

# **Psychiatric Medications in Pregnancy and the Postpartum**

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Columbia, SC

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# Disclaimer

- I have nothing to disclose
- All discussion of medications is off label as no medications are FDA approved in pregnancy



# Who we are

- Stephanie Berg, MD
  - Psychiatrist
    - Primary focus is psychiatric medication management and diagnosis of mental health difficulties in women



# Particular interests

- Mood disorders in **pregnancy**
- Mood disorders in the **postpartum** period
- Psychiatric aspects of **chronic pelvic pain**
- **Eating disorders**
- Mood changes with **menopause**
- Mood changes with **premenstrual** disorders
- Mood disorders in victims of **interpersonal violence**

# Who we are

- Kelly Helms, LISW-CP
  - Clinical Social Worker
  - Primary focus is EMDR as well as individual and family therapy for women, infants, and children



# Particular Interests

- **Trauma** recovery therapy
  - EMDR (Eye Movement Desensitization and Reprocessing)
    - For women with history of
      - Assault
      - Post-traumatic stress disorder
      - Anxiety disorder
      - Abuse history
- **Perinatal** mood disorders
- Individual and couple counseling for difficulties with **intimacy**

# Objectives

- Introduction
- Antidepressant medications
  - Pregnancy
  - Breastfeeding
- Mood stabilizer medications
- Antipsychotic medications
- Antianxiety medications



# Perinatal Psychiatric Disorders

- Pregnancy Depression
- Postpartum Blues
- Postpartum Depression
- Postpartum Psychosis
- Postpartum Obsessive-Compulsive Disorder
- Exacerbation of other illness

# Major Depressive Episode

- At least 2 weeks
  - Sadness or irritability
  - Interest
  - Guilt
  - Energy
  - Concentration
  - Appetite
  - Feeling restless or slowed
  - Sleep
  - Suicidality



# Antidepressant medications

- SSRIs
  - Fluoxetine (Prozac)
  - Sertraline (Zoloft)
  - Paroxetine (Paxil)
  - Fluvoxamine (Luvox)
  - Citalopram (Celexa)
  - Escitalopram (Lexapro)
- SNRIs
  - Venlafaxine (Effexor)
  - Duloxetine (Cymbalta)
  - Desvenlafaxine (Pristiq)

# Antidepressant medications

- Other
  - Bupropion (Wellbutrin)
    - Norepinephrine and dopamine
  - Trazodone (Desyrel)
  - Mirtazapine (Remeron)
- Tricyclic Antidepressants
  - Amitriptyline (Elavil)
  - Nortriptyline (Pamelor)
  - Imipramine (Tofranil)
  - Clomipramine (Anafranil)
- MAOIs
  - Phenylzine (Nardil)
  - Tranylcypromine (Parnate)

# Anxiety medications

- Benzodiazepines
- Buspirone (Buspar)
- Hydroxyzine (Vistaril)

# Mood Stabilizers

- Lithium
- Carbamazepine (Tegretol)
- Valproic Acid (Depakote, Depakene)
- Atypical Antipsychotics

# Perinatal Mood Disorder Examples



# Treating MDD in Pregnancy: The Ideal Situation

- Ms. J has a long history of recurrent depression. She is currently stable on sertraline (Zoloft). She would like to become pregnant. What should she do?



# Versus

- Ms. J has had a difficult time becoming pregnant. She is not taking psychiatric medications. Two months after finding out she is pregnant, she notices she feels down and is unsure if she even wants to continue the pregnancy. What should she do?



# Versus

- Ms. J has a long history of depression and just found out she is pregnant. She is currently taking fluoxetine (Prozac). What should she do?



# Depression in pregnancy is common

First trimester	7 %
Second trimester	13 %
Third trimester	12 %

- Up to 30% in low-income populations



# Detection of Perinatal Depression

- Edinburgh Postnatal Depression Scale (EPDS)
  - Can be used during pregnancy and postpartum
  - 10-item, self-administered
  - Easy to score
  - Score of at least 10-13 indicates depression
  - Validated in at least 12 languages

**Name:**  
**Date:**  
**Address:**  
**Baby's Age:**

---

As you have recently had a baby, we would like to know how you are feeling. Please UNDERLINE the answer which comes closest to how you have felt **IN THE PAST 7 DAYS**, not just how you feel today.

---

Here is an example, already completed.

I have felt happy:

Yes, all the time

Yes, most of the time

No, not very often

No, not at all

This would mean: "I have felt happy most of the time" during the past week. Please complete the other questions in the same way.

