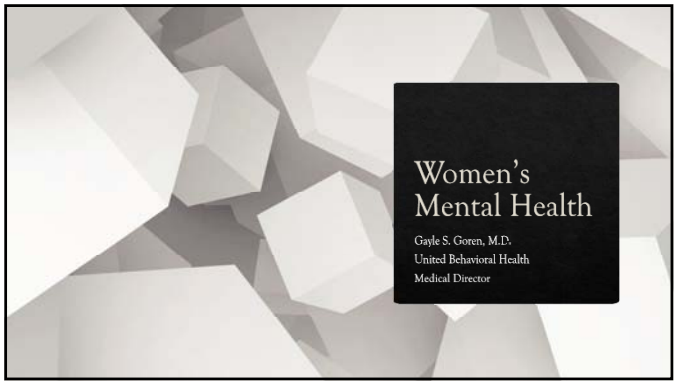

1

Lifetime Prevalence of Psychiatric Disorders in Women and Men

DISORDER	WOMEN	MEN
Depression	21.3	12.7
Dysthymia	8.0	4.8
Bipolar I disorder	0.9	0.7
Bipolar II disorder	0.5	0.4
Seasonal affective disorder	6.3	1.0
Panic disorder	5.0	2.0

A Clinical Primer

2

Lifetime Prevalence of Psychiatric Disorders in Women and Men

DISORDER	WOMEN	MEN
Social Phobia	15.5	11.1
Generalized Anxiety Disorder	6.6	3.6
Schizophrenia	1.7	1.2
Alcohol Dependence	8.2	20.1
Alcohol abuse without dependence	6.4	12.5
Drug Dependence	5.9	9.2

3

Lifetime Prevalence of Psychiatric Disorders in Women and Men

DISORDER	WOMEN	MEN
Drug abuse without dependence	3.5	5.4
Anorexia Nervosa	0.5	0.05
Bulimia	1.1	0.1

4

Gender Differences in Psychiatric Disorders

- There are difference in lifetime prevalence in psychiatric disorders.
- There are differences in the expression, comorbidities and course of illness between men and women.
- Depressed women are more likely than men to experience anxious, somatic symptoms.
  - Increased sleep
  - Appetite disturbances
  - Physical pain

5

Gender Differences in Psychiatric Disorders

- Women with chronic depression have a younger age of onset, greater family history of mood disorders, worse social adjustment and worse quality of life than men with chronic depression.
- Bipolar Disorder has equal prevalence in both genders, but women are more prone to rapid cycling.
- In schizophrenia, women experience a later age of onset, fewer negative symptoms and better treatment response than men.

6

Gender Differences in Psychopharmacology

- Women are 50% more likely than men to receive an antidepressant or anxiolytic agent during a medical visit.
- There is increasing evidence that there are differences in how the body metabolizes medications.
  - The liver may metabolize medications differently because of estrogen's effects on hepatic enzymes. (e.g., oral contraceptives and lamotrigine)
  - Progesterone may slow gastric emptying, influencing drug absorption.
  - Estrogen and progesterone are strongly bound to proteins and may compete with psychotropic medications for proteir-binding sites. May affect available drug in the blood stream.

7

Important Laboratory Considerations

8

Important Laboratory Considerations

- Assessment for thyroid dysfunction, especially with changes in energy, weight, anxiety and mood.
- Assessment in middle-aged women for Follicle-Stimulating Hormone (FSH) and Estradiol Levels – may be helpful in identifying perimenopausal and menopausal status.
- Pregnancy must be ruled-out.

9

Important Laboratory Considerations

- Irregular, or absent menses – should check prolactin levels (prolactin secreting tumor, side effects of antipsychotic medications) and thyroid levels.
- For women with a history of an eating disorder, an evaluation should include a physical exam, dental exam, lab tests for kidney function, electrolytes, liver function, amylase, serum protein levels and ECG.

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Premenstrual Dysphoric Disorder (PMDD)

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Premenstrual Dysphoric Disorder

- PMDD is an official diagnosis in the DSM V.
- Criteria include:
  - A. Timing of symptoms – at least 5 symptoms must be present in the final week before onset of menses, start to improve within a few days of onset of menses, and become minimal or absent in the week post-menses.

