Asthma in Children

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Preface

Rapid advances have been made in our understanding of asthma during the past two decades, particularly in the physiology and immunopharmacology. In addition, powerful new chemotherapeutic agents have become available. Nevertheless, although the road to therapeutic success as always is paved with good intentions, treatment is still difficult and failure not unusual. How common it is to see a child who has had every conceivable form of treatment, yet the parents are at their wits' end because the result has been an abysmal failure.

Starling was right of course when he said that the physiology of today becomes the clinical medicine of tomorrow and this is true of other disciplines. One object of this monograph is to hasten that process. It seemed appropriate at this juncture, therefore, to bring together current knowledge in all aspects of the subject and to emphasize the therapeutic implications. The clinical sections of the book are set out with the object of correlating clinical features with the physiology, immunopharmacology and pathology.

Despite recent advances, the therapeutic weapons available to us often do not control the disease completely and the physician must rely on the art as well as the science of medicine as his forebears had to do. This implies making clinical judgements which will bring maximum benefit, bearing in mind the individual's specific abnormalities and the therapeutic methods available. Experience surely teaches that therapeutic success depends not only upon choosing the right weapons but equally upon the skill with which they are applied. I have made full use of knowledge available in the literature but at the same time have not hesitated to draw upon my own clinical and physiological experience, so to this extent the book is an expression of personal views. In this context it is appropriate to add a word about the chapter on psychosomatic relationships. It is usual for this subject to be dealt with by a psychiatrist, who naturally approaches it from the psychological point of view. This has the disadvantage, however, that the clinician tends to regard the subject as a somewhat mysterious and specialized sphere which he can safely ignore and leave to a psychiatrist, an attitude which it is hoped this book will help to dispel. The subject is approached here from the point of view of the clinician, since it is

he who has to grapple with it in the first instance. Moreover, all treatment including the use of drugs has psychosomatic implications, so that it is an over-simplification to confine a discussion of the subject to its psychological ramifications. Recent advances in our understanding of the physiology of the bronchiole have helped to clarify the relationships between the psyche and the complex somatic component, the latter including as it does the impact of chemotherapy on the individual's pattern of pathophysiology and immunopharmacology.

I am greatly indebted to many friends and colleagues for their advice and encouragement, in particular Professor O. P. Gray, Dr. R. P. Orange, Dr. M. I. Blackhall, Dr. N. B. Pride and Dr. R. E. C. Altounyan. I wish to thank Mr. H. Greenwood and the Committee of the Children's Research Fund for financial support of the physiological research out of which this work grew. In particular Ruth, my wife, has offered valuable support and guidance at all stages. Miss D. M. Hartley, my secretary, whose enthusiasm, patience and forbearance never failed, performed many tasks including the typing of the manuscript. Lastly, I wish to thank the publishers for their encouragement and guidance throughout the preparation of this book.

R. S. J.

Contents

I Introduction

Asthma is a disease which commands attention because it is common although the incidence is in dispute, morbidity is high, views on management are contradictory, and a definition defeats even the erudite. Despite this state of affairs, much progress has been made during the past decade and it is appropriate therefore to assemble available information, especially from the point of view of its bearing on management. Although all aspects of the subject will be discussed, the early chapters are concerned with basic knowledge of prevalence, immunology, physiology, pathology and chemotherapy. A consideration of psychosomatic relationships is then followed by chapters on details of management. These are described within the framework of a classification suggested by the author since it is believed that this approach is more informative than alternative physiological or clinical grading systems.

Prevalence

The prevalence reported has varied from 1 to 14% of the population. An incidence of 0·73% for the whole of Sweden, but 1·37% for Stockholm was reported by Kraepelien (1954). A U.S. National Health Survey (1959–61) reported a prevalence figure for allergic diseases as a whole of 7·4%, with asthma 2·6%, hayfever without asthma 2·5% and other allergy 2·4%. Out of all chronic diseases of childhood under 17 years of age, asthma accounted for 11·4% (Table 1.1).

Table 1.1 Incidence of Chronic Disease in Children

Asthma	11·4%
Hay fever	10·8%
Other allergy	10·6%
Other respiratory disease	15·1%
All other chronic disease	52·1%
	100%

Data from U.S. National Health Survey (1959–61).

