



# Postpartum Mood and Anxiety Disorders

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# Disclosure Statement

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# Learning Objectives

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- Discuss the presentation of postpartum depression
- Discuss the risk factors for and the presentation of postpartum psychosis
- Review the treatment of mood disorders in the postpartum

# Postpartum Mood and Anxiety Disorders

Postpartum Blues

Postpartum Depression (PPD)

- DSM5: Peripartum onset specifier
- Onset within 4 weeks of delivery

Postpartum Psychosis

Postpartum Episodes of Bipolar Disorder

Postpartum Anxiety Disorders or Symptoms

# Postpartum Depression

- 10-15% of women experience major depressive episodes after delivery (25-40% of women with histories of MDD)
- Symptoms similar to non-puerperal major depressive episodes
  - Depressed mood, insomnia, fatigue, anhedonia, suicidal ideation
  - Anxiety is prominent, often marked obsessions, hypochondriasis are present
- Impairment of functioning



# Negative Effects of Maternal Depression on the Child

- Insecure attachment
- Behavioral problems
- Cognitive function
- Increased risk of abuse, neglect
- Childhood psychiatric diagnoses & symptoms
- Compliance with preventative measures
- Thoughts of harming infant

Civic & Holt, 2000; Cicchetti et al., 1988; Feldman et al., 1999; Murray et al., 1999; Murray et al., 1996; Sharp et al., 1995; Kotch et al., 1999; Cadzow et al., 1999; Jennings et al., 1999; McLennan & Kotelchuck, 2000; Weissman et al., 2006.

# Postpartum Depression: Obsessions and Compulsions

- Obsessions are often present
- Obsessions more common than compulsions/rituals
- Obsessions more common in PPD (57%) than in non-puerperal MDD (36%)
- OCD in 9-11% of postpartum women
- 37.5% report subsyndromal OCD
- Aggressive obsessions > contamination > checking rituals

Miller et al., *J Women's Health* 2015; Wisner et al. *J Clin Psychiatry* 1999; Zambaldi et al. *Compr Psychiatry* 2009; Arnold *Prim Care Companion J Clin Psychiatry* 1999.

# Differentiating OCD and Psychosis

- Postpartum OCD
  - Thoughts are ego-dystonic
  - Disturbed by thoughts
  - Avoid objects or being with their newborn
  - Very common disorder
  - Low risk of harm to baby
- Postpartum Psychosis
  - Thoughts are ego-syntonic
  - May not be distressed by thoughts
  - May not show avoidant behaviors
  - Not common disorder
  - High risk of harm to baby



# Breastfeeding

- ...The experience of breastfeeding is special for so many reasons – the joyful bonding with your baby, the cost savings, and the health benefits for both mother and baby...
  - <http://www.womenshealth.gov/breastfeeding/why-breastfeeding-is-important/index.html>
- ...Time to declare an end to the breastfeeding dictatorship that is drowning women in guilt and worry just when they most need support...

Gayle Tzemach Lemmon, **Breastfeeding is a Choice, Let's Treat it that Way**  
Posted: 05/11/2012 [http://www.huffingtonpost.com/gayle-tzemach/breastfeeding\\_b\\_1509658.html](http://www.huffingtonpost.com/gayle-tzemach/breastfeeding_b_1509658.html)



# Postpartum Depression: Etiology and Risk Factors

# Risk for Postpartum Depression: Hormonal Variables

- Inconsistent findings: no one hormone has been implicated in the cause of PPD
- Thyroid dysfunction is common- either hypo- or hyperthyroidism (hypothyroidism more common; thyroiditis with acute hyperthyroidism may occur)
- Behavioral sensitivity to gonadal steroids in women with PPD has been demonstrated
  - Models of hormone withdrawal to simulate postpartum hormonal decreases in estrogen and progesterone can reproduce depressive symptoms in small studies of women with histories of PPD (*Bloch Am J Psychiatry 2000*)

