



- Name of Disorder: Epilepsy
- Essay Title: Sudden Unexplained Death in Epilepsy
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- Date: 28/06/2013

- Content:

Sudden Unexplained Death in Epilepsy

Epilepsy is the most prevalent neurological disorder, and is estimated to affect 50 million people worldwide. It is a condition of recurrent unprovoked seizures that can clinically manifest as alterations in sensory perception, motor control, behaviour and autonomic function (Chang et al., 2003). While these symptoms and the recurrent nature of epilepsy confer significant morbidity for affected patients, individuals suffering from epilepsy are also at a reported 24 times greater risk of sudden unexplained death than the general population. (Ficker et al., 1998) This condition is termed sudden unexpected death in epileptic patients (SUDEP).

One of the earliest medical observations of SUDEP was made in 1868, when the English physician Bacon identified 3 types of death linked to epilepsy; 'sudden deaths in a fit' 'deaths after a rapid succession of fits' and 'deaths from accidents (Bacon 1868). Non-medical observations of sudden unexplained death in epilepsy had occurred prior to Bacon's writings however. The most famous of which was the death of Patsy Custis, the step daughter of George Washington. Patsy's epilepsy began at the age 6, and in 1768 Washington described her as "seized with fits" (Doherty 2004). Prior to the development of effective anti-epileptic medication, the treatment available to Patsy was rudimentary and informed by superstition and misinformation. These treatments included bleeding, valerian root, musk, ether, cinchona, healing waters and even an iron ring to ward off seizures. Unfortunately these treatments were of little benefit to Patsy, who died suddenly during a seizure in 1773. In a letter, Washington described the death:

She rose from dinner about four o'clock in better health and spirits than she appeared to have been in for some time; soon after which she was seized with one of her usual Fits, and expired in it, in less than two minutes without uttering a word, a groan, or scarce a sigh (George Washington) .

SUDEP is formally defined as:

The sudden, unexpected, witnessed or unwitnessed, non-traumatic and non-drowning death in patients with epilepsy, with or without evidence for a seizure and excluding documented status epilepticus, in which post mortem examination does not reveal a toxicologic or anatomic cause for death (Nashef 1997).

The process of diagnosing SUDEP is one of excluding other potential causes of death. While subtle cardiac and neural pathology are often found, these must be judged to be not sufficient to themselves explain death. The incidence of SUDEP depends on the populations studied, and the choice of control group, but across studies of refractory patients is approximately 3.5 per 1000 patient years. In candidates for epilepsy surgery, prevalence may be as high as 9.3 per 1000 person-years (Tomson et al., 2008). Determining which clinical and demographic features are associated with an increased SUDEP risk is complicated by differences in populations, and study design. Across studies however, identified risks include a young age (between 20-40 years old), a long history of seizures,



generalized tonic-clonic seizures (GTCS), refractory epilepsy, and polytherapy with AEDs (which is likely to be another proxy for poorly controlled or refractory epilepsy).

Providing definitive evidence of the mechanisms underlying SUDEP is a challenging task. There have been only a handful of cases where epilepsy patients who were undergoing observational (video-EEG) monitoring in hospital died from SUDEP. One informative case was reported by Dasheiff and Dickinson (1986). Macromi Nei and Nicole Simpkins, in the excellent textbook "Sudden Death in Epilepsy; Clinical and Forensic Issues" describe the case like this:

The patient was a 48-year-old man with a history of prior myocardial infarction and refractory focal epilepsy who had been implanted with depth electrodes for seizure focus localization. He had two secondarily generalized tonic-clonic seizures within 1 hour of each other. After the second seizure, the patient complained of chest and left arm pain. An EKG revealed ST segment elevation and inverted T waves. One hour later, the patient complained of chest pain, then was witnessed to have a complex partial seizure, becoming cyanotic and apneic. The first available EKG revealed coarse ventricular fibrillation, followed by asystole. Cardiopulmonary resuscitation was ineffective. Postmortem examination revealed no acute coronary artery thromboses or pulmonary emboli but did reveal an old myocardial infarction (Mei et al., 2012; Dasheiff et al., 1986).

Current findings suggest that there may be a number of causes underlying cases of SUDEP. The two predominant mechanisms are respiratory failure and cardiovascular failure (Shorovon et al., 2011). While some examples of respiratory related SUDEP and reflect obstruction of the airways during seizure, some examples do suggest a pronounced reduction or disturbance of autonomic drive to the lungs. This mechanism may be related to the presumed mechanism of cardiac SUDEP, seizure associated disruption of autonomic drive or homeostatic regulation of the heart. Research into the underlying mechanisms however is scarce and the careful application of neuroimaging techniques to identify the neural basis of cardiac autonomic dysfunction has not yet been undertaken. This is an area of much needed research. Despite the 240 years since Patsy Curtis died, we have made little progress in understanding the mechanisms underlying this devastating consequence of epilepsy.

These cases continue today. Gerome Schacter, in his forward to the textbook "Sudden Death in Epilepsy; Clinical and Forensic Issues" relays the comments of a colleague (Lathers et al., 2012):

As a doctor and an epileptologist, I experience the deepest frustration when I am notified of the sudden and unexpected death of one of my patients. Often these patients have been found dead in bed, lying dead on the floor of their apartment, or drowned in the bathtub. They are invariably young and are often at the beginning of their lives. I never forget them...One of my young patients, a 25-year-old man, died last year while in bed. His parents had encouraged him to live alone so that his life would be as normal as possible. They had visited him that evening and had eaten dinner with him. He had a girlfriend, but she had not been there that night. The next morning he was found lying face down on his bed, fully dressed. No one was sure whether or not he had experienced a seizure. When his parents called me, we talked about the problem of sudden death and epilepsy (Schacter, 2008).

This clinical problem needs urgent attention. A promising avenue for progress is the sophisticated application of neuroimaging methods to characterise autonomic cardiovascular control within the brain. With effort and expertise, SUDEP may one day be as infrequent as small pox.



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