

Postpartum Depression

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OUTLINE

1. Overview of Mood Disorders in Perinatal period
2. Diagnosis of Postpartum Depression
3. Etiology of Postpartum Depression
4. Treatment guidelines and review of antidepressant medication use in pregnancy and lactation

Overview

- Women are twice as likely as men to suffer from mood disorders
- Gender differences exist in prevalence, expression, co-morbidity and course of the illnesses
- Gender differences may be due to psychosocial factors and biological factors
- Gonadal steroids and synthetic estrogens and progesterone may play a role in psychiatric disorders

Postpartum Blues or “Baby blues”

- Postpartum Blues is a very common syndrome found in about 50% to 75% of new mothers
- Onset is within the first 2 weeks postpartum and lasts up to 10 days
- Symptoms :
 1. Feeling “very emotional”
 2. Increased “moodiness”
 3. Anxiety
 4. Poor appetite
 5. Fatigue
 6. Insomnia and irritability



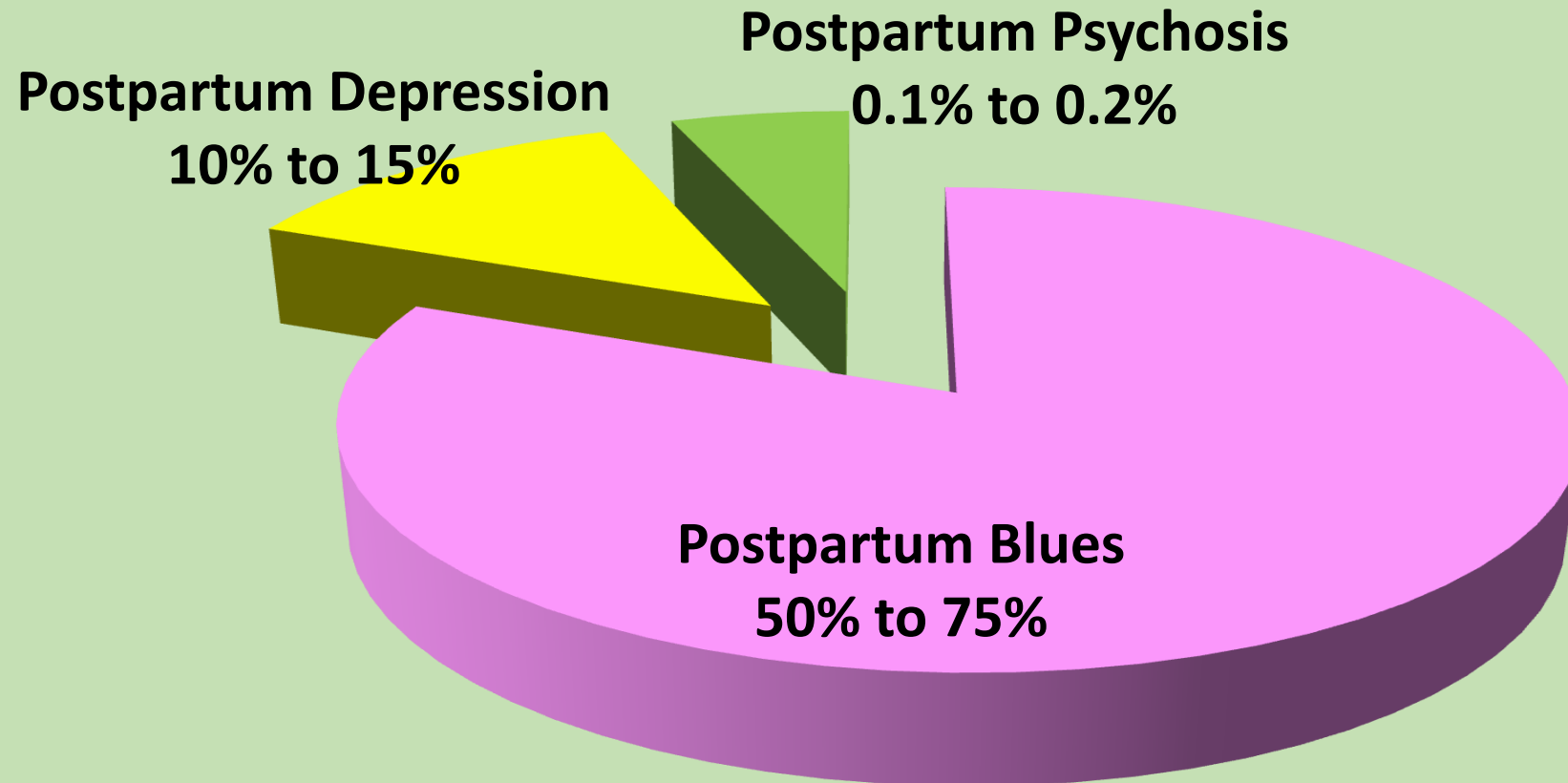
Postpartum Blues

- Transitory with minimal functional impairment and spontaneous resolution of symptoms.
- The key therapeutic interventions:
 - ✓ Support and Reassurance
 - ✓ Adequate sleep and periodic “rest breaks”
 - ✓ Consider short-term use of Hypnotics if necessary.