# Postpartum Depression Predictors Inventory

## Stronger Predictors:

- History of depression
- Depression in pregnancy
- Anxiety in pregnancy
- Stressful life events
- Marital dissatisfaction
- Child care stress
- Inadequate social supports
- Difficult infant temperament
- Low self-esteem
- Family History of Postpartum Depression – heritability 44-54% (from twin and sibling studies)

## Weaker Predictors:

- Unwanted or unplanned pregnancy
- Lower socioeconomic status
- Being single
- Postpartum blues

# Risk for Postpartum Illness: History of Psychiatric Illness

- Depression during pregnancy is a robust predictor of postpartum illness
- History of PPD or PP psychosis: 50-70% risk of recurrence
- History of bipolar disorder: 30-50% risk of PP illness
- History of recurrent MDD: Up to 30% risk of PPD

Cohen et al. *Psychiatr Clin North Am.* 2010; Pearlstein et al. *Am J Obstet Gynecol* 2009.

# Screening for Postpartum Depression

# PPD, Screening, and Large Scale Efforts

- Federal legislation includes provisions for postpartum depression
  - Language on screening for PPD and increased funding for its treatment and research
- Several states have already implemented universal screening or are in the process of implementing screening
- Political impetus to screen for PPD

# Postpartum Psychiatric Illness: Detection

- PPD is frequently missed
- Overlap with “normal” postpartum experience: decreased sleep, fatigue, overwhelmed, anxiety (“normal” or not)
- Multiple contacts with health care providers provides opportunity for detection
- Edinburgh Postnatal Depression Scale (EPDS): frequently used, 10-item, self-rated

Cox et al. *Br J Psychiatry*. 150:782-786.



# Screening for Depression in Adults

## US Preventive Services Task Force Recommendation Statement

**DESCRIPTION** Update of the 2009 US Preventive Services Task Force (USPSTF) recommendation on screening for depression in adults.

**METHODS** The USPSTF reviewed the evidence on the benefits and harms of screening for depression in adult populations, including older adults and pregnant and postpartum women; the accuracy of depression screening instruments; and the benefits and harms of depression treatment in these populations.

**POPULATION** This recommendation applies to adults 18 years and older.

**RECOMMENDATION** The USPSTF recommends screening for depression in the general adult population, including pregnant and postpartum women. Screening should be implemented with adequate systems in place to ensure accurate diagnosis, effective treatment, and appropriate follow-up. (B recommendation)

JAMA. 2016;315(4):380-387. doi:10.1001/jama.2015.18392

# Postpartum Depression Screening

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## PPD Screening:

- 1) Does it translate into treatment engagement?
- 2) Does it yield better outcomes?

# Pitfalls: Risks of Screening Without a Net

## Screening itself does not lead to better outcomes

- Several studies indicate that screening in obstetric setting has not yielded higher rates of treatment engagement
- Women receiving care often receive suboptimal treatment
- Low rates of follow-up on referrals, especially if mental health treatment is offsite
- Recent review: No evidence from any well designed studies that screening leads to better depression outcomes
- 22% rate of treatment engagement after screening (review, Byatt et al., 2015)
- Increased with health care provider education and provision of interventions

## Screening must be accompanied by:

- Adequate numbers of well-trained treaters to provide assessments and care to women who screen positive for PPD
- Care needs to be available and delivered in a timely fashion
- Treatment options must reflect heterogeneity of depression detected and patient preferences

Yonkers et al. *Psychiatric Serv* 2009; Flynn et al. *J Womens Health* 2006; Smith et al. *Gen Hosp Psychiatry* 2010; Nelson et al. *J Matern Fetal Neonatal Med.* 2013. Thombs et al., *J Psychosom Res.* 2014.; Byatt et al., *Obstet & Gynecol* 2015

# Postpartum Depression: Treatment

# Treatment Recommendations: Postpartum Depression

- Moderate to severe depression
  - Consider role of antidepressants; discuss risks and benefits with mother
- Use lowest effective doses
- Consultation with perinatal/reproductive psychiatry specialists as needed
- Maximize non-medication alternatives



# Postpartum Depression: Non-Pharmacologic Strategies

- Maximize social supports
- Psychoeducation of patient and family members
- Group therapy and support groups
- Interpersonal therapy (IPT)
- Cognitive-behavioral therapy (CBT)
  - Similar results: fluoxetine vs. 6 sessions CBT

Cohen et al. *Psychiatr Clin North Am.* 2010; Perlstein et al. *Am J Obstet Gynecol* 2009; Appleby et al., 1997.

