Women's Mood Disorders in the Perinatal and Post-Partum Period

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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

Screening for Perinatal Mood and Anxiety Disorders

- Any clinician who treats perinatal women, including obstetrical, primary care, and mental health professionals, should be screening for depression and anxiety.
- Major professional organizations including the American College of Obstetricians and Gynecologists, American Academy of Pediatrics, U.S. Preventive Services Task Force, and others recommend universal screening for depression during pregnancy and postpartum.
- The most common screening tool is the Edinburgh Postnatal Depression Scale (EPDS).

Edinburgh Postnatal Depression Scale (EPDS)

Cox JL, Holden JM Sagovsky R (1987) Detection of postnatal depression: development of the 10-item Edinburgh postnatal depression scale. Brit J Psychiatry 150 782-86. Reproduced with permission.

Name: _____ Date: _____

We would like to know how you have been feeling in the past week. Please indicate which of the following comes closest to how you have been feeling over the past seven days, not just how you feel today. Please tick one circle for each question that comes closest to how you have felt in the **last seven days.**

Here is an example already completed.

I have felt happy:

- ☐ Yes, all of the time
- ■ Yes, most of the time
- ☐ No, not very often
- ☐ No, not at all

This would mean: 'I have felt happy most of the time during the past week'.

Please complete the other questions in the same way.

1. I have been able to laugh and see the funny side of things

- ☐ As much as I always could
- ☐ Not quite so much now
- ☐ Definitely not so much now
- ☐ Not at all

2. I have looked forward with enjoyment to things

- ☐ As much as I ever did
- ☐ Rather less than I used to
- ☐ Definitely less than I used to
- ☐ Hardly at all

3. I have blamed myself unnecessarily when things went wrong

- ☐ Yes, most of the time
- ☐ Yes, some of the time
- ☐ Not very often
- ☐ No, never

4. I have been anxious or worried for no good reason

- ☐ No, not at all
- ☐ Hardly ever
- ☐ Yes, sometimes
- ☐ Yes, very often

5. I have felt scared or panicky for no very good reason

- ☐ Yes, quite a lot
- ☐ Yes, sometimes
- ☐ No, not much
- ☐ No, not at all

6. Things have been getting on top of me

- ☐ Yes, most of the time I haven't been able to cope at all
- ☐ Yes, sometimes I haven't been coping as well as usual
- ☐ No, most of the time I have coped quite well
- ☐ No, I have been coping as well as ever

7. I have been so unhappy that I have had difficulty sleeping

- ☐ Yes, most of the time
- ☐ Yes, sometimes
- ☐ Not very often
- ☐ No, not at all

8. I have felt sad or miserable

- ☐ Yes, most of the time
- ☐ Yes, quite often
- ☐ Not very often
- ☐ No, not at all

9. I have been so unhappy that I have been crying

- ☐ Yes, most of the time
- ☐ Yes, quite often
- ☐ Only occasionally
- ☐ No, never

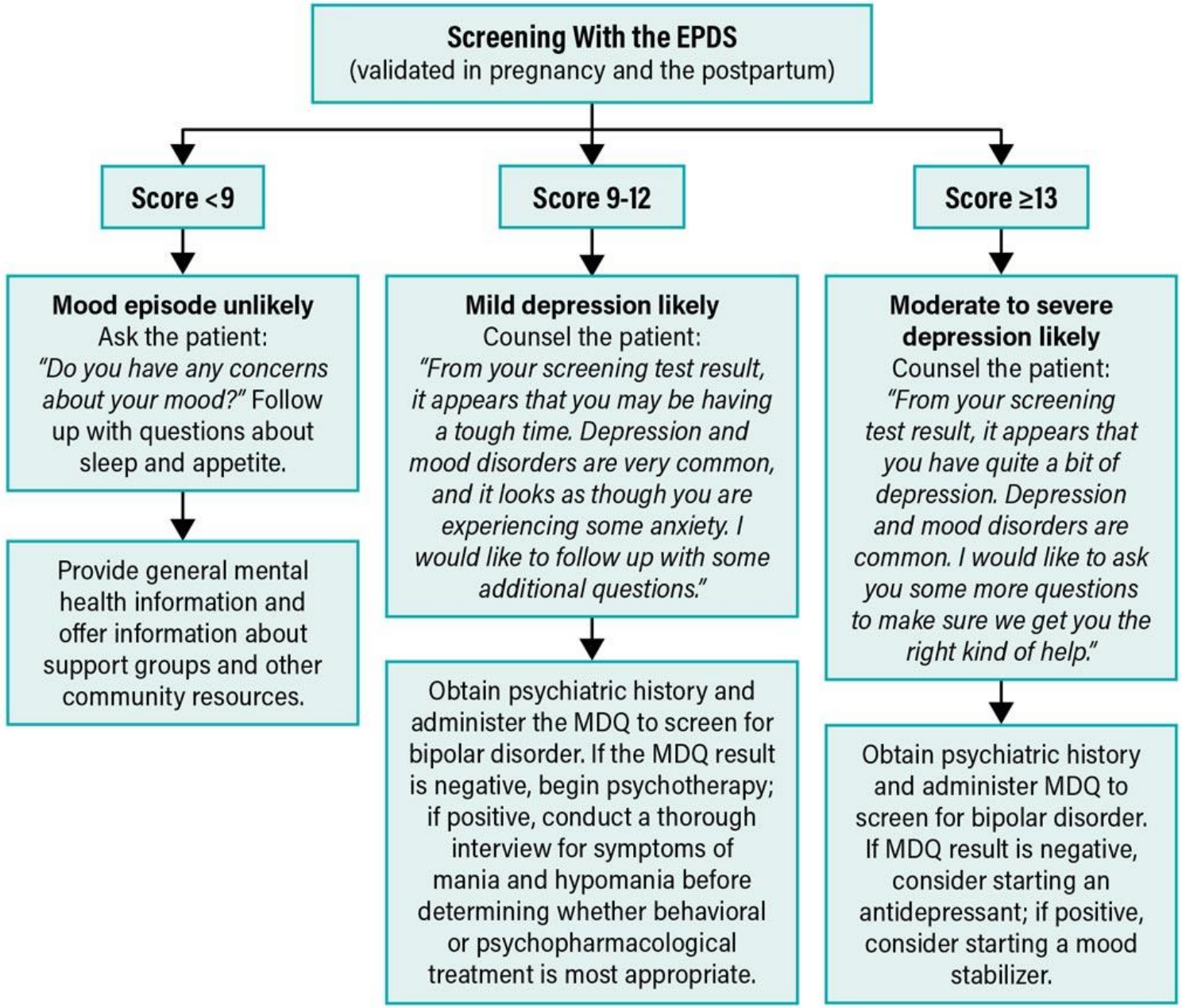
10. The thought of harming myself has occurred to me

