Assessment and Management of Depression Over the Female Life Cycle

Stephen A. Young, MD
Regional Medical Officer/Psychiatry
US Department of State, American Embassy, Tokyo
Office of Personnel Management statistics on DOS personnel as of 9/30/2013 (population about 15,000):

<table>
<thead>
<tr>
<th>Gender</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Civil Service</td>
<td>55.48%</td>
<td>44.52%</td>
</tr>
<tr>
<td>FS Generalist</td>
<td>39.68%</td>
<td>60.32%</td>
</tr>
<tr>
<td>FS Specialist</td>
<td>28.13%</td>
<td>71.87%</td>
</tr>
<tr>
<td>Total</td>
<td>43.95%</td>
<td>56.05%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gender</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>SES</td>
<td>40.64%</td>
<td>59.36%</td>
</tr>
<tr>
<td>SFS</td>
<td>30.46%</td>
<td>69.54%</td>
</tr>
</tbody>
</table>
In addition to employees:

- Spouses (including Foreign Born Spouses)
- Parents
- Children (into young adulthood)
- Additional agencies (Peace Corps, DOD, affiliated agencies)
- Locally employed staff in crisis
Women Get Depressed More Frequently

**Figure 3-1** Proportion of population who met the criteria for depression during previous 12 months, by age and sex, Canada, 2002

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Women</th>
<th>Men</th>
<th>Both</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-24 years</td>
<td>8.3</td>
<td>4.5</td>
<td>6.4</td>
</tr>
<tr>
<td>25-44 years</td>
<td>6.8</td>
<td>4.0</td>
<td>5.4</td>
</tr>
<tr>
<td>45-64 years</td>
<td>5.6</td>
<td>3.5</td>
<td>4.6</td>
</tr>
<tr>
<td>65+ years</td>
<td>1.9</td>
<td>2.1*</td>
<td>2.0</td>
</tr>
</tbody>
</table>

* Small sample size. Interpret with caution.


Possible Etiologies for Gender Differences

• Fluctuations in Gonadal Steroids
• Multiple Social roles and Demands
Theories Still Unclear

- CNS effects not necessarily proportional or equivalent to Peripheral Effect
- Distinct association between rates of depression and menopause unproven
- Estrogen and Progesterone flux may trigger underlying vulnerability to Affective Disorder
CoMorbid Factors

• Incidence of Thyroid and Panic Disorders by Gender
I'm fine. I hate you.
I love you. I want ice cream. Come here.
Get away. Oranges?
PMDD: Introduction

• Frequently Misdiagnosed and Minimized

• Up to 75% of Women Report Mild Symptoms

• 3-9% May Meet Criteria for Premenstrual Dysphoric Disorder (PMDD)
PMDD: Patterns of Presentation

• 25% No symptoms
• 33% Mild symptoms
• 33% Increase in symptoms of underlying medical or psychiatric problem
• 2-9% severe PMDD
• Onset in late 20’s, peaks during 30’s
DSM-V Criteria for PreMenstrual Dysphoric Disorder

• Occurs during the majority of cycles
• Symptoms during the last week (Late Luteal Phase)
• Symptoms improve within a few days of the onset of menses and become minimal or absent in the week post menses
• Symptoms markedly interfere with work, school, or social relationships
• Must have prospective rating of symptoms
# Prospective Reporting

**CALENDAR OF PREMENSTRUAL EXPERIENCES**

Begin your calendar on the first day of your menstrual cycle. Enter the calendar date below the cycle day. Day 1 is your first day of bleeding. Shade the box above the cycle day if you have bleeding (■). Put an X for spotting (∨).

If more than one symptom is listed in a category, i.e., nausea, diarrhea, constipation, you do not need to experience all of these. Rate the most disturbing of the symptoms on the 1-3 scale.

**Weight:** Weigh yourself before breakfast. Record weight in pounds in the box below date.

**Symptoms:** Indicate the severity of your symptoms by using the scale below. Rate each symptom at about the same time each evening.

