society, aided by certain voluntary funds, gives assistance to asthmatic children in two ways in Birmingham. Small numbers of children are sent to Davos in Switzerland for periods of about six months, and others are sent to Beech Hill Convalescent Home in Berkshire for periods of about three months. The children who go to Beech Hill have any specific treatment carried on so that every endeavour is made to prevent relapse on return home. This principle has always been considered important at the Jewish National Home for Asthmatic Children in Denver, Colorado, (Glaser - 1958). The altitude of Denver is similar to that of Davos- just over 5,000 feet - and it appears that many children with perennial asthma who are sensitive to dust and to atmospheric pollution become free of asthma at this altitude. The greater benefit is probably obtained by sending to Switzerland the severely affected child who has failed to obtain any significant benefit from out-patient treatment or from a residential open-air school in this country, and who is severely under-nourished and under-weight as a result of asthma present since infancy. Only a few exceptionally severe cases fail to obtain relief while in Davos. Experience in Birmingham so far covers 15 children who have been to Beech Hill. In all but two, the immediate

result was excellent although only six were still well after being home again for six months. With regard to Davos the results have been similar. Twenty-two children have been to Davos and all but one were well and free or almost free, of asthma. None failed to improve in general health but six months after return all were having asthma again although 14 of them were still better than they had been before going to Switzerland. Apart from the benefit to the child there is an undoubted benefit to the rest of the family, particularly the mother, from a period of rest, relief and renewed hope which these schemes provide. Kraepelien (1956) discussed the question of homes for asthmatic children and concluded that high altitude was seldom necessary and that there was much to be said in favour of a home not far removed from the centre of population from which the children came and under the guidance of a paediatrician interested in asthma. Altitude has, however, a definite effect as Wissler (1956) says and in a few cases will give relief when all else has failed.

PSYCHOTHERAPY.

The place of psychotherapy in the treatment of asthma is not yet defined. No doubt any good physician in the course of unhurried and careful clinical work carries out some psychotherapy. With children such is the case when the physician listens with care to the mother's story, not once but every week for months and even years as happens in the Birmingham clinic. Only rarely are children referred to a child psychiatrist and given psycho-therapeutic treatment at the child guidance clinic. The results are not dramatic but in

a few obviously disturbed children they have been beneficial. The disturbed patient with asthma requires psycho-therapy and it will help him but is unlikely to cure his asthma. Dennis Leigh (1953) feels that ideally the family practitioner should be able to carry out psycho-therapy but that conditions of modern practice seldom allow enough time to do so. Stokvis (1959) says, "in certain cases, psycho-therapy is indeed indicated, our experience has shown that the patient very often benefits from it, although the results are still conducive to modesty".

HYPNOSIS.

Treatment by hypnosis is only separated from the wider field of psycho-therapy because it has been the subject of a special study in Birmingham. During the period September, 1958 to March, 1959, this study was carried out with the help of a senior child psychiatrist - Dr. C.L.C. Burns. Initially it was planned to conduct a controlled trial since a search of the literature failed to reveal more than occasional vague reference to a limited number of cases so treated, and no planned study of the value of hypnosis in asthma could be found. A set of random numbers was supplied by a statistician and according to these either treatment with hypnosis or a simple interview with the psychiatrist was to be given on four occasions at weekly intervals. Assessment was planned to show both an immediate improvement or a delayed improvement should either, or both, occur. Respiratory function tests were made the week before treatment, before and after treatment on each occasion, and finally, the week after treatment. The tests used were the forced expiratory volume in one second and the vital capacity. In addition, a simple

symptom record card such as was in general use in the clinic, was used. Any definite evidence of improvement, of any degree, was sought.

Having treated 30 cases in this way, it was obvious that there was no objective improvement in any so that the statistical diagram for sequential analysis remained blank. It was decided, therefore, to abandon the controlled trial but further children were included for hypnosis only. A total of 25 children, 17 boys and 8 girls, were treated by this method but none showed any objective evidence of improvement. The finding was most unexpected and very disappointing to the psychiatrist. The children proved good subjects for hypnosis and suggestion is generally believed to be capable of giving up to 40% of positive results in asthma. Placebo results were 33% in a carefully controlled trial of pollen vaccine reported by Frankland and Augustin (1954) and 14% in a similar trial of hydro-cortisone by inhalation (Smith, 1958). These positive results with placebos may, however, have arisen because of the use of a largely subjective assessment or because of natural fluctuation of the course of the asthma and not necessarily as a result of suggestion as is usually supposed. The children chosen for the hypnosis trial had particularly chronic asthma with little spontaneous improvement and the assessment was objective.

