CHAPTER 5 ■ INCIDENCE AND PREVALENCE

POONAM NINA BANERJEE AND W. ALLEN HAUSER

INTRODUCTION

To develop optimal approaches to the treatment of epilepsy, to evaluate the effectiveness of treatment strategies, and more importantly, to identify interventions that may prevent the development of epilepsy, valid information regarding the frequency, cause, and natural history of the condition is necessary. Such information is provided by descriptive and hypothesis-testing epidemiologic studies. Early reports of the prevalence of epilepsy, which used information from selective service records, provided data similar to those of contemporary studies undertaken in industrialized countries, such as the United States, for the same age groups.[27] Approaches to the study of the epidemiology of epilepsy have become increasingly sophisticated; current epidemiologic studies provide a much more comprehensive picture of the characteristics of persons with epilepsy, which has led to considerable improvement in understanding epidemiologic features of the seizure disorders in general and epilepsy in particular. These improved methods include the development of clear definitions of the condition being studied; use of data provided by incidence studies of the convulsive disorders; and use of these incidence cases and other inception cohorts to determine natural history and identify risk factors. Unfortunately, incidence studies are expensive and difficult to do. Therefore, there are relatively few reports dealing with total populations. Relying on less expensive and relatively less complex studies of prevalence to gain epidemiologic insights can be compared to an epileptologist performing epilepsy surgery based on clinical history alone. One may have some of the pieces, and a correct decision may be made, but in many cases, an inappropriate procedure will be undertaken.

The following discussion reviews data regarding the incidence of seizure disorders and epilepsy, and the risk factors for epilepsy as suggested by these studies. In addition, potential insights provided by prevalence studies are highlighted. Definitions are important in epidemiologic studies. In the present discussion, the term *epilepsy* represents a condition characterized by two or more unprovoked seizures. For other definitions, the reader is referred to the report of the Commission on Epidemiology and Prognosis of the International League Against Epilepsy (ILAE).[46]

INCIDENCE OF EPILEPSY

Total Population Studies

There are relatively few studies of incidence of epilepsy in total populations. In developed countries, the age-adjusted incidence of epilepsy (recurrent unprovoked seizures) ranges from 24 to 53 per 100,000 person-years.[6,30,44,50,57–60,72,95,100] Total population studies reporting the incidence of a first diagnosis of unprovoked seizures (differing from incidence of epilepsy by the inclusion of persons with a single unprovoked seizure as well as those with recurrent unprovoked seizures) provides estimates of incidence ranging from 26 to 70 per 100,000 person-years [37,51,57,60,72,90,112] (see Table 1). Given methodologic differences, the incidence in studies of predominantly Western, industrialized countries seems remarkably consistent across geographic areas. This seems particularly true of reports for the last two decades (1986 to 2005).

Several recent studies provide incidence from developing countries. An incidence of epilepsy that is considerably higher than that reported in industrialized countries (114 per 100,000 person-years) has been reported from a rural area of Chile.[66] A study in Tanzania[106] reported the incidence of epilepsy to be 77 per 100,000. These are two to three times the incidence reported in industrialized countries in which similar definitions have been used. A study in Ethiopia reported an incidence of 64, but this fell to 46 after age adjustment, underscoring the importance of age adjustment if comparisons are to be made. A large population-based survey in Ecuador[97] identified all individuals with a history of seizures. Included were all persons with newly occurring nonfebrile seizures (including acute symptomatic seizures) and some children with multiple febrile seizures. Based on the number of people seen with seizures in the year preceding the survey, incidence was higher than that of most other reports (190 per 100,000), although incidence for neurologically confirmed cases was about 30% lower. In studies in France[72] and Rochester, Minnesota,[50] about half of newly occurring afebrile seizures do not fulfill criteria for epilepsy. Because of the broader case-inclusion criteria in the study from Ecuador and uncertainty regarding age-specific distribution and cause of acute symptomatic seizures, there is no way to compare these incidence studies. Nonetheless, the incidence of epilepsy may likely be higher in developing countries than in industrialized countries.

Studies in Selected Age Groups

A number of studies report the incidence of epilepsy in specific age groups. These include studies of children,[14,15,20,22,24,33,36,38,84,102,111,112,117] adults,[37,50,64,90,95] and the elderly.[71,76,105,115] Evaluation of these studies again requires consideration of definitions used, but in general, information is complementary to and consistent with incidence in total-population studies when age-specific rates are evaluated. For example, the more comprehensive studies limited to children[111,117] include children with neonatal seizures and children with a single unprovoked seizure as incidence cases of epilepsy. Taking this into account, incidence in the youngest

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TABLE 1

INCIDENCE OF EPILEPSY IN SELECT POPULATION-BASED STUDIES OF ALL AGE GROUPS

Reference	Publication date	Region	Population/ person-years	Number of cases	Incidence	
					Crude	Age-adjusted (U.S. 2000 census)
Brewis[21]	1966	England	497,707	141	29	28
De Graaf[30]	1974	Norway	213,116	70	33	26
Granieri et al.[44]	1983	Italy	697,100	230	33	33
Joensen[59]	1986	Faroe Islands	452,584	194	43	37
Rwiza et al.[106]	1992	Tanzania	165,684	122	74	51
Lavados et al.[66]	1992	Chile	90,596	102	113	92
Hauser[50]	1993	Rochester, MN 1975–1984	573,152	275	48	51
Sidenvall et al. and Forsgren et al.[37,112]	1993 & 1996	Sweden	152,275	226	—	58[a]
Olafsson et al.[89]	1996	Iceland	90,237	42	47	43
Tekle-Haimanot[116]	1997	Ethiopia	215,901	139	64	43
Jallon et al.[58]	1997	Switzerland	384,657	176	46	—
Jallon et al.[57]	1999	Martinique	383,596	246	64	—
Annegers et al.[6]	1999	Texas	601,448	197	33	28
MacDonald et al.[77]	2000	England	100,230	69	46	79
Olafsson et al.[90]	2005	Iceland	882,151	501	57[a]	52[a]

[a] All unprovoked seizures.

age group in studies limited to children are, in general, similar to those reported in total population studies.

Age-specific Incidence

Contrary to popular belief, epilepsy is a disease with onset at the extremes of life (Fig. 1), at least in industrialized countries. Where provided, age-specific incidence is consistently high in the youngest age groups, with highest incidence occurring during the first few months of life. Incidence falls dramatically after the first year of life, seems relatively stable through the first decade of life, and falls again during adolescence.[22,51,90]

In virtually all studies conducted in industrialized countries, age-specific incidence is lowest during the adult years. Contemporary incidence studies, most of which are in Western countries, show an increasing incidence—at times dramatic—in the elderly.[37,50,71,88] In Western countries, the incidence of epilepsy is higher after the age of 70 years than during the first 10 years of life. Only about 50% of cases of epilepsy start in childhood or adolescence.[50,90] A British general practice survey reported that almost 25% of all newly identified seizures (not epilepsy) occurred in persons aged 60 years and older.[108]

The reported patterns of age-specific incidence are quite different in developing countries. In studies from Africa and South America, the peak incidence of epilepsy occurs in young adults, and the dramatic increase in incidence in the elderly has not been identified (Fig. 2).[66,106,116] It is likely that patterns of incidence, and therefore risks for epilepsy, are different in these populations.

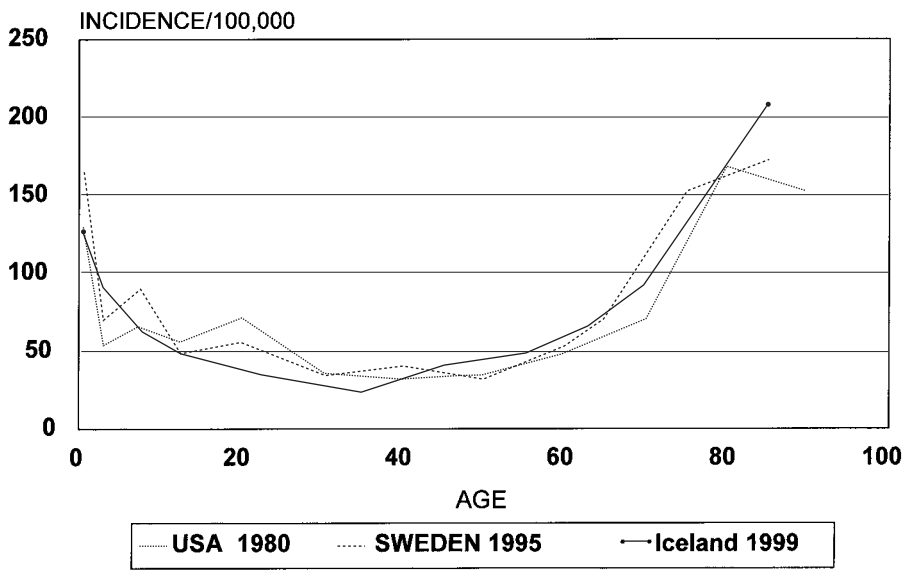

FIGURE 1. Age-specific incidence of epilepsy in industrialized countries.

