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SPECIAL REPORT

Report of the American Epilepsy Society and the Epilepsy Foundation Joint Task Force on Sudden Unexplained Death in Epilepsy

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Summary

The American Epilepsy Society and the Epilepsy Foundation jointly convened a task force to assess the state of knowledge about sudden unexplained death in epilepsy (SUDEP). The task force had five charges: (1) develop a position statement describing if, when, what, and how SUDEP should be discussed with patients and their families and caregivers; (2) design methods by which the medical and lay communities become aware of the risk of SUDEP; (3) recommend research directions in SUDEP; (4) explore steps that organizations can take to perform large-scale, prospective studies of SUDEP to identify risk factors; and (5) identify possible preventive strategies for SUDEP. Some of the major task force recommendations include convening a multidisciplinary workshop to refine current lines of investigation and to identify additional areas of research for mechanisms underlying SUDEP; performing a survey of patients and their families and caregivers to identify effective means of education that will enhance participation in SUDEP research; conducting a campaign aimed at patients, families, caregivers, coroners, and medical examiners that emphasizes the need for complete autopsy examinations for patients with suspected SUDEP; and securing infrastructure grants to fund a consortium of centers that will conduct prospective clinical and basic research studies to identify preventable risk factors and mechanisms underlying SUDEP. For now, the principal effort in preventing SUDEP should be prompt and optimal control of seizures, especially generalized convulsive seizures.

KEY WORDS: Patient care, Preventive measures, Risk factors, Seizures.

The phenomenon of sudden unexplained death in epilepsy (SUDEP) is a devastating event that occurs at a rate of 1 in 150 person-years in persons with uncontrolled seizures (Tomson et al., 2005). Despite intense interest in SUDEP from the medical and lay communities in the last two decades, the mechanisms of SUDEP and methods to prevent SUDEP are still largely unknown. In March 2007, the American Epilepsy Society and the Epilepsy Foundation jointly convened a task force to assess the state of knowledge about SUDEP. The task force had five charges: (1) develop a position statement describing if, when, what, and how SUDEP should be discussed with patients and their families and caregivers; (2) design methods by which

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the medical and lay communities become aware of the risk of SUDEP; (3) recommend research directions in SUDEP; (4) explore steps that organizations can take to perform large-scale, prospective studies of SUDEP to identify risk factors; and (5) identify possible preventive strategies for SUDEP.

The task force consisted of members with different clinical and research backgrounds and also included members who were patient advocates and legal advisors. The task force was divided into two work groups: one focusing on scientific aspects of epilepsy and the other on epilepsy education and advocacy. Recommendations from each work group were assessed by the entire task force, and we offer this report to help further the goal of understanding and eliminating SUDEP.

Charge 1: Develop a Position Statement Describing If, When, What, and How SUDEP Should Be Discussed with Patients and Their Families and Caregivers

The literature pertinent to this charge is limited, but the task force specifically considered guidelines from the National Institute for Health and Clinical Excellence (2007), which were developed in the United Kingdom for the diagnosis and management of epilepsy. These guidelines indicate that information on SUDEP should be tailored to the individual's relative risk of SUDEP and that information should be provided as part of a comprehensive counseling program for patients with epilepsy and their families and caregivers. However, adherence to the guidelines has varied, and a survey showed that most neurologists in the United Kingdom discussed SUDEP with only a few of their patients with epilepsy (Morton et al., 2006).

The task force assessed the implications and nuances of discussing SUDEP with patients and their families and caregivers. Discussing SUDEP may diminish emphasis on the recommendation that most patients with epilepsy live a normal life, but the discussion also is consistent with the need to accept that some persons with epilepsy have increased risks of morbidity and death (Berg et al., 2004; Hitiris et al., 2007). Discussing SUDEP may provoke undue distress and impair quality of life for some patients and for certain clinical situations, but the discussion may be reassuring for others. Patients with absence epilepsy or benign epilepsy syndromes may be relieved to know that their risk of SUDEP is negligible, but some patients with new-onset convulsive seizures may be dismayed to learn about SUDEP in addition to the potential psychosocial consequences of an epilepsy diagnosis.