---

**In the past 7 days:**

- |  |  |
|--|--|
| <p>1. I have been able to laugh and see the funny side of things<br/>As much as I always could<br/>Not quite so much now<br/>Definitely not so much now<br/>Not at all</p> <p>2. I have looked forward with enjoyment to things<br/>As much as I ever did<br/>Rather less than I used to<br/>Definitely less than I used to<br/>Hardly at all</p> <p>*3. I have blamed myself unnecessarily when things went wrong<br/>Yes, most of the time<br/>Yes, some of the time<br/>Not very often<br/>No, never</p> <p>4. I have been anxious or worried for no good reason<br/>No, not at all<br/>Hardly ever<br/>Yes, sometimes<br/>Yes, very often</p> <p>*5. I have felt scared or panicky for no very good reason<br/>Yes, quite a lot<br/>Yes, sometimes<br/>No, not much<br/>No, not at all</p> | <p>*6. Things have been getting on top of me<br/>Yes, most of the time I haven't been able to cope at all<br/>Yes, sometimes I haven't been coping as well as usual<br/>No, most of the time I have coped quite well<br/>No, have been coping as well as ever</p> <p>*7. I have been so unhappy that I have had difficulty sleeping<br/>Yes, most of the time<br/>Yes, sometimes<br/>Not very often<br/>No, not at all</p> <p>*8. I have felt sad or miserable<br/>Yes, most of the time<br/>Yes, quite often<br/>Not very often<br/>No, not at all</p> <p>*9. I have been so unhappy that I have been crying<br/>Yes, most of the time<br/>Yes, quite often<br/>Only occasionally<br/>No, never</p> <p>*10. The thought of harming myself has occurred to me<br/>Yes, quite often<br/>Sometimes<br/>Hardly ever<br/>Never</p> |
|--|--|

# Depression in Pregnancy

- Risks of untreated depression
  - Preeclampsia
  - Placenta abnormalities
  - Low birth weight
  - Developmental delay



# Depression in Pregnancy

- Women with depression have **twice** the risk of preterm delivery
  - Related to
    - Low educational level
    - History of fertility difficulties
    - Obesity
    - Stressful life events
  - Antidepressants do not contribute to preterm labor



# Depression in Pregnancy

- Risks of untreated depression
  - Poor follow up with OB appointments
  - Malnutrition, less likely to take folate
  - More likely to smoke, use alcohol, or other substances
  - Greater likelihood to develop postpartum depression

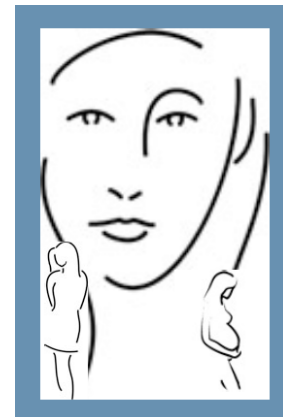


# Postpartum Depression

<b>Previous Condition</b>	<b>Risk of PPD</b>
Major depressive disorder	24 %
Depression in pregnancy	35 %
Previous PPD	50 %

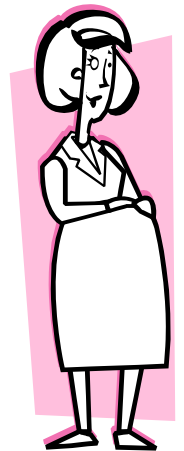
# Depression in pregnancy goes untreated

- Less than 1/3 of women receive treatment for depression during pregnancy
  - Who does get treatment?
    - History of depression
    - History of psychiatric treatment
    - Depression severity



# What happens to the untreated?

- High relapse risk
  - Relapse rate of 26% with continuing antidepressants
  - Relapse rate 68% with discontinuing antidepressants
  - 90% of relapses occur by 2<sup>nd</sup> trimester



# Medication Choice

**An individual decision  
that's made on a case by  
case basis!**



# Medication choices

- Pre-conception taper
- Stop medications entirely
- Stop and restart if symptoms
- Stop and restart after 1<sup>st</sup> trimester
- Continue through pregnancy
- Decrease dose
- Reduce or discontinue in late pregnancy
- Transition to psychotherapy

# General Guidelines

- Document Document Document
  - “I have explained the risks, benefits, and alternatives of psychiatric medications in pregnancy. Ms. X (and her partner) have given consent.”