* * * *

SPECIFIC TREATMENT.

Specific treatment in any allergic disease consists either of the removal of the allergen from the patient or some method whereby the patient's allergic hypersensitivity may be diminished so that the effect of an allergen which cannot be removed will be less. To break the contact between the patient and the factor in the environment which gives rise to the symptoms is the more desirable aim. Unfortunately it is only the rare patient who is allergic to an uncommon and unessential food, an easily avoided animal or air-borne allergen. Such simple problems are usually dealt with by the patients themselves or their family doctor and those referred to the asthma clinic for special treatment usually display evidence of allergic sensitivity to environmental factors which are almost impossible to escape. This does not, however, mean that nothing can be done to control the environment or to reduce exposure to known allergens. The work of the health visitor attached to the asthma clinic has been described by Miss C. Butt (1956). Much can be done by tuition and encouragement in the limitation of the amount of house dust inhaled by asthmatic patients. This is particularly true of the bedroom which should be made as bare and hygienic as a hospital ward. Limiting factors are usually economic in this field but many mild cases will respond to these measures without any additional treatment. Frequently feather pillows have already been replaced when the patient first attends the clinic but it may not be appreciated that kapok and cotton flock are also common inhalant allergens. Nothing so dramatic occurs in

Birmingham as the effects of removal of pillows stuffed with rabbit fur which were used on the beds of Jewish children in New York and often gave rise to asthma. Of the animals the cat is the most important and the horse has now become a rarity in Birmingham, although true sensitivity to horse dander is occasionally encountered in girls from middle and upper class families who ride and groom horses during their leisure.

A recent investigation of the manufacture of a very popular brand of spring-interior mattress revealed that the usual packing material in all but the most expensive mattresses consists of cotton with some coarse vegetable fibre added in places. In the expensive mattresses mixed hair is used to some extent and in the most expensive of all pure horse-hair. Few of the patients attending the Birmingham clinic had such expensive mattresses. The new synthetic fibres like terralene are now used in the making of pillows and quilts and should give rise to less dust and be very suitable for asthmatics. Foam rubber pillows and mattresses are often advised. It should be recognised that even the most careful methods of dust limitation will only attain relative success and that in the more severe cases this will make no apparent difference clinically. As previously explained, the air at an altitude of 5000 feet is much clearer and most children with asthma are relieved there. It is, however, impracticable to maintain them all indefinitely in places such as Davos.

An interesting and possibly informative experiment might be carried out by placing several children with chronic and manifest asthma in a really efficiently air-conditioned room for, say, an hour and measuring their

forced expiratory volume at intervals. The air-conditioning system would have to be such that all particulate matter would be removed from the air and all such gases as sulphur dioxide and chlorine which are irritants. If the particulate matter and the irritant gases could be separately removed, or not, at will, the effect of each might be assessed. Such an experiment has not, as yet, been carried out owing to the absence of a suitable air-conditioning plant. Such apparatus does exist in certain factories where ampoules are filled with sterile material but unfortunately these factories are mainly on the outskirts of London and none are available near Birmingham.

Seasonal allergens can be avoided fairly easily if the patient has the leisure and the money to take a sea voyage during the summer season or to reside on a small island such as the Isle of Sark. For most people with pollen allergy, however, simple advice such as avoidance of outdoor games, gardening and summer holidays in June and July is sufficient. Most of them will require anti-histamine treatment or hypo-sensitisation, or both as well. It is, however, unwise for the subject with pollen allergy or allergy to a common group of moulds such as *Cladosporium* to walk through fields at the height of the season when the allergen is most prevalent. Such an action might give rise to a very severe attack of asthma. Occasionally it may be necessary to give advice on a prophylactic basis regarding avoidance of allergens. Should a child belonging to a family with a high incidence of hay fever show a marked skin reaction to grass pollen it would be unwise to allow that child to help in hay-making.