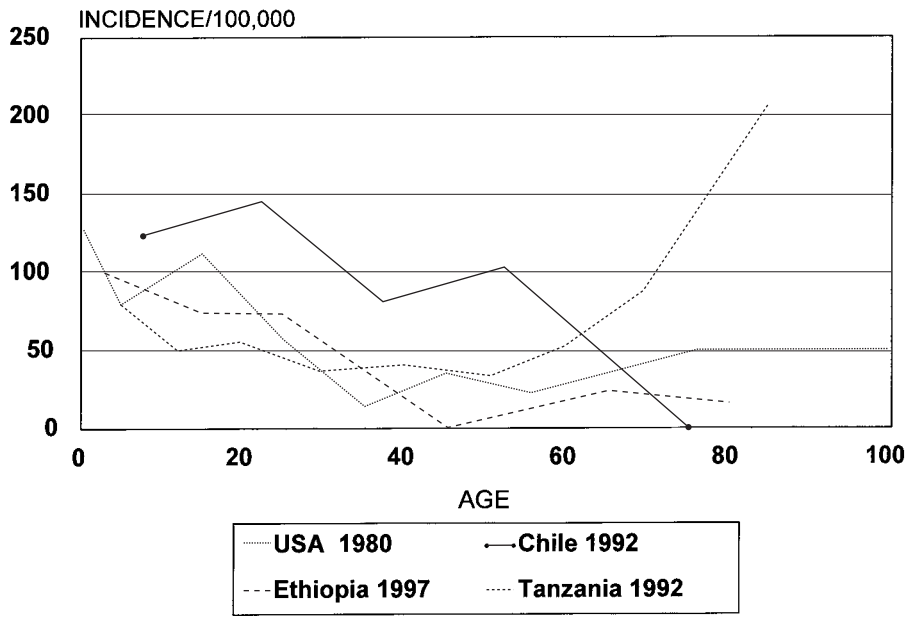

FIGURE 2. Age-specific incidence of epilepsy in developing countries.

Sex

In most total population studies, incidence of epilepsy or of unprovoked seizures is higher in males than in females. This seems true even after the higher incidence in males of definitive risk factors for epilepsy (i.e., head injury, stroke, central nervous system infection) is taken into account. One exception is the study from Ecuador,[97] in which the male-to-female ratio is 0.8, although this study cannot be used for comparison as it included persons with acute symptomatic as well as unprovoked seizures. The other exception is the study of incidence in children in Sweden (male-to-female ratio of 0.7).[112] For most but not all incidence studies, sex-specific differences in incidence are not statistically significant. The consistency of the male-to-female difference across studies suggests that males are at higher risk than females for unprovoked seizures and epilepsy.

Seizure Type

Seizure-specific incidence or proportions of cases with a specific seizure type based on the International Classification of Epileptic Seizures[100] are provided in several contemporary incidence studies (Table 2). A detailed distribution from the Iceland study[90] is provided in Figure 3. In studies in Rochester, Minnesota,[50] the Faeroe Islands,[59] and Chile,[66] slightly more than 50% of incidence cases were classified as partial seizures. Partial seizures are also the predominant seizure type in Sweden in adults after information from the separate studies of adults and children is combined.[37,112]

Race

Most total population incidence studies have been performed in white populations of European extraction. Even in

TABLE 2

CLASSIFICATION OF SEIZURE TYPE IN SELECT INCIDENCE STUDIES

Reference	Publication date	Region	Partial (%)	Generalized (%)	Unclassifiable (%)
Brewis[21]	1966	England	—	—	—
De Graaf[30]	1974	Norway	—	—	—
Granieri et al.[44]	1983	Italy	32	59	9
Joensen[59]	1986	Faroe Islands	51	39	10
Rwiza et al.[106]	1992	Tanzania	32	58	10
Lavados et al.[66]	1992	Chile	54	38	8
Hauser[50]	1993	Minnesota	57	40	3
Sidenvall et al. and Forsgren et al.[37,112]	1993 1996	Sweden	60	27	13
Olafsson et al.[89]	1996	Iceland	31	69	—
Tekle-Haimanot et al.[116]	1997	Ethiopia	20	69	11
Jallon et al.[58]	1997	Switzerland	—	—	—
Jallon et al.[57]	1999	Martinique	—	—	—
Annegers et al.[6]	1999	Texas	—	—	—
MacDonald et al.[77]	2000	England	—	—	—
Olafsson et al.[90]	2005	Iceland	40	58	2

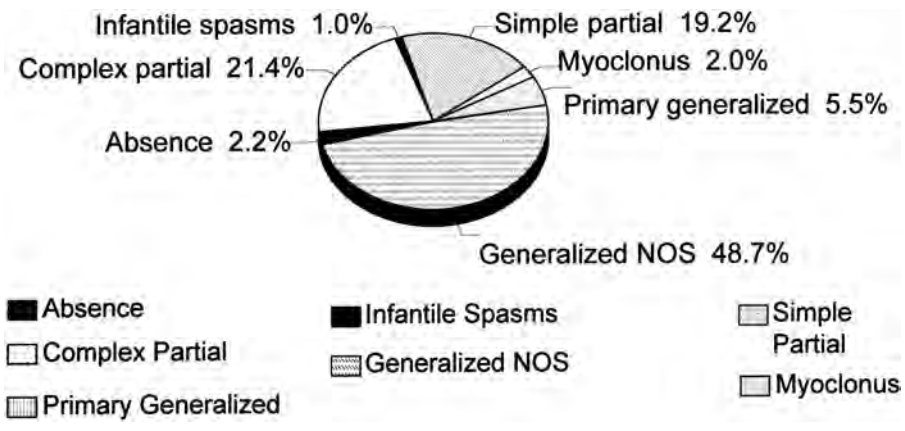

FIGURE 3. Distribution of seizure type in Iceland incidence cases, 1995–1999. NOS, not otherwise specified.

studies of incidence in Asian or African populations, study groups have been homogeneous. Racial differences have been examined only in incidence or cohort studies in children. In the National Collaborative Perinatal Project,[83] incidence of afebrile seizures did not differ across racial groups through the age of 7 years. In studies of Japanese children in Tokyo[117] and Caucasian children in Rochester, Minnesota,[50] age-specific incidence and incidence by seizure type through the age of 14 years were virtually identical. Definitions of epilepsy were similar in these two studies, although methodology was different. A study of children in New Haven, Connecticut,[111] reported incidence of epilepsy through age 15 years to be 1.7 times greater in blacks than in whites, although the definition of epilepsy was quite different from those used in many of the studies mentioned above. This study also made an ecologic comparison based on mean neighborhood socioeconomic level. After controlling for race, incidence of epilepsy was significantly higher in lower socioeconomic classes.

Time Trends

Information on time trends of incidence is provided in the studies from Copparo, Italy,[44] and Rochester, Minnesota.[50] In the Italian study, the incidence of epilepsy decreased over three time intervals from 1964 to 1978, although this may be related to methodologic issues (Fig. 4). The Minnesota study reports a more than 50% decrease in the incidence of epilepsy in those under the age of 10 years from 1935 to 1984. During these same years, there was an increase in incidence in those over age 60 years, causing the age-adjusted incidence in this community over the entire 50-year interval to show little change.

