Psychiatry Bootcamp V

Perinatal Psychiatry

Pre-menstrual Dysphoric Disorder
Management of Perinatal and Postpartum Mood and Anxiety Disorders
ADHD in Pregnancy and Postpartum
Postpartum OCD
Infertility
Menopause

Stacy Greeter, MD
Child/adolescent and Adult Psychiatrist
941-413-0834
stacygreetermd.com

Belle

- 28 y/o, 8 weeks pregnant with her first child
- MDD, GAD, and social phobia
- Medication List
  - Fluoxetine 60mg daily
  - Xanax 0.25mg at bedtime

Her story…..

- Belle was bullied in childhood and has struggled with anxiety from a young age, especially in social situations.
- Belle began experiencing depressive symptoms in her mid-20s and has been on and off of various SSRIs since then.
- She describes past trials of Lexapro (escitalopram) which was effective, but she stopped it due to weight gain.
- When her symptoms returned after 6 months, she restarted escitalopram and struggled with low sex drive and anorgasmia while trying to conceive. Also, escitalopram seemed to poop out on her.
- Belle switched to fluoxetine with titration to 60mg daily with remission of depression for the past 4 months and just discovered that she is pregnant.

My friend said that pregnancy protects women from mental health issues.

She was “the happiest of her life” during her pregnancy.

All the forest creatures were extra nice to her. The birds flew her ice cream and the squirrels did her dishes.

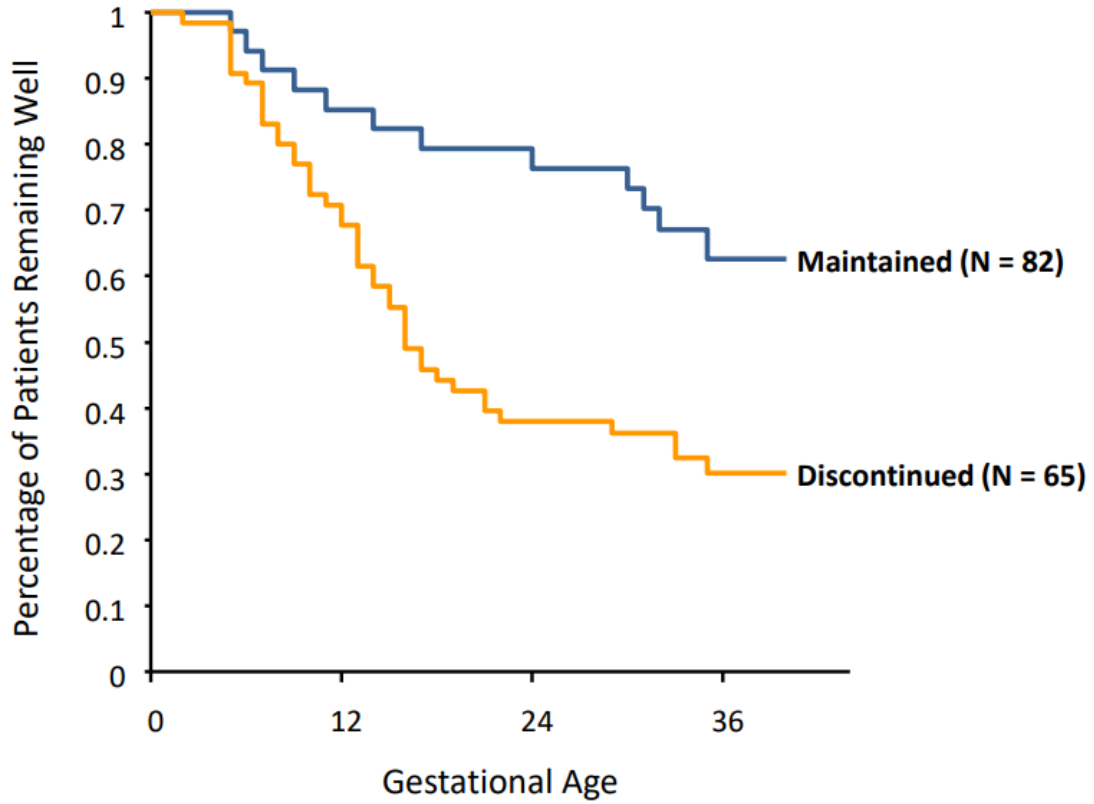
Rates of Relapse During Pregnancy

For women who discontinue their medication during pregnancy, rates of relapse during the first trimester:

- 68% for Major Depressive Disorder
- 81-85.5% for women with Bipolar Disorder
- 50% for women with Schizophrenia

- Bayrampour H, Kapoor A, Bunka M, Ryan D. The Risk of Relapse of Depression During Pregnancy After Discontinuation of Antidepressants: A Systematic Review and Meta-Analysis. J Clin Psychiatry. 2020 Jun 9;81(4):19r13134.
- Perry A, Gordon-Smith K, Di Florio A, Craddock N, Jones L, Jones I. Mood episodes in pregnancy and risk of postpartum recurrence in bipolar disorder: The Bipolar Disorder Research Network Pregnancy Study. *J Affect Disord*. 2021;294:714-722.

Time to Relapse in Patients Who Maintained or Discontinued Antidepressant



Cohen LS, et al. *JAMA*. 2006

MASSACHUSETTS GENERAL HOSPITAL
PSYCHIATRY ACADEMY

www.mghcme.org

Credit to Dr. Lee S. Cohen, Direct, Ammon-Pinizotto Center for Women's Mental Health
Massachusetts General Hospital Psychiatry Academy

Should I just grin and bear it though?

Isn’t stress bad for the baby too?

Depression and Anxiety During Pregnancy

- Lower maternal weight gain
- Increased rates of pre-term birth
  - Elevated cortisol releasing hormone stimulates labor.
- Low birth weight
  - Elevated cortisol levels decrease placental blood flow.
- **Higher rates of maternal cigarette, alcohol, and substance abuse**
- Higher rates of pre-eclampsia
- Higher rates of gestational diabetes
- Less excitement about the upcoming baby

And after the birth….what about baby?

- Children exposed to maternal depression in utero have higher cortisol levels and this finding can continue through adolescence.
- Maternal stress has been shown to impact infant temperament.
- Treatment of depression during pregnancy can normalize infant cortisol levels.

Polte C, Junge C, von Soest T, Seidler A, Eberhard-Gran M, Garthus-Niegel S. Impact of Maternal Perinatal Anxiety on Social-Emotional Development of 2-Year-Olds, A Prospective Study of Norwegian Mothers and Their Offspring : The Impact of Perinatal Anxiety on Child Development. Matern Child Health J. 2019 Jan 4.

Post-partum depression associated with…..

- Lower IQ
- Slower language development
- Increased risk of behavioral problems and psychiatric illness
  - A prospective study followed children of depressed parents over a 20-year period to gauge how they fared in adulthood. They found that they were 3 times more likely to develop mental health and substance abuse disorders than children whose parents weren't depressed.
    - Weissman, et al. 2006 Am J Psychiatry

“I did my research and antidepressants are associated with autism and heart defects.”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Antidepressants during pregnancy doubles the risk of autism

Major research suggests that taking antidepressants during the second or third trimester of pregnancy doubles the risk that children will develop autism

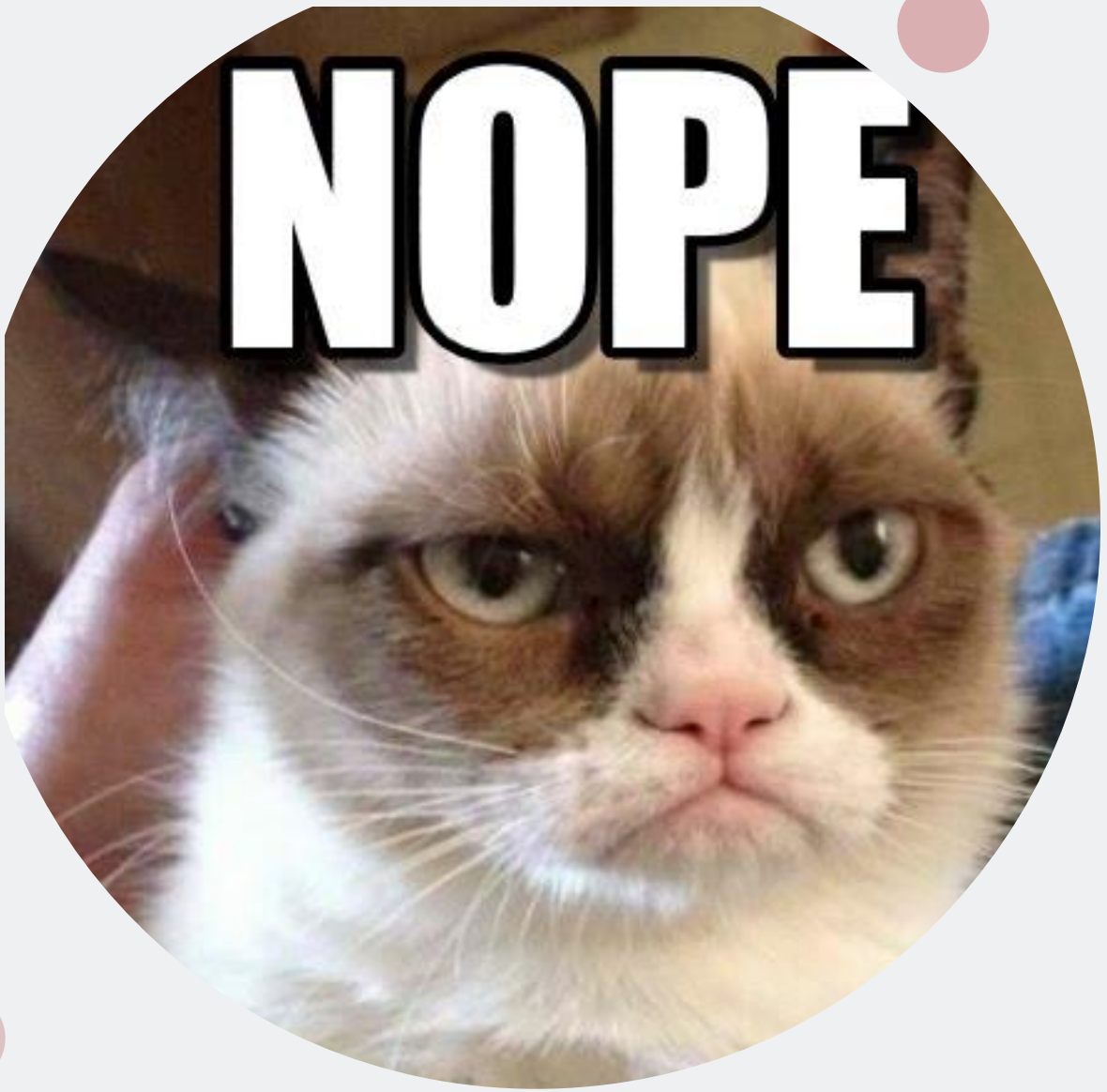
The story of confounding factors…

- Most studies have not controlled for underlying psychiatric illness as a confounding factor, comparing pregnant women with depression on SSRIs to pregnant women **without** any psychiatric illness.
- Studies that compare pregnant women on SSRIs to pregnant women with depression who defer medication treatment have not found an increased risk.
- In fact, one study of pregnant women with depression who declined treatment with SSRIs during pregnancy found an increased risk of heart defects in untreated women with depression.
- Likewise, studies suggest that previous concerns about increased risk of autism and SSRIs are likely due to risk of underlying illness, rather than use of antidepressants.

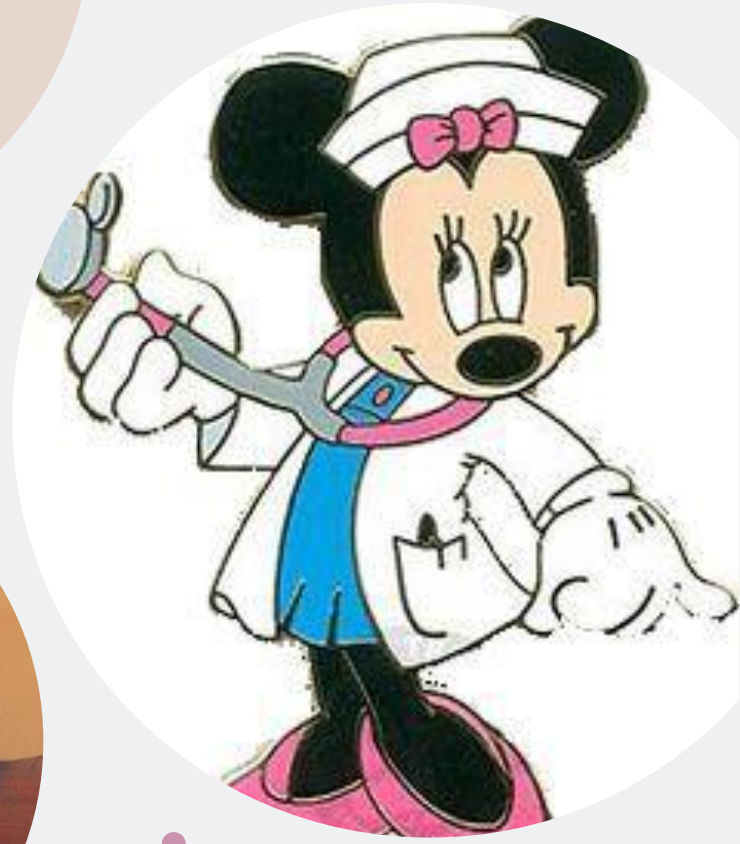
My pharmacist Mrs. Potts said sertraline is the safest. Should I switch to that?

Let's play this out….

- Sertraline is started at 25mg, then increased to 50mg.
- Fluoxetine is tapered to 40mg, then 20mg.
- She becomes depressed again and anxious and is on fluoxetine 20mg and sertraline 50mg.
- Now baby has been exposed to two different SSRIs plus maternal mental illness.
- **Generally, the best antidepressant for mom while pregnant is the best antidepressant for mom while not pregnant.**



My nurse friend said antidepressants can affect how my baby is breathing after birth!?