# General guidelines

- Treat a woman as if she could become pregnant at any time...
  - Up to 80% of pregnancies are unanticipated
  - Document use of birth control
  - Encourage use of folic acid and multivitamin



# FDA labels

- Patients read them
- They will change
- They will be changing
  - Standard information on background rates
  - Fetal risk data
  - Clinical considerations
  - Registry information



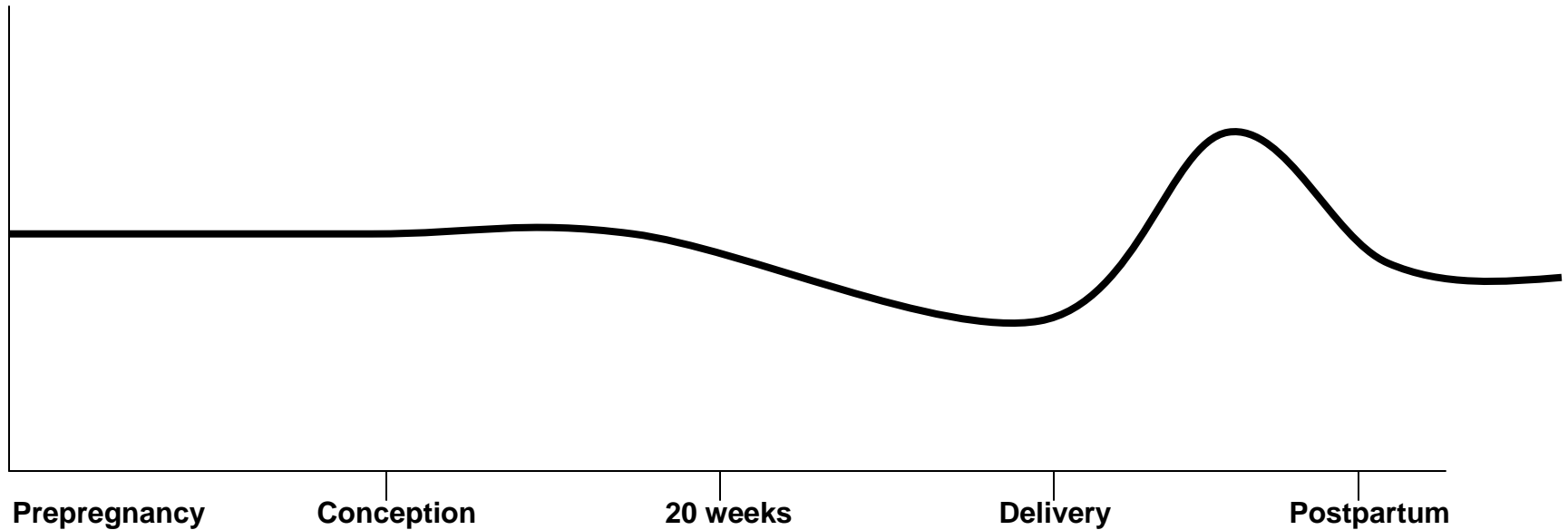
# FDA Classifications

- Most psychotropics are C
- None are A
- No antidepressants are FDA approved for pregnancy
  - No drug is “safe”
  - No good randomized, placebo-controlled studies
  - Most studies are retrospective, case reports, and registry data

# Treating Depression in Pregnancy

- Think **Sertraline** (Zoloft)
- Or whichever medication maintains stable mood

# SSRI Blood Levels and Pregnancy



Adapted from Sit et al 2008

# What should we be concerned about?

1. Organ malformation (teratogenicity)
  - Miscarriage is worst outcome of this
2. Neonatal Adaptation
  - Physical and behavioral symptoms noted shortly after birth
3. Long term behavioral abnormalities



# Medication Background

- Incidence of major birth defects in US is 2 to 4%
  - 65 – 70% of unknown cause
  - 2 – 4% medication related
- Period of maximum vulnerability for birth defects of the nervous system is 14 – 35 days post conception

# Medication Background

- Women usually find out when already 5-7 weeks gestation
- Therefore, may want to keep same medication if it's working



# Risk of miscarriage

- Increased slightly with SSRIs
  - 1.45 relative risk of miscarriage
  - Within normal population rates
- Bupropion (Chun-Fai-Chen 2005)
  - N = 136
  - Higher rate of spontaneous abortions
    - 15.4 % vs. 6.7 %
    - 12.4 % other antidepressants

# SSRIs and NEJM – article #1

- Alwan et al, 2007
  - N = 9622 with major birth defects
  - N = 4062 without birth defects
  - No overall congenital heart defects
  - As a group, SSRIs associated with increased risk of
    - Anencephaly (OR 2.4)
      - Baseline rate 20:100,000
    - Craniosynostosis (OR 2.5)
      - Baseline rate 5:10,000
    - Omphalocele (OR 2.8)
      - Baseline rate 1:10,000



