J. med. Genet. (1968). **5**, 262.

Incidence of Fibrocystic Disease in Wessex*

BRYAN D. HALL and M. J. SIMPKISS

From The Bournemouth and East Dorset Hospital Group

Since the description of fibrocystic disease as a definite entity in 1936, many varied incidence figures have been published. The wide range in these figures has left doubt as to its true incidence. The present paper attempts to avoid previous sources of error, and the resultant values are expected to represent a reliable guide for future surveys. The condition is autosomal recessive, and until recently almost all those affected have died in childhood. It is the commonest recessive lethal in Europe and North America, and its incidence is almost certainly too high to be determined simply by mutation.

Methods

The Wessex region† was used as the case finding area. It is staffed by 7 consultant paediatricians who work in 7 centrally located hospitals. These hospitals are in the counties of Hampshire (Christchurch, Portsmouth, Southampton, Winchester), Dorset (Dorchester), Wiltshire (Salisbury), and the Isle of Wight (Ryde). The area in mid-1965 encompassed a population of 1,875,719.

The base hospital of each consultant paediatrician was used as the primary area of research. These base hospitals admit all of the paediatric patients in Wessex as well as having the only adequate laboratory facilities for the diagnosis of cystic fibrosis in the study area. Most of the necropsies done on Wessex children were carried out at these hospitals, and, invariably, any child with cystic fibrosis would be under the care of the consultant paediatricians at the base hospital.

Between August 1, 1966 and December 31, 1966, one of us (B.D.H.) systematically visited each hospital. The initial day at the hospital was spent with the consultant paediatrician discussing the most fruitful approach to finding the cases diagnosed and treated there. He provided an introduction to all the necessary departments (e.g. pathology, medical records, physiotherapy), and also furnished any names of involved children if he had such a list available. From that point on an intense search was made of the following sources: (1) hospital diagnostic index; (2) nursing records; (3) necropsy reports; (4) laboratory data books; and (5) physiotherapy departments.

The diagnostic index was available in 5 of the 7 hospitals, and in each went back to 1960 and in some as far back as 1950. Any cases coded as fibrocystic disease or associated conditions (e.g. meconium ileus, prolapsed rectum, chronic pneumonia, failure to thrive, chronic diarrhoea) were examined. Similarly, all the necropsies of patients less than 20 years of age were reviewed, and if any of the above conditions were present, the chart and slides, when necessary, were scrutinized. The nursing records, which included admission books, daily cards, and outpatient visits, were examined whenever available. The laboratory data tables for the results of sweat test and duodenal juice tryptic activity were retained by 4 hospitals, and the notes of any children with abnormal values were checked. Five Departments of Physical Medicine supplied names of affected children whom they had treated, and their notes were evaluated.

Once all the known cases were accumulated each record was checked for the date and place of birth, the clinical and laboratory findings, and the history of sibs with the disease. Any child not born in Wessex between 1960 and 1965, inclusive, was excluded, and where the birthplace was doubtful the family doctor and the parents were asked.

The criteria for inclusion in the incidence study were that the child had been born in Wessex from 1960–1965, inclusive, and that he presented the clinical picture characteristic of the illness. He must have demonstrated at least one of the following: (1) increased sweat sodium and/or chlorides; (2) decreased or absent duodenal juice tryptic activity; and (3) histological necropsy evidence of fibrocystic disease. No 'borderline' or 'probable' cases were included.

After the hospital sources were exhausted the secondary sources were approached. The local Wessex branches of the Cystic Fibrosis Research Foundation Trust supplied names of children whose parents were members of that association. A questionary was sent to all Wessex general practitioners asking the name, sex, and date and place of birth of any individual children who had been under their care, or who were otherwise known to them. A second and similar questionary was sent to all the parents in Wessex of affected children, but in addition they were asked to give details of any affected

Received December 7, 1967.

* Supported in part by the Cystic Fibrosis Research Foundation Trust, The Wessex Regional Hospital Board, and The Hospital for Sick Children, Great Ormond Street, London W.C.1.