Postpartum Blues

**Increase risk for Post-partum
Depression!!!!!!!!!!!!**

Postpartum Depression



Post-partum Mood Disorders

- Most common complication of childbirth, incidence 10% to 15 % of deliveries
- DSM-V: “**peripartum onset**” specifier assigned to Major Depression episode (MDE)
- Onset of mood sx's during pregnancy or within 4 weeks after birth
- Between 3%-5% women will experience the onset of MDE during pregnancy or in the weeks or months following delivery
- 50% of PPD episodes actually begin during the pregnancy
- Onset typically within 2-12 weeks, most vulnerable period is first 3 months, overall risk could last up to 1 year postpartum

Post-partum Mood Disorders

- Prevalence:
 - 9.4% to 12.7% of U.S women
 - 7.1% of U.S women in the first 3 month
 - 21.1% of U.S women in the first 12 month (**Gaynes et al.2005, AHRQ**)
- Women with peripartum MDE often have severe anxiety and even panic attacks
- Peripartum onset of mood episodes can be with or without psychotic features – 1 in 500 to 1 in 1000 deliveries; typically with more severe mood sx's and increase risk for infanticide!
- The risk of recurrence of postpartum mood episode with psychosis with each subsequent delivery is between 30% and 50%

Major Depression: DSM V

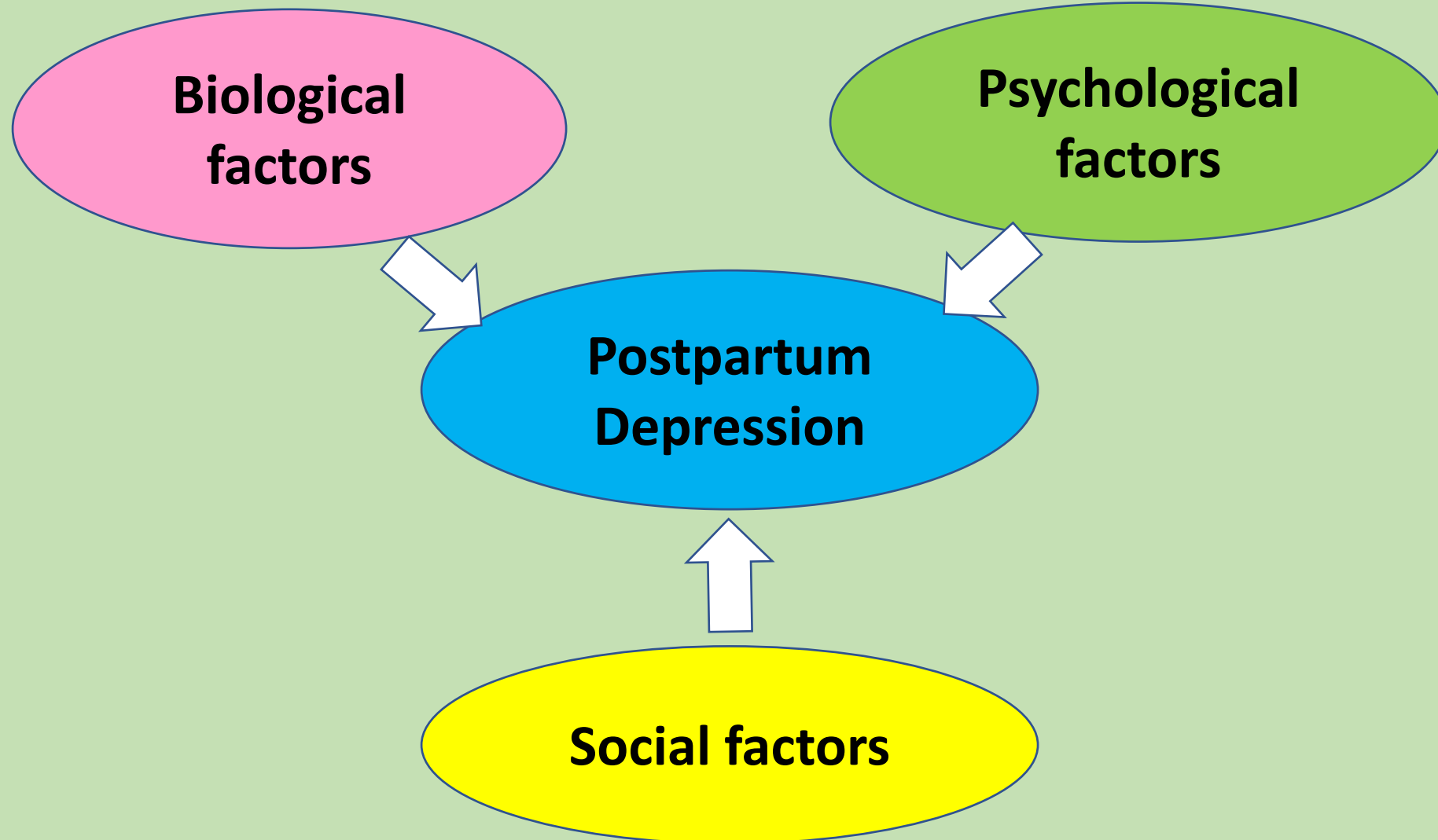
- **5 or more** of the following present during the same **2-week period** and **at least 1 of the sx's is either (1) or (2)**:

