Cystic fibrosis in Northern Ireland

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SUMMARY In a retrospective study of cystic fibrosis in Northern Ireland for 1961 to 1971, the incidence was 1 in 1857 livebirths, which is comparable to figures from Great Britain and the Republic of Ireland.

In Northern Ireland, the incidence of some genetic and partly genetic diseases is higher than in the rest of the United Kingdom. This is especially true of neural tube defects, with an incidence of 8.6 per 1000 total births (Nevin *et al.*, 1978), and of phenylketonuria, with an incidence of 1 in 5000 livebirths (N. A. J. Carson, 1978, personal communication). Recent neonatal screening surveys, using the meconium test for cystic fibrosis, the commonest autosomal recessive disorder in Western communities, have indicated that the incidence may be as high as 1 in 1600 (Carter, 1977). In Northern Ireland, Stevenson (1959) found an incidence of 1 in 1666. The present paper describes a survey of patients with cystic fibrosis born in Northern Ireland 1961 to 1971.

Methods

In the mid-1960s the population of Northern Ireland was 1 484 800, with a birth rate of 22.5 per 1000. The Province is divided, for the purposes of health and social services, into four areas, each of which has at least one major hospital with paediatric facilities. Any infant or child suspected of having cystic fibrosis would be referred to one of these hospitals. During the survey period the majority of necropsies were performed at one centre.

Ascertainment of cases of cystic fibrosis was made from many sources, including consultant paediatricians' diagnostic lists, hospital diagnostic indices, records of the genetic counselling clinics, necropsy records, and laboratory records of patients undergoing sweat and trypsin analyses. In addition, a questionnaire requesting names and addresses of patients with cystic fibrosis was circulated to all family doctors.

A diagnostic index was available at each of the hospitals covering the period of the survey. Cases

coded as cystic fibrosis or associated conditions were noted, and the hospital records in each case examined for relevant data to confirm the diagnosis. Similarly the necropsy index was also examined, and all reports of patients less than 20 years of age were reviewed. When a necropsy with definite diagnosis of cystic fibrosis was found, the relevant hospital records were examined and relevant data abstracted. As the hospital laboratories that performed the trypsin and sweat electrolyte analyses did not index these tests separately, little information was obtained in a trial attempt to scan laboratory request books, and this source of ascertainment was abandoned.

A questionnaire was sent to 741 general practitioners requesting information regarding name, address, date of birth, and hospital attended of any of their patients diagnosed as having cystic fibrosis. Of the returns, 65 contained information on patients with cystic fibrosis, of which 36 fell within the survey period. Case histories of any previously unidentified patients were reviewed to confirm the diagnosis.

For each patient identified, the following information was recorded: date and place of birth, clinical symptoms, age at diagnosis, and confirmatory laboratory findings. Each family was visited and a family history obtained. Criteria for inclusion in the survey as a proven case of cystic fibrosis were as follows. The patient had to be born in Northern Ireland between the years 1961 and 1971, have a typical clinical picture, and, in addition, have one of the following.

- (1) Increased sweat chloride and/or sodium;
- (2) decreased or absent duodenal juice tryptic activity; and
- (3) necropsy evidence of cystic fibrosis.

Some patients were considered to be probable cases of cystic fibrosis. These included patients with a positive family history and raised sweat electrolytes, but with no clinical symptoms. Possible cases of

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cystic fibrosis included all patients reported as having cystic fibrosis, but with incomplete information on diagnostic methods and results.

New cases detected during the period of survey were also included, provided they conformed with the stated criteria. Table 1 shows the sources of ascertainment.

Results

A total of 200 cases of cystic fibrosis was born during the period 1961 to 1971. There were 184 proven cases documented in the period and the total of livebirths was 362 224. Of the remaining 16, 2 were considered to be probable cases of cystic fibrosis and 9 to be possible cases of cystic fibrosis. Five cases were eliminated as 2 were born outside Northern Ireland, and 3, on review, were considered not to have the disease. Table 2 indicates the variation in the number of patients by year.

If only the proven cases of cystic fibrosis are considered, the incidence is 1 in 1969 livebirths, ranging from 1 in 1210 in 1965 to 1 in 3713 in 1967. However, when the possible and probable cases are included, the incidence is 1 in 1857.

Discussion

Surveys of cystic fibrosis from many countries, particularly Europe, show an incidence ranging from 1 in 550 births to more than 1 in 10 000 (Ten Kate, 1977). Though figures are available from several

areas of Great Britain, only two reports have been concerned with Ireland. O'Reilly *et al.* (1974) found an incidence of 1 in 1757 livebirths for the Republic of Ireland. This study was based solely on hospital admissions of patients under 15 years old with cystic fibrosis in 1972. In a survey of congenital and hereditary disorders in Northern Ireland, Stevenson (1959), for cystic fibrosis, noted an incidence of 1 in 1666 livebirths. However, he commented that ascertainment for cystic fibrosis was probably incomplete.

Because of its geographical situation, Northern Ireland, with a population of 1.5 million and a birth rate of 23 per 1000 (mid-1960s), is ideal for population surveys of genetic disorders. Interestingly, only two families with cystic fibrosis children had left Northern Ireland in the period of the survey; both these patients have been included.

A pilot investigation for this study revealed few cases recorded before 1960. This determined the starting date of the survey, while the length was such as to provide sufficient cases and to allow adequate time for diagnosis. Thus, a child born in 1971 would have been aged 5 to 6 years old when the survey was undertaken. Other workers have reported fewer documented cases of cystic fibrosis in the 1950s. Kramm *et al.* (1962), Selander (1962), and Pugh and Pickup (1967) found that the majority of their cases were in the latter part of their surveys. Our study shows as many patients with cystic fibrosis in the early part as in the latter part of the survey (Table 2). Indeed, the incidence of proven cases of cystic fibrosis in 1961 to 1965 was 1 in 1845, and 1 in 2106 in 1966 to 1970.

Previous reports have employed different sources of ascertainment, including paediatric clinic patient lists (Selander, 1962), questionnaires and death records (Goodman and Reed, 1952), hospital records and questionnaires (Danks *et al.*, 1965), and a neonatal survey including lists of patients from cystic fibrosis organisations (Honeyman and Siker, 1965). Hall and Simkiss (1968) and Ten Kate (1977) have employed multiple sources of ascertainment. We have adopted a similar approach.

Similarly, the criteria for inclusion of patients have varied in individual studies, making comparisons difficult. While some studies have stated definite criteria (Danks *et al.*, 1965; Hall and Simkiss, 1968), other studies (Goodman and Reed, 1952; Ten Kate, 1977) have also included probable and possible cases of cystic fibrosis. In our study, if only those patients with proven cystic fibrosis are considered, the incidence is 1 in 1969, whereas if probable and possible cases are also included the incidence is 1 in 1857. Even this is probably an underestimate of the true incidence.

Table 1 Number of patients found in relation to initial source

Hospital diagnostic index	118
Necropsy records	24
Cystic Fibrosis Research Trust	18
General practitioners	12
Medical genetic clinic index	25
Laboratory records	3
Total cases	200

Table 2 Total livebirths and number of proven cases of cystic fibrosis by year of birth

Year	Livebirths (NI)	Cystic fibrosis cases
1961	31 915	16
1962	32 565	10
1963	33 414	15
1964	34 345	21
1965	33 890	28
1966	33 228	17
1967	33 415	9
1968	33 173	15
1969	32 428	17
1970	32 086	20
1971	31 765	16
Total	362 224	184

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