Obstetric Critical Care Symposium

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Dallas, Texas

Seizures and Status Epilepticus in Obstetric Critical Care

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Disclosures

- Biogen, Inc ALS trial
- NFL Unaffiliated neurotrauma consultation

Breakdown

Patients with epilepsy

Patients with new onset seizures

Patients with status epilepticus

Background

- 2.9 million patients with active epilepsy in the USA (1%)
- Women of reproductive age have same risk as average population of having active epilepsy therefore second most common neurologic coexisting condition (headache being most common)
- Maternal morbidity and mortality
  - 36.9 vs 25.4 per 1,000 deliveries

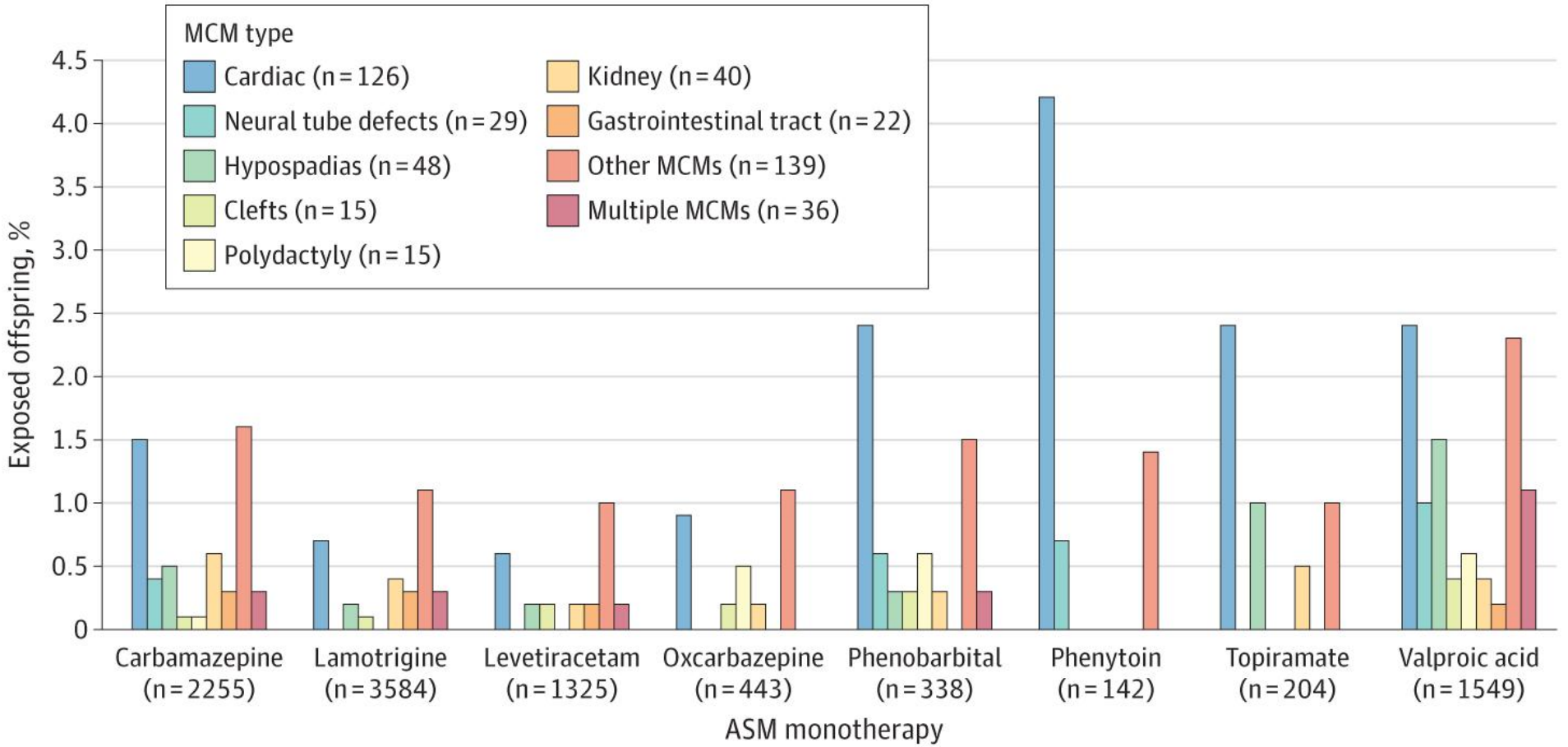
Considerations with comorbid epilepsy

- Risks:
  - Worsening of underlying epilepsy
  - ASM associated with higher severe maternal morbidity among women with epilepsy
    - Cohort of 35K mothers with epilepsy, 16.2K exposed to ASMs.
    - Severe preeclampsia & eclampsia
    - HELLP syndrome
    - Embolism
    - Cerebrovascular events
    - Severe mental health conditions
    - Infants w/ HIE, neonatal convulsions, respiratory distress syndrome, retinopathy of prematurity.

