ProjectTEACH
FAMILIES THRIVE WITH GOOD MENTAL HEALTH

Presenter:

Elizabeth Fitelson, M.D.

Associate Professor of Psychiatry at CUIMC
Director, The Women's Program
Columbia University Department of Psychiatry

Contact:
eem36@cumc.columbia.edu

ProjectTEACH
FAMILIES THRIVE WITH GOOD MENTAL HEALTH

Bipolar Disorder

What Obstetric Clinicians Need to Know

NEW YORK STATE | Office of Mental Health

ProjectTEACH
FAMILIES THRIVE WITH GOOD MENTAL HEALTH

Disclosures

No relevant disclosures

NEW YORK STATE | Office of Mental Health

Outline:

- What is Bipolar Disorder?
  - How do we distinguish it from other psychiatric disorders?
- Why is it important for obstetric clinicians to know about Bipolar Disorder?
  - Pre-pregnancy medications and interactions with birth control
  - Risks in pregnancy
  - Risks postpartum
- Posptartum Psychosis: A Psychiatric Emergency
- Brief Overview of Mood Stabilizers in Pregnancy
- Managing the Postpartum Bipolar Patient
  - Acute Management
  - Beyond the “Fourth Trimester”

Case: 24yo woman with Bipolar 1 Disorder

- 24yo married woman presented for consultation about managing Bipolar 1 Disorder in pregnancy. She had been hospitalized twice for mania with psychosis. Her first episode was right after she graduated from college. She demonstrated pressured speech, was only sleeping 2 hours a night, was agitated, and had a delusion that one of her teachers was sending her telepathic signals. She was stabilized on valproate and olanzapine. Tapered off of both after one year with her psychiatrist, but within 2 months became acutely agitated and paranoid, and was physically aggressive. Stabilized on lithium and olanzapine. Olanzapine was tapered off after several months due to weight gain. Became depressed, and citalopram was added. At the time of presentation she had been stable for 3 years on the combination of lithium 1200mg daily and citalopram 20mg daily. She and her husband planned to start a family within the next year.

ProjectTEACH
FAMILIES THRIVE WITH GOOD MENTAL HEALTH

What is Bipolar Disorder?

Diagnostic Criteria

Screening tools

Distinguishing from other psychiatric and medical illness

DSM-5 diagnostic criteria for manic episode

A. A distinct period of abnormally and persistently elevated, expansive, or irritable mood and abnormally and persistently increased activity or energy, lasting at least 1 week and present most of the day, nearly every day (or any duration if hospitalization is necessary).

B. During the period of mood disturbance and increased energy or activity, 3 (or more) of the following symptoms (4 if the mood is only irritable) are present to a significant degree and represent a noticeable change from usual behavior:

1) Inflated self-esteem or grandiosity.

2) Decreased need for sleep (eg, feels rested after only 3 hours of sleep).

3) More talkative than usual or pressure to keep talking.

4) Flight of ideas or subjective experience that thoughts are racing.

5) Distractibility (ie, attention too easily drawn to unimportant or irrelevant external stimuli), as reported or observed.

6) Increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation (ie, purposeless non-goal-directed activity).

7) Excessive involvement in activities that have a high potential for painful consequences (eg, engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments).

C. The mood disturbance is sufficiently severe to cause marked impairment in social or occupational functioning or to necessitate hospitalization to prevent harm to self or others, or there are psychotic features.

D. The episode is not attributable to the physiological effects of a substance (eg, a drug of abuse, a medication, other treatment) or to another medical condition.

NOTE: A full manic episode that emerges during antidepressant treatment (eg, medication, electroconvulsive therapy) but persists at a fully syndromal level beyond the physiological effect of that treatment is sufficient evidence for a manic episode and, therefore, a bipolar I diagnosis.

NOTE: Criteria A through D constitute a manic episode. At least one lifetime manic episode is required for the diagnosis of bipolar I disorder.

DSM-5 diagnostic criteria for hypomanic episode

A. A distinct period of abnormally and persistently elevated, expansive, or irritable mood and abnormally and persistently increased activity or energy, lasting at least 4 consecutive days and present most of the day, nearly every day.

B. During the period of mood disturbance and increased energy and activity, 3 (or more) of the following symptoms (4 if the mood is only irritable) have persisted, represent a noticeable change from usual behavior, and have been present to a significant degree:

1) Inflated self-esteem or grandiosity.