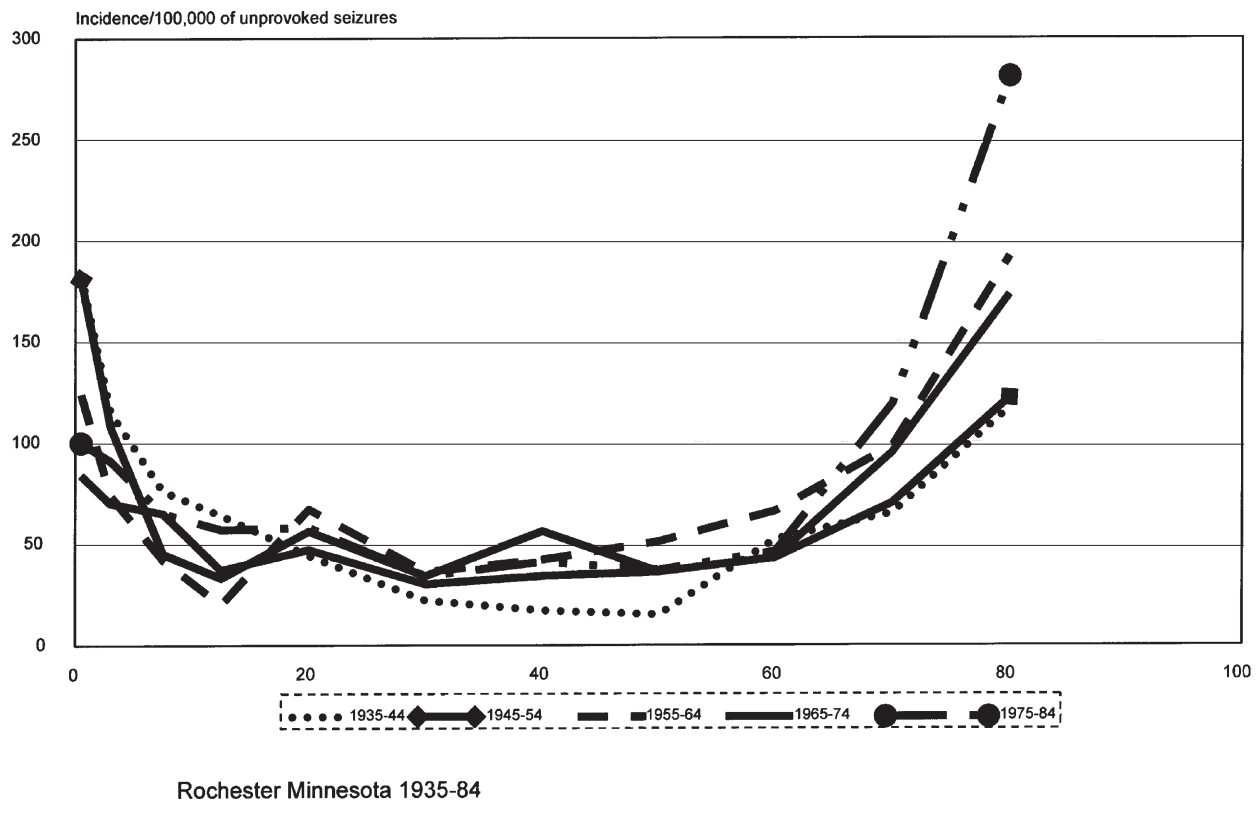

FIGURE 4. Time trends in Rochester, Minnesota, 1935–1984.

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The fall in the middle decades of this century is largely unexplained, but the increase after 1975 may be related to increased survivorship of very-low-birth-weight infants. The findings of this study underscore the potential pitfalls in relying on total incidence of epilepsy in children.

In the studies of a British general practice that included all afebrile seizures, incidence under age 20 was 172 per 100,000 between 1964 and 1973, 152 per 100,000 between 1974 and 1983, and significantly lower (61 per 100,000) from 1984 to 1993.[26] This difference may be explained partially by inclusion in the earlier period of nonepileptic episodes, but even cautious interpretation of these data suggest dramatic reductions in the incidence of childhood-onset epilepsy in industrialized countries. The reduction in incidence over time in children is not readily explained by current epidemiologic or clinical data and deserves further investigation.

It appears that the incidence of epilepsy in the elderly is increasing—at least in the United States. This may be related, at least in part, to an increase in the proportion of the population with a history of stroke.[4] Although the incidence of stroke is decreasing, the prevalence is increasing as more people are surviving strokes.

Epileptic Syndromes

There are few total population incidence studies that present the distribution of epilepsy syndromes such as the study conducted in Bordeaux,[72] studies from Rochester,[50] and studies from Iceland.[90] Some studies provide the distribution of epilepsy syndromes among newly diagnosed cases of epilepsy.[63,72,78,112,121]

In Bordeaux, the incidence of idiopathic localization-related epilepsy was 1.7 per 100,000 (7% of all cases). An additional 13.6 per 100,000 (56%) had symptomatic localization-related epilepsy. Thus, if the same criteria are used as in most other contemporary incidence studies, about 60% of cases can be classified as partial seizures. Each of the following syndromes accounted for about 1% of new cases: Juvenile myoclonic epilepsy, awakening grand mal, and West syndrome. About 2% had pyknolepsy. These proportions are similar to those provided by the Rochester, Minnesota, studies.[9] Crude incidence for all epilepsy (about 24.5 per 100,000) was about half that reported in studies in industrialized countries.[37,44,59,89,90] A few reports of incidence of specific epileptic syndromes in other total population studies provide data consistent with the above figures.[37,59,90]

The incidence of nonfebrile situation-related epilepsy in the French study was about 30 per 100,000.[72] Incidence for this class of seizure in Rochester, Minnesota, was about 40 per 100,000.[85] Isolated unprovoked seizures occurred in 18 per 100,000 population in the French study, which is similar to that in Rochester[50] and considerably less than that reported from Iceland.[90]

There are some reports of the incidence of specific syndromes. West syndrome has been studied in different geographic areas,[48,75,90] with an incidence ranging from 2 to 7 per 10,000 live births. Benign rolandic epilepsy is thought to be among the more frequently occurring childhood epileptic syndromes; one Italian study[24] reported this to account for 24% of incidence cases in children with epilepsy between the ages of 4 and 15 years. In Sweden, the incidence of benign rolandic epilepsy in children under 15 years of age was 10.7, accounting for about 14% of childhood epilepsies.[112] In Iceland, benign rolandic epilepsy accounted for 5% all newly diagnosed cases.[90] The incidence of juvenile myoclonic epilepsy in the Faeroe Islands was 1.1 per 100,000 per year, or about 2.5% of cases.[59] In Sweden, five children under the age of 15 years had a diagnosis of juvenile myoclonic epilepsy, making the incidence 6 per 100,000,[112] and in Iceland, juvenile myoclonic epilepsy occurred in 1% of patients,[90] providing an incidence of 0.7 per 100,000 person-years. Data from the Rochester cohort studies suggest that the incidence of juvenile myoclonic epilepsy is about 1 per 100,000 per year.[50] These data seem to be reasonably consistent and suggest a lower frequency of juvenile myoclonic epilepsy than has been suggested in recent clinical studies. Lastly, childhood absence epilepsy occurred in seven patients in Iceland (1%; incidence of 0.8 per 100,000 person-years).[90]

ETIOLOGY OF EPILEPSY IN INCIDENCE COHORTS

Most of the population-based incidence studies provide information regarding presumed etiology (Table 3). Rarely have definitions for inclusion been provided, but the proportion of cases with an identified antecedent (remote symptomatic epilepsy) is relatively consistent, ranging from 23% to 39%[50](Fig. 5). In children, epilepsy associated with neurologic deficits from birth seems to be the most important single etiologic relationship, whereas cerebrovascular disease is the most commonly identified cause among adults.

Classic Risk Factors

Most physicians have preconceived notions about postnatal antecedents of epilepsy. Head (brain) trauma, stroke, central nervous system infection, and degenerative brain disease are frequently identified.[5,7,9,107] Specific causes of epilepsy may differ across geographic areas, but whether incidence studies are undertaken in developing countries or in developed countries, a definitive etiology has been identified in only about one third of all newly diagnosed cases. In industrialized countries, cerebrovascular disease is the most frequently identified "cause" of epilepsy, accounting for about 12% of all new cases and about one third of cases with an identified cause (Fig. 6).[50,90] In South America, the most frequently identified cause is infection of the central nervous system. In developing and developed countries, cerebral palsy is associated with a large proportion of cases, particularly in children. In incidence studies in endemic areas, neurocysticercosis accounts for about 10% of newly diagnosed cases of epilepsy, confirming the importance of this factor.[23]

Risk Factors Identified in Epidemiologic Studies

Epidemiologic studies have not only confirmed the importance of postnatal insults, but also qualified the risk. As shown in Figure 7, a risk ratio of 1 implies no increase in risk, a risk ratio of ≤ 1 suggests a protective effect, and a risk ratio of >1 suggests an increase in risk. The risk for epilepsy among persons with penetrating head injuries acquired during military service is more than 500 times that expected in the general population.[107] In contrast, individuals who have had brain injury associated with loss of consciousness or amnesia of ≤ 30 minutes' duration have no increase in risk.[5] Studies have also identified other factors (drug and alcohol abuse, depressive illness, suicidality, migraine with aura, hypertension, and risk factors for stroke) that increase the risk for epilepsy—at times as much as or more than the classic risk factors.[2,52,54,55,70,74,85,86,109]

There is a continued belief that adverse prenatal and perinatal events are associated with an increased risk for epilepsy (Fig. 8). Although at times these may be risk factors for cerebral palsy, they have not yet been demonstrated, at least in

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TABLE 3

ETIOLOGY IN INCIDENT CASES OF EPILEPSY OR ALL UNPROVOKED SEIZURES

Reference	Publication date	Region	Symptomatic (%)		Idiopathic (%)	Cryptogenic (%)	Unclassified (%)
			Progressive	Remote			
Brewis[21]	1966	England	—	—	—	—	—
De Graaf et al.[30]	1974	Norway	—	—	—	—	—
Granieri et al.[44]	1983	Italy	39	61	—	—	—
Joensen[59]	1986	Faroe Islands					
Rwiza et al.[106]	1992	Tanzania	25	75	—	—	—
Lavados et al.[66]	1992	Chile					
Hauser[50]	1993	Minnesota	8	25	66	—	—
Sidenvall et al. and Forsgren et al.[37,112]	1993 1996	Sweden	15	28	56	—	—
Olafsson et al.[89]	1996	Iceland	10	21	69	—	—
Tekle-Haimonot et al.[116]	1997	Ethiopia	14	—	86	—	—
Jallon et al.[58]	1997	Switzerland	15	39	10	35	—
Jallon et al.[57]	1999	Martinique	7	30	10	53	—
Annegers et al.[6]	1999	Texas	25	—	75	—	—
MacDonald et al.[77]	2000	England					
Olafsson et al.[90]	2005	Iceland	12	17	14	53	1

developed countries, to be risk factors for epilepsy in the absence of overt neurologic handicap. Separate or together, pre- or perinatal factors pose little increase in risk, and for most of these factors the differences are not significant. Epidemiologic evidence does not support a causal association between febrile convulsions and epilepsy.