Persistent Pulmonary Hypertension of the Newborn

- Resistance of pulmonary vasculature fails to decrease at birth to allow proper oxygenation.
- 10-20% mortality rate and often requires intubation
- There is an FDA alert based on a 2006 study which compared infants diagnosed with PPHN to infants without PPHN and found higher rates of SSRI exposure in infants with PPHN (14 infants) compared to infants without PPHN (6 infants). However, follow up studies adjusting for confounders have not found this association.
- Maternal smoking, diabetes, and obesity which are associated with depression, contribute to risk of PPHN.
- It is important to consider **absolute risk, not just relative risk**.
  - It is rare, affecting 1-2 infants in 1000
  - If SSRI use increases the odds of PPHN by a factor of six, then now 6-12 per 1000 infants exposed to SSRIs may have PPHN, so 0.6-1.2% of infants
  - Thus, 99% of women who take SSRIs during pregnancy will have healthy babies!

Huybrechts KF, Bateman BT, Palmsten K, et al. Antidepressant Use Late in Pregnancy and Risk of Persistent Pulmonary Hypertension of the Newborn. JAMA. 2015 Jun 2;313(21):2142-2151.

Poor Neonatal Adaptation Syndrome (PNAS)

- Originally thought to be related to withdrawal from the mother's SSRI or SNRI in babies, but requires further study to fully characterize the physiological mechanism of this syndrome.
  - Higher levels of the serotonin metabolite 5-HIAA in the blood levels of infants exposed to SSRIs with PNAS compared to infants exposed to SSRIs without PNAS suggest this syndrome may be due to increased serotonergic tone in the newborn.
  - Infants born to women with untreated depression and anxiety, but with no exposure to antidepressants during pregnancy, also exhibit symptoms of poor neonatal adaptation, suggesting higher cortisol levels and dysregulation of the HPA axis may be involved.

- **Most cases are self-limited and mild, but it can include jitteriness, restlessness, irritability, increased muscle tone, and rapid breathing.**

Can pregnancy affect how well my meds work?

Pharmacokinetic and Pharmacodynamic Changes in Pregnancy

- 50% increase in plasma volume, increased body fat, increased volume of distribution
- Renal blood flow, glomerular filtration rate, and elimination of drugs can increase.
- Hormonal changes can affect liver enzyme activity.
  - CYP1A2 activity may decrease
  - CYP 2D6 and CYP3A4 activity may increase

- **Given that the concentration of medication in her blood may decrease both to increased blood volume and increased CYP2D6 activity, Belle may need a higher dose of fluoxetine as she nears her third trimester.**
- Also consider referral to couple's therapy cause well…. The Beast.

Why Belle and Beast should go to therapy……

- How well a parent has made sense of their own childhood history in therapy is one of the biggest predictors of their child's social-emotional health.

"We elicit from the world what we project into the world and what you project is based upon what happened to you as a child." – Bruce D. Perry

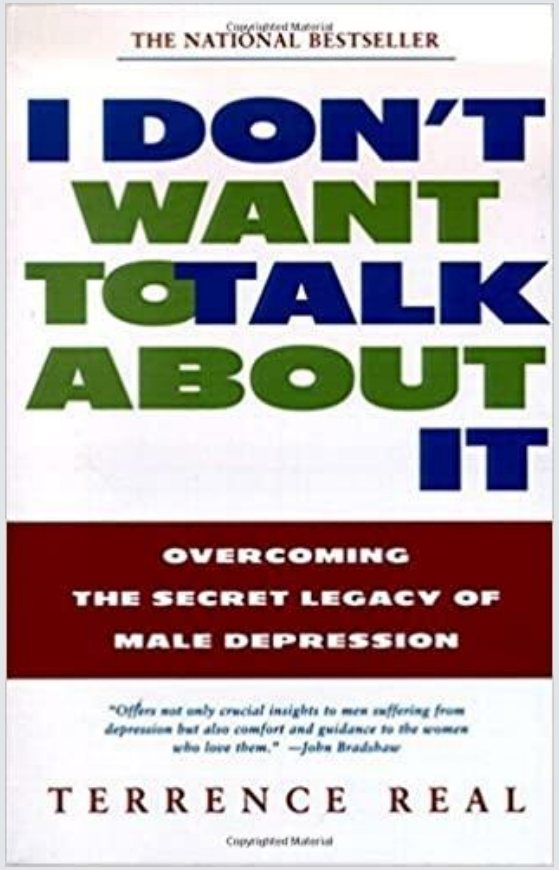
- We cannot give what we never received ourselves.
- HOW parents disagree is more important than how often they agree.

And they all went to therapy and lived happily ever after….

Beast was able to stop using power and control as a surrogate for self-esteem.

He gained the emotional regulation skills to manage his anxiety and anger so that he could tolerate the emotional vulnerability he needed to authentically emotionally connect to his family.

Let's not forget fathers….

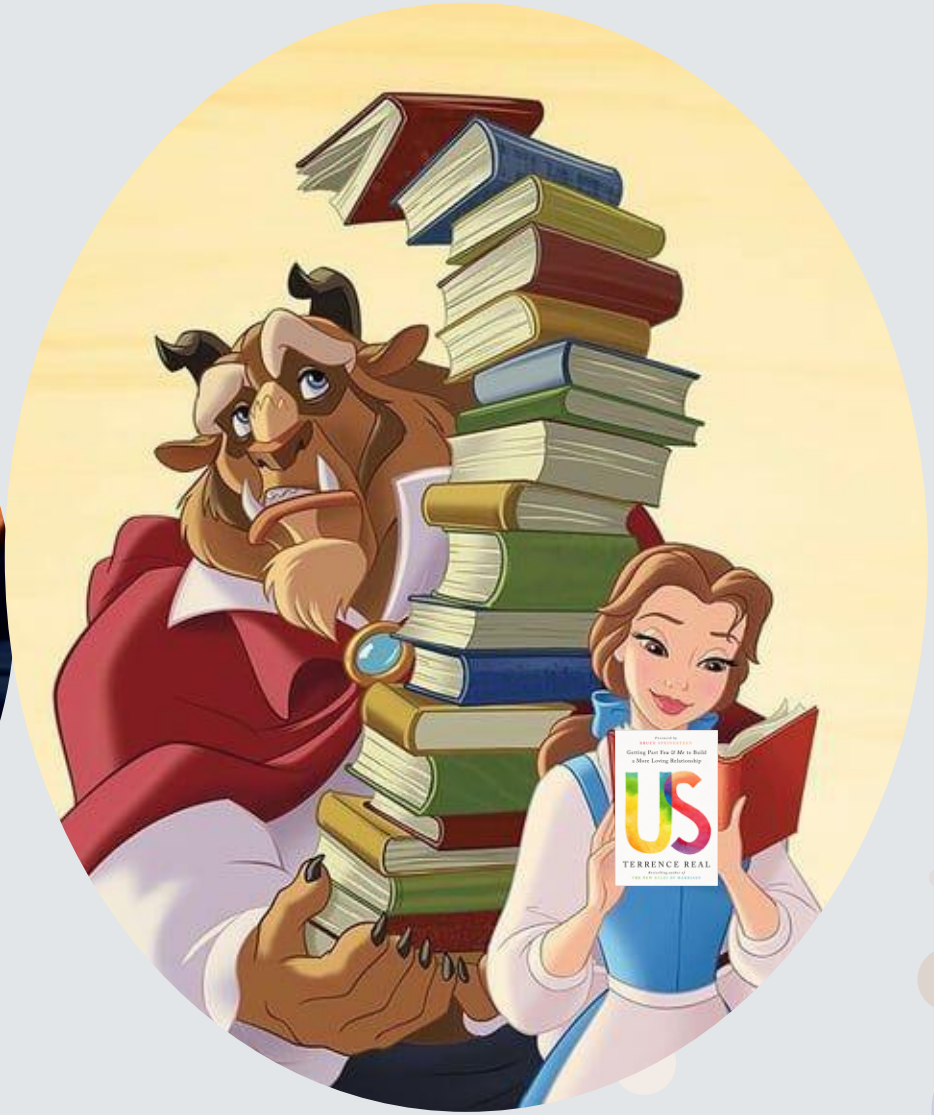


FATHERING TOGETHER

DADVOCATES
FLORIDA FATHERS NETWORK

Belle and Beast's library gets an upgrade…..

- Hold Me Tight by Sue Johnson.
- Feeling Good Together by David Burns
- Solving the Moment: A Collaborative Couple Therapy Manual by Dan Wile, PhD
- Us: Getting Past You and Me to Build a More Loving Relationship by Terrence Real



Ok, let's continue my fluoxetine, but what about my Xanax?

Benzodiazepine medication in pregnancy

- While earlier studies suggested an association between prenatal exposure to benzodiazepines and cleft palate, a more recent meta-analysis of 8 prospective cohort studies did not find an increased risk of cleft palate.

- A meta-analysis of 4 studies did not find an increased risk of cardiac malformations in prenatal exposure to benzodiazepines. However, one study found that benzodiazepine medication plus an SSRI, but not an SSRI alone, increased the incidence of congenital heart defects, but the absolute risk was small.
  - A common limitation of studies is lack of controlling for other medication exposures.

Grigoriadis S, Graves L, Peer M, Mamisashvili L, Dennis CL, Vigod SN, Steiner M, Brown C, Cheung A, Dawson H, Rector N, Guenette M, Richter M. Benzodiazepine Use During Pregnancy Alone or in Combination With an Antidepressant and Congenital Malformations: Systematic Review and Meta-Analysis. J Clin Psychiatry. 2019 Jul 9;80(4).

There are so many different studies and most of my library is out of date. How do I keep up with all this information?

Ariel has been saying I need to buy a laptop…. But which sources of information can I trust on the internet?

NATIONAL CURRICULUM IN REPRODUCTIVE PSYCHIATRY

https://ncrptraining.org/

REPROTOX®

https://www.reprotox.org/

MGH CENTER for Women's Mental Health

Reproductive Psychiatry Resource & Information Center

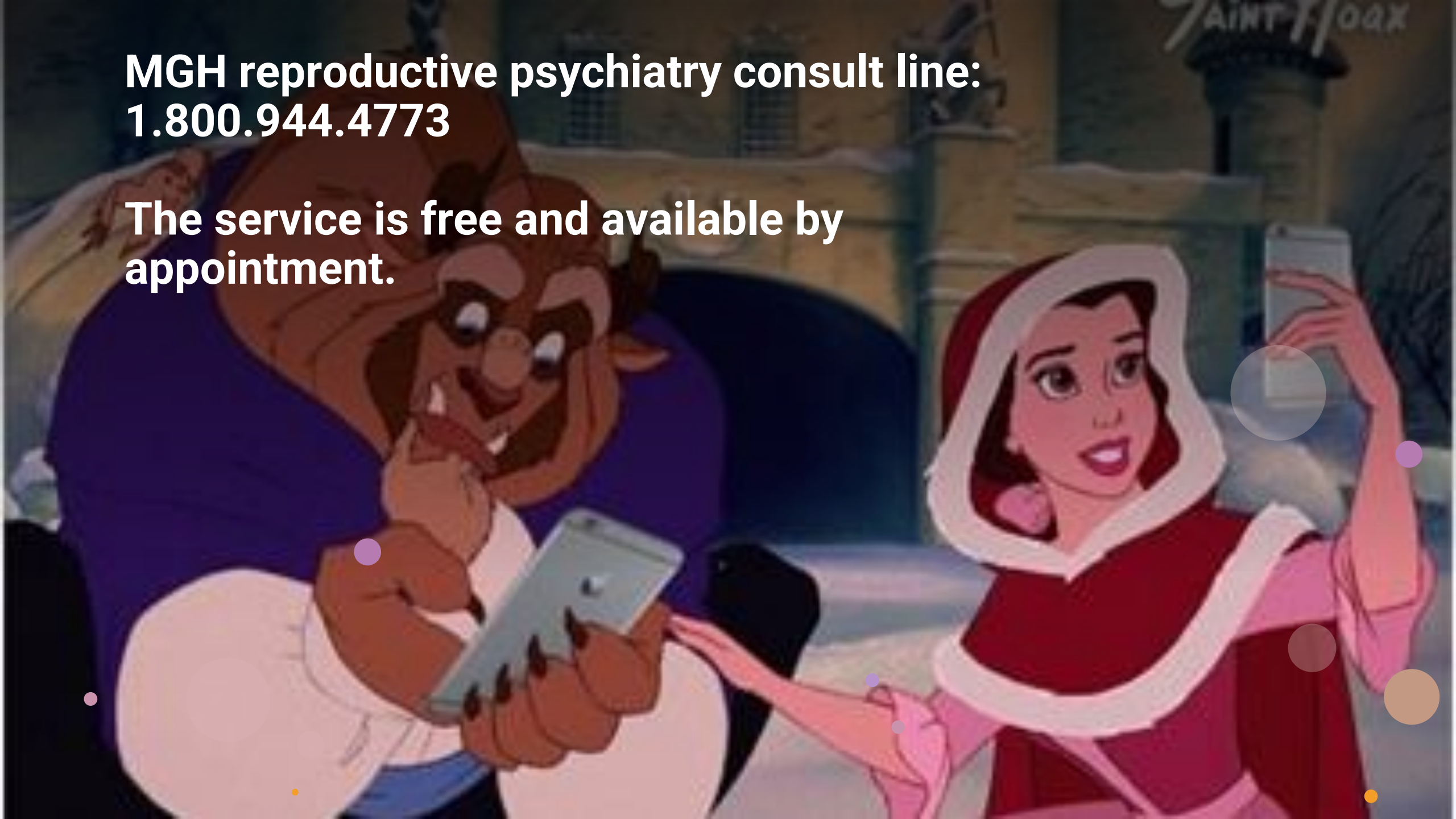
https://womensmentalhealth.org/resource-2/for-providers/#:~:text=The%20service%20is%20free%20and,944.4773%2C%20ext%204.

The International Marcé Society for Perinatal Mental Health

https://marcesociety.com/

MotherToBaby

https://mothertobaby.org/fact-sheets/


MGH reproductive psychiatry consult line:
1.800.944.4773
The service is free and available by appointment.

