

Prevention of Postpartum Depression



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Postpartum Depression: Who is at Risk?

- * 10-15% of women in general population
- * 25-50% of women with a pre-existing mood disorder
- * 70-90% of women with a pre-existing mood disorder who stop their meds for pregnancy
- * Genetics play a role
- * Environment plays a role

**Myth #1: Women Should Tolerate
Being Depressed During Pregnancy
for the Sake of the Baby**

**Truth #1: Depression During
Pregnancy Leads to Poor Outcomes
for Mom and Baby**

Why Treat Depression during Pregnancy?

- * Depression during pregnancy is associated with....
 - * Preterm delivery
 - * Low birth weight
 - * Decreased motor tone and activity in the baby
 - * Higher cortisol levels in the baby
 - * Poor reflexes in the baby
 - * ADHD and behavioral problems, particularly in boys

Depression During Pregnancy and Postpartum Depression

- * Depression during pregnancy is one of the biggest risk factors for Postpartum Depression (PPD)
- * Suicide is a major cause of maternal death in pregnancy and accounts for up to **20%** of all postpartum deaths
- * PPD is associated with the following in exposed children:
 - * Lower IQ
 - * Slower language development
 - * ADHD
 - * Behavioral problems
 - * Psychiatric illness

Myth #2: Antidepressants During
Pregnancy are Associated with
Poor Outcomes for the Infant

Truth #2: Well-Controlled Studies Do
NOT Find Associations with Adverse
Long-Term Infant Outcomes

Antidepressant Use in Pregnancy

- * In Utero Antidepressant Exposure has been associated with:
 - * Preterm Birth
 - * Low Birth Weight
 - * Cardiac Defects
 - * Persistent Pulmonary Hypertension
 - * Autism

- * BUT.....

Problems with the Literature

- * Most studies don't control for:
 - * The underlying psychiatric illness
 - * Severity of psychiatric illness
 - * Risk factors that are found in a higher rate in the psychiatric population
 - * Diabetes, Smoking, Substance Use, Obesity etc
 - * Whether or not the mother was psychiatrically ill during pregnancy
 - * Multiple medications

Factors Associated with Antidepressants Confound Studies on Infant Outcomes

Antidepressant use during pregnancy is a **MARKER** for a population of women, different from the general population of women, with attendant risk factors and behaviors that can affect birth outcomes



Apples to Apples

Studies of women with depression who didn't take meds during pregnancy show higher rates of pre-term birth and low birth weight

- * Studies which compare women with depression taking meds and women with depression not taking meds during pregnancies do NOT find associations between antidepressants and
 - * Heart Defects
 - * Persistent Pulmonary Hypertension
 - * Autism

Hype: Google Search- October 2015

- * Search of “Antidepressants, Pregnancy”
 - * 8,950,000 results
- * Added “Harm”
 - * 9,160,000 results
- * Deleted “Harm,” added “Safe”
 - * 529,000 results

A Scary Story is a Popular Story

Comparison of the Wrong Risks

The Myth

- * Antidepressant Use

versus

- * No Antidepressant Use

Reality

- * Antidepressant Use

versus

- * Risks of Untreated Major Depression

Stigma

WHAT IF WE
TREATED ALL
ILLNESS LIKE
WE TREAT
MENTAL
ILLNESS?

REACH
OUT.COM

*I'm getting
very tired of
this 'cancer'
of yours.*

*Yeah.. you just
think you need
your Asthma puffa
because you can't
deal with
reality.*

*Sigh. I had to
work over time
again because
Adam went and
had a heart
attack or some
shit.*

Prevention: The Way Forward

- * Education
 - * General Population
 - * Physicians
- * Research
- * Screening
 - * The US Preventative Task Force recently recommended universal screening during and after pregnancy
- * Psychosocial support programs

Psychotherapy

- * There have been a number of studies of various types of psychotherapy for depression during and after pregnancy
- * Interpersonal Therapy best studied
- * Cognitive Behavioral Therapy also shows promise
- * Mindfulness Based CBT also shows promise
- * Need more well-designed, randomized trials
- * There are numerous barriers to using psychotherapy for many women

