

# Epilepsy: Female Issues

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# Epilepsy in Women

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- Role of hormones in epilepsy
- Contraception
- Epilepsy and sexuality
- Pregnancy and epilepsy
- Postpartum period and epilepsy
- Bone health and epilepsy
  
- Epilepsy in adolescence
- Epilepsy in menopause

# Epilepsy in Women

## Hormones and Seizures

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Female hormones change the excitability of the brain and alter the threshold for seizures

Estrogen—decreases threshold

Progesteron-increases threshold

# Hormone sensitive seizures Catamenial epilepsy

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In 1/3 of female patients there is substantial relationship between seizures and menstrual cycle.

*Gr. Katamenios* = monthly

# Catamenial Epilepsy

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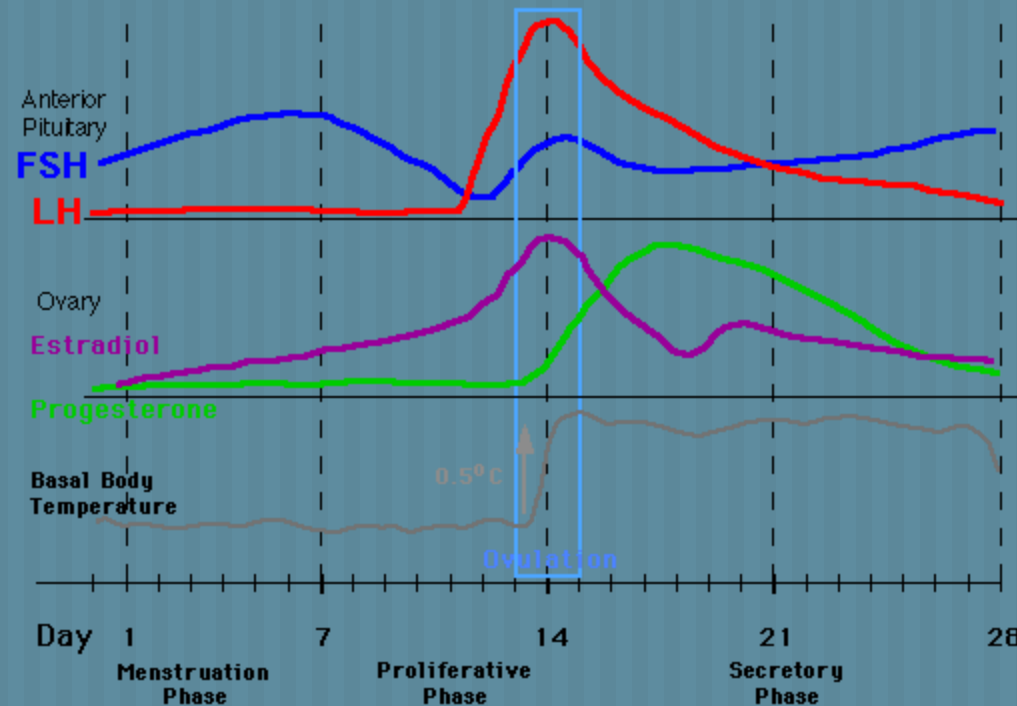


Seizures that tend to cluster in relationship to menstrual periods

- High levels of estrogen
- Low levels of progesterone
- Fluid and electrolyte imbalance
- Psychological Stress
- Decrease in levels of AEDs

# Epilepsy in Women

## Catamenial Epilepsy



# Catamenial epilepsy

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Pattern 1 – just before menstruation  
(steep decline in progesterone)

Pattern 2 – just before ovulation ~day  
14 (steep elevation in estrogen)

# Catamenial epilepsy

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- Pattern 3- in second half of menstrual cycle
- Anovulatory cycles (ovulation does not occur) are more frequent in women with epilepsy
- There is no elevation of progesterone

# Epilepsy in Women

## Management of Catamenial Seizures

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- Hormone treatment
- Supplemental AED at expected time of seizures
- Diamox

# Management of catamenial epilepsy-hormone treatment

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- Cyclic
  - Natural progesterone seems to work better
- Suppressive
  - Depo-provera

# Contraception



- The efficacy of oral contraceptive pills and subdermal progesterone (Norplant) can be lowered by hepatic enzyme inducing AEDs due to enhanced metabolism of estrogen and progesterone
  - Carbamazepine (Tegretol)
  - Phenobarbital
  - Phentoin (Dilantin)
  - Primidone
  - Topiramate (Topamax) \*higher doses
  - Oxcarbazepine (Trileptal) \*higher doses

# Contraception

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- AED's that have no influence on levels of steroids
  - Gabapentin (Neurontin)
  - Lamotrigine (Lamictal)
  - Levetiracetam (Keppra)
  - Tiagabine (Gabatril)
  - Zonisamide (Zonegran)
  - Pregabalin (Lyrica)

# Contraception

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- AED's that may increase level of steroids:
  - Valproate (Depakote)
  - Felbamate (Felbatol)