# Antidepressant Trials for the Treatment of PPD

Study	Design and Size	Medication studied, result
Appleby et al., 1997	Placebo-controlled, N=87 CBT studied in same trial	Fluoxetine - superior to placebo
Yonkers et al, 2008	placebo controlled, N=70	Paroxetine - not superior to placebo)
Wisner et al., 2006	RCT, Setraline vs. Nortriptyline, N=109	Sertraline vs. Nortriptyline - no significant difference
Hantsoo et al., 2013	Placebo-controlled RCT, N=36	Setraline- superior to placebo
Bloch et al., 2012	N=40, all received brief psychodynamic therapy, RCT to sertraline or placebo	Both groups improved – no significant difference for sertraline vs. placebo
Sharp et al., 2010	RCT, AD selected by general practitioner or counseling, N=254	Antidepressants- superior to placebo
Misri et al., 2012	Open trial, N=15	Citalopram – open study
Misri et al., 2004	N=35, all received parox, half randomized to CBT also	Paroxetine – no control group
Stowe et al., 1995	Open-label; N=21	Sertraline – open study
Cohen et al., 1997	Open-label; N=19	Venlafaxine- open study
Suri et al., 2001	Open-label; N=6	Fluvoxamine - open
Nonacs et al., 2005	Open-label; N=8	Bupropion- open

# Antidepressant Treatment During Breastfeeding

Most studies of infant exposure to antidepressants show low levels of drug in breast milk and infant serum

Weissman et al., 2004; Burt et al., 2001



# Breastfeeding and Antidepressants

<b>Fluoxetine</b>	<p>Due to long half life, may be more likely to be found at detectable levels in infant serum, especially at higher doses.</p> <ul style="list-style-type: none"><li>• Reasonable for use if a woman has had a good previous response to it and reasonable to consider if used during pregnancy.</li></ul>
<b>Sertraline</b>	<ul style="list-style-type: none"><li>• Consistent reports of low levels of exposure, relatively large amount of study</li></ul>
<b>Citalopram, escitalopram</b>	<ul style="list-style-type: none"><li>• Less systematic study of mom-baby pairs compared with sertraline and paroxetine, observed low levels of exposure to infant via breastfeeding</li></ul>
<b>Paroxetine</b>	<ul style="list-style-type: none"><li>• Consistent reports of low levels of exposure, relatively large amount of study</li><li>• Use limited by commonly experienced withdrawal symptoms, maybe more sedating than other SSRIs</li></ul>
<b>Bupropion</b>	<ul style="list-style-type: none"><li>• Paucity of systematic study; a few case reports in older infants that demonstrate low levels of exposure via breastfeeding</li><li>• May be advantageous in smokers</li><li>• Reasonable for use if women have had good previous response</li><li>• One case report of possible infant seizure</li></ul>
<b>Venlafaxine, Desmethyl venlafaxine</b>	<ul style="list-style-type: none"><li>• Higher levels of desmethylvenlafaxine found in breastmilk than venlafaxine</li><li>• No adverse events reported</li></ul>
<b>Tricyclic Antidepressants</b>	<ul style="list-style-type: none"><li>• Considered reasonable for breastfeeding if use clinically warranted; few adverse effects in babies and generally low levels of exposure reported</li></ul>
<b>Mirtazapine, nefazodone, MAOIs, duloxetine</b>	<ul style="list-style-type: none"><li>• Systematic human lacking in the context of breastfeeding</li></ul>