Family History as Risk Factors

A small proportion of cases of epilepsy may be attributable to single-gene disorders. In two syndromes with mendelian inheritance patterns, a chromosomal localization has been achieved. Benign familial neonatal convulsions with a dominant inheritance pattern was initially localized to chromosome 20,[67] but genetic heterogeneity has been demonstrated by a more recent localization to chromosome 8.[68] A gene for progressive myoclonic epilepsy has been localized to chromosome 21.[35] A gene for partial epilepsy with auditory features has been localized to chromosome 10, and several sodium and potassium channelopathies have been identified in association with Dravet syndrome and generalized epileptic seizures plus (GES+) syndromes.[17,119] Although the mode of inheritance is obscure, a localization for juvenile myoclonic epilepsy and other juvenile-onset disorders has been proposed.[35,45] Others question this finding.[120] Localizations for several other epilepsy syndromes have been identified.

Even though a small proportion of cases follow mendelian inheritance patterns, in epidemiologic terms family history may be considered an important risk factor for epilepsy. In the absence of other information, epilepsy in a first-degree relative increases the risk threefold.[8] The absolute increase is modified by which first-degree relative is affected (sibling, mother, father), the seizure type and etiology of epilepsy in the affected relative, and the electroencephalographic pattern in the relative or individual in question.

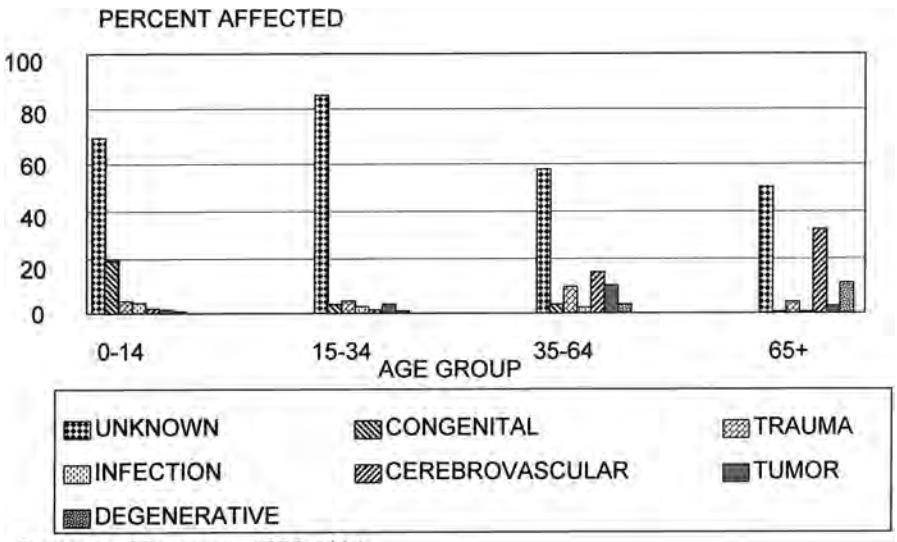

FIGURE 5. Age of onset attributable to various antecedents.

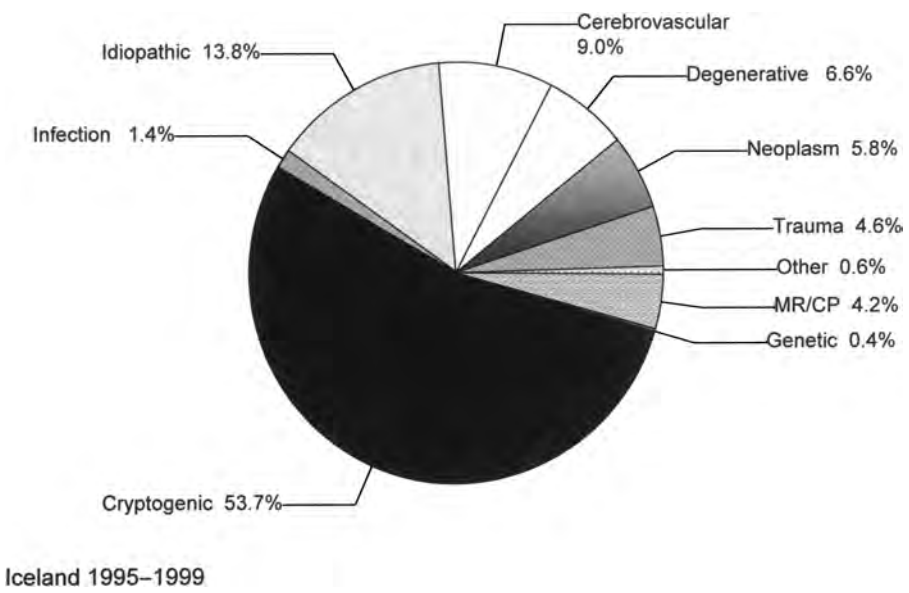

FIGURE 6. Classic risk factors.

Cumulative Incidence

Cumulative incidence is the summation of age incidence. Given the modest alteration mortality among people with epilepsy, cumulative incidence provides an estimate of the proportion of the total population that has been affected with epilepsy by a specific age. Estimates of cumulative incidence of epilepsy have been provided in four total population studies.[50,60,89,90] In Denmark, the risk for having epilepsy by the age of 80 years was 1.3%,[60] a substantially lower number than the cumulative incidence of epilepsy for the same age in Rochester, Minnesota (4% for epilepsy and more than 5% for all unprovoked seizures)[50] or the rate of 5.4% for all unprovoked seizures to age 85 from the Iceland study.[90] This difference can be explained by the considerably higher incidence in the elderly in the Minnesota study. As would be expected from age-specific incidence rates, cumulative incidences of epilepsy through childhood are almost identical in Japan and Rochester.[50,117] In Rochester, the cumulative incidence for epilepsy and unprovoked seizures is significantly greater for males than females.

Incidence of All Afebrile Seizures

There are a few studies that include all afebrile seizures in their definitions of epilepsy, and this definition is consistent with some recent recommendations of the ILAE.[57,58,97] Table 4 includes studies from which incidence using this definition have been provided. The incidence is substantially increased in Ecuador,[97] although it is not clear if this is due to a methodologic approach or reflects differences in the burden of epilepsy between developed and developing countries.

PREVALENCE OF EPILEPSY

Because it is easier to obtain information about prevalence than about incidence, many prevalence studies of epilepsy from diverse populations have been reported.[1,10,11,13,16,18,19,25,31,32,34,39–43,47,53,61,62,69,73,79–81,87,92,94,96,101,103,104,110,113,114] Prevalence is a measure of the interaction of obvious factors such as incidence, death, and remission of illness, and except for

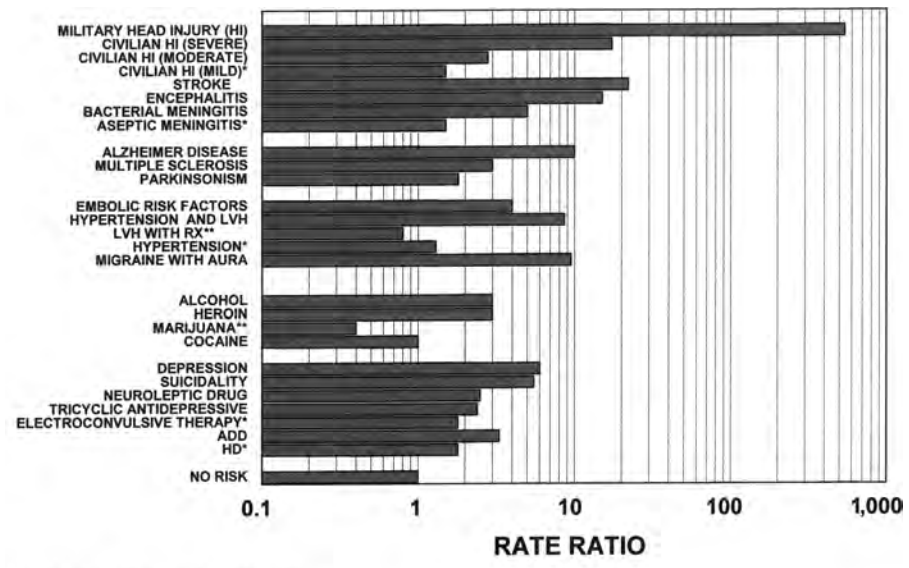

FIGURE 7. Change in risk for epilepsy in association with specific antecedents. ADD, attention deficit disorder; HD, hyperactivity disorder; LVH, left ventricular hypertrophy.

