Psychiatric Drug Treatment and Pregnancy

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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 2nd and 3rd 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

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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

Category	Interpretation
A	Adequate, well-controlled studies in pregnant women have not shown an increased risk of fetal abnormalities to the fetus in any trimester of pregnancy.
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)

Rampano J, et al. Placental transfer of SSRI and SNRI antidepressants and effects on the neonate. Pharmacopsychiatry 2009;42:95-100.

Reproductive Risk

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

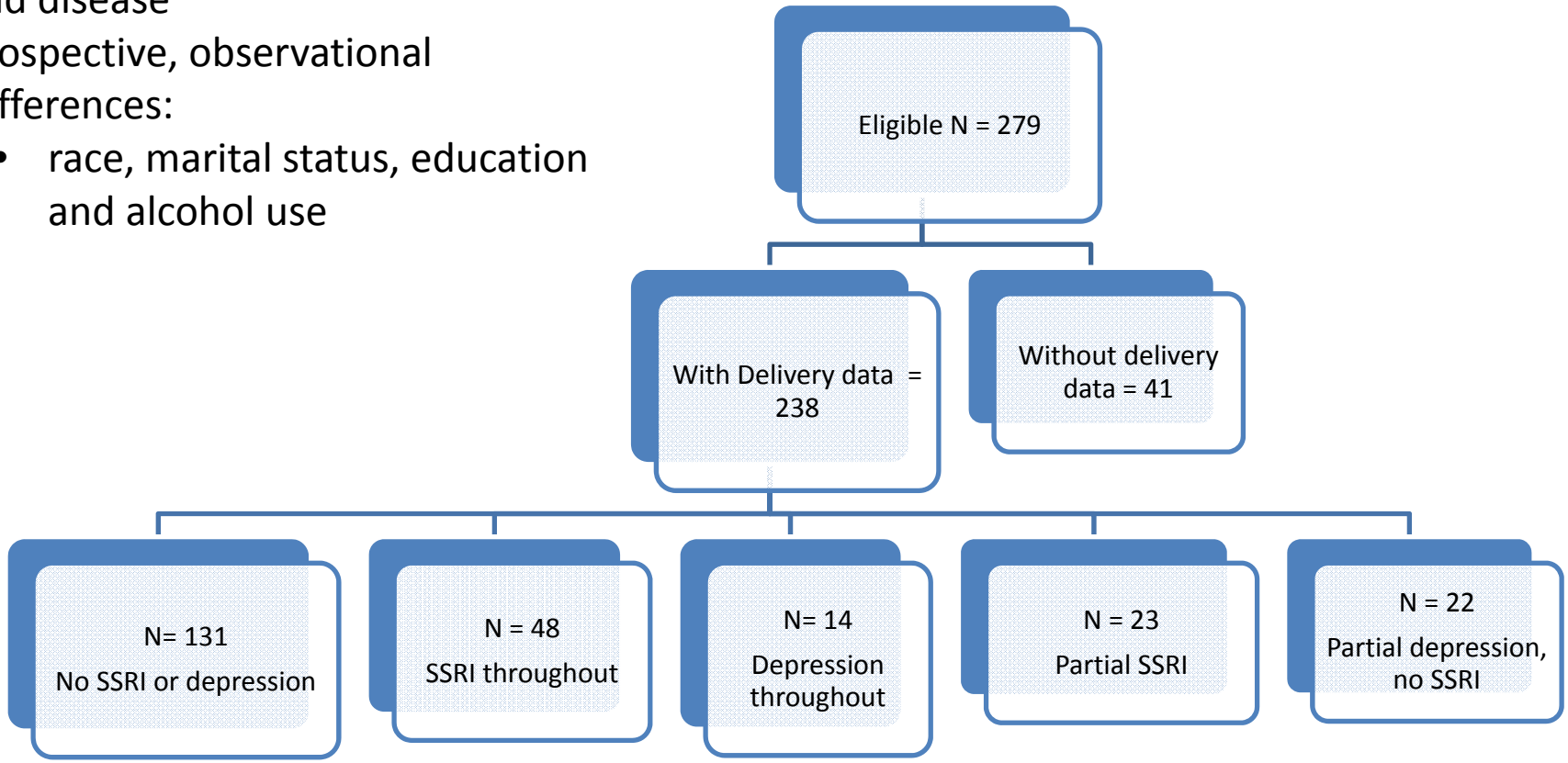
Spontaneous Abortion

- 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

Ann Pharmacother 2005;39:803-9
