



Epilepsy in Pregnancy

SCOTT A SULLIVAN MD

DIRECTOR, MATERNAL-FETAL MEDICINE, INOVA HEALTH

PROFESSOR, UNIV OF VIRGINIA

AUGUST, 2022

Disclosures

- ▶ No conflicts to declare



Objectives

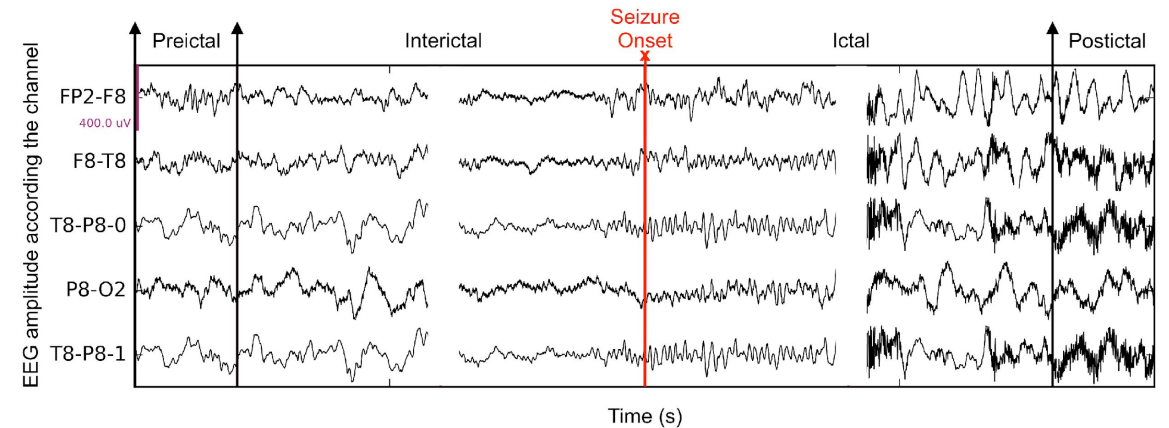
- ▶ Review the numbers
- ▶ Discuss the risks
- ▶ ASD use and risks
- ▶ Best practices / Metrics

Incidence

- ▶ Estimated to be 1/200 pregnancies (0.3-1 %)
1.5 million women of child bearing age
24,000 deliveries/year
- ▶ Most common neurologic complication
- ▶ Modest increase w family history (3x)