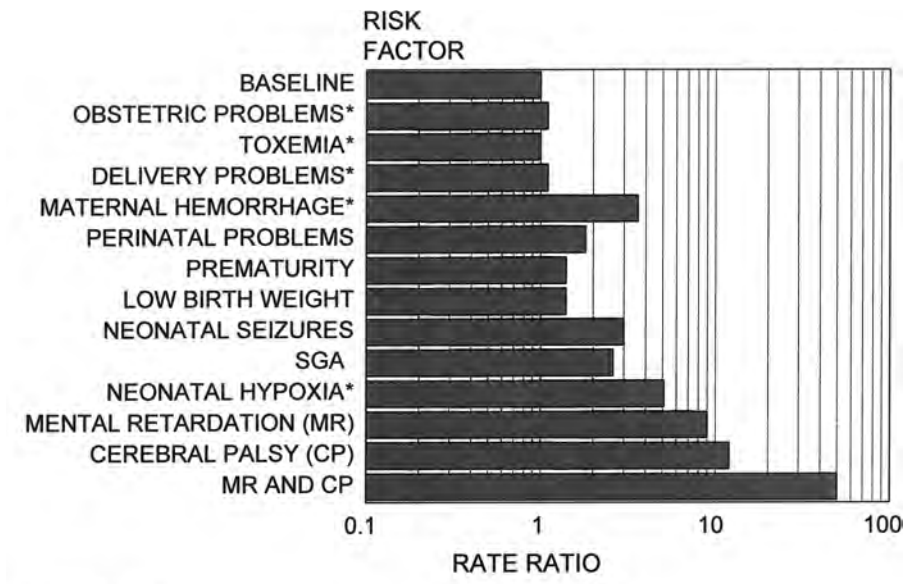

FIGURE 8. Adverse prenatal and perinatal events and risk for epilepsy. SGA, small for gestational age.

geographic isolates such as Iceland, prevalence is also affected by factors such as migration or access to multiple sources of medical care. Prevalence is more a reflection of survival and severity or chronicity of illness than of frequency of illness. Little reliable information regarding etiology or prognosis can be derived from prevalence studies, although they can provide intriguing clues to guide hypotheses that can be tested in properly designed studies. Prevalence data are primarily of value in planning for health care.

There are some well-known difficulties in interpreting prevalence data, related to difficulties in interpreting mortality and remission. Other difficulties stem from inconsistencies in definitions or in the fact that only crude prevalence is reported. Age-specific prevalence in developed and developing countries is difficult to compare, given the dramatic differences in age structure of the populations and the wide variation in age-specific prevalence. Age standardization should be used if any comparisons are to be made, as wide variations in apparent prevalence are demonstrated even in studies of contiguous populations.

Age-Adjusted Prevalence

Age-adjusted prevalence per 1,000 population varies widely—from 2.7 to more than 40, although most studies show a range from four to eight.[49] Even when the same investigators have used similar protocols, definitions of epilepsy, and methodologies, the prevalence of "active" epilepsy ranges from 3.6 to 41.3.[18,93] Somewhat higher prevalence (ranging from 14 to 57 per 1,000) has been reported in pilot studies using a standardized World Health Organization (WHO) protocol in Panama,[43] Ecuador,[97] and Colombia.[99] However, the same protocol used in large-scale population surveys yielded low prevalence in India[18,65] and China.[69]

The high prevalence of epilepsy reported in Central and South America by those using the WHO protocol may be a reflection of methodology. One study[97] using the International Community Based Epilepsy Research Group (ICBERG) protocol in rural Ecuador found the prevalence to be considerably lower (8 per 1,000) than that reported in a pilot study[29] by investigators using the WHO protocol in the same region (18.5 per 1,000). The difference may be related to more stringent case verification in the ICBERG study, but this cannot account for all the differences. A recent population survey in a village in rural Mexico, which was age adjusted to the 1980 U.S. population, revealed a prevalence of active epilepsy of 5.9 per 1,000.[53,94] The prevalence in Pakistan is about 10 per 1,000,[12] and in rural Ethiopia about 5 per 1,000.[116]

Age-Specific Prevalence

Although epilepsy is a disease acquired throughout life, the reported patterns of age-specific prevalence seldom reflect

TABLE 4

INCIDENCE OF ALL AFEBRILE SEIZURES IN POPULATION-BASED STUDIES OF ALL AGES

Reference	Publication date	Region	Population	Number of cases	Incidence	
					Crude	Age-adjusted
Placencia et al.[97]	1992	Ecuador	72,121	137	190	174
Hauser[50]	1993	Minnesota 1975–1984	573,152	639	111	110
Jallon et al.[58]	1997	Switzerland	384,657	273	71	70
Jallon et al.[57]	1999	Martinique	383,596	309	81	83

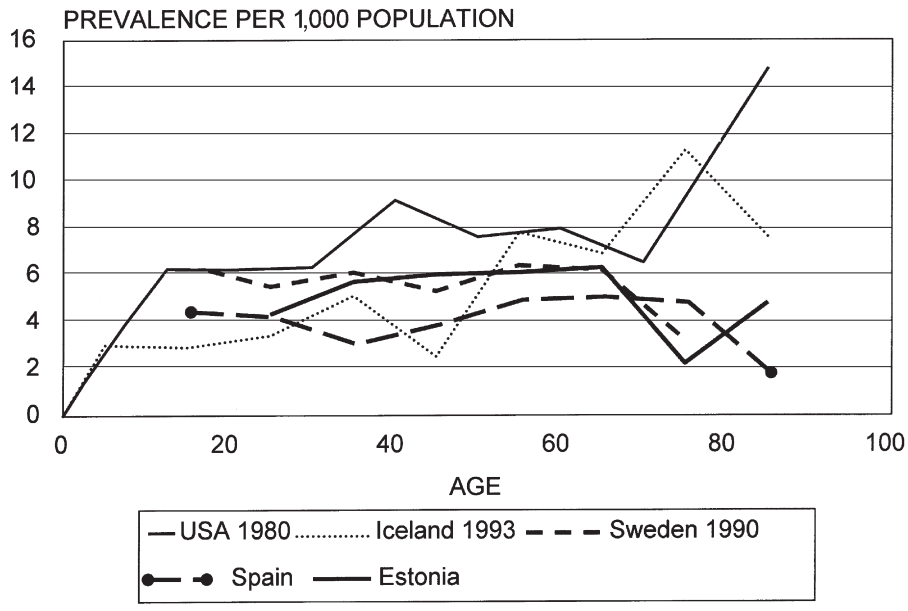

FIGURE 9. Prevalence of epilepsy in industrialized countries.

this. This is particularly striking, as many of the prevalence studies provide data for lifetime prevalence (which should approximate cumulative incidence) rather than for active prevalence (which measures current seizures or current use of antiepileptic drugs). In the studies of prevalence from Rochester, Minnesota,[49] and from Iceland,[91] there is a pattern of active prevalence increasing in each subsequent age group, with the highest prevalence occurring in the elderly (Fig. 9). Studies from other European countries[64,118] and the Faroe Islands[59] report a relatively constant prevalence in adults. In many cases, age-specific estimates are unstable because of small numbers within age groups. Most studies, particularly those from developing countries, report the highest prevalence in the second and third decades of life, with lower prevalence in the elderly[29,53] (Fig. 10).

Gender

As is the case with incidence studies, most studies of prevalence report a higher prevalence in males than in females.

Etiology

For all total population studies providing information, the majority of cases, typically between 55% and 89% (Fig. 11), even in developing countries, have no identified cause.[1,10,11,13,16,18,19,25,31,32,34,39–43,49,53,61,62,65,73,81,87,92–94,99,101,103,104,113]

Race

Race seems more of an issue in the United States than in most other countries, and most studies addressing race or ethnic issues are from this geographic area. There are few studies that provide data on the prevalence of epilepsy in underrepresented populations in the United States.[49] Most studies provide data on prevalence in African-Americans. When comparable data were available, all report a higher prevalence than in the white population, although as usual, definitions cause difficulties in comparison. In Copiah County, Mississippi, the entire population was screened and follow-up evaluations were scheduled with symptoms of seizures or epilepsy to determine the

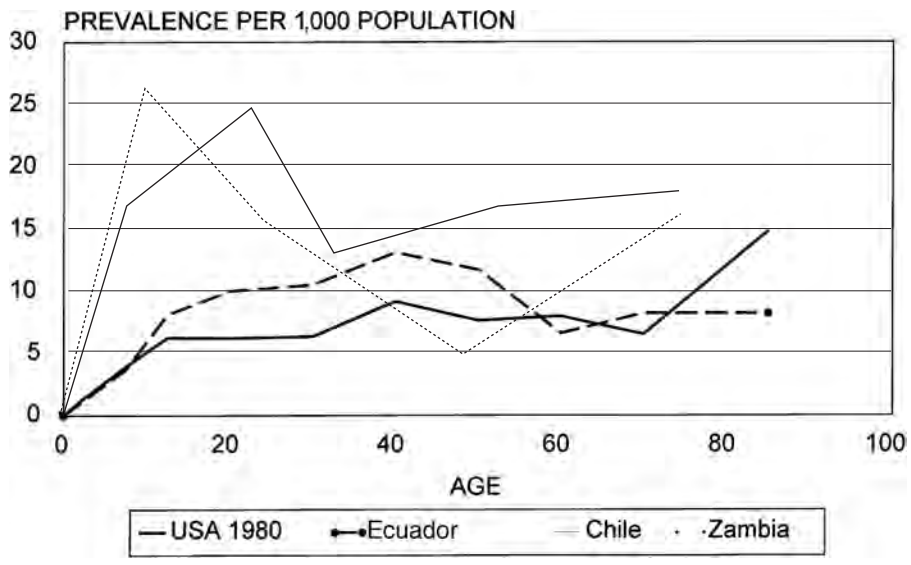

FIGURE 10. Prevalence of epilepsy in developing countries.

