Plenary 2
Mortality in Children
June 24, 2016
10:30 a.m. - noon

Moderator: Elizabeth Donner, MD, FRCP(C), The Hospital for Sick Children

- Parent Speaker: Shannon Bursick, MS and Joe Bursick
- The Facts about Mortality in Pediatric Epilepsy – Anne Berg, PhD, Feinberg School of Medicine
- SUDEP in Children: Compare and Contrast with Adult Literature - Sanjeev Kothare, MD, NYU Langone Medical Center
- Lessons Learned in Sudden Unexpected Death in Childhood (SUDC) Research and Advocacy – Laura Crandall, The SUDC Foundation

Panel Discussion: Why is SUDEP reported to be less common in children?
Learning Objectives

Following participation in this activity, learners should be able to:

- Describe and explain the burden and causes of mortality
- In the first 2 decades of life in the general population
- In children and young people with epilepsy
- In the different types of pediatric epilepsies

Standardized mortality ratios (SMR) for people with epilepsy

Mortality

Force of mortality and reasons for death vary

- By Country
- By subgroups
- Gender
- Socio-economic status
- AGE

Population death rates by age US - 2013

[Graph showing death rates by age with a link to the CDC report]
Cumulative mortality from birth

When deaths occur in young people, what are the most common reasons?

Epilepsy associated mortality

Mortality in young people with epilepsy compared to the population

Epilepsy associated mortality

Short-cut definition

- **“Complicated Presentation”** ~25%
  - Associated with recognized brain disorder
  - Early life insults
  - Infections
  - Trauma
  - Autoimmune
  - Genetic (including structural) causes
  - Neurodisability

- **“Uncomplicated Presentation”** ~75%
  - No recognized associated brain disorder
  - Neurologically, no impairment
  - “Neurotypical”

Epilepsy associated mortality

- Relative force of mortality $\leftrightarrow$ depends on overall force of mortality
- Epidemiology of epilepsy $\leftrightarrow$ epidemiology of neurological morbidity

- Force of mortality of epilepsy $\leftrightarrow$ force of mortality of causes of epilepsy and their consequences

“Complicated” vs “Uncomplicated epilepsy presentations compared to general population

Mortality rates in 4 pediatric epilepsy cohorts and overall US population, 2013

Impact on mortality of Developmental Disability Without Epilepsy

Impact on mortality of developmental disability with and without epilepsy

Impact of epilepsy on mortality in people with developmental or comparable acquired disability
Mortality in young people with epilepsy in the absence of neurodisability?

Distribution of types of pediatric epilepsies

Number and causes of death by type of epilepsy

Impact on Clinical Care and Practice
Learning Objectives

Following participation in this activity, learners should be able to:

• Be knowledgeable on cardiorespiratory abnormalities observed during seizures in children.
• Be aware of the differences in these abnormalities in adults as compared to children.
• Be aware of differing epidemiology and possible mechanisms to explain SUDEP in children as compared to SUDEP in adults.

Some Basic Facts Concerning SUDEP

• The epilepsy usually begins before age 16 years.
• There must be a high seizure burden.
• Long standing chronic refractory epilepsy (usually 20 years duration).
• Type of epilepsy: tonic, secondary generalized, prolonged, in prone position in sleep.
• Must continue to have refractory seizures at the time of occurrence of SUDEP.
Summary

- 101 seizures in 26 children were recorded (average age 3.9 years).
- Ictal central apnea was more prevalent in patients with younger age, temporal lobe, left-sided, symptomatic generalized, longer duration seizures, with desaturation, ictal bradycardia, and more antiepileptic drugs.
- Ictal bradycardia was more prevalent in left sided, symptomatic generalized seizures, with desaturation, ictal bradycardia, and more antiepileptic drugs.
- Ictal tachypnea was more prevalent in left sided, symptomatic generalized seizures, and with brain MRI lesions.
- Ictal bradypnea was more prevalent in older age, female gender, right-sided seizures, fewer AEDs, and less prevalent in symptomatic generalized seizures.
- Desaturations were more prevalent in longer-duration seizures, with ictal apnea, ictal bradycardia, and with more AEDs.

Multiple Mechanism to Explain SIDS

Prematurity, VLBW
Vulnerable infant

SIDS
1.4 months, prone

Multiple stressors
Co-sleeping, passive smoke, overheating

Triple risk model for SIDS.

