Perinatal Mood and Anxiety Disorders (PMAD)
Project ECHO Pediatric Mental Health

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Disclosures: Katherine M. Moore, M.D.

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None

Off-Label/Investigational Uses

None

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Learning Objectives

- Review epidemiology of perinatal mood and anxiety disorders (PMAD)
- Review presenting signs and symptoms of PMAD
- Review use of screening tools in clinical settings
- Review psychotropic medication use during pregnancy and lactation
- Highlight useful provider and patient resources

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PMAD (Perinatal Mood and Anxiety Disorder) Epidemiology

- Common
- Perinatal depression: 1 in 7 women
- Estimates of prenatal anxiety: 13%-21% women affected
- Postpartum anxiety: estimated at 11%-17%
- Pregnant or postpartum women up to 2x more likely to experience OCD (Russel, 2013)
- 60% of women with perinatal depression have pre-existing comorbid psychiatric disorders

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Kendig S et al. Obstet Gynecol 2017;129: 422-30.

Women of childbearing age

- At a sociodemographic disadvantage
  - Nearly 55% live in poverty
- Maternal mental illness is common and associated with adverse maternal, fetal, and infant outcomes
  - Placental abnormalities
  - SGA fetuses
  - Fetal distress
  - Preterm delivery
  - Neonatal hypoglycemia
  - Adverse neurodevelopmental outcomes
  - Disordered attachment
  - High-risk behaviors
  - Less prenatal care
  - Alcohol, cigarettes, substances
  - Suicide
  - Infanticide

https://www.statista.com/statistics/233154/us-poverty-rate-by-gender/.

Preconception consultation is preferable to during pregnancy

- More time to make necessary changes
- Adjust to appropriate regimen
- Check concentrations at stability in nonpregnant state
- Add prenatal and additional folate (if recommended)

"Pregnant Women Get Sick-Sick Women Get Pregnant"

(Wisner KL et al. JAMA Psychiatry 2016;73(9):901-903.)

Screening

https://safehealthcareforeverywoman.org/patient-safety-bundles/maternal-mental-health-depression-and-anxiety/

Identify mental health screening tools to be made available in every clinical setting (outpatient obstetric clinics and inpatient facilities)

Without consistent screening, PMAD may go unrecognized

- Underreporting of symptoms
- Edinburgh Postnatal Depression Scale (EPDS)
- Patient Health Questionnaire 9 (PHQ-9)
- Consider screening for bipolar disorder (Mood Disorders Questionnaire—MDQ)

Whitton A et al. Br J Gen Pract 1996;46:427-428; Cox JL et al, Br J Psychiatry 1987;150:782-786;
Kroenke K et al. J Gen Intern Med 2001;16:606-613; Hirschfeld RM. Prim Care Companion J Clin Psychiatry 2002; 4:9-11

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Management of depression during pregnancy: principles

- If already utilizing psychotropic medications, plan ahead! Assume reproductive-age women will get pregnant!
- Ask about reproductive plans and contraception
- For mild to moderate illness, consider nonpharmacological interventions (psychotherapy: CBT or IPT)
- Best to do medication changes prior to pregnancy, if possible
- Consider history and diagnosis (ie, reconsider off-label use)
- Ideally, a woman should be stable psychiatrically for at least 3-6 months before attempting pregnancy

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PayneJL, Meltzer-Brody S. Clin Obstet Gynecol. 2009 Sept; 52(3):469-482.
Yonkers KA et al. Ob Gyn 2009;114:703.
Yonkers KA , Wisner KL et al. Gen Hosp Psych . 2009; 31:403-413.

General principles, continued

- Single medication at a higher dose favored over multiple medications
- Use lowest effective dose
- Limit changing of medication: decreases exposure to the fetus
- Consider prior exposure during pregnancy
- Available reproductive safety information

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ACOG Practice Bulletin, "Use of Psychiatric Medications During Pregnancy and Lactation", Obstr & Gyn, 110 (5), Nov 2007

Pharmacological treatment strongly considered for:

- Moderate to severe depression
- Active suicidal ideation
- Psychotic symptoms
- History of highly recurrent depression
- History of depressive relapse after stopping medication
- Clinical need for faster response