- ☐ Yes, quite often
- ☐ Sometimes
- ☐ Hardly ever
- ☐ Never

Edinburgh Postnatal Depression Rating Scale

- The EPDS is the most widely used screening tool for post-partum depression.
- It is the most validated screening tool for pregnant and post-partum patients and is available in over 60 languages.
- A score of 10 or greater is a possible indication of minor (score of 9/10) or major (12/13) depression.
- It is a screening instrument and a diagnosis can only be established by a structured and formal clinical interview.

Figure 1. Using the Edinburgh Postnatal Depression Scale (EPDS)



MDQ: Mood Disorders Questionnaire

Mood Disorder Questionnaire

- The Mood Disorder Questionnaire (MDQ) is a validated screening tool for Bipolar Spectrum Disorders (Bipolar I, Bipolar II, Cyclothymia, Bipolar NOS).
- Previous studies have shown that one-quarter of women with bipolar disorder relapse during pregnancy, and nearly half of bipolar women relapse during the postpartum period.
- The perinatal period is also associated with an elevated risk for new-onset mood disorder.
- Bipolar disorder is often unrecognized, and there is often a significant delay between illness onset and proper diagnosis and treatment.

THE MOOD DISORDER QUESTIONNAIRE

Instructions: Please answer each question to the best of your ability.

	YES	NO
1. Has there ever been a period of time when you were not your usual self and...		
...you felt so good or so hyper that other people thought you were not your normal self or you were so hyper that you got into trouble?	○	○
...you were so irritable that you shouted at people or started fights or arguments?	○	○
...you felt much more self-confident than usual?	○	○
...you got much less sleep than usual and found you didn't really miss it?	○	○
...you were much more talkative or spoke much faster than usual?	○	○
...thoughts raced through your head or you couldn't slow your mind down?	○	○
...you were so easily distracted by things around you that you had trouble concentrating or staying on track?	○	○
...you had much more energy than usual?	○	○
...you were much more active or did many more things than usual?	○	○
...you were much more social or outgoing than usual, for example, you telephoned friends in the middle of the night?	○	○
...you were much more interested in sex than usual?	○	○
...you did things that were unusual for you or that other people might have thought were excessive, foolish, or risky?	○	○
...spending money got you or your family into trouble?	○	○
2. If you checked YES to more than one of the above, have several of these ever happened during the same period of time?	○	○
3. How much of a problem did any of these cause you – like being unable to work; having family, money or legal troubles; getting into arguments or fights? *Please circle one response only.* No Problem Minor Problem Moderate Problem Serious Problem		
4. Have any of your blood relatives (i.e. children, siblings, parents, grandparents, aunts, uncles) had manic-depressive illness or bipolar disorder?	○	○
5. Has a health professional ever told you that you have manic-depressive illness or bipolar disorder?	○	○

How to Use the MDQ Questionnaire

- It takes less than 5 minutes to complete.
- Patients simply check the yes or no boxes in response to the questions.
- The last question pertains to the patient's level of functional impairment.
- How to Score Further medical assessment for bipolar disorder is clearly warranted if patient: • Answers Yes to 7 or more of the events in question #1 AND • Answers Yes to question #2 AND • Answers Moderate problem or Serious problem to question #3

Psychiatric Disorders in Pregnancy

Psychiatric Disorders in Pregnancy

- Psychiatric Disorders affect both the mother's well-being as well as that of the developing fetus.
- 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.