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Premenstrual Dysphoric Disorder

B. One (or more) of the following symptoms:

1. Marked affective lability (e.g., mood swings, feeling suddenly tearful or sad, or increased sensitivity to rejection
2. Marked irritability, anger or increased interpersonal conflict
3. Markedly depressed mood, feelings of hopelessness or self-deprecating thoughts
4. Marked anxiety, tension and/or feeling on edge.

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Premenstrual Dysphoric Disorder

C. One (or more) of the following symptoms:

1. Decreased interest in usual activities
2. Subjective difficulty in concentration
3. Lethargy, easy fatigability, or marked lack of energy
4. Marked changes in appetite, over-eating or specific food cravings
5. Hypersomnia or insomnia
6. Sense of being overwhelmed or out of control
7. Physical symptoms = breast tenderness or swelling, joint or muscle pain, "bloating," or weight gain

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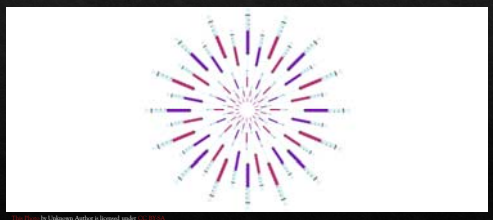
Hormonal Contraception and Effects on Mood



15

Advantages of Oral Contraceptives on Mood

- Regulation of menses
- Reduction in the rise of endometrial and ovarian cancer
- Reduction in ovarian cysts
- Reduction in ectopic pregnancies
- Reduction of incidence of iron deficiency anemia due to heavy menses

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Increased Risk of Adverse Events

- Thromboembolism
- Cerebrovascular events
- Hypertension
- Gallstones
- Benign Hepatic tumors
- Post-usage amenorrhea (loss of menses)

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Psychiatric Disorders in Pregnancy

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Psychiatric Disorders in Pregnancy

- Psychiatric Disorders affect both the mother's well-being and the pregnancy.
- Mood symptoms, anxiety, and psychotic symptoms during pregnancy are linked with an increased risk of preeclampsia, placental abnormalities, low birth weight, pre-term labor and fetal distress.

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U.S. Food and Drug Administration Use-In-Pregnancy Ratings

Rating	Interpretation
A	**Controlled studies show no risk** – Adequate, well-controlled studies in pregnant women have failed to demonstrate risk to the fetus in any trimester of pregnancy.
B	**No evidence of risk in humans** – Adequate, well-controlled studies in pregnant women have not shown increased risk of fetal abnormalities despite adverse findings in animals, or, in the absence of adequate human studies, animal studies show no fetal risk. The chance of fetal harm is remote but remains a possibility.
C	**Risk cannot be ruled out** – Adequate, well-controlled human studies are lacking, and animal studies have shown a risk to the fetus or are lacking as well. There is a chance of fetal harm if the drug is administered during pregnancy, but the potential benefits may outweigh the potential risk.
D	**Positive evidence of risk** – studies in human, or investigation or postmarketing data, have demonstrated fetal risk. Nevertheless, potential benefits from the use of the drug may outweigh the potential risk.
X	**Contraindicated in pregnancy** – studies in animals or humans, or investigational or postmarketing reports have demonstrated positive evidence of fetal abnormalities or risk which clearly outweighs any possible benefit to the patient.

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Stats about Depression in Women During the Reproductive Years

- 18.4% of women suffer from antenatal depressive and anxiety disorders
- 19.2% of mothers develop a depressive disorder within weeks of delivery
- 21.7% of women develop anxiety disorders during the 3rd trimester of pregnancy, 11.1% during the first 3 post-partum months
- Depression in pregnancy can lead to inadequate nutrition, maternal weight gain and substance abuse
- Depression in pregnancy associated with preeclampsia, preterm birth, increase risk of low-birth-weight infant, elective termination of pregnancy, post-partum depression and anxiety, fetal distress and increased risk of neonatal care unit admissions and c-sections

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Summary of Effects of in utero Exposure to Antidepressants

ANTIDEPRESSANT	TERATOGENICITY	POTENTIAL PERINATAL SIDE EFFECTS
SSRIs	See below for each agent	For SSRIs in general, some reports describe increased risk of perinatal complications (jitteriness, tachypnea, respiratory distress, hypoglycemia, poor tone, lower Apgar scores, premature delivery, lower birth weight when used in third trimester). Some report (2 studies) of pulmonary hypertension in the newborn. Other studies do not show this effect.
Fluoxetine (Prozac) Class C	• No evidence of major congenital abnormalities. • Long-term follow up to age 7 years suggests no adverse neurobehavioral abnormalities.	Transmission of fluoxetine in breastmilk occurs, there is no evidence of adverse effects.