1. Depressed Mood
2. Anhedonia/Lack of pleasure
3. Sleep difficulties (insomnia or hypersomnia)
4. Appetite changes (increased or decreased)
5. Poor energy levels
6. Feelings of inappropriate guilt/Worthlessness
7. Poor concentration/Indecisiveness
8. Agitation or Retardation
9. Suicidal ideations

Postpartum Depression (PPD)

- The symptoms differ in some ways from those of non-puerperal cases:
 - ✓ Predominance of severe worry, anxiety, obsessional features and/or agitation
 - ✓ High rates of recurrence
 - ✓ PPD may cluster in families
 - ✓ Postpartum depression risk factors include history of affective instability at other times of hormonal change, such as history of PMDD and OCP mood symptoms

Biopsychosocial Model

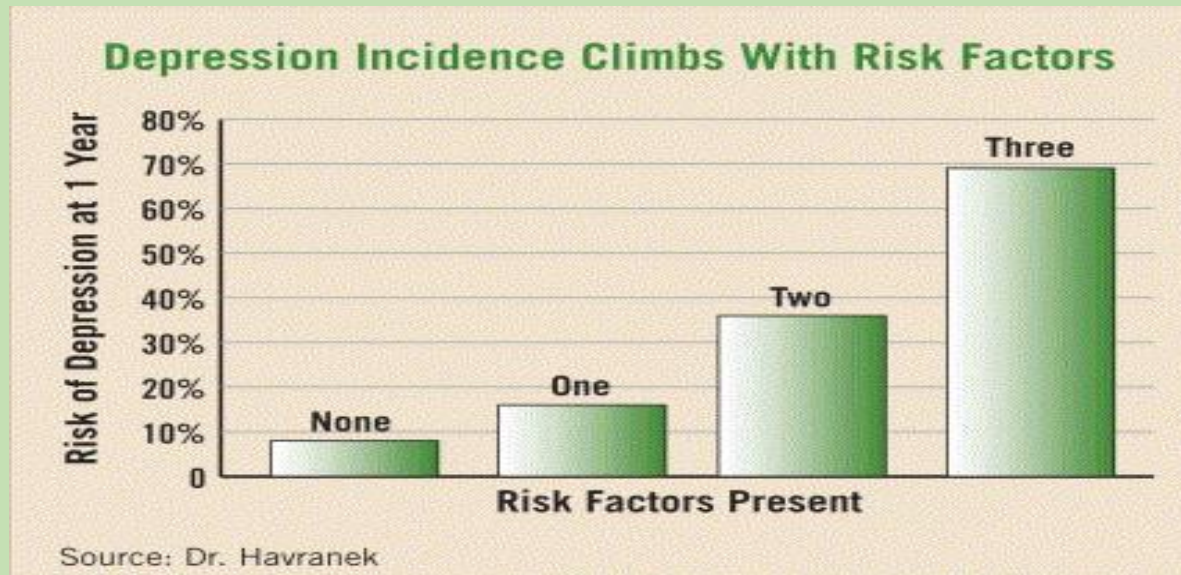


Biological Factors

- Family Hx
- It is a period of series of neuro-chemical changes:
 - ✓ Disturbances in the serotonin (5-HT) system
 - ✓ Disturbances in Limbic Hypothalamic-Pituitary-Adrenal (LHPA) axis
 - ✓ High levels of stress provokes the release of increased amounts of cortisol which is regulated by LHPA axis - Hyperactivity of LHPA axis is well documented in depression
- Presence of co-morbid medical illnesses
- Sleep changes
- Prospective studies have indicated that mood and anxiety sx's during pregnancy as well as "baby blues" increase the risk of peripartum MDE

Psychological factors

- Anxiety/ambivalence about being a new mother
- Re-experiencing difficulties with own childhood/mother
- Loss of control/perfectionism
- Grief of previous pregnancy losses
- Feeling overwhelmed
- Unhappy with physical appearances/loss of sexuality
- Poor Self-care



Social factors

- Role/identity change
- Limited social contact with peers
- Change in relationship with husband
- Absence from the workplace
- Reaction from other children at home
- Financial strain

Can Postpartum Depression Be Prevented?

- Estimated risk for postpartum depression in a woman with a previous history of depression: unknown
- Estimated risk for recurrence of postpartum depression: 25%
- Limited research available for guiding treatment recommendations
- Postpartum antidepressant “prophylaxis” trials:
 - Nortriptyline no more effective than placebo in a RDB study
 - Sertraline more effective than placebo (7% vs. 50%) in RDB study

(Wisner et al, 2001; Wisner et al, 2004)

Peripartum Depression Screening

- High prevalence in the general population
- High morbidity and mortality risks if untreated
- Readily treatable conditions
- Greatly improved short and long-term outcome for mothers and for their children
- Availability of validated, easy to use and standardized screening tools
- High rates of detection and diagnosis using the screening tools