I don't want to risk it with my Xanax but I can't sleep without it.

Should I just give up on good sleep for a while?

Insomnia and Pregnancy

- Up to 95% of women experience sleep problems during pregnancy.
- Insomnia during pregnancy increases risk of both perinatal and post-partum mood and anxiety disorders.
- Mid-pregnancy insomnia also predicts risk of postpartum OCD.
- Pregnancy presents a higher risk of restless leg syndrome and obstructive sleep apnea.
- A small study of 54 women asked whether treatment of insomnia with diphenhydramine and trazodone could help prevent post-partum depression and found that:
    - Both sleep efficiency and total sleep time improved in women treated with trazodone and diphenhydramine during the third trimester of pregnancy and reduced the severity of post-partum depression symptoms assessed at 2 wks and 6 wks after delivery.
    - Sedating tricyclic antidepressants, such as amitriptyline or nortriptyline have not been associated with an increased risk of congenital malformations.
    - Benzodiazepine medication and Z-drug (zolpidem, eszopiclone, zaleplon) use in pregnancy remains controversial.

Khazaie H, Ghadami MR, Knight DC, Emamian F, Tahmasian M. Insomnia treatment in the third trimester of pregnancy reduces postpartum depression symptoms: a randomized clinical trial. Psychiatry Res. 2013; 210(3):901-5.

Maybe I should use marijuana for sleep.

All the villagers say it works great for them!

It's natural so that means its safe right?

Cannabis and Pregnancy

- Data suggest that prenatal cannabis exposure increases risk of …
  - Intrauterine growth retardation and low birth weight
  - Smaller head circumference in some studies
  - Increased chance of NICU admission upon delivery
  - Deficits in memory, attention, and learning in childhood and adolescence
  - Several studies indicate increased risk of cannabis and nicotine use in adolescence with prenatal exposure to cannabis.
- Overall, there is a growing body of literature that the developing brain is particularly vulnerable to exposure to cannabis and may increase risk of psychotic disorders.

- Paul SE, Hatoum AS, Fine JD, Johnson EC, Hansen I, Karcher NR, Moreau AL, Bondy E, Qu Y, Carter EB, Rogers CE, Agrawal A, Barch DM, Bogdan R. Associations Between Prenatal Cannabis Exposure and Childhood Outcomes: Results From the ABCD Study. JAMA Psychiatry. 2020 Sep 23.
- Hurd YL, Manzoni OJ, Pletnikov MV, Lee FS, Bhattacharyya S, Melis M. Cannabis and the Developing Brain: Insights into Its Long-Lasting Effects. J Neurosci. 2019 Oct 16;39(42):8250-8258. Free article.
- Gunn JK, Rosales CB, Center KE, Nuñez A, Gibson SJ, Christ C, Ehiri JE. Prenatal exposure to cannabis and maternal and child health outcomes: a systematic review and meta-analysis. BMJ Open. 2016 Apr 5. Free article.
- Roncero C, Valriberas-Herrero I, Mezzatesta-Gava M, Villegas JL, Aguilar L, Grau-López L. Cannabis use during pregnancy and its relationship with fetal developmental outcomes and psychiatric disorders. A systematic review. Reprod Health. 2020 Feb 17;17(1):25.

- Data suggests that the use of cannabis in pregnancy has increased in frequency and is often under-reported, so the American College of Obstetricians and Gynecologists (ACOG) recommends universal screening for cannabis use and counseling re risks at the first prenatal visit

“Ursula says she’s holistic and uses only natural ingredients!”
-Ariel

Addressing the Naturalistic Fallacy…

- Whether a substance is natural or man-made has no bearing on its safety, effectiveness, or side effects.
- A truly wholistic approach means utilizing all tools/resources, including medication, exercise, psychotherapy, pursuit of meaningful activities.

What do we do about Belle's sleep?

- Because she is on a **low** dosage, Belle and her doctor decide to discontinue Xanax during her pregnancy.
- She switches to diphenydramine first 50mg at bedtime.
- Because she owns a laptop now, she reads data supporting the use of CBT-I during pregnancy on the MGH women's mental health website: https://womensmentalhealth.org/posts/essential-reads-cognitive-behavioral-therapy-for-insomnia-during-pregnancy/
- Belle starts a CBT-I program which teaches her:
  - Sleep hygiene
  - Relaxation training
  - How to correct her cognitive distortions re sleep.

Ariel

- 22 y/o, 24 wks pregnant with her first child
- ADHD and PTSD from complex childhood trauma
- Medication List
  - Concerta (methylphenidate ER) 36mg daily
  - Intuniv (guanfacine ER) 3mg in the evening

Treating ADHD in pregnancy: No one right answer for everyone!

- Depending on the severity of ADHD symptoms, women may or may not need to continue stimulant medication during pregnancy.
- Untreated ADHD does include increased risk of motor vehicle accidents, loss of employment, substance abuse, financial distress and other risk-taking behaviors.
- Some employers may be able to offer extra accommodations and support for ADHD.
- Previous trends were towards discontinuation of stimulants in pregnancy. Concerns were based on studies of women who **abused** stimulant medication and had higher rates of prematurity, growth retardation, and withdrawal.

No one right answer for everyone!

- More recent findings have not demonstrated a significant increase in risk of major malformations in children with exposure to methylphenidate or amphetamine, but it is possible there is a slight increased risk in cardiac malformations.
    - Huybrechts KF, Bröms G, Christensen LB, Einarsdóttir K, et al. Association Between Methylphenidate and Amphetamine Use in Pregnancy and Risk of Congenital Malformations: A Cohort Study From the International Pregnancy Safety Study Consortium. JAMA Psychiatry. 2017 Dec 13.
- Women on stimulants during pregnancy should be carefully monitored for hypertension and potential for reduced weight gain due to appetite suppression.

We ask Ariel questions to help her make a choice that is right for her…..

How have you functioned in the past without the use of medication?

"I couldn't find any of my whozits and whatzits!

I forgot my Dad's concert!

Honestly, the hardest part was when I was fighting with Eric because I let him down."

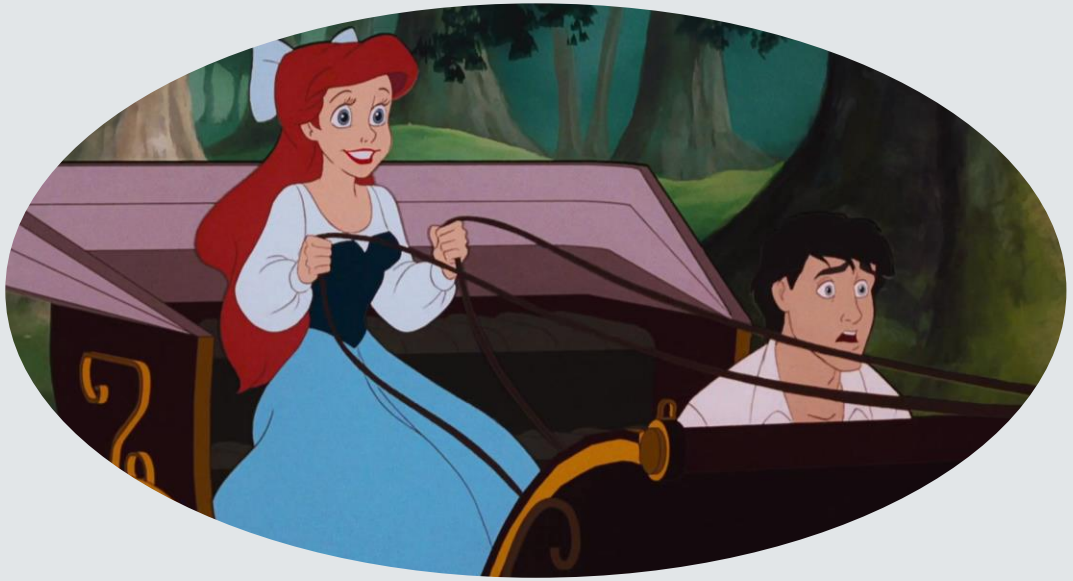
Impulsive risky behaviors?

"I made a really bad deal with a sea witch….

Oh, I forgot pants!"

How does your ADHD impact your safety driving?

"Well….. Now that you mention it…"



Other ADHD medications and pregnancy

- **Bupropion**
  - Relatively reassuring data, but not as well studied as other antidepressants in pregnancy and not as efficacious as stimulant medication
  - If patient is already doing well on it, can stay on it.
  - Evidence does NOT justify switching from stimulant to bupropion if patient is doing well on stimulant
- **Atomoxetine**
  - Very small studies have not found congenital malformations
  - We don't know.
- **Guanfacine and Clonidine**
  - Very small studies have not found congenital malformations.
  - We don't know.

Nörby U, Winbladh B, Källén K. Perinatal Outcomes After Treatment With ADHD Medication During Pregnancy. *Pediatrics*. 2017 Dec;140(6).

Help patients understand how to interpret data and evaluate risks/benefits.

- Absence of evidence of risk is NOT evidence of its absence!
- Otherwise, Patients may erroneously view medications with large studies showing evidence of low absolute risks as scarier than very small studies which show no risk.
- Explain the significance of confounding factors and that we are not comparing the risk of medication to the risk of nothing. We are comparing risks of medication to risk of untreated maternal psychiatric illness.

What does Ariel decide…

- Ariel stays on Concerta (methylphenidate ER), taking her typical 36mg dosage for driving and long castle meetings and a lower dosage 18mg or skips on less intense days.
- We monitor her blood pressure, pulse, and intrauterine growth carefully.
- Ariel decides to taper and discontinue Intuniv (guanfacine ER) because she finds this medication less integral to her functioning and is more concerned by the absence of safety data.
- Additionally, we discussed risk of guanfacine worsening orthostatic hypotension during pregnancy.

Ariel addresses her childhood trauma

To gain better control of her PTSD symptoms without guanfacine, she undergoes a combination of EMDR (eye movement desensitization and reprocessing) therapy and psychodynamic-oriented psychotherapy and elicits support from her family and employer.

She then asks…

"I lost my mom at a young age.

How will I know how to be a mom to my baby?

I've been reading about how human babies can't just be left alone like a clutch of fish eggs. How do I connect to my baby when no one did that for me?"

Circle of Security®

Parent Attending To The Child's Needs

I need you to...

Support My Exploration

- Watch over me
- Delight in me
- Help me
- Enjoy with me

SECURE BASE

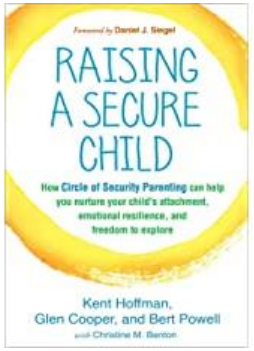
I need you to...

SAFE HAVEN

- Protect me
- Comfort me
- Delight in me
- Organize my feelings

Welcome My Coming To You

ALWAYS BE: BIGGER, STRONGER, WISER & KIND.
WHENEVER POSSIBLE: FOLLOW MY CHILD'S NEED.
WHENEVER NECESSARY: TAKE CHARGE.

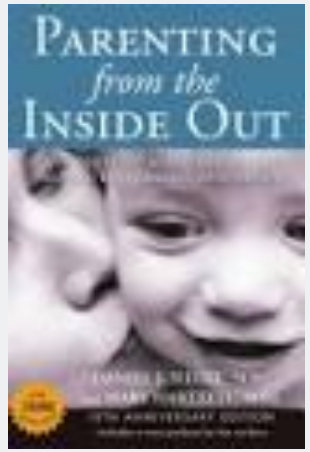


https://www.circleofsecurityinternational.com/circle-of-security-model/what-is-the-circle-of-security/

Secure Attachment Make children feel….

Safe	Seen	Secure	Soothed
• Parent will protect the child from harm and will not be a source of fear for their child themselves. • Children have a sense that home is a haven.	• Parents demonstrate that they understand how a child feels and what they are thinking, or that they are at least curious and want to understand. • Parents do not shame or judge the child. • Parents are open and empathic.	• Parents are reliable and consistently present. • Parents will repair the relationship after disagreements. • Connect before you correct.	• Parents are attentive to child's emotional needs. • They help comfort the child and teach them emotional regulation skills.

Ariel's story continues…..



Ariel works hard with her therapist to understand how her early childhood experiences impact her effectiveness as a parent. She recognizes that her hoarding stems from early childhood neglect and her tendency toward helicopter parenting stems from her fear of not protecting her child as she herself was not protected swimming alone in shark infested waters. She struggles initially with limit setting because she does not want to be like her authoritarian father but is eventually able to grow in confidence as a parent.

Now I collect empowering information instead of whosits and whatsits!