# SSRIs and NEJM – article #2

- Louik et al, 2007
  - N = 9849 infants with birth defects
  - N = 5860 infants without birth defects
  - No overall birth defects for SSRIs as a group
  - Sertraline
    - omphalocele (OR 5.7)
    - Septal defects (OR 2.0)
  - Paroxetine
    - Right ventricular outflow tract obstruction defects (OR 3.3)

# Pedersen et al 2009 BMJ

- n = 493,113
- SSRIs overall increase risk of septal defects (OR 1.99)
  - Sertraline 3.25
  - Citalopram 2.52
  - Fluoxetine 1.34
  - Multiple SSRIs 4.70
- Risk increases 0.5% to 0.9%

# Paroxetine

- Has FDA warning against using in first trimester due to increased risk of cardiac defects

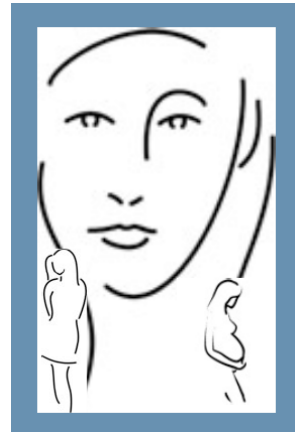


# Paroxetine

- Berard 2007
  - Looked at paroxetine vs. other ADs
  - 1403 women
    - 101 with major malformations
      - 24 of these were cardiac
  - Paroxetine OR = 1.38 vs. other 0.89
    - Not significant
  - However OR = 2.25 when paroxetine dose > 25mg daily

# Paroxetine

- Einarson et al. 2008
  - N = 3235 infants
  - Cardiac malformations
    - Paroxetine group 0.7%
    - Unexposed group 0.7%
- Paxil is not associated with heart defects in this group



# SSRIs and Persistent Pulmonary Hypertension of the Newborn

- 1 % risk in babies born to mothers taking SRIs after 20 weeks gestation
- Risk increases from 2/1000 to 6/1000
- Most recent studies have not shown an association

Chambers 2006 NEJM

Wichman 2009 Mayo Clinic Proceedings

Andrade 2009 Pharmacoepi Drug Safety

# Neonatal Adaptation Syndrome

- Present in 30% of babies born to mothers taking antidepressants late in pregnancy
- Peak
  - 3 days for term
  - 5 days for premies
- Monitor for 48 hours after delivery



Moses-Kolko EL et al, 2005 JAMA

Levinson-Castiel R, 2006 Arch Pediatr Adolesc Med

# Neonatal Adaptation Syndrome

- Tremors
- Increased muscle tone
- Feeding difficulties
- Irritability
- Respiratory problems
- Increased reflexes
- Increased crying
- Sleep changes
- Seizures



# SSRI Long Term Effects

- Children's IQ, language, development, temperament assessed and compared
  - Ages 15 -71 months
- No differences between groups
  - IQ negatively associated with duration of depression
  - Language negative associated with # MDD episodes after delivery

# Tricyclics in pregnancy

- The studies are conflicting
- Fetal tachycardia?
  - One case report
- Neonatal symptoms
  - Tachypnea
  - Tachycardia
  - Cyanosis
  - Irritability
  - Hypertonia
  - Clonus
  - Spasm



# MAOIs

- Not recommended in pregnancy
- Can be dangerous with medications used around the time of delivery
  - Tocolytics – terbutaline
- Increased congenital malformations x 3.4



# Electroconvulsive Therapy

- Safe and effective treatment
  - 70% of patients who have not responded to medications respond well to ECT
  - Effective for major depressive episode
    - Especially with psychosis or melancholic features
  - Effective for manic episode
  - Effective for acute schizophrenia episode

# ECT in Postpartum

- Medications with minimal risk to breastfeeding infant
- Monitor mother's memory and ability to care for child



# Non pharmacological treatments

- Decrease caffeine, nicotine, alcohol
- Improve sleep
- Increase relaxation
  - Pregnancy massage, yoga
- Psychotherapy
  - Interpersonal
  - Cognitive Behavioral
- Support groups
- Education
- Marital counseling
- Decrease psychosocial stressors
- Communicate with obstetrical team



# Postpartum Mood Disorders



# Postpartum Depression

- Two weeks after Ms. J's son is born, she begins to lose interest in life. Even though she is continually exhausted, she has trouble falling asleep when her baby sleeps. She has repetitive thoughts of her baby falling out the window but these thoughts scare her and she states she would never act on it.

