The first formal description of sudden cardiac death (SCD) was made as early as 4th century BC by the father of medicine, Hippocrates of Kos, which stated in his aphorisms that those who are subject to frequent and severe fainting attacks without obvious cause die suddenly. Presently, in most textbooks SCD is defined as an unexpected death occurring within one hour from onset of symptoms in an individual with stable clinical conditions before the onset of the life-threatening arrhythmic event. The magnitude of the problem is reflected on the fact that more than 7 million lives per year are lost to SCD worldwide. In Europe, approximately 350,000 individuals die each year due to SCD with unsuccessful out-of-hospital cardiopulmonary resuscitation. The incidence of SCD in the United States ranges between 180,000 and 450,000 cases annually, depending on the definition used. In a more specific way, prospective studies using multiple sources developed in the United States, Netherlands, Ireland, and China have shown that SCD rates ranging from 50 to 100 per 100,000 in the general population. The global burden of SCD remains high despite the fact that several factors have already been described which increase the risk of SCD in the general population. It should not be ignored that epilepsy and seizures can have a profound effect on cardiovascular function and in some cases may be fatal. A number of questions should be raise to elucidate clearly the exact relationship between SCD and epilepsy.

WHERE? Epilepsy is one of the most common neurological conditions affecting at least 65 million people worldwide. Individuals of all ages can be affected by it. It is treatable but often requires lifelong medication and sometimes surgery to control seizures. Despite this, seizures in up to 40% of people with epilepsy do not respond properly to antiepileptic drugs or other treatments. In these individuals with refractory epilepsy, high rates of premature death compared with the general population have recorded. Sudden unexpected death in epilepsy (SUDEP) is a major cause of death in those people. WHAT? The lack of autopsy results and

1Universidade Federal de São Paulo, Escola Paulista de Medicina, Disciplina de Neurociência, Departamento de Neurologia/Neurocirurgia, São Paulo SP, Brasil; 2Pontifícia Universidade Católica do Rio Grande do Sul, Hospital São Lucas e Instituto do Cérebro do Rio Grande do Sul, Serviço de Neurologia, Porto Alegre RS, Brasil. 
Correspondence: Fulvio A. Scorza; Rua Pedro de Toledo, 669 / 10 andar; 04039-032 São Paulo SP, Brasil; E-mail: scorza.nexp@epm.br
Conflict of interest: There is no conflict of interest to declare.
Support: This study has been supported by the following grants: FAPESP (Fundação de Amparo à Pesquisa do Estado de São Paulo); CNPq (Conselho Nacional de Desenvolvimento Científico e Tecnológico); Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES); CEPID/FAPESP; FAPESP/PRONEX and FAPESP/CNPq/MCT (Instituto Nacional de Neurociência Translacional). 
Received 08 May 2016; Accepted 16 May 2016.
the rarely witnessed or monitored cases of SUDEP pose difficulties with regard to its pathophysiology and definitions. SUDEP is generally defined as sudden, unexpected, witnessed or unwitnessed, nontraumatic and nondrowning death in patients with epilepsy, with or without evidence of a seizure and excluding documented status epilepticus, in which postmortem examination does not reveal a toxicologic or anatomical cause of death. **WHEN?** The incidence of SUDEP is largely underestimated due to differences in patient populations, study design, incomplete level of documentation and the criteria for diagnosing SUDEP. Over the years, further refinements to knowledge of SUDEP incidence have been made. Briefly, it has been reported that SUDEP is responsible for up to 17% of all deaths in epilepsy with an incidence rate among adults between 1:500 and 1:1,000 patient-years. Considering the guidelines, we agree with suggestions that patients with epilepsy, especially those at highest risk of SUDEP, should follow the comprehensive cardiovascular screening protocols (ECG, Holter-monitoring, echocardiography, genetic analysis, ergometric exercise test and myocardial scintigraphy, and, if abnormalities were found, coronary angiography). Despite this SUDEP mechanisms are still a mystery, and the recent discoveries of genes and molecular systems involved in epilepsy and cardiovascular system are a cause for optimism that this issue could be solved quicker than anticipated.

Knowledge makes us wiser. In this sense, clinical and animal research is critical to understand accurately the close association between SUDEP and seizures, and obviously, this is the primary goal of decreasing epilepsy-related deaths which figure high each year in mortality statistics.

**Acknowledgements**

The authors acknowledge the many valuable suggestions made by Dr Ley Sander, Professor of Neurology and Clinical Epilepsy, UCL Institute of Neurology, Honorary Consultant Neurologist at the National Hospital for Neurology and Neurosurgery, Queen Square, London, UK and Director for Scientific Research at SEIN – Stichting Epilepsie Instellingen Nederland in Heemstede, Netherlands.