Table 3. Maternal and Perinatal Mortality and Severe Morbidity Among Women With Epilepsy by Antiseizure Medications (ASM) Use During Pregnancies in 5 Nordic Countries (1997 to 2017)

Outcome	No ASM (n = 19 013)		Any ASM (n = 16 240)		
	No. of events	Rate per 1000 deliveries/births (95% CI)	No. of events	Rate per 1000 deliveries/births (95% CI)	Unadjusted odds ratio (95% CI)[a,b]
Maternal morbidity and mortality outcome					
Composite maternal mortality/maternal morbidity[c]	655	34.6 (32.1-37.3)	636	39.6 (36.7-42.8)	1.16 (1.04-1.30)
Maternal mortality[c]	<5	NA[d]	<5	NA[d]	NA[d]
Composite severe maternal morbidity	656	34.5 (32.0-37.2)	642	39.6 (36.7-42.7)	1.17 (1.04-1.30)
Severe maternal morbidity					
Severe preeclampsia, HELLP, eclampsia	278	14.6 (13.0-16.4)	281	17.3 (15.4-19.4)	1.20 (1.01-1.43)
Severe hemorrhage	123	6.5 (5.4-7.7)	137	8.4 (7.1-10.0)	1.31 (1.02-1.67)
Pulmonary and obstetric embolism, DIC, shock	20	1.1 (0.7-1.6)	24	1.5 (1.0-2.2)	1.42 (0.77-2.61)
Sepsis	137	7.2 (6.1-8.5)	91	5.6 (4.6-6.9)	0.78 (0.60-1.02)
Acute kidney failure	<5	NA[d]	<5	NA[d]	NA[d]
Cardiac complications	11	0.6 (0.3-1.0)	6	0.4 (0.2-0.8)	0.64 (0.24-1.73)
Complications of anesthesia	<5	NA[d]	<5	NA[d]	NA[d]
Cerebrovascular accidents	19	1.0 (0.6-1.6)	34	2.1 (1.5-2.9)	2.15 (1.21-3.82)
Surgical complications	22	1.0 (0.6-1.6)	20	2.1 (1.5-2.9)	2.15 (1.21-3.82)
Severe mental health conditions	56	2.9 (2.3-3.8)	61	3.8 (2.9-4.8)	1.28 (0.89-1.85)
Uterine rupture	21	1.1 (0.7-1.7)	21	1.3 (0.8-2.0)	1.16 (0.62-2.17)
Fetal/infant mortality and morbidity outcome[e]					
Composite perinatal death/severe neonatal morbidity[d]	760	39.9 (37.2-42.8)	912	56.2 (52.7-59.8)	1.17 (0.84-1.64)
Perinatal death[f]					
Stillbirth[f]	69	3.62 (2.86-4.59)	69	4.25 (3.36-5.38)	2.65 (1.62-4.33)
Neonatal death[g]	23	1.21 (0.81-1.82)	52	3.22 (2.45-4.22)	1.55 (1.18-2.03)
Perinatal death[f]	92	4.83 (3.94-5.92)	121	7.45 (6.24-8.90)	1.42 (1.28-1.58)
Compos morbidi		36.1 (33.5-38.8)	812	50.2 (47.0-53.7)	1.42 (1.28-1.58)

Antiseizure medications in pregnancy



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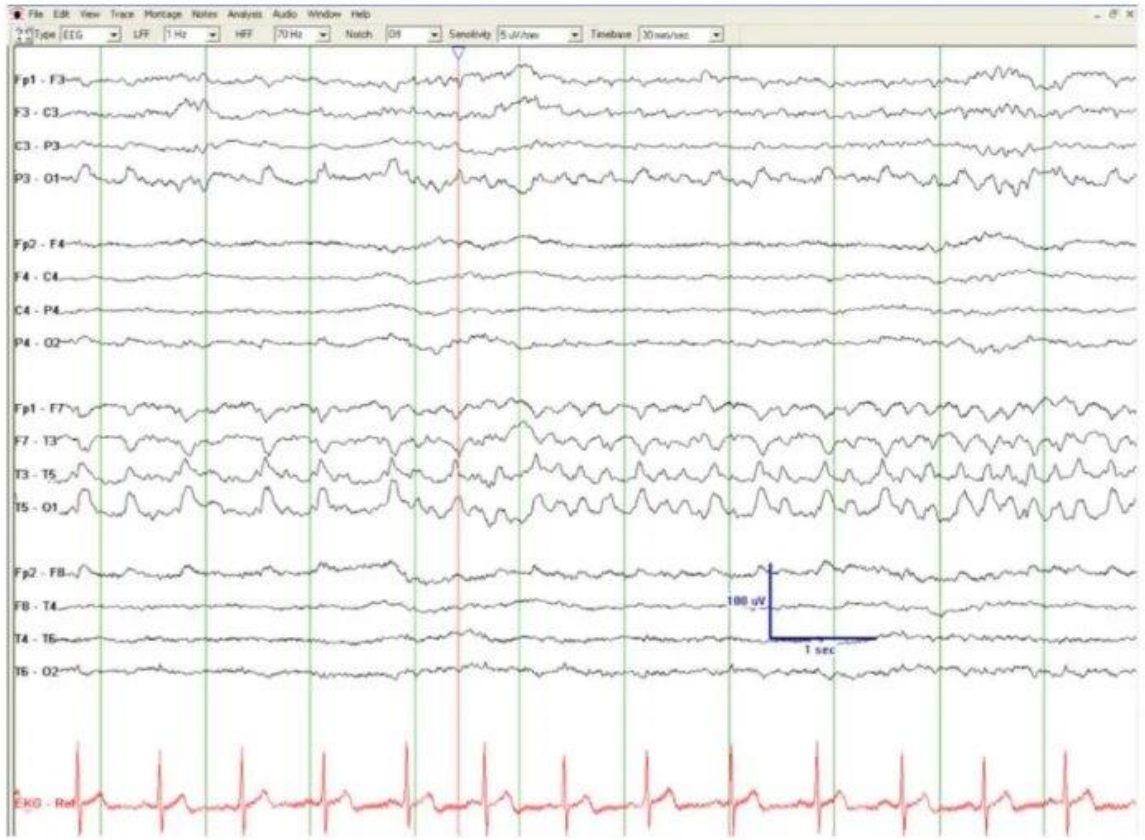
Start, stop, or stay the course