# Postpartum Psychiatric Disorders

Disorder	Incidence	Time Course	Clinical Features
Postpartum Blues	70 – 80 %	Within first week and ends by 14 days	<ul style="list-style-type: none"><li>•Tearfulness</li><li>•Anxiety</li><li>•Insomnia</li><li>•Mood Instability</li></ul>
Postpartum Depression	13 - 20 %	Within first month and can last for a year	<ul style="list-style-type: none"><li>•Depression</li><li>•Guilt</li><li>•Anxiety</li><li>•Fear of harm to baby</li><li>•Obsessions</li></ul>
Postpartum Psychosis	0.1 – 0.2 %	Within first month	<ul style="list-style-type: none"><li>•Disorientation</li><li>•Confusion</li><li>•Delusions</li><li>•Hallucinations</li><li>•Rapid Mood Cycling</li></ul>

# Postpartum Depression

- Symptoms
  - Depression, crying
  - Inability to sleep when the baby sleeps
  - Intrusive thoughts
    - Thoughts of hurting the baby
    - Thoughts of hurting self
  - Suicidal thoughts
  - Loss of appetite
  - Lack of interest in the baby
  - Anxiety and panic attacks



# Postpartum Depression

- Places child at risk down the road
  - Lower self-esteem
  - More acting out
  - Nursing infants gain less weight
  - Duration of mother's episode correlated with degree of impairment in child



# Breastfeeding

- Most medications excreted into breast milk
  - **Most important determinant of drug penetration is mother's plasma levels**
- Drug levels in breastmilk are less than what crosses the placenta

# Medications in breastfeeding

- Avoid long half life or sustained release medications
- Schedule medication dosing immediately after feeding or right before long rest period
- Advise mother to monitor for oversedation, especially with cosleeping

# SSRIs with Breastfeeding

- Monitor baby's behavior with any medication
  - Half life may be extended in infant
  - Case reports of severe colic, fussiness, crying, poor weight gain



# Antidepressants and Breastfeeding

- N = 78 breastfed infants of mothers taking antidepressants
  - Mothers mood assessed at 6, 12, and 18 months
- Results
  - No difference in child weights with population norms
  - Infants of mothers with MDD relapse (> 2 months duration) weighed less than those with euthymic mothers and those with a relapse < 2 months

# Antidepressants and Breastfeeding

- No detectable or low levels in infant
  - Nortriptyline
  - Paroxetine
  - Sertraline
- Increased levels
  - Citalopram 17 % of the cases
  - Fluoxetine 22 % of the cases

# Antidepressants and Breastfeeding

- Paroxetine (Stowe 2000)
  - N = 16 pairs
  - Level of paroxetine increased in hindmilk
  - No level found in infants
- Sertraline (Stowe 2005)
  - N = 11
    - Levels of sertraline in 3 infants
    - Levels of desmethylsertraline in 6 infants

# Antidepressants in Breastfeeding

- Tricyclic antidepressants OK
  - Not doxepin though
    - Due to concern of respiratory depression



# Postpartum **Depression** – Nonpharmacological Treatment

- Check thyroid function
- Increase support
- Psychotherapy
  - Interpersonal Psychotherapy
- Phototherapy
- ECT



# Treating Bipolar Disorder in Pregnancy

- Ms. B has bipolar disorder but is stable on lithium and sertraline. She asks about medication for her bipolar disorder during pregnancy and breastfeeding. What do you tell her?

# Risk of Relapse of Bipolar Disorder in Pregnancy

- Viguera 2007
  - N = 89 pregnant women with BPAD I or II
  - Continue medications - 37% relapse
  - Discontinue medications - 85% relapse