Foods seldom need to be avoided on account of asthma in children of school

age but in those who suffer from eczema and who still show exacerbation of the children after eating certain foods, these should be avoided as far as possible. It is, however, the commonest foods which are most often involved such as egg, milk, fish, wheat and oats. Egg is probably the most important and often worth taking special care with. Fish may be avoided and be known to cause symptoms and yet some proprietary tonic containing fish oil is given by a misguided mother. Such simple errors can be corrected if sought and the health visitor should include a careful discussion regarding diet in her visit to the home.

Taking naturally occurring allergic disease as an abnormal reaction to the environment, using the latter term in its widest sense, it is of obvious importance to have as close a contact with and as much control over the environment as possible. This object is achieved as far as it can be by the use of trained health visitors who also act as clinic nurses in the asthma clinic. This aspect of the work of an asthma clinic is considered to be just as important as it has been generally accepted to be in relation to the work of a tuberculosis clinic. Asthma in childhood should be regarded as a family disease in much the same way as we have learned to regard tuberculosis.

HYPO-SENSITISATION.

This aspect of the treatment of asthma is the most controversial, even now, fifty years after its introduction by Noon and Freeman (Noon 1911, Freeman 1911). On one hand we have reports such as those of Conybeare and Witts (1935) and of Boland (1938) and Boland and Lintott (1939) which appear

to demonstrate the futility of hypo-sensitisation, and on the other hand, Bruun (1957) reports excellent results. The mechanism of hypo-sensitisation is not fully understood. The accepted belief at present is that blocking antibodies are produced and that the circulating reagins are not reduced. Cooke, Barnard, Hebal and Stall (1935) thought that transfusion of blood from hypo-sensitised hay fever sufferers might improve other sufferers from the same condition who had not received hypo-sensitisation and claimed good results in 16 out of 20 patients so treated. This blocking antibody is apparently thermostable, whereas the skin-sensitising reagin is thermolabile (Loveless, 1940, 1943). The whole question of the mechanism of hypo-sensitisation is discussed by Bruun (1959). From a clinical point of view the important thing to know is to what extent, and in which cases, can successful relief of asthma be obtained by this tedious and potentially dangerous method of treatment. The clinical result may vary within wide limits depending not on the procedure itself but upon other factors, such as the skill and experience of the physician, the suitability of the solution used, the dosage and duration of treatment and other non-specific factors such as the climate, air pollution, humidity and the age of the patients treated. It is conceivable that the poor results obtained at Guys Hospital in London in 1935 might be due to the prevalence of the "bronchitic element" among the patients for London has been noted for bronchitis among its residents since the time of the Roman occupation 2000 years ago. The mixed inhalant solution used by the physicians at Guys Hospital might well be inferior as a specific antigen in their patients to the house dust solution

used by Bruun in his patients. There is in all reported results of treatment in asthma an element of uncertainty introduced by the largely subjective methods of assessment used by most observers which can alter the conclusions from the work materially.

The house dust antigen is not yet fully understood; Maunsell (1956) states that house dust contains living organisms, mould spores and materials from buildings, furniture, etc. of plant and animal origin which may be broken down by bacterial action. It varies in potency as an allergen geographically and may also vary in content. In spite of this the most remarkable thing about it as an antigen or allergen is its relative uniformity. It is less remarkable that there may be a difference in the skin responses produced by house dust collected in London and in Davos than there should be a very close similarity between the reactions produced by house dust collected in London and in Birmingham. Maunsell has studied the effect of mould growth on the potency of house dust as an antigen and it did appear reasonable to suppose that the antigen in house dust might be dependent upon mould growth and the presence of mould spores for much of its potency. The strongest samples of dust which Mrs. Maunsell obtained were from damp houses with a high content of penicillium spores. However, at the Fourth European Congress of Allergy in London in 1959, she reported that the deliberate attempt to enhance the antigenicity of house dust samples by growing species of penicillium on them for five weeks failed and, in fact, had the opposite effect.