# Brexanolone (SAGE-547)

## Allopregnanolone/Neurosteroids

- FDA approval in 2019
- IV delivered analogue of allopregnanolone
- Allosteric modulator of GABA receptors
- Two positive, controlled trials in postpartum depression (onset during late pregnancy or postpartum, presented within six months postpartum with MDD)
- Rapid onset of benefit, durable efficacy to 30 days
- Implementation challenges: cost, in hospital

# Prevention of Postpartum Depression



# US Preventative Task Force 2019

JAMA | US Preventive Services Task Force | RECOMMENDATION STATEMENT

## Interventions to Prevent Perinatal Depression: US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

**IMPORTANCE** Perinatal depression, which is the occurrence of a depressive disorder during pregnancy or following childbirth, affects as many as 1 in 7 women and is one of the most common complications of pregnancy and the postpartum period. It is well established that perinatal depression can result in adverse short- and long-term effects on both the woman and child.

**OBJECTIVE** To issue a new US Preventive Services Task Force (USPSTF) recommendation on interventions to prevent perinatal depression.

**EVIDENCE REVIEW** The USPSTF reviewed the evidence on the benefits and harms of preventive interventions for perinatal depression in pregnant or postpartum women or their children. The USPSTF reviewed contextual information on the accuracy of tools used to identify women at increased risk of perinatal depression and the most effective timing for preventive interventions. Interventions reviewed included counseling, health system interventions, physical activity, education, supportive interventions, and other behavioral interventions, such as infant sleep training and expressive writing. Pharmacological approaches included the use of nortriptyline, sertraline, and omega-3 fatty acids.

**FINDINGS** The USPSTF found convincing evidence that counseling interventions, such as cognitive behavioral therapy and interpersonal therapy, are effective in preventing perinatal depression. Women with a history of depression, current depressive symptoms, or certain socioeconomic risk factors (eg, low income or young or single parenthood) would benefit from counseling interventions and could be considered at increased risk. The USPSTF found adequate evidence to bound the potential harms of counseling interventions as no greater than small, based on the nature of the intervention and the low likelihood of serious harms. The USPSTF found inadequate evidence to assess the benefits and harms of other noncounseling interventions. The USPSTF concludes with moderate certainty that providing or referring pregnant or postpartum women at increased risk to counseling interventions has a moderate net benefit in preventing perinatal depression.

**CONCLUSIONS AND RECOMMENDATION** The USPSTF recommends that clinicians provide or refer pregnant and postpartum persons who are at increased risk of perinatal depression to counseling interventions. (B recommendation)

# PPD Prevention: non-pharmacologic

- Interpersonal Psychotherapy
- Cognitive behavioral therapy
- Groups and individual psychotherapies

US Preventative Task Force, JAMA 2019  
Zlotnick et al., 2016, Werner et al., 2014; Kozinsky et al., 2012

# RCTs of Antidepressants for Prevention of PPD in women at risk

Study	High Risk defined by...	Intervention	N	Findings
Wisner et al., 1994	Past h/o postpartum MDD	Open trial; monitoring alone vs. monitoring + a medication that had been effective for the previous episode or nortriptyline (pt selected monitoring vs. monitoring + med)	N=23; monitoring compared to medication +monitoring	Significantly greater proportion of the women who elected <b>monitoring alone (62.5 percent) suffered recurrence</b> compared to monitoring plus medication (6.7 percent) (p = .0086)
Wisner et al., 2001	Past h/o postpartum MDD	RCT: Nortriptyline vs. placebo (started immediately postpartum) x 20 wks	N=51 (N=26 Nortrip; N=25 placebo)	No significant differences between groups; <b>about 25% recurrences for both</b> (6/25 relapsed on placebo; 6/26 on nortrip)
Wisner et al., 2004	Past h/o postpartum MDD	RCT: Sertraline v. Placebo (started immediately postpartum) x 17 wks (followed for 20 wks)	N=22 (N=14 sert, N=8 placebo)	7% recurrence with sert; <b>50% recurrence with placebo</b> (significantly different)