# Postpartum **Psychosis**

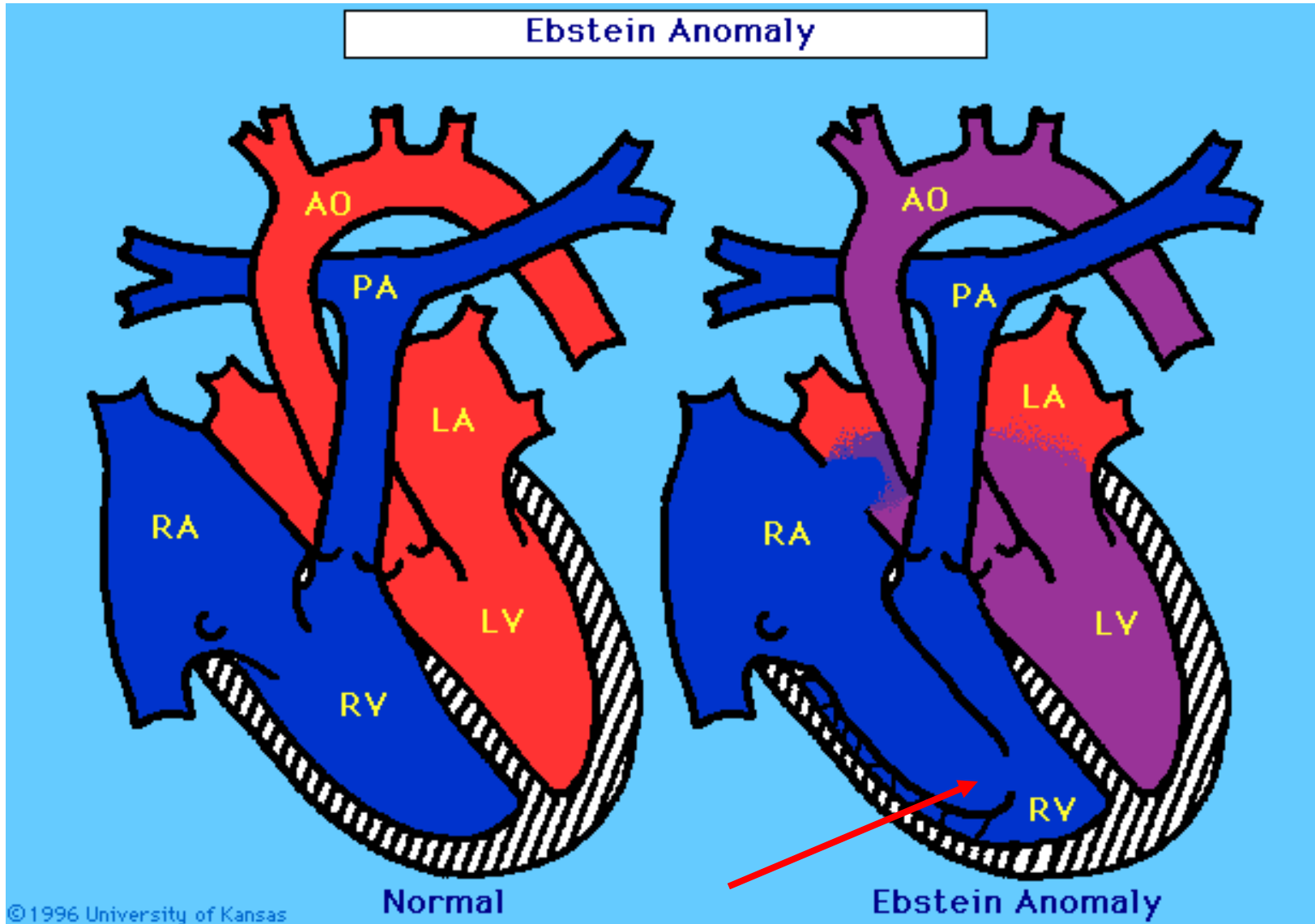
- Related to bipolar disorder
  - History of Bipolar Disorder leads to 35% risk postpartum psychosis
  - 60 % risk of recurrent affective illness after Postpartum psychotic episode
- Significant danger to child
  - Risk of abuse, neglect, infanticide, suicide
  - HOSPITALIZE

# Lithium in Pregnancy

- Lithium Register 1980 (N = 225 1st trimester exposures)
  - Ebstein's anomaly = 1% (400 X normal)
- More recent estimate at 10-20 x general population
  - Baseline risk = 1:20,000 (0.005%)
  - Lithium risk = 1:1,000 (0.1%)



# Ebstein's Anomaly



# Lithium

- Neonatal toxicity
  - “floppy baby”: cyanosis, hypertonicity
- Neurobehavioral
  - 5 year follow-up study (n = 60) – 2<sup>nd</sup> and 3<sup>rd</sup> trimester exposure
    - Parents given questionnaires
    - Exposed children compared with non-exposed siblings
    - No significant differences in developmental anomalies between groups

# Lithium in Pregnancy

- May require higher doses to achieve pre pregnancy therapeutic levels
  - Increased volume of distribution
  - Increased renal plasma flow, increased renal clearance

# Lithium in Pregnancy

- Newport et al 2005 Lithium Guidelines
  - Monitor Li Closely
    - Check Li levels weekly (at least monthly in first trimester)
    - avoid salt restriction and diuretics
    - Stop Li with delivery
      - 24-48 hours before planned induction or c-section
      - At onset of labor
    - Restart at pre-pregnancy dose after delivery

# Lithium and Breastfeeding

- Breast milk Lithium concentration = 30-100% mother serum Lithium concentration
  - Cyanosis, ↓ muscle tone, T-wave changes
- **Not recommended**



# Anticonvulsants

- All studies done in women receiving anticonvulsants for epilepsy
  - None in women with primary psychiatric disorder
  - Women with epilepsy bear more children with malformations
    - 3.5 %