Screening tools for perinatal depression

- Edinburgh Postnatal Depression Scale (EPDS)
 - Best validated screening for peripartum populations
- Post-partum Depression Screening Scale (PDSS)
 - It is a 35-item self report questionnaire designed for postpartum period.
 - Easy to administer
 - Measures severity and type of depressive symptoms
- Patient Health Questionnaire-9 (PHQ-9)
 - Best validated for tracking response to treatment

Risks of untreated antenatal depression

■ Neonatal Risks:

- ✓ low birth weight
- ✓ Prematurity
- ✓ pre-eclampsia
- ✓ irritability in the newborn
- ✓ cortisol elevation in the newborn

■ Risks during infancy and early adolescence

- ✓ poorer growth
- ✓ increased risk of infections
- ✓ more difficult temperament

Risks of untreated peripartum depression

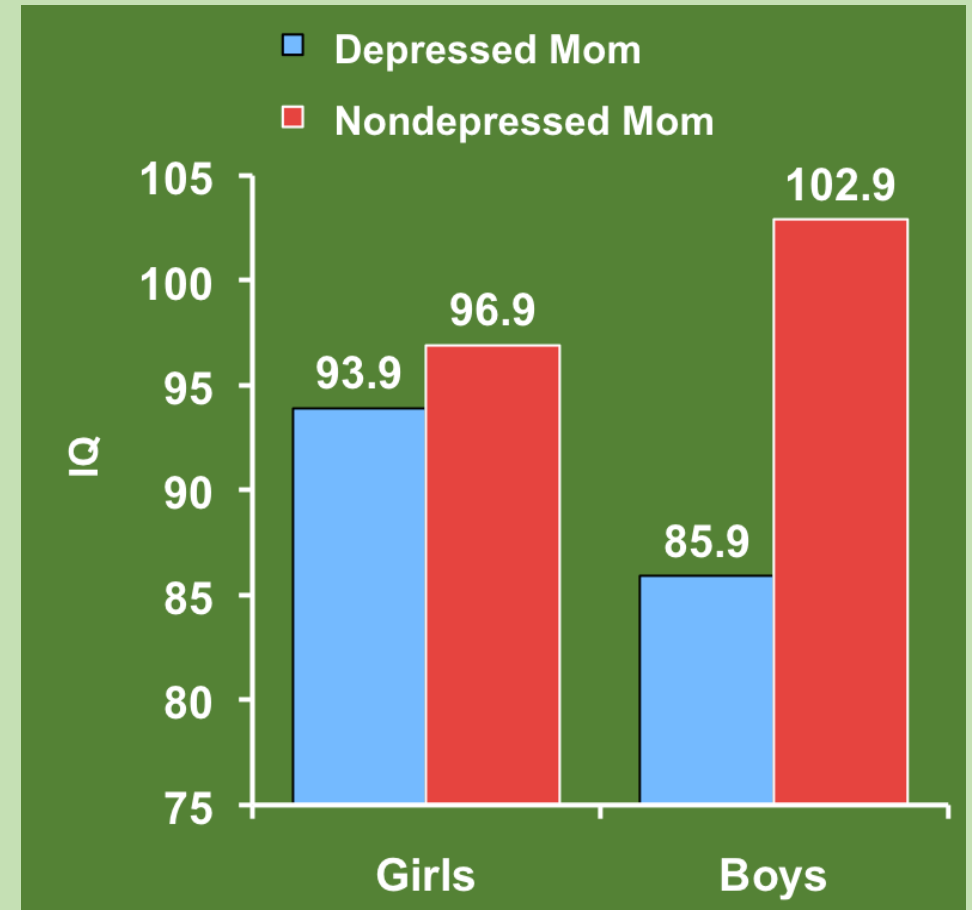
- Predicts future episodes of Depression
- Depressed mother has:
 - ✓ reduced ability to read baby's cues
 - ✓ reduced ability to communicate range of emotions
 - ✓ reduced enrichment (e.g; reading, singing, story telling)
 - ✓ less healthy sleeping and feeding practices
 - ✓ less attention to baby's health needs
 - ✓ practices poor preventive health practices and safety measures
 - ✓ overwhelming guilt
 - ✓ anger outbursts and irritability

Risks of untreated peripartum depression in babies and children

- Failure to thrive
- Delayed and/or impaired cognitive and motor development
- Emotional problems, including depression
- Behavioral problems- conduct disorders, school truancy
- Life-long increased neurophysiologic reactivity to stress

Post-partum Depression: Long-Term Effects on IQ and Cognitive Function

- 148 women enrolled at 3 months postpartum
- Children (n = 132) assessed at 11 years
- Lower IQ
- Attention, mathematical reasoning deficits
- Conduct problems
- Outcomes worse in children exposed to recurrent MDD (although exposure to one episode of MDD had negative effects)



Treatment Considerations

- Referral to Mental Health provider
- Inpatient/Outpatient
- Family involvement-Who?
- Treatment modality
 - Pharmacotherapy
 - Psychotherapy



Psychological Treatment

➤ **Interpersonal Therapy:**

- Effective for pregnant women with depression
- Brief, structured
- Addresses disoutes, feelings of isolation, role adjustment, grief related to loss

➤ **Cognitive-Behavioral Therapy:**

- Effective for depression in pregnancy
- Brief, structured
- Involves cognitive restructuring and behavioral modification

Psychological Treatment

➤ **Supportive Therapy:**

- supportive listening
- foster pt's strengths and coping abilities

➤ **Group Therapy:**

- value of support
- short-term best

➤ **Marital Therapy:**

- engaging the couple in treatment

➤ **Family Therapy:**

- treat family as unit
- engage all

(Sockol LE. *J Affective Dis.* 2015; 177: 7-21)

Sockol LE et al. *Clin Psychol Rev.* 2011;31(5):839-49.