Allergy to mould spores in Britain has been investigated by Hyde, Richards and Williams (1956) and their experience indicates that this is not very common

but that Cladosporium is not only the most abundant group producing spores in the air, particularly in the country, but that it is clinically much more important than the others. Alternaria is less common and less important than it appears to be in North America. Penicillium might be expected to be of importance especially in patients also sensitive to house dust but this does not appear to be so. Of the rest Botrytis, Rhoma, Pullularia and Candida seem to be of little significance, but recently, Aspergillus fumigatus has been shown to cause a well-marked group of cases of asthma of both clinical and theoretical importance (Pepys, 1959). Hyde, Richards and Williams found 4% of their patients had clinically significant allergy to Cladosporium and 1% to Alternaria but none to the other groups. Mould allergy in Birmingham children is rare and nothing can be said about the results of treatment. Hyde, Richards and Williams, however, report good results with hypo-sensitisation in cases of Cladosporium allergy and this has been borne out in three cases so treated in Birmingham with pre-seasonal hypo-sensitisation.

Hypo-sensitisation in hay-fever and pollen asthma is a much more clearly defined subject. Here there is no doubt that a high degree of success is obtainable and the trial conducted by Frankland and Augustin (1954) has provided clear scientific confirmation of this. Pollen allergy occurs more commonly as a single uncomplicated condition. The season is short so that non-specific changes are less likely to occur especially in summer and the condition is less likely than perennial asthma or rhinitis to become self-perpetuating. The treatment can easily be carried out when the subject is free from natural exposure to the allergen. All these circumstances may contribute

towards the highly satisfactory results obtained.

Among the Birmingham children the results of hypo-sensitisation are given below. There were 63 cases of hay fever and pollen asthma with an average age of 10 years. Of these 43 were boys and 20 girls. Thirty-four had only one season of treatment, while 29 had more than one season. The results were better ~~than~~ in those who had more than one season and the practice usually adopted is to give at least three years treatment before stopping to see if the symptoms will recur without further courses.

TABLE XXIII.

MIXED POLLEN VACCINE TREATMENT.

Single Season	-	Symptom free	13	(38.5%)
		Improved	15	(44.1%)
		Not improved	<u>6</u>	(17.4%)
		Total	<u>34</u>	
Multiple Seasons	-	Symptom free	21	(72.42%)
		Improved	5	(17.24%)
		Not improved	<u>3</u>	(10.34%)
		Total	29	
All Cases	-	Symptom free	34	(55.46%)
		Improved	20	(30.67%)
		Not improved	<u>9</u>	(13.87%)
		Total	<u>63</u>	

Hypo-sensitisation with house dust solution was given to 122 children for at least six months. Of these 85 were boys and 37 girls, a ratio of 2.3 to 1 which is not very different from the pollen cases. The average age was, however, lower, 8.8 years. Assessment of results was more difficult than with the pollen cases and less certain.

HOUSE DUST VACCINE TREATMENT.TABLE XXV.

Much improved	-	60	(49.18%)
Slightly improved	-	24	(19.67%)
Not improved	-	<u>38</u>	(31.15%)
Total		<u>122</u>	

The cases who had shown considerable improvement did not differ from the group as a whole in respect of the average age at the onset of treatment (8.8 years). The sex ratio of the successful cases was 2.15 to 1 in favour of the boys which was similar to that of the whole group (2.3 to 1). The duration of treatment was over a year in a higher proportion of the successful cases than in the group as a whole, but the difference was not very great.

DURATION OF TREATMENT WITH HOUSE DUST.TABLE XXVI.

Successful cases - over 6 months	13	(21.7%)
over 1 year	31	(51.7%)
over 1½ years	5	(8.3%)
over 2 years	<u>11</u>	(18.3%)
Total	<u>60</u>	
All cases - over 6 months	39	(32%)
over 1 year	50	(41%)
over 1½ years	13	(10%)
over 2 years	<u>20</u>	(17%)
	<u>122</u>	

Brunn (1957) claims 88.2% of good results after 6 - 12 months but almost 30% relapsed at three years, whereas with at least three years of treatment

he obtained sustained improvement in 83.4% of patients. All this is very difficult to assess, particularly in children where, as has been shown, there is a natural tendency towards recovery which makes assessment of any long term therapy doubtful. The follow-up studies of asthmatic children by Rache mann and Edwards (1952) and by Unger, Unger and Wolf (1952) are difficult to evaluate because of this. Almost anything can happen in 20 -30 years, irrespective of the treatment given. The results given by Maunsell (1956) approximate to those obtained in Birmingham.

