Postpartum Disorders

- Who do they effect? EVERYONE!!
- Celebrities who have been vocal about their struggles with postpartum depression:

  Brooke's Story.
Postpartum Depression

- Quote from ‘Down Came the Rain,’ by Brooke Shields.
- And then one day, finally, she became pregnant. She was thrilled beyond belief. She had a wonderful pregnancy and a perfect baby girl. At long last, her dream of being a mommy had come true. But instead of being happy, all she could do was cry.

Postpartum Disorders

- Women are most vulnerable to mood disorders during the post partum period.
- If depression, anxiety, bipolar disorder or psychosis is going to surface, it typically happens during this time.
- The postpartum period involves numerous physiologic, psychological and sociocultural changes which all may be etiologic factors in postpartum disorders.
- Hospitalization rates to psychiatric hospitals are 7 times higher in the first 30 days postpartum than any other time in a woman’s life.

Postpartum Disorders Gender Differences

- The lifetime prevalence for MDD in women is 10-25% and in men is 5-12%.
- In pre-pubertal children, the rate of depression for boys is greater than the rate for girls.
- Between the beginning of puberty and age 50 years, the rate for depression in women is twice the rate for depression in men.
- After age 50 years, the rates of depression for men and women are equal.

Postpartum Blues

- Let’s start with the Blues…
Postpartum Blues

- Postpartum blues are a common, benign, transitory condition occurring within the first 10 days postpartum and occur in approximately 50-90% of females.
- Peak of symptoms occurs around days 4-5.
- The most frequent reported symptom is weeping.
- Other symptoms include irritability, lack of affect for baby, hostility towards husband or partner, sleep disturbance, headache, exhaustion, restlessness, derealization, depersonalization.

Postpartum Depression

- On to depression...
Postpartum Depression

- Postpartum depression is the most common of the postpartum mood disorders and affects 10-15% of women after delivery. (May be seen in 26% of adolescent mothers.)
- For 60% of women with PPD, this represents their first episode of depression.
- DSM-IV categorizes this disorder as major depressive disorder, with postpartum onset if symptoms occur within 4 weeks following childbirth. (Modifier applies to MDD, Bipolar I and Bipolar II)
- Some sources consider depression as ‘postpartum’ if it occurs anytime during the first year after delivery.
- Onset is usually gradual but can be very rapid and occur immediately after delivery. Symptoms usually peak between 3-6 months postpartum.

How is it different?

- Postpartum depression presents with more prominent and more sustained depressive symptoms than postpartum blues and may be accompanied by hopelessness, a sense of failure as a parent, and suicidal/homicidal thoughts.
- Symptoms: excessive worry (almost of an obsessional nature), anger, feelings of guilt, sadness, hopelessness, problems sleeping, uneasiness around the baby, poor concentration, loss of pleasure, decreased sex drive, changes in appetite.

Postpartum Depression Quotes

- My life is over.
- I will never feel connected to my child.
- I am a horrible mother.
- I made a terrible mistake.
- I am so alone in how I feel.
- I am the only person in the world who won’t ever be happy or in love with her child.
- I hate myself and I hate life.
- My child will never love me.
Postpartum Depression Quotes

- The voices in my head kept screaming and I felt so sad.
- I kept waiting for my baby’s real mother to arrive.
- I thought it was okay if my baby dies because this is a bad world to grow up in.
- My friend couldn’t walk by the microwave without wanting to put her baby in it.
- My husband had to remove the sharp objects from the house.
- I couldn’t stand the sound of my baby’s cry.
- I did not feel attached to my baby at all.

Postpartum Depression

- 25% of mother’s who do not receive treatment for postpartum depression remain depressed after the first year.
- Once a woman has one episode of postpartum depression, she is at risk for another occurrence (50%) with each subsequent pregnancy.
- 30% of women with postpartum depression may later develop nonpuerperal mood disorders.
- Postpartum depression can occur after the birth of any child, not only the first child.

Postpartum Depression Estrogen

- Let’s talk about Estrogen...