# Bipolar Disorder: Postpartum Considerations

# Pregnancy & Postpartum: Risks of Discontinuing Medication

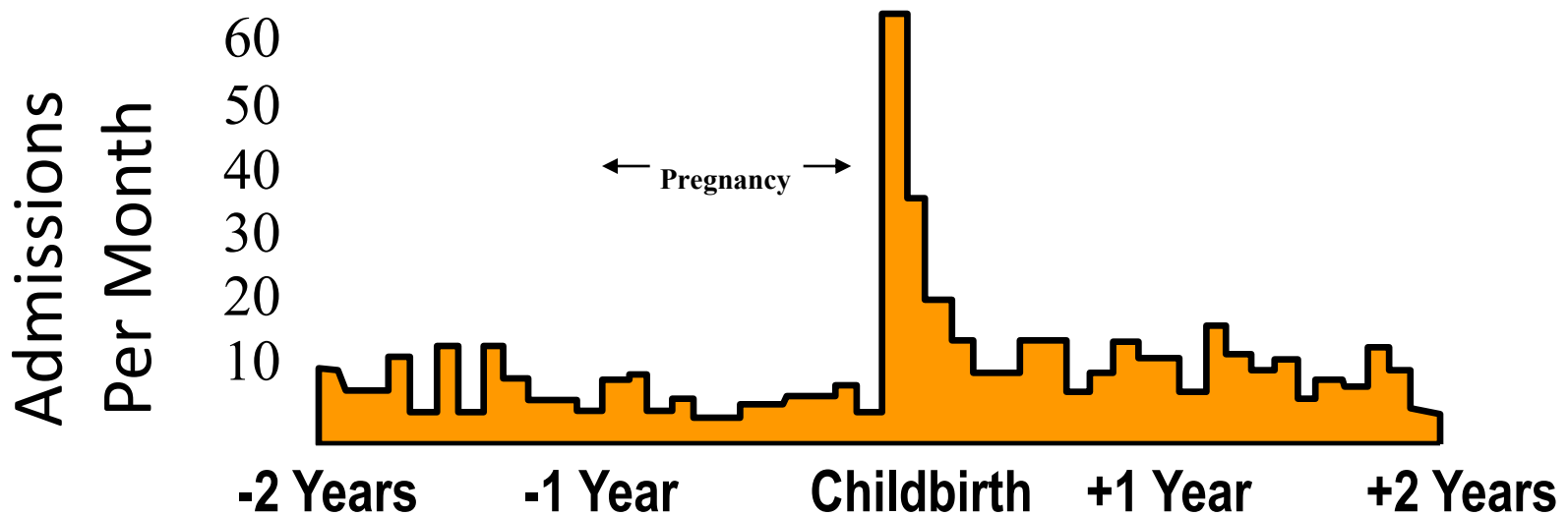
## Viguera, et al. 2000:

- Retrospective comparison of recurrence rates, pregnant (N=42) vs. nonpregnant women (N=59) with bipolar disorder
- Rates of recurrence after discontinuation of medication
  - Similar for pregnant and nonpregnant women, except more depressive episodes in pregnant women (**overall recurrence rate = 55%**)
  - **Women at increased risk of recurrence postpartum (70% vs. 24%; 2.9 x more likely to have recurrence than nonpregnant women after same time course)**
  - **Recurrence risk greater after rapid discontinuation ( $\leq 2$  wks) than gradual (2-4 wks)**

Viguera, et al. 2000



# Risk of Psychiatric Hospitalization During Pregnancy and Postpartum



Kendell et al. *Br J Psychiatry*. 1987;150:662.