Diagnosis

- ▶ 2 unprovoked seizures
- ▶ 1 seizure + EEG/MRI evidence
- ▶ History/ ASD use

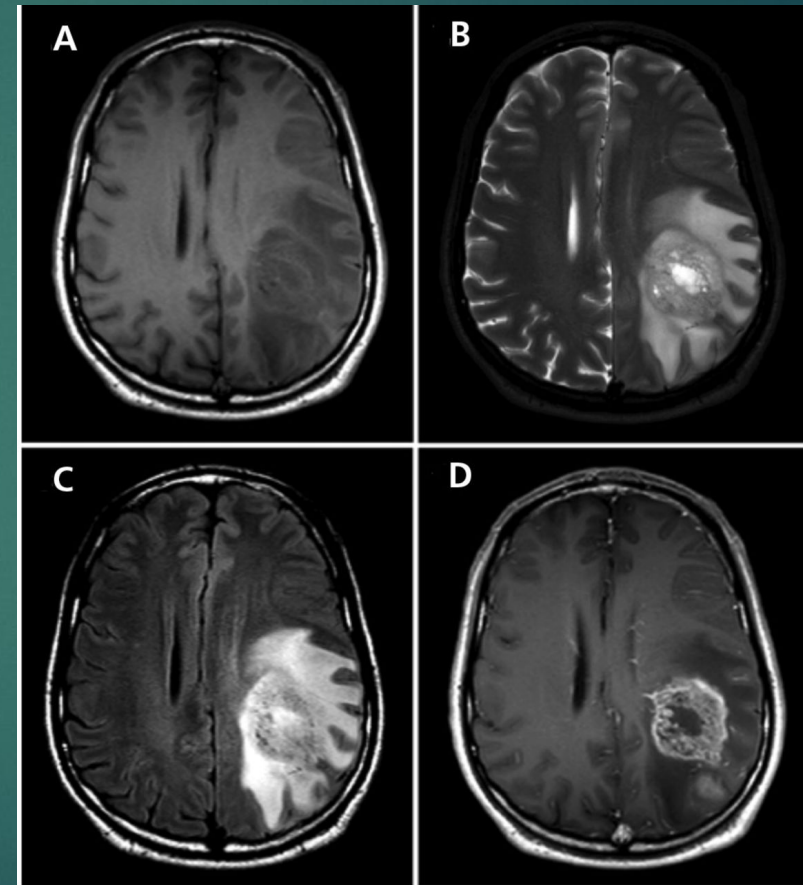


Subtypes

- ▶ Focal
- ▶ Focal with preserved awareness
- ▶ Focal with altered awareness
- ▶ Generalized
- ▶ Bilateral tonic-clonic

Differential Diagnosis

- ▶ Eclampsia
- ▶ Tumors
- ▶ Vascular Malformation
- ▶ Infections
- ▶ Auto-immune
- ▶ Trauma
- ▶ Metabolic
- ▶ Genetic
- ▶ Medications



Overlapping diagnoses

- ▶ Migraines
- ▶ CVA / TIA
- ▶ Arrhythmias
- ▶ Syncope
- ▶ Sleep disorders
- ▶ Movement disorders

- ▶ Psychogenic nonepileptic seizure (pseudo-seizure)

A word on Fertility

- ▶ Increased rates of :
 - PCOS
 - Anovulation
 - Irregular menses
- ▶ Meds? Hypothalamus?
- ▶ Infertility? Data is conflicting

Pre-conception Counseling

- ▶ Ideal for risk reduction
- ▶ Medication review – change, adjust
- ▶ 9-12 months seizure free
- ▶ 0.4 mg Folic acid
- ▶ Only 15-20 % of patients



Genetic Counseling

- ▶ Risk of inheritance :
 - generalized 8.3 % [1.4 – 15.4]
 - focal 4.4 % [1.4 – 7.4]
- ▶ Autosomal dominant pattern (ADFLE), SCN1A gene
- ▶ Many syndromes have seizure activity as a risk
- ▶ Family history, option for prenatal diagnosis

Pregnancy Risks

- ▶ Preterm Birth
- ▶ Pre-eclampsia
- ▶ Fetal growth restriction (FGR)
- ▶ Cesarean delivery
- ▶ Post-partum hemorrhage

SUDEP

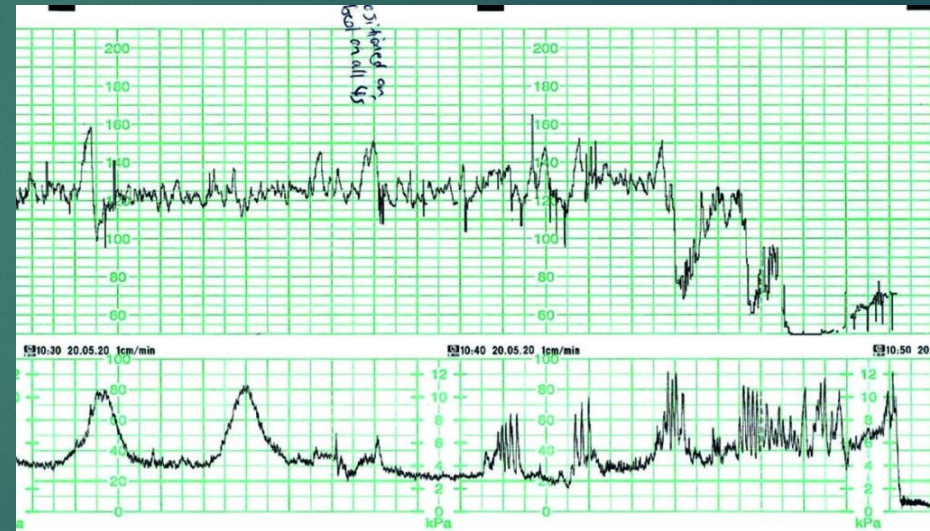
“Sudden Unexpected
Death in Epilepsy”