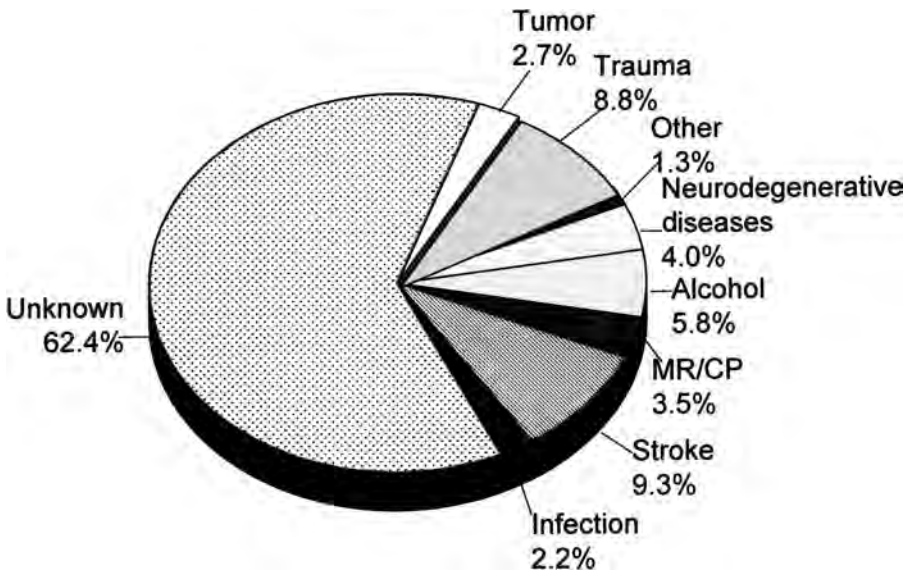

FIGURE 11. Distribution of etiology of epilepsy cases. CP, cerebral palsy; MR, mental retardation.

prevalence of epilepsy.[3,47] Definitions used in this study would include some people now categorized as acute symptomatic epilepsy in other studies such as those in Rochester, Minnesota. The age-adjusted active prevalence in blacks defined as recent seizures or current medication use was 8 per 1,000. This was about 60% greater than the age-adjusted prevalence in the white population in the same county.

A study in a rural Alabama county reported a lifetime prevalence of epilepsy of about 12 per 1,000 in the 2,200 black residents based upon clinic record review. This was almost double the prevalence in whites determined in a similar fashion.[56]

There are reports of prevalence of epilepsy limited to children that include information regarding the prevalence in minorities. The prevalence of epilepsy was determined in three counties in Oklahoma using multiple sources for case identification.[28] The active prevalence in black children of 5.7 per 1,000 compared to 4.2 per 1,000 in white children. The overall prevalence in "others," including Native American and Hispanic children, was 4.5 per 1,000. Prevalence was higher in males than in females for all ethnic groups. The excess in black children seemed attributable to a higher prevalence of generalized seizures and was present for all age groups. No further information is provided for the "other" group.

In Atlanta, multiple sources were used to identify potential cases that were screened to identify children with epilepsy. The lifetime prevalence of epilepsy in black children at age 10 was 6.4 per 1,000, not significantly higher than the prevalence in white children (5.7 per 1,000).[82] The prevalence of generalized seizures was significantly greater in black children than in white children.

Studies of prevalence in minority populations are inexorably confounded by socioeconomic status. Few studies attempt to address the relationship of socioeconomic status and the prevalence of epilepsy. In Ecuador, prevalence was inversely correlated with community ranking by socioeconomic class.[97,98] The prevalence of epilepsy in Pakistan has been reported to be greater in rural than in urban areas.

SUMMARY AND CONCLUSIONS

As more insight is gained into the epidemiologic characteristics of the epilepsies, apparent discrepancies between epidemiologic and clinical studies will be resolved. In addition, more pointed questions will be asked, and the prime epidemiologic goal of preventing epilepsy and its consequences will be addressed.

References

1. Al Rajeh S, Awada A, Bademosi O, et al. The prevalence of epilepsy and other seizure disorders in an Arab population: a community-based study. *Seizure*. 2001;10(6):410–414.
2. Amatniek JC, Hauser WA, DelCastillo-Castaneda C, et al. Incidence and predictors of seizures in patients with Alzheimer's disease. *Epilepsia*. 2006; 47(5):867–872.
3. Anderson DW, Schoenberg BS, Haerer AF. Prevalence surveys of neurologic disorders: methodologic implications of the Copiah County Study. *J Clin Epidemiol*. 1988;41(4):339–345.
4. Annegers JF, Hauser WA, Lee JR, et al. Incidence of acute symptomatic seizures in Rochester, Minnesota, 1935-1984. *Epilepsia*. 1995;36(4):327–333.
5. Annegers JF, Grabow JD, Kurland LT, et al. Seizures after head trauma: a population study. *Neurology*. 1980;30(7 Pt 1):683–689.
6. Annegers JF, Dubinsky S, Coan SP, et al. The incidence of epilepsy and unprovoked seizures in multiethnic, urban health maintenance organizations. *Epilepsia*. 1999;40(4):502–506.
7. Annegers JF, Hauser WA, Beghi E, et al. The risk of unprovoked seizures after encephalitis and meningitis. *Neurology*. 1988;38(9):1407–1410.
8. Annegers JF, Hauser WA, Anderson VE, et al. The risks of seizure disorders among relatives of patients with childhood onset epilepsy. *Neurology*. 1982;32(2):174–179.
9. Annegers JF, Rocca WA, Hauser WA. Causes of epilepsy: contributions of the Rochester epidemiology project. *Mayo Clin Proc*. 1996;71(6):570–575.
10. Attia-Romdhane N, Mrabet A, Ben Hamida M. Prevalence of epilepsy in Kelibia, Tunisia. *Epilepsia*. 1993;34(6):1028–1032.
11. Aziz H, Gavener A, Akhtar SW, et al. Comparative epidemiology of epilepsy in Pakistan and Turkey: population-based studies using identical protocols. *Epilepsia*. 1997;38(6):716–722.
12. Aziz H, Ali SM, Frances P, et al. Epilepsy in Pakistan: a population-based epidemiologic study. *Epilepsia*. 1994;35(5):950–958.
13. Basch EM, Cruz ME, Tapia D, et al. Prevalence of epilepsy in a migrant population near Quito, Ecuador. *Neuroepidemiology*. 1997;16(2): 94–98.
14. Beilmann A, Napa A, Hamarik M, et al. Incidence of childhood epilepsy in Estonia. *Brain Dev*. 1999;21(3):166–174.
15. Benna P, Ferrero P, Bianco C, et al. Epidemiological aspects of epilepsy in the children of a Piedmontese district (Alba-Bra). *Panminerva Med*. 1984;26(2):113–118.
16. Beran RG, Hall L, Michelazzi J. An accurate assessment of the prevalence ratio of epilepsy adequately adjusted by influencing factors. *Neuroepidemiology*. 1985;4(2):71–81.
17. Berten P, Cuelemans MD. Clinical correlations of mutations in the SCN1A gene: from febrile seizures to severe myoclonic epilepsy in infancy. *Pediatr Neurol*. 2004;30(4):236–243.
18. Bharucha NE, Bharucha EP, Bharucha AE, et al. Prevalence of epilepsy in the Parsi community of Bombay. *Epilepsia*. 1988;29(2):111–115.
19. Birbeck GL, Kalichi EM. Epilepsy prevalence in rural Zambia: a door-to-door survey. *Trop Med Int Health*. 2004;9(1):92–95.
20. Blom S, Heijbel J, Bergfors PG. Incidence of epilepsy in children: a follow-up study three years after the first seizure. *Epilepsia*. 1978;19(4):343–350.
21. Brewis M. Neurological disease in an English city. *Acta Neurol Scand*. 1966;Suppl 24:89.