- 0 = None (symptom not present)
- 1 = Mild (noticeable but not troublesome)
- 2 = Moderate (interferes with normal activities)
- 3 = Severe (involuntary, unable to perform normal activities)

**Other Symptoms:** If there are other symptoms you experience, list and indicate severity.

**Medications:** List any medications taken. Put an X on the corresponding day(s).

| Bleeding |  |  |  |  | • | • | • |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Cycle Day| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 |
| Date     |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Weight   | 120 | 120 | 120 | 120 | 120 | 120 | 120 | 120 | 120 | 120 | 120 | 120 | 120 | 120 | 120 | 120 | 120 | 120 | 120 | 120 | 120 | 120 | 120 | 120 |
| **SYMPTOMS** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Acne     | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 1 |
| Bloating | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Breast tenderness | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Cramping, abdominal | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Fatigue  | 2 | 2 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Headache | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Swelling (hands, ankles, breast) | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Angy outbursts, arguments, violent tendencies | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Anxiety, tension, nervousness | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Clumsiness | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Confusion, difficulty concentrating | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Crying easily | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Depression | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Food cravings (sweets, salts) | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Forgetfulness | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Irritability | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Increased appetite | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Mood swings | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Sexual desire/activity change | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Want to be alone | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| **Other Symptoms** | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Nausea | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| **Medications** | 1 | Acetaminophen | 2 | Aspirin/Butalbital | 3 | Pseudoephedrine | 4 | 5 | 6 |
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
| 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 |
| 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 |

Physical Symptoms

- Acne
- Bloatedness
- Breast Tenderness
- Headaches
- GI Complaints
- Swelling (hands, ankles, breast)

from the Calendar of PreMenstrual Experience (Obstet Gynecol 1990;76:302-7)
Behavioral Symptoms

- Angry Outbursts/Irritability
- Confusion, Difficulty Concentrating
- Anxiety, Tension, Nervousness
- Depression, Mood Swings
- Crying Easily
- Food Cravings

from the Calendar of PreMenstrual Experience (Obstet Gynecol 1990;76:302-7)
Differential Diagnosis

- Mood Disorders (Premenstrual Exacerbation)
- Thyroid
- Anemia
- Hepatitis
- Personality Disorders
Non Somatic Treatments

• Diet
  • Decrease caffeine, salt
  • multiple small meals (high carbohydrates)

• Exercise

• Stress Management
Gonadal Steroids Cause PMS in Vulnerable Women

Biosynthesis of Neurosteroids in the Human Brain

Cholesterol $\xrightarrow{P \, 450_{\text{sc}}}$ Pregnenolone $\xrightarrow{3\beta\text{HSD}}$ Progesterone

Progesterone $\xrightarrow{20\alpha\text{-} \text{Dihydro-Progesterone (}20\alpha\text{DH-PROG)}}$ 20\alpha\text{- Hydroxysteroid oxidoreductase}$

Progesterone $\xrightarrow{5\alpha\text{-reductase}}$ 5\alpha\text{-Pregnane -3.20 - DIONE (}5\alpha\text{DH} - \text{PROG})$

Progesterone $\xrightarrow{3\beta\text{HSD}}$ Androstenedione $\xrightarrow{17\beta\text{-Hydroxysteroid oxidoreductase}}$ Testosterone

Testosterone $\xrightarrow{P \, 450}$ Estradiol

Adapted from Beaulieu EE Recent Progress in Hormone Research 1997;52:1-32.
GABA Receptor modulated by multiple biologically active substances

- Decrease:
  - Flumazenil
  - Convulsants
  - Pregnenolone

- Increase:
  - GABA
  - Benzodiazepines
  - Barbiturates
  - Allopregnanolone
  - Alcohol

Sundstrom P, Smith S. GABA Receptors, Progesterone and Premenstrual Dysphoric Disorder
Arch Wom Mental Health, 6(1), Feb 2003, 23-41
The role of Progestin metabolites in PMDD and possibly MDD