Freeman and Johnson (1964) sampled over 2,000 children from the school population of Denver, Colorado, and reported a prevalence of asthma of 2·8%, hayfever 19·1% and perennial rhinitis 6·4%, with an approximate over-all figure for allergic disease of 24·3%, varying from 14% in the lower socio-economic group to 35% in the upper group. There was a family history of atopy in 73%. Dawson *et al.* (1969), in a similar survey in Aberdeen, reported an incidence of asthma of 4·8% and of these 61% had other forms of allergic disease, 37% eczema, 29% allergic rhinitis and 8% urticaria. There was a history of asthma in 53% of first degree relatives. There was an excess of severe asthma in the lower social classes and larger families. On the other hand, Graham *et al.* (1967), studying children aged from 9 to 11 years in the Isle of Wight, reported an incidence of 2–3% with predominance of asthma in the upper rather than the lower social classes.

A major difficulty not overcome in the surveys mentioned is that of defining asthma. Williams and McNicol (1969) overcame this by dividing the sample of 7-year-old schoolchildren in Melbourne into a control group, a 'mild' wheezy bronchitis group in which the children had wheezed in fewer than five illnesses and always in association with bronchitis, a 'wheezy bronchitis' group who had wheezed more than five times, always in association with bronchitis, and finally a group of definite asthma and wheeze unassociated with respiratory infection. They compared the controls with the three disease groups in respect of recurrent bronchitis, persistent or recurrent nasal discharge, a history of hay fever, wheeze in siblings, nasal eosinophilia, skin sensitivity to various allergens and serum histamine binding capacity. They found that in respect of all these comparisons the disease groups differed significantly from the control group, and they concluded that this 'strongly supports the proposition that the patients from the three groups belonged to a single population with a common defect'. The group with mild and infrequent wheezing comprised 7·7% of the population, with wheezy bronchitis 7·7% and with unequivocal asthma 3·7% of the population. They arrived at the tentative conclusion that the true incidence of asthma is of the order of 11·4% and may be higher. This is in line with physiological evidence that even slight wheezing is associated with an abnormal lability index if other diseases have been ruled out (p. 187).

Onset and Course of the Disease

The age of onset reported has been very variable. Ford (1969), in Australia, reviewing almost 12,000 asthmatics found an age of onset < 5 years in 24%, 5–14 years in 16%, 15–29 years in 27%, 30–44 years in 14%, 45–59 years in 15% and > 60 years in 3%. This gives a figure of 40% with onset under 15 years, compared with 25% for males and 16% for females for age of onset under 18 years reported by Fagerberg (1958), and the much higher incidence reported by Derrick (1971) of 72% for males and 55% for females with an onset before the age of 10 years. In

making comparisons between children and adults it must be borne in mind that most childhood asthma is of the extrinsic type (that is, it affects atopic individuals who demonstrate hypersensitivity as indicated by associated allergic diseases, family history, positive skin tests and reaginic (IgE) antibodies) whereas most adults exhibit intrinsic asthma in which these features are absent.

Rackeman and Edwards (1952) followed up 449 asthmatics first seen under the age of 13 years. Of these, 30·7% lost their asthma at an average age of 14·7 years, but varying from 5 to 30 years. Four, or 1%, died of the disease. Out of the 370 who were hypersensitive, as shown by skin tests, only 20·3% lost their asthma, whereas 63% of the 79 with negative skin tests lost their asthma. In a more recent study, Barr and Logan (1964) followed 767 asthmatics for 17–27 years, 65% with onset < 5 years of age: 40–50% lost their asthma, the figure being lower if there was another allergic disease present and higher for boys than girls, the age of onset not affecting the issue. The last point was also noted by Johnstone (1968) in a prospective study of 63 children: 22% lost their asthma at 16 years, there being no correlation between loss of asthma in adolescence and age of onset (Table 1.2), sex or severity of symptoms.

Table 1.2 Age of Onset and Incidence of Asthma at 16 Years in 63 Children

Age of onset:	<1 year	1–3 years	3–6 years	>6 years
Asthma present at 16 years	11	11	18	9
Asthma absent at 16 years	4	2	7	1

Adapted from Johnstone (1968).

Severity of Asthma

Buffum and Settipane (1966), reporting on 518 children followed for 10 years and 136 of these for a further 10 years, reported rather different findings (Table 1.3). Only 5·6% were severely handicapped at the first follow-up and 5·1% at

Table 1.3 Prognosis of Asthma in Children

Followed for	Total No.	Well: No.	%	Mild: No.	%	Severe: No.	%	Dead: No.	%
10 years	518	212	41·0	272	52·4	29	5·6	5	1·0
20 years	136	75	55·1	51	37·5	7	5·1	3	2·2

From Buffum and Settipane (1966).

the second. An onset under the age of 2 years, positive skin tests and the presence of atopic dermatitis were all associated with more severe and persistent asthma. Out of 29 with severe symptoms after 10 years, 21 had or had had atopic

dermatitis, 14 a positive skin test, 15 food sensitivity and in 20 the onset was before the age of 2 years. In all these it continued to be severe after the 10-year follow-up.