# Valproic Acid and Pregnancy

- Associated with
  - Neural tube defects
  - Atrial septal defects
  - Cleft palate
  - Hypospadias
  - Polydactyly
  - Craniosynostosis

# Valproic Acid with Breastfeeding

- Breast milk / infants
  - < 1% - 10% concentration
  - Thrombocytopenic purpura
  - Anemia
  - **Generally felt to be reasonable**

# Carbamazepine

- Fingernail hypoplasia (26%)
- Developmental delay (20%)
- Craniofacial defects (11%)
- Don't forget neural tube defects (0.5% to 1%)
- Intrauterine growth retardation
- Transient cholestatic hepatitis
- Urinary tract abnormalities
- Cardiovascular abnormalities
- Fetal Vitamin K deficiency
  - Take 20mg daily oral Vitamin K
  - Pediatric dose of Vitamin K 1mg IM

# Carbamazepine in Breastfeeding

- “Probably safe”
- Possible effects
  - Transient cholestatic hepatitis
  - hyperbilirubinemia



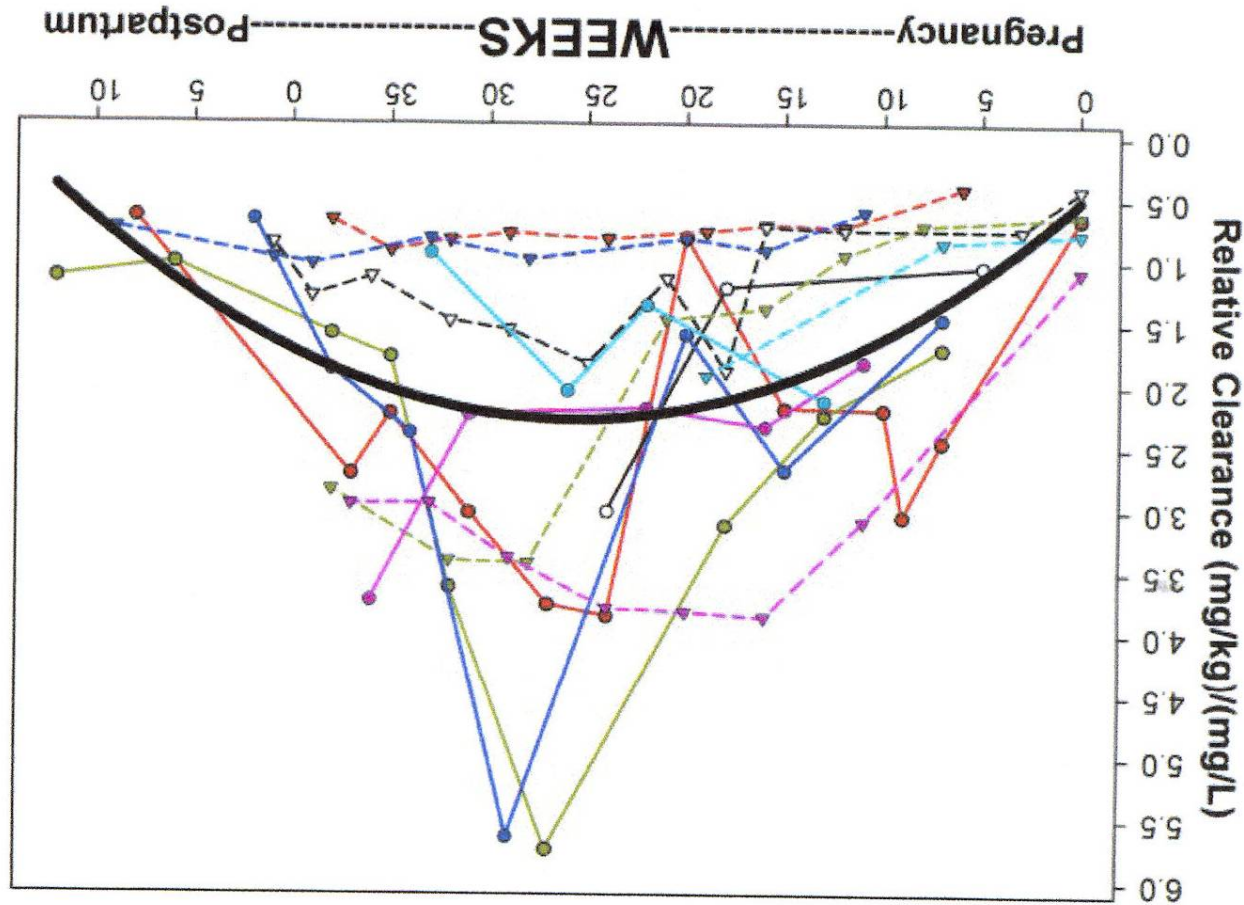
# Lamotrigine in Pregnancy

- Cunnington (2004)
  - N = 414 Lamotrigine
    - 2.9 % Major Congenital Malformations monotherapy
    - 12.5 % MCM when polytherapy with VPA
    - No specific pattern
    - Concerns
      - Poor neonatal adaptation
      - thrombocytopenia