- When Progestin levels fall:
  - Allopregnanolone production decreases
  - A4 subunit of GABA_A receptor increases
  - Reduced Allopregnanolone levels may cause GABA like withdrawal (irritability, insomnia, etc)

Andréena L, Nyberg S: Sex steroid induced negative mood may be explained by the paradoxical effect mediated by GABA_A modulators Psychoneuroendocrinology 34 (8) 2009, 1121–1132
Serotonin Enhances Allopregnanolone Production in the Brain

Cholesterol → Pregnenolone → Brain Progesterone

3α-hydroxysteroid dehydrogenase

Allopregnanolone + Serotonin → GABA Receptor

Adapted from Beaulieu EE. Recent Progress in Hormone Research. 1997;52:1-32.
## Medication Trials for PMDD

<table>
<thead>
<tr>
<th>Year</th>
<th>Medication</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1984</td>
<td>GnRH Agonist</td>
<td>Effective</td>
</tr>
<tr>
<td>1989</td>
<td>Nortriptyline</td>
<td>Ineffective</td>
</tr>
<tr>
<td>1989</td>
<td>Buspirone</td>
<td>Ineffective</td>
</tr>
<tr>
<td>1990</td>
<td>Danazol</td>
<td>Moderate</td>
</tr>
<tr>
<td>1993</td>
<td>Light Therapy</td>
<td>Ineffective</td>
</tr>
<tr>
<td>1993</td>
<td>Alprazolam</td>
<td>Ineffective</td>
</tr>
<tr>
<td>1993</td>
<td>Depakote</td>
<td>Ineffective</td>
</tr>
</tbody>
</table>
### SSRI Trials in PMDD

<table>
<thead>
<tr>
<th>Year</th>
<th>Medication</th>
<th>Author</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1992</td>
<td>Fluoxetine</td>
<td>Menkes DB</td>
<td>Effective</td>
</tr>
<tr>
<td>1995</td>
<td>Fluoxetine</td>
<td>Steiner M*</td>
<td>Effective</td>
</tr>
<tr>
<td>1996</td>
<td>Sertraline</td>
<td>Yonkers KA*</td>
<td>Effective</td>
</tr>
<tr>
<td>1998</td>
<td>Sertraline</td>
<td>Young SA</td>
<td>Effective</td>
</tr>
<tr>
<td>2005</td>
<td>Paroxetine</td>
<td>Steiner M*</td>
<td>Effective</td>
</tr>
</tbody>
</table>

* * Multi Center Trials
Birth control pills

• 14 Randomized trials found no efficacy of progesterone alone

• Two studies have shown some efficacy with drospirenone plus ethinyl estradiol (Yaz)

• Other BCPs regulate cycle and dysmenorrhea – less well documented for treating PMDD


PMDD: Why Treat?

• Patients symptomatic 25% of the time
• Increased lifetime prevalence of Major Depression
• Increased risk for Post Partum Depression
• 20-25% meet criteria for Dysthymia
• Increased suicidal, aggressive, and psychotic behavior associated with luteal phase
When Pregnancy and Depression Intersect

- Patient in treatment seeks advice prior to becoming pregnant
- Patient in treatment becomes pregnant
- Pregnant patient is referred for treatment of depression
- Patient with hx of post partum depression seeks advice re: current pregnancy
- Patient who requires treatment for depression wishes to breast feed her newborn
Is Pregnancy Protective?

- Rates of Depression Similar
- 14-23% of Women Meet Diagnostic Criteria for Depression During Pregnancy\(^1\)
- BMJ Reported higher rates of Depression at 32 wks compared to 8 weeks Post Partum\(^2\)
- OCD May increase
- High Rate of Relapse for Bipolar Patients who discontinue meds

\(^1\) Gaynes Evid Re/Technol Assess (Summ) 2005:1-8
\(^2\) Evans Br Med Jnl 2001;323:257-60
“Let’s try getting up every night at 2:00 AM to feed the cat. If we enjoy doing that, then we can talk about having a baby.”
Non Biologic Factors on Mood State During Pregnancy

