Psychiatric Drug Treatment and Pregnancy

Ann Ebert, PharmD
Perinatal Clinical Pharmacy Specialist
Meriter-UnityPoint Health
Madison, WI
Learning Objectives

1. Describe the risks of untreated depression in pregnancy
2. Discuss the limitations of reproductive safety data for psychotropic medications
3. Compare and contrast antidepressant medications with regards to their safety in pregnancy
4. Choose an appropriate psychotropic medication given a specific clinical scenario
Outline

• Methodological problems with determining risks of medications in pregnancy
• Defining the clinical problem
• Risks of depression during pregnancy
• Reproductive benefits and risks of treatment
• Additional psychotropic medications
  – antipsychotics
  – lithium
  – antiepileptic agents (used for psychiatric disorders)
Methodological Limitations

1. Controls do not take antidepressants during pregnancy
2. Lack of objective confirmation of antidepressant exposure
3. Reliance on maternal self-report for other exposures
4. Reliance on retrospective recall for medication exposures and psychiatric symptoms
Facts about Perinatal Depression

• 50% is unrecognized or untreated
• Women who are depressed are more likely to:
  – smoke, drink alcohol, miss prenatal appointments
• Most women do not refill prescriptions for antidepressants in 2\textsuperscript{nd} and 3\textsuperscript{rd} trimesters of pregnancy
• Relapse during pregnancy is significant
• Rates of depression are higher in the perinatal period than at any other time in a woman’s life
• Women who take SSRIs are more likely to be:
  – older, caucasian, married and more educated

O’Keefe V, Marsh M. BMJ 2007;334:1003-1005
Risk
maternal disease
drug therapy

Benefit
drug therapy
Depression

• Clinical Problem
  – 14-23% of pregnant women experience a depressive disorder
    • Post partum depression in 10-15% of women
  – 8.7% fill a prescription for an antidepressant during pregnancy
  – Treatment during pregnancy increasing
  – Discontinuation during pregnancy is also increasing
  – Reproductive safety of SSRIs and SNRIs have undergone considerable scrutiny

Yonkers KA et al. Obstet Gyn 2009; 114; 703-13
Ray S, Stowe ZN. Best Pract Ob Gyn 2014; 28: 71-83
Risks of depression – pregnancy outcomes

• Pregnancy
  – Poor antenatal care
  – Decreased appetite/weight gain
  – Increased use of alcohol, tobacco, other drugs

• Birth outcomes
  – Preterm birth
  – Lower birth weight
  – Smaller head circumference
  – Lower APGAR scores

• Neurobehavioral alterations
  – Problems with affect, cognition, interpersonal relationships
  – Neuroendocrine and brain functioning
## FDA Pregnancy Risk Categories

<table>
<thead>
<tr>
<th>Category</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Adequate, well-controlled studies in pregnant women have not shown an increased risk of fetal abnormalities to the fetus in any trimester of pregnancy.</td>
</tr>
</tbody>
</table>
| B        | Animal studies have revealed no evidence of harm to the fetus, however, there are no adequate and well-controlled studies in pregnant women.  
OR  
Animal studies have shown an adverse effect, but adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus in any trimester |
| C        | Animal studies have shown an adverse effect and there are no adequate and well-controlled studies in pregnant women.  
OR  
No animal studies have been conducted and there are no adequate and well-controlled studies in pregnant women. |
| D        | Adequate well-controlled or observational studies in pregnant women have demonstrated a risk to the fetus. However, the benefits of therapy may outweigh the potential risk. |
| X        | Adequate well-controlled or observational studies in animals or pregnant women have demonstrated positive evidence of fetal abnormalities or risks. The use of the product is contraindicated in women who are or may become pregnant. |
Pregnancy Risk – FDA Proposal

• Eliminate categories from medication labeling
  – Confusing and misleading for providers and patients
  – Animal vs human data
  – Risks weighed against benefits

