

Sudden Unexpected Death in Epilepsy

A Retrospective Study

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Abstract: Patients with epilepsy have a mortality rate higher than that of the general population; sudden unexpected death represents a significant category of mortality in these patients. The precise frequency of occurrence of sudden unexpected death in epilepsy (SUDEP) is not well defined, with a range of 1 in 370 to 1100 in the general epileptic population. A major difficulty with incidence studies is the continued reluctance in using the term SUDEP as a cause of death, making reliance solely on death certificates inconsistent and incomplete. Knowledge about SUDEP remains limited, as no single common risk factor has yet been identified, although predisposing conditions have been suggested. The purpose of this study is to review the association between several clinical variables and SUDEP to elucidate risk factors. The characteristics of the 67 cases in this series correlate with published findings in previous studies. Attributes that may be used to define an at-risk group of epileptics include age less than 40 years, male gender, long history of seizure disorder, undermedication or poorly controlled seizure activity, and mental or physical stress. Education of physicians as to the existence of SUDEP and risk factors is imperative in improving patient education and reduction in mortality.

Key Words: sudden unexpected death, epilepsy, antiepileptic drugs, seizure disorder, risk factors

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Patients with epilepsy have a mortality rate higher than that of the general population; causes of death contributing to the mortality rate in this population include status epilepticus, progression of the underlying brain process, trauma or drowning directly precipitated by seizure activity, and disease processes unrelated to epilepsy. Sudden unexpected death

also represents a significant category of mortality in the population of patients with chronic epilepsy. The term *sudden unexpected death in epilepsy*, or SUDEP, encompasses sudden unexpected, witnessed or unwitnessed, nontraumatic and nondrowning deaths in epileptic patients where postmortem examination does not reveal a toxicologic or anatomic cause of death, with or without evidence of a seizure and excluding documented status epilepticus.¹

Most of these deaths are unwitnessed, although it is generally believed that most cases of SUDEP are preceded by seizures with consequent postictal respiratory arrest or terminal cardiac arrhythmia. Several reports describe respiratory arrest and hypoventilation as primary mechanisms in SUDEP deaths, including a report of a series of witnessed deaths² and several animal models.^{3,4} An abundance of literature also documents a variety of seizure-related cardiac dysrhythmias captured on ECG. These observed arrhythmias include lengthening of the QT interval,^{5–7} ST depression and T-wave inversion,⁸ ventricular fibrillation and asystole,^{9–13} bradyarrhythmias,^{14,15} as well as atrial fibrillation, atrial and ventricular premature depolarizations, and sinus and supraventricular tachycardias.^{12,16,17} While the arrhythmogenic effect of seizure activity is certainly hypothesized to play a role in cardiac instability, seizure-related apnea and hypoxia may also play a central part in potentiating cardiac arrhythmias, with subsequent hypoxia acting as an additional contributing factor in cardiorespiratory arrest.^{14,18}

The precise frequency of occurrence of SUDEP is not well defined; the incidence is reported as ranging from 1 in 100 in therapy-resistant epilepsy surgery candidates¹⁰ to 1 in 370 to 1100 in the general epileptic population.^{19,20} Overall, it is felt that approximately 1 in 200 patients with severe chronic epilepsy die each year from SUDEP,^{21,22} and 5% to 30% of deaths in patients with epilepsy are attributable to SUDEP.^{19,23–25} A major difficulty with incidence studies is the continued reluctance in using the term *SUDEP* as a cause of death, making death certificate information particularly inconsistent and therefore unreliable. The occurrence of SUDEP is well recognized in Europe and Canada, where a majority of the published research has been conducted. Fewer studies have come out of the United States, and the general

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medical community has been slower to promote SUDEP as a legitimate risk to epileptic patients, as epilepsy is portrayed as a disease that one lives with, not necessarily a condition from which one could die. This is partially due to the fact that knowledge about SUDEP remains limited; despite thorough documentation in the literature, no single common risk factor has yet been identified; therefore, it is difficult to identify patients at risk and impossible to implement steps to prevent its occurrence. Previous studies have implicated numerous clinical scenarios, suggesting the possibility of multiple mechanisms. A variety of predisposing conditions have been suggested, but contradictory literature addresses many of these risk factors. Several conditions that have been previously proposed include low antiepileptic drug (AED) levels and poor compliance with medications, treatment with carbamazepine, amygdalal sclerosis, number of antiepileptic medications taken concurrently, and frequency of seizure activity. The objective of this study is to review the association between several clinical variables and sudden unexpected death in epileptic patients to identify possible risk factors.