Social Interventions

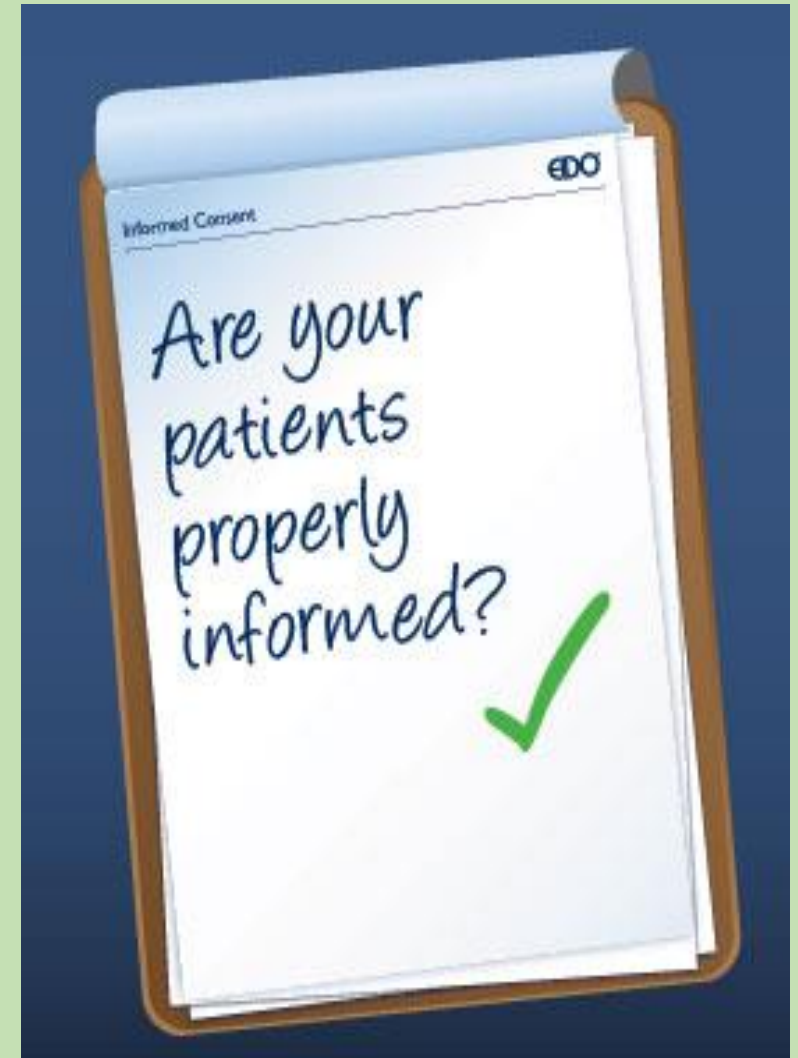
- Financial Resources
- Community Resources: including childcare classes, support groups, suicide hotline numbers
- Identifying abuse in the home- contacting DCFS
- Encouraging maternal self-care
- Eliciting support from relatives
- Home Health Care
- Linkage to mental health providers skilled with this population

Fetal Exposure !!!!!!!!!!!!!!!!



Fetus will be
exposed either
to the medication
or
the illness

- ✓ Risk of psychiatric illness in pregnancy and postpartum
- ✓ Non-pharmacological treatment options
- ✓ Risks of psychotropic exposure to developing fetus/breastfeeding infant
- ✓ Potential adverse effects to mother
- ✓ Benefits of psychotropic use in treatment of psychiatric illness



Risk of Medication Treatment vs. Risk Depression

- Miscarriage
- Congenital malformations
- “Behavioral teratogenesis”
- Perinatal complications
 - ✓ Preterm Delivery
 - ✓ LBW/SGA
 - ✓ Persistent Pulmonary Hypertension
 - ✓ Neonatal Adaptation Syndrome

- Mothers’ poor self care
- Suicide
- Termination of pregnancy
- Risk of postpartum depression
- ? Hypercortisolemia
 - ✓ Low birth weight
 - ✓ Premature labor
 - ✓ Gestational Hypertension/Preeclampsia
 - ✓ Neurodevelopmental problems

Pharmacotherapy Risks

Depression Risks

Relapse of Major Depression During Pregnancy

Women Who Maintain or Discontinue Antidepressant Treatment

Table 3. Relapse of Major Depression During Pregnancy

Relapse Status	All Women	Medication Status			
		Maintained	Increased	Decreased	Discontinued
No relapse	115 (57.2)	61 (74.4)	11 (55.0)	22 (64.7)	21 (32.3)
Relapse by trimester					
All	86 (42.8)	21 (25.6)	9 (45.0)	12 (35.3)	44 (67.7)
First	44 (51.2)	11 (52.4)	7 (77.8)	5 (41.7)	21 (47.7)
Second	31 (36.0)	9 (42.9)	2 (22.2)	3 (25.0)	19 (43.2)
Third	11 (12.8)	1 (4.8)	0 (0.0)	4 (33.3)	4 (9.1)