• New categorization proposal:
  – Pregnancy Subsection
    • Fetal risk summary
    • Clinical considerations
    • Inadvertent exposure
    • Prescribing decisions for pregnant women
    • Data
    • Pregnancy exposure registries
    • General statement about background risk
Antidepressants

• SSRI
  – Fluoxetine (Prozac®)
  – Sertraline (Zoloft®)
  – Paroxetine (Paxil®)
  – Citalopram (Celexa®)
  – Escitalopram (Lexapro®)
  – Fluvoxamine (Luvox®)
  – Vilazodone (Viibryd®)

• SNRI
  – Venlafaxine (Effexor®)
  – Duloxetine (Cymbalta®)
  – Milnacepran (Savella®)
  – Levomilnacepran (Fetzima®)

• TCA
  – Desipramine (Norpramine®)
  – Nortriptyliine (Pamelor®)

• Others
  – Buproprion (Wellbutrin®)
  – Mirtazapine (Remeron®)
  – Trazadone
  – Nefazadone
Placenta Transfer

- 56 mother-infant pairs
  - 38 SSRI/SNRI
  - 18 controls
- Mean cord/maternal ratio range
  - 0.15-0.83
  - Lowest = paroxetine (n=1)
  - Sertraline (6) = 0.33 (0.29-0.36)
  - Citalopram (9) = 0.83 (0.77-0.86)
  - Venlafaxine (11) = 0.72 (0.41-1.11)

Reproductive Risk

- Intrauterine death
- Prematurity
- Low birth weight
- Teratogenic effects
- Behavioral teratogenicity
- Neonatal toxicity
- Neonatal effects
Spontaneous Abortion

- Controversial
- Evidence is not strong
- Meta-analysis -
  - 6 articles included
  - Baseline rate of spontaneous abortion (SA) = 8.7%
  - SA for women on antidepressants = 12.4%
    - RR 1.45 (1.19-1.77)
    - Many limitations of this type of analysis

- More recently:
  - 3 studies included in analysis
  - OR 1.47 (95% CI, 0.99-2.17)
  - Comparison with depressed control not possible due to lack of data

- None of the studies controlled for underlying psychiatric illness or other confounding variables

Ross LE, et al. JAMA Psych 2013;70:436-43
Depression and Treatment: Impact on Premature Birth

- One of first comparing treatment and disease
- Prospective, observational
- Differences:
  - race, marital status, education and alcohol use

Gestational Age and SSRI Exposure

Maternal exposure during pregnancy

<table>
<thead>
<tr>
<th>Maternal Exposure</th>
<th>Full term</th>
<th>Preterm</th>
</tr>
</thead>
<tbody>
<tr>
<td>No SSRI or depression</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>Cont. SSRI</td>
<td>80</td>
<td>20</td>
</tr>
<tr>
<td>Cont dep/No SSRI</td>
<td>60</td>
<td>40</td>
</tr>
<tr>
<td>Partial SSRI</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>Partial depression/No SSRI</td>
<td>100</td>
<td>0</td>
</tr>
</tbody>
</table>
**Premature Delivery**

- Recent meta-analysis: (23 studies included in total)
  - 13 studies evaluated for preterm birth
  - Prematurity defined as < 37 weeks (10 studies) or < 36 weeks (2 studies)
  - Pooled OR of 1.55 (95% CI 1.38-1.74) p<0.001
  - Similar effect size when compared to depressed mothers (5 studies)
    - Was not statistically significant

Ross LE, et al. JAMA Psych 2013;70:436-43
Premature Delivery

• Cohort study: (228,876 pregnancies)
  • Retrospective review
  • Filling of prescriptions in the 2\(^{nd}\) trimester
    – Associated with progressive decrease in gestational age at birth
      » Filling of 1, 2 or ≥3 prescriptions →
      » Shortened by 2.6 – 5.8 – 6.6 days, respectively (p < 0.0001)
  • Filling prescriptions in the 3\(^{rd}\) trimester:
    – Positive association with longer gestation
      » Filling of 1, 2, ≥3 prescriptions →
      » 0.90 – 1.8 – 6.4 days longer