• Lack of partner, family and social support
• Previous problems (colicky sibling)
• Prior Mental Illness
• Prior Induced Abortion
• Marital Status
• Concurrent medical complications, e.g., “high risk” pregnancy
Risks of Not Treating in Pregnancy

- Suicide
- Poor self care, nutrition, sleep
- Drug, Alcohol, and tobacco use
- Exposure to other medications
- Maternal stress may alter fetal HPA axis\(^1\)
- Possible association with pre-term delivery, low birth weight, developmental delay, behavioral problems\(^2,3\)

\(^1\) Stowe ZN CNS Spectrums 2002 6(2):150-66
\(^2\) Chaudron LH Am J Psychiatry 2013; 170:12-20
\(^3\) Dayan J Psychosom Med 2006;68:938-46
Risk of Treatment

- Miscarriage
- Structural Malformations
- Gestational Age Effects
- Growth Effects
- Neonatal Behavioral Outcomes
- Persistent Pulmonary Hypertension (PPHN)

Miscarriage

• Increased risk reported with use early in pregnancy – 12.4% exposed versus 8.7% unexposed
• No differences among various classes of antidepressants
• Confounding health habits (smoking, drug use, age) were variably controlled among studies contributing to the meta-analysis

Structural Malformations

- Majority of Tricyclics, SSRIs, SNRIs, and Bupropion are Pregnancy Category C

- Paroxetine is Category D – based primarily due to reports of cardiac malformations

- Meta analyses of data on tricyclics revealed no increased incidence\(^1\)

- Best data with SSRIs – Fluoxetine – 2400 exposures documented without increase\(^2\) and Citalopram\(^3\)

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\(^1\) Stowe ZN APA Textbook Psychopharmacology 2\(^{nd}\) Ed 2000
\(^2\) Cohen LS Currents in Affective Illness May 2001
Paroxetine

- NEJM 2007¹,²
- 9849 infants with birth defects, 5860 controls
- 2x risk of septal defects with Sertraline and 3x risk of R vent outflow obstruction with Paroxetine
- Comprehensive Meta-Analysis did NOT replicate the results³

Einarson A Am J Psychiatry 2008;165:749-52³
• Low Birth Weights associated with SSRI use – studies difficult to interpret due to poor replication and difficulty quantifying exposure

• Majority of evidence supports an association between pre-term births but modest differences of one week or less for those exposed compared to not exposed
Neonatal Behavioral Outcome

• Irritability, feeding difficulties, diaphoresis
• Anticholinergic side effects, e.g., gastrointestinal or bladder dysfunction reported with maternal TCA use
• “Poor Neonatal Adaptation” in 15-30% of women taking SSRIs in late pregnancy
• Symptoms generally resolve spontaneously within 2 weeks or less
• Nonrandomized 228 women and 254 controls
• Divided: “early” exposure (n=101) and late (n=73)
• No difference in major birth defects
• Increase in minor anomalies 15.5% vs. 6.5%
• Premature birth increased in late exposed group
• Poor neonatal adaptation in 31% of late exposed vs. 8.9% of early exposed group
• Issue may be related to half life of Fluoxetine
Persistent Pulmonary Hypertension

• Baseline risk between 0.5 to 2/1000
• Multiple studies have reported increased risk with exposure to SSRIs (not TCAs)
• Most recent study\(^1\): 30,000 exposures – about 1/3 after week 20
• PPHT occurred in 3/1000 compared with background incidence of 1.2/1000
• Incidence was consistent regardless of SSRI exposure – suggesting a class effect

\(^1\)Kieler H, Artama M BMJ 2012;344:d7642
Behavioral Teratogenicity
• 80 infants exposed to a TCA, 55 infants exposed to Fluoxetine, 84 controls
• Assessed between 16 and 86 months of age (mean 33, ± 14)
• No differences between groups in language development, IQ, temperament, mood, distractibility or behavior problems
Impact of Maternal Depression Across the First 6 Years of Life on the Child’s Mental Health, Social Engagement, and Empathy: The Moderating Role of Oxytocin