The ethical principle of patient autonomy in health care entails the patient's right to know about his or her own medical condition and prognosis. However, the patient's right to not know about certain aspects of a medical condition also should be respected (Black, 2005). In some situations, the physician may have to exercise therapeutic privilege, which is defined as a ''unique situation, within medical care, in which it is deemed to be in the patient's best interests for the doctor to withhold information'' (Beran et al., 2004). In the light of the preceding assessment, the task force has developed recommendations for discussing SUDEP with patients and their families and caregivers.

Should SUDEP be discussed?

The potentially increased risk of death associated with epilepsy should be disclosed in the context of a comprehensive education program provided to all patients and their families and caregivers. No seizure type or epilepsy syndrome precludes the need to discuss or provide information about SUDEP at some point during the patient's care. The risk of SUDEP may need to be emphasized to encourage compliance with medical therapy or consideration of epilepsy surgery. Furthermore, SUDEP discussion can be reassuring to patients whose epilepsies are associated with very low SUDEP risk.

When should SUDEP be discussed?

SUDEP should not be discussed until the diagnosis of epilepsy is made. Information should be provided promptly to patients and their families and caregivers if they ask about the potential adverse consequences of the seizures or about the mortality risk associated with epilepsy. Those who do not ask about SUDEP should still be given the information in the context of a comprehensive epilepsy education. In this situation, the timing of a SUDEP discussion and the relative emphasis placed on SUDEP are determined by the presence of risk factors and the physician's awareness of the patient's preparedness to receive the information.

Discussing SUDEP risk becomes a priority for patients who are noncompliant with their medications and for those who are excellent candidates for epilepsy surgery. However, the urgency of discussing SUDEP is diminished for patients who are seizure free or for patients whose epilepsy is not associated with an increased risk of death.

What should be discussed?

The task force stresses the key concept of individualizing SUDEP information according to each patient's SUDEP risk and to the background of the patients and their families and caregivers in terms of culture, education, emotional state, and support systems. Discussion should focus on the individual's SUDEP risk when information is specifically requested or when the information could improve medication compliance or guide decisions for epilepsy surgery. In addition, SUDEP discussion can be augmented in most patients and their families and caregivers by describing ongoing research efforts in SUDEP.

How should SUDEP be discussed?

SUDEP should not be discussed until the diagnosis of epilepsy is made. In most instances, SUDEP should not be discussed in isolation from other topics regarding epilepsy care and prognosis. The task force recognizes that SUDEP information can be provided in many ways and that the most effective methods will vary depending on the patients and clinical situations. The most suitable method of providing SUDEP information can be determined by making the following assessments for each patient: (1) Readiness to learn—education and counseling will have little effect on those who are preoccupied or overwhelmed by a new diagnosis of a seizure disorder; (2) Preferred learning style—some may prefer one learning format over another, but SUDEP information may be best conveyed through a combination of face-to-face discussion, written materials, and video presentations; (3) Expectations as a learner—the appropriate information content should be determined by what patients and their families and caregivers desire to know and what the physician judges to be appropriate and sufficient for the clinical situation; and (4) Suitable venue for education and counseling—most SUDEP discussions are expected to occur during regular office visits. However, a knowledgeable health care professional can provide individual or group education and counseling.

Although the task force recommends discussing SUDEP with patients and their families and caregivers, no information currently is available that indicates how SUDEP information can best be conveyed. In view of this, the task force recommends conducting research to determine what patients and their families and caregivers want to know about SUDEP, how SUDEP information is best delivered, and the outcome or consequence of SUDEP discussions. We also recommend development of a checklist of topics for discussion and counseling throughout the patient's epilepsy care and development of informational content for Web sites and print publications. Web sites for the American Epilepsy Society, the Epilepsy Foundation, and other organizations can host up-to-date SUDEP educational materials.