Risks of Untreated Depression

- Depression in pregnancy can lead to inadequate nutrition, inadequate 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

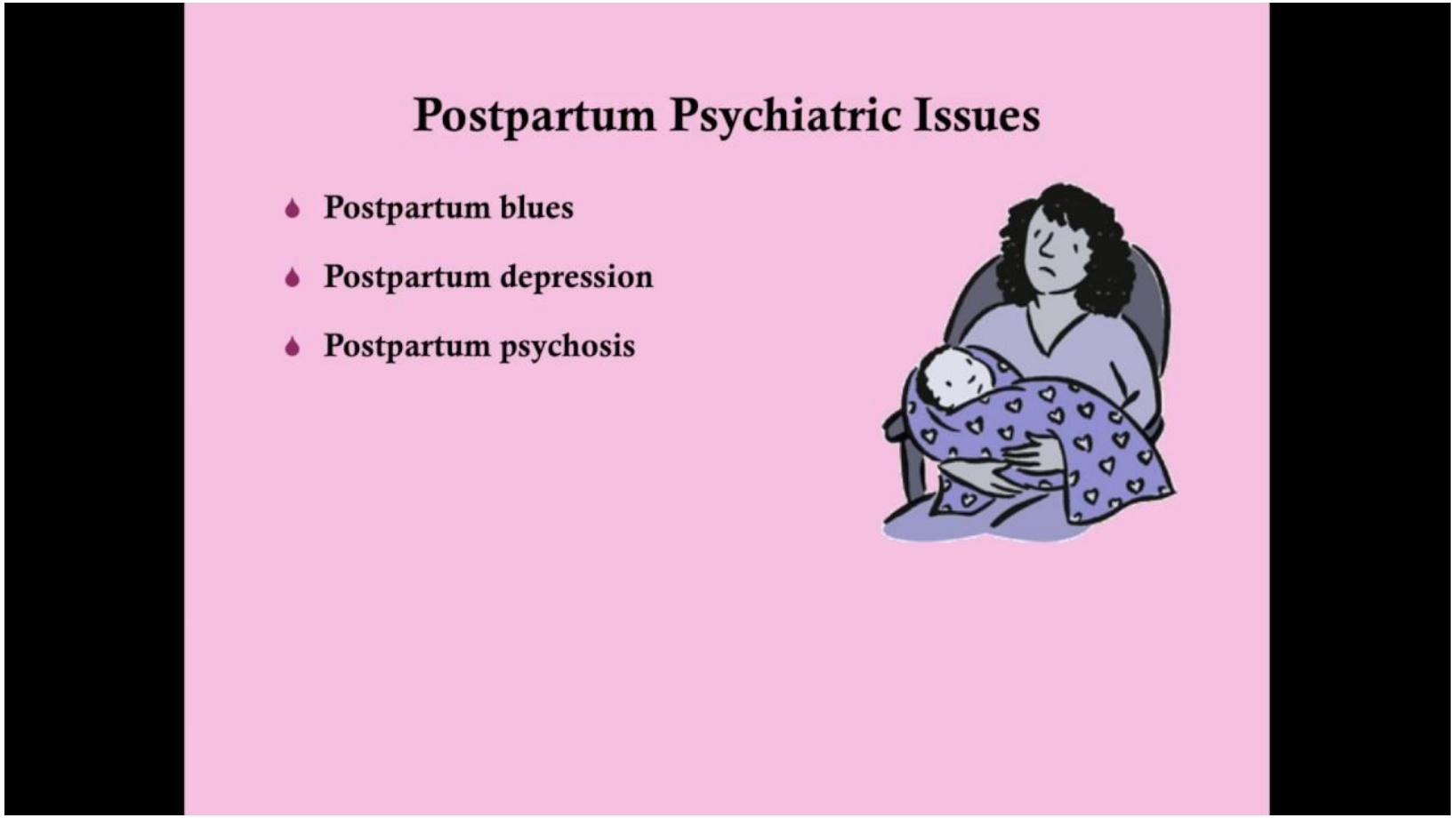
Risks of Untreated Bipolar Illness for Mother

- 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)

Risks of Untreated Bipolar Illness to Baby

- Pre-term birth
- Small for gestational age – in utero
- Low birth weight – at delivery
- Poor developmental outcomes

Post-Partum Psychiatric Disorders



Risk Factors for Postpartum Psychiatric Disorders

DISORDER	RISK FACTORS
Postpartum blues	Depressive symptoms during pregnancy History of depression History of premenstrual dysphoric disorder
Postpartum depression	Depression during pregnancy History of depression, especially postpartum depression Stress within the marital/partner relationship Inadequate social supports Stressful life events during pregnancy
Postpartum psychosis	History of Bipolar DO Primiparity Previous Postpartum psychosis

Post-Partum Psychiatric Disorders: incidence, time course, and clinical features

DISORDER	INCIDENCE (%)	TIME COURSE	CLINICAL FEATURES
Postpartum blues	70 – 85	Onset with first postpartum week, abates after 10 – 14 days	Mood instability, tearfulness, anxiety, insomnia
Postpartum depression	10	Onset within first postpartum month; duration similar to that of major depressive episodes	Depressed mood, guilt, anxiety, fear of harm coming baby, obsessional features
Postpartum psychosis	0.1 – 0.2	Onset within first postpartum month; duration variable – weeks to months	Disorientation, confusion, delusions, hallucinations, often rapid mood-cycling