Snow White

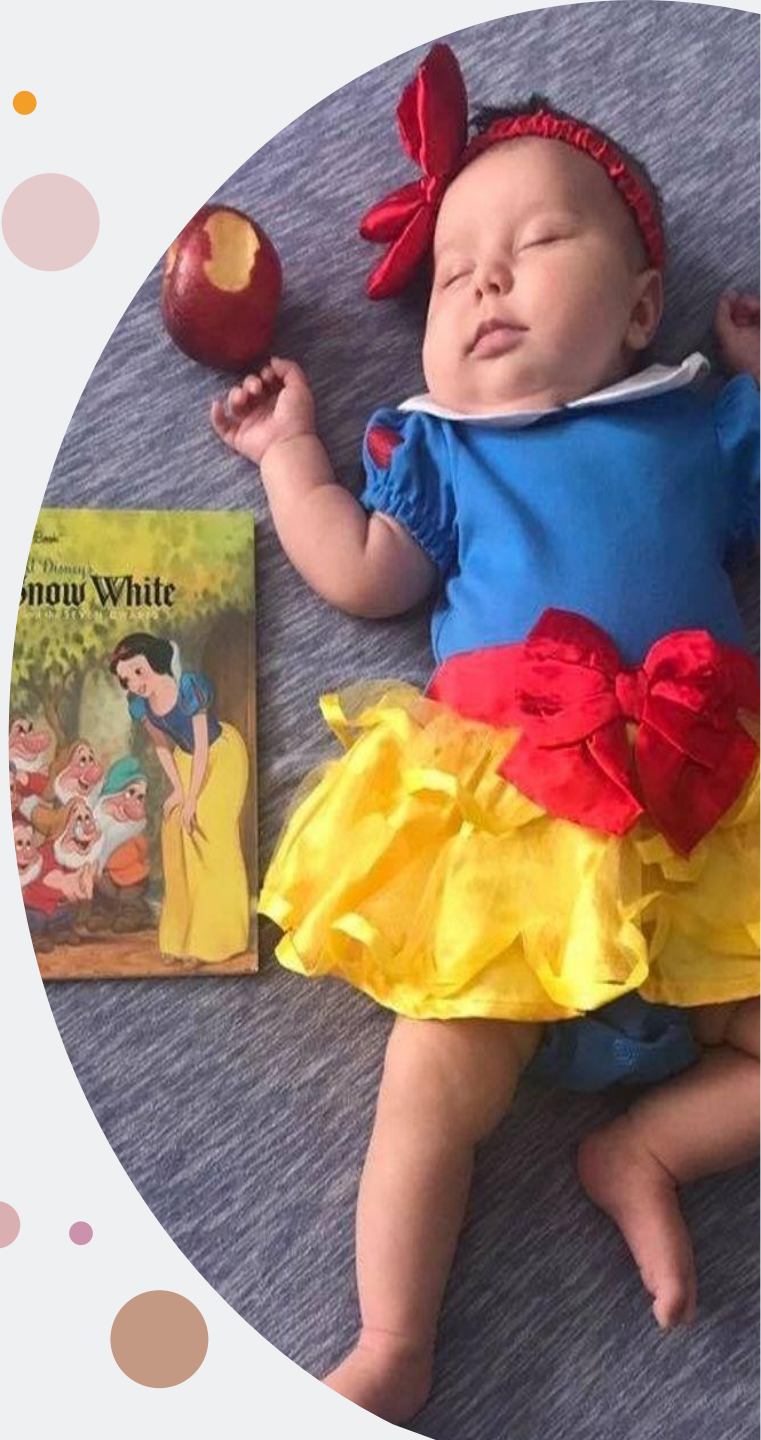
- 22 y/o female 8 wks post-partum
- Reluctant to speak….
- No current medications

Fear of contamination

Snow White reluctantly discloses that she is plagued by fears of accidentally poisoning her infant through contamination. She is spending 5 hours a day cleaning and makes the dwarves wash their hands, show her their hands, and wash their hands again before entering the baby's room.

Compulsive checking

Snow white goes into the baby's room at night over and over again checking that her baby is breathing, unable to sleep due to a fear that her baby will go to sleep and never wake up. She tries to go back to sleep, but thinks "what if this time, my baby isn't breathing?"



Her doctor asks directly and nonjudgmentally…

"Some new mothers have thoughts of harming their baby. Has this happened to you?"

Snow White answers….

"I've been afraid to tell anyone, but I have this image in my mind of smothering my infant with a pillow. I can't get rid of it. I'm so afraid that I don't want to hold my baby. I don't want to hurt her!"

Post-partum OCD

- New onset OCD and worsening of pre-existing OCD is common in the post-partum period.
  - Studies have estimated prevalence of OCD of 7-11% across the perinatal period, with peak prevalence 8 weeks post-partum.
- This may lead mothers to avoid holding their infant and affected mothers may engage family members in compulsive rituals.
  - Support and education are key to maintain appropriate bonding with baby.
- Women are especially afraid to disclose these symptoms due to shame, so direct screening is important.

Fairbrother N, Collardeau F, Albert AYK, et al. High prevalence and incidence of obsessive-compulsive disorder among women across pregnancy and the postpartum. J Clin Psychiatry, March 2021.

Reducing Shame and Stigma

Normalization

- You are not the only one struggling with this.

Psychoeducation for Patient and Family

- Educate family members as well as the patient that there is no an increased risk of harming the infant.
- Encourage family members not to enable the compulsive behaviors or help with rituals.

Externalization of the Disorder

- How can the family attack “The OCD” together
- Separate OCD thoughts from the patient’s identity as a mother

Connection

- I can handle whatever you need to tell me.
- You are not alone. I’m with you in this.
- Who else do you feel safe sharing this with?

Shame thrives in the darkness of secrecy and solitude. It cannot survive the light of open acceptance and human connection.

Post-partum OCD vs Post-partum Psychosis

Post-partum OCD

- No increased risk of harm to infant or self.
- Thought process is organized.
- Ego-dystonic thoughts
  - Patient is afraid of harming baby and wants thoughts to go away.
- Common:
  - 7-11% of women
- Provide reassurance, education, and referral to therapy
- SSRIs are first line

Post-partum Psychosis

- Increased risk of harm to infant and harm to self.
- Thoughts process is disorganized. Mood changes are present. Behavior is bizarre.
- Ego-syntonic thoughts
  - Patient believes harming themselves or baby may be for a greater good (delusion of altruism).
- Rare
  - 0.1% of women or 1-2 per 1000 women
- Provide emergency hospitalization.
- Lithium is first line

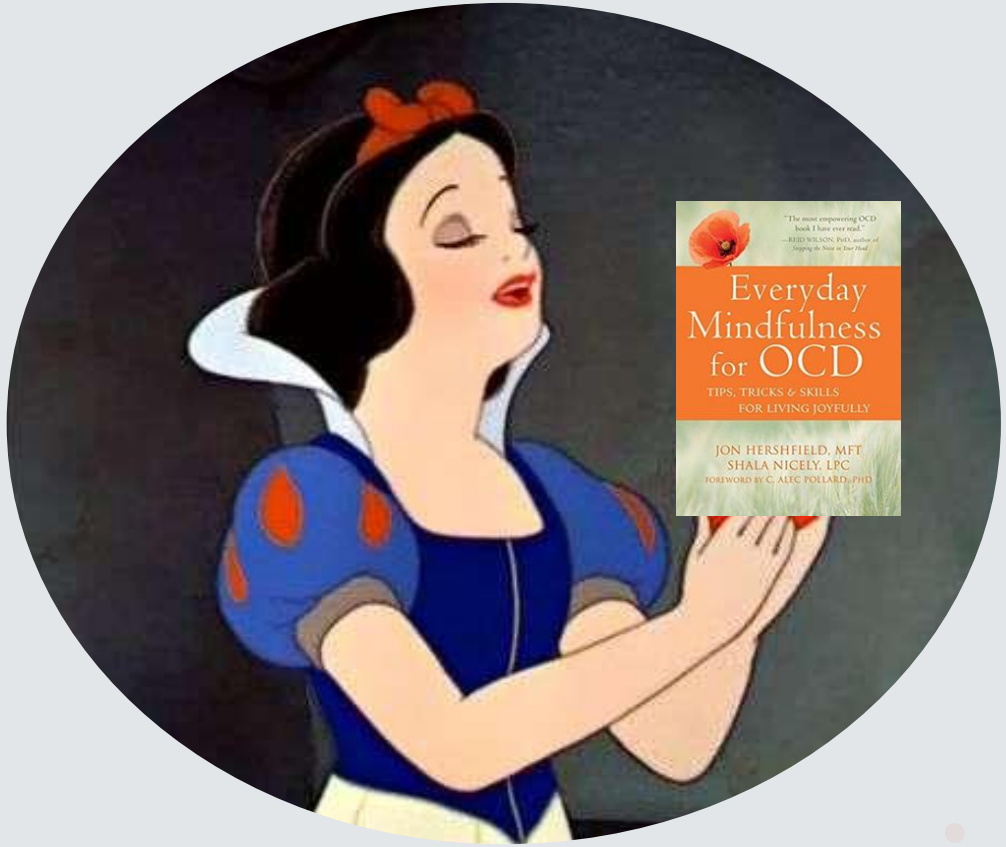
Post-partum Psychosis

- The post-partum period is a very risky time for women's mental health.
  - A woman's risk of first-onset psychosis in the post-partum period is 23 times higher than any other time during that woman's life.
- Who is most at risk?
  - Women with a family hx of bipolar disorder or hx bipolar disorder themselves
- What does the future look like?
  - Women with post-partum psychosis have a 50%-80% chance of experiencing another severe psychiatric episode, usually within the bipolar spectrum.
  - In 20%-50% of women, psychosis is limited to the postpartum period.
- Treatment
  - Lithium has shown the most benefit in treating and preventing post-partum psychotic episodes.

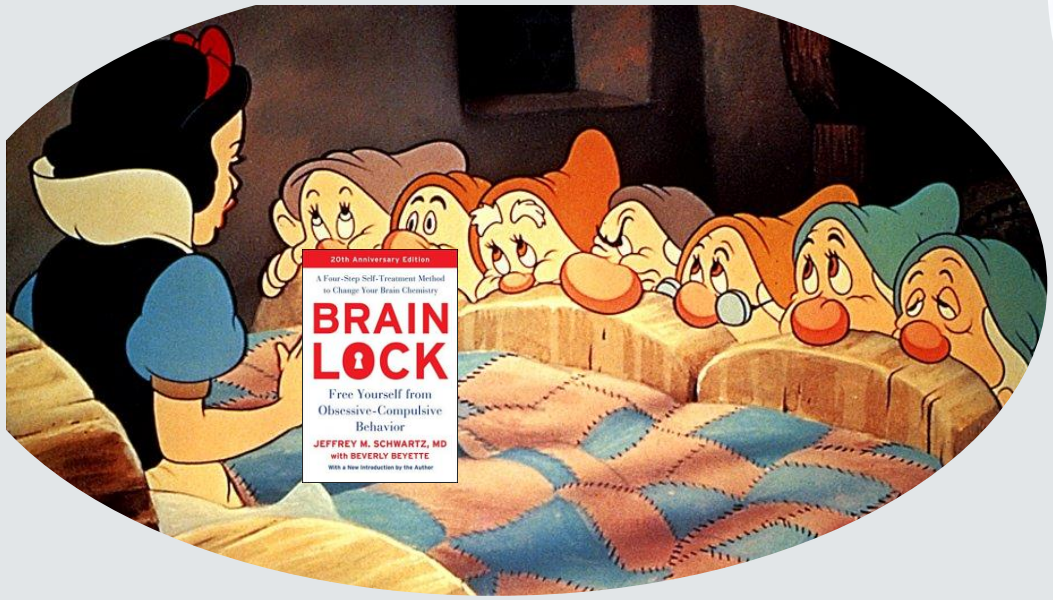
Gilden J, Kamperman AM, Munk-Olsen T, Hoogendijk WJG, Kushner SA, Bergink V. Long-term outcomes of postpartum psychosis: a systematic review and meta-analysis. J Clin Psychiatry. 2020.

Snow White's Recovery

- Snow White starts sertraline which is titrated up to 300mg daily.
  - Yes, sometimes we need to go that high with OCD.
- Snow White undergoes CBT (cognitive behavioral therapy) and ERT (exposure and response prevention therapy).
  - She labels her OCD thoughts and practices doing the opposite and spending time with her baby. She practices various levels of exposure to contaminants.



- Charming and the dwarves participate in her treatment. They read <u>When a Family Member has OCD</u> by John Hershfield. They stop participating in Snow White's compulsive rituals and provide positive affirmations instead of reassurance.



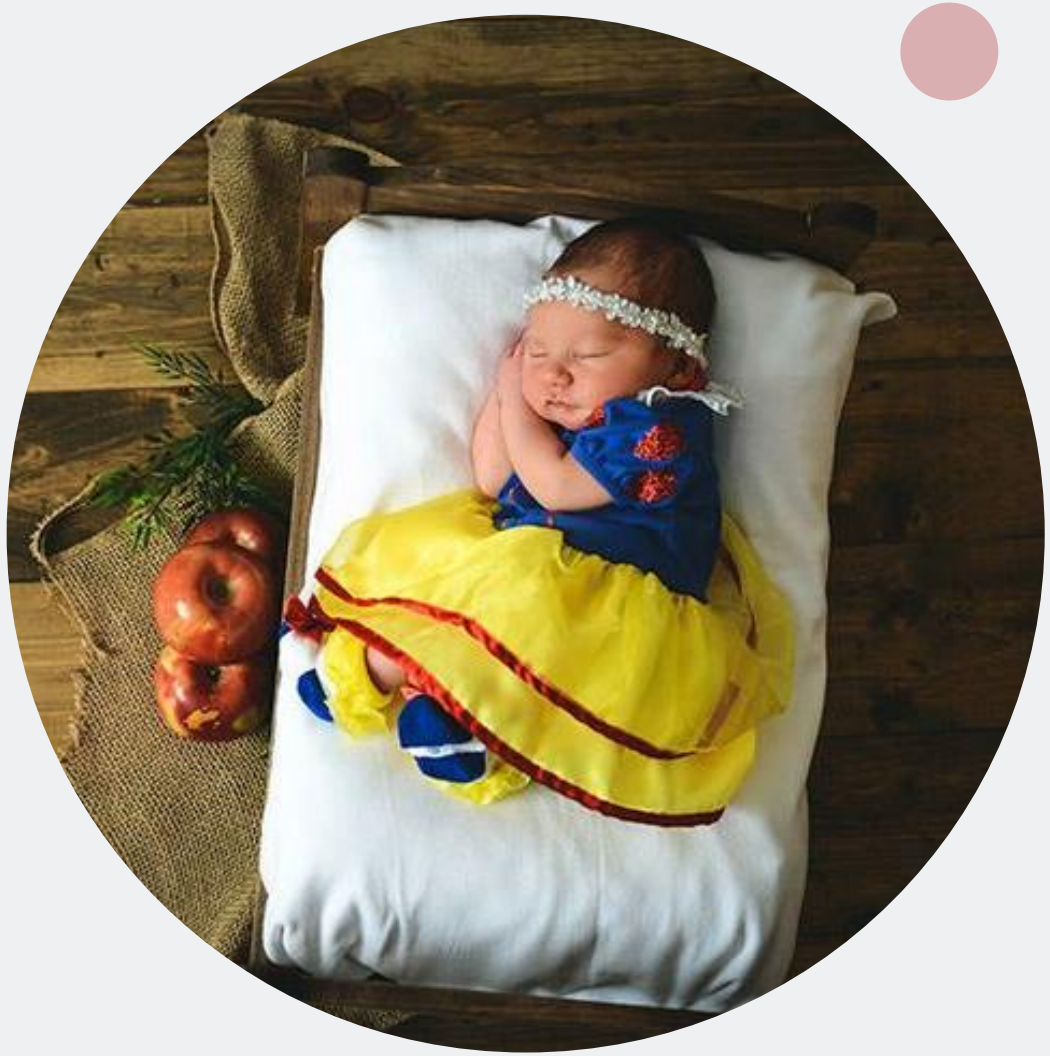
Breastfeeding and Antidepressants: An Overview

- During the first month of an infant's life, their hepatic capacity for drug metabolism is about 1/5 to 1/3 of adult capacity.
- Hepatic metabolism increases rapidly and by 2-3 mo of age, hepatic capacity surpasses that of adults.
- "Pumping and dumping" is not recommended or supported by evidence.