METHODS

Reviewed were cases of sudden death in known epileptic patients from autopsies performed from January 1993 through December 2000 at the Arapahoe County Coroners Office (a suburban area with a population of approximately 506,000) and from January 1996 through September 2000 at the Denver Office of the Medical Examiner (an urban area with a population of approximately 555,000). Information was acquired from several sources, including death certificates, autopsy reports, and scene information. Included were only nontraumatic, nondrowning deaths in the absence of documented status epilepticus and without significant natural disease. The clinical histories and autopsy data were reviewed, including available laboratory studies and neuropathology, with the goal of elucidating risk factors for SUDEP. Details considered in investigation of the clinical data of each case include the age at death, duration of disease, degree of seizure control, past medical history and current medications, recent illnesses, and use of alcohol or other drugs of abuse. Cases were excluded from the study if cocaine or other drugs of abuse to which death could be attributed were found. Postmortem information recorded included details of the scene of death, circumstances surrounding the event, autopsy findings, antiepileptic medication levels, and postmortem toxicologic studies including antiepileptic medication levels.

RESULTS

Sixty-seven cases were identified, 48 male and 19 female. The age range was 2 to 58 years, with an average age of 35.5 years. All cases except 2 occurred in patients 13 years or older. Table 1 summarizes the characteristics of each case.

Documentation of seizure histories was often limited, and there was limited availability of clinical medical records, including classification of seizure type and duration of disease. Most cases of epilepsy were known to be longstanding (often since childhood), with a mean duration of disease of 18.4 years in the 43 patients in which extent was known and documented. Duration of seizure disorder ranged from 4 months to 53 years. Thirty-four cases (51%) had idiopathic epilepsy with no known cause, 14 (21%) were posttraumatic, and 7 (10%) had other known causes, including infections, mass lesions, or cerebral palsy. Five patients had seizures of presumed multifactorial etiology, while no reliable seizure history was obtained in 7 cases (unknown etiology). Of the 54 patients being treated with known antiepileptic medications, 21 (39%) were on multiple medications. The most common medications included phenytoin, phenobarbital, carbamazepine, and valproic acid. Other medications included felbamate, lamotrigine, topiramate, primidone, gabapentin, respidal, and clorazepate. Of the 54 cases with a prescribed antiepileptic therapy, postmortem drug levels were therapeutic in only 12 cases (22%), subtherapeutic in 36 cases (67%), and undetectable in 4 (7%). Two cases had postmortem antiepileptic levels greater than the upper limit of the reported therapeutic range. In 13 of the cases with prescribed antiepileptic medications, there was a known history of poor compliance. Ten patients were not being treated with any antiepileptic medications.

Medical histories included substance abuse (18 cases), psychiatric disorders (9 cases) including schizophrenia and major depression, mental retardation (9 cases), chronic infection (3), cerebral palsy (3), malignancy (2), and a variety of other miscellaneous conditions (17). Six patients were receiving antibiotics at the time of death, and in a total of 19 cases, a report of recent viral symptoms was provided. Other recent stressors recorded included injury (5 cases), travel (4), and arrest by law enforcement (1). Four patients were homeless. Postmortem toxicologic studies revealed drugs of abuse in 15 cases including only alcohol, marijuana, or both. Four of the patients had a known history of hypertension, and arteriosclerotic cardiovascular disease was discovered at autopsy in 14 (21%). Other autopsy findings included hepatic steatosis (19 cases), cirrhosis (6), and obvious bacterial infection (pneumonia and acute pyelonephritis, 1 each). A variety of other incidental findings were present.