Ross LE, et al. JAMA Psych 2013;70:436-43

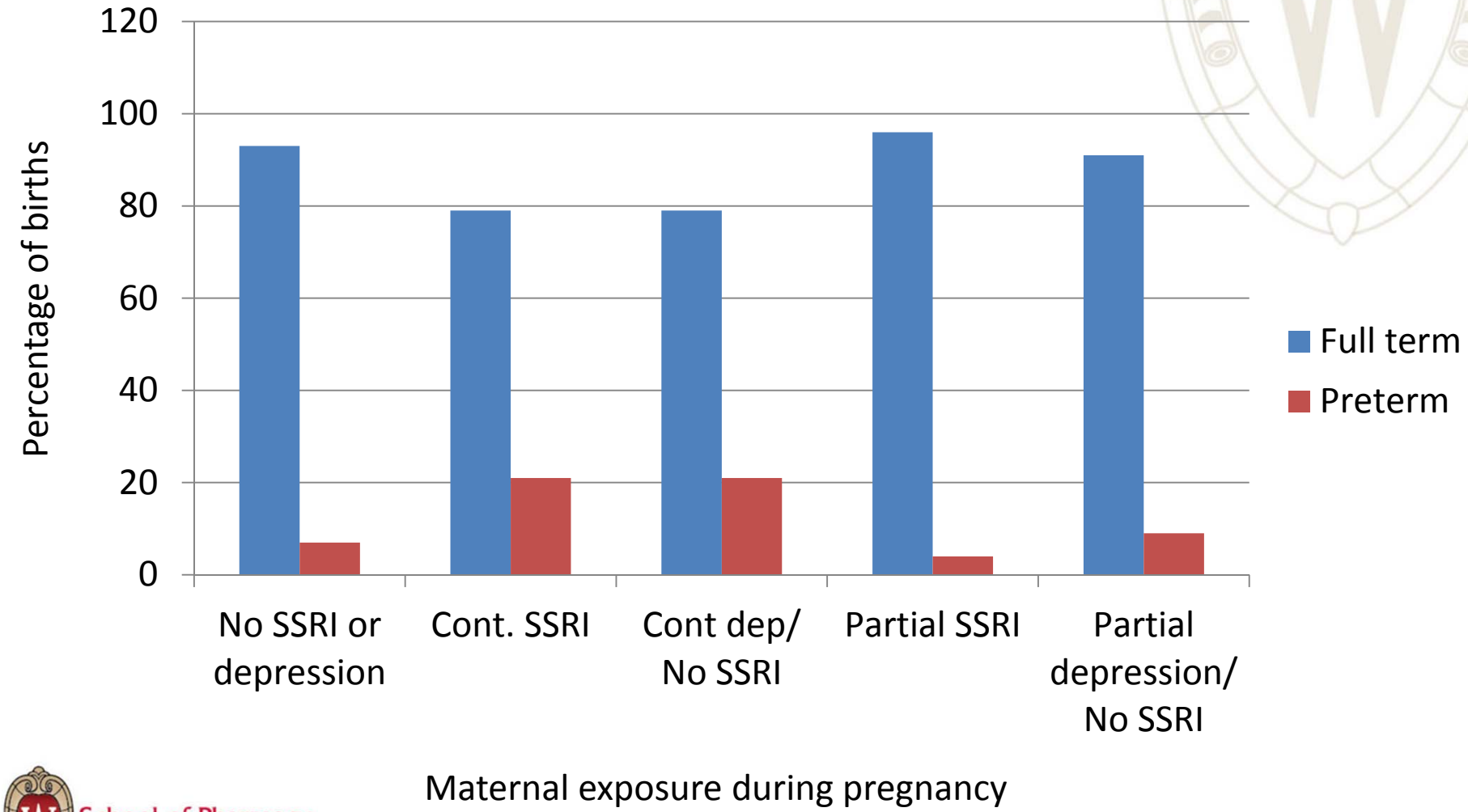
Depression and Treatment: Impact on Premature Birth

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



Wisner, et al. Am J Psych 2009

Gestational Age and SSRI Exposure



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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 2nd 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 3rd 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

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Hayes RM et al. Am J Ob Gyn 2012;207:e1-9

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 5th and 8th 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

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

n = number of studies

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Koren G et al. Antidepressant use during pregnancy: the benefit-risk ratio. Am J Ob Gyn Sept 2012;157-163.