Charge 2: Design Methods by Which the Medical and Lay Communities Become Aware of SUDEP

The task force recognizes that awareness of SUDEP must be raised in the medical and lay communities, and that information regarding SUDEP must be readily available. Raising SUDEP awareness requires a concerted effort that should include a multimedia campaign targeting newspapers; broadcasts for television, radio, and handheld devices; and the Internet. This effort must provide comprehensive and balanced information that is easily accessible. Established epilepsy organizations and institutions (e.g., Epilepsy Foundation, American Epilepsy Society, Citizens United for Research in Epilepsy, National Institutes of Health, and http://www.epilepsy.com) are ideal hosts for SUDEP information. To broaden opportunities for educating medical and lay communities, SUDEP information also should be available from professional organizations with wide interests and backgrounds (e.g., American Medical Association, American Academy of Neurology, Child Neurology Society, American Academy of Nurse Practitioners, American Academy of Family Physicians, American Association of Neuroscience Nurses, and American Academy of Pediatrics). In addition, consideration should be given to making the information available at Web sites that promote general health and wellness.

The task force recognizes specific challenges in educating medical and lay communities about SUDEP. The devastating nature of SUDEP may overwhelm patients and their families and caregivers. Lay persons and medical professionals also need to understand that the causes of SUDEP are still unknown and that SUDEP risk varies among persons with epilepsy. Moreover, the lack of definitive preventive measures against SUDEP may be upsetting to some individuals. Therefore, the task force formulated the following specific recommendations to educate lay and medical communities about SUDEP: (1) consider performing a survey to determine the method preferred by lay persons for learning about SUDEP; (2) develop SUDEP information that is comprehensive and balanced; (3) incorporate SUDEP education into programs of patient education and counseling (e.g., programs at the Epilepsy Foundation and their chapters); (4) develop SUDEP information materials for lay and medical audiences; (5) include appropriate SUDEP information in the curricula of health science schools (e.g., medical, nursing, and allied heath schools); (6) regularly conduct symposia and establish special interest groups for SUDEP at national and international meetings of epilepsy organizations; and (7) convene national or international meetings that focus on SUDEP.

Charge 3: Recommend Research Directions in SUDEP

There is a tremendous need for basic and clinical research in SUDEP. Although confirming the SUDEP incidence rate in the general population is important, research priorities should be given to identification of causative mechanisms and prevention. For this purpose, animal studies are of vital importance. Our review of the literature showed encouraging evidence of animal models of SUDEP, but no long-term animal studies have

been performed that investigate specific mechanisms of SUDEP.

The task force concluded that single-center studies would not identify a sufficient number of cases to yield new SUDEP knowledge. Prospective, multicenter studies are required to conduct investigations that have reasonable probability of yielding meaningful information regarding the causation and prevention of SUDEP. Multicenter studies should be able to enroll a sufficient number of patients with high risk of SUDEP (i.e., patients with medically refractory epilepsy and convulsive seizures) in a reasonable period. After reviewing the SUDEP literature, the task force identified the following several areas for possible investigations of SUDEP in humans or in animal models: (1) age-group–specific incidence rates and the change in risk levels over time; (2) risk factors among high-risk patients with medically refractory epilepsy; (3) role of genetics; (4) role of structural and functional cardiac abnormalities; (5) role of autonomic dysfunction; (6) morphologic, molecular, and biochemical studies of the heart, lungs, and brain of affected patients; (7) role of respiratory mechanisms; (8) role of sleep mechanisms; (9) role of antiepileptic and nonantiepileptic drug use; (10) role of serotonin and other neurotransmitters; (11) medical and psychologic comorbid conditions; (12) premorbid circumstances of SUDEP (e.g., living situation, sleep position, time of SUDEP event); (13) effect of epilepsy surgery in reducing SUDEP risk; (14) role of nocturnal supervision and device-based seizure and apnea detection in preventing SUDEP; and (15) role of long-term implantable devices for monitoring cardiovascular, respiratory, and neurophysiologic functions.