22

Summary of Effects of in utero Exposure to Antidepressants

ANTIDEPRESSANT	TERATOGENICITY	POTENTIAL PERINATAL SIDE EFFECTS
Sertraline (Zoloft) Category C	No evidence of major anomalies. No evidence of long-term neurobehavioral abnormalities.	No evidence of cardiac malformations. Low transmission in breast milk.
Paroxetine (Paxil) Category D	In the Fall of 2005, GlaxoSmithKline published a study that infants exposed to Paxil were at higher risk of cardiac malformations (septal defects) – Contraindicated in pregnancy.	
Citalopram (Celexa), Escitalopram (Lexapro) Category C	No evidence of major anomalies, no evidence of long-term behavioral abnormalities.	Citalopram is transmitted in breast milk in a relatively high amount, escitalopram is transmitted in a low amount. No evidence of adverse effects with either medication.

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Summary of Effects of in utero Exposure to Antidepressants

ANTIDEPRESSANT	TERATOGENICITY	POTENTIAL PERINATAL EFFECTS
Fluvoxamine (Luvox), Venlafaxine (Effexor), Duloxetine (Cymbalta) Category C	No evidence of major congenital anomalies. No long-term neurobehavioral adverse outcomes. The risk of spontaneous abortion for Cymbalta is not increased over the general population.	Not adequate data to comment on the risk of preterm delivery, low birth weight, poor neonatal adaptation, and persistent pulmonary hypertension of the newborn.
Trazodone, Nefazodone Category C	No evidence of major congenital anomalies. No long-term neurobehavioral adverse outcomes.	No increased risk of perinatal complications.
Tricyclic Antidepressants Category C	Appear to be safe: Nortriptyline and Desipramine preferred. Long-term f/up to age 7 years suggests no adverse neurobehavioral abnormalities.	Toxicity and withdrawal sxs have been reported, including lethargy, hypotonia, jitteriness, irritability, anticholinergic effects (e.g., constipation, tachycardia, urinary retention).
Monoamine Oxidase Inhibitors (Category C)	Increased rate of congenital anomalies in animal studies.	Contraindicated: potential hypertensive crisis if tocolytic agents needed.
Buproprion (Wellbutrin) Category B	No association with congenital malformations.	Two small studies showed a possible association with a higher risk of spontaneous abortion. Other studies have not shown this association.

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Risks of Untreated Bipolar Illness for Mother

- Increased risk of mood episodes 8.5% if medications stopped
- Increased risk of c-section
- Placental abnormalities
- Antepartum hemorrhage
- Pre-eclampsia (high blood pressure with possible damage to kidney/liver; occurs after week 20 of pregnancy)

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Risks of Untreated Bipolar Illness to Baby

- Pre-term birth
- Small for gestational age
- Low birth weight
- Poor developmental outcomes

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Summary of Effects of in utero Exposure to Mood Stabilizers

MEDICATION	TERATOGENICITY	POTENTIAL PERINATAL EFFECTS
Lithium Category D	Increased risk of cardiac malformations with first trimester use (Ebstein's anomaly).	Case reports suggest: diabetes insipidus, hypotonia, transient hypothyroidism, respiratory problems, poor suck reflex, cyanosis, hypoglycemia, tremor, tachycardia, neuromuscular complications. Lithium crosses the placenta. Lithium concentration in milk is substantially less than in utero exposure
Lamictal Category C	Considered first-line among anti-epileptics. Potential increased risk of cleft palate, from 1 study, not replicated in 5 other studies.	No evidence of perinatal complications. High dose folic acid is recommended. Variable passage into breast milk
Valproate (Depakote) Category D	Significantly increased risk of neural tube defects with first trimester exposure. Significantly increased risk of developmental delay, craniofacial defects and fingernail hypoplasia	Reports of hypoglycemia and hepatic dysfunction. Low levels passed in breast milk.