Risk of Maternal Death 10x
higher w Epilepsy Dx

80 % are SUDEP

Fetal response

- ▶ Hypoxia/acidosis
- ▶ Decelerations
- ▶ Iatrogenic prematurity
- ▶ Trauma



Fetal Demise

- ▶ IUFD

OR 1.27 [1.17-1.38]

- ▶ SAB

OR 1.13 [1.04-1.24]

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Changes in Seizure Frequency and Antiepileptic Therapy during Pregnancy

Page B. Pennell, M.D., Jacqueline A. French, M.D., Ryan C. May, Ph.D.,
Elizabeth Gerard, M.D., Laura Kalayjian, M.D., Patricia Penovich, M.D.,
Evan Gedzelman, M.D., Jennifer Cavitt, M.D., Sean Hwang, M.D.,
Alison M. Pack, M.D., Maria Sam, M.D., John W. Miller, M.D., Ph.D.,
Steffanie H. Wilson, Ph.D., Carrie Brown, M.S., Angela K. Birnbaum, Ph.D.,
and Kimford J. Meador, M.D., for the MONEAD Study Group*

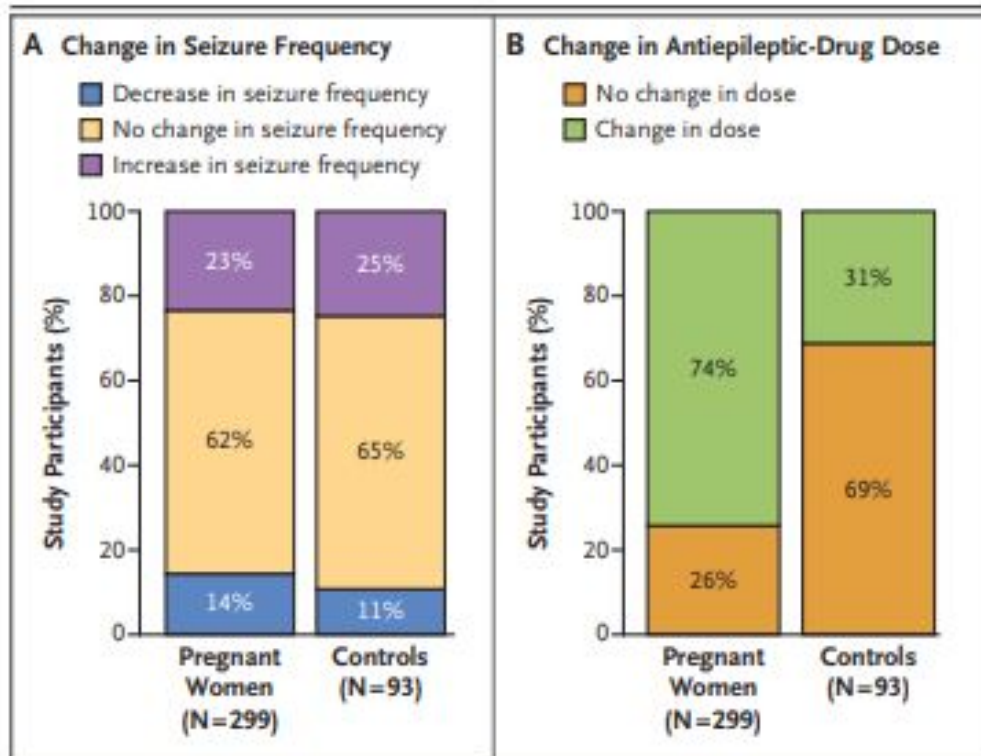
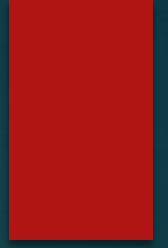


Figure 3. Changes in Seizure Frequency and Antiepileptic-Drug Dose.

