Women's Mental Health Across the Lifespan

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LA County Department of Mental Health Workshop
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Objectives

- Discuss concept of women's mental health, with particular attention to Asian-American women
- Understand periods of vulnerability: menses, perinatal period, perimenopause
- Review presentation, assessment, and evidence-based treatment

Women and Mental Health

- Lifetime prevalence rates for depression in women: 20% (twice that of men)
- Higher rates for every anxiety diagnosis except OCD
- Rates start to differ at menarche
- Return to men's rates in menopause

Faravelli C, Alessandra Scarpato M, Castellini G, Lo Sauro C. Gender differences in depression and anxiety: the role of age. *Psychiatry Res.* 2013; 210(3):1301-3.

Suicide and Asian-American Women

- Compared with women of all other racial groups, Asian American females are at the HIGHEST risk of suicide:
  - Between ages 15-24
  - Older than age 65

Kramer EJ, Wang CB, Kwong K, Lee E, and Chung H. "Culture and Medicine: cultural factors influencing the mental health of Asian Americans." *WJM.* 2002; 176:227-231.

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What Makes Asian-American Women More Vulnerable to Mental Illness?

- Females have a lower status from birth onward
- Women expected to bend to husband's will to promote family peace
- These traditional values at odds with American independence, self-sufficiency, putting one's own needs before others
- Can lead to inner conflict, stress, and either 1) "acting out" or 2) depression / low self-esteem

Kramer E et al.

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Biological Windows of Vulnerability

- Menses
- Pregnancy / Postpartum
- Perimenopause
- Other issues:
  - Infertility
  - Pregnancy Loss
  - Female-specific Cancers

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Hormones and Mental Health

- Estrogen and serotonin work closely together
- The brain is an "estrogen sensitive organ"
- As estrogen levels shift, serotonin function is impacted
- Some women are particularly vulnerable to these shifts: genetic predisposition
- The result? Mood and anxiety symptoms

Lokuge S et al. Depression in Women: Windows of Vulnerability and New Insights Into the Link Between Estrogen and Serotonin. *J Clin Psychiatry.* 2011; 72(11): e1563-e1569.

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Mood and the Menstrual Cycle

Key Point: Mood symptoms around the menstrual cycle should be included in every woman's mental health assessment

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Prevalence of PMS and PMDD

- PMS: >50%
- PMDD: 2-8%
- Premenstrual exacerbation of symptoms: unmeasured

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Premenstrual Dysphoric Disorder (PMDD)

- In most cycles for the past year, during the days prior to onset of menses.
- Must have one of the following:
  - Marked depressed mood, hopelessness
  - Marked anxiety, tension
  - Marked affective lability
  - Marked anger or irritability

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders (5th ed.).* Arlington, VA: American Psychiatric Publishing.

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PMDD DSM-V con't:

Other symptoms can include (need a total of 5 for diagnosis):

- Decreased interest in activities
- Concentration difficulties
- Marked lethargy or lack of energy
- Change in appetite, overeating, or food cravings
- Hypersomnia or insomnia
- Feeling overwhelmed or out of control
- Physical symptoms: bloating, breast tenderness

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How to tell the difference? PMS v. PMDD v. MDD

	Predominant Mood Symptoms	Predominant Physical Symptoms	Marked Social Impairment	Monthly Cyclicity	Respond to SSRIs?
PMS	-	+	-	+	-
PMDD	+	+/-	+	+	+
MDD	+	-	+	-	+

Adapted from Burt VK.

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PMDD: Evidence-Based Treatments

- SSRIs: standard of care; intermittent dosing
- Oral contraceptives: some positive data (drosperinone plus ethinyl estradiol)
- Calcium carbonate: 1200 mg/day
- Lifestyle modifications

Jarvis CI, Lynch AM, Morin AK. Management strategies for premenstrual syndrome / premenstrual dysphoric disorder. *Ann Pharmacother.* 2008; 42(7):967-78.
Lopez LM, Kaptein AA, Helmerhorst FM. Oral contraceptives containing drospirenone for premenstrual syndrome. *Cochrane Database Syst Rev.* 2012; 2:CD006586.
Ghanbari Z, Haghollahi F, Shariat M, Foroshani AR, Ashrafi M. Effects of calcium supplement therapy in women with premenstrual syndrome. *Taiwan J Obstet Gynecol.* 2009; 48(2):124-9.