# Lamotrigine Pharmacokinetics

294 NEUROLOGY 62 January (2 of 2) 2004



# Antipsychotics in Pregnancy

- Risperidone
  - 300 cases in pregnancy – probably OK
  - Breastfeeding
    - Data is conflicting on whether level present in infants
- Olanzapine
  - Lilly registry
    - No increased risk of complications
    - Metabolic problems
    - Lower birth weight
  - Low levels in breastmilk but some adverse effects
    - Cardiac problems, jaundice, lethargy, poor suckling, sleep problems, EPS, transient neurodevelopmental delay

# Antipsychotics in Pregnancy

- Quetiapine
  - 8 cases of congenital anomalies out of 487 reports
  - Low levels in breastmilk without difficulties



# Treating Anxiety in Pregnancy

- Ms. F has severe panic disorder and has a difficult time managing her anxiety without the use of a benzodiazepine. Now she is pregnant. What should she do?



# Benzodiazepines

- Teratogenicity
  - Oral clefts
    - General population = 0.06% (6:10,000)
    - 3 studies (diazepam): odds ratio = 2.4 (CI: 1.4 – 4.03)
    - 1 study (alprazolam): risk increased to 0.7% (7:1000)
      - Controversy over risk
  - Clonazepam
    - Animal studies show low to no risk
    - Case reports in women with no adverse effects

# Benzodiazepines

- Neonatal effects
  - 3<sup>rd</sup> trimester or parturition exposure
    - Sedation, muscular hypotonicity, failure to feed, impaired temperature regulation, apnea, and low Apgar scores.
    - Withdrawal signs: hypertonia, restlessness, irritability, seizures, inconsolable crying, tremors, etc.
      - Can appear after delivery to 3 weeks after birth
      - May last several months

# Benzodiazepines

- Behavioral effects
  - Impaired learning and memory, absence of startle reflexes, other sustained/subtle behavior
  - Data is conflicting



# Benzodiazepines and Pregnancy

Generally, if must use BZs in pregnancy, stick with ones that are short acting and don't have metabolites, e.g. lorazepam



# Take Home Points

- Depression in pregnancy is common
- Untreated depression in pregnancy carries risks for both the mother and the child
- No antidepressants are FDA approved in pregnancy
  - But sertraline is generally agreed to be “safest”
- Must weigh risks and benefits with the mother (and partner) on an individual basis

# Take Home Points

- SSRIs may be associated with septal defects, PPHN, and a neonatal syndrome.
- SSRIs are tolerated well in breastfeeding
  - Sertraline and paroxetine probably safest
- ECT is safe with pregnancy and breastfeeding



# Take Home Points

- Lithium is moderately safe in pregnancy but not with breastfeeding
- Carbamazepine and Valproic Acid are not safe in pregnancy but moderately safe with breastfeeding
- Lamotrigine and the atypical antipsychotics seem to be relatively safe in pregnancy but need more data
- Benzodiazepines may be associated with clefting



Midlands Postpartum Coalition

## Postpartum Depression and the Family Conference

October 7, 2011

Place: Dorn VA Medical Center  
6439 Garner's Ferry Rd.  
Columbia, SC 29209



Fee: \$45.00 if received by September 1, 2011

\$55.00 if received after September 1, 2011

Registration must be received by September 30, 2011.

**Mental Health America of South Carolina**  
**Attn: Postpartum Depression and the Family**

**1823 Gadsden St.**  
**Columbia, SC 29201**  
**or fax: 803-929-6147**

**For more information please call Anita Baker at 803-779-5363**  
**or by email [atbaker@mha-sc.org](mailto:atbaker@mha-sc.org).**

**Credit Card payments can also be made at**  
**[www.mha-sc.org](http://www.mha-sc.org)**

# Perinatal Mood Disorders

# Questions ?



# Resources

- <http://www.womensmentalhealth.org>
- [www.Motherisk.org](http://www.Motherisk.org)
- <http://www.emorywomensprogram.org>
- [www.postpartumprogress.com](http://www.postpartumprogress.com)
- Yonkers et al, 2009 APA and ACOG  
Consensus Statement, *General Hospital  
Psychiatry and Obstetrics and Gynecology*