- **For the majority of psychiatric medications, the benefits of breastfeeding outweigh risks of medication.**
  - *Weissman AM, Levy BT, Hartz AJ et al. Pooled analysis of antidepressant levels in lactating mothers, breast milk, and nursing infants. Am J Psychiatry. 2004;161:1066-78.*
  - Julie Demetree, MD's presentation on breastfeeding and psychiatric medications
    - https://ubmm.med.buffalo.edu/uploads/MMU3/6-8-2018%20Grand%20Rounds%20Handout.pdf

While Breastfeeding avoid:

- Clozapine
  - infant serum levels 279% that of mother's serum level
  - case reports of agranulocytosis, cardiovascular instability, sedation
- Doxepin
  - has been linked to infant death in one case and respiratory depression in another



Antidepressant levels in breastmilk

- Relatively lower levels in breastmilk:
  - Sertraline- only 0.04-0.5% in milk
  - Paroxetine
  - Cymbalta (very limited date though)
  - Mirtazapine (very limited data)
  - Bupropion – 8 case reports found nondetectable levels
- Relatively higher levels
  - Fluoxetine – higher levels, but still advisable to breastfeed
    - study of 238 infants found that 18% had levels over 10% of maternal level
  - Citalopram/escitalopram –
  - Venlafaxine / desvenlafaxine
- No Data Yet:
  - Trintellix (vortioxetine)Viibryd (vilazodone), Rexulti (brexpiprazole), Fetzima (levomilnacipran)

ADHD medication in breastmilk

- Methylphenidate
  - undetectable levels in 4 infants
  - no adverse events
  - possible increase in prolactin level
  - monitor for agitation and appropriate weight gain
- Adderall
  - up to 15% maternal serum level in infant serum
  - no adverse events
  - may increase in prolactin
- Clonidine
  - infant levels range from undetectable to 66% maternal level
  - several reports of hypotonia, seizure, apnea, possible galactorrhea
- No data on guanfacine or atomoxetine

Antipsychotics and Breastfeeding

- Relatively reassuring data on
  - Quetiapine
  - Olanzapine
  - Risperidone
    - Can cause galactorrhea
- Can inhibit lactation and decrease milk supply
  - Abilify (aripiprazole)

Sedatives in breastmilk

- Sleep Medication
  - Trazodone
    - 0.6% of maternal dose in infant serum, no adverse effects
  - Limited data on safety of diphenhydramine and melatonin
- Benzodiazepines
  - lorazepam is the safest
    - lower levels in breast milk
    - can cause sedation in infant
  - Clonazepam – multiple reports of adverse events
  - Diazepam – infant serum levels are unpredictable and can get very high, reports of sedation and weight loss
  - Alprazolam – one case of infant withdrawal

Cannabis in breastmilk

- High milk to serum plasma levels
  - estimated that infants will receive 2.5% of maternal dose (range 0.4-8.7%)
- Delayed motor development
- Less frequent and shorter feeds

The postpartum period is no fairytale…..

- Breastfeeding improves infant immune systems, decreases risk of sudden infant death, decreases risk of diabetes and obesity, and improves cognitive development.
- For mothers, breast feeding improves post-pregnancy weight loss, protects against breast and ovarian cancer, and facilitates bonding.
- For women whose expectations of breast feeding are not met or who struggle to breast feed due to low milk supply, breast/nipple pain, or inadequate latching, there is an increased risk of anxiety, depression, and guilt.
    - In select cases, the maternal mental health effects associated with breast feeding may outweigh the potential physical benefits of breastfeeding.

Post-partum sexual dysfunction

- Pain
  - Studies estimate about 50% of women experience persistent (lasting at least 3 mo) pelvic and genital pain postpartum, often exacerbated by sexual activity.
    - Laurel Q P Paterson et. Al. J. Sex Med. 2009 Jan
- Reduced sex drive and anorgasmia
  - Lactation lowers estrogen levels which lowers sex drive and increases vaginal dryness.
  - Pelvic floor muscle weakness and nerve damage due to birth and delivery cause pain and anorgasmia.
  - Also…. Sleep deprivation, breast tenderness, anxiety…..

Managing SSRI induced sexual dysfunction

- **Cialis (tadalafil)** 5-20mg or **Viagra (sildenafil)** 50-100mg about 30mins to an hour before intercourse
  - most effective for anorgasmia
- **Buspar (buspirone)** 7.5mg to 30mg twice daily
  - most effective for low libido
- **Wellbutrin (bupropion)** 150-300mg daily
  - Mildly helpful
- **Mirtazapine** 7.5mg- 45mg qhs
  - Mildly helpful

“No one told me pooping after pregnancy could be more painful than childbirth!”

-Snow White

- Pelvic floor dysfunction after childbirth causes pain with intercourse as well as…..
  - Urinary incontinence
  - Fecal incontinence
  - Severe constipation
    - Dehydration due to lactation combined with pelvic floor weakness often results in painful defecation.
  - Vaginal or rectal prolapse
- Low back pain
- Pelvic pain
- Separation of the abdominal muscles (diastasis recti)

It’s important to check in with women post-partum about how they’re doing ….. down there.

Snow White and Charming

- Snow White works with a pelvic floor physical therapist, improves her hydration, takes stool softener, and gets a squatty potty.
- Snow White and Charming work with a couple's therapist.
  - Snow White learns to stop treating Charming as another child, cleaning up after him all the time. Charming learns to take initiative with household chores.
  - Charming no longer views Snow White's anorgasmia as a failure on his part or threat to his masculinity. He is able to understand her need for personal space when her breasts are tender.
  - Snow White is able to approach her sexuality with less shame and communicate assertively to Charming what conditions she needs to feel sexual again (ie sleep, alone time, Charming does the dishes).
- Snow White starts buspirone 15mg BID with her sertraline and Cialis 10mg PRN 30 mins prior to intercourse.

Snow White and Charming's New Book Club


The Better Sex through Mindfulness Workbook
A GUIDE TO CULTIVATING DESIRE
Lori A. Brotto, PhD
FOREWORD BY DR. JEN GUNTER

Snow White and Charming Thank their Treatment Team….

"If you hadn't directly asked me about my pelvic pain and sexual dysfunction I never would have told you. I would be too embarrassed. I am so glad you referred me to the pelvic floor physical therapist and helped me to understand I wasn't permanently damaged or alone."

"I thought I was going crazy when I had those thoughts of harming my baby and I was so ashamed and scared. When you told me other women have those thoughts too and that it was postpartum OCD I felt so relieved to be accepted and seen and know that I wasn't a bad mother for taking medication."

"Thank you for having Charming listen to the Motherhood Meets Medicine Podcast *https://podcasts.apple.com/us/podcast/motherhood-meets-medicine/id1553782780* episode on Pelvic Floor Issues and read those books on OCD. Charming downloaded Come as You Are by Emily Nagoski on audiobook, which made for a very entertaining listen while riding to and from our neighboring Kingdom.

All the villagers love Massachusetts General Hospital's Women's Mental Health website!

https://womensmentalhealth.org/blog/essential-reads/

Elsa

30 y/o nulliparous women struggling with severe irritability, hopelessness, and anxiety that causes interpersonal conflicts starting about 10 day prior to menstruation, peaking four days beforehand, and resolving with menstruation.

PMDD
Pre-Menstrual Dysphoric Disorder

- Estimated to affect 3-9% of women
- Causes marked impairment in functioning and relationships.
- At least 2 consecutive months of at least 5 of these symptoms:
  - Markedly depressed mood, hopelessness, or low self-worth
  - Severe emotional lability
  - Anxiety
  - Irritability and anger leading to interpersonal conflicts
  - Low motivation, lack of interest, low energy
  - Sense of being overwhelmed or out of control
  - Physical symptoms, such as breast tenderness or swelling, headaches, joint or muscle pain, a sensation of “bloating”

PMDD (Pre-Menstrual Dysphoric Disorder)

- Symptoms occur during the luteal phase (ovulation to menstruation)
  - about 2 weeks prior to menstruation
  - severity of symptoms generally peeks about 2 days before menses
- Symptoms resolve with menstruation and mood remains normal during the follicular phase.
  - If symptoms are present but milder during follicular phase, it is called PME (pre-menstrual exacerbation)

- Commonly co-morbid with other mood disorders such as Major Depressive Disorder and Bipolar Disorder.
- An estimated 38-46% of women with PMDD also meet criteria for Seasonal Affective Disorder.

- PMDD Daily Record of Severity of Problems
  - https://psychscenehub.com/wp-content/uploads/2020/10/Daily-Record-of-Severity-of-Problems-PMDD.pdf

Daily Record of Severity of Problems

Symptoms	Day of menstrual cycle (day 1 should be the start of the menstrual period)																																
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35
Felt depressed, sad, down, or blue																																			
Felt hopeless																																			
Felt worthless or guilty																																			
Felt anxious, tense, keyed up, or on edge																																			
Had mood swings (e.g., suddenly felt sad or tearful)																																			
Was more sensitive to rejection or feelings were more easily hurt																																			
Felt angry, irritable																																			
Had conflicts or problems with people																																			
Had less interest in usual activities (e.g., work, school, friends, hobbies)																																			
Had difficulty concentrating																																			
Felt lethargic, tired, fatigued, or had a lack of energy																																			
Had increased appetite or overate																																			
Had cravings for specific foods																																			
Slept more, took naps, found it hard to get up when intended																																			
Had trouble getting to sleep or staying asleep																																			
Felt overwhelmed or that I could not cope																																			
Felt out of control																																			
Had breast tenderness																																			
Had breast swelling, felt bloated, or had weight gain																																			
Had headache																																			
Had joint or muscle pain																																			
At work, school, home, or in daily routine, at least one of the problems noted above caused reduced productivity or inefficiency																																			
At least one of the problems noted above interfered with hobbies or social activities (e.g., avoided or did less)																																			
At least one of the problems noted above interfered with relationships with others																																			
Menstrual flow: H = heavy, M = medium, L = light or spotting; leave blank for no bleeding																																			
Totals																																			

Directions:

Record the score for each item on each day using the following scale of 1 to 6: 1 = not at all, 2 = minimal, 3 = mild, 4 = moderate, 5 = severe, 6 = extreme.

Add the scores in the column for the first day of menses. If the total score is less than 50, consider a diagnosis other than premenstrual syndrome. If the total score is greater than 50, record two cycles of symptoms. If more than three items have an average score of more than 3 (mild) during the luteal phase, add the scores of five-day intervals during the luteal and follicular phases. A luteal phase score that is 30 percent greater than the follicular phase score indicates a diagnosis of premenstrual syndrome.

Figure 1. Daily scoring sheet for patients to track symptoms related to premenstrual syndrome and premenstrual dysphoric disorder.

Adapted with permission from Endicott J, Nee J, Harrison W. Daily Record of Severity of Problems (DRSP): reliability and validity. Arch Womens Ment Health. Springer-Verlag, Wein. 2006;9(1):43.

PMDD treatment

- **SSRI and SNRI medication – response rate of 60-90%**
  - Work faster for PMDD than for anxiety and depression, allowing some patients to only take them during the 14 day luteal phase prior to menstruation, **can take lower dosage than for MDD**
  - Paroxetine, sertraline, and fluoxetine are specifically FDA-approved for PMDD but other SSRIs and SNRIs are also effective
- **Combination (estrogen and progesterone) oral contraceptives**
  - Can skip placebo pills to optimize emotional regulation for very sensitive patients
  - Yaz (drospirenone and ethinyl estradiol) has shown efficacy in RCTs and is FDA approved, has shorter placebo pill duration (4 days instead of 7)
- **GnRH (gonadotropin releasing hormone) agonists** such as leuprolide – about 60-70% of women respond
  - Reserved for those non-responsive to SSRIs or contraceptives due to side effects
  - Night sweats, hot flashes, vaginal dryness, risk of endometrial hyperplasia
- Can also consider supplementation with:
  - **Vitamin B6** up to 100mg daily
    - Only has support from small studies
    - Neuropathy can occur with doses of 200mg/day or higher
  - **Calcium**
    - 600mg twice daily, mild effect
  - **chasteberry**

Magnesium –weak evidence
Vitamin E –weak evidence

Reduce Caffeine and Alcohol

For physicians who want to learn how to prescribe contraception…..

https://ncrptraining.org/learning-modules/f-reproductive-life-cycle/

NATIONAL CURRICULUM IN REPRODUCTIVE PSYCHIATRY

Facilitator Modules Logout

Topic: The Reproductive Life Cycle

This unit reviews the basic science of the reproductive life cycle, including the menstrual cycle, pregnancy, and perimenopause, as well as the basic science of contraception and lactation. Classroom activities include a progressive case conference concerning a woman at different reproductive stages, a contraception case conference, and a conference about drug interations between contraceptives and psychotropics. The media module covers weight and body image in pregnancy and postpartum.

The recommended order of modules is:

Self-Study: Reproductive Life Cycle 101
Self-Study: Emergency Contraception, Pregnancy Termination
Classroom: Stages of reproductive cycle progressive case conference
Classroom: Birth Control Case
Classroom: Drug Interactions
Media Module

Objectives

US Medical Eligibility Criteria (US MEC) for Contraceptive Use, 2016
https://www.cdc.gov/reproductivehealth/contraception/mmwr/mec/summary.html

- Elsa tracks her mood symptoms for 3 months, confirming diagnosis of PMDD.
- She starts fluoxetine 10mg for 7 days, then 20mg thereafter.
- She does not want to try oral contraceptive because she plans to undergo egg retrieval.