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Summary of Effects of in utero Exposure to Mood Stabilizers

MEDICATION	TERATOGENICITY	POTENTIAL PERINATAL EFFECTS
Carbamezapine (Tegretol) Category D	Significantly increased risk of neural tube defects with first trimester exposure. Increased risk for developmental delay, craniofacial defects, cardiovascular and urinary abnormalities, and fingernail hypoplasia	Hypoglycemia, hepatic dysfunction, bleeding disorders. Passed in higher levels in breastmilk. No known impact on growth and development.
Oxcarbazepine (Trileptal) Category D	Data are limited. Rates of congenital malformations appear to be similar to the general population	Limited data, no known adverse outcomes.
Topiramate (Topamax) Category D	Not first line in bipolar DO. Data are limited. No adverse outcomes in limited case reports.	Limited data.
Gabapentin (Neurontin) Category C	Not first line in Bipolar DO. Limited data.	Limited data.

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Antipsychotic Medications

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Antipsychotic Medications in Pregnancy

- Schizophrenia, independent of the use of treatment – is associated with an increased risk of major neurological malformations, preterm delivery, low birth weight and small for gestational age babies.
- Consideration around risks and benefits associated with First Generation (FGA) and Second Generation (SGA) antipsychotic medications.
- Both appear to be associated with an increase risk of neonatal complications.
- Most SGAs appear to increase the risk of gestational, metabolic complications and babies large for gestational age as compared to FGAs.
- Low potency FGAs – phenothiazines like chlorpromazine (Thorazine), perphenazine (Trilafor), Thioridazine (Mellaril) – appear to increase the risk of nonspecific congenital anomalies over high-potency antipsychotics (e.g., haloperidol – Haldol).

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Summary of Effects of in utero Exposure to Antipsychotic Medications

MEDICATION	TERATOGENICITY	POTENTIAL PERINATAL EFFECTS
Olanzapine (Zyprexa)	No associated major congenital malformations. FDA category C	Has not been associated with perinatal complications.
Risperidone (Risperdal)	Small number of case reports indicate no adverse birth outcomes. FDA category C.	Small number of case reports noted no adverse birth outcomes.
Quetiapine (Seroquel)	Small number of case indicate no adverse birth outcomes. Lowest amount of placental passage when compared to Haldol, Risperdal and Zyprexa. FDA category C.	Small number of case reports noted no adverse birth outcomes.
Aripiprazole (Abilify)	Limited data, but no clinical reports of adverse outcomes. FDA category C.	Limited data. Unknown amount excreted in human mild.

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Summary of Effects of in utero Exposure to Antipsychotic Medications

MEDICATION	TERATOGENICITY	POTENTIAL PERNATAL EFFECTS
Ziprasidone (Geodon)	Limited data, no clinical reports of adverse outcomes. FDA category C.	Limited data. Excretion in human milk is not known.
Clozapine (Clozaril)	No clinical reports linking its use to congenital defects. FDA category C.	Sedation, decreased suckling, restlessness, irritability, risk of seizures and cardiovascular instability
High-potency antipsychotic agents (haloperidol, trifluoperazine)	Not associated with major congenital anomalies. Haldol and Stelazine. FDA category C.	Transient perinatal syndrome of motor restlessness, tremor, hypotonia, hyperreflexia, irritability, and poor feeding in infants exposed near term.
Low potency agents (mellaril, Thorazine)	May increase the risk of nonspecific congenital malformations. No neurobehavioral sequelae have been observed in long-term follow-up. FDA category not assigned.	Transient perinatal syndrome of motor restlessness, tremor, hypotonia, hyperreflexia, irritability, and poor feeding in infants exposed near term.

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Summary of Effects of Benzodiazepines

- Mixed evidence — Some studies (meta-analyses) did not find an association between benzodiazepine use in utero and major malformations.
- Another study by the same authors showed a small risk (relative risk of 0.8) of oral clefts.
- Risk noted especially for alprazolam (Xanax) and diazepam (Valium).
- Recommended to avoid the use of benzodiazepines during weeks 5-10 of pregnancy as the fetal palate forms at this time.
- Use of benzodiazepines late in the third trimester may be associated with perinatal syndromes — hypotonicity, withdrawal, failure to feed, apnea and low Apgar scores.
- Lorazepam (Ativan) — best choice as it has fewest metabolites and crosses the placenta at a lower rate than other agents.