2) Decreased need for sleep (eg, feels rested after only 3 hours of sleep).

3) More talkative than usual or pressure to keep talking.

4) Flight of ideas or subjective experience that thoughts are racing.

5) Distractibility (ie, attention too easily drawn to unimportant or irrelevant external stimuli), as reported or observed.

6) Increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation.

7) Excessive involvement in activities that have a high potential for painful consequences (eg, engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments).

C. The episode is associated with an unequivocal change in functioning that is uncharacteristic of the individual when not symptomatic.

D. The disturbance in mood and the change in functioning are observable by others.

E. The episode is not severe enough to cause marked impairment in social or occupational functioning or to necessitate hospitalization. If there are psychotic features, the episode is, by definition, manic.

F. The episode is not attributable to the physiological effects of a substance (eg, a drug of abuse, a medication, or other treatment).

NOTE: A full hypomanic episode that emerges during antidepressant treatment (eg, medication, electroconvulsive therapy) but persists at a fully syndromal level beyond the physiological effect of that treatment is sufficient evidence for a hypomanic episode diagnosis. However, caution is indicated so that one or two symptoms (particularly increased irritability, edginess, or agitation following antidepressant use) are not taken as sufficient for a diagnosis of a hypomanic episode, nor necessarily indicative of a bipolar diathesis.

NOTE: Criteria A through F constitute a hypomanic episode. Hypomanic episodes are common in bipolar I disorder but are not required for the diagnosis of bipolar I disorder.

Bipolar Disorder DSM-V

Comparison of DSM-5 criteria for bipolar I disorder and bipolar II disorder

	Bipolar I disorder	Bipolar II disorder
Manic episode(s)	Yes	No
Hypomanic episode (s)	Commonly occur, but not required	Yes
Major depressive episode(s)	Usually occur, but not required	Yes
Mixed features	May occur	May occur
Anxious distress	May occur	May occur
Rapid cycling	May occur	May occur
Psychotic features	May occur	May occur
Catatonia	May occur	May occur

Data from: American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, American Psychiatric Association, Arlington, VA, 2013.

ProjectTEACH
FAMILIES THRIVE WITH GOOD MENTAL HEALTH

UpToDate®

Bipolar Epidemiology and Course

- 1-3% lifetime prevalence (bipolar 1 and 2)
- Age of onset (diagnosis or 1st manic) in women early to mid 20's (late teens men), later dx possible
- Chronic, relapsing remitting course
- Depression is more frequent than mania (bipolar patients spend more time depressed than manic or hypomanic)
- Antidepressants without mood stabilizers can precipitate mania, mixed states, and more mood cycling
- Lifetime suicide risk is 15x general population
- Treatment mainstay is mood stabilizing medication, psychosocial support and attention to sleep and health

Differential and Comorbidity

- **Differential Dx:**
- Schizophrenia/schizoaffective
- Trauma/PTSD
- Substance Use Disorders
- Severe Anxiety D/o
- Thyroid Disorders
- Cushing's Dx
- Delirium (in medically ill)
- Iatrogenic (ie steroids)

- **Comorbidity:**
- Trauma/PTSD
- Substance Use Disorders
- Anxiety Disorders
- Obesity
- DM2
- Hyperlipidemia
- Obstructive Sleep Apnea
- Thyroid, other immune disorders

ProjectTEACH
FAMILIES THRIVE WITH GOOD MENTAL HEALTH

Screening:

EDPS or PHQ for Depression

Screen for Substance and Alcohol Use

Mood Disorders Questionnaire screens for mood elevation (but low specificity)

If you have concerns based on:

- Family history of bipolar
- Past diagnosis or medications suggestive of bipolar dx
- Presentation of mania/hypomania, mixed symptoms, or psychotic sx
- Unusual response to antidepressants (escalating agitation e.g.)

