Febrile Convulsions in Families:

Findings in an Epidemiologic Survey

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In a well-studied community of 3,953 individuals under 20 years of age, 142 or 3.6 per cent had a history of one or more proven febrile seizures. Certain families are more FC-prone. An unexpectedly strong relationship was found between children with febrile convulsions and sibs with mental retardation.

BECAUSE the pathogenesis and natural history of febrile convulsions in early childhood are still poorly understood,[3, 4, 8–10] it seemed to us that the epidemiologic approach might throw new light on this problem. Such an approach must of necessity begin with considering the entire family in which the child with febrile convulsions lives.

A Southeastern Michigan community of approximately 3,500 families provided us with an unusually favorable setting, in that almost 90 per cent of the inhabitants are already participating in an on-going clinical and epidemiologic study of considerable depth and breadth.[5–7] As part of the general health picture of each family, detailed pediatric histories have been recorded; and review of these records reveals that 142 out of 3,953 individuals under 20 years of age had had at least one true febrile convulsion (FC) (Table 1).

Each case with a positive history was reviewed by a physician using a standard set of questions and criteria.* By excluding those individuals in whom the convulsions had accompanied encephalitis or meningitis and those in whom seizures had been diagnosed or treated by the attending physician as epilepsy, the figure of 142 actual cases was arrived at. The diagnosis of FC was applied only in those cases that had been so-called by the attending physician, or when the seizures or loss of consciousness had occurred only during febrile illnesses.

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Copies of this questionnaire are available from the authors on request.

Observations Made

Prevalence of febrile convulsions. Despite the limitations of the retrospective approach, even for an episode as memorable as a typical febrile seizure, this study provides a reasonable estimate of the prevalence of this common childhood condition. Actually, our cumulative figure of febrile convulsions affecting 3.6 per cent of children is less than the 6 to 8 per cent figure cited elsewhere.[1]

By extrapolation and projection of our findings, however, this lower figure suggests that among persons aged 20 years or less there are an estimated 132,000 persons in Michigan and 2,736,000 in the United States who have experienced at least one febrile seizure.[2] The higher incidence among males than females—1.68 boys to each girl in our series—confirms the clinical experience of most physicians.

TABLE 1. *Frequency of Febrile Convulsions (FC)**

	Male	Female	Total
Number of FC cases reported	89	53	142
Persons at risk and examined	1,999	1,954	3,953
Prevalence of FC cases in per cent	4.5	2.7	3.6

* Among persons under 20 years of age at the time of examination in 1959–60, Tecumseh, Michigan

Frequency of convulsions. Forty-two of the 142 children had had more than one febrile seizure. The average number of episodes per child was 1.70 (Table 2).

Does the age of onset affect the number of subsequent episodes? Slightly only (Table 3)—the average number of subsequent episodes of FC was virtually the same for the group of children whose seizures began before 23 months, and for the group whose onset was after 24 months.

Age of occurrence of first and last episodes. Figure 1 shows that febrile or "infantile convulsions" are aptly named, since over 50 per cent of children have their first episode by two years of age. By age four, 75 per cent have had their last episode. While highly characteristic, the self-limited, transitory nature of FC's is still largely unexplained. In exceptional cases, when seizures persist or recur or change in character, the early FC episode may have to be reclassified in retrospect as being atypical of the so called "simple" FC syndrome.