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Perimenopause and Mood

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A Few Definitions: Perimenopause

1) Irregular menstrual cycles (if woman previously regular)
2) Amenorrhea between 3 and 11 months
3) Lab values (checked on day 3 of cycle):
   - FSH > 25 IU/l
   - Estradiol < 40 pg/ml

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A Few Definitions: Menopause

1) Amenorrhea of 12 or more months
2) Can be natural or surgical (hysterectomy)
3) Lab values:
   - FSH > 40 IU/l
   - Estrogens < 25 pg/ml

The Stats

- Average age of menopause is 52
- Most women have symptoms for at least 8 years previously
- Women now living over a third of their lives in menopause
- Symptoms frequently minimized

Peri/Menopausal Symptoms

- Vasomotor
  - Hot flashes, night sweats
  - Palpitations
- Somatic
  - Dizziness
  - Fatigue
  - Insomnia
  - Joint pain, paresthesia
  - Headache

Peri/Menopausal Symptoms

- Affective
  - Sad mood, pessimistic
  - No pleasure / joy (anhedonia)
- Anxious
  - Tension, persistent worry
  - Irritability
- Cognitive
  - Lack of concentration
  - Poor memory

Perimenopausal Depression

- Same criteria as classic MDE
- One difference: more "emotional withdrawal" or anhedonia
- Can also be "subsyndromal"

What are risk factors for perimenopausal depression?

- A personal or family history of depression
- Background of PMDD or postpartum depression
- Presence of severe hot flashes / night sweats
- Longer duration of perimenopause
- Recent negative life circumstances

Gibbs Z, Lee S, Kulkarni J. Factors associated with depression during the perimenopausal tradition. (2013). Womens Health Issues (23)5:e301-7.

What leads to perimenopausal depression?

- Neurobiological theory
- Domino theory
- Psychosocial theory

Ayubi-Moak I and Parry BL. (2002) Psychiatric Aspects of Menopause: Depression. In Kornstein S and Clayton AH (Eds.) *Women's Mental Health,* (pp.132-43). NY: The Guilford Press.

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Neurobiological Theory

- Estrogen receptors found throughout brain and body
- No clear data on "hormone levels" and mood
- What matters? Variability / falls in estrogen
- Checking labs not meaningful

Flores-Ramos M, Moreno J, Heinze G, Aguilera-Perez R, Pellicer Graham F. Gonadal hormone levels and platelet tryptophan and serotonin concentrations in perimenopausal women with or without depressive symptoms. (2014) *Gynecol Endocrinol* (30)3:232-5.

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Domino Theory

- Symptoms of perimenopause have a bidirectional relationship with depression
  - Insomnia
  - Hot flushes / night sweats
- Can become an escalating cycle

Worsley R, Bell R, Kulkarni J, Davis SR. The association between vasomotor symptoms and depression during perimenopause: A systematic review. *Maturitas.* 2013; 77(2):111-7.
Moreno-Frias C, Figueroa-Vega N, Malacara JM. Relationship of sleep alterations with perimenopausal and postmenopausal symptoms. *Menopause.* 2014; 21(9):1-17-22.

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Psychosocial Theory

- Roles change:
  - "Empty nest" syndrome
  - Aging / dying parents
- Cultural connotations: high expectations of caregiving with little room for emotional expression
- Positive: elderly more respected

Kramer E et al.

How to help? Treatment Options

- Psychotherapy
- Antidepressants
- Hormone replacement therapy?

Psychotherapy

- Very few studies specific to perimenopause
- Mild to moderate cases: can be first-line
- More severe cases: use as adjunct
- Interpersonal Psychotherapy (IPT)

Green SM, Key BL, McCabe RE. Cognitive-behavioral, behavioral, and mindfulness-based theories for menopausal depression: a review. *Maturitas* 2015. 80(1):37-47.

Antidepressants

- Start with what worked best in the past
- Otherwise, start with an SNRI (venlafaxine, duloxetine, desvenlafaxine)
- Peri- and postmenopausal women may respond better to "double neurotransmitter" effect as estrogen levels drop

Soares C. N. Depression in Peri- and Postmenopausal Women: Prevalence, Pathophysiology and Pharmacological Management. *Drugs Aging* 2013; 30:677-685.
Thase ME et al. Relative Antidepressant Efficacy of Venlafaxine and SSRIs: Sex-Age Interactions. *Journal of Women's Health.* November 2005; 14(7):609-616.