Similar Models to Explain SUDEP

Seizure Burden
Vulnerable Age, State, Environment.
Genetic Predisposition
Autonomic changes following generalized tonic clonic seizures: An analysis of adult and pediatric patients with epilepsy
Barri A. Sarkis, Signide Thome-Souza, Ming-Zhe Poh, Nichelle Lewellyn, Jarquelyn Kiem, Joseph R. Madson, Rosaline Picard, Page B. Precelli, Barbara A. Swartzl, Tobias Loddenkemper, Class Reinberger

Objective: Sudden unexpected death in epilepsy (SUDEP) is the most common cause of mortality directly related to epilepsy in adults and in younger children, but there is little data available on pediatric SUDEP. The current study, we aimed to analyze post-seizure autonomic changes following ECS in adult and pediatric epilepsy.

Methods: Patients admitted to the epilepsy monitoring unit were prospectively recruited, and were an electroencephalogram (EEG) while continuously monitored sympathetic activity while using non-invasive mic-EDG and BiCG electrodes. Pre-ictal EDG parameters were assessed at a session of 60 s pre-ictal intervals. Post-ictal EDG parameters were assessed at 1, 5, 10, 30, and 60 min post-ictal intervals. The analysis included the following: (1) Heart rate variability (HRV): The duration of the post-ictal generalized EEG suppression (GSES) was also measured. (2) The occurrence of PGLS (primary generalized epilepsy with absence seizures) was also measured. (3) The occurrence of PGLS (primary generalized epilepsy with absence seizures) was also measured. (4) The occurrence of PGLS (primary generalized epilepsy with absence seizures) was also measured.

Results: Age and sex are a significant determinant of the sympathetic and parasympathetic response following a ECS, which the younger patients suppressed autonomic response whereas older patients did not. Older patients exhibited a higher degree of autonomic dysregulation. The occurrence of PGLS (primary generalized epilepsy with absence seizures) was also measured. In adult patients, the occurrence of PGLS (primary generalized epilepsy with absence seizures) was also measured. In pediatric patients, the occurrence of PGLS (primary generalized epilepsy with absence seizures) was also measured. In pediatric patients, the occurrence of PGLS (primary generalized epilepsy with absence seizures) was also measured. In pediatric patients, the occurrence of PGLS (primary generalized epilepsy with absence seizures) was also measured. In pediatric patients, the occurrence of PGLS (primary generalized epilepsy with absence seizures) was also measured. In pediatric patients, the occurrence of PGLS (primary generalized epilepsy with absence seizures) was also measured.

Conclusions: The occurrence of PGLS (primary generalized epilepsy with absence seizures) was also measured. The occurrence of PGLS (primary generalized epilepsy with absence seizures) was also measured. The occurrence of PGLS (primary generalized epilepsy with absence seizures) was also measured. The occurrence of PGLS (primary generalized epilepsy with absence seizures) was also measured. The occurrence of PGLS (primary generalized epilepsy with absence seizures) was also measured. The occurrence of PGLS (primary generalized epilepsy with absence seizures) was also measured. The occurrence of PGLS (primary generalized epilepsy with absence seizures) was also measured. The occurrence of PGLS (primary generalized epilepsy with absence seizures) was also measured. The occurrence of PGLS (primary generalized epilepsy with absence seizures) was also measured. The occurrence of PGLS (primary generalized epilepsy with absence seizures) was also measured. The occurrence of PGLS (primary generalized epilepsy with absence seizures) was also measured. The occurrence of PGLS (primary generalized epilepsy with absence seizures) was also measured. The occurrence of PGLS (primary generalized epilepsy with absence seizures) was also measured. The occurrence of PGLS (primary generalized epilepsy with absence seizures) was also measured. The occurrence of PGLS (primary generalized epilepsy with absence seizures) was also measured.

Impact on Clinical Care and Practice

- Very little data available on pediatric SUDEP.
- Multi-centric longitudinal studies are needed.
- More data needs to be available from SUDC sites.
Lessons Learned From Sudden Unexplained Death In Childhood: Research and Advocacy

Laura Crandall, MA
NYU Langone Medical Center

JUNE 2016

Learning Objectives

- History of SUDC and Febrile Seizures
- Advocacy Efforts in SUDC
- Research
- Networking with Medical Examiners & Coroners
- Promoting Death Investigation and Autopsy Standards
- Legislative Advocacy
- U.S. Federal Efforts
- Working with your Medicolegal Death Investigation System

SUDC is currently defined as...