- Guidelines emphasize ASM and doses to optimize seizure control and fetal outcomes at earliest possible opportunity.
- Once pregnant, avoid removing or replacing ASM this is controlling GTC/focal-to-bilateral tonic clonic seizure even if fetal risk.
- 0.4 mg folic acid** then1-4 mg FA

Hirsch LJ et al. PMID 33475321

Breakdown

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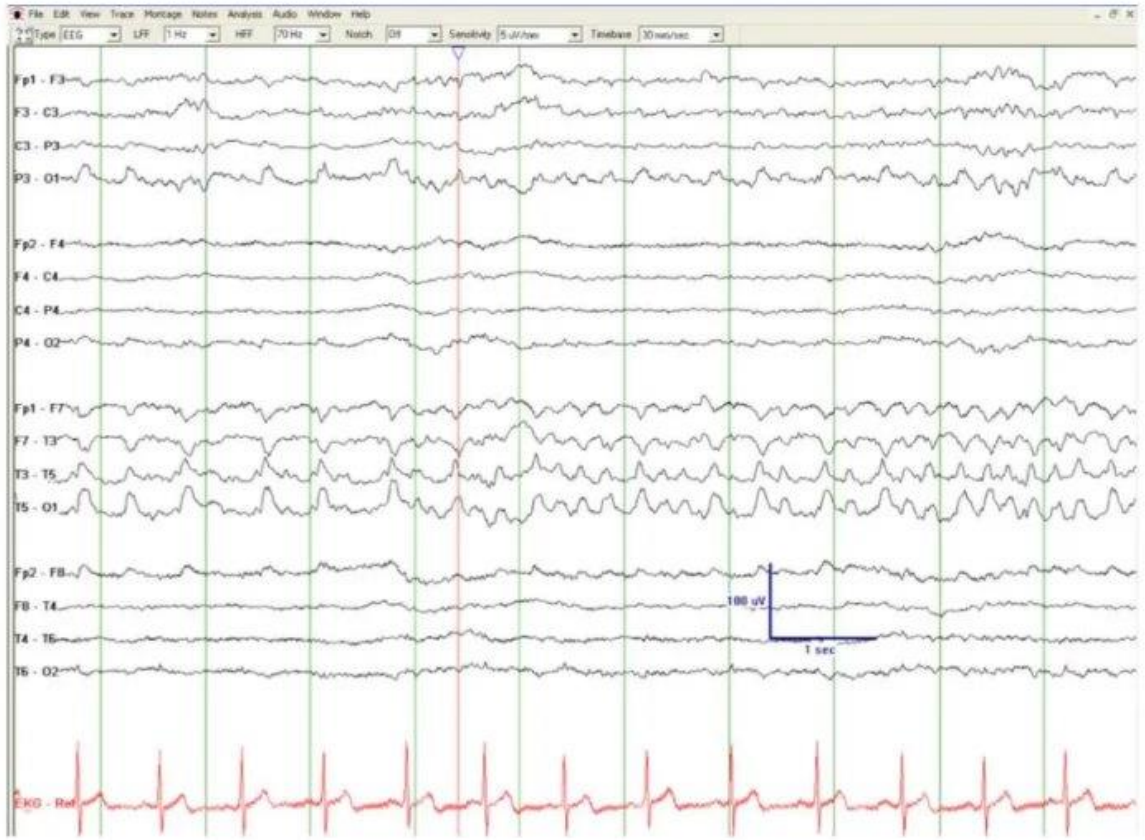
Patients with new onset seizures

Patients with status epilepticus

New seizure? High risk for more seizures? Do we treat?



- One seizure ≠ epilepsy
- Standard ASM treatment depending on etiology and workup
- What are high risk features for more seizures?