Highest risk of hospitalization for new mothers 10-19 days postpartum, increased outpt contacts 1<sup>st</sup> three months

-Munk-Olsen et al., *JAMA*, 2006

# Postpartum Psychosis

# Postpartum Psychosis

- 1 to 2 per 1000 pregnancies
- Rapid, dramatic onset within first 2 weeks
- **High risk of harm to self and infant**
- **Suspect Bipolar disorder:**
  - Underlying diagnosis: affective psychosis (bipolar disorder or schizoaffective disorder)
  - Family and genetic studies, index episode follow-up

Nonacs and Cohen, 1998; Jones & Craddock, 2001;  
Spinelli, AJP, April 2009

# Diagnosis?

- Majority have bipolar disorder or schizoaffective disorder (72-80%)
- Schizophrenia (12%)
- More likely to be related to an affective disorder than not
- Risk factors:
  - history of postpartum psychosis
  - previous psychosis
  - bipolar disorder
  - previous psychiatric hospitalizations

Spinelli, AJP, 2004

# Postpartum Psychosis

- Psychiatric emergency
- Estimated that 4% of women with postpartum psychosis commit infanticide
  - Actual rates of infanticide are difficult to estimate, as infanticide may be under-reported

Spinelli, AJP 2004; Spinelli, AJP 2009

Risk Factor	% that developed postpartum psychosis
Hospitalization for psychotic episode <b>during</b> the pregnancy	44%
Hospitalization for a past psychotic episode <b>prior</b> to the pregnancy	14.5%
Any previous psychiatric hospitalization	9.2%
Previous hospitalization for bipolar mood episode	2.0%
Baseline population risk	0.07%

Harlow et al, Arch Gen Psychiatry 2007

# Acute Treatment

- Inpatient psychiatric hospitalization
- Rule out medical conditions
- Length of stay depends on clinical condition
- Many women will need to stop breastfeeding
- Primary pharmacotherapy: mood stabilizer and an antipsychotic, with medications for anxiety, insomnia, and agitation as needed
  - Sequential use of benzodiazepines, antipsychotics, lithium and ECT proposed

Sit et al., J Women's Health, 2006; Bergink et al., AJP 2015

# Acute Treatment

- Inpatient Protocol: Sequential use: N=64
  - Step 1: Benzodiazepine (lorazepam), 3 days - 6% remitted (N=4)
  - Step 2: Antipsychotic: haloperidol or atypical – 19% remitted (N=12)
  - Step 3: lithium – 73% remitted (N=48)
  - Step 4: ECT – none underwent
  - Total of 98% remission; only 1 patient did not fully remit
    - Most women responded to by addition of lithium
  - Sustained remission at 9 months postpartum in 80%
    - Affective diagnosis more associated with remission than non-affective
    - Relapse rates higher with antipsychotics than with lithium

Bergink et al., AJP 2015



# Treatment After Discharge

- Little data to inform length of care
  - 6-12 months of pharmacotherapy
  - psychotherapy and close monitoring
- Treatment planning for adequate sleep, support, help in meeting the needs of caring for a baby
- Close monitoring is required for safety
  - Psychoeducation of family and friends

# Postpartum Relapse: Bipolar Disorder

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- Pharmacotherapy strongly influences rate of relapse

# Prevention of Postpartum Psychosis

- Are outcomes different in women who have only had postpartum psychotic episodes and no other mood episodes?
- When should medication prophylaxis be initiated?
  - Most using lithium
  - Advised to use lithium prophylaxis immediately after delivery

Bergink et al., AJP 2012

# Prevention of Postpartum Bipolar Episodes and Postpartum Psychosis

Group	During Pregnancy	With postpartum prophylaxis	Did not start postpartum prophylaxis	
Women with histories of <b>psychosis in the postpartum only</b>	<b>All (29/29) remained stable</b> off of medication during pregnancy	Started Postpartum Prophylaxis: No relapses (N=20)	Did not start Postpartum Prophylaxis: 44% relapse (N=9)	
Women with bipolar disorder	<b>24.4% relapse:</b> 75.6% on maintenance meds Relapse rates: 19.4% on meds 40% off meds	Of those who stayed well during pregnancy: postpartum relapse rate 7.7% on prophylaxis	Of those who stayed well during pregnancy: 20% relapse rate not on prophylaxis	<b>60% postpartum relapse among those who experienced mood episodes during pregnancy</b>