Severity in terms of clinical grading was associated with early onset (<5 years) (Table 1.4) in the study of Dawson *et al.* (1969). Out of 20 children with severe

Table 1.4 Age of Onset of Asthma and Severity

Age (years)	Mild: No.	%	Moderate: No.	%	Severe: No.	%	All cases: No.	%
0–2	20	40	20	40	13	65	53	44
3–5	18	36	23	45	4	20	45	37
6–8	6	12	3	6	0	0	9	7
9–13	6	12	5	9	3	15	14	12
All ages	50	100	51	100	20	100	121	100

From Dawson *et al.* (1969).

asthma, 16 were boys; there was a family history in 53%; heights and weights were below normal and they were mostly from lower social classes and larger families.

Sex Ratio

Most reports give a ratio of boys to girls of 2 : 1 but this tends to vary with age, which is well brought out in Table 1.5. In several reports it has been noted that more boys than girls cease to have asthma in adolescence.

Table 1.5 Sex Ratio in Different Age Groups

Age (years)	Boys	Girls	Total	Ratio (boys/girls)
10	20	6	26	3·3/1
11	14	5	19	2·8/1
12	20	8	28	2·5/1
13	18	9	27	2·0/1
14/15	12	9	21	1·3/1
10–15	84	37	121	2·2/1

From Dawson *et al.* (1969).

Social and Psychiatric Status

Although severity was noted above to be associated with lower social status,

the actual incidence in most reports is higher in the upper social strata (Table 1.6). The Table also outlines the relationship to other handicapping diseases.

Table 1.6 Social Class Distribution of Physically Handicapped Children

Group	Controls	Handicapped children			
		Asthmatic	Maladjusted	Neuro-epileptic	Other
Proportion of population percentage	—	2·3	5·7	1·9	1·1
Percentage male	50·1	56·0	64·5	59·6	47·4
Social class (percentage)					
I and II	15·7	39·7	14·3	21·7	26·3
III (non-manual)	15·7	13·7	14·3	21·7	21·1
III (manual)	43·6	35·6	42·8	33·3	26·3
IV and V	23·0	10·9	28·6	23·3	26·3
No. of children in group	147	76	126	63	38

From Graham *et al.* (1967).

This report by Graham *et al.* (1967) is on 3,300 children, aged from 9 to 11 years, in the Isle of Wight and shows the prevalence of asthma to be 2·3%. Intelligence and educational attainment were slightly above average, which is in line with other reports. Concomitant psychiatric disorder was rather more common in the asthmatic (10·5%) than in the general population (6·3%), but there was no difference between children with other physical disorders and asthmatic children. Of the asthmatic children in this study, 35·1% had attacks which appeared to be precipitated by emotional factors. This was thought to be a minimum figure and that psychological factors play a part in the genesis of attacks in both allergic and non-allergic asthmatics. They arrived at the important conclusion that one is almost as likely to find psychological mechanisms at work when organic factors are obvious, as when they are absent. Leigh and Marley (1967) studied asthmatics together with their first and second degree relatives from two general practices in the London area with a total of 18,000 subjects. A greater number of asthmatic than control subjects under the age of 12 years suffered from psychiatric disturbance, and this was also more severe. Females were affected more than males. These authors reviewed the literature in which electroencephalographic abnormalities had been reported frequently but the finding was of uncertain significance.

The importance of emotional factors has been recognized for many years. French (1939) identified the following groups of precipitants of an attack:

sudden intense emotion such as anger or fear; crying, which may relieve or precipitate an attack; disturbance of a dependent relationship such as between mother and child; danger to a near relative; fear of respiratory disease and, hence, of death; utilization of an attack for the purpose of 'gain', real or imaginary. The literature has recently been reviewed by Pinkerton and Weaver (1970).

Mortality

For a hundred years the death rate for the age range 5–34 years remained fairly constant at about 1 per 100,000 persons (Fig. 1.1). The striking increase in the 1960s is brought out by the Registrar General's figures from 1949 onwards (Table 1.7).