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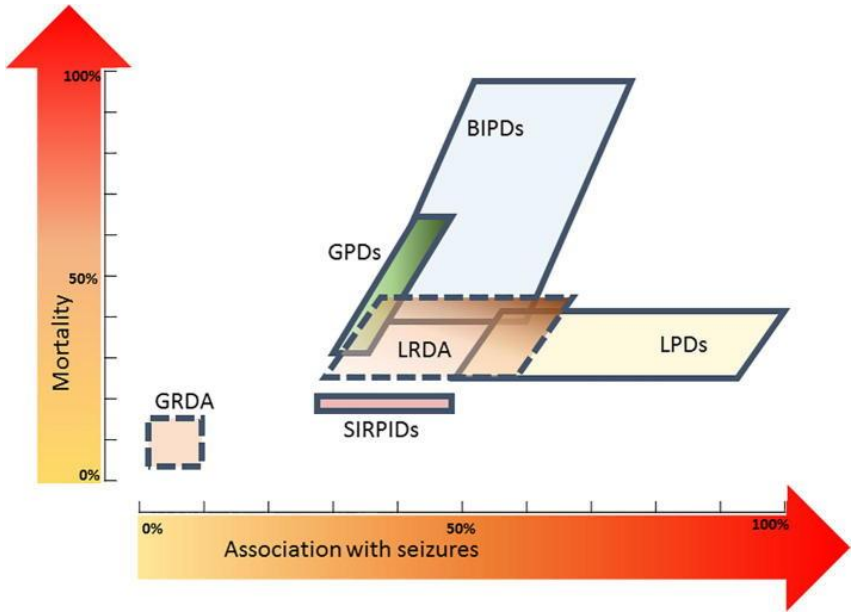
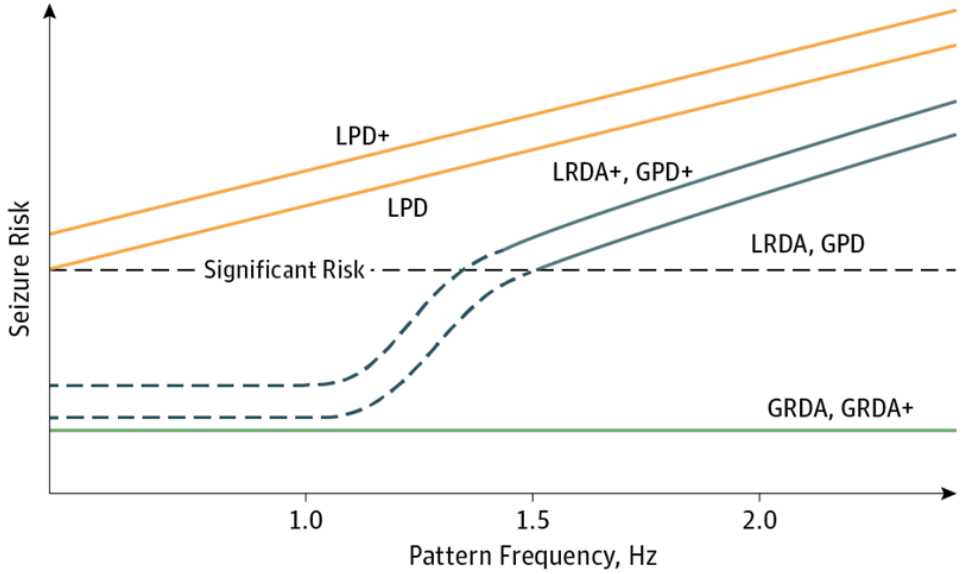
Evaluation of new-onset seizures in pregnancy

- Differential Diagnosis
- Clinical Presentation
- Diagnostic Considerations





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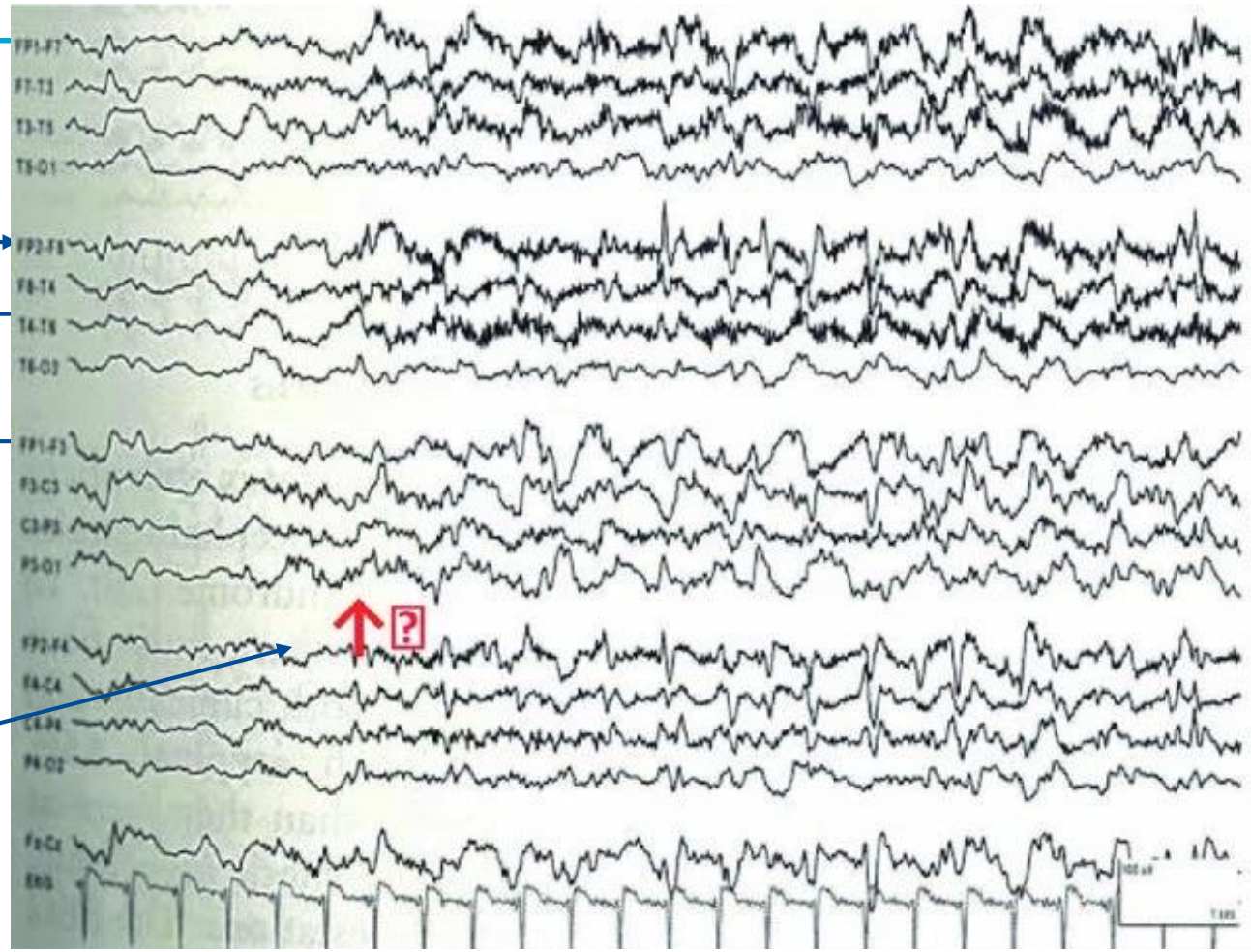
Treatment of new-onset seizures in pregnancy