- Women, compared to men, are at increased risk of depression (2:1), especially at several reproductive related life cycle points.
- As estrogen levels vary, risk of depression in women also varies. Women are at greatest risk when reproductive hormones fluctuate.
  - Puberty – estrogen rises and the onset of depression is associated with puberty onset.
  - Mood disturbances associated with menstrual cycles (Premenstrual symptoms) and taking oral contraceptives signal a risk for a full blown MDD.
  - Women of childbearing age are at highest risk for mood disorders (pregnancy and postpartum).
  - Infertility, miscarriage and prenatal loss are also times of increased depression.
  - Lowered estrogen levels after menopause causes the risk of depression in females to EQUAL the risk of depression in males.
Postpartum Depression (Stahl, 2009)

- During pregnancy, estrogen levels skyrocket to much higher levels than even the peak of the estrogen cycle in non pregnant females.
- What happens after delivery?
  - Estrogen levels dramatically plummet.
  - Prolactin is no longer blocked by estrogen and lactation is initiated.
  - Beta endorphin levels (peak immediately before delivery) decline.
- Regular hormonal cycles do not resume until after a woman stops nursing.

Postpartum Depression Estrogen (Stahl, 2009)

- The data supporting a role for estrogen in depression is also supported by basic science.
- There are estrogen receptors distributed in brain regions and this may be associated with the symptoms of mood disorders.
  - Hippocampus, cortex – depressed mood and cognitive dysfunction
  - Amygdala - anxiety

Postpartum Depression

- Incidence of depression in women across the lifecycle
- Higher than in men at the same age
- Estrogen levels and depression
- Postpartum period
- Prolactin
- Beta endorphin
- Other hormonal changes
- Hormonal cycles resume after a woman stops nursing
- Depression risk remains high for the first year postpartum
- Hormonal changes may contribute to mood disturbances
- Treatment options may be necessary

Postpartum Depression

- The risk of depressive symptoms in women is affected by several occurrences: puberty, menstrual cycles, postpartum period, and perimenopause.

*Relative risk of depression in women, where the greatest risk of depressive moods occur during postpartum period can perimenopause.*

*PHYSIOLOGICAL CHANGES RELATED TO HORMONAL CYCLES*
Postpartum Depression

- Estrogen is a hormone that can affect levels of neurotransmitters and neural proteins.
- When we treat depression, we target the 3 neurotransmitters most implicated in depression (5HT, NE, DA) by using antidepressants to block reuptake at specific neurotransmitter reuptake transporters.
- There are other agents (besides antidepressants) that can modulate all three neurotransmitters without inhibiting the monoamine transporters.
- These agents are called “Trimonoamine modulators” and include:
  - Thyroid hormone
  - L-methylfolate
  - ESTROGEN
  - Lithium
  - Psychotherapy

Postpartum Depression

Estrogen and 5HT

- Estrogen treatment increases protein levels of tryptophan hydroxylase (key synthetic enzyme for serotonin) and increases serotonin content in raphe neurons.
- Estrogen treatment increases firing rate of rat raphe neurons.

Estrogen and Serotonin

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Postpartum Depression
Estrogen and NE

- In the locus coeruleus of female monkeys an estrogen infusion increased the expression of mRNA for tyrosine hydroxylase (key synthetic enzyme for NE) and caused dramatic release of NE into the hypothalamus.

Estrogen and DA

- Animal studies have demonstrated that DA release and reuptake in the nucleus accumbens fluctuates over the estrous cycle.
- As estrogen levels peak, DA release is also increased, indicating a possible role for estrogen in facilitating DA release.
There’s another important hormone... 

- Corticotrophin Releasing Hormone (CRH)

CRH is central in the regulation of the hypothalamic pituitary adrenal axis (HPA).

- Increased levels of CRH may be a risk factor for depression and plays an important role in the etiology of depression in the NON-pregnant state.

- Depressed patients have shown in increased number of CRH neurons.

**Corticotrophin Releasing Hormone (CRH)**

HPA Axis Dysregulation Observed in Some Depressed Patients:

<table>
<thead>
<tr>
<th>HPA Axis Component</th>
<th>Observation in Depressed Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortisol production</td>
<td>Elevated</td>
</tr>
<tr>
<td>CRH production</td>
<td>Elevated</td>
</tr>
<tr>
<td>CRF receptors in paraventricular nucleus</td>
<td>Downregulated (perhaps due to excess CRF signals)</td>
</tr>
<tr>
<td>Hippocampus</td>
<td>Atrophied</td>
</tr>
</tbody>
</table>