# Lamictal

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Does not lower efficacy of oral birth control pills, but oral birth control pill can decrease levels of Lamictal

# Contraception

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- Consider AEDs that don't induce liver enzymes
- Consider other methods of contraception (barrier, IUD)

# Contraception

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- OCP with higher doses of estrogen (50 micrograms)
- Depo-Provera - more frequent (6-8 weeks)
- If breakthrough bleeding
  - Increase dose of estrogen
  - add barrier method
    - Condoms
    - Cervical diaphragm or cervical cap
    - Spermicides

# Epilepsy and reproductive function

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- Higher risk of infertility (effect of both seizures and AED's)
  - Irregular menstrual cycles
  - Polycystic ovaries
  - Endocrine disorders

# Epilepsy and sexuality

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- AED's effect on hormone binding and metabolism (elevations in prolactin and gonadotropin level can suppress libido)
- AED's effect on cortical function (sedative effect)
- Dysfunction of frontal/temporal lobes due to seizures
- Psychological/social factors

# Epilepsy and Pregnancy

## Fetal Risks

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- Late fetal loss (after 20 weeks)-twice as often in infants of mothers with epilepsy.
- Infant mortality- two to three times more likely than others to die soon after birth - more uncontrolled the mother's seizures, the higher the infant mortality rate.

# Epilepsy and Pregnancy

## Fetal Risks

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The risk of major congenital fetal anomalies in the general population is about 2-4%

The risk is 4-8 % in women with epilepsy, regardless of AEDs

# Epilepsy and Pregnancy

## Fetal Risks

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- Most common major malformations:
  - Neural tube defects
  - Heart abnormalities
  - Orofacial clefts

# Epilepsy and Pregnancy

## Fetal Risks

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- Low birth weight -twice as often in infants of mothers with epilepsy.
- Developmental delay and learning disability-polypharmacy and possibly valproate (depakote) increase risk.
- Hereditary epilepsy- 2% of the children whose mothers (but not fathers) have epilepsy will have epilepsy

# Epilepsy and Pregnancy

## Folic acid

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- Folic deficiency is associated with increase in risk of neural tube defects.
- AED's that are linked to folic acid malabsorption/metabolism are
  - Phenytoin (Dilantin)
  - Carbamazepine (Tegretol)
  - Barbiturates
  - Valproate (Depakote)

# Epilepsy and Pregnancy

## AED's in pregnancy

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- More birth defects with:
  - Polypharmacy (two or more AED's)
  - Higher levels of medications

# Hemorrhagic disorder or neonate

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- AED's compete with vitamin K across the placenta
- Associated with in utero exposure to
  - Carbamazepine (tegretol)
  - Barbiturates (phenobarbital and primidone)
  - Phenytoin (dilantin)
- Risk can be decreased by vitamin K in last month of pregnancy

# Epilepsy and Pregnancy

## Fetal Risks

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90% of women with epilepsy have a successful and healthy newborn

# Epilepsy and Pregnancy



- Discuss before planning pregnancy
- May need to change AED drug/dosage
- Folic Acid: start before pregnant
- Close supervision with neurologist
- High-risk pregnancy OB is preferred

# Epilepsy and Pregnancy

## Guidelines for AED use during pregnancy



- Attempt AED withdrawal prior to conception if possible
- Use the most effective AED in monotherapy at lowest possible dose
- If family hx of neural tube defects, and there are acceptable alternatives, avoid Depakote and Tegretol
- Monitor free (nonprotein-bound) AED during each trimester, before delivery, 4-8 wks after delivery