Call Project TEACH to discuss before initiating treatment or for management

Mood Disorder Questionnaire

Patient Name _____ Date of Visit _____

Please answer each question to the best of your ability

1. Has there ever been a period of time when you were not your usual self and...	YES	NO
...you felt so good or so hyper that other people thought you were not your normal self or you were so hyper that you got into trouble?	☐	☐
...you were so irritable that you shouted at people or started fights or arguments?	☐	☐
...you felt much more self-confident than usual?	☐	☐
...you got much less sleep than usual and found that you didn't really miss it?	☐	☐
...you were more talkative or spoke much faster than usual?	☐	☐
...thoughts raced through your head or you couldn't slow your mind down?	☐	☐
...you were so easily distracted by things around you that you had trouble concentrating or staying on track?	☐	☐
...you had more energy than usual?	☐	☐
...you were much more active or did many more things than usual?	☐	☐
...you were much more social or outgoing than usual, for example, you telephoned friends in the middle of the night?	☐	☐
...you were much more interested in sex than usual?	☐	☐
...you did things that were unusual for you or that other people might have thought were excessive, foolish, or risky?	☐	☐
...spending money got you or your family in trouble?	☐	☐
2. If you checked YES to more than one of the above, have several of these ever happened during the same period of time?	☐	☐

3. How much of a problem did any of these cause you - like being unable to work; having family, money or legal troubles; getting into arguments or fights?

☐ No problems ☐ Minor problem ☐ Moderate problem ☐ Serious problem

ProjectTEACH
FAMILIES THRIVE WITH GOOD MENTAL HEALTH

ProjectTEACH
FAMILIES THRIVE WITH GOOD MENTAL HEALTH

What Is Important to Know About Bipolar Disorder in Reproductive Age Women?

Pre-pregnancy medications and interactions with birth control

Risks in pregnancy

Risks postpartum

50% of Pregnancies are Unplanned!

- Likely higher in bipolar patients
- Mood stabilizers have important interactions with hormonal birth control
- Bipolar disorder has high morbidity in the perinatal period for mom, fetus, and family

Interactions Between Mood Stabilizers and Reproductive Health

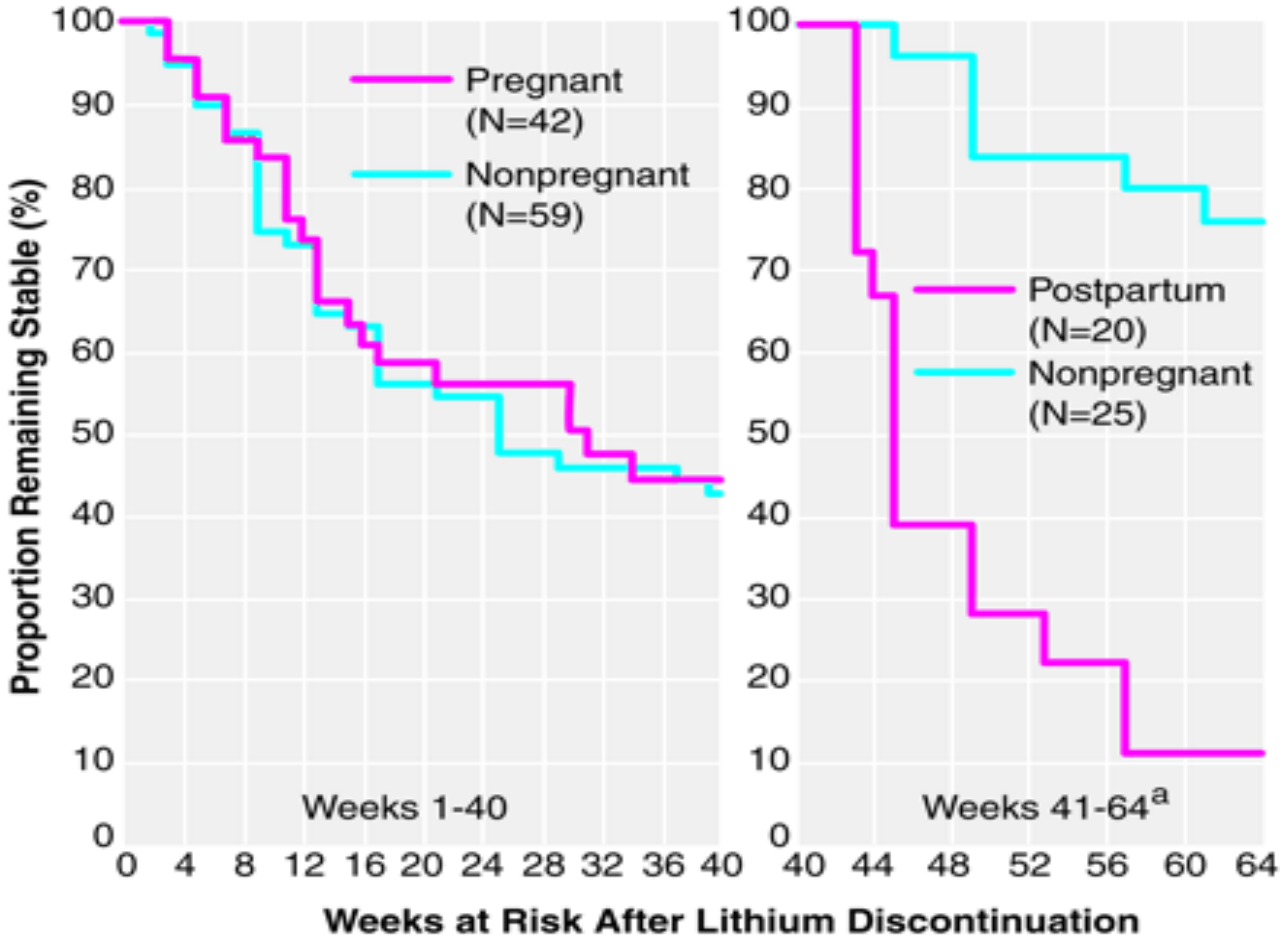
Drug	Menstrual/Hormonal Interactions	Pregnancy
Valproic Acid (Depakote)	Can cause PCOS OCP's lower VPA levels	Teratogenic in every trimester *should not be 1st line in reproductive age women!*
Lamotrigine	OCP's lower LMG levels 50%	No clear teratogenicity
Antipsychotics	Can elevate prolactin levels (impact on menses, fertility, bone health)	No clear teratogenicity; weight gain and metabolic monitoring; neonatal EPS (rare)
Carbamazepine/Oxcarbazepine	Lowers OCP effectiveness	First trimester NTD's, craniofacial abnormalities, low VitK
Lithium	None	Cardiac defects (slt), polyhydramnios, neonatal effects
Topiramate	Lowers OCP effectiveness	Some signal of teratogenic risk >200mg