The scenes of death showed remarkable similarities, with 58 of 67 cases (87%) found at home; the remaining 9 cases included 3 found at homeless shelters, 1 in jail, 1 at work, and 4 discovered at outdoor locations. Thirty-eight cases were found on a bed or a couch. In a majority of cases, the body was found in the prone position (37 cases, 67%). Only 16 of the deaths were witnessed (Table 2), with reports of seizure activity in 12. Fourteen of these patients received medical attention (transported to an emergency department or

TABLE 1. Summary of Cases

Case #	Demographics	Duration of Disease	Etiology	AEDs	Postmortem AED Levels	Recent Stressors	Scene Location	Body Position
1	47M cauc	20 years	Posttraumatic	None	Negative	—	Home in bed	Unknown
2	2M greek	1.5 years	Idiopathic	1	Subtherapeutic	—	Home in parents' bed	Prone
3	28M cauc	Longstanding	Idiopathic	3	Therapeutic (1)	URI on antibiotics	Home in bed	Prone
4	13F cauc	Longstanding	Idiopathic	1	Subtherapeutic	URI on antibiotics	Home in bed	Prone
5	39M cauc	Longstanding	Idiopathic	2	Therapeutic (1)	—	On floor	Prone
6	17M cauc	10 years	Idiopathic	1	Subtherapeutic	—	Home in bed	Prone
7	29M cauc	Longstanding	Idiopathic	1	Therapeutic	—	Home in bed	Prone
8	29M cauc	Longstanding	Idiopathic	2	Subtherapeutic	—	Home on floor	Unknown
9	45F cauc	Longstanding	Idiopathic	2	Subtherapeutic	Flu sx 2 days PTD, on antibiotics	Home in bed	Supine
10	24M cauc	24 years	Idiopathic	2	Subtherapeutic	—	Home living room	Prone
11	39F cauc	37 years	Idiopathic	1	Therapeutic	Increasing HA, seizure 1 day PTD	Home in bed	Prone
12	46M cauc	Unknown	Idiopathic	1	Subtherapeutic	—	Home on floor	Prone
13	27M cauc	3 years	Multifactorial	None	Negative	Dislocated shoulder 7 days PTD Jailed day of death	Jail in bed	Prone
14	36M asian	4 months (0.33 years)	Hippocampal anomaly	1	Negative	Surgery resident	Home in bed	Prone
15	22M black	Unknown	Idiopathic	3	Therapeutic (1)	Psych admission 1 month PTD	Seizure at home	NA
16	44M black	Longstanding	Idiopathic	1	Subtherapeutic	On antibiotics	Home in bed	Prone
17	30M black	29 years	Idiopathic	1	Subtherapeutic	Flu sx 1 week	Home in bed	Prone
18	58F cauc	53 years	Idiopathic	1	Subtherapeutic	—	Home bathroom floor	Other
19	52M cauc	14 years	Cerebral palsy	None	Negative	Bronchitis 2 weeks	Home under bed	Prone
20	26M cauc	6 years	Idiopathic	1	Subtherapeutic	Travel 1 day PTD	Home bedroom floor	Prone
21	34M cauc	Longstanding	Posttraumatic	1	Negative	—	Home porch	Prone
22	17F cauc	4 years	Idiopathic	3	Subtherapeutic	C/o increased stress	Home on couch	Prone
23	23M black	17 years	Idiopathic	3	Therapeutic (2)	Relocation 1 month PTD	Home on air mattress Living room floor	Prone
24	40M cauc	40 years	Idiopathic	3	Subtherapeutic	Flu sx 3 days PTD Anorexia 3 days	Home in bed	Other
25	38F cauc	2 years	Posttraumatic	1	Subtherapeutic	Recent diarrhea	Home on couch	Other
26	36M cauc	Longstanding	Idiopathic	2	Subtherapeutic	—	Home in bed	Prone
27	27M cauc	Unknown	Idiopathic	1	Subtherapeutic	—	Home in bathroom	Other
28	48M cauc	Unknown	Unknown	Unknown	Negative	Homeless	Shelter	NA

(Continued)

TABLE 1. (Continued)