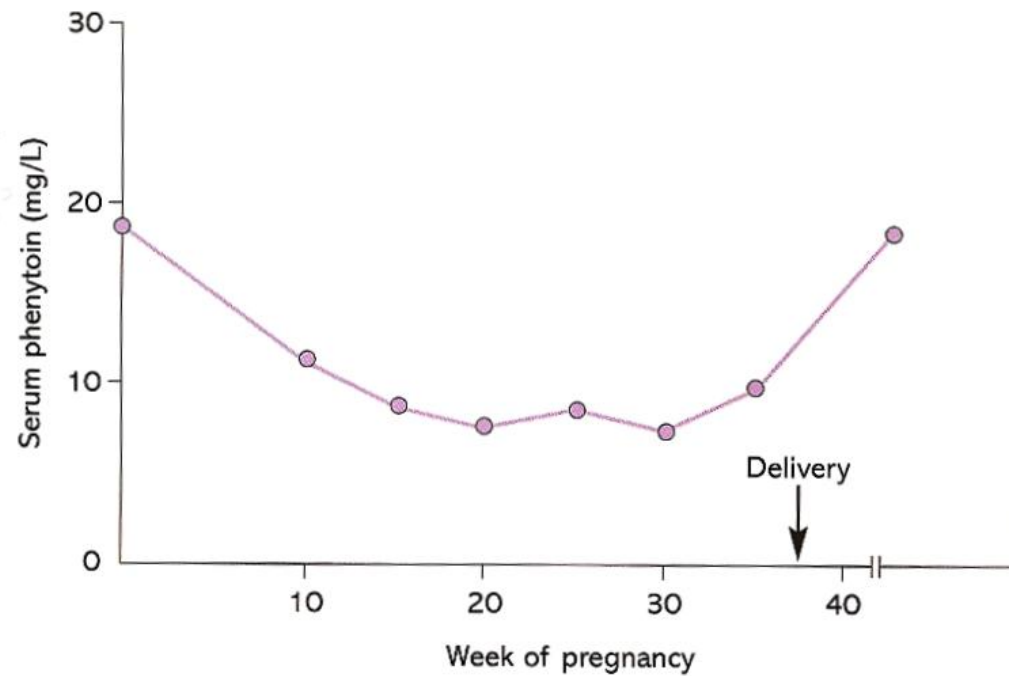
# Epilepsy and Pregnancy

## Guidelines for AED use during pregnancy

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- Levels of AED's drop in second trimester due to:
  - Increase in drug clearance
  - Increase in maternal plasma volume
  - Decreased protein binding

# Epilepsy and Pregnancy



**Figure 8.1** Serum phenytoin concentrations during pregnancy and delivery in a woman taking an established dose of 300 mg daily.

# Epilepsy in Women

## Guidelines

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- Adjust AED dosage according to nonprotein-bound (free) level
- Folic Acid 0.4 to 4 mg daily before conception and throughout gestation
- Vitamin K 10 mg daily during last month of gestation and IM to neonate at birth if on enzyme inducing AED's

# Epilepsy in Women

## Prenatal Testing

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- Anatomical ultrasound
- Maternal serum alpha-fetoprotein: increased concentration in mom's blood and amniotic fluid raise suspicion of neural tube defects

# Epilepsy and Pregnancy

## AED National Pregnancy Registry

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- Tracks use of AEDs and pregnancy outcomes
- All information confidential
- Can greatly improve our knowledge



# Epilepsy in Women

## Pregnancy Registry Resources

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- Epilepsy Foundation
  - 800 – EFA – 1000
  - [www.efa.org](http://www.efa.org)
- North American Pregnancy Registry
  - 888 – 233 - 2334

# Postpartum issues

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- AED levels may rise – close monitoring of levels is necessary
- Sleep deprivation and stress may increase frequency of seizures
- Child safety/lifestyle adaptation

# Breastfeeding

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Benefits of breastfeeding are felt to outweigh potential risk of continued exposure of neonate and infant to AEDs (AAN and AAP)

- Protein bound drugs have low concentrations in breast milk
- Observe breastfeeding infant for irritability, poor sleep patterns, or inadequate weight gain

# Epilepsy in adolescence

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- Most seizure disorders are not altered by onset of puberty
- Certain types of epilepsy start at approximate age (JME) or improve (benign rolandic epilepsy, absence epilepsy)
- Rapid growth may account for poor seizure control

# Epilepsy in adolescence

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- Menarche (first period)
  - Discuss hormone sensitive seizures
  - Interactions of AED's with contraceptive pills
  - Start folic acid supplementation
  - Discuss planning of pregnancy

# Epilepsy in adolescence

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- Discuss
  - Choice of medications
  - Substance abuse
  - Sleep deprivation
  - Compliance to medications
  - Driving
  - Sports safety
  - Choice of profession

# Epilepsy and menopause

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- Premature menopause is more common in WWE
- Effect on seizure frequency is unclear as both estrogen and progesterone levels drop
- Catamenial epilepsy seems to improve

# Epilepsy and menopause

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- Doses of AED's may need to be changed due to changes in metabolism
- Polypharmacy due to other medical conditions may affect efficacy of AED's and seizure
- Bone health
- Hormone replacement therapy

# Epilepsy & Bone health

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- Fractures are more likely in people with epilepsy due to:
  - Falls due to seizures and due to side effects of AED's, and
  - Altered bone density due to certain AED's

# Epilepsy & Bone health

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- Altered bone density due to AED's is associated with:
  - Phenytoin (dilantin)
  - Carbamazepine (tegretol)
  - Barbiturates
  - Valproate (depakote)

# Epilepsy & Bone health

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Prevention and therapy >6mo AEDs

- exercise, balanced diet, stop smoking, moderate alcohol, moderate caffeine
- calcium and vitamin D supplements
- measure Ca, ALP, 25-hydroxy vit D yearly
- Baseline DXA scan

# Epilepsy & Bone health

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Refer for possible treatment to endocrinologist if:

- osteopenia/osteoporosis
- Abnormal calcium or vit D levels
- fracture

# Epilepsy & HRT

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- HRT increases estrogen levels and may increase seizure frequency – concomitant use of natural progesterone may help
- AED's may affect HRT efficacy

# Women and epilepsy

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- Women with epilepsy face particular challenges
- Most women with epilepsy can lead normal lives and deliver healthy children