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

Exposure Group	Total # women	Any cardiac malformation	RVOTO	VSD	Other cardiac malformation
		No./10,000	No./10,000	No./10,000	No./10,000
No exposure	885,115	72.3	11.8	36.3	36.5
Any antidep	64,389	90.1	13.0	44.4	49.4
SSRI	46,144	90.2	13.2	43.6	49.0
- Paroxetine	11,126	83.6	14.4	39.5	43.1
- Sertraline	14,040	91.9	12.1	44.9	50.6
- Fluoxetine	11,048	89.6	14.5	43.4	49.8
TCA	5954	70.5	13.4	40.3	30.2
SNRI	6904	108.6	17.4	56.5	55.0
Bupropion	8856	85.8	12.4	44.0	55.3
Other	7055	104.9	11.3	43.9	65.2

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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 0.1.58-7.02; P=0.002)
  - 5 - late pregnancy
    - Pooled OR = 2.5 (95% CI 1.32-4.73; P=0.005)

Grigoriadis S, et al. BMJ 2013; 348: 1-11

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

Common Symptoms	Less Common Symptoms
Neurological Jitteriness Muscle tone regulation Tremors Sleeping difficulties High pitched/frequent crying Agitation/irritability Myoclonia Gastrointestinal Feeding difficulties Respiratory Respiratory distress	Neurological Convulsions Hyper-reflexia Lethargy Gastrointestinal Diarrhea Uncoordinated/weak sucking Vomiting/regurgitation Autonomous Temperature instability Mottling Excessive sweating Nasal stuffiness

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

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

Kieviet, etal. 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

Grigoriadis S et al. J Clin Psych 2013;74(4):e309-20

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

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Sanz EJ, et al. Selective serotonin reuptake inhibitors in pregnant women and neonatal withdrawal syndrome: a database analysis. *Lancet* 2005;365:482-487.

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 effect IQ, language, or behavior in preschool children

Nulman I, et al, N Engl J Med 1997;336(4):258-62.

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

Marroun HE, et al. Eur Child Adolesc Psychiatry 2014; May 27 [epub ahead of print]

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

Toh S, et al. Arch Womens Ment Health. 2013;16:149-157

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%)

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Toh S, et al. Arch Womens Ment Health. 2013;16:149-157

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

Marroun HE, et al. Eur Child Adolesc Psychiatry 2014; May 27 [epub ahead of print]

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

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ANTIDEPRESSANT MEDICATION CHART

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

Data current as of April 2012

Antidepressants	Trade Name	Usual Daily Dose	Benefits	Maternal Risks	Fetal/Neonatal Risks	Breastfeeding: Relative infant dose=(RID)	Breastfeeding: Half-life (t1/2)/ metabolites	Breastfeeding: Reported side effects in breastfed infants
DRUG CLASS: Selective Serotonin Reuptake Inhibitors (SSRIs)								
Citalopram	Celexa®	20-40mg	• No adverse morphologic consequences for infant found • Few interactions with other medications	• Side effects include nausea, insomnia, dizziness, and somnolence	• Behavioral consequences for infant unknown • Possible increased risk of growth restriction • Possible increased risk of neural tube defects and cardiac defects (ASD)	3.60%	• Drug has intermediate t1/2 (1-2 days) • 3 weak metabolites with little activity	• Somnolence • Decreased feeding • Weight loss
Escitalopram	Lexapro®	10-20mg	• Few interactions with other medications • No adverse morphologic consequences for infant found	• Side effects include nausea, insomnia, somnolence, dizziness, fatigue, diarrhea, sexual dysfunction, and dry mouth	• No systematic studies in human pregnancy • Morphologic and behavioral consequences for infant unknown • Possible increased risk of growth restriction • Possible increased risk of necrotizing enterocolitis	5.2-8%	• Drug and active metabolite have intermediate t1/2 (1-2 days)	• Somnolence • Decreased feeding • Weight loss
Fluoxetine	Prozac®	20-60mg	• More studies in human pregnancy, including meta-analysis and neurodevelopmental follow-up • No adverse behavioral consequences for infant found	• Side effects include nausea, drowsiness, and sexual dysfunction • Possible drug interactions	• More reports of neonatal side effects than some other antidepressants • Possible morphological changes	1.6-14.6%	• Drug and active metabolites have very long t1/2 (days to weeks) • Serum levels similar to those in adults reported in some symptomatic infants	• Severe colic • Fussiness • Crying
Fluvoxamine	Luvox®	50-200mg	• No adverse morphologic consequences for infant found	• Side effects include nausea, drowsiness, anorexia, anxiety, and sexual dysfunction • Possible drug interactions	• Behavioral consequences for infant unknown	0.3-1.4%	• Drug has short t1/2 (hours) • Major metabolite not active	• No reported concerns
Paroxetine	Paxil®	20-60mg	• None--avoid during pregnancy if possible	• May increase risk of miscarriage • Side effects include nausea, drowsiness, fatigue, dizziness, and sexual dysfunction.	• Behavioral consequences for infant unknown • More reports of neonatal side effects than most other antidepressants • Possible association with cardiovascular malformations in infant	1.2-2.8%	• Drug has relatively short t1/2, but variable (hours to days) • No active metabolites	• Numerous studies suggest minimal to no effect on breastfed infants
Sertraline	Zoloft®	50-200mg	• Relatively well-studied in human pregnancy • No adverse behavioral consequences for infants found • Fewer reports of neonatal side effects than other antidepressants	• Side effects include nausea, loose stools, tremors, insomnia, and sexual dysfunction • Possible drug interactions	• Possible specific association with omphalocele and cardiac septal defects	0.4-2.2%	• Drug and weakly active metabolite have intermediate t1/2 (1-2 days) • Detectable levels in some infants, but no adverse effects	• 1 report of benign neonatal sleep myoclonus (relationship unknown)