• Difficult to ascertain the reason

Low Birth Weight

• Association with low birth weight and small for gestational age and SSRIs
• Many studies lack power to detect differences
• LBW may be attributable to early delivery
• Several studies have attempted to control for possible effects of maternal factors
  — Recent meta-analysis: 20 studies included
    • The mean difference was -74 gm (95% CI -117 to -31; p=0.001)
    • When compared to control group of depressed mothers – the difference was null
  — Absolute risk is small

Oberlander T, et al. Arch Gen Psychiatry 2006;63:898-906
Ross LE, et al. JAMA Psych 2013;70:436-43
Teratogenicity

• Period of greatest risk is between the 5\textsuperscript{th} and 8\textsuperscript{th} week of pregnancy
  – Before most women realize they are pregnant
• Few drugs have been tested for teratogenicity in controlled clinical trials
• Risk based on epidemiological studies, individual case reporting and extrapolation from animal studies
## Fetal Malformation - Summary

<table>
<thead>
<tr>
<th>No malformation risk (n)</th>
<th>Malformation risk (n)</th>
<th>Malformation noted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paroxetine (15)</td>
<td>Paroxetine (8)</td>
<td>General congenital anomalies</td>
</tr>
<tr>
<td>Fluoxetine (12)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Citalopram (9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sertraline (8)</td>
<td></td>
<td>Cardiovascular, gastroschisis, anencephaly</td>
</tr>
<tr>
<td>Fluvoxamine (7)</td>
<td>Sertraline (2)</td>
<td>Anencephaly, cardiovascular</td>
</tr>
<tr>
<td>Escitalopram (4)</td>
<td>Fluoxetine (3)</td>
<td>Cardiac, general</td>
</tr>
<tr>
<td>Venlafaxine (2)</td>
<td>SSRIs – general (6)</td>
<td>Cardiovascular, craniosynostosis</td>
</tr>
<tr>
<td></td>
<td>Citalopram (3)</td>
<td>Cardiovascular, neural tube defects</td>
</tr>
</tbody>
</table>

*n = number of studies*

Antidepressants - Risk of Cardiac Defects

• Cohort study: 2000-2007
  – Medicaid Analytic eXtract for 46 states & Wash DC
  – Women 12-55 years of age
    • linked to live-born infants
  – Evaluated exposure in the first trimester of pregnancy
  – 949,504 eligible pregnancies identified
    • 64,389 (6.8%) used an antidepressant
    • Sertraline > paroxetine > fluoxetine

Huybrechts KF, et al. NEJM 2014;370:2397-2407
# Risk of Cardiac Defects

<table>
<thead>
<tr>
<th>Exposure Group</th>
<th>Total # women</th>
<th>Any cardiac malformation</th>
<th>RVOTO</th>
<th>VSD</th>
<th>Other cardiac malformation</th>
</tr>
</thead>
<tbody>
<tr>
<td>No exposure</td>
<td>885,115</td>
<td>72.3</td>
<td>11.8</td>
<td>36.3</td>
<td>36.5</td>
</tr>
<tr>
<td>Any antidep</td>
<td>64,389</td>
<td>90.1</td>
<td>13.0</td>
<td>44.4</td>
<td>49.4</td>
</tr>
<tr>
<td>SSRI</td>
<td>46,144</td>
<td>90.2</td>
<td>13.2</td>
<td>43.6</td>
<td>49.0</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>11,126</td>
<td>83.6</td>
<td>14.4</td>
<td>39.5</td>
<td>43.1</td>
</tr>
<tr>
<td>Sertraline</td>
<td>14,040</td>
<td>91.9</td>
<td>12.1</td>
<td>44.9</td>
<td>50.6</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>11,048</td>
<td>89.6</td>
<td>14.5</td>
<td>43.4</td>
<td>49.8</td>
</tr>
<tr>
<td>TCA</td>
<td>5954</td>
<td>70.5</td>
<td>13.4</td>
<td>40.3</td>
<td>30.2</td>
</tr>
<tr>
<td>SNRI</td>
<td>6904</td>
<td>108.6</td>
<td>17.4</td>
<td>56.5</td>
<td>55.0</td>
</tr>
<tr>
<td>Bupropion</td>
<td>8856</td>
<td>85.8</td>
<td>12.4</td>
<td>44.0</td>
<td>55.3</td>
</tr>
<tr>
<td>Other</td>
<td>7055</td>
<td>104.9</td>
<td>11.3</td>
<td>43.9</td>
<td>65.2</td>
</tr>
</tbody>
</table>

