Mood Disorders in Women: Issues Related to Pregnancy and Post-Partum

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Disclosure Declaration

- Nothing to disclose.

Leading causes of Disease Burden

Women aged 15-44 in High Income Countries (WHO)

1. Unipolar Disorder
2. Bipolar Disorder
3. Schizophrenia
4. Migraine
5. Alcohol Use Disorder
6. Road Traffic Accidents
7. Refractory Error
8. Hearing Loss
9. COPD
10. Panic Disorder

*Measured in years lived with a disability.
Global Burden of Disease, World Health Organization Study, 2004 estimates

Mood Disorders in Women

Twofold Increase in Women: Men Ratio

- Risk factors
  - Gender-related--reproductive transition events, i.e. menstrual cycles, postpartum states, perimenopause; subclinical thyroid disease; anemia
  - Care giver role
  - Inadequate income
  - Domestic violence

Reproductive Life Events:
Increased Risk of Depressive Symptoms

- Infertility treatments
- Hormonal contraceptives
- Miscarriage
- Menstrual cycles
- Pregnancy
- Postpartum states and lactation
- Hysterectomy + oophorectomy
- Peri- and postmenopausal

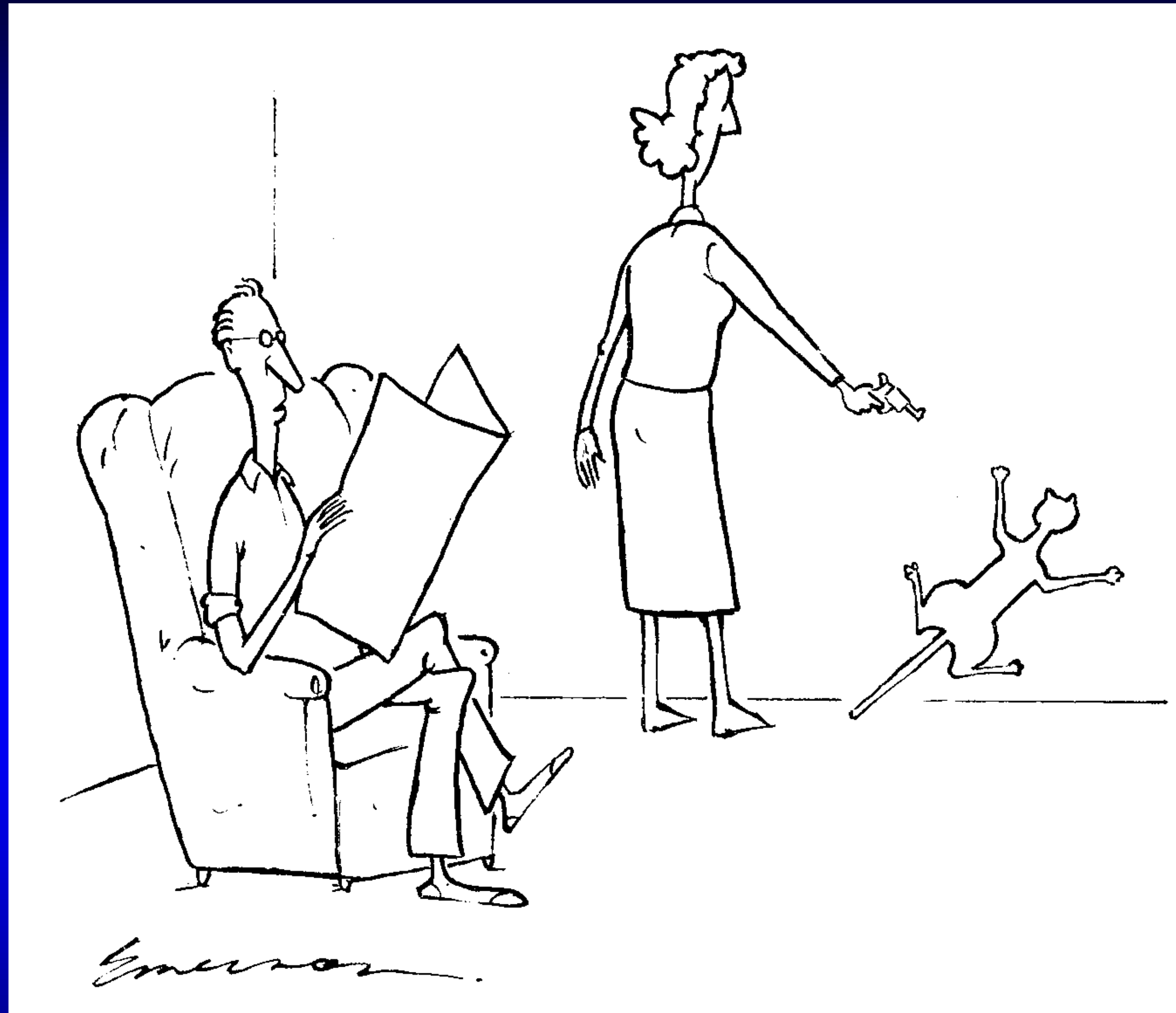
Warnock JK. Female Hypoactive Sexual Desire Disorder: Epidemiology, Diagnosis and Treatment. CNS Drugs. 2002; 16 (11):745-753.