Then you receive a frantic phone call from her sister……

“After starting that new medication you prescribed, Elsa’s not acting like herself.

These past two weeks, she’s only slept 2 hours a night at most. She’s talking so fast, I can’t understand her. My sister is usually so reserved. She’s wearing more revealing clothing. She turned our entire kingdom into ice!

I think she’s out in the snow singing loudly to herself right now!

-Anna

Screen for history of manic episode before prescribing an antidepressant

- **Manic episode**
  - Grandiosity (extremely high self-esteem, making lots of grand plans)
  - Euphoria/intense irritability
  - Risk-taking behaviors that are out of character (Running red lights, spending sprees)
  - Decreased need for sleep (doesn't sleep AND doesn't feel tired after not sleeping)
  - Increased activity
  - Feeling invincible
  - Hallucinations and Delusions (often religious or grand)
- **ADHD**
  - Overlap in symptoms (impulsivity, talking fast, risk-taking) but ADHD symptoms represent the patient's baseline and are not episodic
  - Does not included increased sex drive, decreased need for sleep, or sudden increase in self-esteem
- **Mood swings**
  - Last hours, not days
  - Usually do not include behavior that is very out of character for that individual
  - No decreased need for sleep for many nights in a row

If suspicious, consult a family member and refer to psychiatry!

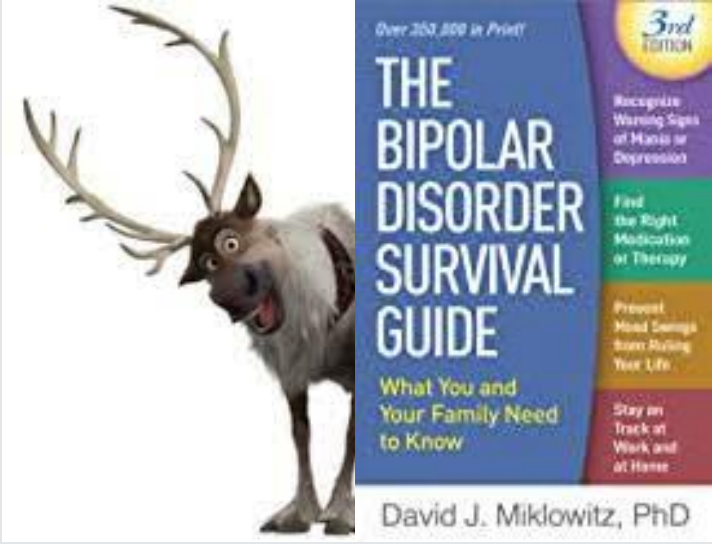
How we stabilize Elsa….

- Elsa starts olanzapine 10mg and lithium 600mg qhs. Lithium level collected 5 days later is 0.4.
- Lithium is titrated to 1200mg qhs with lithium level 0.9 and manic symptoms have resolved.
- Six months later, symptom free, olanzapine is tapered and discontinued to minimize metabolic risk.
- Later, lamotrigine titrated to 200mg qhs is added as lithium monotherapy alone did not prevent depressive episodes.
- However, breakthrough hypomania and depressive episodes still occur, so she is transitioned from lamotrigine to quetiapine titrated gradually to 300mg qhs plus metformin 500mg BID to mitigate metabolic risk.
- After 6 mo without mania, lithium is reduced to 1050mg qhs with level of 0.7 to protect kidney function.
- Elsa is provided with an emergency sample of “mayday medicine” and asked to designate a family member point of contact who she trusts.
    - Elsa is given olanzapine 10mg tablets with instructions to both Elsa and her sister Anna to call the office immediately and restart olanzapine 10mg daily in the evening for any early signs of oncoming manic episode (not sleeping, elevated self-esteem, etc). Both sisters are provided with a list of warning symptoms of mania.
- Her creatinine, GFR, TSH, HbA1c, and PTH are regularly monitored with a yearly ECG.

PMDD and Bipolar Disorder

- Avg age of onset of bipolar disorder in females is 15-23.
- Data suggests that women with bipolar disorder are particularly vulnerable to mood episodes during menarche, pregnancy, post-partum, and peri-menopause.
- Women with bipolar disorder are also particularly vulnerable to severe mood symptoms in response to hormonal fluctuations of the menstrual cycle.
- Women with PMDD have an 8 fold higher risk of bipolar disorder than other women.
  - Wittchen HU, Becker E, Lieb R, Krause P. Prevalence, incidence and stability of premenstrual dysphoric disorder in the community. *Psychol Med.* (2002) 32:119–32. 10.1017/S0033291701004925
  - A prospective study (STEP-BD) of 293 females with bipolar disorder found that those with premenstrual mood exacerbation, had more severe depressive and manic symptoms with higher numbers of depressive episodes. Having PMDD increased risk of rapid cycling.
  - Dias RS, Lafer B, Russo C, Del Debbio A, Nierenberg AA, Sachs GS, et al.. Longitudinal follow-up of bipolar disorder in women with premenstrual exacerbation: findings from STEP-BD. *Am J Psychiatry.* (2011) 168:386–94. 10.1176/appi.ajp.2010.09121816
- Women with comorbid PMDD and bipolar disorder are more likely to experience severe mood side effects of oral contraceptives.
- Eliminating menstruation via leuprolide (GnRH agonist) eliminates PMDD symptoms
- Treatment of PMDD with dutasteride, a 5α-reductase inhibitor which blocks the conversion of progesterone into allopregnanolone, reduces PMDD symptoms during the late luteal phase

In addition to medication…..



- Elsa and Anna read The Bipolar Disorder Survival Guide.
  - Elsa participates in a free bipolar disorder support group through The Depression and Bipolar Support Alliance https://www.dbsalliance.org/.
  - Anna and Olaf join National Alliance for Mental Illness (NAMI)'s free Family to Family Class to understand how to support Elsa. Occasionally Kristoff and Sven come to group too.
    - https://namisarasotamanatee.org/support-and-education/mental-health-education/family-to-family-class/

- Her doctor explains the importance of regular sleep, avoidance of caffeine, avoidance of medications that interact with her lithium, such as NSAIDs, signs of lithium toxicity, and warning signs that she is becoming manic. This information is provided both written and verbally.
- Elsa's doctor makes sure a release of information is signed for her therapist and her closest family members, Anna and Olaf.

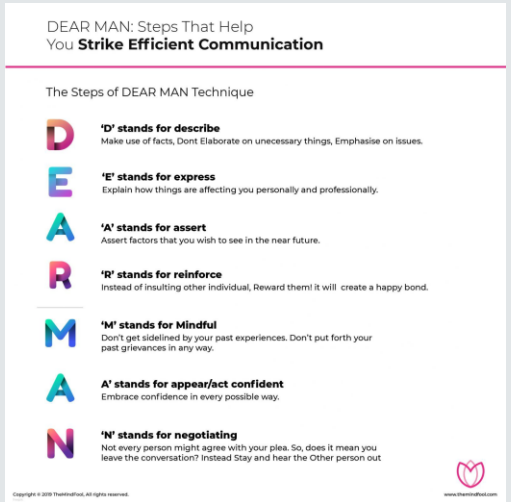
Elsa and Anna enjoy the validation and sense of “Not being alone with this” in their support groups so much that they decide to join a local DBT (dialectical behavioral therapy) group together as well.

“After completing the interpersonal effectiveness module and using the DEAR MAN skill, Elsa and I can communicate assertively about difficult topics and respect each other’s perspectives.”

-Anna

“I just completed the distress tolerance module. With mindfulness and my radical acceptance DBT skill, now I can REALLY let it go!”

-Elsa


DEAR MAN: Steps That Help
You **Strike Efficient Communication**

The Steps of DEAR MAN Technique

‘D’ stands for describe
Make use of facts, Dont Elaborate on unecessary things, Emphasise on issues.

‘E’ stands for express
Explain how things are affecting you personally and professionally.

‘A’ stands for assert
Assert factors that you wish to see in the near future.

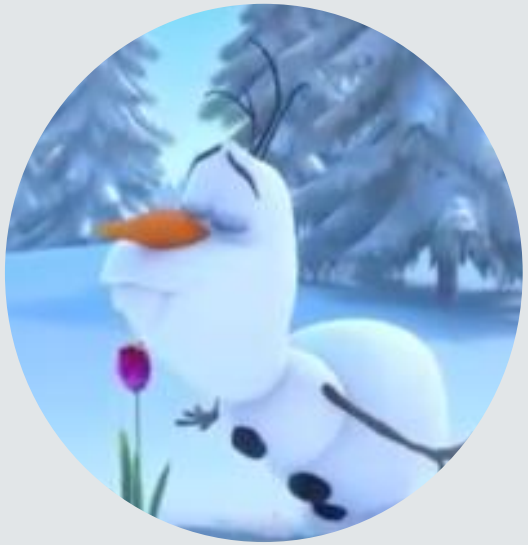
‘R’ stands for reinforce
Instead of insulting other individual, Reward them! It will create a happy bond.

‘M’ stands for Mindful
Don’t get sidelined by your past experiences. Don’t put forth your past grievances in any way.

A’ stands for appear/act confident
Embrace confidence in every possible way.

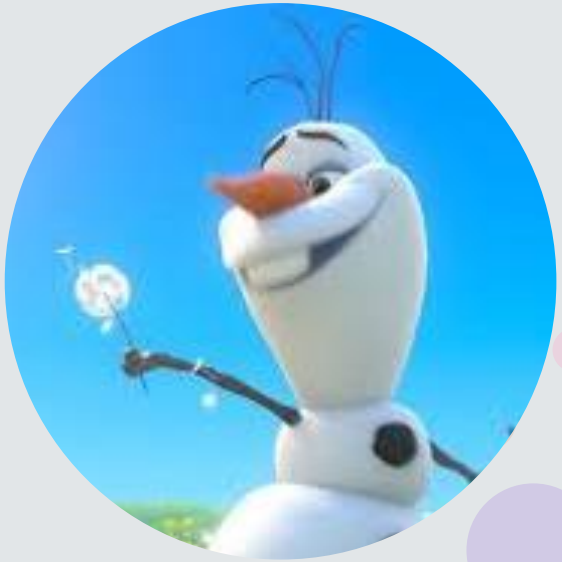
‘N’ stands for negotiating
Not every person might agree with your plea. So, does it mean you leave the conversation? Instead Stay and hear the Other person out

Olaf Practicing Mindfulness Skills



“I love warm hugs and engaging my 5 senses…..”

-Olaf



Lithium

- **Pregnancy**
  - Gold-standard for treatment of bipolar disorder
  - First trimester exposure confers 1/1000 risk of Ebstein's anomaly
    - Thus, over 99% of lithium exposed infants will not develop this cardiac defect
  - Dosage may need to be increased during pregnancy and it should be held with initiation of labor and resumed at pre-pregnancy dose upon delivery.
- **Breastfeeding**
  - A study conducted at MGH on 10 mother-infant pairs found lithium concentrations in breast milk ranging from 17-73% of maternal serum levels. Infant serum levels averaged 0.15. There were no adverse events reported in 9 or 10 infants and one infant had an elevated TSH which normalized when the mother discontinued lithium treatment.
    - Lithium in breast milk and nursing infants: clinical implications. Viguera AC, Newport DJ, Ritchie J, Stowe Z, Whitfield T, Mogielnicki J, Baldessarini RJ, Zurick A, Cohen LS. Am J Psychiatry. 2007 Feb;164(2):342-5.
  - There are case reports of lithium toxicity in infants due to dehydration, as well as lethargy, hypotonia, and decreased renal function.
  - Requires close monitoring of lithium levels, TSH, CBC, BUN and creatinine while the child is nursing.
  - Supplementation with formula feeding does have additional advantages for women with bipolar disorder who are vulnerable to decreased sleep as it allows a partner to feed the infant and protect mom's sleep.

Lamotrigine during Pregnancy

- Previously there were concerns about increased risk of cleft palate (2006, Holmes et al)
- However, a more recent meta-analysis did not find increased risk.
  - *Dolk et al population-based study of 3.9 million births and a meta-analysis of 21 studies by Pariente et. al. CNS Drugs. 2017 Apr 22.*
- Dosage often needs to be increased during pregnancy….
  - Rising levels of estrogen induce the liver enzymes that metabolize lamotrigine
    - If possible, prior to pregnancy, obtain a lamotrigine blood level while the woman is stable at an effective dosage
    - Measure lamotrigine blood level every 4 weeks and if it drops below the baseline non-pregnancy level, increase the dosage by 20-25% at a time.
    - Measure lamotrigine blood level within a week or two post-delivery and reduce the dosage by 20-25% if blood level rises.

Lamotrigine and Breastfeeding

- High serum lamotrigine concentrations may be observed in the breastfed neonate, average milk/plasma ratio of 0.61.
- However, adverse effects in infants are rarely reported.
  - Adverse events include mild thrombocytosis and one case report describing apnea in an infant whose mother used high doses of lamotrigine after delivery.
  - No reports of Stevens Johnson Syndrome
  - Monitor for rash, respiratory depression, CBC, blood level
- No clear right answer.

Meador, KJ . Breastfeeding and antiepileptic drugs. JAMA 2014; 311: 1797–1798.