Reported etiologies, association with seizures, and mortality of periodic and rhythmic patterns.

Feature	Common causes		Association with seizures	Mortality
Lateralized Periodic Discharges (LPDs)	Stroke Tumor Infection	Hemorrhage	50–100%	24–41%
Bilateral Independent Periodic Discharges (BIPDs)	Stroke Anoxic injury Metabolic disorders	Infection Tumors	43–78%	39–100%
Generalized Periodic Discharges (GPDs)	Metabolic Sepsis Anoxic	Stroke	29–50%	30–64%
Lateralized Rhythmic Delta Activity (LRDA)	Hemorrhage Stroke Tumor	TBI Infection	25–63%	
Generalized Rhythmic Delta Activity (GRDA)	Encephalopathy Stroke Hemorrhage	Tumor Infection Drug induced	No additional association with seizures compared to controls without GRDA	
Stimulus-Induced Rhythmic, Periodic, or Ictal Discharges (SIRPIDs)	Hemorrhage Anoxic injury Drug toxicity	Metabolic TBI	27–51% One large study found no increase in seizures when features had stimulus-induced compared to spontaneous patterns	17%



Breakdown

Patients with epilepsy

Patients with new onset seizures

Patients with status epilepticus

Treatment of status epilepticus in pregnancy

1. Initial stabilization
   a) Secure the airway*
   b) Establish IV access
   c) Call appropriate consults (OB/MFM, neurology, anesthesia, neonatology)
   d) Admit to ICU
   e) Protect and perfuse the fetus (injury precautions, lateral recumbent position).
   f) Initial history (if available).
   g) Baseline laboratory studies (CBC, glucose, calcium, electrolytes, phosphorous, ABG, UA, ASM levels if relevant)

Treatment of status epilepticus in pregnancy

2. Therapeutic trials (to be administered sequentially)

Medication	Dosage	Intent	Considerations
Glucose	50mL of D50 IV	Correct hypoglycemia	
Thiamine (vitamin B1)	100 mg IV followed by 50-100 mg IM/IV QD	Correct Wernicke's encephalopathy	
Magnesium sulfate	Standard obstetric regimen	Treatment of eclamptic confusions if clinically suspected	MgSO4 is NOT a treatment for status epilepticus

Treatment of status epilepticus in pregnancy

3. Initiate first line anticonvulsants ONE from EACH class

Class	Drug	Dosage	Therapeutic / max levels	Considerations
Benzodiazepine	Diazepam Lorazepam Midazolam	5-10 mg IV q10-15min 4 mg IV; repeat x 1 in 10-15min 0.2 mg/kg up to 10 mg IM	Max dose 30 mg Max dose 8mg/12h Max dose 8mg/12h	Magnesium sulfate more effective than phenytoin or diazepam in eclamptic seizures only
ASM	Levetiracetam Fosphenytoin Phenytoin	40-60 mg/kg iv x 1 20 mg/kg IV x 1 then maintenance q12h thereafter 20 mg/kg IV q30 min prn and maintenance q12h	 Total=10-20 µg/mL Free=1-2 µg/mL Total = 10-20	 Continuous EEG and BP monitoring during infusion, use non-glucose

Treatment of status epilepticus in pregnancy

4. Intubation and sedation
    a) Intubation
    b) Sedation:
        a) Phenobarbital (20-25 mg/kg, do not exceed 100 mg/min)
        b) Midazolam (0.02-0.10 mg/kg/h)
        c) Propofol (5-50 µg/kg/min, start at 5 µg/kg/min IV x 5 min then inc by 5 µg/kg/min q 5-10 min until desired effect)