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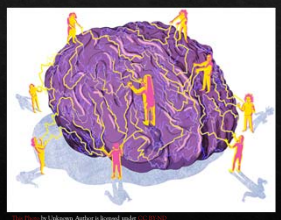
Electroconvulsive Therapy (ECT)



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ECT

- Studies have indicated that when carried out with a comprehensive treatment team consisting of a psychiatrist, anesthesiologist, and obstetrician, ECT appears to be a safe and effective treatment modality.
- Treatment of choice when rapid stabilization is essential (delusional depression, uncontrollable mania).

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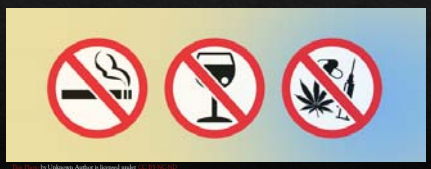
Substance Abuse and Pregnancy



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Substance Abuse and Pregnancy

- TOBACCO: Implicated in spontaneous abortion, placenta previa and abruptio placenta. Cigarette smoking has been linked to intrauterine growth retardation and low birth weight.
- ALCOHOL: Negative effects on pregnancy and the developing fetus are due to a combination of pharmacological, lifestyle and nutritional factors.
  - Alcohol displaces proteins, vitamins, and essential fats needed for proper fetal development. Its metabolite, acetaldehyde, is directly toxic to fetal cellular growth and metabolism
    - Fetal alcohol effects are isolated abnormalities seen in 3-5 per 1,000 live births
    - Fetal Alcohol Syndrome 1-2 per 1,000 births – irreversible cognitive and growth delays

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Fetal Alcohol Syndrome

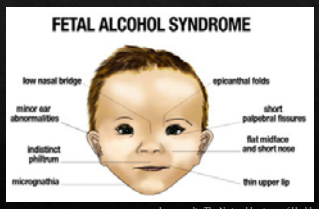

Image credit: The National Institutes of Health

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Principal Features of Fetal Alcohol Syndrome

- Structural
  - Shortened palpebral fissures (the opening for the eyes between the eyelids)
  - Hypoplastic philtrum (dimple of upper lip) and maxilla
  - Thinned upper vermilion border of lip
  - Retrognathia (backwards displacement of jaw) in infancy
  - Micrognathia/prognathia in adolescence (i.e., small or prominent jaw)
  - Diminished adipose tissue

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Principal Features of Fetal Alcohol Syndrome

- Cognitive
  - Mild to moderate cognitive delay
- Developmental
  - Poor coordination, hypotonia
  - Irritability in infancy
  - Attention deficit with hyperactivity in childhood
  - Growth retardation
  - Height and weight below 95th percentile

Substance Abuse and Pregnancy

- COCAINE: Produces maternal hypertension and tachycardia leading to lessened blood flow to the placenta, vasoconstriction and reduced oxygen to the fetus.
  - Exposure to cocaine in utero appears to increase the risk of genitourinary tract malformations.
  - A prolonged abstinence syndrome, lasting up to four months — characterized by tremulousness, abnormal motor development, persistence of primitive reflexes and impaired bonding can occur.
  - Some, but not all studies, have reported mood dysfunction and impaired attention in children born to cocaine-abusing mothers.

Substance Abuse and Pregnancy

- HEROIN/OPIATES:
  - Associated with intrauterine growth retardation, premature rupture of membranes, pregnancy-induced hypertension, abruptio placentae, neonatal meconium aspiration, maternal and neonatal infections, and stillbirth
  - Perinatal withdrawal syndrome – irritability, decreased feeding, respiratory difficulties, sweating and tremulousness
  - Women who receive MAT (e.g., Methadone Maintenance) and proper prenatal care have improved obstetrical outcomes compared with untreated opiate use.
  - Other adverse effects include: low birth weight, decreased head circumference, and increased risk of sudden infant death syndrome.