Out of the Shadows: Postpartum

- https://vimeo.com/258504759/be69227bc8

Depressive Disorders
DSM V

- Depressive Disorders
  - Disruptive Mood Dysregulation Disorder
  - Major Depression
  - Dysthymia (Persistent Depressive Disorder)
  - Premenstrual Dysphoric Disorder
  - Substance/Medication Induced Depressive Disorder
  - Depressive Disorder due to another Medical Condition



"Your time of month again, Marge?"

MILWAUKIE-PORTLAND
OREGON
PMS24-7
10
03
Would you pass a car with this license place?

Real women don't have hot flashes they have

POWER SURGES

Criteria for Perinatal Depression

- DSM V
  - Presence of major depressive episode
  - Episode occurs within peripartum-onset specifier:
    - During pregnancy
    - Within 4 weeks of delivery
  - PPD is not a separate Dx
- ACOG
  - Presence of a major or minor depressive episode(s)
  - Episode(s) may occur:
    - During pregnancy
    - Within 12 months of delivery
  - PPD is a complication of pregnancy, occurs in 1 in 7 women

DSM V, 2013; Committee of Obstetric Practice. Obstet Gynecol. 2015;125:1268-1271.

Peripartum Depression:
Risk Factors

- FH or personal history of MDD, bipolar disorder, Premenstrual mood changes, H/O mood symptoms with OCPs
- Stressful life circumstances: low SES, DV, poor sleep & nutrition
- Mother and baby: High-risk pregnancy, labor complications, low birth weight, preterm birth, problems breast feeding

Becker M et al Curr Psychiatry 2016; 18(3):32

Peripartum Depression: Facts

- Peripartum onset mood episodes can present either with or without psychotic features.
- Infanticide is most often ass with PP psychotic episodes with command hallucinations to kill the infant.
- PP mood episodes with psychotic features occur in 1 in 500 to 1 in 1000 deliveries.

DSM-V 2013

Peripartum Depression: Facts

- Suicide is the second-leading cause of postpartum death
  - Accounts for 20% of postpartum deaths
- Thoughts of self-harm/harm to baby with a Plan, Intent and Delusions are a Psychiatric Emergency
- PP psychosis needs to be distinguished from delirium with a fluctuating level of awareness

Lindahl V et al Arch Women's Ment Health, 2005;8:77-87; Suicide Prevention Resource Center Website.

Peripartum Depression: Facts

- Untreated PPD is associated with
  - Suicide
  - Infanticide
  - Lactation challenges
  - Attachment difficulties with the infant
  - Low martial satisfaction

Meltzer-Brody S.et al Best Pract Res Obstet Gynacol 2014: 28(1) 49-60.

Peripartum Depression: Facts

- 30% to 50% of women who experience PPD will have recurrent PPD in subsequent pregnancies
- 50% of cases are not recognized
- ACOG recommends that all pregnant women be screened during the perinatal period
- OK statute, SB 419, Nov. 1, 2019, requires OK hospitals and licensed providers to educate and screen patients for perinatal mental health disorders.