Panel A shows the changes in the frequency of seizures that impaired awareness during epoch 1 as compared with epoch 2 in pregnant women and in controls (odds ratio for an increase in seizure frequency during pregnancy, 0.93; 95% confidence interval [CI], 0.54 to 1.60). Panel B shows the changes in the dose of an antiepileptic drug by the time of delivery in pregnant women and by 9 months after enrollment in controls (odds ratio for a change in dose during pregnancy, 6.36; 95% CI, 3.82 to 10.59).

Pennell,
2020

Anti-Seizure Medications (ASM)



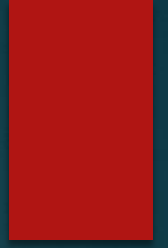
- ▶ Higher Risk

- ▶ Valproate
- ▶ Phenytoin
- ▶ Phenobarbital
- ▶ Carbamazepine

- ▶ Lower Risk

- ▶ Topiramate
- ▶ Lamotrigine
- ▶ Levetiracetam
- ▶ Zonisamide

ASM

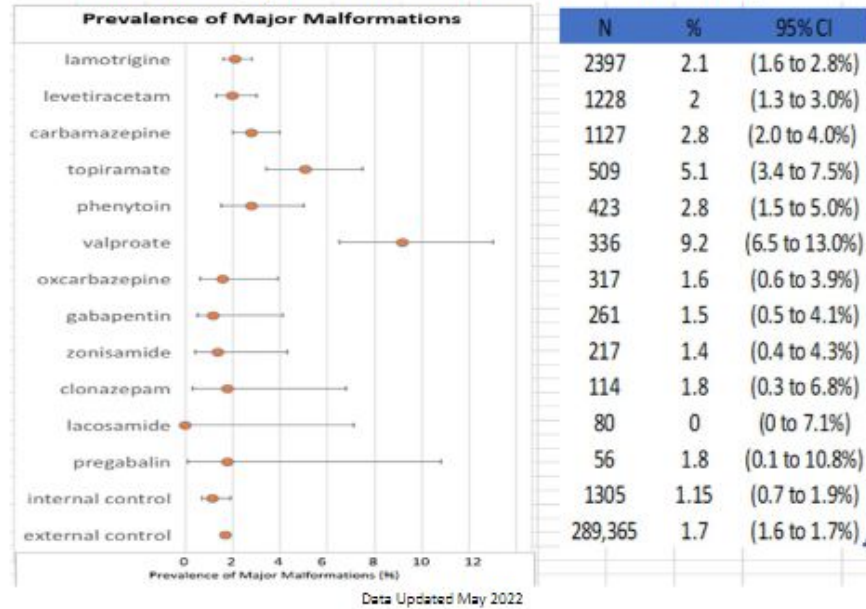


- ▶ Monotherapy preferred
- ▶ No one superior agent
- ▶ Levels
- ▶ Misinformation