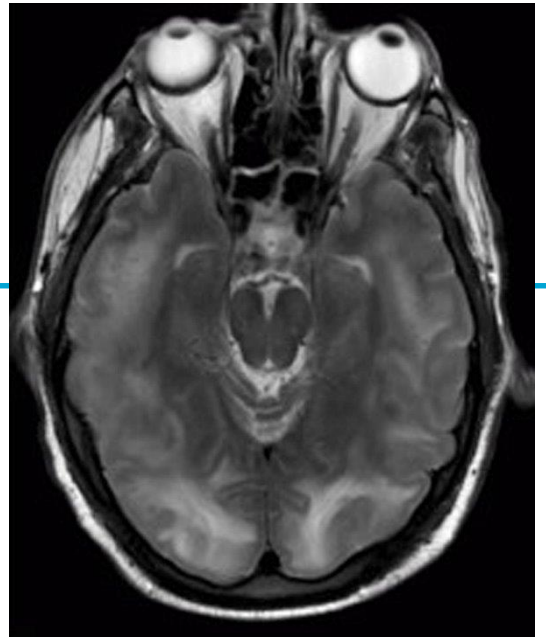
Treatment of status epilepticus in pregnancy

5. Refractory status epilepticus
   a) If seizures persist, consider general anesthesia and NMJ blockade
   b) Consider steroids / IVIG
   c) ECT
   d) Delivery for failure to control super-refractory status epilepticus

6. Further differential diagnoses
   a) Toxicology
   b) Lumbar puncture
   c) Imaging
   d) Expanded liver panel (rule out HE)

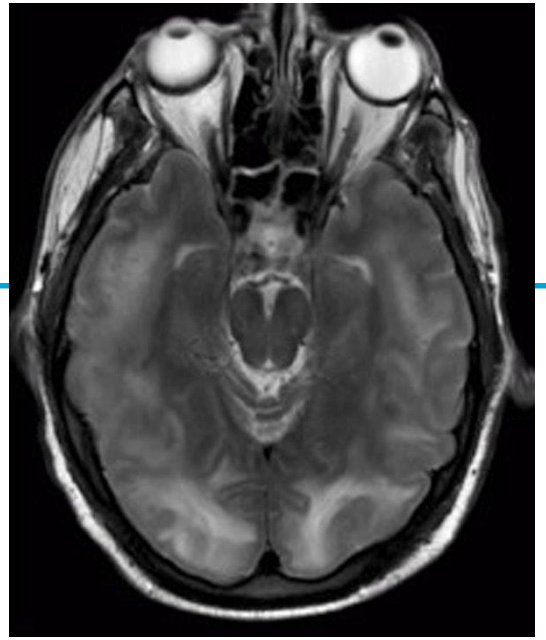
Posterior Reversible Encephalopathy Syndrome