Committee on Obstetric Practice. Obstet Gynecol. 2015;125(5):1268-1271; DSM-V 2013.
https://content.govdelivery.com/accounts/OKOMB/bulletins/2663530

Postpartum Depression:
Impact on Children

- Poorer infant motor development by 15 months
- Higher morbidity associated with GI and lower respiratory tract infections
- Lower cognitive outcomes, including language and intelligence
- Increased risk of teenage depressive and anxiety disorders

Meltzer-Brody S.et al Best Pract Res Obstet Gynacol 2014: 28(1) 49-60.

Peripartum Depression:

Validated Rating Scales in Pregnancy and Postpartum

- Edinburgh Postnatal Depression Scale EPDS
  - Commonly employed
  - 10 question, self rated, past 7 days
  - English and Spanish versions
- PHQ-9
  - 9 Questions
  - Over the past 2 weeks

Cox J et al Br J Psychiatry 1987;150:782-786

Kroenke K, et al J Gen Intern Med. 2001; 16: 606-613

Cases of Baby Blues vs PPD

Baby Blues

- Pt is 2 weeks postpartum
- Pt reports the following, which started 1 week earlier
  - Being emotional and crying
  - Does not feel bad about herself, but irritable
  - Is able to function
  - Still enjoy activities
  - No major changes to sleep, appetite or concentration
  - EPDS =9

PPD

- Pt is 6 weeks post partum
- Pt reports the following which has been going on several weeks:
  - Not enjoying activities
  - Depressed mood most days
  - Trouble sleeping
  - Difficulty concentrating and making decisions
  - Feels guilty and bad about herself
  - Appetite is impacted
  - EPDS = 16

PPD:
Medical and Other Considerations

- Medical Differential Dx:
  - Thyroid disease
  - Other metabolic conditions
  - Anemia
  - B12 and folate deficiency
- R/O Substance Use Disorders:
  - PP alcohol use ranges from 30% to 49%
  - Drug use ranges from 4.5 to 8.5 %
  - PPD symptoms in women with a current or h/o substance use: ranges from 19 to 46%

Chapman SLC, et al Women Health. 2013;53:479-503.

PPD: Wisner Study

Screen-positive findings

- Episodes began:
  - 40% postpartum
  - 33% during pregnancy
  - 27% before pregnancy
- Most common primary diagnosis:
  - 69% unipolar depressive disorder
  - 23% bipolar disorders
  - 6% anxiety disorders
- 1 in 5 screen positive could have undiagnosed bipolar disorder.

Wisner KL, et al. JAMA Psychiatry.2013;70:490-498

Potential Endocrine Influences on PPD

- Reproductive Hormones
  - Increase in Estrogens (estradiol 100 fold & estriol 1000 fold) and progesterone
  - Placenta produced
  - Removal results in abrupt decline to pregravid levels by day 5.
- HPA Axis
  - CRH increased during pregnancy and falls rapidly after delivery
  - Environmental risk factors for PPD increase stress levels and alter the HPA axis

Postpartum

Hormonal Treatment

- Investigate assoc b/w E_2 & postpartum psychosis
- 10 women with estrogen deficiency and postpartum psychosis
- Baseline E_2 levels = postmenopausal levels; Baseline BPRS total score mean=78
- Week 1 sublingual E_2, BPRS $\downarrow$ to mean=18; by Wk 2=9; by Wk 4=0.9
- Note 1 pt D/C E_2 after 5 wks; her BPRS increased from 0 at wk 4 to 53 at wk 6
- Findings suggest a connection b/w E_2 and serotonin and dopamine

Ahokas A et al. Positive tx effect of E2 in postpartum psychosis: a pilot study. J Clin Psychiatry 2000;61:166-169

Allopregnanolone analogue

Brexanolone IV (Sage 547) & Oral (Sage 217)

- Positive allosteric modulator of both synaptic and extrasynaptic GABA-A receptors
- Reduced levels of allopregnanolone ass. with MDD, anxiety, PMDD,
- FDA approval of Sage 547 (Zulresso) 3/19/19. Two Placebo controlled trials: Superiority over placebo at the end of infusion in moderate and severe PPD. Improvement maintained 30 days post infusion.
- Sage 217 Phase 3 trial, remission in 45% vs. 23% placebo, in 2 weeks. Pending FDA approval