There is no doubt that a carefully planned controlled trial would still be worth while and it is proposed to carry out such a trial in Birmingham with assessment over a period of six months during which weekly respiratory function tests will be done. Brunn carried out a controlled trial in Copenhagen in 1947-48 and in 189 cases and claimed that 78% of those treated specifically were improved compared with 34% of the placebo cases. He states (1959) that "it is true that a certain percentage of asthmatic children are apparently spontaneously freed from the disease at the time of puberty; however, a sober analysis shows that this applies at most to about 20% of the cases. In contrast with this it may be stated that the corresponding percentage of improvement in asthmatic children subjected to specific hypo-sensitisation is about 85 per cent". Experience in Birmingham suggests that much more than 20% of children show spontaneous improvement and that significant improvement cannot be obtained in such a high proportion as 85 per cent with hypo-sensitisation.

Bacterial vaccines have not been used at all in the Birmingham clinic.

A controlled trial carried out at St. Mary's Hospital, London, by Frankland, Hughes and Gorrill (1955) in 200 cases of "infective asthma", using autogenous bacterial vaccines resulted in 50% improvement in the treated cases and 50% improvement in the controls who received carbol saline injections.

DIFFICULTIES AND DANGERS WITH HYPO-SENSITISATION.

Collapse and death may follow the injection of an allergen into a subject allergic to that allergen. The British Medical Journal (1958) discusses the hazards of such treatment which apply mainly to pollen extracts. In children the dangers of reactions are probably greater than in adults. In the Birmingham clinic very great care is taken. Each patient starting pollen vaccine injections for the first time has a test dose of the weakest strength diluted 1 in 10 or 1 in 100 before the ordinary vaccine is begun. All vaccines are ordered annually at the beginning of the season and no pollen vaccine is kept over to the second year. Thus difficulty has not been experienced with instability as has been reported by Hyorth (1957). An opened bottle is rarely used after one week. The patients have record cards showing each dose given and a duplicate record is kept in the case notes. Each single dose is prescribed by a physician and checked and given by a nurse. The patient must wait at least 20 minutes before departing and any evidence of local or general reaction is recorded. Antihistamine tablets are given if the local reaction is significant. This careful procedure is time-consuming but no serious reaction has been experienced in six years using such methods. In adults dust solutions give rise to very little trouble but in children every care must be taken with every type of injection. Continuation courses are

given by general practitioners in some cases, particularly in grammar school children, to whom the loss of school time involved in a visit to the clinic may be serious. Thus 9 out of 122 dust cases have been passed on to their family doctors but only one of 63 pollen cases.

There is one final but important point about hypo-sensitisation which applies to children receiving steroid treatment concurrently. It is important that this should never be stopped without the knowledge of the physician as an unexpected severe reaction may occur which could have been avoided had it been known that the steroid had been omitted. One such incident has occurred in Birmingham due to the fact that a general practitioner prescribed a course of steroid treatment unknown to the clinic physician and when this was suddenly stopped the next injection given gave rise to an unexpected reaction, fortunately, only local. It is of the greatest importance that the liaison between family doctor and the clinic physician should be close and cordial.

* * * * *

... and special facilities. ...
... the care of asthmatic children so that it is ...
... for the family doctor to undertake, and ...
... a clinic can provide new knowledge of the ...

C O N C L U S I O N S

The study of the prevalence of asthma in children attending Birmingham schools has shown that it is a very common condition in childhood. The overall prevalence of 1.76 per cent is likely to be a low estimate of the amount of active asthma between the ages of five and fifteen years. It agrees well with figures from Sweden and Norway of 1.37 per cent and 1.77 per cent respectively and is appreciably higher than some figures reported from the United States of America.