The task force also developed recommendations for improving SUDEP research. First, future studies should be hypothesis driven. Consideration should be given to studies designed to assess effects of preventive interventions. Second, a workshop featuring clinical and basic scientists in disciplines relevant to sudden death should be organized. By including experts in sudden cardiac death, sudden infant death syndrome, genetic disorders, and autonomic dysfunction, a workshop could yield additional avenues for future investigations and refine current investigations of SUDEP mechanisms. Third, drug trial databases and national or large community-based databases could be new sources of SUDEP cases. Such databases could be assessed for future studies.

A serious shortcoming in SUDEP research is the low autopsy rate of patients with suspected SUDEP and the incompleteness of autopsy information (Coyle et al., 1994; Schraeder et al., 2006). A campaign should be waged to enhance SUDEP awareness, autopsy rates, and autopsy completeness. In addition to informing patients with epilepsy and their families and caregivers, the campaign should also be directed toward medical examiners and coroners.

Charge 4: Explore Steps That Organizations Can Take to Perform Large-Scale, Prospective Studies of SUDEP to Identify Risk Factors

The task force affirmed that large-scale, prospective, national or international studies are necessary for future SUDEP investigations. We considered the traditional study design—a National Institutes of Health–funded multicenter study that prospectively enrolled large cohorts of patients with refractory epilepsy from different geographic regions—but decided that this type of study would be cost-prohibitive and unfeasible for a long-term study, particularly because the SUDEP rate in medically refractory patients is 1 in 150 person-years.

An alternative to the traditional study model would be a consortium of study centers that follow specific arrangements. First, criteria for SUDEP determination and autopsy protocols should be standardized for all centers participating in the consortium. Second, selected tissues should be prepared and transported in a specified manner to investigators who will use them for specific molecular, genetic, or biochemical research studies. Third, funding sources for the consortium could include nongovernmental organizations, government agencies, and the medical industry. A master grant would be needed to support core activities of the consortium, but we anticipate that individual investigators will also need independent funding to pursue investigations of specific SUDEP mechanisms.

Charge 5: Identify Possible Preventive Strategies for SUDEP

Because the pathologic mechanisms underlying SUDEP currently are unknown, preventive measures against SUDEP are directed only at its risk factors. Numerous SUDEP risk factors have been reported in the literature, but only a few are identified consistently in case–control studies (Tellez-Zenteno et al., 2005; Tomson et al., 2005; So, 2006; Nashef et al., 2007). Factors such as patient age, early onset of epilepsy, and intelligence quotient are not modifiable, but others may be attenuated to potentially lower SUDEP risk. These factors include uncontrolled seizures (especially generalized tonic–clonic seizures), long epilepsy duration, subtherapeutic antiepileptic drug (AED) levels, and number of AEDs used.

To reduce SUDEP risk, the task force recommends adherence to several established principles in the treatment of epilepsy. First, seizure control should be optimized as promptly as possible. Physicians should re-evaluate the epilepsy diagnosis and treatment as soon as two AEDs fail

to control seizures or when generalized tonic–clonic seizures occur frequently despite initial AED treatment. The reevaluation should be directed toward epilepsy surgery treatment if appropriate. Persons with surgically remediable epilepsy should be identified promptly, and they and their families and caregivers should carefully consider the option of surgery for controlling seizures. Second, patients should comply with medication intake. Poor compliance is a common but reversible cause of uncontrolled seizures and breakthrough seizures. Third, patients should use the smallest number of AEDs to control seizures.

Although nighttime supervision and special precautions have been reported to be associated with reduced SUDEP risk (Nashef et al., 1995; Langan et al., 2000), evidence for the effectiveness and feasibility of these measures currently is insufficient for the task force to recommend them. Devices for monitoring heart rate, oxygen saturation, and body movements are available, but the reliability of these devices in detecting seizures or in identifying high-risk persons is unproven. Further studies are needed to determine whether these measures have a role in the prevention of SUDEP events.