“...the sudden death of a child older than one year of age which remains unexplained after a thorough case investigation, including review of the clinical history and circumstances of death, and performance of a complete autopsy with appropriate ancillary testing.” Krous et al., Ped Dev Path 2005

Background

- No definition until 2005
- Incidence of SUDC among children 1-18 years of age
- 344 deaths/year
- 20% (~60%) SUDC deaths among children ages 1-4 yrs
- Limited awareness and research greatly impact our understanding
- Lack of ICD code impairs ability to track
- In contrast to Sudden Infant Death Syndrome (SIDS), where genetic discoveries and extensive risk reduction public awareness programs have decreased rates by 50% over the past two decades, very little progress has been made towards understanding the pathogenesis of SUDC and rates of SUDC have doubled during this period.

R99= Undetermined
SUDC Funding & Research

- **FUNDING** Deaths
  - SIDS 156,000; >500 Million last 20 years
  - SUDEP >27,000/yr - <75 million last 20 years
  - SUDC ~380/yr - <10 million last 20 years
  - Bike accidents (1-19 yrs): 97/year
  - Fires and burns (1-14 yrs): 281/year
  - Motor vehicle accidents (1-14) - 1,083/yr
  - **RESEARCH** (PubMed)
  - SIDS 10,000
  - SUDC 1,000
  - Electrocution accidents children 616
  - Sudden vehicle accidents children 8,372

Sudden Unexplained Death in Childhood (SUDC)

- Sudden death of a child >12 mos; unexplained after thorough autopsy & case investigation.
  - **Categories of deaths that elude us**
  - SUDC: Case Referrals to SUDC Foundation (2011-14)
  - Predominantly male, ages 1-3 yr
  - Seizures up to 60% of cases
  - Possible SUDC as mechanism
  - Infants born at term as singletons
  - Most found prone, often face down
  - Minor pathologic findings common, but does not explain death

Diagnoses of Exclusion

- **SUID**: SIDS
- **SIDS**: SUDEP
- **SUDEP**: SUDC

Factors to SUDC Research

- Lack of awareness
- MDI and law enforcement investigations
- Lack autopsy standards
  - Retention of brain not common
  - Retention of viable specimen for genetics not universal
- Variations in MDI policies re: retention and release
- Variability/lack of criteria for COD
- Difficulty in admitting “I don’t know” - Real incidence of SUDC is unknown
- Limited resources of MDI offices
- Families living with great uncertainty and inconsistent treatment!

SUDCRRC

- Review the child's death, medical and family history
  - by FP panel for cause of death
- Neuroimaging/neuropathology consultations
- Genetic analysis (whole exome sequencing) on SUDC child, biological parents and symptomatic relatives
- Study the risks that lead to SUDC
- Provide families with study report
- Identify at-risk individuals to establish prevention strategies

http://sudc.org/Research/SUDCRRC
first bullet- change to equal or greater than 12 months. (SIDS is less than 12 months, so SUDC covers deaths on the first birthday.

Laura Crandall, 12/13/2015
The Unexpected, Unexplained and Often Undetermined

Federal Efforts
2009 NAS Report: Strengthening Forensic Science in the United States: A Path Forward
- National Commission on Forensic Science (by DOJ)
- Organization of Scientific Area Committees (by NIST and DOJ)
- Sudden Unexpected Death Data Enhancement And Awareness Act (passed into law 12.18.14)
- Sudden Death in the Young Registry (NIH and CDC)
- SUID Case Registry (CDC)

Research Efforts
- What are the policies of ME/C offices around Child Death investigations?
- What are the experiences of families?
  - A commentary on lack of protocols affecting mourning rituals. Are practical barriers to science?

International Efforts
- Work with Medical Examiners- Coroners
  - National Association of Medical Examiners (NAME)
  - Member
  - Annual Exhibitor
  - Genetic Specimen Standard
  - International Association of Coroners & Medical Examiners
    - Involvement on SAB
    - Offering Resources from the SUDC Foundation
    - Help For Families Brochure

NAME Interim Scientific Program
February 23, 2016

250 Attendees
29 Countries

UUUgh!
The Unexpected, Unexplained and Often Undetermined

Working “WITH” Your Medicolegal Death Investigation System

What are your goals?
What are the barriers?
Why do the barriers exist?
- What is the history behind them?
- Get to Know your Medical Examiner/Coroner- BEFORE you need them!
Recognize...

- You are all the same page
- Scope of Work
- Statutory Authority
- Department they reside
- Limited resources-personnel, time, $
- Their mandate
- Varying systems with varying viewpoints on role in public health

Impact on Clinical Care and Practice

- Communication with Medical Examiners
- Make Connections Now
- How can you help them? What can you offer them?
- How can you work together?
- Partnering with Advocacy Groups
- Strategic Plans: Health Policy, Legislative and/or ME/C Offices
- Coordination of Family and Medical Professional Efforts