The prevalence study also revealed a hitherto unreported sex difference which has long been suspected because more boys than girls attend for treatment. With increasing age there was a tendency for the sex difference to become less marked owing to a decreasing prevalence in boys. It seems most unlikely that this sex difference can be explained on an environmental basis. The explanation may be hormonal and its elucidation may have to await further advances in the techniques of hormone assay. New light may be thrown eventually upon the pathogenesis of asthma which at present is only partly understood.

The investigation and treatment of asthma in children is tedious and requires special knowledge and special facilities. Here lies the need for a clinic for the care of asthmatic children so that techniques, difficult and time-consuming for the family doctor to undertake, can be carried out. In addition such a clinic can provide new knowledge of the disease and serve as a suitable unit for clinical trial of new methods of treatment. The close association with the other departments of the school health service is of

value both in relation to diagnostic help such as may be afforded by the child guidance clinics and therapeutic help such as may be obtained through the special schools department.

In Birmingham it has been possible to accumulate information about the natural history of asthma and related disorders and about the family background of the affected children. It has also been possible to evaluate such methods of investigation as the skin tests to common inhalation and food allergens and to add something to existing knowledge of the etiology of the condition.

With regard to treatment, it has been possible to obtain experience of the most suitable palliative treatment for children, including the use of steroid preparations in severe chronic cases. The value both of specific and of non-specific methods of treatment have been studied and several clinical trials undertaken. Experience gained in clinical practice in this way is invaluable, particularly in relation to a condition such as asthma where so much uncertainty has existed and so much controversy arisen about the value of various methods of treatment. Wherever possible objective methods of assessment have been used in reaching a conclusion about the results.

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S U M M A R Y

1. A prevalence study carried out in children attending Birmingham Schools revealed that between the ages of 5 and 15 years the overall prevalence of asthma was 1.76 per cent. The prevalence in boys fell from 2.58 per cent at 5 - 6 years, 1.96 per cent between 13 and 15 years, while in girls, the prevalence was 1.02 per cent at 5 - 6 years, and 1.21 per cent at 13 to 15 years.
2. Experience in a special clinic within the School Health Service in Birmingham, for the treatment of asthma and related disorders over a period of six years and more than 500 patients is reported.
3. Family size and circumstances were not found to have a marked influence on the occurrence of asthma, but a strong hereditary tendency was evident.
4. The most important associated disorders were found to be infantile eczema, which often preceded asthma, and hay fever, which often developed at a later age.
5. Investigation of individual cases had to be very thorough and include careful enquiry into personal and environmental history, together with physical, radiological and other special methods of investigation.
6. Of the special methods of investigation the skin tests were found to be the most generally applicable, simple, safe and reliable but then to apply the results to clinical assessment and treatment required understanding and experience. In the absence of such experience and understanding, the results would undoubtedly be misleading.

7. Asthma in children was found to have a predominantly allergic background, but many other factors also played a part. The most important allergic factors were house dust in perennial cases, and grass pollen in seasonal cases. The most important non-allergic factors were infection, emotion and non-specific irritation of the respiratory tract from air pollution. A self-perpetuating trend such as is evident in infantile eczema may also be present.

8. Palliative treatment in children requires special consideration and experience with Prednisolone given by mouth in minimal amount over prolonged periods to the most severely affected cases, has proved of great benefit without resulting in side effects. Clinical trials of hydrocortisone given by inhalation and of the active isomers of Glycyrrhetic acid given by mouth failed to demonstrate any useful effect from either.

9. Non-specific treatment was found to be of great importance owing to uncertain results of specific treatment. Antibiotic therapy of infections of the respiratory tract, breathing exercises and open-air schools proved to be of great value in many cases. Hypnotic suggestion and tonsillectomy failed to result in significant benefit.

10. Specific treatment by removal of an offending allergen is often difficult or only partly applicable. Hypo-sensitisation to inhalant allergens proved most successful in seasonal cases with pollen allergy where 55 per cent could be rendered symptom-free, and a further 30 per cent improved. Hypo-sensitisation with house dust solution in perennial cases was less successful, but 49 per cent were much improved after at least six months treatment, and a further 19 per cent slightly improved.

11. Both experience and great care are necessary in administering hypo-sensitisation treatment to children, but given these no serious accident has occurred.

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