Case #	Demographics	Duration of Disease	Etiology	AEDs	Postmortem AED Levels	Recent Stressors	Scene Location	Body Position
29	39M cauc	23 years	Idiopathic	None	Negative	Friend's funeral 1 day PTD	Home in bed	Prone
30	41F cauc	39 years	Posttraumatic	2	Subtherapeutic	—	Home in bed	Prone
31	33M nat am	Unknown	Unknown	Unknown	Negative	—	Outside on ground	Other
32	38F hisp	36 years	Idiopathic	2	Therapeutic (1)	—	Home in bed	NA
33	7M cauc	7 years	Posttraumatic	1	Subtherapeutic	Fever 105°F	Home	NA
34	36M black	24 years	Idiopathic	1	Negative	Heavy drinking	Home living room floor	Prone
35	44F cauc	Unknown	Unknown	None	Negative	Depression	Home bedroom floor	Prone
36	36F cauc	30 years	Posttraumatic	2	Subtherapeutic	—	Home in bed	Prone
37	49M black	3 years	Meningioma	1	Subtherapeutic	—	Home hallway floor	Other
38	31M hisp	28 years	Measels/febrile	None	Negative	—	Home in bed	Prone
39	29F hisp	20 years	Idiopathic	1	Subtherapeutic	—	Home bedroom floor	Prone
40	47M cauc	Longstanding	Idiopathic	1	Therapeutic	Stomach ache/ hematemesis Odd behavior 3 days PTD	Floor at work	Supine
41	30M hisp	15 years	Idiopathic	1	Therapeutic	—	Home in bed	Prone
42	38M cauc	38 years	Congenital Hydrocephalus	1	Subtherapeutic	Pneumonia, on antibiotics	Home in makeshift bed	Other
43	52F cauc	2 years	Idiopathic	2	Elevated	—	Home in bed	Supine
44	40M cauc	7 years	Multifactorial	1	Elevated	Fall down stairs Multiple blunt impact trauma	Unresponsive at home	NA
45	33M cauc	33 years	Porencephaly	1	Subtherapeutic	Car stolen, ticketed Upcoming travel	Seizure at home	NA
46	45M hisp	Recent onset	Multifactorial	1	Subtherapeutic	Assault 1 month PTD	Home in bed	Prone
47	51F hisp	Unknown	Unknown	2	Subtherapeutic	Fever 108°F Acute cholecystitis/ vomiting	Group home in bed	Other
48	34M cauc	1 year	Multifactorial	None	Negative	Homeless	River bank in bed	Prone
49	21F cauc	8 years	Posttraumatic	1	Subtherapeutic	On cold medications	Home bedroom floor	Prone
50	44M black	15 years	Posttraumatic	1	Subtherapeutic	To ED c/o HA, "Preictal" state	Home in bed	Supine
51	54M cauc	39 years	Posttraumatic	2	Subtherapeutic	Felt ill, vomiting	In car outside ED	NA
52	52F cauc	23 years	Posttraumatic	1	Subtherapeutic	Flu sx 2 days PTD on antibiotics	Home on couch	Supine
53	37M black	2 years	Idiopathic	1	Therapeutic	—	Home on bed	Prone
54	40M hisp	8 years	Posttraumatic	1	Subtherapeutic	—	Home in bed	Unknown
55	41F hisp	Unknown	Unknown	Unknown	Negative	—	Home in bed	Prone

(Continued)

TABLE 1. (Continued)

Case #	Demographics	Duration of Disease	Etiology	AEDs	Postmortem AED Levels	Recent Stressors	Scene Location	Body Position
56	37M cauc	Unknown	Unknown	2	Subtherapeutic	Recent apartment break-in	Home living room floor	Prone
57	36F cauc	35 years	Idiopathic	3	Subtherapeutic	Cholecystectomy Nasuea/vomiting PTD	Home in bed	Prone
58	38M cauc	23 years	Posttraumatic	2	Subtherapeutic	Struck by car 1 month PTD Assault 6 months PTD	Home bedroom floor	Prone
59	18M hisp	Unknown	Idiopathic	None	Negative	—	Home	NA
60	32F black/hisp	Longstanding	Idiopathic	2	Subtherapeutic	—	Home bedroom floor	Prone
61	44M cauc	43 years	Posttraumatic	1	Therapeutic	—	On street	NA
62	33M cauc	4 years	Viral meningitis	1	Therapeutic	—	Home in bed	Other
63	42M cauc	3 years	Multifactorial	None	Not done	Assault few days PTD Homeless	Shelter bathroom floor	Other
64	39M cauc	Unknown	Unknown	1	Negative	Homeless shelter few days PTD	Shelter in bed	Supine
65	28F black	14 years	Posttraumatic	2	Subtherapeutic	Moved new house 1 day PTD	Home in bed	Prone
66	45M cauc	Unknown	Idiopathic	None	Negative	Vomiting hours PTD	Home in bed	Supine
67	31M hisp	6 years	Idiopathic	1	Subtherapeutic	Recent cold sx	Home in bed	NA

M indicates male; F, female; cauc, Caucasian; hisp, Hispanic; nat am, Native American; NA, not applicable; AED, antiepileptic drug; ED, emergency department; sx, symptoms; PTD, prior to death; HA, headache; c/o, complained of; URI, upper respiratory infection.

attended by paramedics or other medical personnel) but were unresuscitatable.