22. Camfield CS, Camfield PR, Gordon K, et al. Incidence of epilepsy in childhood and adolescence: a population-based study in Nova Scotia from 1977 to 1985. *Epilepsia*. 1996;37(1):19–23.
23. Carpio A, Escobar A, Hauser WA. Cysticercosis and epilepsy: a critical review. *Epilepsia*. 1998;39(10):1025–1040.
24. Cavazzuti GB. Epidemiology of different types of epilepsy in school age children of Modena, Italy. *Epilepsia*. 1980;21(1):57–62.
25. Chiofalo N, Kirschbaum A, Fuentes A, et al. Prevalence of epilepsy in children of Melipilla, Chile. *Epilepsia*. 1979;20(3):261–266.
26. Cockerell OC, Eckle I, Goodridge DM, et al. Epilepsy in a population of 6000 re-examined: secular trends in first attendance rates, prevalence, and prognosis. *J Neurol Neurosurg Psychiatry*. 1995;58(5):570–576.
27. Cornaggia CM, Canevini MP, Christe W, et al. Epidemiologic survey of epilepsy among Army draftees in Lombardy, Italy. *Epilepsia*. 1990;31(1): 27–32.
28. Cowan LD, Bodensteiner JB, Leviton A, et al. Prevalence of the epilepsies in children and adolescents. *Epilepsia*. 1989;30(1):94–106.
29. Cruz ME, Schoenberg BS, Ruales J, et al. Pilot study to detect neurologic disease in Ecuador among a population with a high prevalence of endemic goiter. *Neuroepidemiology*. 1985;4(2):108–116.
30. de Graaf AS. Epidemiological aspects of epilepsy in northern Norway. *Epilepsia*. 1974;15(3):291–299.
31. de la Court A, Breteler MM, Meinardi H, et al. Prevalence of epilepsy in the elderly: the Rotterdam Study. *Epilepsia*. 1996;37(2):141–147.
32. Dent W, Helbok R, Matuja WB, et al. Prevalence of active epilepsy in a rural area in South Tanzania: a door-to-door survey. *Epilepsia*. 2005;46(12):1963–1969.
33. Doose H, Sitepu B. Childhood epilepsy in a German city. *Neuropediatrics*. 1983;14(4):220–224.
34. Dumas M, Grunitzky K, Belo M, et al. [Cysticercosis and neurocysticercosis: epidemiological survey in North Togo]. *Bull Soc Pathol Exot*. 1990;83(2):263–274.
35. Durner M, Sander J, Greenberg DA, et al. Localization of idiopathic generalized epilepsy on chromosome 6p in families of juvenile myoclonic epilepsy patients. *Neurology*. 1991;41(10):1651–1655.
36. Ellenberg JH, Hirtz DG, Nelson KB. Age at onset of seizures in young children. *Ann Neurol*. 1984;15(2):127–134.
37. Forsgren L, Bucht G, Eriksson S, et al. Incidence and clinical characterization of unprovoked seizures in adults: a prospective population-based study. *Epilepsia*. 1996;37(3):224–229.
38. Freitag CM, May TW, Pfafflin M, et al. Incidence of epilepsies and epileptic syndromes in children and adolescents: a population-based prospective study in Germany. *Epilepsia*. 2001;42(8):979–985.
39. Gallitto G, Serra S, LaSpina P, et al. Prevalence and characteristics of epilepsy in the Aeolian islands. *Epilepsia*. 2005;46(11):1828–1835.
40. Garcia-Pedroza F, Rubio-Donnadieu F, Garcia-Ramos F, et al. Prevalence of epilepsy in children: Tlalpan, Mexico City, Mexico. *Neuroepidemiology*. 1983;2:16–23.
41. Gomez JG, Arciniegas E, Torres J. Prevalence of epilepsy in Bogota, Colombia. *Neurology*. 1978;28(1):90–94.
42. Goudsmit J, van der Waals FW. Endemic epilepsy in an isolated region of Liberia. *Lancet*. 1983;1(8323):528–529.
43. Gracia F, de Lao SL, Castillo L, et al. Epidemiology of epilepsy in Guaymi Indians from Bocas del Toro Province, Republic of Panama. *Epilepsia*. 1990;31(6):718–723.
44. Granieri E, Rosati G, Tola R, et al. A descriptive study of epilepsy in the district of Copparo, Italy, 1964-1978. *Epilepsia*. 1983;24(4):502–514.
45. Greenberg DA, Delgado-Escueta AV, Widelitz H, et al. Juvenile myoclonic epilepsy (JME) may be linked to the BF and HLA loci on human chromosome 6. *Am J Med Genet*. 1988;31(1):185–192.
46. Guidelines for epidemiologic studies on epilepsy. Commission on Epidemiology and Prognosis, International League Against Epilepsy. *Epilepsia*. 1993;34(4):592–596.
47. Haerer AF, Anderson DW, Schoenberg BS. Prevalence and clinical features of epilepsy in a biracial United States population. *Epilepsia*. 1986;27(1):66–75.
48. Hauser WA, Annegers JF, Gomez M. The incidence of West Syndrome in Rochester, Minnesota. *Epilepsia*. 1991;1991(32):83–88.
49. Hauser WA, Annegers JF, Kurland LT, Prevalence of epilepsy in Rochester, Minnesota: 1940-1980. *Epilepsia*. 1991;32(4):429–445.
50. Hauser WA, Annegers JF, Kurland LT. Incidence of epilepsy and unprovoked seizures in Rochester, Minnesota: 1935-1984. *Epilepsia*. 1993;34(3):453–468.
51. Hauser WA, Annegers JF, Rocca WA. Descriptive epidemiology of epilepsy: contributions of population-based studies from Rochester, Minnesota. *Mayo Clin Proc*. 1996;71(6):576–586.
52. Hauser WA, Ng SK, Brust JC. Alcohol, seizures, and epilepsy. *Epilepsia*. 1988;29(Suppl 2):S66–78.
53. Hauser WA. Prevalence of epilepsy in Guanajuato, Mexico. Presented at the American Epilepsy Society Conference, 1990.
54. Hesdorffer DC, Hauser WA, Olafsson E, et al. Depression and suicide attempt as risk factors for incident unprovoked seizures. *Ann Neurol*. 2006;59(1):35–41.
55. Hesdorffer DC, Hauser WA, Annegers JF, et al. Severe, uncontrolled hypertension and adult-onset seizures: a case-control study in Rochester, Minnesota. *Epilepsia*. 1996;37(8):736–741.
56. Hollingsworth J. *Mental Retardation, Cerebral Palsy and Epilepsy in Alabama; a Sociological Analysis*. Tuscaloosa, Alabama: University of Alabama Press; 1978.
57. Jallon P, Smadja D, Cabre P, et al. EPIMART: prospective incidence study of epileptic seizures in newly referred patients in a French Carribean island (Martinique). *Epilepsia*. 1999;40(8):1103–1109.
58. Jallon P, Goumaz M, Haenggeli C, et al. Incidence of first epileptic seizures in the canton of Geneva, Switzerland. *Epilepsia*. 1997;38(5):547–552.
59. Joensen P. Prevalence, incidence, and classification of epilepsy in the Faroes. *Acta Neurol Scand*. 1986;74(2):150–155.
60. Juul-Jensen P, Foldspang A. Natural history of epileptic seizures. *Epilepsia*. 1983;24(3):297–312.
61. Kaiser C, Kipp W, Asaba G. et al. The prevalence of epilepsy follows the distribution of onchocerciasis in a west Ugandan focus. *Bull World Health Organ*. 1996;74(4):361–367.
62. Karaagac N, Yeni SN, Senocak M, et al. Prevalence of epilepsy in Silivri, a rural area of Turkey. *Epilepsia*. 1999;40(5):637–642.
63. Kellinghaus C, Loddenkemper T, Najm IM, et al. Specific epileptic syndromes are rare even in tertiary epilepsy centers: a patient-oriented approach to epilepsy classification. *Epilepsia*. 2004;45(3):268–275.
64. Keranen T, Riekkinen PJ, Sillanpaa M. Incidence and prevalence of epilepsy in adults in eastern Finland. *Epilepsia*. 1989;30(4):413–421.
65. Koul R, Razdan S, Motta A. Prevalence and pattern of epilepsy (Lath/Mirgi/Laran) in rural Kashmir, India. *Epilepsia*. 1988;29(2):116–122.
66. Lavados J, Germain L, Morales A, et al. A descriptive study of epilepsy in the district of El Salvador, Chile, 1984-1988. *Acta Neurol Scand*. 1992;85(4):249–256.
67. Leppert M, Anderson VE, Quattlebaum T, et al. Benign familial neonatal convulsions linked to genetic markers on chromosome 20. *Nature*. 1989; 337(6208):647–648.
68. Lewis TB, Leach RJ, Ward K, et al. Genetic heterogeneity in benign familial neonatal convulsions: identification of a new locus on chromosome 8q. *Am J Hum Genet*. 1993;53(3):670–675.
69. Li SC, Schoenberg BS, Wang CC, et al. Epidemiology of epilepsy in urban areas of the People's Republic of China. *Epilepsia*. 1985;26(5):391–394.
70. Li X, Breteler MM, de Bruyne MC, et al. Vascular determinants of epilepsy: the Rotterdam Study. *Epilepsia*. 1997;38(11):1216–1220.
71. Loiseau J, Loiseau P, Duche B, et al. A survey of epileptic disorders in southwest France: seizures in elderly patients. *Ann Neurol*. 1990;27(3):232–237.
72. Loiseau J, Loiseau P, Guyot M, et al. Survey of seizure disorders in the French southwest. I. Incidence of epileptic syndromes. *Epilepsia*. 1990;31(4):391–396.
73. Longe AC, Osuntokun BO. Prevalence of neurological disorders in Udo, a rural community in southern Nigeria. *Trop Geogr Med*. 1989;41(1): 36–40.
74. Ludvigsson P, Hesdorffer D, Olafsson E, et al. Migraine with aura is a risk factor for unprovoked seizures in children. *Ann Neurol*. 2006;59(1):210–213.
75. Ludvigsson P, Olafsson E, Sigurdardottir S, et al. Epidemiological features of infantile spasms in Iceland. *Epilepsia*. 1994;35:802–805.
76. Luhdorf K, Jensen LK, Plesner AM. Epilepsy in the elderly: incidence, social function, and disability. *Epilepsia*. 1986;27(2):135–141.
77. MacDonald BK, et al. The incidence and lifetime prevalence of neurological disorders in a prospective community-based study in the UK. *Brain*. 2000;123(Pt 4):665–676.
78. Manford M, Hart YM, Sander JW, et al. The National General Practice Study of Epilepsy. The syndromic classification of the International League Against Epilepsy applied to epilepsy in a general population. *Arch Neurol*. 1992;49(8):801–808.
79. Maremmani C, Rossi G, Bonuccelli U, et al. Descriptive epidemiologic study of epilepsy syndromes in a district of northwest Tuscany, Italy. *Epilepsia*. 1991;32(3):294–298.
80. Mathai KV, Dunn DP, Kurland LT, et al. Convulsive disorders in the Mariana Islands. *Epilepsia*. 1968;9(2):77–85.
81. Medina MT, Duron RM, Martinez L, et al. Prevalence, incidence, and etiology of epilepsies in rural Honduras: the Salama Study. *Epilepsia*. 2005;46(1):124–131.
82. Murphy CC, Trevathan E, Yeargin-Allsopp M. Prevalence of epilepsy and epileptic seizures in 10-year-old children: results from the Metropolitan Atlanta Developmental Disabilities Study. *Epilepsia*. 1995;36(9):866–872.
83. National Collaborative Perinatal Project, Hauser W, Nelson KB. Epidemiology of epilepsy in children. *Cleve Clin J Med*. 1989;56(Suppl 2):S185–194.
84. Nelson KB, Ellenberg JH. Antecedents of seizure disorders in early childhood. *Am J Dis Child*. 1986;140(10):1053–1061.
85. Ng SK, Hauser WA, Brust JC, et al. Alcohol consumption and withdrawal in new-onset seizures. *N Engl J Med*. 1988;319(11):666–673.
86. Ng SK, Hauser WA, Brust JC, et al. Hypertension and the risk of new-onset unprovoked seizures. *Neurology*. 1993;43(2):425–428.
87. Nicoletti A, Reggio A, Bartoloni A, et al. Prevalence of epilepsy in rural Bolivia: a door-to-door survey. *Neurology*. 1999;53(9):2064–2069.
88. Ohtahara S, Oka, E, Ohtasuka Y, et al. An Investigation on the Epidemiology of Epilepsy, in Frequency, Causes and Prevention of Neurological, Psychiatric and Muscular Disorders. Ministry of Health and Welfare, Japan. 1993: 55–60.