Antidepressants for the Treatment of PPD

- Serotonin Reuptake Inhibitors (SSRIs) are the most frequently studied antidepressants in perinatal mood disorders
- SRIs have higher depression response and remission rates than placebo or “care as usual” in meta-analysis
- To date, few trials comparing antidepressants and psychotherapy

Risks Associated with Antidepressant Use in Pregnancy

- Antidepressants and Spontaneous Abortion (SA):
 - ✓ Variable findings in individual studies of differing antidepressants
 - ✓ Large registry-based study reports increased rates of SA in antidepressant exposed pregnancy related to maternal mental health (depression) and lifestyle
(Johansen et al. *Paediatric Perinatal Epidemiol* , 2014)

- ✓ Results of meta-analysis evaluating all published studies reported the following risks for SA in 6 carefully evaluated cohort studies:
 - Nonexposed = 8.7% (7.5%-9.9%); N=1,534
 - Exposed= 12.4% (8.8%-14.1%); N=2,033
 - Relative Risk = 1.45
 - No difference between antidepressants (Nefazodone, Trazodone, Venlafaxine, SSRIs)
(Hemels et al, 2005; *Ann Pharmacother* 39: 803-9)

Risks for Spontaneous Abortion

- Meta-analysis and systematic review did not find significant association between antidepressant exposure and spontaneous abortion

(Ross et al. JAMA Psychiatry. 2013; 70(4): 436-43)

- Estimated risk in general population: 12% of pregnancies
- Estimated risk is less in patients with previous history of successful pregnancy (4-5%) and greatest in a history of recurrent miscarriage (24-50%)

Regan et al, BMJ, 1989; 26: 54-58

Confounding Variables

- Increased risk of recurrent spontaneous abortion has been linked with untreated Major depression

(Bergant et al, 1997; Sugiura-Ogasawara et al, 2002)

- Studies compared depressed patients on antidepressants to non-depressed controls and not controlled for reproductive history of the patient

Are Antidepressants Associated with Congenital Malformations?

History of the Controversy:

- Pre-2005:
 - ✓ No studies showed an increased risk of major congenital malformations
 - ✓ Chambers et al. reported an increased risk of “minor” malformations in babies exposed to fluoxetine in utero
- September 2005: Preliminary GSK Report:
 - ✓ Increased rate of congenital malformations in paroxetine exposed infants compared to other antidepressants (4%) OR=1.82
 - ✓ Increased risk of cardiac malformations compared to other antidepressants (2%) OR=1.79

(Chambers et al, 1996 *NEJM*; 335: 1010-5)

SSRI group and Malformations

Study	Findings
Swedish Medical Birth Registry 2005	RR = 0.97 SSRI vs unmedicated
National Birth Defects Prevention Study	No association between SSRI use and CM
Slone Epidemiology Birth Defects Study	Overall SSRI use not associated with a significantly increased risk of omphalocele, craniosynostosis or heart defects

(Kallen and Olausson, 2007; Alwan S, et al. *NEJM* 2007; 356:2684-2692);
Louik C, et al. *NEJM* 2007; 356:2675-2683

Specific SSRIs and Malformations:

Glaxo-Smith-Kline	<u>Paroxetine</u> vs other AD: Cong Malf OR 1.82 <u>Paroxetine</u> vs other AD: Cardiac Def OR 1.63
Swedish Medical Birth Registry 2005	Cardiac Defects RR 1.63 <u>Paroxetine</u> vs Sertraline, Fluoxetine or Citalopram
National Birth Defects Prevention Study Case-Control	Fluoxetine: craniosynostis OR=2.8; CI=1.3-6.1 Sertraline: anencephale OR=3.2; CI=1.1-9.3 <u>Paroxetine</u> : anencephale OR=5.1; CI=1.7-15.3 omphalocele OR=8.1, CI=1.7-15.3 RV cardiac OR=2.5 CI=1-6; gastroschisis OR=2.9; CI=1-8.4
Slone Epidemiology Birth Defects	Sertraline: omphalocele OR=5.7 CI=1.6-20.7 <u>Paroxetine</u> : RV outflow tract obstr. OR=3.3 CI=1.3-8.8;

Paxil Update: Association with cardiac defects may be less severe

- Meta-analysis of unpublished cases and register cases found:
 - ✓ 2,061 unpublished cases: cardiac defect rate of infants exposed to Paroxetine: 1.5%
 - ✓ 1,174 teratology register cases: cardiac defect infants exposed to Paroxetine: 0.7%
- Authors suggest previous findings may be due to a detection bias:
 - ✓ Women taking Paroxetine had twice the rate of US and Echo
 - ✓ Women with anxiety disorders more likely to take Paroxetine than other SSRIs

Conclusions: Antidepressants and Congenital Malformations

- Majority of studies do not report an association between antidepressant use and increased risk for congenital malformation
- No specific type of congenital malformation has been linked to specific antidepressants (other than the conflicting reports of an association of Paroxetine with cardiac malformations)