Atypical Antipsychotics During Pregnancy

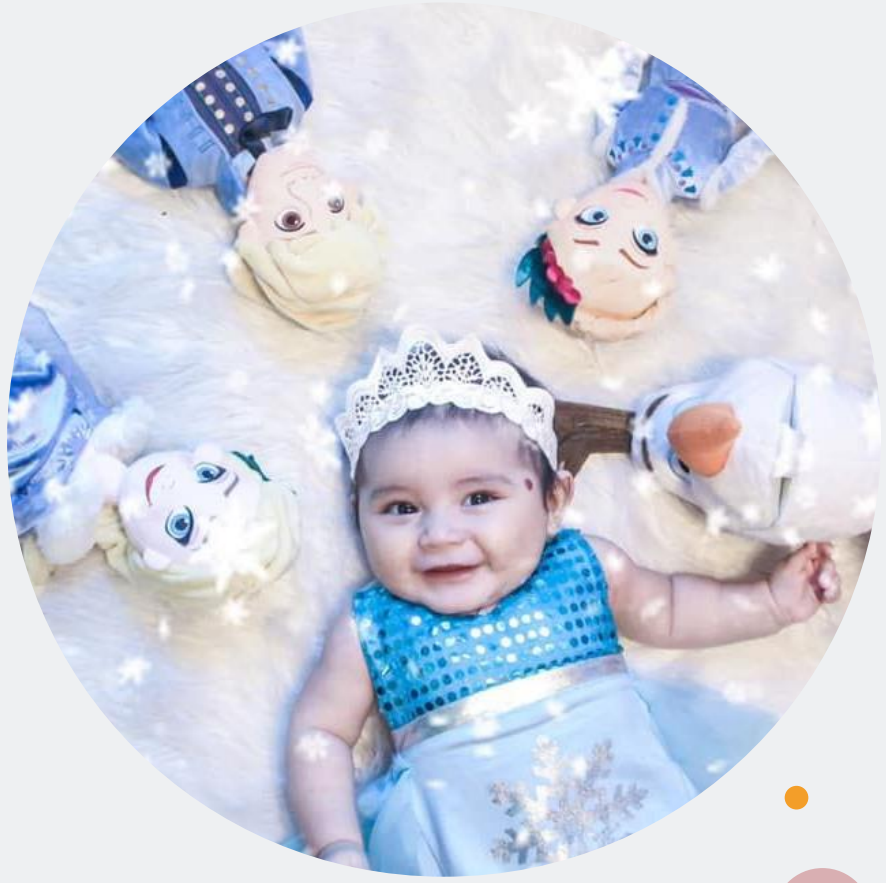
- Prospective data has been collected on 640 live births exposed to atypical antipsychotics compared to 704 live births in the control group via the **National Pregnancy Registry for Atypical Antipsychotics** which has found no significant difference in birth defects.
  - There are not enough patients in the cohort yet to analyze each antipsychotic separately except for quetiapine.
  - Viguera AC, Freeman MP, Góez-Mogollón L, Sosinsky AZ, McElheny SA, Church TR, Young AV, Caplin PS, Chitayat D, Hernández-Díaz S, Cohen LS. Reproductive Safety of Second-Generation Antipsychotics: Updated Data From the Massachusetts General Hospital National Pregnancy Registry for Atypical Antipsychotics. J Clin Psychiatry. 2021 Aug 3.
- 152 women with first-trimester exposure to quetiapine were compared with 205 control subjects without any exposure and found no increased risk of birth defects.
- **So, consider quetiapine….**

What about gestational diabetes?

- In light of a recent large Swedish study, we should warn patients that there may be a small but significant increased risk of gestational diabetes and large for gestational age baby with second generation antipsychotics.
    - Heinonen E, Forsberg L, Nörby U, Wide K, Källén K. Antipsychotic Use During Pregnancy and Risk for Gestational Diabetes: A National Register-Based Cohort Study in Sweden. CNS Drugs. 2022 May;36(5):529-539.

Antipsychotics and Breastfeeding?

- Avoid clozapine – infant serum levels 279% that of mother's serum level
  - Case reports of agranulocytosis, cardiovascular instability, sedation.
- **Reassuring data on**
  - **Olanzapine** (many case reports of undetectable levels in infant) – most preferred antipsychotic in breastfeeding
  - **Quetiapine** – relatively reassuring data, no known adverse events
  - **Risperidone-** levels undetectable in 4 breastfed infants, no adverse events, can cause galactorrhea
- **Less Ideal**
  - Abilify – lowers prolactin which decreases milk supply
- No data on
  - asenapine, paliperidone, iloperidone, and lurasidone



Depakote (valproic acid)

Pregnancy

- Avoid in women of childbearing age
- If valproic acid is the only option, women should be counseled re contraception.
- In the setting of unplanned pregnancy, women should take 4mg of folic acid daily.
    - First trimester use of valproate (often prior to discovery of pregnancy) has been associated with 3-5% risk of neural tube defects, as well as increased risk of other malformations affecting the heart, limbs, and genitals.
    - Prenatal exposure to valproate may also result in lower IQ and increased risk of autism.

Depakote (valproic acid)

Breastfeeding

- Relatively safe in breastfeeding without known adverse effects, though infants should be monitored for signs of jaundice due to risk of hepatoxicity as well as bruising.
  - Monitor LFTs, valproic acid level, platelets.
- One study found higher IQ in infants breastfed while mother was on valproic acid than in infants formula fed while mother was on valproic acid.
  - Meador KJ, Baker GA, Browning N et al. Breastfeeding in children of women taking antiepileptic drugs: Cognitive outcomes at age 6 years. JAMA Pediatr. 2014;168:729-36.

“I want to freeze my eggs.”
Mental Health and Infertility Treatment


Anna and Kristoff Face Infertility

Grieving the Loss of the Reproductive Story

As way back as I can remember, I thought about becoming a mother. I stuffed pillows in my shirt and played with dolls.

I promised myself that I would be there for my little girl and never leave her alone like my mom did.

I wanted to honor my mother by becoming a mom myself.

-Anna

Loss of the Reproductive Story

- Because a reproductive story comprises a fundamental part of one's identity, the loss of this story is experienced as a loss of identity and fragmentation of self.
- Patients often feel psychologically stuck as neither a child nor a full adult.
- Women feel less feminine and men may feel less virile and competent.
- Parenthood presents opportunities for self-development and growth/healing which infertile couples may be longing for.
  - i.e. Anna's desire to overcome the loss of her mother and childhood by becoming a mother herself and making this happen for her own biological child.
- **Patients are mourning not just a potential child, but also missed opportunities for self-development and their entire identity prior to the trauma of infertility.**

"I faced down giants, saved my kingdom, and rescued my sister from herself. But I can't make this happen. Maybe I'm not trying hard enough. I used to be so strong and now I feel so weak."

-Anna

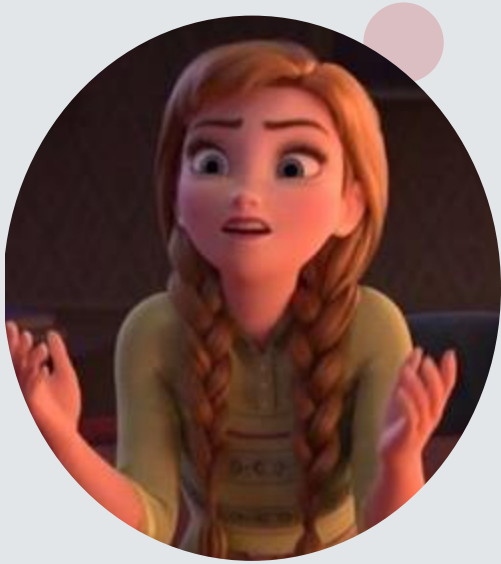
- Patients tend to see infertility as a psychological failing of not wanting a baby enough or not trying hard enough instead of a medical condition.
  - Historically in psychiatry, infertility was thought to be caused by a women's ambivalence about becoming a mother or unresolved issues/conflict with her own mother.
- Help patients understand that infertility is NOT a skill that they just haven't "mastered" yet. Fertilization of an egg by a sperm is a biological process, not a psychological one.
- Successful women think *"When I work hard at something and do it right, I am successful. Therefore, I must be doing something wrong. I must be to blame."*

"These patients are not unlike solders who repeatedly are sent back into battle to conquer the same ever-elusive hill."

Reproductive Trauma: Psychotherapy with Infertility and Pregnancy Loss Clients by Janet Jaffe, PhD and Martha Diamond, PhD

"I know Kristoff loves me and it makes no sense, but I can't stop thinking he deserves to be with someone who isn't barren. When we try to make love….I just feel so tarnished. I never was insecure like this before. It's crazy."

-Anna



It's not crazy….. It's human.

- Patients often feel enormously guilty and wonder if their partner will continue to love them if they cannot produce a child.
- Men often feel helpless to "fix" things for their partner.
- **Normalizing the insecurity and vulnerability of the experience of infertility is powerfully therapeutic.**

Lean in……have courage

- Get ready to **lean into your patient's pain** even though it is uncomfortable.
  - Well-meaning friends, family, and clinicians may inadvertently invalidate patients by minimizing the loss.
- Validating and normalizing painful feelings gives patient's permission to be human.
- Patients commonly feel **anger and envy** when hearing of a friend's pregnancy and subsequent **guilt and shame** for feeling this way.
- They may need to avoid a baby shower or family gathering full of children and then feel like a bad friend.
- Even seemingly innocuous situations, like walking down the baby aisle of the grocery story can trigger an unexpected onslaught of painful emotions.
- Patients often describe an emotional roller coaster of renewed hope and then bitter disappointment as they go through infertility treatment.
- **Clinicians can play a pivotal validating role here.**


Anger
Fear
Inadequacy
Failure
Envy
Defectiveness
Helplessness

When Others Get Pregnant

I want people to know that every pregnancy announcement is devastating. Not because you're not happy for them, but because you're sad for you.

-- Jennifer Brynn Jones


Isolation

Early Pregnancy Loss

- Early pregnancy loss is common, affecting up to 25% of pregnancies.
  - Compared to women with viable pregnancies, women who had an early pregnancy loss were about twice as likely to report moderate to severe anxiety (odds ratio 2.14) and nearly four times as likely to report moderate to severe depression (OR 3.88).
    - Farren J, Jalmbrant M, Falconieri N, Mitchell-Jones N, Bobdiwala S, Al-Memar M, Tapp S, Van Calster B, Wynants L, Timmerman D, Bourne T. Posttraumatic stress, anxiety and depression following miscarriage and ectopic pregnancy: a multicenter, prospective, cohort study. Am J Obstet Gynecol. 2019 Dec 13.
- Women who have an early pregnancy loss and their partners usually do not receive any specific medical or psychological follow up even though they are extremely vulnerable to depression, anxiety, and PTSD.

“The “if-only’s” that would-be mothers ruminate on can fill an entire book. Rationally, these women know they did nothing to harm their baby, but emotionally they feel they must have done something wrong.”

Reproductive Trauma: Psychotherapy with Infertility and Pregnancy Loss Clients by Janet Jaffe, PhD and Martha Diamond, PhD

Pregnancy and Infant Loss Support website:
https://nationalshare.org/florida/

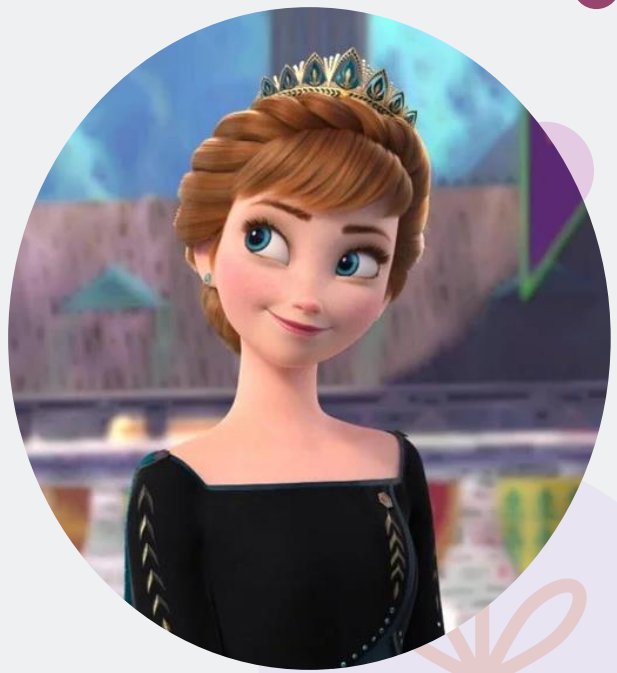
“Even before Kristoff proposed, I imagined having a little boy with strawberry blonde hair and Kristoff’s eyes and an adventurous little girl we would teach to drive his sleigh.”

-Anna

- *“Listening for and reviewing both the obvious and the less apparent losses with patients will make clear the enormity of the trauma they have experienced and will help them understand the depth of their pain. The challenge for clients is to acknowledge that these losses have forever changed them – they are not the person they once were- and to incorporate these losses into a new sense of self.”*
    - Reproductive Trauma: Psychotherapy with Infertility and Pregnancy Loss Clients by Janet Jaffe, PhD and Martha Diamond, PhD
- It is only after patients understand the enormous impact of their loss that they can fully mourn.