† Defined for the purpose of this study as that area under the jurisdiction of the Wessex Regional Hospital Board.

sibs, or details of any relevant family death. This was done during the latter part of the study when most of the cases were found and the list of parents was essentially complete. Any new cases not found during the hospital investigations were reviewed and were accepted if they met the stated criteria.

During the study it was obvious that some children living along the periphery of Wessex had been cared for by non-Wessex hospitals which were closer to the patient's residence. Consequently, hospitals in Berkshire (Reading) and Somerset (Yeovil) were checked, and any new Wessex cases that met the criteria were included. Two other hospitals outside Wessex were also checked because they form the main specialized referral centres for the study area. The Hospital for Sick Children (Great Ormond Street, London) and the Royal Hospital for Sick Children (Bristol) treat a number of Wessex infants with meconium ileus. Any new cases among this group were added to the study.

A number of miscellaneous sources added certain negative information. These included chest hospitals and children's convalescent homes. The Medical Officers of Health were usually able to confirm previously known cases, and the Isle of Wight M.R.C. Survey produced no new cases.

The consultant paediatricians kept us informed of any newly diagnosed cases from January 1, 1967 to May 1, 1967. This 4-month period added to the previous 12 months (1966) allowed 16 months for any new cases to be diagnosed after the end of the study period.

Results

A total of 159 cases was documented from 1946 until 1966. In all, 89 cases were born during the study period (1960–1965). Of these, 9 were eliminated because their birthplace was not in Wessex. Thus, 80 were discovered between 1960–1965, inclusive. During this period there were 188,613 live births, with a resultant incidence of 1 in 2358 births. Table I separates the total live births and the total cases of cystic fibrosis into the various years of the study. Table II breaks down the number of cases found in regard to the initial source, and Table III gives some miscellaneous findings.

TABLE I

TOTAL LIVE BIRTHS PER YEAR AND NUMBER OF CYSTIC FIBROSIS CASES BY YEAR OF BIRTH

Year	Live Wessex Births	Cystic Fibrosis Cases
1960	29,464*	13
1961	29,469*	18
1962	31,358*	14
1963	32,453*	7
1964	33,028	10
1965	32,841	18
Total	188,613	80

* Stillbirth figures available only for 1964 and 1965; thus, average of these two years subtracted from each year (1960–1963) to attain above figures.

TABLE II

NUMBER OF CASES FOUND IN REGARD TO INITIAL SOURCE

Primary Sources	No. of Cases	Secondary Sources	No. of Cases
Hospital diagnostic index	43	Cystic Fibrosis Research Foundation Trust	3
Nurse notes	9	Wessex general practitioners	6
Necropsies	9	Peripheral hospitals	3
Laboratory data books	2	Specialized referral centres	2
Physiotherapy department	1	Parents of children with cystic fibrosis	2
Total cases (80)	64		16

TABLE III

MISCELLANEOUS FINDINGS IN 80 CASES

Sex		Meconium Ileus		Prolapsed Rectum		Mortality	
M	F	M	F	M	F	M	F
46	34	6	10	7	2	15	11
Incidence (%)		20		11·3		32·5	

Discussion

Incidence studies have always produced controversy. This is especially true for cystic fibrosis. Figures from 1 in 600 births (Andersen and Hodges, 1946) to 1 in 1000–10,000 (Carter, 1952) served to stimulate a number of more recent reports. The first extensive study (Goodman and Reed, 1952) laboured under the burden of a recently discovered disease which was neither well known nor easily diagnosed. One can see from Table IV that the incidence figures given for studies originating from 1945 up to 1952 are variable. This point is clarified if one notes in reports given by Selander (1962), Kramm *et al.* (1962), and Pugh and Pickup (1967) that the number of cases documented during the latter part of their surveys greatly exceeded the cases found during the first few years. Therefore, one must assume that case finding was not accurate up to about 1955. Since then the results of most studies from many different countries (Danks, Allan, and Anderson, 1965; Honeyman and Siker, 1965; Houštěk and Vávrová, 1962; Merritt *et al.*, 1962) have been similar to ours.

Other factors are involved in incidence accuracy.