Febrile-seizure-prone families. Can the common clinical impression be documented that some families are more FC-prone than others? Figure 2 summarizes evidence of a familial

TABLE 2. *Single and Multiple Episodes of Febrile Convulsion*

Number of Episodes Reported	No.	%
1	100	70.4
2	21	14.8
3	13	9.2
4	2	1.4
5	2	1.4
6 or more	4	2.8
Total	142	100.0

TABLE 3. *Occurrence of Febrile Convulsions, by Age of Onset*

	0–23 Months	24 Months or More	Total
No. of FC cases	72	70	142
No. and per cent of FC cases with subsequent FC's	29 (40.3%)	14 (20.0%)	43 (30.3%)
Average No. of subsequent FC's	2.1	1.9	2.0
Average interval in months between first and last FC	16.2	24.0	18.9

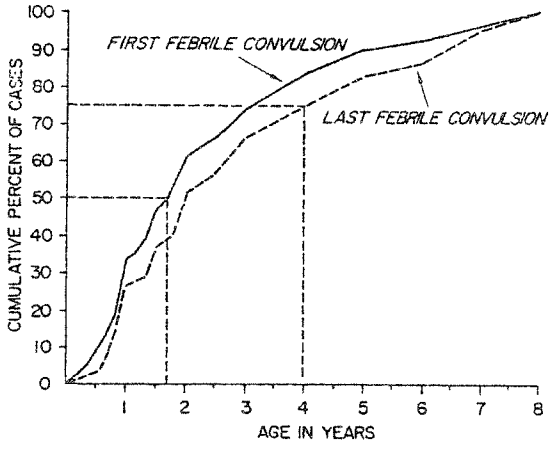

FIG. 1. Age at first and last febrile convulsion, as a cumulative frequency.

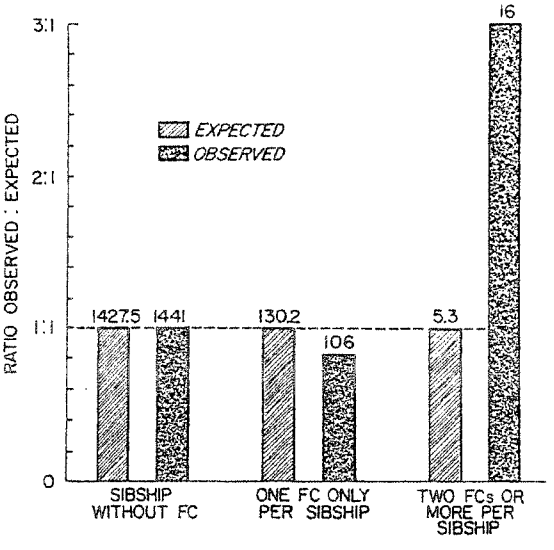

FIG. 2. Number of febrile convulsion (FC) cases per sibship, observed and expected.

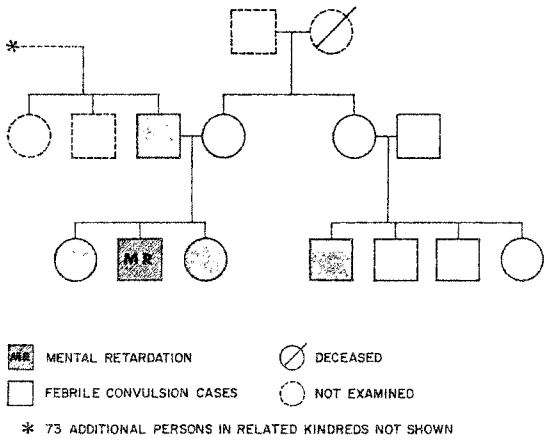

FIG. 3. A selected pedigree showing febrile seizure cases.

aggregation of febrile seizures beyond the expectation derived from over-all incidence figures in this community and after careful allowance is made for sibships of varying sizes.* The pedigree in Figure 3 illustrates a family pattern of a sort well-known to may readers.

For a condition occurring as frequently as febrile convulsions, the possibility of a recessive trait for FC-susceptibility may stir the genetically-inclined to calculate a carrier frequency using the Hardy-Weinberg formula. The frequency in one community is quite high, $2pq = 30.8$ per cent carriers, suggesting opportunities for more genetic research into this problem.