Table 1.7 Deaths from Asthma 1949–72, England and Wales

	Age groups (years)				
Year	0–4	5–9	10–14	15–19	20–24
1949	23	7	8	22	33
1950	26	2	5	21	29
1951	31	9	15	28	29
1952	24	3	9	23	31
1953	36	9	8	24	27
1954	34	6	8	25	37
1955	29	8	9	15	39
1956	33	10	18	18	34
1957	24	11	10	19	29
1958	33	8	13	26	42
1959	25	6	12	19	24
1960	29	12	13	17	27
1961	31	6	24	24	28
1962	21	6	29	39	32
1963	37	9	41	36	56
1964	21	23	53	62	51
1965	41	18	66	73	79
1966	20	17	80	92	83
1967	19	30	68	57	61
1968	24	17	41	52	40
1969	26	8	33	37	39
1970	16	11	24	33	36
1971	26	10	22	35	35

Compiled from the Registrar General's Statistical Review.

The increase commenced in 1961, especially in the age group 10–14 years, leaving the young and the old unaffected (Fig. 1.2). For the 10–14 years group the rate per 100,000 increased from 0·33 in 1959 to 2·45 in 1966: almost eightfold (Speizer *et al.*, 1968a). The same authors have pointed out that for this

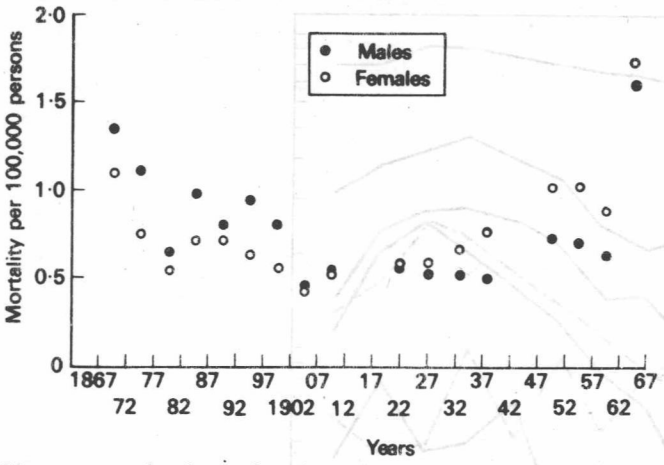

Fig. 1.1 Mortality from asthma for England and Wales, 1867–1966, in males and females aged from 5 to 34 years. From Speizer and Doll, 1968; data from Annual Report of the Registrar General for the years 1867–1966.)

age group asthma accounted for 1% of all deaths in 1959, but increased to 5·7% in 1965 (Table 1.8), reaching a peak of 7·2% in 1966.

The increase was not uniform, being marked in the U.K. but not appreciable, for example, in the U.S.A. (Fraser and Doll, 1971). Speizer *et al.* (1968b), Inman

Table 1.8 Ten Major Causes of Death in England and Wales in Children aged from 10–14 Years for the Year 1965

Cause of Death (International Classification of Diseases—I.C.D.)	No.		Total	Percentage of total deaths in age group
	Male	Female		
1. All motor accidents (I.C.D. E810–E825)	127	66	193	16·6
2. Malignant neoplasms other than leukaemia (I.C.D. 140–203, 205)	85	39	124	10·7
3. All congenital malformations (I.C.D. 750–759)	50	51	101	8·7
4. All diseases of nervous system (I.C.D. 330–398)	53	37	90	7·8
5. Leukaemia and aleukaemia (I.C.D. 204)	39	35	74	6·4
6. Asthma (I.C.D. 241)	43	23	66	5·7
7. All pneumonia (I.C.D. 490–493)	27	36	63	5·4
8. Drowning (I.C.D. E929)	44	9	53	4·6
9. All gastrointestinal diseases (I.C.D. 530–587)	31	19	50	4·3
10. All genitourinary diseases (I.C.D. 590–637)	14	33	47	4·1
All other diseases	190	109	299	25·8
Total all diseases	703	457	1,160	100·0

From Speizer, Doll and Heaf (1968) quoting the Registrar General's Statistical Review of England and Wales for the Year 1965.