Risks of BD and Pregnancy

- Poor self-care, poor nutrition, prenatal care, risks of substance use, poor judgment, fetal abuse/injury
- Effects on family system
- Adverse effects on fetal growth (premature birth, low birth weight, pre-eclampsia)
- Postpartum psychosis
- Suicide, infanticide

Wadhwa, 1993; Kurki 2000; Jablensky 2005

Bipolar Disorder and Pregnancy



Viguera et al, 2000

ProjectTEACH
FAMILIES THRIVE WITH GOOD MENTAL HEALTH

Postpartum Period is Particularly High Risk for Women with Bipolar Illness

- Lack of sleep
- Infant temperament
- Family stressors, role transition
- Sudden change in hormone levels
- Breastfeeding
- Immunological factors?

ProjectTEACH
FAMILIES THRIVE WITH GOOD MENTAL HEALTH

Postpartum Psychosis

A Psychiatric Emergency

Postpartum Psychosis

- Women with BD have highest risk for PPP
  - Baseline rate 1-2/1000
  - Bipolar women significantly higher risk (up to 20%)
  - 72-88% women with PPP have dx BD
- Onset 2 days to 4 weeks, waxing/waning course
- Paranoid, grandiose, or bizarre delusions,
- Mood swings, grossly disorganized behavior, confusion, cognitive disruption
- Risk for suicide, infanticide
- Psychiatric Emergency

Sit et al 2006; Chaudron 2003

Postpartum Psychosis (cont'd)

- Distinguish from pre-existing stable psychotic disorder
- Patient needs immediate psychiatric evaluation and cannot be alone with the infant (usually needs psych ER)
- If in doubt, call Project TEACH
- Medical workup: look for other causes of delirium, intoxication, immune dysfunction
  - CBC, LFTs, TFTs, BMP, B12, Folate, Utox
  - Consider imaging if focal findings

If you have a patient you are concerned may have PPP, send to ER AND/OR call Project TEACH!