Differential Diagnosis

Characteristics	Postpartum Blues	Postpartum Depression	Postpartum Psychosis
Incidence	26-85%	10-15%	0.1 - 0.2%
Timing	Within first week	Within 12 months	Within first two weeks
Onset	Gradual	Insidious	Dramatic and rapid
Duration	Hours to few days	>2weeks to months	>4 days to months
Symptoms	• Fluctuating mood, depressed mood, irritability, tearfulness • Insomnia	• Mood lability, depressed mood • Insomnia	• Mood lability, depressed or elated mood, irritability • Insomnia

Differential Diagnosis, continued

Characteristics	Postpartum Blues	Postpartum Depression	Postpartum Psychosis
Symptoms	• Anxiety • Absence of suicidal/infanticidal thoughts • Mild and temporary decreased interest or pleasure, guilt, appetite change, decreased libido	• Excessive anxiety, agitation • Possible presence of suicidal/infanticidal thoughts • Decreased interest or pleasure, inappropriate guilt, appetite/weight change, obsessions, decreased libido	• Agitation, disorganized behavior • Possible presence of suicidal/infanticidal thoughts • Psychotic symptoms which can include delusions, hallucinations, confusion/disorientation

Specific features or symptoms of Post-Partum Depression

- Depressed mood with tearfulness, irritability, loss of interest in usual activities, insomnia, fatigue and loss of appetite.
- Expression of ambivalence or negative feelings about the infant. Sometimes there is an expression of doubt or concern around the mother's ability to care for the infant.
- Anxiety can be prominent – often presenting with Generalized Anxiety, Panic or Health Anxiety. Comorbid Obsessive Compulsive DO is not felt to be common but women with Post Partum Depression can experience intrusive, obsessive ruminations that are ego-dystonic and with intact reality testing.
- Suicide rates appear to be relatively low in women with non-psychotic Post Partum Depression.

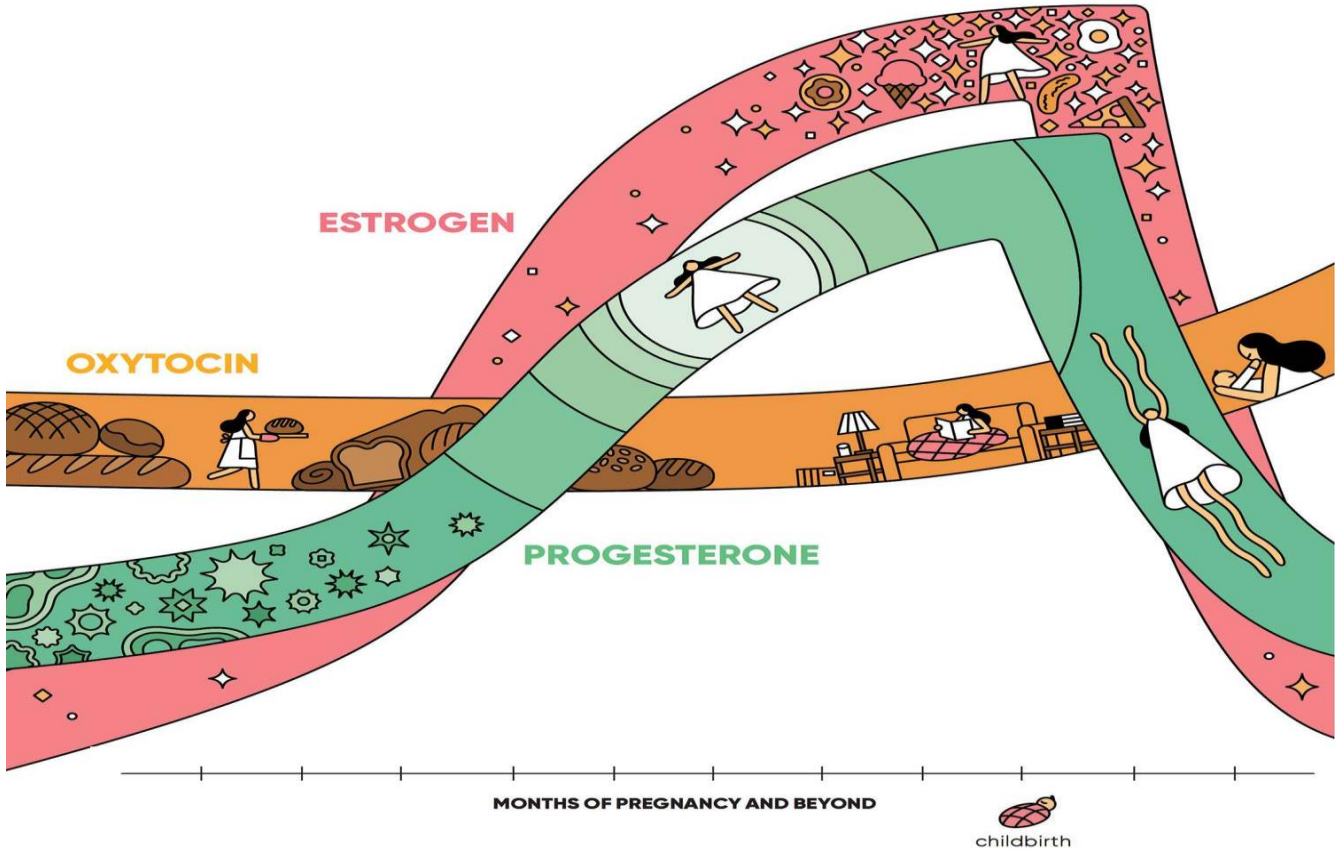
Specific features or symptoms of Post Partum Psychosis