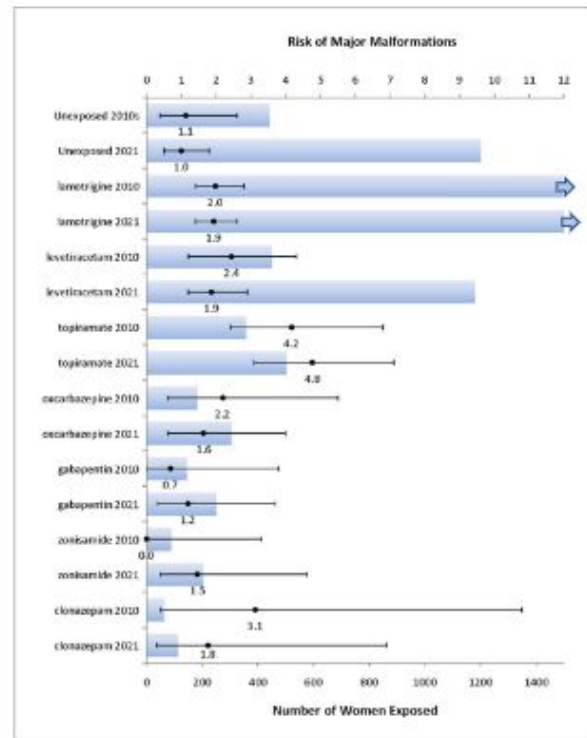
Risk of Malformations (MCM)

- ▶ Difficult to study, time consuming
- ▶ Registries
- ▶ Epilepsy background rate?
- ▶ Teratogenic principles – consistency, dosing

Risk of Malformation for Specific AED in Monotherapy 1st Trimester and the Control Groups



MCMs



Risk of malformations for specific AED in monotherapy 1st trimester and the control groups

By 2010 &
By 2021

Management

- ▶ Clearance significantly increases
 - Lamictal – 191 %
 - Keppra – 207 %
- ▶ Up to 1/3 of new seizures if not adjusted
- ▶ Inconsistent guidelines, reference ranges

Lamotrigine

- ▶ (Lamictal)
- ▶ 8 registry studies – MCM rates 2-4.6 %
- ▶ Possible increased clefts, cardiac, NTD
- ▶ 6 week titration schedule
- ▶ Stevens-Johnson

Carbamazepine

- ▶ (Tegretol)
- ▶ Registry Data – 2.6 – 5.5 % MCMs
- ▶ Cardiac, hip, renal
- ▶ IQ / behavior ?
- ▶ Oxcarbazepine (Trileptal)

Topiramate

- ▶ (Topamax)
- ▶ Registry studies – 3.9 – 4.2 %
- ▶ Oral clefts (6X)
- ▶ Increased risks of SGR

Levetiracetam

- ▶ (Keppra)
- ▶ Registry data - 0 – 2.8 % MCMs
- ▶ No consistent pattern of anomalies
- ▶ Rapid onset

Alternative Treatments

- ▶ “Drug Resistant Epilepsy” (DRE)
- ▶ CNS surgeries
- ▶ Vagal stimulation
- ▶ Deep brain stimulation
- ▶ Ketogenic diet
- ▶ Limited OB data

Pregnancy Management

- ▶ Multi-disciplinary care
- ▶ ASM levels
- ▶ Detailed anatomy 19-21 weeks
- ▶ Fetal echocardiogram ?
- ▶ Serial fetal growth ?
- ▶ Antenatal testing?
- ▶ Delivery timing?

New onset seizures

- ▶ “Eclampsia until proven otherwise” +/-
- ▶ Mortality may be higher
- ▶ Magnesium
- ▶ Rapid and broad workup
- ▶ Imaging
- ▶ AMS

- ▶ Stay calm
- ▶ Simulations

Vitamin K?

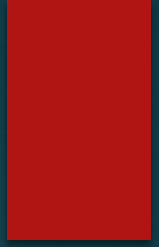
- ▶ Enzyme-inducing ASMs
- ▶ Phenobarbital, phenytoin, carbamazepine
- ▶ Concern for Vitamin K depletion, risk for ICH, neonatal bleeding
- ▶ Not evidenced based

Post-Partum

- ▶ Dose adjustments 2-4 weeks PP
- ▶ Neonatal safety
- ▶ Breast-feeding
- ▶ Contraception
- ▶ Neurology continuity of care



ACOG Monograph



Conclusions

- ▶ Maternal / fetal risks
- ▶ Preconception counseling
- ▶ Multi-disciplinary care
- ▶ Use a low-risk monotherapy if possible
- ▶ Levels/dosing adjustments

Thank you