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

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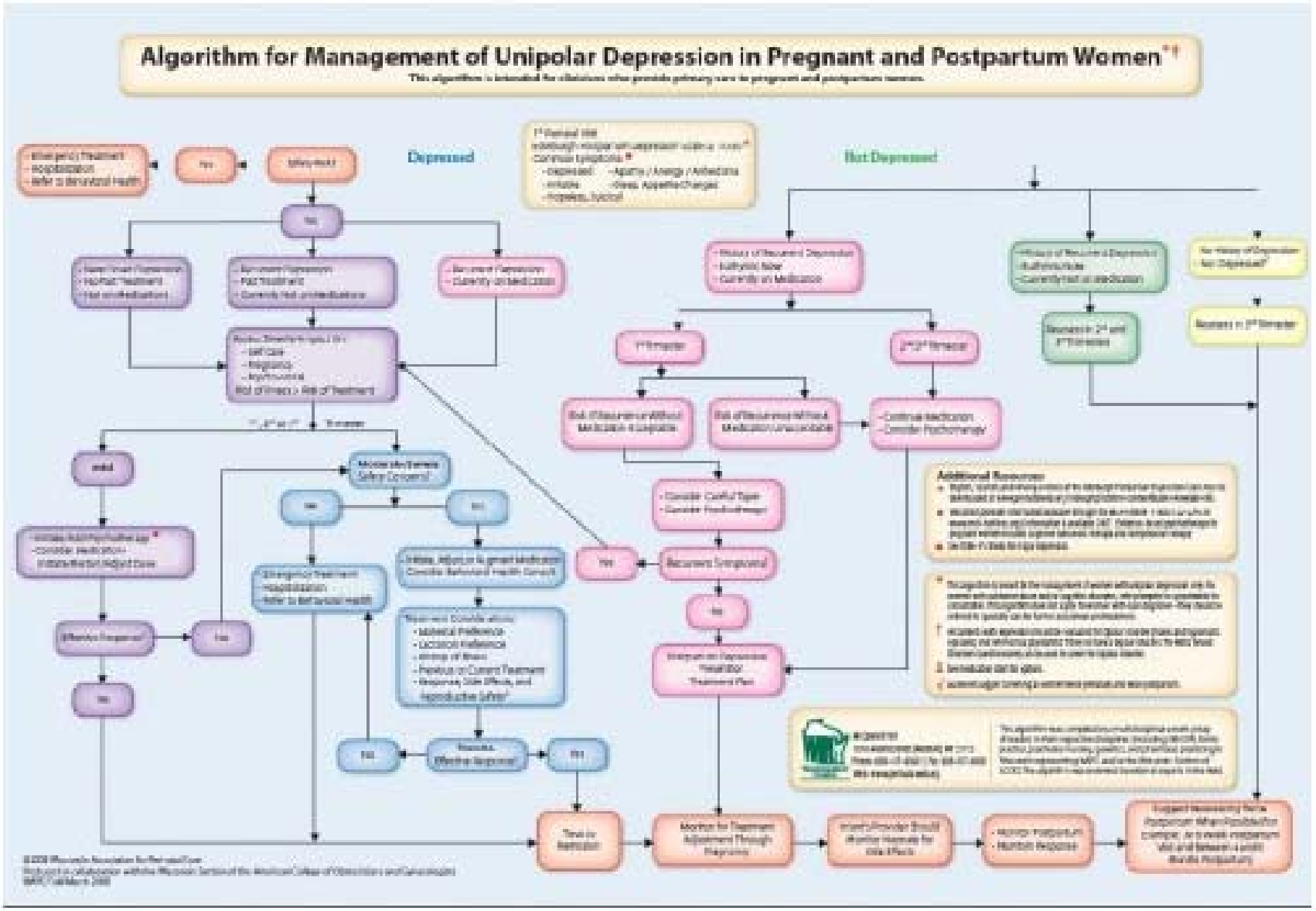
ANTIDEPRESSANT MEDICATION CHART