- Children of depressed and non-depressed Moms followed up at age 6
- 61% of children with depressed Moms had Axis I disorders (15% of controls)
- Salivary oxytocin lower in moms, children, and Dads!
- Presence of specific genotype in depressed Moms markedly decreased risk of child psychopathology
Treatment During Pregnancy

• This is a longitudinal analysis that stretches from pre-conception through the post partum period
• Risk of relapse for those with hx of severe depression (at least four previous episodes) is significant but relapse risk decreases in those with milder histories
• Consider the whole picture: previous history, support network, patient’s choice
Treatment During Pregnancy (cont)

- There is always a risk, even if only perceived must be weighted against risk of untreated depression

- Some data has correlated low birth weight\(^1\) and preterm delivery\(^2\) with untreated depression

- Avoid psychotropic during first trimester, use effective dose and avoid concurrent benzodiazepine use

- Always document the discussion of risks/benefits for treatment and non-treatment

\(^1\) Dayan J Psychsom Med 2006;68:938-46
\(^2\) Orr, Miller Epidemiol Rev., 1995
Breastfeeding and Antidepressants

- 50% of new mothers plan to nurse
- All psychotropic medications secreted in breast milk to some degree, generally higher concentration in samples with higher fat content (fore vs. hind milk)
- Always have to assess risk of treatment vs. non-treatment
Considerations in the Breastfeeding Mother Taking Antidepressants

• Exposure measured in M/P ratio – amount of drug in milk vs. mother’s blood level
• Higher the number, greater the exposure

• Exposure in infant related to a number of factors:
  • Less protein binding
  • Less drug metabolized
  • Less drug excreted
  • Blood brain barrier more permeable
Managing Psychiatric Medications in the Breast Feeding Woman

Suri RA, Altshuler LL et al Medscape Woman’s Health 3(1), 1998

- 13 reports on TCAs, 7 reports on SSRIs, and case reports on Bupropion, Trazodone
- 22 infants exposed to TCAs - nondetectable levels in 16
- 17 infants exposed to SSRIs - nondetectable levels in 14 (Sertraline), 1 (Fluoxetine), but detectable in 2 others
Methods to Determine Exposure

• Quantitative – Measure levels in mother’s sera, milk, and infant sera
• Functional – Measure activity of drug
• Outcome – Changes in developing CNS?
Use of Sertraline, Paroxetine, and Fluvoxamine by Nursing Women
Hendricks V Br Jnl Psychiatry 2001; 179:163-6

• 50 Mother – Infant pairs (34% had taken the medication while pregnant as well)
• 16 Paxil, 4 Fluvoxamine, and 30 Sertraline
• Blood samples from mother and infant minimum of 2 weeks following delivery
• Undetectable levels in all Paxil and Fluvoxamine infants
• Detectable in 24% of Sertraline infants – low levels, correlated with mother’s dose
• No poor outcomes
19 Mother-Infant Pairs taking Sertraline 25-200 mg/d
- Drug exposure measured in terms of Serotonin content of platelets
- Mothers showed decline of 70-96% in platelet Serotonin content
- Infants had little (2.5%) to no decrease in platelet 5HT content
Breastfeeding and SSRIs

- Paroxetine – 3 reports, 32 infants exposed
  - Infants had 3% or less of Maternal Paxil dose: No bad outcomes

- Sertraline – 4 reports, 25 infants exposed
  - Non detectable levels in most cases, some had N-desmethylsertraline level: No bad outcomes

- Fluoxetine – Multiple Reports
  - Fluox and Norfluox present in infant sera in higher concentrations: 3 reports of colic, irritability, tremulousness.