Huybrechts KF, et al. NEJM 2014;370:2397-2407
Persistent Pulmonary Hypertension (PPHN)

- Baseline prevalence of 1.9/1000 live births
- Normally – pulmonary vasculature relaxes after birth
- Symptoms:
  - Respiratory distress, hypoxia
- 2006 – FDA issued an advisory – possible association of SSRI’s with PPHN
- 2011 – revised – conflicting information – difficult to reach any conclusions
PPHN: Meta-analysis

• Pooled data based on timing of exposure
• 7 studies included:
  – 3 - early pregnancy
    • Pooled OR = 1.23 (95% CI 0.58-2.6; P=0.58)
  – 2 - any time during pregnancy
    • Pooled OR = 1.55 (95% CI 0.79-3.04; P=0.20)
  – 2 - most or all of pregnancy
    • Pooled OR = 3.33 (95% CI 0.158-7.02; P=0.002)
  – 5 - late pregnancy
    • Pooled OR = 2.5 (95% CI 1.32-4.73; P=0.005)

PPHN: Results

• Risk increased with exposure later in pregnancy
• Absolute risk is relatively low
  – 2.85/1000 live births
• Number needed to harm
  – 351 women treated
• Limited number of studies available for analysis
• None of the studies evaluated the effect of maternal depression on PPHN
PPHN: Conclusions

• Preliminary information
• Limitations of retrospective study
• Absolute risk is relatively low
• Further study needed to determine overall effects
Neonatal Behavioral Outcomes

- Least understood area of teratology
- No good animal models
- Neurotransmitters are reliably detected in the human brain in early gestation
- Effects of antidepressants are difficult to assess
- Potential area of concern
# Poor Neonatal Adaptation

<table>
<thead>
<tr>
<th>Common Symptoms</th>
<th>Less Common Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neurological</strong></td>
<td><strong>Neurological</strong></td>
</tr>
<tr>
<td>Jitteriness</td>
<td>Convulsions</td>
</tr>
<tr>
<td>Muscle tone regulation</td>
<td>Hyper-reflexia</td>
</tr>
<tr>
<td>Tremors</td>
<td>Lethargy</td>
</tr>
<tr>
<td>Sleeping difficulties</td>
<td>Gastrointestinal</td>
</tr>
<tr>
<td>High pitched/frequent crying</td>
<td>Diarrhea</td>
</tr>
<tr>
<td>Agitation/irritability</td>
<td>Uncoordinated/weak sucking</td>
</tr>
<tr>
<td>Myoclonia</td>
<td>Vomiting/regurgitation</td>
</tr>
<tr>
<td><strong>Gastrointestinal</strong></td>
<td><strong>Autonomous</strong></td>
</tr>
<tr>
<td>Feeding difficulties</td>
<td>Temperature instability</td>
</tr>
<tr>
<td><strong>Respiratory</strong></td>
<td><strong>Mottling</strong></td>
</tr>
<tr>
<td>Respiratory distress</td>
<td>Excessive sweating</td>
</tr>
<tr>
<td></td>
<td><strong>Nasal stuffiness</strong></td>
</tr>
</tbody>
</table>
Poor Neonatal Adaptation