Brexanolone IV (Zulresso)

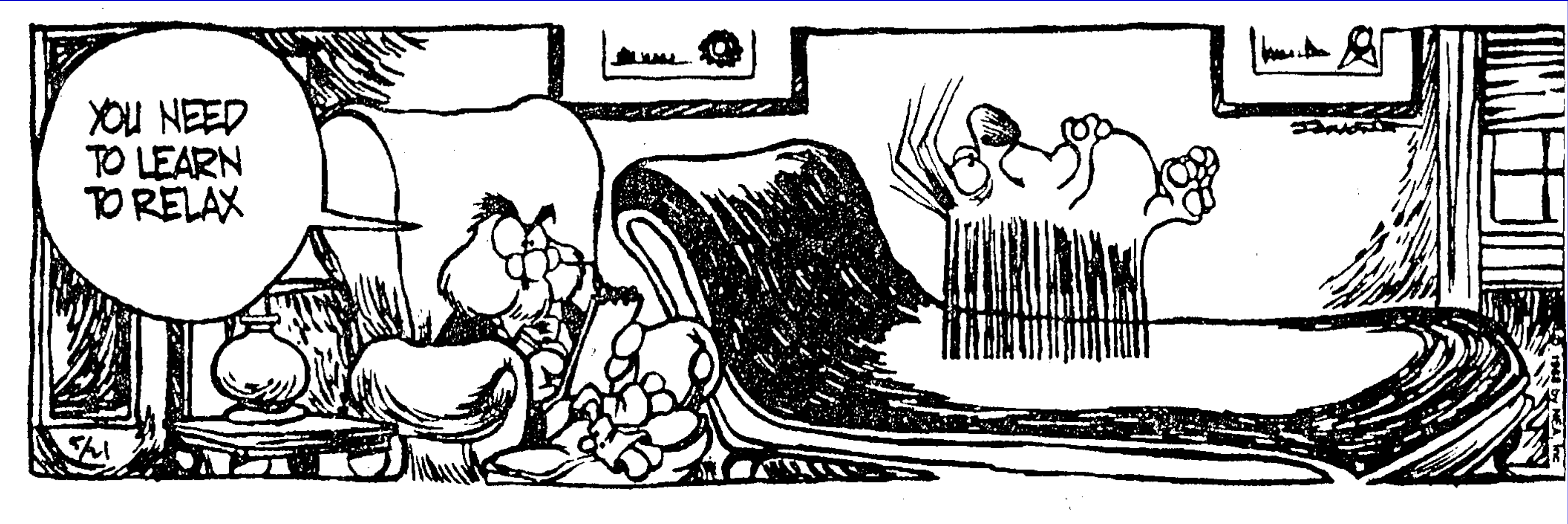
- First drug approved specifically for PPD
- Available only through a restricted program called Zulresso REMS "Risk Evaluation and Mitigation Strategy" Program.
- Administered with medical supervision, continuous IV infusion, over 60 hours at certified facilities, with pulse oximetry and cannot be left alone with child(ren).
- Risks: excessive sedation, sudden loss of consciousness; thus, No dangerous activities until sedation dissipates.

Treatment of Mood Disorders in Women

- **Psychotherapy**
- **Phototherapy**
- **Pharmacotherapy**
- **ECT**
- **Vagal Nerve Stimulation**
- **Repetitive Transcranial Magnetic Stimulation**
- **Deep Brain Stimulation**

Treatment of Postpartum Depression
Psychotherapeutic Approaches

- Get support for mom; cleaning, bathing
- Support Groups-i.e. Facebook
- Lactation specialist, if needed
- Exercise – walking, yoga, etc.
- Sleep hygiene techniques
- Relaxation exercises
- Nutritional modification & preparation
  - Eat regular, well balanced meals
- Mindfulness Training
- Massage
- Develop appropriate coping strategies
- Counseling-Cognitive Behavioral; ITP