Posterior Reversible Encephalopathy Syndrome

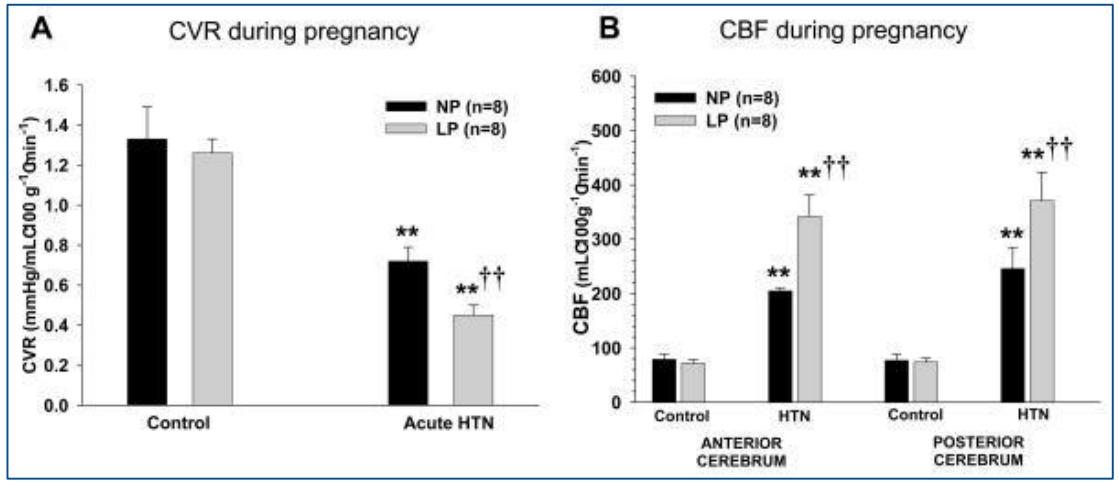


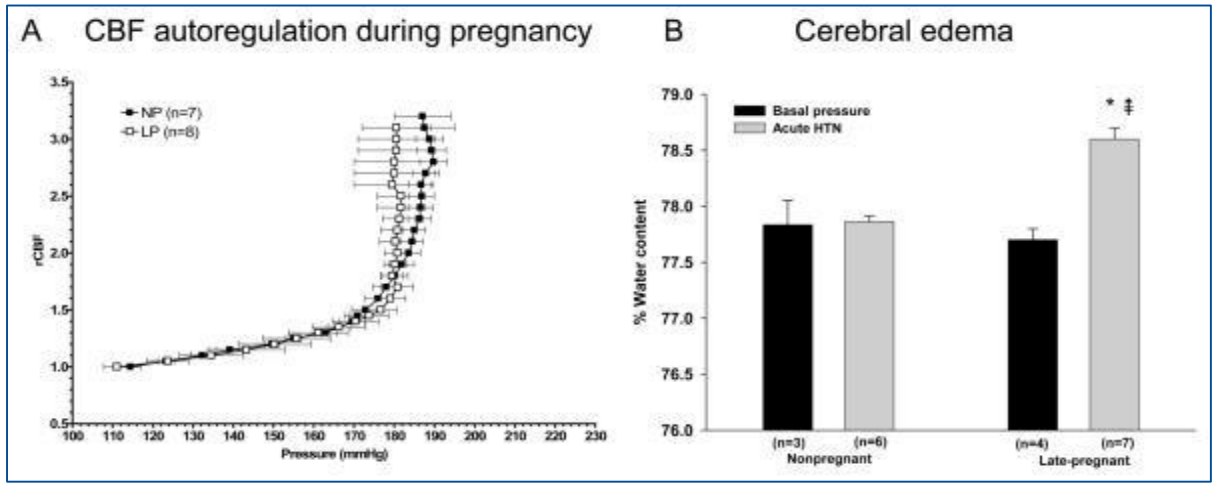
- Etiology (50% of eclampsia cases)
  - Preeclampsia / eclampsia (cytokine activation, autoantibodies, complement activation, proinflammatory mediators ➔ endothelial dysfunction
  - HELLP (seizures, altered sensorium, HA, HTN in 3rd trimester/postpartum
  - Acute hypertensive crisis (present in 80%; risk associated with absolute elevation and rate of rise)
  - Renal failure (independent risk factors vs volume/hypertension)
  - Autoimmune/ thrombotic microangiopathies
  - Immunosuppressive agents (post-transplant pregnancy)

Posterior Reversible Encephalopathy Syndrome



- Etiology
- DDx: RCVS, CVT, iCVA, ICH





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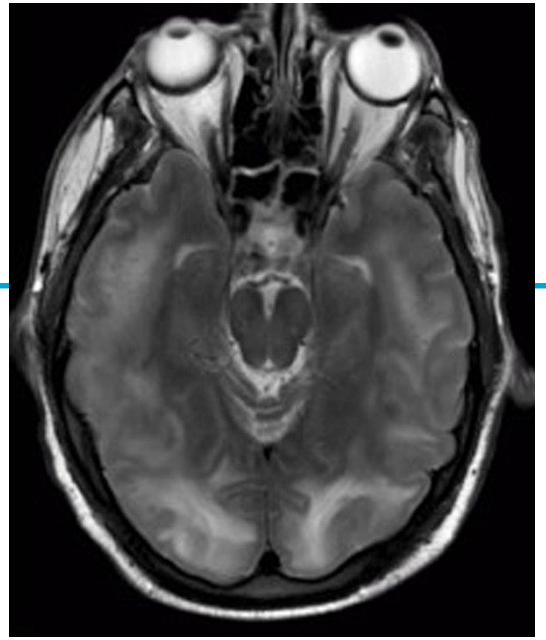
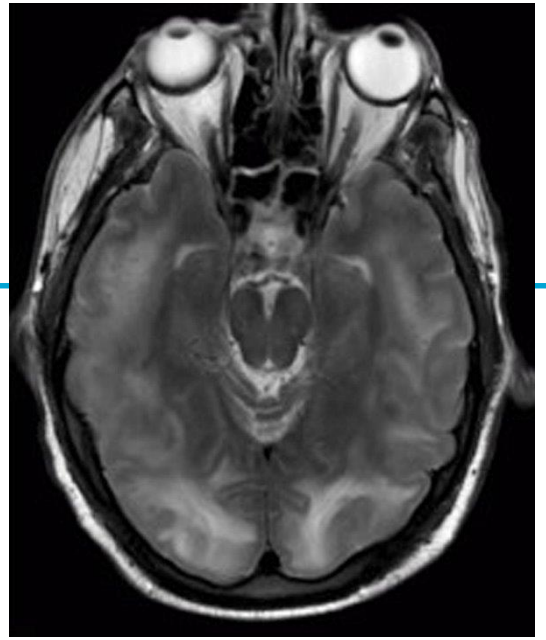
Posterior Reversible Encephalopathy Syndrome



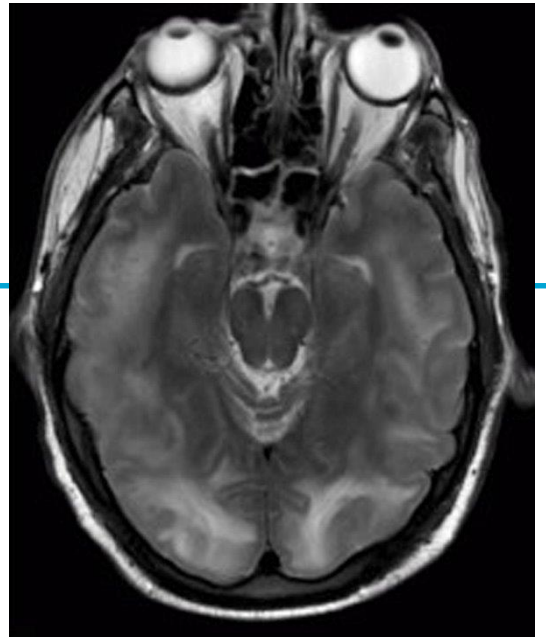
- Etiology
- DDx: RCVS, CVT, iCVA, ICH
- Labs: check for liver/ renal dysfunction, hemolysis, consider ADAMSTS13 activity/smear.
- Imaging: MRI w/ FLAIR and T2 weighted sequence to detect vasogenic edema
- LP: elevated protein without pleocytosis

