PERC meeting AES 12/1/12

See additional file for meeting participants

1. Update on funding
	1. AES infrastructure grant
		1. Continuation approved for next year, only a 2 year grant
	2. Current budget - $25-35K/yr
		1. Funds IS registry, meetings – study funding is separate
		2. For larger new onset database which is currently at 13 centers, estimated $400,000/yr for database, data coordinators, RA
	3. Other potential funding sources – goal is self-sustaining support which can accommodate growth as other centers join
		1. Clinical trials planning grant – speak to Brandi or Vicky from NINDS – requires an end point
		2. Work some group funding into a study grant
		3. Philanthropy groups
		4. PERF – Anne is writing grant (this is for new onset epilepsy database)
	4. We will avoid pharmaceutical funding
	5. Examples: NICU consortium – individual hospitals pay for database and research coordinators, have developed automated info gathering from EMR and billing
2. Ongoing studies
	1. Infantile spasms registry
		1. 14 centers are IRB approved, 27 children enrolled to date
		2. Based on counting exercise, has potential for 250 children/yr (could counting during the winter months have made a difference in numbers?)
	2. Full database
		1. Only up and running in Chicago – grant in process
3. New studies proposed
	1. Prehyps study - John Millichap and Doug Nordli
		1. See description from John below
		2. Pilot study – 12 pt enrolled (those with abnl EEG in neonatal period and PVL/HIE), 50% had abnormal EEG at 3 months and several of those went on to develop spasms
		3. Prehyps = 150uV slow waves and multifocal spikes
		4. Discussion as to whether 3 month EEG is standard of care – In Chicago, if abnormal neonatal EEG, NICU follow up clinic will order EEG at 3 months
			1. 3 months is “sweet point” to determine prehyps in prior studies
			2. Could consider survey to neurologists and neonatologists to determine if 3 month EEG would be standard of care
		5. 2nd milestone – determine if 2 weeks low dose ACTH improves EEG – no randomization, using historical controls
			1. Could blind EEG reading and track those who decline treatment as controls
		6. Awaiting CURE decision on funding (likely January) – Proposal to repeat this with multicenter study
	2. KCNQ2 encephalopathy (Dr. Cooper)
		1. In April – 8/80 pt with sz in first week of life and encephalopathy have de novo KCNQ2 mutations
			1. One pt – father had BFNS (mosaic) and child had more severe form
		2. Letter in Annals – ¼ Ohtahara pts had de novo KCNQ2 mutations
		3. Informal network of several centers – 17 more pt identified
		4. AES infrastructure grant submitted – awaiting decision
		5. First goal – collect data, second – create resource for rapid sequencing (GeneDx takes 3 months), third – evaluate treatable mutations ie. with ezogabine
		6. Please refer any KCNQ2 mut pts to Dr. Cooper – ecc1@bccm.edu
	3. Pediatric SUDEP registry – Dr. Donner
		1. Objectives – incidence, modifiable risk factors, inc awareness among pediatricians
		2. Age cutoff 19
		3. Funding from CURE and Ontario Brain Institute
		4. Currently enrolling pts through CPEN (Canadian equivalent of PERC)
		5. Funding available to add US centers should IRB approval be obtained – provider data collection
			1. North American SUDEP registry uses family provided info – not as reliable
			2. Unclear international HIPAA regulations – has been achieved in other studies: IPSS (International Pediatric Stroke Survey)
		6. Goal for case-control study – not ready for prime time
		7. NIH – institute without walls planning grant – could allow for collaboration between groups looking at different aspects of SUDEP
		8. CDC is expanding “SIDS” program to sudden deaths up to age 24
		9. Contact info: sudep.registry@sickkids.ca, 416-813-7654 (ext 3654)
	4. SUDEP Tissue Bank – Alicia Goldman
		1. STOP SUDEP program funded through her RO1
		2. NINDS sponsored tissue collection and registry until age 40 – goal to find molecular risk factors for SUDEP
		3. Partnerships with parent org, epilepsy foundation, SUDEP aware to identify pt – then they will contact the medical examiner immediately and the family at a later date for blood samples
		4. Even if no autopsy – can often get a blood sample (Guthrie card)
		5. Goal for repository – develop cell lines
		6. Can contact group via SUDEPaware and epilepsy foundation
4. Websites
	1. PERC – temporary website up and running
		1. Infrastructure grant includes money for professional website
		2. We need a logo
	2. Database – contact Sana Khan with any concerns
5. Additional subgroups
	1. Genetic/metabolic subgroup – May be redundant – epi4K is looking at spasms (Heather Medford), Baylor also has infrastructure for testing. – Jayson Coryell, Rusty Novotny Julianne Paolicchi
	2. EEG subgroup – Zach G, John Myt, John Mil, Sucheta, Lucy, Nicole
	3. Publications subgroup – not necessary yet
6. Meeting dates
	1. Large group – second Monday of even numbered months
	2. Infantile spasms – third Monday of the month

Prehyps Study Summary – courtesy of John Millichap

The best way to modify a disease process is to prevent it in the first place. Neonatal hypoxic ischemic encephalopathy (HIE) is a significant risk factor for West Syndrome (WS). WS is characterized by a special seizure type called infantile spasms, a chaotic EEG pattern known as hypsarhythmia, and developmental regression. Evolution to WS does not happen overnight, but follows a highly predictable trajectory. Certain progressive EEG features are highly predictive of future progression to WS. Adrenocorticotrophin hormone (ACTH) is known as the best treatment for WS. Yet, for 160 years since the first description of WS, not a single randomized study has utilized a preemptive strategy to halt the evolution of this devastating epileptogenic process.

We hypothesize that a specific EEG pattern, pre-hypsarhythmia, appears within the months prior to the development of WS. This reliable biomarker will predict development of WS. The aims of the study are to (1)confirm pre-hypsarhythmia is a reliable biomarker for WS in a large multi-institutional cohort; (2)determine whether ACTH improves the EEG in infants with pre-hypsarhythmia and decreases the likelihood of progression to WS; and (3)determine the neonatal features predictive of pre-hypsarhythmia and WS.

We will use the resources of the Pediatric Epilepsy Research Consortium (PERC) to enroll subjects from multiple pediatric epilepsy centers simultaneously. We will prospectively identify the specific EEG pattern prior to hypsarhythmia in infants with high risk of developing symptomatic WS. Each subject will have serial EEGs from 3 to 12 months old that is rated from normal to hypsarhythmia. The primary end point is presence or absence of WS. We estimate it will take one year to complete this milestone.

After achieving the first milestone that establishes pre-hypsarhythmia as a reliable biomarker for development of WS, we will perform a single treatment arm exploratory study utilizing a two-stage design and the EEG as the surrogate marker for clinical response. Screening of infants with neonatal HIE will occur according to the protocol established in milestone 1. If pre-hypsarhythmia develops, treatment with low-dose ACTH will be given.  Primary outcome measure is improvement of EEG.  The two-stage design exposes treatment to a small number of subjects and provides information on adverse events and short-term clinical response with a short duration and at a low cost. We estimate it will take 1-1.5 years for this milestone.

If the objectives for milestones 1 and 2 are achieved, the neonatal records, including primary review of MRI and EEG, will be analyzed for predictive factors for pre-hypsarhythmia and WS. Successful completion of all 3 milestones will lay the groundwork for more multicenter studies to determine the ideal dose and duration of ACTH. Funding this study provides a unique opportunity for CURE to achieve the goal of “No seizures and no side effects” by actually preventing epilepsy.