At autopsy, evidence suggesting recent seizure activity (tongue lacerations and contusions and/or superficial cutaneous abrasions and contusions) was detected in 39 cases (58%). Other findings included visceral congestion (16 cases), pulmonary edema (10), or both (29). Structural brain lesions thought to be the underlying cause of the seizure disorder were identified in 4 cases (meningioma, hippocampal developmental abnormality, temporal cystic degeneration, and hydrocephalus).

In these 67 cases, the cause of death listed on the death certificate was termed SUDEP in only 8 cases (12%). A majority of cases were signed out as seizure disorder or complications thereof (38 cases, 57%) or probable seizure (18 cases, 28%). Three cases listed other causes on the death certificate, including positional asphyxia and complications of blunt impact trauma to the head.

DISCUSSION

The characteristics of the sixty-seven cases in this series correlate with published findings in previous studies.^{13,19,26-29} These frequently described attributes, which may be used to define an at-risk group within the epileptic population, include a younger age group (mean age 35.5 years old) and a striking male predominance (72%, or approximately 3:1 male to female ratio). The data are skewed to a younger age group by the very definition of SUDEP, as in older populations more significant natural disease is present at autopsy to which the cause of death is attributable. Although some series report a shorter duration of disease,^{13,19,28,29} our data do agree with more recent indications that SUDEP tends to occur in epilepsy of long duration.^{26,27,30} Although the duration of epilepsy was only known in 64% of our cases (Table 1), a majority of these cases (60% of the 43 cases with a known history) had

TABLE 2. Witnessed Deaths

Case No.	Witnessed Seizure	Circumstances
13	Yes	Seizure activity in jail, unresuscitatable by paramedics in postictal state
15	Yes	Seizure at home, transported to ED, unresuscitatable
21	Yes	3-year-old daughter witnessed seizure, found dead by family friend after an unknown period of time
25	Yes	Seizure at home, unresuscitatable by paramedics
28	Yes	Seizure at homeless shelter, transported to ED, unresuscitatable
31	No	Found unresponsive outside apartment building, transported to ED, unresuscitatable
32	Yes	Seizure at home, transported to ED, unresuscitatable
33	Yes	Seizure at home with prolonged postictal state, transported to ED, unresuscitatable
44	No	Found unresponsive at home, transported to ED, unresuscitatable
45	Yes	Seizure at home, apnic, unresuscitatable by paramedics
49	No	Found unresponsive at home in asystole, transported to ED, unresuscitatable
51	No	Collapsed in car outside hospital, taken to ED in asystole, unresuscitatable
59	Yes	Seizure at home, transported to ED in ventricular fibrillation, unresuscitatable
61	Yes	Seizure on the street, transported to ED, unresuscitatable
65	Yes	Seizure at home felt by spouse overnight, was dead in the morning when spouse awoke
67	Yes	Seizure at home, unresuscitatable by paramedics

experienced their first seizure at least 10 years prior to death. Also in concordance with other studies our cohort group showed a predominance of idiopathic epilepsy (51%) versus identifiable (secondary) causes; only a minority of cases (6%) displayed underlying neuropathologic lesions to which seizures were attributed.

Sleep acts a potent activator of interictal epileptiform discharges in certain epilepsies, and sleep deprivation can also in turn trigger seizure activity.^{31,32} In concordance with this well-recognized relationship between epilepsy and sleep, in a majority of our cases the decedents were found either in bed or on a couch (57%) with a large number of the remaining patients found in close proximity, giving the appearance of having fallen from bed during seizure activity. Of the 16 witnessed deaths, 44% were sleep-related.

At autopsy, there was evidence of seizure activity in 58% of cases, manifested by tongue lacerations/contusions (19 cases) and superficial cutaneous injuries (5) or both (15), for a total of 39 out of 67 cases. For many of these patients, the seizure was the first epileptic activity over a long period of time, while in other cases history was obtained indicating the deceased experienced frequent seizure activity. These results contrast somewhat with previously published data in that almost half of our cases (43%) were relatively seizure-free for an extended period of time, while other studies^{20,25,28-30} indicate a higher risk for SUDEP in therapy-resistant patients with poorly controlled seizures. Although 56% of cases (25 of 45 cases with known seizure history) displayed seizure activity within the month prior to death, only 8 patients reported regular, frequent seizures, and a

history of therapy resistance was obtained in only 4 of these patients. Of particular interest, 40 of 54 patients (74%) with prescribed AEDs had negative or subtherapeutic AED levels at autopsy, but a history of noncompliance or recent discontinuation of AEDs was obtained in 24% of cases, highlighting the need for patient education and regular follow-up.