Conditions associated with FC. In 113 of the 142 cases the parents recalled a variety of conditions or infections preceding the first dramatic episode (Table 4). Not surprisingly, acute respiratory infections and the communicable diseases lead the list. Conditions peculiar to infancy, such as roseola and teething, accounted for 19 of the 142 cases. The contents of this list would obviously be different if we were to include the so-called afebrile convulsions of early childhood.[4] It is noteworthy that only three reports of FC associated with immunization occurred in our 1960 data, which predate the introduction of measles vaccine.

*Sibships rather than families are shown because only histories of persons under 20 years were used in this analysis.

FC linkage to other conditions. Although association does not establish causation, it is inherent in the epidemiologic approach to compare the have's (FC's) with the have-not's (non FC's) in as many important aspects as possible. The total community setting in our study is extremely important because all persons were interviewed and examined in a standard way with no special interest whatsoever in febrile convulsions at the time; furthermore, at each stage of the analysis, the 142 children with FC and their 213 siblings were compared with some 3,562 controls in the remainder of the similarly studied population. These factors are summarized in Figure 4.

A systematic search of a number of possibly associated conditions turned up only a single striking finding; namely, that there was an excess of mental retardation (MR) within FC sibships. Ten of the 23 probable diagnoses of MR in the community occurred among the total 355 persons in FC sibships, and these constituted less than ten per cent of the population at risk.*

This unexpected finding was subjected to rigorous statistical testing as illustrated in Figure 5. Expected frequencies of MR and FC were calculated for sibships of varying sizes, utilizing the over-all observed prevalence rates; then, taking MR cases and their sibs

* Our diagnostic criteria for MR included any of the following: 1. Already previously diagnosed; 2. Illiteracy or inability to work because of low intelligence; 3. Our clinical impression of probable MR.

TABLE 4. *Reported Conditions or Infections Preceding Febrile Convulsions*

	No.	%
Respiratory infection	84	59.2
Upper respiratory (48)		
Lower respiratory (23)		
Teething (13)		
Communicable diseases	19	13.3
Measles (4)		
Roseola (6)		
Other (9)		
Gastro-intestinal infection	5	3.5
Immunization	3	2.1
Trauma, breath-holding (?)	2	1.4
None reported	29	20.4
Total	142	99.9

as the index cases (Fig. 5, left portion), the numbers of observed and expected FC cases are calculated. Results show an excess of observed FC to expected FC, 13 : 2.4 (chi-square, one d.f. = 48.2, $p < .005$).

Another approach (shown on the right portion of Fig. 5) begins with FC cases and their sibs and calculates expected and observed frequencies of MR. There is a resultant excess of MR of 10 : 2.0 (chi-square, one d.f. = 33.7, $p < .005$).

The degree of overlap of the presumably independent conditions, mental retardation and febrile convulsions, is illustrated in the pedigree in Figure 3—the boy with MR has two sisters with FC. Fortunately, the number of persons with FC is much larger than the number with MR, but the pattern of overlap is unlikely to be explained by either chance or, in this total community study, by the use of a selected or biased sample.

Medical Care after First Episode. A practical question concerns the availability of medical care to the affected families. Throughout the period covered in this study, the level of medical and hospital care was well above average for this region; in addition, two university medical centers are nearby.

The original episode of FC in most of the 142 cases was reported to have been attended

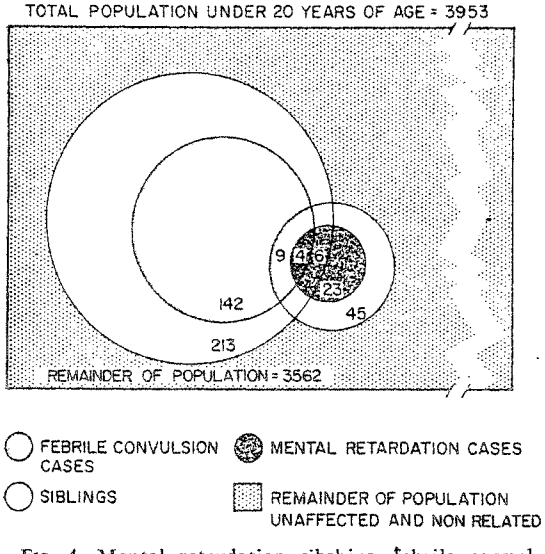

FIG. 4. Mental retardation sibships, febrile convulsion sibships, and the total study population, as an area (Venn) diagram.