YOU NEED TO LEARN TO RELAX

FRANK AND ERNEST
PSYCHO THERAPIST
THAT'S SUPPOSED TO BE ONE WORD!
THAVES
E-mail: FarcE@bobT@AOL.COM
6-11

Pharmacologic Treatment Guidelines
PPD

- NO decision is risk free
- Must weigh the risk of Antidepressant medication vs. untreated depression
- Use the lowest dose that "Gets You Well"
- Considerations regarding patients decision and ability to breastfeed

Psychotropics, Pregnancy and Breastfeeding: Lactation

- No randomized controlled trials
- Studies are small and variable
- Adverse effects (i.e. irritability, poor feeding or sleep disorders) observed in babies who are exposed to antidepressants through breast milk are often nonspecific and may be due to other causes, i.e. viral infections
- Nationwide database of reports of adverse reactions to drugs transmitted through breast milk (n= 174) Antidepressants were not on the list of frequently implicated

Molyneaux E et al. Cochrane Database Syst Rev. 2014: 9CD002018; Soussan C et al Eur J Clin Pharmacol. 2014:70(11):1361-1366; National Institiutes of Health. LactMed, a TOXNET Database. https://toxnet.nim.nih.gov/newtoxnet/lactmed.htm. Accessed 9/2018.

Psychotropics, Pregnancy & Breastfeeding: Lactation

- Infant exposure to SSRIs, SNRIs, & atypical AD through lactation generally low to negligible
- Infant serum concentrations appear to be **lower** with **sertraline and nortriptyline**, & higher with citalopram, fluoxetine, venlafaxine and desvenlafaxine
- Most reproductive psychiatrists suggest it is best to use the medication that works for the patient.

Sriraman NK et al. Breastfeed Med. 2015;10(6):290-299; Weisskopf E et al. expert Opin Drug Saf. 2015;14(3):413-427.

Lactation Resource
LactMed

- Drugs and Lactation Database (LactMed)
  - National Library of Medicine and Toxicology Data Network
  - A peer reviewed and referenced database of drugs to which breastfeeding mothers may be exposed
  - Among the data are maternal and infant blood levels of drugs and the possible effects on breastfed infants.
- https://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm
- Also available at the app store

FDA Classification Medication

CLASS	DESCRIPTION	MEDICATION
A	Controlled studies in humans have demonstrated no fetal risk	Prenatal vitamins
B	Animal studies indicate no fetal risks, but no human studies; OR adverse effects in animals but not in well-controlled human studies	Buspirone, bupropion clozapine
C	No adequate studies in animal or human OR there are adverse fetal effects in animal studies, but not available human data	Sertraline, trazadone, fluoxetine, clomipramine, carbamazepine, haloperidol, risperidone, olanzapine
D	Evidence of fetal risk but benefits may be acceptable despite the risk	Alprazolam, diazepam, lithium, chlordiazepoxide, lorazepam, valproic acid
X	Proven fetal risks that clearly outweighs any benefits	

Goldberg HL. Psychotropic drugs in pregnancy & lactation. Int J Psych in Medicine 1994;24:129-149

Psychotropic Medication - Pregnancy

Lithium: Clinical Implication

- Little consistent evidence that pregnancy conveys protection from mood instability in women with bipolar disorder
- No evidence that pregnancy lessens need for antimanic prophylaxis
- Compelling evidence suggesting significant morbidity with untreated bipolar disorder - lost productivity, economic burden
- Gradual tapering of lithium dose is preferable to abrupt discontinuation
- Lithium can be continued until first missed menstrual period. Taper over next 10 days. Avoid lithium during embryonic period - wks. 4-12 after LMP
- Counsel women, lightly higher risk of congenital malformations including cardiovascular. Fetal ultrasound and fetal echocardiograph at 16-18 wks. - Reassuring

Delivery & Postpartum

Lithium

- Taper lithium by 25% to 50% prior to delivery to minimize toxicity of mother given the rapid fluid shifts
- Best not discontinued entirely b/c puerperium appears to be a period of particular risk for bipolar pts.
- 4 to 5 fold increase for postpartum decompensation. Lithium has been shown to significantly decrease such risk, especially if given 48 hours postpartum

Stuart et al . Prophylactic lithium in puerperal psychosis: the experience of three centers. Br J Psychiatry 1991;158:393-397