HPA= hypothalamic-pituitary-adrenal, CRF= corticotrophin releasing factor, CRH= Corticotrophin releasing hormone type 1.
Corticotrophin Releasing Hormone

- CRH is produced in the paraventricular nucleus of the hypothalamus and released to the pituitary to stimulate ACTH which then binds to the adrenal glands (cortex) and causes the release of cortisol.
- Cortisol is part of a negative feedback loop to the HPA axis.
- However, pregnancy is different because the placenta also produces pCRH which rise exponentially in pregnancy and reach levels of a normal person under severe stress.
- The sudden disappearance of the placenta after delivery results in a sharp drop of pCRH levels which causes withdrawal and transient suppression of the hypothalamus CRH release and HPA axis dysregulation.
- This may explain PPD.

Postpartum Depression

- Psychosocial factors affect the mother’s emotional state and exacerbate postpartum depression.
- Psychosocial risks: moving, poor partner support, social isolation, single marital status, ambivalence about motherhood, multiple offspring, financial hardship (annual income <$20,000.00), less than college education, low occupational prestige.
- Transition to parenthood has significant impact on both men and women, their relationship as a couple and their work and social activities.

Postpartum Depression

- Mood symptom history: a personal history of mood disorders (MDD, BPD), a history of depression or anxiety in pregnancy or postpartum, a history of mood symptoms associated with the menstrual cycle or mood symptoms when taking oral contraceptives, family history of depression.
- Other risk factors: illness, health problems with mother or baby, history of thyroid dysfunction, chronic sleep deprivation, past trauma.
Postpartum Depression

- Warning Signs / Behaviors to Watch:
  - Missing doctor appointments
  - Requiring someone to accompany her to appointments
  - Worrying excessively about her (mother’s) health or health of the baby
  - Physical complaints without any apparent cause
  - Significant weight loss or gain
  - Problems sleeping at night when the baby is sleeping
  - Loss of appetite
  - Poor milk production (which may be a thyroid problem)
  - Evading questions about herself
  - Crying easily

- All medical professionals should give patients who are pregnant or postpartum information about postpartum mood disorders.

- Even if the patient is doing well at that moment and is not considered high risk, she may not be well in a couple of days or weeks.

- It is best to NORMALIZE things for your patient: If you start feeling any of these symptoms, don’t worry. This is very treatable. Depression and anxiety are very common during the postpartum period. This doesn’t mean you are not a good or competent mother.

- The more matter of factly this information is delivered, the more relaxed the patient will be.

Postpartum Depression

- How do we screen?
  - Edinburg Postnatal Depression Scale (EPDS) is a 10 item, self rated measure that does not include items on somatic symptoms.
  - Postpartum Depression Checklist is intended for use by health professionals.
• If a woman remains untreated, there is an increased risk of her children developing psychiatric disturbances.

• There is also the potential for child abuse or neglect, an increased risk of the mother developing chronic depression or relapsing, and the possibility of a negative impact on the marriage and other family relationships.

• The serious consequences of untreated maternal depression on children has been studied extensively.

• Infants of depressed mothers:
  • often weigh less, vocalize less, have fewer facial expressions and increased heart rates.
  • may have poor peer relationships, poor self control, neurological delays and attentional problems.
  • exhibit poor verbal comprehension, fewer expressive language skills, more problem behaviors and perform poorly on measures of school readiness.
Postpartum Depression

- The earlier a woman receives help, the faster she recovers and the better the prognosis.

- Treatments include:
  - In cases of mild depression treatment with psychotherapy alone should be first line. (CBT, IPT and Psychodynamic Psychotherapy).
  - Also group therapy (focus on mothering role); Couples therapy.
  - SSRI’s are first line for medication treatment.
  - Start prophylactic antidepressants either in late pregnancy or the early postpartum period.

*Women with a history of PPD have a 65% risk of recurrence, whereas only 10% of that risk exists if such patients take antidepressants.

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Postpartum Depression

- Treatment:
  - Dispel the woman’s fears of physical disease or personal inadequacy
  - Personal and professional support
  - Phototherapy
  - Specific nutrition to support health brain chemistry (omega 3 fatty acids) / omega 3 supplements
  - Increase melatonin intakes (to help with sleep)
  - Add estrogen to augment the antidepressant
  - Regular exercise (when cleared by OBGYN)
  - Regular breaks during the daytime and a few hours of uninterrupted night time sleep
  - Thyroid assessment and treatment (The best time to test a new mother for a thyroid imbalance is between 2-3 months postpartum since the thyroid may shift from hypothyroid to hyperactivity until then.)