ProjectTEACH
FAMILIES THRIVE WITH GOOD MENTAL HEALTH

ProjectTEACH
FAMILIES THRIVE WITH GOOD MENTAL HEALTH

Brief Overview of Mood Stabilizers in Pregnancy

Treatment Principals for Prescribing Psychotropics in Pregnancy

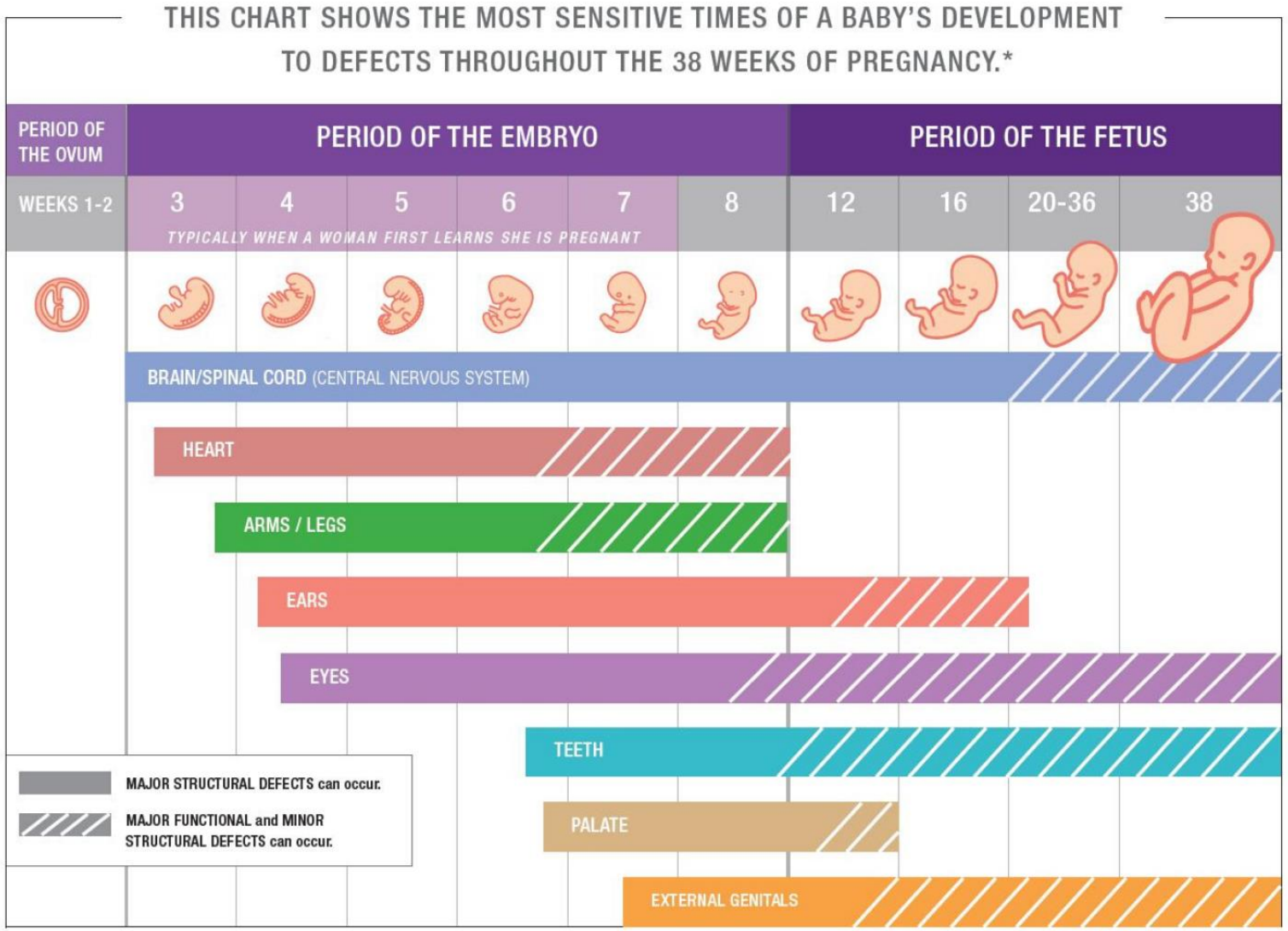
1. Know what you are treating
2. There are no risk-free decisions. Where there is illness, there is risk.
3. Cases by case, “risk of no/under treatment vs risks of treatment”
4. Maximize non-medication therapeutic options even when meds indicated
5. The best medication is usually the one that works for the patient
6. Avoid polypharmacy when possible
7. Use the lowest EFFECTIVE dose of medications
8. Re-screen, monitor effectiveness, changes across puerperium
9. Involve family/partner when possible, consider family system in risk
10. Communication and education with patient, supports, treatment team