Antidepressants and Hot Flashes

- Venlafaxine
- Escitalopram
- Fluoxetine
- Paroxetine

Brisdelle

- Paroxetine 7.5 mg
- Approved in May 2014 for hot flushes
- Advisory committee voted against, but FDA approved anyway
- First non-hormonal alternative for hot flushes
- Caution with tamoxifen: decreases conversion to active metabolite by 64%

Orleans RJ, Kim MJ, Guo J, Soghan M, Soule L, and Joffe HV. FDA Approval of Paroxetine for Menopausal Hot Flushes. *N Engl J Med* 2014; 370:1777-1779.

Antidepressants

- Carefully review possible side effects:
  - Decreased libido; anorgasmia
  - Fatigue / insomnia
  - Weight gain
- May exacerbate already bothersome symptoms of perimenopause
- Consider drug-drug interactions

Hormone Replacement Therapy for Depression?

- If falling estrogen levels lead to depression, shouldn't replacing them help mood?
- Seems to be a "mental tonic" for well or mildly symptomatic women
- Less helpful for women with overt depression unless combined with antidepressant
- General health concerns may limit use

Garcia-Portilla MP. Depression and Perimenopause: A Review. *Actas Esp Psiquiatr* 2009; 37(4):213-221.

Medical Concerns and HRT

- FDA approved uses:
  - Hot flashes / night sweats
  - Vaginal atrophy
  - Osteoporosis if alternate treatments don't work
  - Not recommended to prevent dementia or CAD
- Risks:
  - Increased risk of strokes / PE / DVT?
  - Breast cancer / ovarian cancer with long-term use?

Conclusions on HRT for Depression

- Data is mixed and may depend on phase of menopausal transition
- Health risks may outweigh benefit
- If do use, should be the LOWEST dose for the SHORTEST duration possible
- May be used to augment antidepressants and vice versa

Sleep in Perimenopausal Women

- Impaired on multiple measures: onset, duration, frequency of awakenings
- Can be multifactorial
  - Primary sleep disorder (OSA, RLS)
  - Anxiety or depression
  - Vasomotor symptom
- Should be important target of treatment

Soares CN 2013.

What about CAM Treatments?

- Black cohosh: inconsistent results
- Phytoestrogens
  - Derived from soy; weak estrogenic effects
  - Inconsistent evidence
- Vitamin E: no evidence, but doesn't hurt
- Acupuncture
- Exercise

Perinatal Mood and Anxiety Disorders (PMADs)

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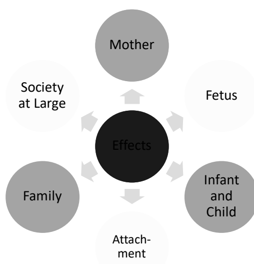
Why Do PMADs Disorders Matter?



- If left untreated can become chronic; impact on woman, child, family then much greater
- Can have multigenerational impact

Vliegen, et al., 2014.

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Postpartum or "Baby Blues"

- Over 80% of women affected
- Tearfulness, mood swings, feelings of being easily overwhelmed
- Occurs in first two to three weeks
- Usually resolves with social support – as provider, draw on patient's family
- 20% goes on to become depression

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Perinatal Depression = MDD

- Officially, same DSM-V criteria as MDD
- Peripartum specifier: “Onset within pregnancy or the first four weeks after delivery”
- In reality, can occur up to one year postpartum

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Where there’s depression, there’s anxiety

- Panic Disorder
- Obsessive Compulsive Disorder
- Post Traumatic Stress Disorder
- Generalized Anxiety Disorder
- “Stress”

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Panic Disorder in Perinatal Period

- General population prevalence: 1.3-2.0%
- Postpartum incidence in first 12 weeks: elevated to 11%
- Rule out hypertension, night sweats, thyroid dysfunction

Ross LE and McLean LM. Anxiety disorders during pregnancy and the postpartum period: a systematic review. *J Clin Pyschiatry.* 2006 Aug; 67(8):1285-1298.