- Symptoms occur in the immediate newborn period
- Affects 15-30% of infants born to mothers on SSRIs
- Symptoms typically resolve by 2 weeks after delivery
- Mechanism is unclear
  - Gene-SSRI interaction
  - “withdrawal” type of syndrome
  - Pharmacologic toxicity
# Characteristics of Toxicity vs Withdrawal

<table>
<thead>
<tr>
<th></th>
<th>Toxicity</th>
<th>Withdrawal</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Onset of symptoms</strong></td>
<td>Immediately post-partum</td>
<td>8-48 hrs</td>
</tr>
<tr>
<td><strong>Medication level in infant</strong></td>
<td>High</td>
<td>Low</td>
</tr>
<tr>
<td><strong>Medication – t ½</strong></td>
<td>Long</td>
<td>Short</td>
</tr>
<tr>
<td><strong>Type of psychotropic med</strong></td>
<td>Antidepressants, Benzodiazepines, Antipsychotics, Lithium</td>
<td>Antidepressants, Benzodiazepines, Antipsychotics</td>
</tr>
<tr>
<td><strong>Common symptoms</strong></td>
<td>Agitation/Irritability, Tremors, Jitteriness, Myoclonia, Respiratory distress, Hyperthermia/sweating, Hyperreflexia, Diarrhea, rigidity</td>
<td>Agitation/Irritability, Tremors, Jitteriness, Myoclonia, Respiratory distress, Feeding difficulties, Vomiting, Sleep difficulties, Hypo/hypertonia</td>
</tr>
</tbody>
</table>

Kieviel, et al. Neuropsych Dis treatment. 2013: 9; 1257-66
Poor Neonatal Adaptation

• Meta-analysis
• 8 studies
  – exposure to any antidepressant
  – risk of PNAS (OR=5.07, 95% CI 3.25 to 7.90) based
    • respiratory distress - OR=2.2 (95% CI 1.81 to 2.66)
    • tremor - OR=7.89 (95% CI 3.33 to 18.73)

  – Limitations
    • unable to adjust for maternal depression
    • studies differ substantially in the confounders included in the adjusted models
    • heterogeneity in the definitions of the outcomes

British Database Study

- WHO database of ADRs
- SSRIs & other antidepressants
- 93 cases of neonatal convulsions or withdrawal syndrome
  - IC = 2.68 (IC-2 SD 0.32)
- Almost 2/3 associated with paroxetine
  - IC = 4.07 (IC-2 SD 0.37)
- Sertraline, fluoxetine, citalopram

Long term effects

- Neurodevelopment of children exposed to antidepressant drugs in utero
  - 3 groups:
    - group 1 - TCA (80)
    - group 2 - fluoxetine (55)
    - group 3 - “control” (84)
    - global IQ and language development tested between 16 and 86 months postnatal age
  - results: no differences
    - major malformations
    - mean global IQ scores
    - language skills
    - temperament
  - conclusions:
    - in utero exposure does not affect IQ, language, or behavior in preschool children

Cognitive & Behavioral Development

• Very limited information available
• Recent systematic review:
  – Some studies show array of issues while others do not
  – Consolidating information and providing clinical recommendations is a challenge
  – Observational studies with methodological weaknesses
  – RCTs – ethical, medical and logistic problems
• Maternal psychiatric disorders/mood
  – impact behavior in off-spring
• No clear correlation between SSRI use & influence on cognitive, emotional, or behavioral development

Additional Neonatal Effects

- Bleeding
  - Effects on platelet aggregation
  - Serotonin in platelets
- Altered Pain reactivity
- Prolonged QT interval
Class or Drug?