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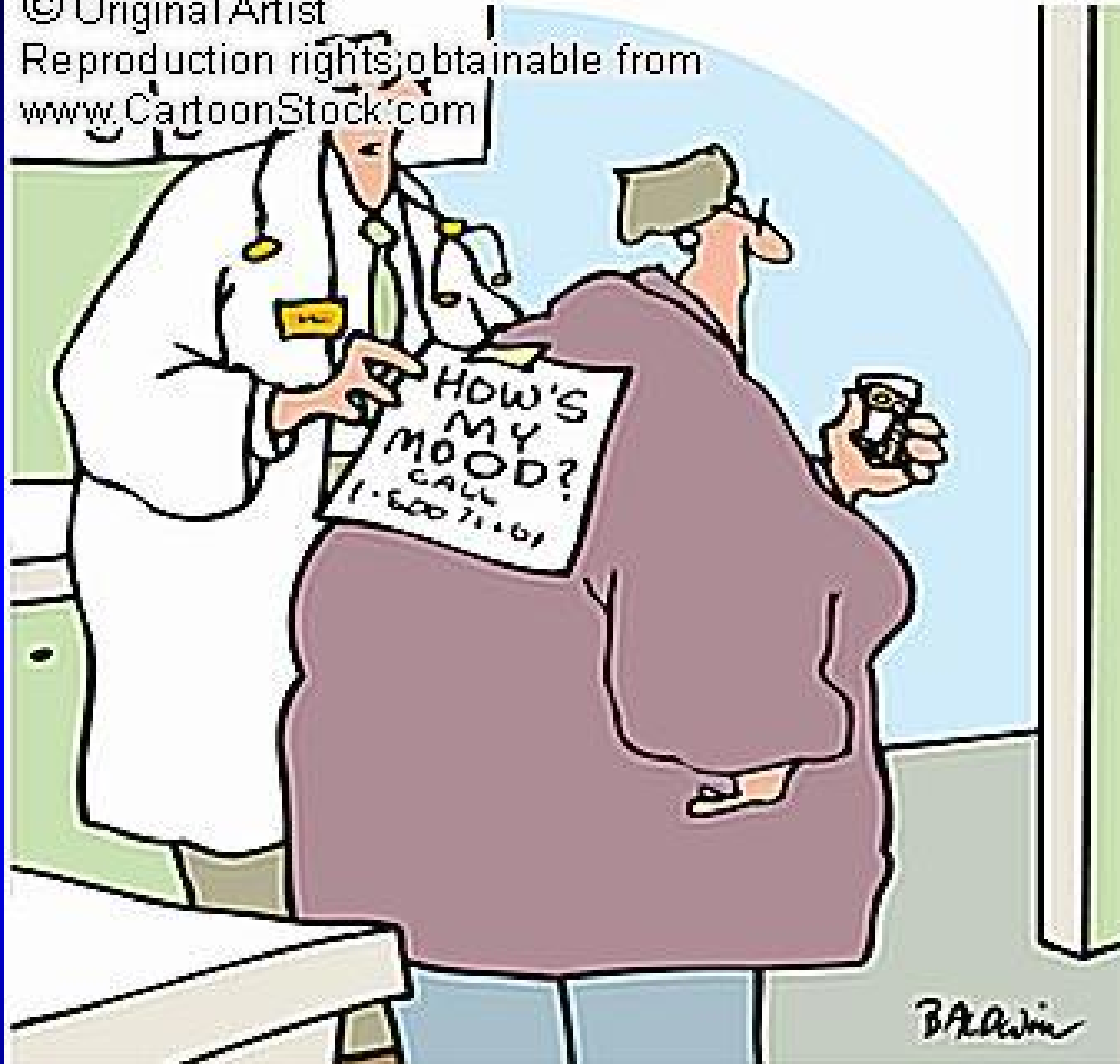
RX
“Take the green pill to feel hunky, the yellow pill to feel dory.”



"It's always best to start with a low dose
and closely monitor the results."

"This shock therapy really works!"

Summary

Postpartum depression

- 1 in 7 pregnant women may have postpartum depression,
- Many factors contribute to the risk, and it is often untreated.
- Increased attention to peripartum depression will result in improved treatment & health in women, their children and our communities.