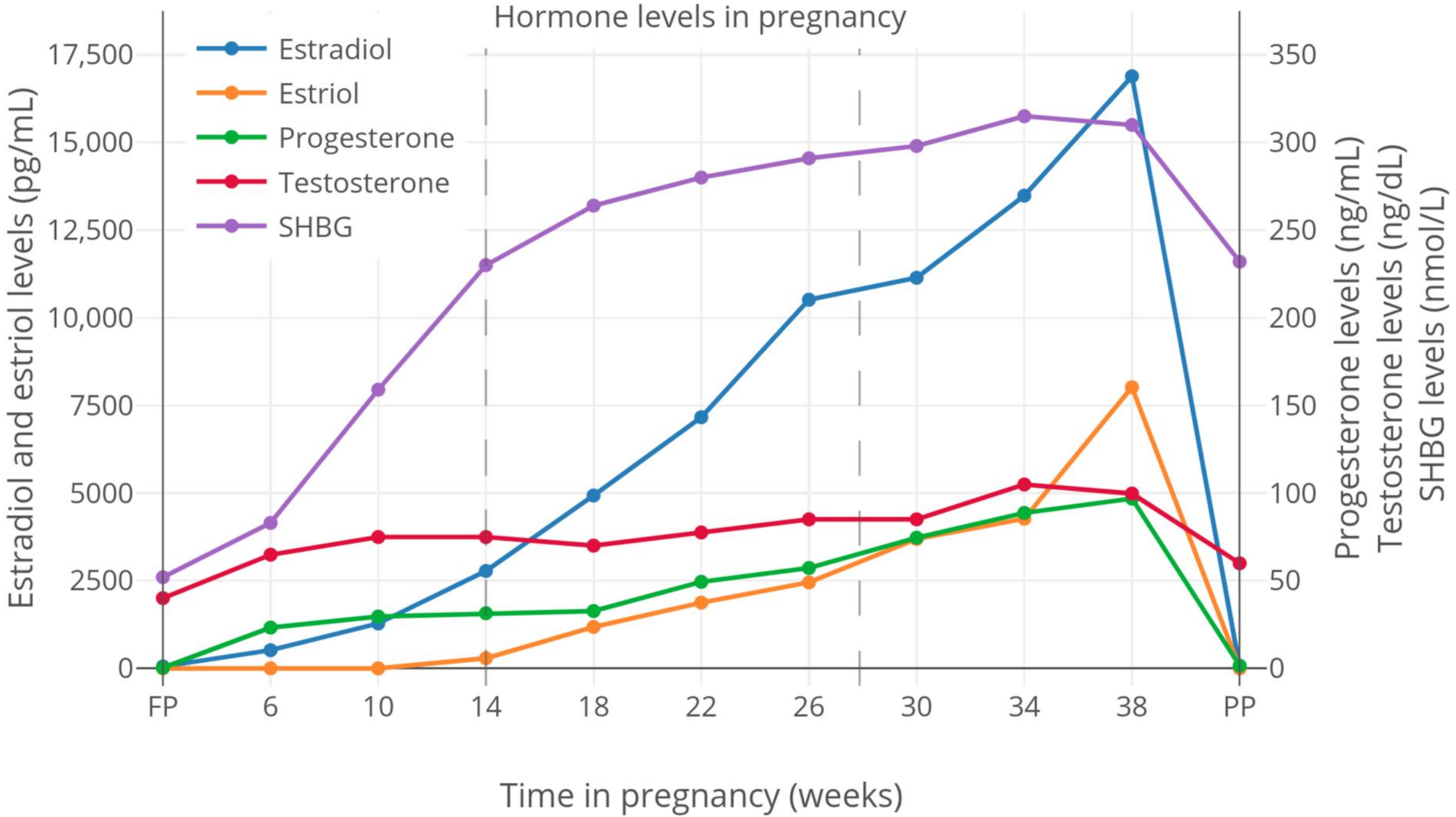
- The DSM 5 does not recognize Post Partum Psychosis as a separate diagnostic entity.
- The abrupt onset of psychotic symptoms following childbirth.
- Incidence rates peak during the first month, especially within the first two weeks following childbirth.
- Insomnia seems to be the most frequent, earliest symptom of Post Partum Psychosis.
- Hospitalization of the patient is usually required.

Specific features or symptoms of Post Partum Psychosis

- Core symptoms present with diurnal fluctuations in intensity of symptoms which include: mood swings, delusions, cognitive impairment with confusion, thought disorganization and bizarre behavior.
- Confusion seems to be a specific symptom of Post Partum Psychosis.
- Hallucinations may be auditory, visual, tactile and/or olfactory.
- Post Partum Psychosis may be considered as a bipolar spectrum mood disorder rather than a primary psychotic disorder.