Rewriting the Reproductive Story With a New Ending

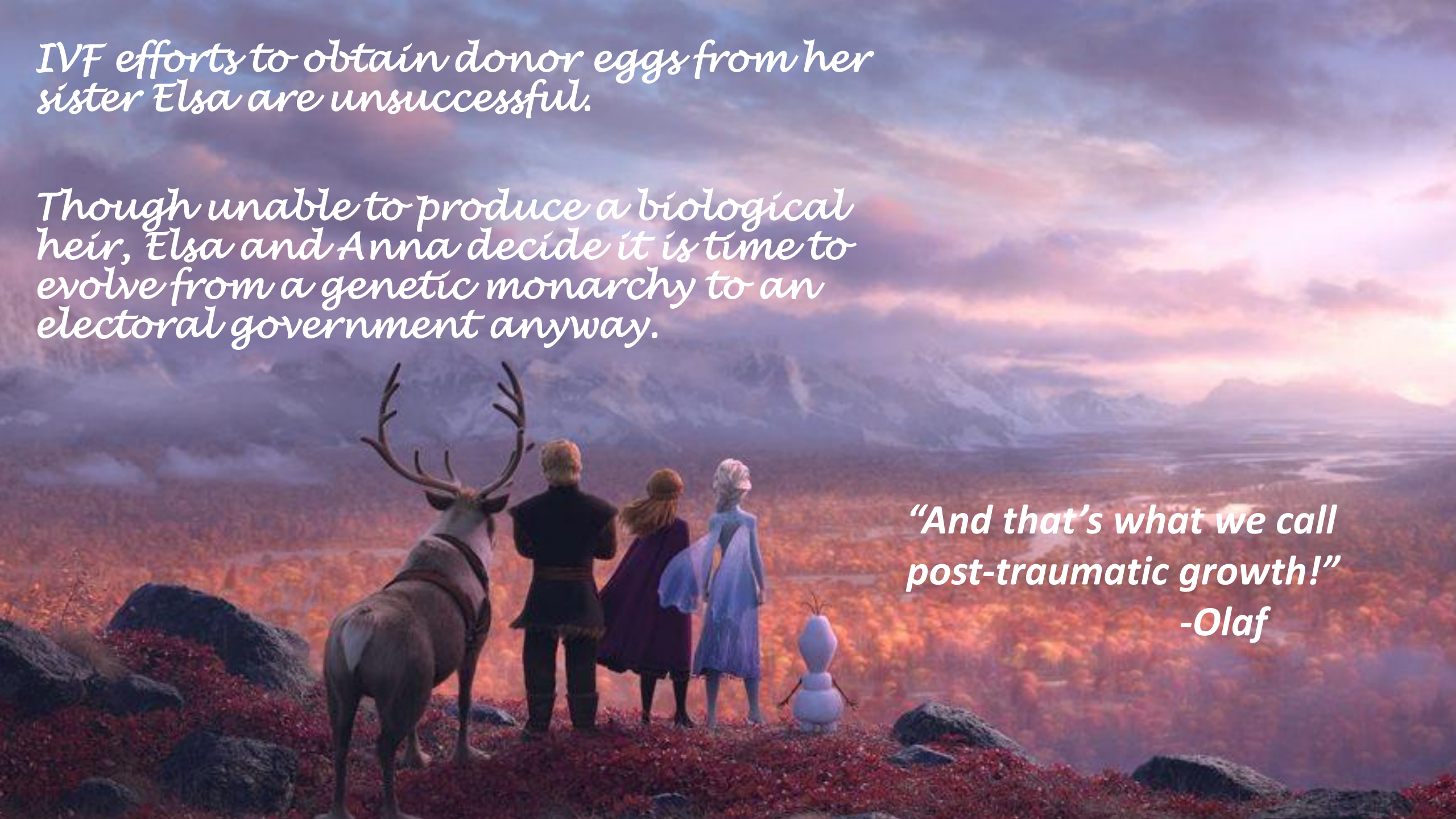
- Therapists can help patients try on different options for building a family or remaining childless to see which one fits best.
- Helps a couple articulate what each partners needs from the other to overcome the trauma.
- Both partners grow and actualize a new possible self.



- **Anna develops her identity as a ruler.**
  - She spearheads social justice programs empowering women in her kingdom, improving relations with indigenous peoples, and addressing systemic racism.
  - Anna fulfills her need for generativity and considers this her legacy to the future.
- **Kristoff finds meaning and fulfillment.**
  - He starts a school and foster program for orphan rock troll babies.
  - He values the opportunity to give back to the rock troll community who adopted and fostered him.

IVF efforts to obtain donor eggs from her sister Elsa are unsuccessful.

Though unable to produce a biological heir, Elsa and Anna decide it is time to evolve from a genetic monarchy to an electoral government anyway.



"And that's what we call post-traumatic growth!"

-Olaf

Psychiatric Side Effects of Infertility Treatments

- Clomid (clomiphene)
  - Mood swings, depression
  - Anxiety, insomnia, irritability
  - Rare cases of psychosis
- GnRH agonists (leuprolide)
  - depression, emotional lability, and changes in libido.

The Trauma Does Not End with a Successful Pregnancy

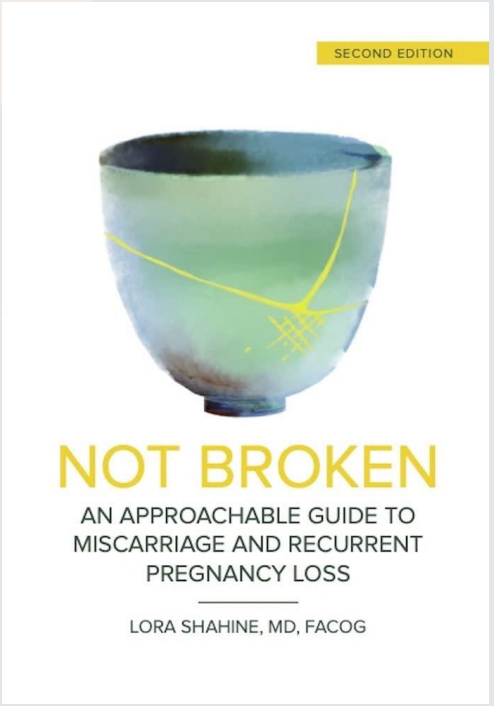
Women struggling with pregnancy loss and infertility often expect their symptoms of PTSD, anxiety, and depression to resolve once their dream of motherhood is achieved.

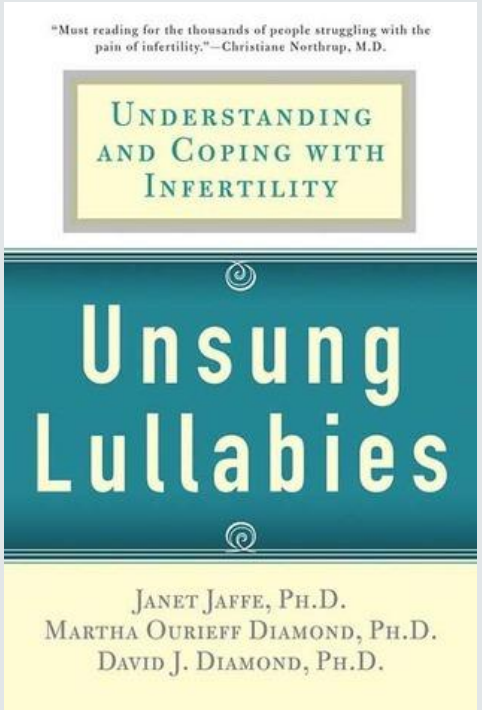
Many women continue to experience anxiety and depression after infertility treatment, even after attaining a successful pregnancy!

- It may be harder for these women to seek treatment as they feel that after becoming pregnant or giving birth they don't "deserve" to feel depressed or this represents ungratefulness.
  - Klock, SC, Greenfield, DA. Psychological status of in vitro fertilization patients during pregnancy: a longitudinal study. Fertil Steril 2000; 73:1159-64.
  - Monti, F, Agostini, F, Fagandini, P, La Sala, GB, Blickstein, I. Depressive symptoms during late pregnancy and early parenthood following assisted reproductive technology. Fertil Steril 2008

Birth Trauma

- While about 40% of women describe their pregnancy as “traumatic,” about 5-6% of women meet criteria for ongoing PTSD following birth.
  - This can lead to avoidance of their infant, decreased bonding, nightmares and re-experiencing of the birth trauma, marital strife, hyper-arousal, anxiety, and decreased utilization of needed healthcare resources.
  - Similar to other traumatic events, mothers commonly experience re-activation of symptoms around the anniversary of the event which coincides with their child’s birthday.
- **Open communication with a woman in labor, putting the locus of control on the patient as much as possible, skin-to-skin contact with baby, and social support after delivery mitigate risk.**

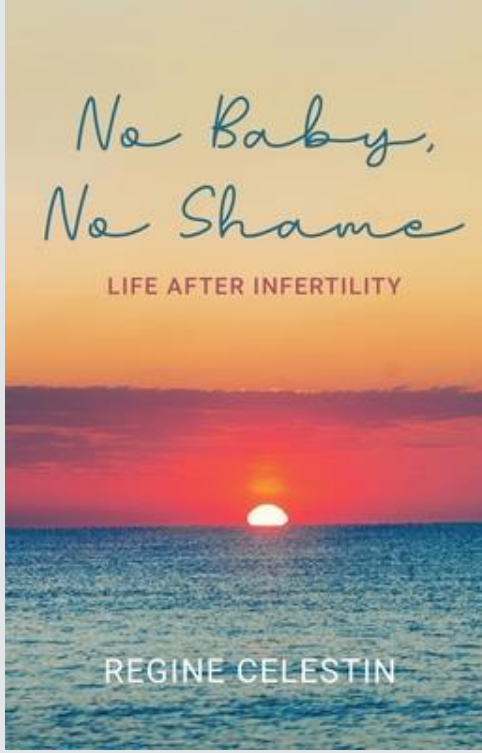


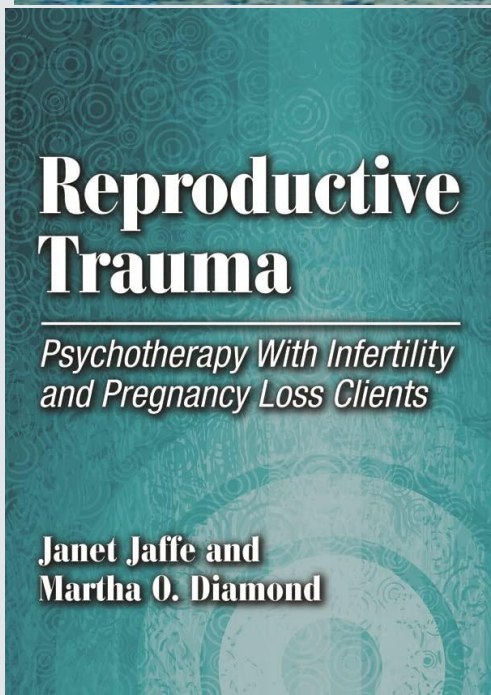


Resources for Further Learning

- https://resolve.org - National Infertility Organization
- Micro-video: The Trauma of Infertility and Pregnancy Loss: Helping Our Patients Heal
  - **Presenters**: Janet Jaffe, Ph.D., Center for Reproductive Psychology; Julie Bindeman, Psy.D., Integrative Therapy of Greater Washington; and Karen Hall, Ph.D., Center for Infertility Counseling and Support
  - https://www.asrm.org/resources/videos/learn-on-the-go---short-videos/micro-videos/2019-micro-videos/trauma-of-infertility-and-pregnancy-loss/

- Women's Wellness Psychiatry podcast by Dr. Anna Glezer
  - https://www.mindbodypregnancy.com/my-podcast
- Motherhood meets medicine podcast episode on infertility
  - https://podcasts.apple.com/us/podcast/a-journey-through-infertility-with-lindsey-horning/id1553782780?i=1000586402258
- Post-traumatic Stress Disorder after Birth Resources
  - https://www.tabs.org.nz/index.htm
- Pregnancy and Infant Loss Support website
  - https://nationalshare.org/florida/





Dr. Cheryl Beck's Research on Treatment of Birth Trauma

- Beck, C.T., & Watson, S. (2019). Mothers' Experiences Interacting with Infants after Traumatic Childbirth. ***The American Journal of Maternal/Child Nursing in Vol. 44, 59***
- Beck, C.T., & Watson, S. (2010). Subsequent Childbirth After a Previous Traumatic Birth. ***Nursing Research, 59***, 241-249.
- Beck, C.T., & Watson, S. (2008). The Impact of Birth Trauma on Breastfeeding: A Tale of Two Pathways. ***Nursing Research, 57 (4)***, 228-236.
- Beck, C.T. (2006). The anniversary of birth trauma: Failure to rescue. ***Nursing Research, 55 (6)***, 381-390.
- Beck, C.T . (2004). Birth Trauma: In the Eye of the Beholder. ***Nursing Research, 53 (1)***, 28-35.
- Beck, C.T. (2004). Post Traumatic Stress Disorder Due to Childbirth: The Aftermath. ***Nursing Research, 53 (4***), 216-224.

Mental Health and Perimenopause

Bibbity Bobbity Boooooooooo……

Mental Health and Peri-menopause

- Peri-menopause is a high risk time for women with rates of depression estimated at 39% by the Study of Women's Health Across the Nation (SWAN).
  - https://www.swanstudy.org/
- Earlier onset of menopause and past history of depression and anxiety are major risk factors.
- In a prospective study at Harvard, premenopausal women with no history of depression who entered the perimenopause were twice as likely to develop significant depressive symptoms when compared with women who remained premenopausal during the period of observation.
  - Cohen L, Soares C, Vitonis A, Otto M, Harlow B. Risk for new onset of depression during the menopausal transition: The Harvard Study of Moods and Cycles. Arch Gen Psychiatry. 2006;63:385-390.

- Antidepressants help with both mood and vasomotor side effects of peri-menopause.
- Be aware that antidepressants that are strong CYP2D6 inhibitors (i.e. fluoxetine, bupropion, paroxetine) can inhibit the conversion of the breast cancer drug Tamoxifen to its active metabolite endoxifen.
  - **Weak Inhibitors** (Use not restricted by treatment with tamoxifen):
    - Venlafaxine (Effexor)
    - Desvenlafaxine (Pristiq)
    - Vortioxetine(Trintellix)
    - Vilazodone (Viibryd)
    - Levomilnacipran (Fetzima)

Perinatal Mental Health in Black Mothers

- Black women are twice as likely to experience severe maternal morbidity and 3-4 times as likely to die of pregnancy related causes.
- Black women are both more likely to experience perinatal mood and anxiety disorders and less likely to receive psychiatric treatment for them.
  - Interview by Dr. Anna Glezer with Dr. Sinmi Bamgbose
    - https://podcasts.apple.com/us/podcast/ep-16-perinatal-mental-health-in-black-mothers/id1596816881?i=1000551146653

For the parents who are not represented by Disney…..

More research is needed…..

Trans and non-binary pregnancy, traumatic birth, and perinatal mental health: a scoping review

Mari Greenfield[a,b] and Zoe Darwin[c]

[a]School of Human & Health Sciences, King's College London, London, United Kingdom of Great Britain and Northern Ireland; [b]School of Human & Health Sciences, University of Hull, Hull, United Kingdom of Great Britain and Northern Ireland; [c]School of Human & Health Sciences, University of Huddersfield, Huddersfield, United Kingdom of Great Britain and Northern Ireland


Thank you for
listening….

How Can We Do Better?