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89. Olafsson E, Hauser WA, Ludvigsson P, et al. Incidence of epilepsy in rural Iceland: a population-based study. *Epilepsia*. 1996;37(10):951–945.
90. Olafsson E, Ludvigsson P, Gudmundsson G, et al. Incidence of unprovoked seizures and epilepsy in Iceland and assessment of the epilepsy syndrome classification: a prospective study. *Lancet Neurol*. 2005;4(10):627–634.
91. Olafsson E, Hauser WA. Prevalence of epilepsy in rural Iceland: a population-based study. *Epilepsia*. 1999;40(11):1529–1534.
92. Onal AE, Tumerdem Y, Ozturk MK, et al. Epilepsy prevalence in a rural area in Istanbul. *Seizure*. 2002;11(6):397–401.
93. Osuntokun BO, Adeuja AO, Nottidge VA, et al. Prevalence of the epilepsies in Nigerian Africans: a community-based study. *Epilepsia*. 1987;28(3):272–279.
94. Osuntokun BO, Schoenberg BS, Nottidge VA. Research protocol for measuring the prevalence of neurologic disorders in developing countries: results of a pilot study in Nigeria. *Neuroepidemiology*. 1982;1:143–153.
95. Oun A, Haldre S, Magi M. Incidence of adult epilepsy in Estonia. *Acta Neurol Scand*. 2003;108(4):245–251.
96. Pisani F, Trunfio C, Oteri G, et al. Prevalence of epilepsy in children of Reggio Calabria, southern Italy. *Acta Neurol (Napoli)*. 1987;9(1):40–43.
97. Placencia M, Shorvon SD, Paredes V, et al. Epileptic seizures in an Andean region of Ecuador. Incidence and prevalence and regional variation. *Brain*. 1992;115(Pt 3):771–782.
98. Placencia M, Sander JW, Shorvon SD, et al. Validation of a screening questionnaire for the detection of epileptic seizures in epidemiological studies. *Brain*. 1992;115(Pt 3):783–794.
99. Pradilla G, Vesga BE, Leon-Sarmiento FE, et al. [Neuroepidemiology in the eastern region of Colombia]. *Rev Neurol*. 2002;34(11):1035–1043.
100. Proposal for revised classification of epilepsies and epileptic syndromes. Commission on Classification and Terminology of the International League Against Epilepsy. *Epilepsia*. 1989;30(4):389–399.
101. Radhakrishnan K, Pandian JD, Santhoshkumar T, et al. Prevalence, knowledge, attitude, and practice of epilepsy in Kerala, South India. *Epilepsia*. 2000;41(8):1027–1035.
102. Ramirez IO, Rodriguez MH, Aparicio Meix JM, et al. Incidencia de las epilepsias y sindromes epilepticos de la infancia en la provincia de Albacete. *An Esp Pediatr*. 1999;51(2):154–158.
103. Reggio A, Failla G, Patti F, et al. Prevalence of epilepsy. A door-to-door survey in the Sicilian community of Riposto. *Ital J Neurol Sci*. 1996;17(2):147–151.
104. Rocca WA, Savettieri G, Anderson DW, et al. Door-to-door prevalence survey of epilepsy in three Sicilian municipalities. *Neuroepidemiology*. 2001;20(4):237–241.
105. Ruggles KH, Haessly SM, Berg RL. Prospective study of seizures in the elderly in the Marshfield Epidemiologic Study Area (MESA). *Epilepsia*. 2001;42(12):1594–1599.
106. Rwiza HT, Kilonzo GP, Haule J, et al. Prevalence and incidence of epilepsy in Ulanga, a rural Tanzanian district: a community-based study. *Epilepsia*. 1992;33(6):1051–1056.
107. Salazar AM, Jabbari B, Vance SC, et al. Epilepsy after penetrating head injury. I. Clinical correlates: a report of the Vietnam Head Injury Study. *Neurology*. 1985;35(10):1406–1414.
108. Sander JW, Hart YM, Johnson AL, et al. National General Practice Study of Epilepsy: newly diagnosed epileptic seizures in a general population. *Lancet*. 1990;336(8726):1267–1271.
109. Schaumann BA, Annegers JF, Johnson SB, et al. Family history of seizures in posttraumatic and alcohol-associated seizure disorders. *Epilepsia*. 1994;35(1):48–52.
110. Senanayake N. Epilepsy control in a developing country - the challenge of tomorrow. *Ceylon Med J*. 1987;32:181–199.
111. Shamansky SL, Glaser GH. Socioeconomic characteristics of childhood seizure disorders in the New Haven area: an epidemiologic study. *Epilepsia*. 1979;20(5):457–474.
112. Sidenvall R, Forsgren L, Blomquist HK, et al. A community-based prospective incidence study of epileptic seizures in children. *Acta Paediatr*. 1993;82(1):60–65.
113. Snow RW, Williams RE, Rogers JE, et al. The prevalence of epilepsy among a rural Kenyan population. Its association with premature mortality. *Trop Geogr Med*. 1994;46(3):175–179.
114. Stanhope JM, Brody JA, Brink E. Convulsions among the Chamorro people of Guam, Mariana Islands. I. Seizure disorders. *Am J Epidemiol*. 1972;95(3):292–298.
115. Tallis R, Hall G, Craig I, et al. How common are epileptic seizures in old age? *Age Ageing*. 1991;20(6):442–448.
116. Tekle-Haimanot R, Forsgren L, Ekstedt J. Incidence of epilepsy in rural central Ethiopia. *Epilepsia*. 1997;38(5):541–546.
117. Tsuboi T. Prevalence and incidence of epilepsy in Tokyo. *Epilepsia*. 1988;29(2):103–110.
118. Wagner AL. A clinical and epidemiological study of adult patients with epilepsy. *Acta Neurol Scand Suppl*. 1983;94:63–72.
119. Wallace RH, Scheffer IE, Barnett S, et al. Neuronal sodium-channel alpha1-subunit mutations in generalized epilepsy with febrile seizures plus. *Am J Hum Genet*. 2001;68(4):859–865.
120. Whitehouse WP, Rees M, Curtis D, et al. Linkage analysis of idiopathic generalized epilepsy (IGE) and marker loci on chromosome 6p in families of patients with juvenile myoclonic epilepsy: no evidence for an epilepsy locus in the HLA region. *Am J Hum Genet*. 1993;53(3):652–662.
121. Zarrelli MM, Beghi E, Rocca WA, et al. Incidence of epileptic syndromes in Rochester, Minnesota: 1980-1984. *Epilepsia*. 1999;40(12):1708–1714.