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Postpartum Depression

- Father’s can suffer too. . .

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Postpartum Depression

- Parent support groups
- Hotlines:
  - 1-800-PPD-MOMS
  - 1-800-SUICIDE

- Postpartum support groups:
  - *Depression after Delivery* is a national support group. (1-800-944-4PPD) [www.depressionafterdelivery.com](http://www.depressionafterdelivery.com)
  - Postpartum assistance for mothers [www.postpartumassistance.com](http://www.postpartumassistance.com)
  - The Massachusetts General Hospital Center for Women’s Mental Health [www.womensmentalhealth.org](http://www.womensmentalhealth.org)
### Postpartum Depression

- 1 in 10 new fathers also experience depression (obviously not caused by reproductive hormones).
- Fathers seem to more often exhibit tension and a short temper as their main symptoms along with fear, anger, frustration and feelings of helplessness.
- They are concerned about their partners, family life and finances.
- They may have increased expectations for themselves and confusion about their new role.

### Postpartum Psychosis

- Mental disturbance following childbirth was first mentioned by Hippocrates but the first good clinical description of postpartum psychosis was written by a French psychiatrist, Louis Marce' in 1858, titled “Insanity in Pregnant, Puerperal, and Lactating Women”.
- DSM II (1968) – ‘psychosis associated with childbirth’ was listed as psychosis caused by organic conditions.
- DSM III (1980) – postpartum psychosis was listed as an example of atypical psychosis.
- DSM IV lists “postpartum onset” as an atypical features modifier of mood disorders and brief psychotic disorder. Also considered psychosis NOS if does not qualify as brief psychotic disorder.

### Postpartum Depression

- The strongest predictor of whether a father will develop postpartum depression is the presence of postpartum depression in the mother. (24-50%)
- Onset is later than seen in the mother.
- Male children are affected the most when fathers are depressed and often have twice as many behavioral problems.
- For more information: [www.postpartumdads.org](http://www.postpartumdads.org)
Postpartum Psychosis

- An uncommon disorder that occurs in 0.1-0.2% of women postpartum. This rate is 100 times higher in women with bipolar disorder or a previous history of postpartum psychosis.

- Typically occurs within the first few days or weeks after childbirth and then again 1-3 months after delivery.

Postpartum Psychosis


- When talking to police she made several statements about why she killed her children:
  - Probably since I realized I have not been a good mother to them.
  - They weren't developing correctly
  - To fulfill the prophecy

- Andrea was sentenced to life in prison in 2002 but after an appeal in 2006 she was found ‘Not guilty by reason of insanity’.

- She was committed to a North Texas State Hospital and later moved to a low security state mental hospital in Texas.

Postpartum Psychosis

- Risk factors include
  - a personal history of bipolar disorder, schizophrenia or thyroid disorders
  - A personal history of postpartum psychosis (70% recurrence risk)
  - Family history of postpartum psychosis
  - Psychosocial stressors
  - Fetal distress or abnormalities
  - Primiparity
Postpartum Psychosis

- http://www.youtube.com/watch?v=FJJuNqQfro

Postpartum Psychosis

- What does recent research tell us?

Postpartum Psychosis

- Kendell et al, using data on 54,000 births over a 12 year period, linked obstetric and psychiatric case registers to determine the temporal relationship of childbirth and psychiatric admissions for postpartum psychosis.
- They found that psychiatric admissions were seven times more likely in the first 30 days after childbirth than in the pre-pregnancy period, suggesting hormonal factors as a cause.
- They also found that among patients who developed postpartum psychosis, 70-80% had bipolar disorder or schizoaffective disorder, while 12% had schizophrenia.
- There is a 2.5 fold increase risk of postpartum psychosis seen after C-section than vaginal delivery.