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Perinatal Panic Disorder: Presentation

- May misconstrue normal physiology of pregnancy as panic (shortness of breath, nausea, dizziness)
- Diarrhea a common complaint
- "Rush of adrenaline"
- Can significantly impact sleep

Perinatal Panic Disorder: Breastfeeding

- Breastfeeding reduces panic?
- Weaning increases panic?
- Data still small but suggestive

Perinatal PTSD

- Can childbirth result in PTSD?
- Poor data to date, but improving
- Postpartum prevalence:
  - Population baseline: 3%
  - At-risk populations: 16%

Grekin R, O'Hara MW. Prevalence and risk factors of postpartum posttraumatic stress disorder: a meta-analysis. *Clin Psychol Rev* 2014 Jul;34(5):389-401.

Perinatal GAD: Presentation

- Some anxiety normal in pregnancy
- Possible red flags:
  - Excessive
  - Uncontrollable
  - Cannot be reassured
  - Physical complaints that don't make sense medically or have negative work-up

Perinatal GAD: Prevalence

- By definition, difficult to diagnosis
- "Adjustment disorder with anxiety"
- Rate in 3rd trimester: 8.5%
- Rate in postpartum: from 4 to 8%

Perinatal Obsessive-Compulsive Disorder: Prevalence

- Prevalence in pregnancy: mixed data, ranging from lower to higher incidence
- Clear that postpartum is high-risk
- 30% increase in risk postpartum if previous OCD
- Highly comorbid with depression: 50-75%

Abramowitz JS, Schwartz SA, Moore KM, LUenzmann KR. Obsessive-compulsive symptoms in pregnancy and the puerperium: a review of the literature. *Anxiety Disorder.* 2003; 17:461-78

Common Presentations

- Health concerns
  - Contamination and cleaning
  - Baby's health / breastfeeding and Internet
- Intrusive images
  - Violent or sexual images
  - Shameful, unwilling to admit
  - Accompanied by panic, anxiety, depression
- Ruminations that don't meet OCD threshold

Perinatal OCD: Outcomes

- Dysfunctional maternal behavior:
  - Avoiding infant
  - Refusing to separate from infant
- Either way, inappropriate attachment

Distinguishing OCD v. Psychosis

Abramowitz JS, Schwartz SA, Moore KM, LUenzmann KR. Obsessive-compulsive symptoms in pregnancy and the puerperium: a review of the literature. *Anxiety Disorder*. 2003; 17:461-78

Postpartum Psychosis v. OCD

Postpartum Psychosis	Postpartum Obsessive Compulsive Disorder
Thoughts of harming infant are not upsetting; in fact, can be soothing	Thoughts are intrusive, meaning they jump into woman's brain against her will, and are extremely upsetting
Feel as if guided by outside force	Thoughts are recognized as "not my own"
Part of larger delusion	Otherwise grounded in reality
Disorganized, "spacey" thoughts	Organized thoughts
Can be manic, depressed, or neither	Often highly anxious, with panic attacks, and/or depressed
Needs hospitalization	Can be treated as an outpatient

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Postpartum Psychosis

- New onset psychotic episode triggered by childbirth
- Can be mania, depression, or neither
- Women often confused, disoriented
- Have auditory, somatic hallucinations
- Have delusions that incorporate baby
- Risk of infanticide: 4%

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Postpartum Psychosis: Epidemiology

- Present in roughly 1 out of 1000 births (absolute risk)
- Relative risk for new onset psychosis is **23 times higher** within four weeks of delivery compared to any other time in life
- Typically occurs within the first 3-10 days postpartum
- 90% within first four weeks
- Does not have an official DSM diagnosis

Di Florio A et al. Perinatal episodes across the mood disorder spectrum. *JAMA Psychiatry*. 2013; 70:168-75.
Spinelli MG. Postpartum Psychosis: Detection of Risk and Management. *Am J Psychiatry*. 2009;166:405-408.
Stewart D, Klompenhouwer J, Kendell R, Van Hulst A: Prophylactic lithium in puerperal psychosis: the experience of three centres. *Br J Psychiatry* 1991; 158:393-397.

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How to Manage Postpartum Psychosis? Acute Care

- Safety must be guaranteed
  - Psychiatric evaluation immediately OR
  - Warm hand-off to the Emergency Room
- Do not leave alone with infant / child
- Psychosis must be controlled
- Document!