• Studies generally grouped drugs together
  – SSRIs/SNRIs, TCAs, others
• Mechanistic differences
  – 5HT/NE selectivity
  – Potency
• Pharmacokinetic differences
  – $T_{1/2}$
Other psychiatric disorders

- Bipolar disorder
- Schizophrenia

- Lower prevalence than depression
- Higher degree of clinical complexity – higher service usage
- Prevalence of these disorders
Prevalence of Use of Antipsychotics

• 2001-2007
  – Medication Exposure in Pregnancy Risk Evaluation Program (MEPREP)
  – Study population:
    • 585,615 deliveries
    • 4223 (0.7%) filled at least one Rx for an atypical antipsychotic
    • 548 (0.09%) typical antipsychotic

Exposure to antipsychotics

- Atypical antipsychotics
  - 2.5 fold increase for over study period (0.33% -> 0.82%)
  - Quetiapine most commonly used (42%)
  - Diagnosis:
    - depression (63%) > bipolar (43%) > schizophrenia (13%)

- Typical antipsychotics
  - Prevalence low = 0.1% - remained stable
  - Patients more likely to have diagnosis of schizophrenia (27% vs 13%)

Psychotropic agents
Risks in pregnancy

• Mood stabilizers
  – Lithium
    • Avoid use in pregnancy if possible - risk of fetal cardiac anomalies
    • Floppy infant syndrome (FIS), thyroid toxicity
  – Anti-epileptic medications (valproate, carbamazepine, lamotrigine)
    • Increased risk of neural tube defects, fetal valproate syndrome, fetal carbamazepine syndrome
    • Limited data with lamotrigine – possible oral clefts

• Antipsychotics
  – Typical / First generation
    • Haloperidol, promethazine, chlorpromazine, etc
    • Risks of malformations appears to be low, potential for withdrawal
  – Atypical / Second generation
    • Olanzapine, quetiapine, clozapine, risperidone, aripiprazole, ziprasidone
    • Limited data – FIS, agranulocytosis, poor neonatal adaptation; induce metabolic syndrome in mother

Practice Points

• Antidepressants/antipsychotics
  – may be the only viable treatment option
• Patient education regarding the risks of antidepressants during pregnancy
• Choice of agent:
  – History of positive response
  – Fetus already exposed
  – New medications have limited or no data
• Dose management in pregnancy
  – Minimal effective dose
  – It may be necessary to increase dose as pregnancy progresses
  – Continue through delivery
• Antidepressants – transition to breastfeeding
  – Use same criteria
  – Exposure is significantly decreased
Patient Case

• DP is a 31 yr old woman, currently 8 weeks pregnant - pregnancy unremarkable to date
• Started fluoxetine ~ 1 yr ago d/t persistent negative thoughts, depressed mood and anxiety, sx’s were similar to a previous episode – received counseling and tried several medications.
• Currently not sleeping well and her mood is not as bright as usual – she prefers to stay home, but is able to get out with friends periodically.
• She has a good support system and feels that she is better on fluoxetine – her current dose is 20 mg daily.
Case - considerations

• Do you agree that the symptoms are consistent with a diagnosis of depression?
• What should be considered in the treatment options for this patient?
• What would you monitor as her pregnancy progresses?
• What counseling would you provide for this patient?
Thoughts regarding the case...

• Likely having some breakthrough symptoms
  – Hard to know if symptoms related to depression
    or early pregnancy
• She has tried several medications in past –
  likely best to continue fluoxetine at this time
  – Data would not suggest increase in fetal adverse
effects
  – May have symptoms following delivery
• Monitor closely for progression of disease
Conclusion

• Weigh risk vs. benefits
  – Pharmacologic treatment generally preferred
  – Neonatal monitoring
• Untreated depression also has risk
• No preferred antidepressant in pregnancy
  – Take into account individual circumstances
• Further studies need to adequately assess fetal and perinatal risk
# Antidepressant Medication Chart

This chart is intended for clinicians who provide primary care to pregnant and postpartum women. Data current as of April 2012.