Summary

The task force recommendations are summarized in the following list: (1) Convene a multidisciplinary workshop to refine current lines of investigation and to identify additional areas of research for mechanisms underlying SUDEP; (2) Perform a survey of patients and their families and caregivers to identify effective means of education that will enhance participation in SUDEP research (including autopsy examination); (3) Conduct a campaign aimed at patients, families, caregivers, coroners, and medical examiners that emphasizes the need for complete autopsy examinations for patients with suspected SUDEP; (4) Secure infrastructure grants to fund a consortium of centers that will conduct prospective clinical and basic research studies to identify preventable risk factors and mechanisms underlying SUDEP; (5) Develop uniform criteria for centers in the study consortium that detail SUDEP determination and protocols for complete autopsy examination; (6) Establish how core functions will be provided to centers in the study consortium; functions include coordination of consortium activities, supervision of database or enrollment registry, monitoring protocol compliance, and tissue repository and distribution; and (7) Facilitate research activities of individual researchers who pursue hypothesis-driven clinical and basic science investigations of SUDEP risk factors and mechanisms.

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We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

References

Beran RG, Weber S, Sungaran R, Venn N, Hung A. (2004) Review of the legal obligations of the doctor to discuss sudden unexplained death in epilepsy (SUDEP): a cohort controlled comparative cross-matched study in an outpatient epilepsy clinic. *Seizure* 13:523–528.

Berg AT, Shinnar S, Testa FM, Levy SR, Smith SN, Beckerman B. (2004) Mortality in childhood-onset epilepsy. *Arch Pediatr Adolesc Med* 158:1147–1152.

Black A. (2005) SUDEP: whether to tell and when? *Med Law* 24:41–49.

Coyle HP, Baker-Brian N, Brown SW. (1994) Coroners' autopsy reporting of sudden unexplained death in epilepsy (SUDEP) in the UK. *Seizure* 3:247–254.

Hitiris N, Mohanraj R, Norrie J, Brodie MJ. (2007) Mortality in epilepsy. *Epilepsy Behav* 10:363–376.

Langan YM, Nashef L, Sander JWA. (2000) Sleeping alone increases the risk of sudden unexpected death in epilepsy (SUDEP) [abstract]. *Epilepsia* 41(Suppl. 7):90–91.

Morton B, Richardson A, Duncan S. (2006) Sudden unexpected death in epilepsy (SUDEP): don't ask, don't tell? *J Neurol Neurosurg Psychiatr* 77:199–202.

Nashef L, Fish DR, Garner S, Sander JW, Shorvon SD. (1995) Sudden death in epilepsy: a study of incidence in a young cohort with epilepsy and learning difficulty. *Epilepsia* 36:1187–1194.

Nashef L, Hindocha N, Makoff A. (2007) Risk factors in sudden death in epilepsy (SUDEP): the quest for mechanisms. *Epilepsia* 48:859–871.

National Institute for Health and Clinical Excellence. (2007) *Epilepsy: the epilepsies: the diagnosis and management of the epilepsies in adults and children in primary and secondary care [CG20] [Internet].* National Institute for Health and Clinical Excellence. Available from: http://www.nice.org.uk/guidance/CG20 (cited February 1, 2007).

Schraeder PL, Delin K, McClelland RL, So EL. (2006) Coroner and medical examiner documentation of sudden unexplained deaths in epilepsy. *Epilepsy Res* 68:137–143.

So EL. (2006) Demystifying sudden unexplained death in epilepsy: are we close? *Epilepsia* 47(Suppl. 1):87–92.

Tellez-Zenteno JF, Ronquillo LH, Wiebe S. (2005) Sudden unexpected death in epilepsy: evidence-based analysis of incidence and risk factors. *Epilepsy Res* 65:101–115.

Tomson T, Walczak T, Sillanpaa M, Sander JW. (2005) Sudden unexpected death in epilepsy: a review of incidence and risk factors. *Epilepsia* 46(Suppl. 11):54–61.

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