Not all of these deaths can be attributed to management failures, however; an additional risk factor that may play a role in SUDEP is the presence of recent stressors prior to death. In 53% of cases, a history of illness, stress, anxiety, or fatigue was obtained. Twenty-eight percent of patients (19 cases) were ill at the time of death, with conditions predominantly described as bacterial or viral infections; 11 of these patients were prescribed antibiotics or were using over-the-counter remedies. For the remaining 21 cases, histories of stress events were obtained which included homelessness, physical trauma, recent relocation or travel, and psychiatric stressors, including suicide of a friend and the rape of a daughter.

There were 16 witnessed deaths in this series (Table 2), with a suggestion of a distinct mechanism; although the purpose of this study was not to define the mechanism behind SUDEP, it bears mentioning. Of witnessed cases, 4 patients were found unresponsive and expired despite paramedic transportation and attempted resuscitation at a local emergency department. In 12 cases, the decedents experienced witnessed seizures and expired in presumed postictal states, again despite resuscitative measures. In none of the witnessed cases was death observed to occur during seizure activity. The observed delay between seizure activity and death is

suggestive of primary respiratory inhibition followed by respiratory arrest, with the development of significant pulmonary edema contributing to the difficulty with resuscitation. Although this does not rule out secondary cardiac arrhythmias, a primary arrhythmia is unlikely due to the delay between seizure activity and death. In addition, autopsy and microscopic evaluation also revealed pulmonary edema in 51%, which is consistent with autopsy findings in other series.^{19,26,27} The edema may be neurogenic, respiratory, or cardiac in origin, although deaths from primary cardiac arrhythmia would in theory be so abrupt as to preclude the development of pulmonary edema, whereas this finding would be consistent with respiratory arrest.

In summary, these data correlate with previously published studies in terms of elucidating possible risk factors in SUDEP. Factors identified here include male gender, age less than 40 years old, a long history of epilepsy, undermedication or poorly controlled seizure activity, and mental or physical stress. Overall, the identified factors represent risk factors for seizure activity, as the seizure itself presents the largest risk for sudden unexpected death. The underlying trigger for SUDEP within any given seizure remains unknown. Although SUDEP strikes only approximately 1 in 1000 epileptic patients, the need for patient education regarding risk factors is obvious and may lead to an even lower incidence with better patient awareness and medication compliance. In addition, appropriate death investigation and pathologic examinations are imperative in seizure-related deaths. As SUDEP is the most common category of epilepsy-related death,³³ classifying these deaths as such would provide better mortality data, as well as facilitate building an accurate database for further research.