Postpartum Psychosis

- Wisener et al. identified a “cognitive disorganization psychosis” in mothers with child bearing onset affective psychosis that was not present in women with affective psychosis not related to childbirth.
- Psychosis associated with child bearing includes: cognitive impairment, bizarre behaviors, thought disorganization, lack of insight, delusions of reference, delusions of persecution, greater levels of homicidal behavior.
- There may be visual, tactile and olfactory hallucinations and a delirium like appearance.
Postpartum Psychosis Current Research

- Chandra et al. found that 53% of women with postpartum psychosis had delusional ideas that were related to the infant:
  - Someone would kill the baby
  - The baby would be harmed by breast milk
  - Something was wrong with the baby

- Oosthuzien et al. found in comparing 20 women with postpartum psychosis and 20 women with bipolar disorder, the women with postpartum psychosis had more rapid shifts in mood, more confusion and more delusions of control, such as feeling under the influence of an overpowering force that made them act completely out of their own control.
  - The majority of postpartum bipolar psychotic females had Schneiderian delusions and hallucinations (thought broadcasting, experiences of alienation, external control).

Postpartum Psychosis Risk Factors

- Risk factors include a family history of bipolar disorder and postpartum psychosis.
  - Jones and Craddock found that:
    - Of women with bipolar disorder AND a first degree relative with postpartum psychosis, 74% suffered from postpartum psychosis
    - Of women with bipolar disorder but no family history of postpartum psychosis, 30% suffered from postpartum psychosis.

Postpartum Psychosis

- Postpartum psychosis is a psychiatric EMERGENCY due to the potential danger to the mother and infant.
  - Inpatient psychiatric treatment is essential to ensure the safety of mother and baby.
  - Up to 5% of women with postpartum psychosis commit suicide and 2-4% pose a direct threat to their infant.
Postpartum Psychosis

Infanticide

• For any mother who presents with a postpartum mood disorder, the clinician must inquire about thoughts of harming herself or the infant and determine whether the thoughts of infanticide are **obsessional** or **psychotic**.

<table>
<thead>
<tr>
<th>Obsessional</th>
<th>Psychotic</th>
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<tbody>
<tr>
<td>Women with postpartum depression often experience co-morbid obsessional, <strong>ego-dystonic</strong> thoughts of harm to their infant. There is preservation of rational judgment and reality testing.</td>
<td>In contrast, delusional thoughts about harming the infant in postpartum psychosis is <strong>ego-syntonic</strong>. This is associated with psychotic beliefs and a loss of reality testing. There is a compulsion to act without the ability to assess the consequences.</td>
</tr>
</tbody>
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Postpartum Psychosis

Suicide

• In women, pregnancy is a time of significant reduced suicide risk.

• Suicide is most likely to occur the first month after delivery and risk continues throughout the post partum period.

Postpartum Psychosis

Less Risk for suicide
- Women with young children in the home

Greater Risk for suicide
- Women with a history of depression
- Women with a history of suicide attempts
- Women previously hospitalized for a post partum disorder
- Teenage mothers
- Low SES
Postpartum Psychosis Treatment

- **Medication therapy**
  - There is no specific method for medication management but you may consider previous successful medication trials for the patient or for the patient’s family members.
  - Acute treatment involves mood stabilizers, antipsychotics and benzodiazepines.
  - Lithium is a good mood stabilizer with the MOST evidence for prophylaxis of psychosis. Some doctors start Lithium in T2, T3 or immediately post delivery.
  - Antidepressants should be avoided because they may induce rapid cycling or mixed states.
  - Insomnia should be treated aggressively.
  - Hormone replacement (sublingual 17β estradiol)
  - Breastfeeding should be discouraged for the infant’s safety and to avoid sleep disruption in the mother.

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Postpartum Psychosis Prognosis

- Despite the severity of their symptoms, in the immediate post partum period, females with postpartum psychosis have a better overall prognosis compared with females who have non-puerperal psychoses, and they are less likely to have recurrent illness beyond the postpartum period.

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Breastfeeding

- Let’s talk about medications and breastfeeding.

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Breastfeeding

- For ethical reasons, adequate controlled trials of antidepressants in pregnancy and lactating women have not been performed. The safety data on the use of AD in this population are based on case reports, case series, birth registries, retrospective surveys and reports from teratology centers.
- ALL psychotropics cross the placenta, are present in amniotic fluid and can enter breast milk.