- Citalopram – 3 reports minimal dosage recommended
  - Swedish Birth Registry – 375 exposed – no bad outcomes
Techniques to Minimize Exposure

- Avoid feeding 3-6 hours after taking medication
- Alternate with bottle feedings
- Use minimum effective dose, Fluoxetine less preferred
- Monitoring levels in infant is not necessary
- Moms exposed to AD much less likely to breastfeed – may need more support education

Breastfeeding Among Women Exposed to Antidepressants during Pregnancy Jnl Human Lactation; published on line 17 FEB 2012
Recommendations for Treatment During Pregnancy and Lactation

• Start with lowest possible dose
• Monotherapy if possible
• Once decision is made, treat effectively
• Patient education and support critical, may need to include husband and grandparents
• Avoid feeding when peak blood levels are present
BABY BLUES

NOW WHAT?

NOW WHAT?

DAY 1.
Post Partum Mood Disorders

• 50-70% - normal “post partum blues”
• 10-20% will develop PostPartum Depression (25% of adolescents)
• PPD frequently severe, 1-2 percent can progress to include psychosis
• PostPartum Psychosis is considered a medical emergency
Risk Factors for Postpartum Depression

- Previous episode of PPD risk 35%
- Family History of Mood Disorder
- History of PMDD
- Marital discord
- Depression/Anxiety During Pregnancy
Untreated Depression in the Postpartum Period

- May have an impact on infant sleeping patterns\(^1\)
- Correlation between persistent depression in mothers and similar symptomatology in fathers\(^2\)
- Crucial period of infant development may be disrupted
- Ripple effect to spouse, grandparents, and siblings

\(^1\) Hiscock H Pediatrics 2001 107(6):1317-22
\(^2\) Zelkowitz P J Nerv Ment Dis 2001 189(9):575-2
Comparison of Post Partum Depressed Patients vs. Normal Controls

<table>
<thead>
<tr>
<th>Cornell Dysthymia Scale Score</th>
<th>Post Partum (n=8)</th>
<th>Comparison (n=8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early Withdrawal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow Up</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Why is Post Partum Psychosis an Emergency?

“…Instead she was essentially abandoned to cope with an overwhelming illness. Her children were murdered, her own future was destroyed, and incalculable suffering was caused to her husband, family community and all who knew her”

Deborah Peel, MD
Texas Medicine 2001 97(9)
I'M STILL HOT, IT JUST COMES IN FLASHES NOW
Depression and Menopause

- Peri-menopausal years typically between ages 45-49 when cycles become irregular
- Mean age is 51
- One study (using FSH levels) found 14x the risk for the 24 months surrounding final menses than for the 31 year pre-menopausal period
- Risks of non-treatment: exacerbation of CVD, osteoporosis, and DM

Schmidt PJ, Haq N Am J Psychiatry 2004;161(12):2238-44
Parry B Int Jnl Womens Health 2010:2 143-51
Estrogen

• Estrogen is a neurotransmitter with receptor rich regions in multiple brain areas
• Effective antidepressant in peri-menopausal women\(^1\), but not post-menopausal women\(^2\)
• HRT use is always a complex analysis based on other risk factors and may not be a first line approach – but has positive effect on mood, vasomotor symptoms, and sleep

\(^1\)Soares CN Arch Gen Psychiatry 2001;58(6):529-34
\(^2\)Morrison MF Biol Psychiatry 2004;55(4):406-12
Antidepressants

- Multiple studies have shown efficacy with SSRIs and other ADs; both as primary agents and as adjunctive agents with Estrogen
- Recent meta analysis showed superiority of Venlafaxine to SSRIs
- In addition to relief of depressive symptoms there was significant relief of somatic symptoms (hot flashes, night sweats etc).
- Paroxetine (Brisdelle) received FDA approval for treatment of hot flashes in June 2013 (7.5 mg at hs)

Soares C: Challenges and Opportunities to Manage Depression During the Menopausal Transition and Beyond Psychiatr Clin N Am 33 (2010) 295-308
Non-pharmacologic approaches

- Supportive psychotherapy focusing on change of life issues
- Relaxation/mindfulness training to assist in management of hot flashes\(^1\)
- Botanicals: Best studied are black cohosh and soy isoflavone – which have shown some efficacy versus placebo

\(^1\)Carmody J Mindfulness Training for Coping with Hot Flashes: Results of a Randomized Trial Menopause 2011 18(6): 611-20
Questions?