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REFERENCES

- Nashef L, Brown S. Epilepsy and sudden death. *Lancet*. 1996;348:1324–1325.
- Langan Y, Nashef L, Sander JWAS. Sudden unexpected death in epilepsy: a series of witnessed deaths. *J Neurol Neurosurg Psychiatry*. 2000;68:211–213.
- Johnston SC, Horn JK, Valente J, et al. The role of hypoventilation in a sheep model of epileptic sudden death. *Ann Neurol*. 1995;37:531–537.
- Johnston SC, Siedenberg R, Min JK, et al. Central apnea and acute cardiac ischemia in a sheep model of epileptic sudden death. *Ann Neurol*. 1997;42:588–594.
- Timmings PL. Sudden unexpected death in epilepsy: is carbamazepine implicated? *Seizure*. 1998;7:289–291.
- Tavernor SJ, Brown SW, Tavernor RM, et al. Electrocardiograph QT lengthening associated with epileptiform EEG discharges: a role in sudden unexpected death in epilepsy? *Seizure*. 1996;5:79–83.
- Drake ME, Reider CR, Kay A. Electrocardiography in epilepsy patients without cardiac symptoms. *Seizure*. 1993;2:63–65.
- Opherck C, Coromilas J, Hirsch LJ. Heart rate and EKG changes in 102 seizures: analysis of influencing factors. *Epilepsy Res*. 2002;52:117–127.
- Dasheiff RM, Dickinson LJ. Sudden unexpected death of epileptic patient due to cardiac arrhythmia after seizure. *Arch Neurol*. 1986;43:194–196.
- Dasheiff RM. Sudden unexpected death in epilepsy: a series from an epilepsy surgery program and speculation on the relationship to sudden cardiac death. *J Clin Neurophysiol*. 1991;8:216–222.
- Howell SJ, Blumhardt LD. Cardiac asystole associated with epileptic seizures: a case report with simultaneous EEG and ECG. *J Neurol Neurosurg Psychiatry*. 1989;52:795–798.
- Nei M, Ho RT, Sperling MR. EKG abnormalities during partial seizures in refractory epilepsy. *Epilepsia*. 2000;41:542–548.
- Leestma JE, Kalelkar MB, Teas SS, et al. Sudden unexpected death associated with seizures: analysis of 66 cases. *Epilepsia*. 1984;25:84–88.
- Nashef L, Walker F, Allen P, et al. Apnoea and bradycardia during epileptic seizures: relation to sudden death in epilepsy. *J Neurol Neurosurg Psychiatry*. 1996;60:297–300.
- Kiok MC, Terrence CF, Fromm GH, et al. Sinus arrest in epilepsy. *Neurology*. 1986;36:115–116.
- Walsh GO, Masland W, Goldensohn ES. Relationship between paroxysmal atrial tachycardia and cerebral discharges. *Bull Los Angeles Neurol Soc*. 1972;37:28–35.
- Mathew NT, Taori GM, Mathai KV, et al. Atrial fibrillation associated with seizure in a case of frontal meningioma. *Neurology*. 1970;20:725–728.
- So EL, Sam MC, Lagerlund TL. Postictal central apnea as a cause of SUDEP: evidence from a near-SUDEP incident. *Epilepsia*. 2000;41:1494–1497.
- Leestma JE, Walczak T, Hughes JR, et al. A prospective study of sudden unexpected death in epilepsy. *Ann Neurol*. 1989;26:195–203.
- Annegers JF, Coan SP. SUDEP: overview of definitions and review of incidence data. *Seizure*. 1999;8:347–352.
- Leestma JE, Annegers JF, Brodie MJ, et al. Sudden unexplained death in epilepsy: observations from a large clinical development program. *Epilepsia*. 1997;38:47–55.
- Nashef L, Fish DR, Sander JW, et al. Incidence of sudden unexpected death in an adult outpatient cohort with epilepsy at a tertiary referral centre. *J Neurol Neurosurg Psychiatry*. 1995;58:462–464.
- Ficker DM. Sudden unexplained death and injury in epilepsy. *Epilepsia*. 2000;41(suppl 2):S7–S12.
- Walczak TS, Leppik IE, D'Amelio M, et al. Incidence and risk factors in sudden unexpected death in epilepsy: a prospective cohort study. *Neurology*. 2001;56:519–525.
- Brenningstall GN. Mortality in pediatric epilepsy. *Pediatr Neurol*. 2001;25:9–16.
- Earnest MP, Thomas GE, Eden RA, et al. The sudden unexplained death syndrome in epilepsy: demographic, clinical, and postmortem features. *Epilepsia*. 1992;33:310–316.
- Kloster R, Engelskjøn T. Sudden unexpected death in epilepsy (SUDEP): a clinical perspective and a search for risk factors. *J Neurol Neurosurg Psychiatry*. 1999;67:439–444.
- Nilsson L, Bergman U, Diwan V, et al. Antiepileptic drug therapy and its management in sudden unexpected death in epilepsy: a case control study. *Epilepsia*. 2001;42:667–673.
- McKee JR, Bodfish JW. Sudden unexpected death in epilepsy in adults with mental retardation. *Am J Ment Retard*. 2000;105:229–235.
- Nilsson L, Farahmand BY, Persson PG, et al. Risk factors for sudden unexpected death in epilepsy: a case-control study. *Lancet*. 1999;353:888–893.
- Dinner DS. Effect of sleep on epilepsy. *J Clin Neurophysiol*. 2002;19:504–513.
- Malow BA. Paroxysmal events in sleep. *J Clin Neurophysiol*. 2002;19:522–534.
- Langan Y, Nashef L, Sander JWAS. Certification of deaths attributable to epilepsy. *J Neurol Neurosurg Psychiatry*. 2002;73:751–752.