Pathophysiology of Hormonal Changes in Pregnancy




Hormone levels in pregnancy
Estradiol
Estriol
Progesterone
Testosterone
SHBG
Estradiol and estriol levels (pg/mL)
17,500
15,000
12,500
10,000
7500
5000
2500
0
Progesterone levels (ng/mL)
Testosterone levels (ng/dL)
SHBG levels (nmol/L)
350
300
250
200
150
100
50
0
FP
6
10
14
18
22
26
30
34
38
PP
Time in pregnancy (weeks)

Pathophysiology of Hormonal Changes In Pregnancy

- There is evidence to suggest that hormonal fluctuations and inflammation play a role in the development of mood episodes during the post – partum period.
- During pregnancy there are escalating serum levels of estrogen, progesterone, prolactin, corticotrophin-releasing hormone and cortisol.
- There is a then a drastic decline of levels following delivery.
- Immunomodulation and inflammation are turned down during pregnancy. During parturition the immune response rapidly readjusts in an unregulated fashion.

Treatment Options for Postpartum Psychiatric Disorders

DISORDER	TREATMENT OPTIONS
Postpartum blues	Education Support Reassurance
Postpartum depression	Reduction of psychosocial stressors Individual and/or group psychotherapy Antidepressant medications ECT Hospitalization
Postpartum psychosis	Hospitalization Medical workup to rule out organic etiology Mood stabilizers Antipsychotics Antidepressants Benzodiazepines ECT

New FDA Approved Treatment for Postpartum Depression

- Zulresso (brexanolone) – an injection for intravenous administration for the treatment of Postpartum Depression
  - Unclear mechanism of action. Binds to GABA receptors. It is a neurosteroid – an analogue of allopregnanolone (by-product of progesterone)
  - Thought to exert its effects on anxiety and depression by modulating the HPA axis which mediates the body's response to stress.
  - Candidate – severe depression and history of failing prior treatment interventions

New FDA Approved Treatment for Postpartum Depression

- Available only through a restricted program called the Zulresso REMS Program. Requires the drug be administered by a health care provider in a certified health care facility
- High cost – Estimated to be $25,000 – 34,000 per infusion with need for inpatient treatment
- Administered as a continuous IV infusion over a total of 60 hours (2.5 days)
- Patients must be monitored for sedation and sudden loss of consciousness. Must have continuous pulse oximetry monitoring
- Works very quickly, within a few days

Psychotherapeutic Interventions

- Perinatal Dyadic Psychotherapy (PDP): a dual-focused mother-infant intervention designed to prevent and/or decrease depressive symptoms in the mother and to improve aspects of the mother-infant relationship related to child development.
- Interpersonal Psychotherapy (IPT): time-limited (12-16 weeks) addressing 4 problem areas:
- 1. Grief: Acknowledging the losses that occur to sense of self, changes in relationships, or more specific loss.
- 2. Role Transitions: Life stage transitions and social transitions including loss of independence and changing social networks.
- 3. Interpersonal Disputes: Ones that frequently occur after the birth of a child including unmet expectations and intimacy struggles within partnerships.
- 4. Interpersonal Deficits: Looking at struggles with attachment in other relationships that may be causing distress.

Psychotherapeutic Interventions

- Cognitive Behavioral Therapy:
- work with a mom to identify and acknowledge her automatic thoughts, evaluate these thoughts and become aware of when these thoughts are not helpful.
- explore and change underlying beliefs, differentiate between realistic and false threats, and develop new and more helpful perspectives.
- CBT helps a mom to develop coping strategies so that she feels better equipped to manage distress.
- CBT uses tools such as homework, relaxation, exposure therapy, thought stopping, mental imagery, and tools for changing catastrophic thoughts and irrational thinking
- Psychodynamic Psychotherapy:
- This type of therapy looks into early experiences that play a role in forming beliefs about ourselves as adults, and identifies those beliefs that are no longer helpful.
- Dialectical Behavior Therapy:
- DBT teaches skills in the following categories: mindfulness, distress tolerance, emotional regulation, and interpersonal effectiveness.

Medications During Pregnancy

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

Summary of Effects of in utero exposure to antidepressants

MEDICATION	TERATOGENICITY	POTENTIAL PERINATAL SIDE EFFECTS
SSRI's	See below for each agent	For SSRI's 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)	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.

Summary of Effects of in utero exposure to antidepressants

MEDICATION	TERATOGENICITY	POTENTIAL PERINATAL SIDE EFFECTS
Sertraline (Zoloft)	No evidence of major anomalies. No evidence of long-term neurobehavioral abnormalities	No evidence of cardiac malformations. Low transmission in breast milk.
Paroxetine (Paxil)	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)	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.

Summary of Effects of in utero exposure to antidepressants

MEDICATION	TERATOGENICITY	POTENTIAL PERINATAL EFFECTS
Fluvoxamine (Luvox), Venlafaxine (Effexor), Duloxetine (Cymbalta)	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	No evidence of major congenital anomalies. No long-term neurobehavioral adverse outcomes.	No increased risk of perinatal complications
Tricyclic Antidepressants	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	Increased rate of congenital anomalies in animal studies	Contraindicated: potential hypertensive crisis if tocolytic agents needed
Buproprion (Wellbutrin)	No association with congenital malformations	Two small studies showed a possible association with a higher risk of spontaneous abortion. Other studies have not show this association.