<table>
<thead>
<tr>
<th>Antidepressants</th>
<th>Trade Name</th>
<th>Usual Daily Dose</th>
<th>Benefits</th>
<th>Maternal Risks</th>
<th>Fetal/Neonatal Risks</th>
<th>Relative infant dose (RID)</th>
<th>Half-life (1/2)</th>
<th>Reported side effects in breastfed infants</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DRUG CLASS:</strong> Selective Serotonin Reuptake Inhibitors (SSRIs)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Citalopram</td>
<td>Celexa*</td>
<td>20–40mg</td>
<td>• No adverse morphologic consequences for infant found</td>
<td>• Side effects include nausea, insomnia, dizziness, and somnolence</td>
<td>• Behavioral consequences for infant unknown</td>
<td>3.60%</td>
<td>• Drug has intermediate 1/2 (1-2 days)</td>
<td>• Severe colic</td>
</tr>
<tr>
<td>Esctalopram</td>
<td>Lexapro*</td>
<td>10–20mg</td>
<td>• Few interactions with other medications</td>
<td>• Side effects include nausea, insomnia, somnolence, dizziness, fatigue, diarrhea, sexual dysfunction, and dry mouth</td>
<td>• No systematic studies in human pregnancy</td>
<td>5.2–8.8%</td>
<td>• Drug and active metabolite have intermediate 1/2 (1-2 days)</td>
<td>• Somnolence</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>Prozac*</td>
<td>20–60mg</td>
<td>• More studies in human pregnancy, including meta-analysis and nonrandomized follow-up</td>
<td>• Side effects include nausea, drowsiness, sexual dysfunction</td>
<td>• More reports of neonatal side effects than other antidepressants</td>
<td>1.6–14.6%</td>
<td>• Drug and active metabolites have very long 1/2 (days to weeks)</td>
<td>• Severe colic</td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td>Luvox*</td>
<td>50–200mg</td>
<td>• No adverse morphologic consequences for infant found</td>
<td>• Side effects include nausea, drowsiness, anorexia, anxiety, and sexual dysfunction</td>
<td>• Behavioral consequences for infant unknown</td>
<td>0.3–1.4%</td>
<td>• Drug has short 1/2 (hours)</td>
<td>• Major metabolite not active</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>Paxil*</td>
<td>20–60mg</td>
<td>• None—avoid during pregnancy if possible</td>
<td>• May increase risk of miscarriage</td>
<td>• Behavioral consequences for infant unknown</td>
<td>1.2–2.8%</td>
<td>• Drug has relatively short 1/2, but variable (hours to days)</td>
<td>• No active metabolites</td>
</tr>
<tr>
<td>Sertraline</td>
<td>Zoloft*</td>
<td>50–200mg</td>
<td>• Relatively well-studied in human pregnancy</td>
<td>• Side effects include nausea, drowsiness, tremors, insomnia, and sexual dysfunction</td>
<td>• Possible specific association with omphalocoele and cardiac septal defects</td>
<td>0.4–2.2%</td>
<td>• Drug and weakly active metabolite have intermediate 1/2 (1-2 days)</td>
<td>• Detectable levels in some infants, but no adverse effects</td>
</tr>
</tbody>
</table>

For additional information contact: Wisconsin Association for Perinatal Care | 211 S. Paterson St., Suite 250 | Madison, WI 53703 | www.perinatalweb.org | Email: wapc@perinatalweb.org
# Antidepressant Medication Chart

This chart is intended for clinicians who provide primary care to pregnant and postpartum women.