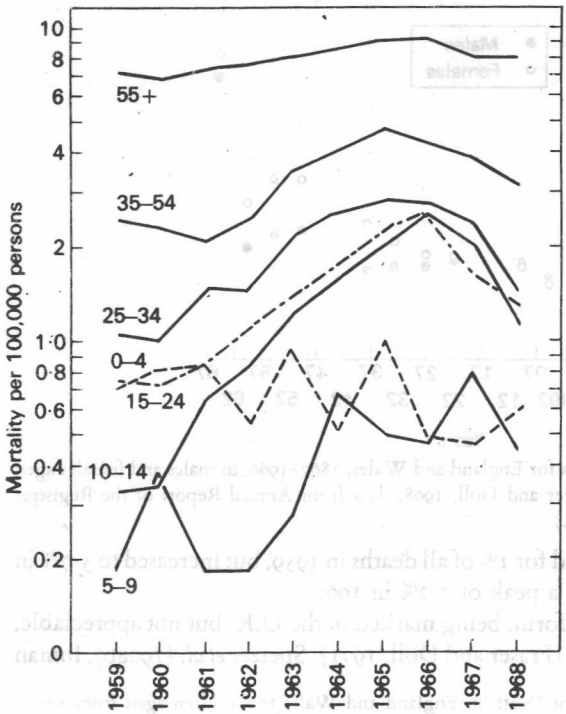

Fig. 1.2. Mortality from asthma (International Classification of Disease 241) in England and Wales expressed as annual age-specific rates per 100,000 living, 1959–68. Figure shows age groups, e.g. age groups 0–4 years. (From Inman and Adelstein, 1969.)

and Adelstein (1969) and many other authors correlated the phenomenon with the increasing use of pressurized bronchodilator aerosols (Fig. 1.3). The mechanism of death is discussed elsewhere (p. 134).

Heredity

Schwartz (1952) made an extensive study of asthmatics, subjects with related allergic diseases and control subjects, concluding that asthma is an inherited disease, genetically related to vasomotor rhinitis and hay fever. He could not distinguish between 'allergic' and 'non-allergic" subgroups of asthmatics. He considered the mode of inheritance to be by a dominant gene with variable penetrance. Many studies have been made of asthmatics and their relatives which report a positive family history in over 20% compared with less than 10% in control subjects, which is in agreement with recent physiological findings (p. 95; König and Godfrey, 1937a and b).

Leigh and Marley (1967) have reviewed the literature, and from their own

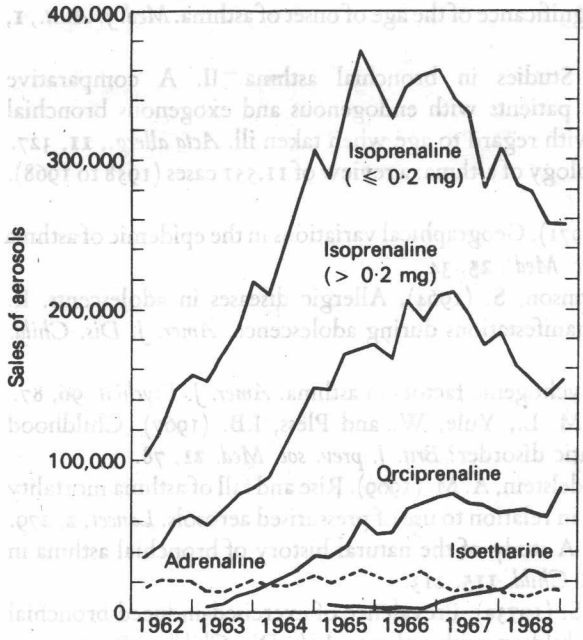

Fig. 1.3. Sales of various pressurized bronchodilating drugs in England and Wales, 1962–68. (From Inman and Adelstein, 1969.)

evidence conclude that the likelihood of developing asthma is greater in the relatives of asthmatics than of control probands, and that by age 65-plus the likelihood of developing asthma in first degree relatives of asthmatics is 43%. They suggest inheritance by a dominant gene with weakened penetrance.

Multifactorial inheritance is also a possibility. Inherited factors could operate to influence various mechanisms such as penetration of the mucosal barrier by allergen, stimulation of antibody production, formation of chemical mediators and their action on target cells. There is also the possibility that stability of the bronchiolar muscle cell may depend upon two separately inherited factors (p. 96).

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2
Aspects of Management

Rational treatment depends upon information derived from the patient and his environment. From the patient it is necessary to consider:

History
Clinical examination
Immunological status
Physiological status
Psychology

Environmental factors are important in all disease but especially so in asthma because of the interrelationship with immunological, physiological and psychological aspects. Factors to be considered are:

Social—primarily home and school
Allergic
Infection
Atmospheric pollution
Climate

Accurate information about clinical events, environmental factors and their interrelationships is important but often difficult to obtain. The value and limitations of the various methods available will be considered in this chapter and enlarged upon in subsequent chapters.

Clinical History

The history obtained from parent or child is intended to supply information about the subject and his environment. It is now appreciated that the extent and particularly the accuracy of information from these sources are limited unless special precautions are taken. These are limited by memory and judgement of events and coloured by the child's psychological reaction to subjective symptoms and by the disturbing influence of environment. Thus the child may be disturbed by events at school but these may or may not be relevant to his asthma. The parents