TABLE IV
COMPARISON OF MORE EXTENSIVE INCIDENCE STUDIES

Reference	Place of Study	Study Type	Years of Study	Total Births	Fibrosis Cystic Cases	Incidence
Goodman and Reed (1952)	Minnesota, U.S.A.	Retrospective	1945–1949	343,604	234	0·7–1·0/1000
Steinberg and Brown (1960)	Ohio, U.S.A.	Retrospective	1950–1953	742,163	198	1/3700
Selander (1962)	Sweden	Retrospective	1950–1957	870,032	113	1/7700
Kramm *et al.* (1962)	N.H., Massachusetts, Vermont, U.S.A.	Retrospective	1952–1958	1,497,300	651	1/2300
Pugh and Pickup (1967)	Leeds, U.K.	Prospective	1952–1962	546,764	132	1/4142
Danks *et al.* (1965)	Victoria, Australia	Retrospective	1955–1960	362,732	138	1/2448
Honeyman and Siker (1965)	Hartford Country, Hartford, Connecticut, U.S.A.	Retrospective and prospective	1957–1965	26,087	14	1/1863*
Hall and Simpkiss (this study)	Wessex, U.K.	Retrospective	1960–1965	188,613	80	1/2358

* Only figure considered by authors to be reliable of three different figures stated in study

The area in which the investigation is carried out is important. Wessex seemed to be ideal because of its geographical and medical stability. It offered no large population turnover such as a large city might do, and its area was small enough to make thorough case finding possible. The population for the most part sought medical attention within the study area, and because the hospitals in the area were governed by a central Board (Wessex Regional Board), a certain advantageous conformity was present.

The next main variables were the sources used in case finding. Previous reports used primarily paediatric clinics (Selander, 1962), questionaries (Kramm *et al.*, 1962), questionaries and death records (Goodman and Reed, 1952; Steinberg and Brown, 1960), and hospital records plus questionaries (Danks *et al.*, 1965). One study relied primarily on reporting by consultant paediatricians (Pugh and Pickup, 1967), while another used a neonatal survey and organizations possessing lists of fibrocystic children (Honeyman and Siker, 1965). The present report used most of the above sources and most closely approaches the methods of Danks *et al.* (1965). It should be pointed out that in this project every case was found by one and verified by both of us; consequently, dependency on second-hand information was minimal.

The criteria for inclusion of cases have varied greatly. We included no 'probable' cases, while one study (Goodman and Reed, 1952) had 177 of 234 cases classified as such. Only 2 papers (Kramm *et al.*, 1962; Danks *et al.*, 1965) stated definite criteria, thus, leaving one great freedom in interpreting the results of other reports.

In criticism of our results, there is the usual lack of accuracy associated with any retrospective study. Our total births and number of cystic fibrosis cases were small, and the hospital diagnostic index was rarely complete. We made no allowance in our figures for Wessex-born children who moved from Wessex before a diagnosis was made, though we excluded all (9) non-Wessex children. The 16 months (1966–May 1967) period of grace before closing the study could have been longer.

The true incidence in Wessex must, of course, be higher than the above figure, but we can estimate what it might be. Among our excluded cases were 7 patients classified as 'probable'. We also felt that at least 7 cases (1 per base hospital) were 'missed', though medically documented. Add to these 7 further cases which might fall into the following categories: (1) Wessex-born children who moved out of the Wessex area before diagnosis; (2) those with mild disease; (3) those children dying of diarrhoea or pneumonia who did not come to necropsy, or who were not diagnosed. These additional 21 cases would give an over-all total of 101 cases, and an incidence of 1 in 1867 births.

Summary

A retrospective incidence study done in Wessex for 1960–1965 revealed a figure of 1 in 2358 live births for the disease, cystic fibrosis. Previous incidence figures and the methods used to attain them are compared and evaluated with the present report.

Our thanks are due to Dr. C. O. Carter of the M.R.C. Clinical Genetics Research Unit for his advice and help. and to the consultant paediatricians of Wessex for their valuable co-operation without which this study would not have been possible.

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