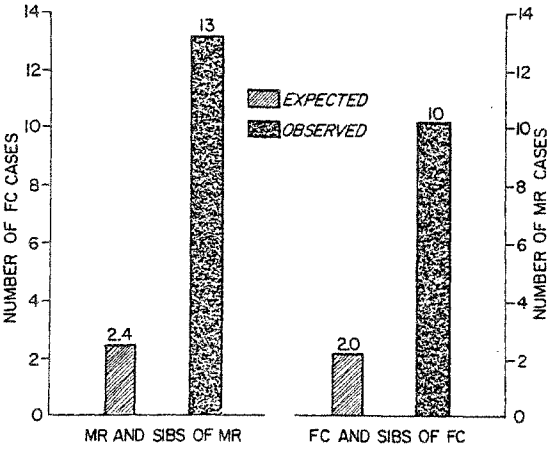

FIG. 5. Occurrence of cases of mental retardation (MR) and febrile convulsion (FC) in sibships, observed and expected.

by the family physician either at home or in a hospital emergency room. Of the 142, 11 were hospitalized for the seizure or associated illness; and five were seen by a specialist, neurologist or pediatrician. Only two recalled the taking of anticonvulsant drugs, even for a short period. These data confirm for us the "garden-variety" nature of the 142 index cases.

Similarities of index families to unaffected families. Several measures of socio-economic status including formal education of the heads of household, area and quality of residence reflecting income were applied to the index and unaffected families. No significant differences were found. An analysis of birth histories as recalled by mothers was made with emphasis on birth weights and complications of delivery; the differences between index and unaffected persons were insignificant.

Discussion and Final Thoughts

Any study of the natural history of febrile convulsions must seek "garden-variety" cases from families in the community; must cover a long enough period of experience; should minimize observer differences; should standardize criteria; and, at each stage, compare the experience of FC cases with an adequate number of non-FC cases. These formidable standards have nowhere yet been met, and

would require a large-scale, prospective population study.

Our retrospective survey of a uniquely studied total community offers some qualitative and quantitative dimensions to the familiar problem of providing care and counselling for parents of one or more children with single or multiple episodes of FC.

We have found that:

1. Febrile convulsions are frequent; at least 3.6 per cent of children, more boys than girls, have experienced at least one FC.

2. There are FC-prone families, with a distinct excess of observed to expected experience—16 : 5.3, observed to expected.

3. An unexplained and unexpectedly strong relationship occurs between two presumably independent conditions—febrile convulsions and mental retardation. There is at least a fivefold risk (13 : 2.4 and 10 : 2 ratios; observed to expected) for a child with FC to have a sibling with MR, or of a child with MR to have a sibling with FC, as compared to a large number of unaffected children in the population. These ratios are based on the findings in 142 cases of FC with 213 sibs, 23 cases of MR with 45 sibs, and 3,562 unaffected children for comparison.

4. No other significant socio-economic, birth history, medical care, or major clinical differences were detected between the index and the unaffected families. The FC cases suggest the "garden-variety" experience of the general practitioner.

5. Any measures effectively reducing the morbidity of febrile conditions, particularly acute respiratory and other communicable diseases of childhood, would probably have prevented at least 70 per cent of the 142 cases in this series.

6. The need for better diagnosis, management, understanding and eventual prevention of febrile convulsions in young children should be more widely recognized. No single approach will suffice; epidemiologic studies of families should provide better estimates of risk factors, etiologic factors, and prognosis in this all-too-frequent complication of early childhood.

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