(No Audio)

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

Data current as of April 2012

Antidepressants	Trade Name	Usual Daily Dose	Benefits	Maternal Risks	Fetal/Neonatal Risks	Breastfeeding: Relative infant dose=(RID)	Breastfeeding: Half-life (t1/2)/ metabolites	Breastfeeding: Reported side effects in breastfed infants
DRUG CLASS: Tricyclic antidepressants (TSAs)								
Desipramine	Norpramin®	100-300mg	• More studies in human pregnancy, including neurodevelopmental follow-up • No adverse morphologic consequences for infant found • No adverse behavioral consequences for infant found • May be useful if sedation desired	• Side effects include sedation, weight gain, dry mouth, constipation, and orthostatic hypotension--baseline ECG recommended • Possible drug interactions	• Fetal and neonatal side effects include tachycardia and urinary retention	0.2-0.9%	• Drug and active metabolite have intermediate t1/2 (1-2 days) • Not detected in infants	• No reported adverse events in infants found
Nortriptyline	Pamelor®	50-150mg	• More studies in human pregnancy, including neurodevelopmental follow-up • No adverse morphologic consequences for infant found • No adverse behavioral consequences for infant found • May be useful if sedation desired	• Side effects include sedation, weight gain, dry mouth, constipation, and orthostatic hypotension--baseline ECG recommended • Possible drug interactions	• Fetal and neonatal side effects include tachycardia and urinary retention	1.7-3.1%	• Drug has intermediate t1/2 (≥1 day) • No active metabolites	• No reported adverse events in infants found
DRUG CLASS: Serotonin Norepinephrine Reuptake Inhibitors (SNRIs)								
Duloxetine	Cymbalta®	40-60mg	• Balanced antidepressant; may be effective when selective agents are not • Low cord to maternal serum ratio suggests limited transfer across the placenta	• Common side effects include nausea, dry mouth, constipation, diarrhea, vomiting, decreased appetite, fatigue, dizziness ,somnolence, tremors, sweating, blurred vision, and insomnia	• No systematic studies in human pregnancy • Morphologic and behavioral consequences for infant unknown	0.10%	• Drug has short t1/2 (hours) • No active metabolites • Relative infant dose low	• No reported adverse events in infants found
Venlafaxine	Effexor®	75-300mg	• Balanced antidepressant; may be effective when selective agents are not • No adverse morphologic consequences for infant found	• May increase risk of miscarriage • Maternal side effects include nausea, sweating, dry mouth, dizziness, insomnia, somnolence, and sexual dysfunction	• No behavioral studies in human pregnancy • Possible neonatal risk of respiratory, cyanosis, apnea, seizures, and temperature instability	6.8-8.1%	• Drug and active metabolite have short t1/2 (approx 5 h)	• Detectable plasma levels in several breastfed infants were not associated with any adverse effects
DRUG CLASS: Other								
Bupropion	Wellbutrin® Zyban®	300-450mg	• No adverse morphologic consequences for infant found • Helps with smoking cessation (never tested in pregnancy)	• May increase risk of miscarriage • Maternal side effects include dizziness, headache, dry mouth, sweating, tremor, agitation, insomnia, and rare seizures • Possible drug interactions	• Behavioral consequences for infant • Possible increased risk of CHD (left outflow tract defects) • Possible increased risk of fetal cardiac arrhythmia	0.6-2%	• Drug and active metabolite have intermediate t1/2 (~ 1 day) • Plasma levels undetectable in breastfed infant	• One reported case of seizure in a 6 month old
Mirtazapine	Remeron®	15-45mg	• No adverse morphologic consequences for infant found • Helps restore appetite in women who are not gaining weight • Less likely to exacerbate nausea and vomiting	• May increase risk of miscarriage • Maternal side effects include somnolence, nausea, weight gain, and dizziness	• Behavioral consequences for infant unknown • May increase risk of preterm birth • Possible hypothermia	1.6-6.3%	• Drug and active metabolite have intermediate t1/2 (1-2 d) • Very low plasma level detected in 1 of 3 infants tested	• No adverse effects reported • Observe for sedation



(No Audio) For additional information contact: Wisconsin Association for Perinatal Care | www.perinatalweb.org

Thank You!

School of Pharmacy
UNIVERSITY OF WISCONSIN–MADISON