How to Manage Postpartum Psychosis? Long-Term Care

- Appropriate medication management
- Supportive psychotherapy
- Psychoeducation of family
- Safety of child / legal involvement
- Involve case managers / social workers / community resources

Treatment Options

- Lithium
- Antipsychotics
- ElectroConvulsive Therapy (ECT)
- Medications for Sleep Support

Sleep Support

- Consider not breastfeeding
- Short-acting benzodiazepines (lorazepam)
  - Lorazepam given at bedtime
  - Wait 6-8 hours before nursing again
  - Do NOT need to "pump and dump"
- Avoid chronic or long-term benzo use
  - Infant sedation and lethargy

"Exposure always occurs, be it to treatment or illness."

Stowe, Z et al., 2001.

Thinking Through Risk and the Individual Patient

- No clear-cut answer
- Risks and benefits
- Evidence changing rapidly
- Clinician as educator
- Clear, up-to-date, and documented informed consent is vital

Acknowledge Patient Concerns

- Fear that medications will hurt fetus or baby
- Guilt that a "bad mother" prioritizes her own well-being
- Belief that depression will remit after delivery
- Misinformation from other sources (friends, Internet)
- Stigma of medication use
- Fear of addiction and withdrawal
- Fear of showing weakness or vulnerability

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Risk of Relapse

- Key Point: if a woman with a significant Axis I disorder is untreated in pregnancy, she will most likely relapse.
- Relapse rates > 70% for depression, anxiety, and bipolar disorder
- Postpartum: rates of hospitalizations for bipolar disorder and psychosis increased significantly

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Preconception Planning

Goals:

- Optimize stability and
- Minimize risks
- NOT necessarily to stop medications

<u>Excellent</u> chance to use plan a healthy pregnancy!

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Reducing Risk

- Remember that studies show ASSOCIATION between medication and outcomes
- The real issue may be behavioral and medical risks that go along with illness and the drug is a MARKER of risk
- Focus should be on reducing risk, not getting off medications (unless clearly indicated)

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Areas of Risk Reduction

- Metabolic syndrome
  - Work closely with OB to monitor weight, blood pressure, glucose levels
- Substance use (including tobacco and MJ)
- Psychosocial issues
  - Poor nutrition
  - Stress of housing insecurity, violence, legal issues

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FDA Categories

- Old system of A,B,C and D is limited
- Newer system: three sub-sections
  - Pregnancy
  - Lactation
  - Females and Males of Reproductive Potential

Requires clinical decision making on a case-by-case basis

http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/UCM431132.pdf

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Basic Guidelines

- Use what has worked before, unless a clear safety reason not to
- Lowest EFFECTIVE dose
- Monotherapy preferable, if possible
- Minimize number of exposures / switching
- Consider breastfeeding early and often
- Do not taper off SSRIs prior to delivery

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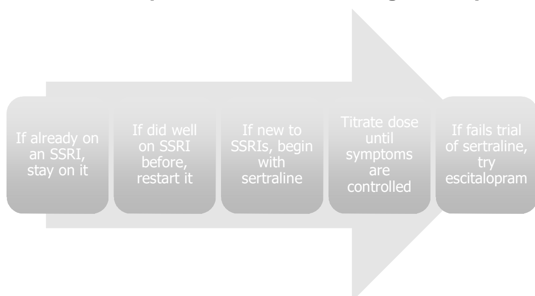
Antidepressants In Pregnancy



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Potential Risks with SSRIs

- No elevated risks of birth defects
- Poor Neonatal Adaptation
- Persistent Pulmonary Hypertension of the Newborn
- Preterm delivery? Probably depression/anxiety
- Autism data increasingly more reassuring

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Perinatal Depression and Sertraline

	Benefits	Risks
Treatment	Remission from symptoms Prevention of postpartum depression or anxiety	No birth defect or miscarriage risk above population; Poor Neonatal Adaptation, PPHN; potential unknown long-term effects; safe in nursing
No Treatment	No medication exposure to fetus or nursing infant	Relapse – 70%, poor self-care, dysregulated stress system, preterm delivery, less breastfeeding, postpartum depression and anxiety, long-term effects

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CONCLUSIONS

- Women's mental health focuses on vulnerability and wellness at times of reproductive change
- Evidence-based, effective treatments are available
- Proactive assessment of symptoms increases chances of health overall

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RESOURCES

- Emily C. Dossett, MD: edossett@dhs.lacounty.gov
- Massachusetts General Hospital Center for Women's Mental Health: blog
- Marce of North America (MONA)
- Postpartum Support International (PSI)
- North American Menopause Society (NAMS)

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