Breastfeeding

- Weigh the risk of infant medication exposure against the benefits of breastfeeding.
- No matter what a woman decides, it is vital not to make her feel guilty.
- Breastfeeding:
  - Facilitates mother–child bonding
- Bottle feeding:
  - Gets husbands more involved
  - Mother can return to work sooner
  - Breastfeeding may change the shape of the breast
  - Some women have difficulty with modesty issues

Breastfeeding

- Two major organizations have published guidelines on using psychotropic drugs during lactation:
  - American College of Gynecology, 2008
  - The American Academy of Pediatrics, Committee on Drugs 2001, classifies psychotropic medications as “Drugs for which the effect on nursing infants is unknown but may be of concern.”

Breastfeeding

- ACOG in 2008, classified psychotropic medications according to their safety during lactation.
  - L1 – Safest
  - L2 – Safer
  - L3 – Moderately safe
  - L4 – Possibly hazardous
  - L5 – Contraindicated
  *Unfortunately ZERO of the psychotropic medications are L1.*
Breastfeeding L2

- L2 – SAFER
  - Trazodone, TCA (except doxepin – respiratory depression), zaleplon (Sonata), valproic acid (one case of thrombocytopenia and anemia), carbamazepine (transient cholestatic hepatitis and hyperbilirubinemia), halodol, olanzapine
- SSRI’s
  - Fluvoxamine
  - Paroxetine
  - Sertraline
  - Fluoxetine in older infants is L2, but considered L3 in the neonatal period (which may be due to the long half life)

Breastfeeding L3

- L3 – Moderately Safe
  - Benzodiazepines (except diazepam is considered L4 if used chronically).
  - Buspar
  - Chloral hydrate, zolpidem
  - Citalopram, escitalopram, buproprion, venlafaxine, mirtazepine
  - Risperidone, clozapine, aripiprazole, lamictal

SSRI

- It has been shown that quantitatively, med exposure during lactation is considerably lower than transplacental exposure to the same SSRI during gestation.
- Fluoxetine (Prozac) is excreted into BM to a greater extent that the other SSRIs but appears to be the safest to use during pregnancy. It has been shown to cause colic, irritability, feeding and sleep disorder and slow weight gain.
- Order of greater to lower transfer into breast milk: fluoxetine > citalopram > paroxetine
- Sertraline is recommended as 1st line as there is a substantial body of evidence showing that sertraline has minimal risk to the infant.
- The concentration of sertraline in breast milk is low and not detectable in the serum of breastfed infants of mothers taking the drug.

Benzodiazepines

- Benzodiazepines can cause fatigue, feeding difficulty, irritability and temperature dysregulation.
- Days 1-4, the infant is unable to conjugate benzodiazepines with glucuronic acid which may result in newborn jaundice.
- Avoid benzos with long half life while breastfeeding.
Breastfeeding

L4

- L4 – Possibly hazardous
- Lithium (Contraindicated)
- Nefazodone
- Ziprasidone, Quetiapine
- Typical antipsychotics

*Duloxetine is unknown at this time.

Lithium

- Li has the potential to rapidly accumulate in breast fed infants to very high levels. (50% of the level in maternal serum)
- Li is excreted into breast milk to a greater extent than divalproex and carbamazepine.
- Due to the substantial risk of lithium toxicity in infants, use of lithium is not recommended while nursing.

Side effects include: lethargy, hypotonia, ECG changes, hypothermia, cyanotic episodes, thyroid and renal dysfunction.

Breastfeeding

- Experts recommend the use of any antidepressant in the postpartum period if it has been used effectively to treat prior depressive episodes in the patient.
- A switch in medication may be necessary if the breastfed infant has adverse effects. (Prozac – Zoloft).

Breastfeeding

- Consider before Prescribing:
  1. Is drug therapy really necessary? (Communicate between the PCP, psychiatrist and OBGYN)
  2. The safest drug should be chosen.
  3. If there is a possibility that a drug may present a risk to the infant consideration should be given to measurement of blood concentration in the infants.
  4. Drug exposure to the infant may be minimized by having the mother take the med just after she breastfeeds or just before the infant is due for a long sleep period.
Postpartum Disorders

• Last but not least...

The End!!!

Postpartum Disorders Closing

• Let your patients know that there is NO shame in having postpartum illness.
• It’s not the patient’s fault.
• She’s not crazy.

References

References

- The transfer of drugs and other chemicals into human milk. Committee on Drugs, Pediatrics 2001; 108; 776-789.