Teratogenicity Time-Table

Time after conception	Organ System	Associated Defect
17 – 30 days	CNS	Neural Tube Defects
21 – 56 days	Cardiac	Ebstein’s Anomaly; Septal defects
8 – 11 weeks	Lips and Palate	Cleft Lip and Palate
6-14 weeks	Limbs	
15-35 weeks	Craniofacial	Craniofacial
Second & third trimester		Neurobehavioral teratogenicity

Persistent Pulmonary Hypertension of the Newborn

- Rare condition in the general population: estimated 1/1000 births
- Possible Causes:
 - ✓ Hypoxia and hypercarbia at birth (meconium aspiration, complicated deliveries)
 - ✓ Increased medial muscle thickness of pulmonary arteries
 - ✓ Vasoactive mediator abnormalities (nitrous oxide, leukotrienes, platelet activating factor)
 - ✓ SSRIs have been associated with an increased risk of PPHN in some, but not all studies

(t Jong et al. *Reprod Toxicol* 2012; 34(3) 293-7)

Neonatal SSRI “Adaptation” Syndrome

- Clinical characteristics:
 - ✓ Respiratory distress
 - ✓ Autonomic instability
 - ✓ Poor feeding
 - ✓ Neurologic symptoms: tremor, myoclonus, seizures
- Neonatal adaptation syndrome occurs in < 30% of neonates exposed to SSRIs in utero, leading to NICU and SCN admits
- Etiology controversial: SSRI withdrawal or serotonergic toxicity?
- Self limited, supportive treatment
- Severe symptoms rare

ACOG and American Psychiatric Association Guidelines



Depression During Pregnancy: Treatment Implications

- To switch antidepressant before or during pregnancy
 - During pregnancy: avoid switching compounds without previous history of response
- To decrease or discontinue antidepressant prior to delivery
 - SSRIs and TCAs have been associated with neonatal complications, including lower Apgar scores and increased rates of admission to special care nurseries
 - No studies to inform decision regarding benefits of tapering or stopping antidepressant on neonate and risk of precipitating depression recurrence in mother if stop
 - Decision based on severity of depression, consultation with OBGYN and perinatologist

Important Medical Differential Postpartum Depression

- Postpartum thyroiditis
- Anemia
 - SSRI and SNRI use in pregnancy is associated with an increased risk of postpartum hemorrhage in some but not all studies
(Hanley GE. et al. Obstet Gynecol. 2016; 127(3): 553-61' Bruning AH et al. Eur J Obstet Gynecol Reprod Bio 2015; 189: 38-47)
- B12 and/or folic acid deficiency

ACOG Recommendations

- If possible, avoid using paroxetine for women who currently PG, or planning. Consider fetal echo if 1st trimester exposure
- Lowest possible effective dose
- Choose with substantial safety data
- Monotherapy preferable
- Use IPT or CBT as alternate Tx or as adjunct

ACOG Recommendations

Maternal psychiatric illness (if inadequately treated), may result in:

- Poor compliance with prenatal care
- Inadequate nutrition
- Exposure to additional medications / herbs
- Increased alcohol / tobacco use
- Deficits in mother-infant bonding
- Disruptions in family environment

ACOG Recommendations

- Multidisciplinary management is ideal
- Single medication exposure best
- Monitoring neonatal serum for drug levels is not recommended
- Individualize treatment with SSRIs/ SNRIs

Breastfeeding and Psychotropic Drug Use

- All psychotropic medications found in breast milk
- Concentrations of medications in breast milk is variable: milk/plasma ratio poor indicator of exposure
- Majority of clinical practice guided by case reports and clinical impression vs systematic data
- Neurodevelopmental follow-up data limited to case reports that examine children in first year of life
- American Academy of Pediatrics recommends that Relative Infant Dose (RID) of a drug be <10% and most antidepressants are < 10%
 - RID is the weight adjusted infant dose relative to weight adjusted maternal dose (dose in infant (mg/kg/day)/dose in mother (mg/kg/day))

Managing Postpartum Depression in Breast-Feeding Women

- Baseline assessment of infant
- Monitor infant clinical status
- Use lowest effective dose
- SSRIs appear to be safest and effective
 - ✓ Sertraline is preferred medication with several studies showing undetectable infant serum levels (including metabolite)
 - ✓ Fluoxetine and Citalopram may have higher infant serum concentrations; a few case reports of increased irritability, poor feeding, agitation
- Consider infant serum levels if using high doses, especially if clinical changes occur in infant

Premature Infants, Lactation and Antidepressants

- All studies investigating plasma concentrations in infants exposed to antidepressants through breastfeeding have included only term infants
- No studies of premature infants
- Liver metabolic enzymes (CYP450) immature until approximately 2 months of age

“Treatment Resistant” PPD

- ✓ No studies to inform treatment decisions
- ✓ Algorithm similar to major depression w/non-postpartum onset except consider breastfeeding issues with augmentation agents such as Lithium
- ✓ Always double check thyroid status
- ✓ Always evaluate family and marital dynamics--
marital problems have been strongly associated with persistent PPD
- ✓ Strongly consider bipolar differential
- ✓ ECT

Brexanolone/Zulresso

- Only FDA approved treatment indicated for the treatment of postpartum depression (PPD) in adults
- ZULRESSO is a neuroactive steroid gamma-aminobutyric acid (GABA) A receptor positive modulator
- The mechanism of action: not fully understood, but is thought to be related to its positive allosteric modulation of GABA-A receptors binding to a site other than the GABA receptor and amplifies the effect of GABA binding to its receptor
- Dysfunctional HPA activity plays a role in PPD. It's thought that enhancement of GABA activity regulates stress-signaling in the hypothalamic-pituitary-adrenal axis (HPA).