## Drug Class: Tricyclic Antidepressants (TCAs)
- **Desipramine**
  - **Trade Name**: Norpramin®
  - **Usual Dose**: 100-300mg
  - **Benefits**: More studies in human pregnancy, including antidepressant and follow-up
    - No adverse side effects for infant found
  - **Maternal Risks**: Side effects include sedation, weight gain, dry mouth, constipation
  - **Fetal/Neonatal Risks**: Fetal and neonatal side effects include tachycardia and primary retention
  - **Relative Infant Dose (RID)**: 0.2-0.9%
  - **Metabolites**: Drug and active metabolite have intermediate metabolism (1-3 days)
  - **Breastfeeding**: Not detected in infants
  - **Reported Side Effects in Breastfed Infants**: No reported adverse events in infants found

- **Nortriptyline**
  - **Trade Name**: Pamelor®
  - **Usual Dose**: 50-150mg
  - **Benefits**: More studies in human pregnancy, including antidepressant and follow-up
    - No adverse side effects for infant found
  - **Maternal Risks**: Side effects include sedation, weight gain, dry mouth, constipation
  - **Fetal/Neonatal Risks**: Fetal and neonatal side effects include tachycardia and primary retention
  - **Relative Infant Dose (RID)**: 1.7-3.1%
  - **Metabolites**: Drug has intermediate metabolism (2-1 day)
  - **Breastfeeding**: No active metabolites
  - **Reported Side Effects in Breastfed Infants**: No reported adverse events in infants found

## Drug Class: Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)
- **Duloxetine**
  - **Trade Name**: Cymbalta®
  - **Usual Dose**: 40-60mg
  - **Benefits**: Balanced antidepressant, may be effective when selective agents are not
    - Low cord-trial serum ratio suggests limited transfer across the placenta
  - **Maternal Risks**: Common side effects include nausea, dry mouth, constipation, dizziness
  - **Fetal/Neonatal Risks**: No systematic studies in human pregnancy
  - **Relative Infant Dose (RID)**: 0.10%
  - **Breastfeeding**: Drug has short 1/2 (2-1 day)
  - **Reported Side Effects in Breastfed Infants**: No reported adverse events in infants found

- **Venlafaxine**
  - **Trade Name**: Effexor®
  - **Usual Dose**: 75-300mg
  - **Benefits**: Balanced antidepressant, may be effective when selective agents are not
    - No adverse morphologic consequences for infant found
  - **Maternal Risks**: May increase risk of miscarriage
  - **Fetal/Neonatal Risks**: No behavioral studies in human pregnancy
  - **Relative Infant Dose (RID)**: 6.8-8.1%
  - **Breastfeeding**: Drug and active metabolite have short 1/2 (approx 5h)
  - **Reported Side Effects in Breastfed Infants**: Detectable plasma levels in some breastfed infants, were not associated with any adverse effects

## Drug Class: Other
- **Bupropion**
  - **Trade Name**: Wellbutrin®, Zyban®
  - **Usual Dose**: 300-450mg
  - **Benefits**: No adverse morphologic consequences for infant found
    - Helps with smoking cessation (nevers tested in pregnancy)
  - **Maternal Risks**: May increase risk of miscarriage
  - **Fetal/Neonatal Risks**: Behavioral consequences for infant
  - **Relative Infant Dose (RID)**: 0.6-2.9%
  - **Breastfeeding**: Drug and active metabolite have intermediate metabolism (1-2 days)
  - **Reported Side Effects in Breastfed Infants**: One reported case of seizure in a 6 month old

- **Mirtazapine**
  - **Trade Name**: Remeron®
  - **Usual Dose**: 15-45mg
  - **Benefits**: No adverse morphologic consequences for infant found
    - Helps to control appetite in women who are not gaining weight
  - **Maternal Risks**: May increase risk of miscarriage
  - **Fetal/Neonatal Risks**: Behavioral consequences for infant unknown
  - **Relative Infant Dose (RID)**: 1.6-6.3%
  - **Breastfeeding**: Drug and active metabolite have intermediate metabolism (1-2 days)
  - **Reported Side Effects in Breastfed Infants**: No adverse effects reported
  - **Observation**: Observe for sedation
Thank You!