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Stewart DE. N Engl J Med 2011;365:1605-11
Yonkers KA et al. Gen Hosp Psychiatry 2009;31:403-13

Medication Use in Pregnancy

- Common (Mitchell, Am J Obstet Gynecol, 2011)
  - 82.3% of women take at least one medication (prescription or OTC, not counting vitamins or iron) during first trimester
  - 48.8% of women take a prescription medication during first trimester
  - 30% of women have exposure to four or more medications during first trimester (prescription or OTC)

- Psychotropics in pregnancy
  - 8% of pregnancy has exposure to an antidepressant (Mitchell, Am J Obstet Gyencol, 2011)
    - 2.8% have exposure to antidepressant throughout pregnancy (Reefhuis, N Engl J Med, 2006)
  - 1.3% of pregnancies have exposure to atypical antipsychotics (Toh, Arch Womens Ment Health, 2013)

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Medications

- FDA Pregnancy and Lactation Labeling Rule (PLLR), 2015 update
  - Clinicians must assess risk of untreated illness as well as potential adverse effects of pharmacotherapy
  - Assess impact on mother, fetus, and infant
  - No longer pregnancy classes for medication safety during pregnancy
    - These were misleading
    - Often based on limited information
      - Latuda- class B

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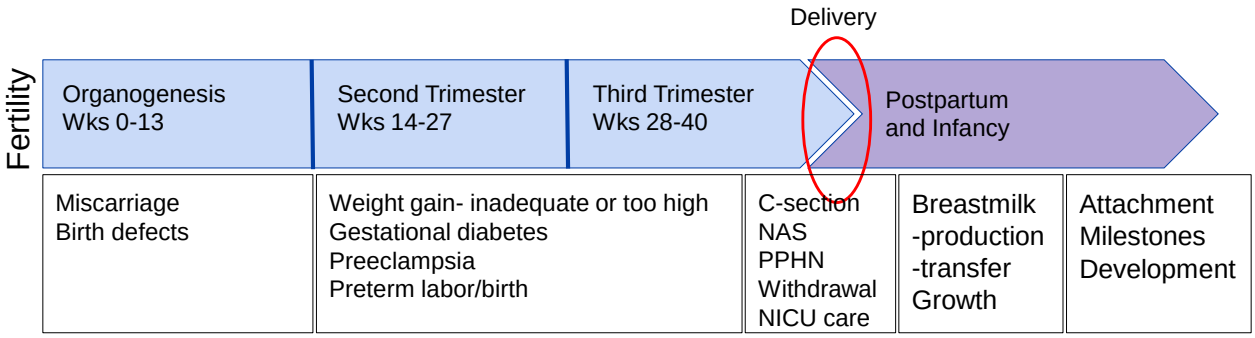
Pregnancy and Postpartum Windows of Effect



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Physiologic changes in pregnancy impact drug metabolism

- Hormonal shifts
- Increased plasma volume
- Increased renal clearance
- Changes in protein binding
- Hepatic metabolism changes
  - Estrogen induces UGT1A4 (lamotrigine)
  - Many of the CYP p450 enzymes

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Depression and Antidepressants

First Trimester:

- Evidence does not suggest that SSRI or SNRI (or TCA's, bupropion, mirtazapine, MAOI) medications increase rate of birth defects (Huybrechts 2014)- even paroxetine.
  - After adjusting for variables associated with underlying disease and restricting the comparison group to women with MDD
- No convincing evidence that antidepressants impact miscarraige rates (although associated)

Preeclampsia

- Risk of preeclampsia is 5.4% in women with depression and no antidepressant exposure
- SNRI and tricyclics during mid pregnancy associated with 1.5 fold increased risk of preeclampsia (Palmsten, Epidemiology, 2013).
- Severity of illness, potential confounder

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Depression and Antidepressants

- Preterm birth (PTB) and growth effects:
  - Mothers with depression are at higher risk for PTB
    - One study showed equivalent rates of PTB in treated and untreated depression (Wisner, Am J Psychiatry, 2009)
    - Another study showed treating the depression (with SSRI) decreased the risk of PTB (Malm, Am J Psychiatry, 2015)
      - Women with depression who also took antidepressants, had lower c-section rates than depressed women who did not take antidepressants (Malm, Am J Psychiatry, 2015)