Recommended Dosage

- Administered as a continuous intravenous infusion over 60 hours (2.5 days) as follows:
 - ✓ 0 to 4 hours: Initiate with a dosage of 30 mcg/kg/hour
 - ✓ 4 to 24 hours: Increase dosage to 60 mcg/kg/hour
 - ✓ 24 to 52 hours: Increase dosage to 90 mcg/kg/hour (alternatively consider a dosage of 60 mcg/kg/hour for those who do not tolerate 90 mcg/kg/hour)
 - ✓ 52 to 56 hours: Decrease dosage to 60 mcg/kg/hour
 - ✓ 56 to 60 hours: Decrease dosage to 30 mcg/kg/hour
- If excessive sedation occurs at any time during the infusion, stop the infusion until the symptoms resolve
- The infusion may be resumed at the same or lower dose as clinically appropriate
- Injection: 100 mg/20 mL (5 mg/mL) single-dose vial
- Dilution required prior to administration

Brexanolone/Zulresso

- A healthcare provider must be available on site to continuously monitor the patient, and intervene as necessary, for the duration of the ZULRESSO infusion
- Monitor patients for hypoxia using continuous pulse oximetry equipped with an alarm
- Assess for excessive sedation every 2 hours during planned, non-sleep periods
- Initiate ZULRESSO treatment early enough during the day to allow for recognition of excessive sedation

Pharmacokinetics:

- Brexanolone exhibited dose proportional pharmacokinetics over a dosage range of 30 mcg/kg/hour to 270 mcg/kg/hour
- The volume of distribution of brexanolone was approximately 3 L/kg, suggesting extensive distribution into tissues
- Plasma protein binding was greater than 99% and is independent of plasma concentrations
- The terminal half-life of brexanolone is approximately 9 hours. The total plasma clearance of brexanolone is approximately 1 L/h/kg

Warnings and Precautions

- Suicidal Thoughts and Behaviors
- Sedation and somnolence requiring dose interruption or reduction in some patients during the infusion: 5% of ZULRESSO-treated patients compared to 0% of placebo-treated patients
- Loss of consciousness or altered state of consciousness during the infusion: 4% of the ZULRESSO-treated patients compared with 0% of the placebo-treated patients
- Time to full recovery from loss or altered state of consciousness, after dose interruption, ranged from 15 to 60 minutes
- There was no clear association between loss or alteration of consciousness and pattern or timing of dose

Warnings and Precautions

- After symptoms resolve, the infusion may be resumed at the same or lower dose as clinically appropriate
- Immediately stop the infusion if pulse oximetry reveals hypoxia. After hypoxia, the infusion should not be resumed
- Caution against engaging in potentially hazardous activities requiring mental alertness, such as driving after infusion
- Patients must be accompanied during interactions with their child(ren) while receiving the infusion because of the potential for excessive sedation and sudden loss of consciousness
- Concomitant use of opioids, antidepressants, or other CNS depressants such as benzodiazepines or alcohol may increase the likelihood or severity of adverse reactions related to sedation

Adverse Effects:

- Most common adverse reactions (incidence $\geq 5\%$ and at least twice the rate of placebo) were:
 - ✓ sedation/somnolence
 - ✓ dry mouth
 - ✓ loss of consciousness, and
 - ✓ flushing/hot flush
- The adverse reactions leading to treatment discontinuation were:
 - ✓ sedation-related - loss of consciousness, vertigo, syncope, and presyncope or
 - ✓ infusion site pain.

	Placebo (n=107)	Maximum dosage 60 mcg/kg/hour (n=38)	Maximum dosage 90 mcg/kg/hour (n=102)
Cardiac Disorders			
Tachycardia	--	--	3%
Gastrointestinal Disorders			
Diarrhea	1%	3%	2%
Dry mouth	1%	11%	3%
Dyspepsia	--	--	2%
Oropharyngeal pain	--	3%	2%
Nervous System Disorders			
Dizziness, presyncope, vertigo	7%	13%	12%
Loss of consciousness	--	5%	3%
Sedation, somnolence	6%	21%	13%
Vascular Disorders			
Flushing, hot flush	--	5%	2%

Zulresso in Lactation:

- Available data from a lactation study in 12 women:
 - ✓ Brexanolone is transferred to breastmilk in nursing mothers
 - ✓ The relative infant dose (RID) is low, 1% to 2% of the maternal weight-adjusted dosage
 - ✓ ZULRESSO has low oral bioavailability (5%) in adults, infant exposure is expected to be low
 - ✓ No reports of effects of ZULRESSO on milk production
 - ✓ No data on the effects of ZULRESSO on a breastfed infant

Questions?