# Main points

- **History of isolated postpartum psychosis**
  - High risk for recurrence **postpartum**
  - Prophylaxis may be deferred to immediately postpartum if mother well throughout pregnancy
- Bipolar disorder
  - **High risk for recurrence throughout pregnancy and the postpartum**, particularly with medication discontinuation
  - High risk postpartum relapse, postpartum prophylaxis decreases risk
  - Clinical picture during pregnancy greatly factors into postpartum prognosis – do not delay treatment

# Postpartum Treatment

- **Prescribe Sleep!**
  - Sleep deprivation – similar to antidepressants regarding risk of induction of mania/hypomania (10%)
- **Prescribe Support!**
  - Good social support associated with quicker recovery, less symptomatic; better prophylaxis against episodes

Colombo, et al. 1999; Johnson, et al. 1999; Stefos, et al. 1996

# Mood Stabilizers & Breastfeeding

- **Lithium**

- Toxicity reported in cases with infant serum levels at 0.1-0.5 times the maternal level
- Contraindicated at one time by the American Academy of Pediatrics<sup>1</sup>
  - Revised to classification “Drugs That Have Been Associated With Significant Effects on Some Nursing Infants and Should Be Given to Nursing Mothers With Caution”

American Academy of Pediatrics 2001

# Mood Stabilizers & Breastfeeding

- **Lithium and Breastfeeding: Recent report**
  - N=10 mother-baby pairs;
    - Mother's stable, lithium monotherapy 600-1200 mg q day
    - Babies' serum levels 0.09-0.3 meq/L (average 0.16)
    - Transient increases in elevated infant TSH, BUN, Cr
  - **Recommendations** –consider when
    - 1) Bipolar disorder in mother that is stable
    - 2) Lithium monotherapy (or simple regimen)
    - 3) Adherence to infant monitoring
      - Monitoring Li level, TSH, BUN, Cr immediately postpartum, 4-6 weeks of age, and then every 8-12 weeks
    - 4) Healthy infant
    - 5) Collaborative pediatrician

Viguera, et al. 2007 (Feb)



# Avoiding Pregnancy

## Ask About Birth Control Methods and Document

## Interactions with Oral Contraceptives Pills (OCPs)

- May Decrease Efficacy of OCPs:
  - Carbamazepine
  - Oxcarbazepine
  - Topiramate
  - St John's Wort
  - Modafinil, armodafil
- Oral contraceptives may decrease lamotrigine levels

# Postpartum Depression in Fathers

- About 10% of fathers experience depression and/or high burden of depressive symptoms in the year postpartum
- Correlation between maternal and paternal depression
- Risk factors: maternal depression, prenatal depressive symptoms, relationship quality, birth concerns, younger age (20' s), financial worry, low education level/socioeconomic status

Bergstrom, Birth 2013; Paulson and Bazemore, JAMA 2010; Gawlik et al., Arch Women' s MH, 2014

# Take Home Points

- The postpartum is a vulnerable window of time for many women
- Women, children, and families are impacted
- Effective, safe, accessible, and acceptable treatments are needed
- Treatment considerations involve risks of medications, risks of the untreated disorder
- Unknowns
  - Warrant collaborative treatment decisions, prioritizing patient preferences

# ARS Question #1

What diagnosis has the strongest association with postpartum psychosis:

- A. Major depressive disorder
- B. Bipolar disorder
- C. Schizophrenia
- D. OCD

## ARS Question #2

Which psychotropic medication is generally not recommended for use during breastfeeding:

- A. Sertraline
- B. Lithium
- C. Valproic acid
- D. paroxetine



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Thank you!

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[www.womensmentalhealth.org](http://www.womensmentalhealth.org)