Posterior Reversible Encephalopathy Syndrome



- Management
  - Antihypertensives
    - Labetalol
    - Hydralazine
    - nifedipine (particularly if RCVS)
    - Avoiding nicardipine/clevidipine due to limited pregnancy safety data
  - Anti-seizure management
    - Magnesium sulfate if eclampsia related
    - Standard antiseizure medications (diazepam, phenytoin, levetiracetam) for refractory seizures
    - ** NCSE in 16% so proceed with cEEG if remain altered **

Posterior Reversible Encephalopathy Syndrome



- Prognosis
  - Mortality 3-6%
  - Severe neurologic injury 10-20%
    - Hydrocephalus, ICH, diffuse cerebral edema
    - Hemiparesis, decreased visual acuity, dizziness
    - Unprovoked seizures / epilepsy 1-10% long term risk
    - Recurrence: 5-12% if uncontrolled hypertension, highest risk in 90 days
  - Complete recovery 75-90%

Infectious Precipitants in Status Epilepticus

Infectious Precipitants to Status Epilepticus

- Infectious considerations
  - HSV encephalitis
  - Neurocysticercosis
  - Cerebral malaria
  - Bacterial meningitis

    - Acyclovir 10 mg/kg q8h
    - Empiric iv antibiotics (ceftriaxone + vancomycin + ampicillin)
    - Antihelmenthic (albendazole, praziquantel + corticosteroids)

Safety of lumbar puncture in pregnancy

- Generally considered safe

Absolute contraindications	Relative contraindications
Non-communicating hydrocephalus Platelet count <20 x 10^9 /L Spinal stenosis or cord compression above the puncture level Local skin infection at puncture site Spinal /cranial abnormalities (Chiari malformation/tethered cord) Cerebral mass lesion with	Platelet count 20-40 x 10^9/L Thienopyridine therapy (clopidogrel, prasugrel) Space occupying brain lesion without elevated ICP

Platelet count thresholds in pregnancy
≥70 × 10^9/L epidural/spinal anesthesia safe without other coagulopathy 50-80 × 10^9/L epidural / spinal anesthesia risk individualized risk assessment 20-40 × 10^9/L risk assessment for LP, likely safe <20 × 10^9/L spinal procedures contraindicated

Research updates

Research Updates

- Placental perfusion during seizures and status epilepticus

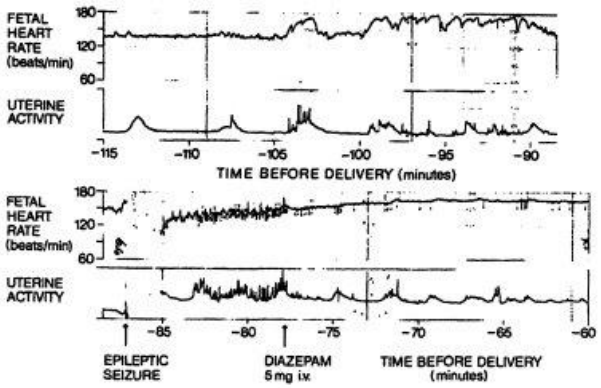
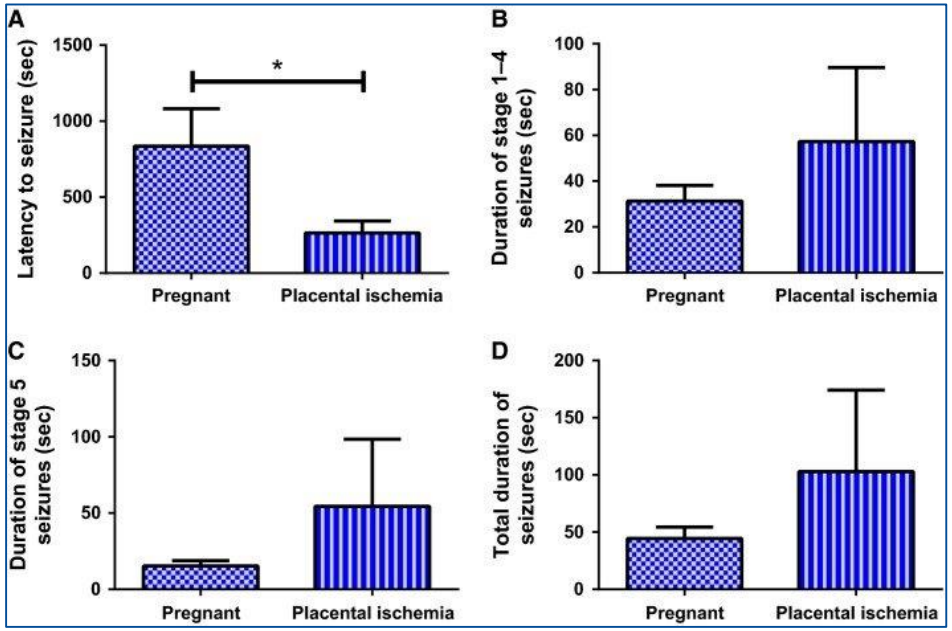


Fig. 2. Fetal heart rate recorded via a scalp electrode and uterine activity before and after a maternal epileptic grand mal seizure during the first stage of labor. The gestation was 292 days. There was a 90-second lag in the recording from the beginning of the epileptic seizure because the mother fell from the bed onto the floor.



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Thank you for your attention

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