Summary of effects of in utero exposure to mood stabilizers

MEDICATION	TERATOGENICITY	POTENTIAL PERINATAL EFFECTS
Lithium	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	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)	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.

Summary of effects of in utero exposure to mood stabilizers

MEDICATION	TERATOGENICITY	POTENTIAL PERINATAL EFFECTS
Carbamezapine (Tegretol)	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)	Data are limited. Rates of congenital malformations appear to be similar to the general population	Limited data, no known adverse outcomes.
Topiramate (Topamax)	Not first line in bipolar DO. Data are limited. No adverse outcomes in limited case reports	Limited data.
Gabapentin (Neurontin)	Not first line in Bipolar DO. Limited date.	Limited data.

Antipsychotic Medications

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 SGA's appear to increase the risk of gestational diabetes, metabolic complications and babies large for gestational age as compared to FGA's.
- Low potency FGA's -- phenothiazines like chlorpromazine (Thorazine), perphenazine (Trilafon), Thioridazine (Mellaril) – appear to increase the risk of nonspecific congenital anomalies over high-potency antipsychotics (e.g. haloperidol –Haldol)

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.

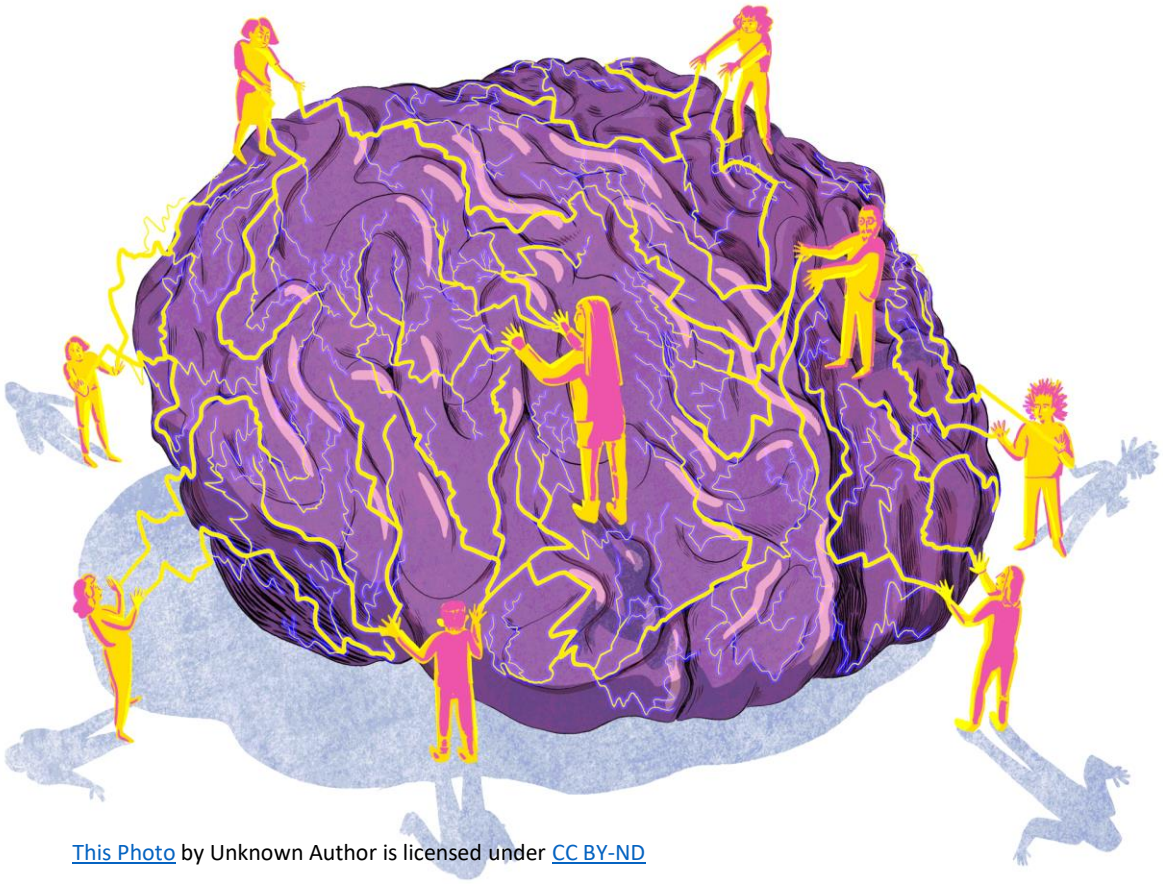
Summary of effects of in utero exposure to Antipsychotic medications

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 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

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.

Electroconvulsive Therapy



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.