ProjectTEACH
FAMILIES THRIVE WITH GOOD MENTAL HEALTH

Non-pharmacologic approaches

- Psychotherapy (IPSRT, CBT, supportive, etc)
- ECT, TMS
- Bright Light Therapy
- Support groups, peer support, telephone
- Acupuncture, yoga, meditation
- Exercise
- Sleep regulation
- Postpartum: Focus on practical and emotional supports

Use of Mood Stabilizers in Pregnancy



*All mood stabilizers cross the placenta; folate supplementation (5 mg/day) pre-conception and throughout pregnancy

mothertobaby.org; Adapted from Moore 1993, and the National Organization of Fetal Alcohol Syndrome (NOFAS) 2009.

ProjectTEACH
FAMILIES THRIVE WITH GOOD MENTAL HEALTH

Lithium

- First line for treatment of bipolar 1: reduces rates of suicide and postpartum psychosis
- MFM consult/monitoring indicated for women on lithium in pregnancy
- Teratogenicity
  - Ebstein's anomaly: abnormalities of tricuspid valve and right ventricle; risk increased from 1:20,000 to 1:2,000
  - Prevalence cardiac defects increased from ~1% -> 2%
  - Risk ratio proportional to dose (3x>900 mg)

Lithium

- Obstetric Complications
  - Hypothyroidism
  - Polyhydramnios
  - Nephrogenic diabetes insipidus
- Neonatal complications
  - Apnea, cyanosis
  - Hyperbilirubinemia
  - Muscle flaccidity and hypotonia
  - Hypothyroidism/hypoglycemia
  - Cardiac rhythm abnormalities
  - Seizures
- Neurodevelopmental outcomes
  - Data are limited but 3 small studies have **not** demonstrated negative outcomes

Jacobson 1992, Schou 1976, Forsberg 2018, Menon 2008

Lithium Management in Pregnancy

- Obtain preconception level and monthly in pregnancy, more frequently 3rd trimester
- Lithium levels *will decrease* in 2nd/3rd trimester (blood volume, renal metabolism)
- Close management with psychiatrist for mood monitoring
- Monitor fluid levels after 24 weeks
- Check more frequently in women at risk for dehydration, ie hyperemesis gravidarum
- No NSAIDS
- Fetal echocardiogram and high resolution ultrasound at 18-20 weeks
- Maintain hydration

Wesseloo 2017

Lithium

- Management postpartum (levels increase)
  - Decrease dose postpartum to preconception dose (unless unstable)
  - Check level 24 hours postpartum and 1-2x weekly first 2 weeks postpartum
- Breastfeeding
  - Only recommended after careful consideration in certain reliable/adherent patients of fullt erm infants who are able to monitor their babies
  - Monitor infant TSH/BUN/Cr

Lamotrigine

- FDA approved for maintenance of bipolar disorder but not effective for treatment of acute mania
  - 2008 study found that 30% of women taking lamotrigine had postpartum bipolar disorder relapses versus 100% of women not taking mood stabilizing medications
- Teratogenicity:
  - No clear evidence of birth defects with first trimester exposure (early concern for orofacial clefts was not confirmed with later data, rate is the same as general population ~0.7/1,000)
- Pregnancy complications
  - No significant differences found in birthweight
- Neurodevelopmental outcomes
  - No significant differences found in IQ

Newport 2008, Dolk 2008

Lamotrigine

- Management during pregnancy:
  - Obtain preconception level
  - Estradiol upregulates UGT1A4 which increases lamotrigine clearance
  - May require dose increase as early as 8 weeks gestation, though usually dosed by clinical sx rather than level
  - Disagreement about following levels, though if patient is on higher doses (>200mg) at the start of pregnancy may be useful q4 weeks
- Management postpartum
  - Taper to preconception dose postpartum(over 1-2 weeks) depending on clinical
  - Reduction 25% PPD 1
  - Lamotrigine clearance normal 4 weeks postpartum
  - Signs of toxicity: diplopia/ataxia/nausea/dizziness
- Breastfeeding
  - Infant serum levels reported 18- 50% maternal serum
  - No reports of neonatal Stevens Johnson Syndrome
  - No evidence of neurobehavioral toxicity