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Depression and Antidepressants

- Persistent Pulmonary Hypertension of the Newborn (PPHN)
  - Large Medicaid database of 3.79 million pregnant women compared outcomes of women taking an SSRI, another class of antidepressant, or no antidepressant in the last 90 days of pregnancy (Huybrechts, JAMA, 2015)
  - After adjusting for confounders, restricting the sample to women with depression, and performing propensity score matching, the OR for PPHN was nonsignificant (OR=1.10; 95% CI, 0.94-1.29) as well as for non-SSRI antidepressants (OR=1.02; 95% CI, 0.77-1.35).
  - The adjusted odds ratio for a specific subtype of primary PPHN (not secondary to aspiration or lung hypoplasia), was 1.28 (95% CI, 1.01-1.64) and for non-SSRI antidepressants was 1.14 (95% CI, 0.74-1.74).
  - The absolute risk of PPHN is extremely small and any contribution for SSRI medications is more modest than previously suggested.

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Depression and Antidepressants

- NICU/supportive cares
  - Infants exposed to maternal depression are at higher risk for NICU admission (Malm, Am J Psych, 2015).
- Poor neonatal adaptation, often termed neonatal adaptation syndrome (NAS)
  - Newborn signs: restlessness, rigidity, tremor, tachypnea, hypoglycemia, temperature instability, and irritability
  - Reported in up to 30% of infants exposed to antidepressants during third trimester
    - More common in infants exposed to venlafaxine, paroxetine, and fluoxetine (Chambers, N Engl J Med, 1996)
  - Mechanism of NAS?
    - increased serotonergic stimulation at birth
    - withdrawal (rapid drug decline after birth)
    - neurobehavioral teratologic effects on fetal brain function

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Depression and Antidepressants:

- Development

  Developmental origins of health and disease hypothesis

  - Newborns exposed to depression in utero have lower attention scores (even compared to those exposed to SSRI) (Salisbury, Depress Anxiety, 2011).
  - In utero exposure to depression linked with difficult temperament in fnancy and childhood behavioral problems as well as psychiatric disorders in adolescence and childhood (Werner, Dev Psychobiol. 2007; Davis, J Am Acad Child Adolesc Psych. 2007; Glover, Best Pract. Res Clin Obstet. 2014; O'Donnell, Dev Psychopathol. 2014).
  - In utero exposure to maternal depression associated with elevated cortisol in infants that persists through adolescence (Velders, Neuropsychopharm. 2012).

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Depression and Antidepressants:

Development, cont:

SSRI exposure and motor development (Santucci, J Clin Psychiatry, 2014)

- Slower at 26 wks and 52 wks, caught up by 78 wks

Cognitive development

- IQ testing at ages 3-7, no difference in exposed vs not exposed (Nulman, Am J Psychiatry, 2002)

Autism

- Large-scale studies that adjust for confounding factors (maternal psychiatric disorders, other diseases, familial risk factors) did not demonstrate an increased risk of autism attributable to in utero exposure to antidepressant (Hviid, N Engl J Med. 2013; Sorensen Clin Epidemiol. 2013; Malm, J Am Acad Child Adolesc Psychiatry. 2016)

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Pregnancy and Antidepressants: Practical

- Data is reassuring for use during pregnancy (SSRIs, SNRIs, tricyclic agents, bupropion, mirtazapine)
- No one ‘right’ choice
- Treat to euthymia
- May need to increase dose later in pregnancy given physiologic changes of pregnancy
- Recommendation to taper and discontinue use around labor and delivery problematic given high risk for recurrence in the postpartum period

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Antidepressants: Lactation and breastfeeding

- All antidepressants are compatible with breastfeeding
- Fluoxetine has relatively higher transfer
- Bupropion: at least 1 case report of seizure in infant

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Resources

- Massachusetts Child Psychiatry Access Project for Moms (MCPAP for Moms) Toolkit
  https://www.mcpapformoms.org/
- MotherToBaby
  https://mothertobaby.org/contact-expert/#ask-an-expert
- Postpartum Support International (PSI)
  http://www.postpartum.net/
- Massachusetts General Hospital Center for Women's Mental Health
  https://womensmentalhealth.org/

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