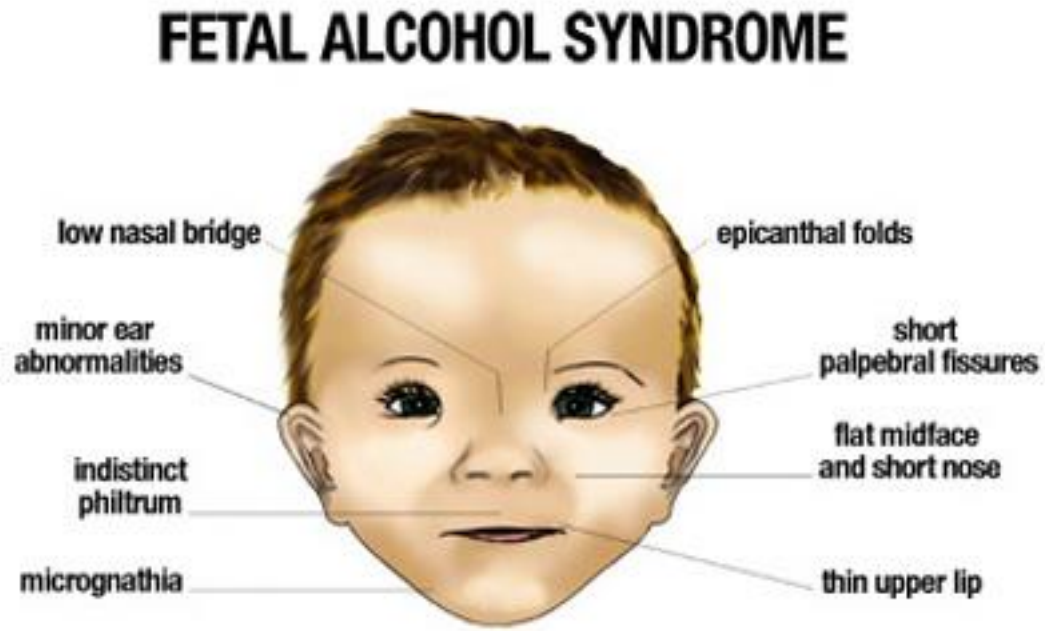
- Treatment of choice when rapid stabilization is essential (delusional depression, uncontrollable mania.)

Substance Abuse and Pregnancy

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

Fetal Alcohol Syndrome



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

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.

Substance Abuse and Pregnancy

- Cannabis:
  - Cannabis is fat soluble and readily crosses the placenta.
  - Cannabis elevates carbon monoxide levels in the mother and decreased fetal oxygenation.

Breast Feeding

Psychotropic Drugs Taken During Breastfeeding

MEDICATION	COMMENT
Antidepressants	
Tricyclic antidepressants	In most cases, the parent compound levels in infant serum are below limits of detection, but metabolite levels are sometimes detectable.
Selective serotonin reuptake inhibitors	Data for fluoxetine: it is found in breast milk and has been associated with colic (irritability, vomiting, diarrhea, less sleep). One study showed no differences shown on neurodevelopmental tests than other babies. Sertraline: no adverse events – the agent of choice; Paxil/Luvox/Celexa/Lexapro – no adverse events
Other antidepressants	No adverse events noted with buproprion, venlafaxine, nefazodone, and mirtazapine. Cymbalta – limited data appears to indicate no adverse events
St. John's Wort	A few case reports with no adverse effects

Psychotropic Drugs Taken During Breastfeeding

MEDICATION	COMMENT
Antianxiety Medications	
Benzodiazepines	Benzodiazepines (especially long-acting agents) may accumulate in neonates because of their immature liver enzymes. Occasional, low doses of short-acting benzodiazepines (e.g. lorazepam, oxazepam, temazepam) are unlikely to be harmful. Reports of sedation and lethargy have been noted with diazepam, and irritability and possible withdrawal have been noted with alprazolam. Cyanosis and impaired respiration (reversible) have been noted with clonazepam
Zolpidem	Found in very low levels in breast milk. No adverse effects noted. More data needed before recommendations can be given
Gabapentin	No data available

Psychotropic Drugs Taken During Breastfeeding

MEDICATION	COMMENT
Antipsychotic agents	• Acceptable for breast-feeding: olanzapine (Zyprexa), quetiapine (Seroquel) • Possible for breast-feeding under medical supervision: chlorpromazine (Thorazine), haloperidol (Haldol), risperidone (Risperdal) • Recommendations can not be given due to limited data: aripiprazole (Abilify), asenapine (Saphris), clozapine (Clozaril), droperidol, fluphenazine, flupenthixol, iloperidone (Fanapt), lurasidone (Latuda), paliperidone (Invega), perphenazine (Trilafon), pimozide (Orap), trifluoperazine (Stelazine), thiothixene (Navane), and ziprasidone (Geodon).

Psychotropic Drugs Taken During Breastfeeding

MEDICATION	COMMENTS
Mood Stabilizers	
Lithium	• Mixed data: some studies report 40-45% of maternal serum level, other reports list up to 77%. Thought to be substantially less than in utero exposure. Studies appear to indicate no adverse developmental effects • Because the neonatal kidney is immature, risk for lithium accumulation is high • The American Association of Pediatrics (AAP) considers lithium contraindicated during breast-feeding
Carbamazepine (Tegretol)	Rapidly metabolized, does not appear in infant serum. The AAP considers it compatible with breast-feeding. Requires careful clinical and lab monitoring
Lamotragine (Lamictal)	Blood levels in infants can reach adult levels, but no adverse effects have been noted.
Topiramate (Topamax)	No adverse effects

On-Line Resources

- MGH Center for Women's Mental Health -- https://womensmentalhealth.org/

- Post-Partum Support International –

https://www.postpartum.net/resources/