First Generation Antipsychotics

- Teratogenicity
  - No evidence of teratogenic risk in high potency typical AP (Haldol/Fluphenazine)
  - Possible teratogenic risk in low potency typical AP (Chlorpromazine)
- Neonatal outcomes
  - Risk of neonatal EPS with late fetal exposure (rare)
- Neurodevelopmental outcomes
  - No known neurobehavioral effects
- Lactation
  - Low transmission
  - No adverse effects reported

ProjectTEACH
FAMILIES THRIVE WITH GOOD MENTAL HEALTH

Gentile 2010, Yaeger 2006

Second Generation Antipsychotics

- Teratogenicity
  - Data does not support increased risk of malformations (*risperidone)
  - Polypharmacy more likely associated with congenital malformations
- Pregnancy outcomes
  - Metabolic risks (GDM), both SGA and LGA reported, ?preterm birth
  - Higher baseline weight, but not usually increased weight gain antepartum
- Neurodevelopmental outcomes
  - Few studies
- Breastfeeding
  - General rec to continue same medication as in pregnancy
  - Lactation: Generally low transmission, quetiapine lowest transmission
  - Monitor for sedation
  - Aripiprazole and brexiprazole may interfere with milk production (dopamine partial agonist effect)

Huybrechts 2016, Sadowski 2013

Second Generation Antipsychotics: Clozapine

- Cessation of clozapine more likely to result in severe relapses
- 2X risk of gestational diabetes
- Risks of neonatal seizures (rare), agranulocytosis (1 case report), low muscle tone
- Lactation: monitoring of infant level and WBC required. Single case report of agranulocytosis in breastfed infant

Mehta 2017

Depakote

- Teratogenicity
  - Neural tube defects (1-9%)-dose-response relationship
  - Neural tube development begins in early weeks of gestation before many women know they are pregnant
  - Increased risks hypospadias, polydactyly, facial clefts, cardiac defects, abnormal facial features
- Neonatal outcomes
  - Irritability/low apgar/hypertonia/feeding problems/hepatotoxicity/hypoglycemia/low fibrinogen
- Neurodevelopmental outcomes
  - Low IQ
  - Increased risk of autism
  - Increased risk ADHD
- Breastfeeding: Low transmission, but not recommended d/t risk of pregnancy in mother

Carbamazepine

- Teratogenicity
  - Risk of neural tube defects 0.5-1%
  - Risk of Craniofacial abnormalities, microcephaly, IUGR
- Neonatal abnormalities
  - Fetal vitamin K deficiency
  - Neonatal bleeding
  - Rec: 20mg/d oral vit K last month of pg, 1mg IM to neonate
- Neurodevelopmental outcomes
  - No association with cognitive dysfunction
- Breastfeeding
  - Case reports of transient hepatic dysfunction
  - OK with monitoring

ProjectTEACH
FAMILIES THRIVE WITH GOOD MENTAL HEALTH

Supporting Bipolar Women through the Postpartum

Patient and Family Support PP

- Frequent outreach
- Emphasize sleep: “Sleep is a mood stabilizer!”
- Discuss breastfeeding, bottle feeding, combination, in non-judgmental, supportive way
- Involve partner and all other support system
- Plan in advance for relapse: “plan for the worst, hope for the best”

Patient and Family Support PP (cont'd)

- Most mental-health related maternal death occurs beyond the "fourth trimester"
- Linkage to ongoing psychiatric care is critical
- Pay attention to comorbidities (ie substances, medical)
- Support resources for families (ie NAMI)

ProjectTEACH
FAMILIES THRIVE WITH GOOD MENTAL HEALTH

Staying Up to Date: Resources

- **Project TEACH**: https://projectteachny.org/
- Mothertobaby.org (free resources including fact sheets for patients)
- Reprotox.org (subscription site)
- Lactmed: https://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm
- Postpartum Support International: www.postpartum.net
- MGH Center for Women's Mental Health www.womensmentalhealth.org

ProjectTEACH
FAMILIES THRIVE WITH GOOD MENTAL HEALTH