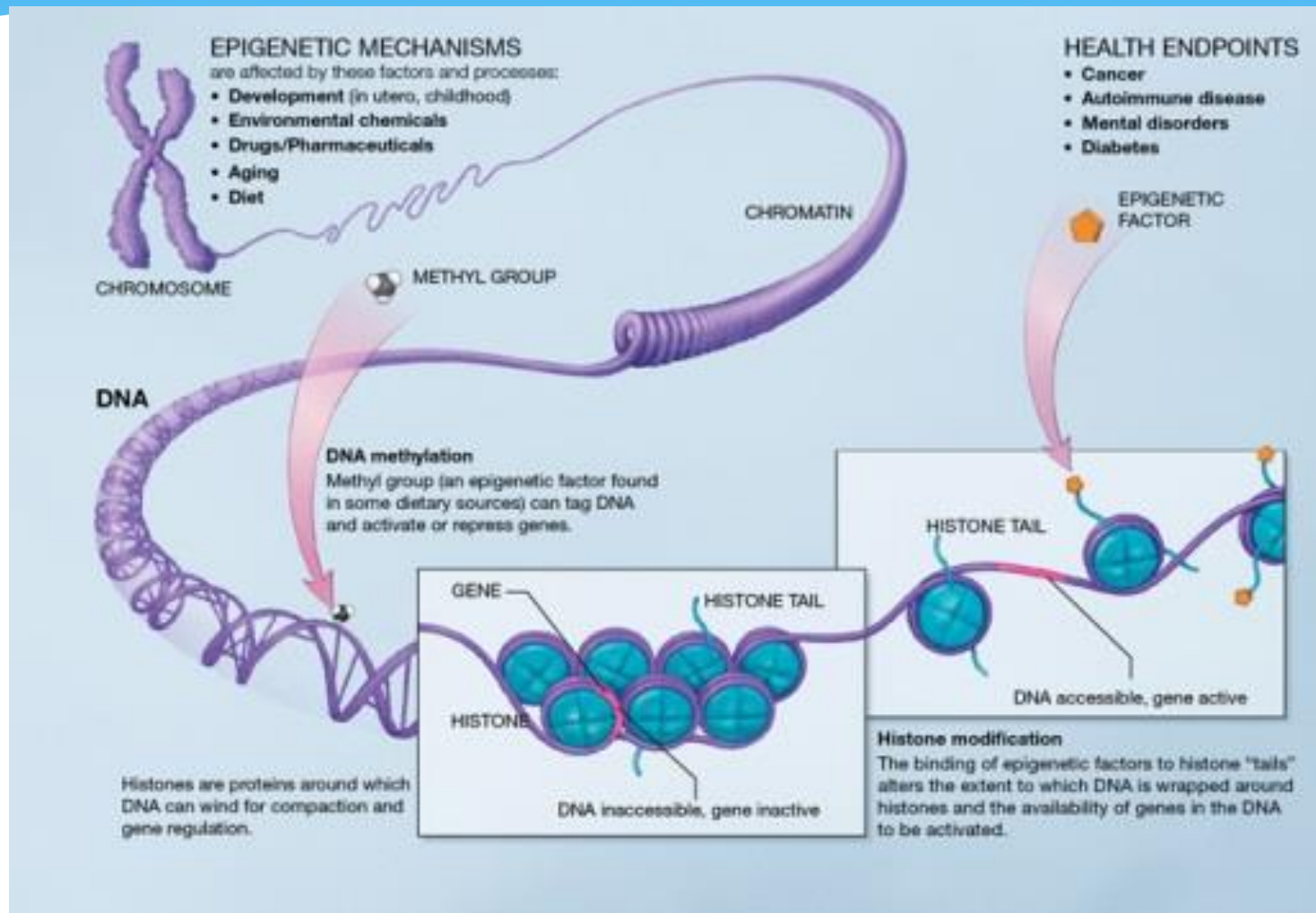
A Great Need for Research

- * No studies on the proper management of antidepressants during pregnancy
 - * FDA recommends tapering antidepressants prior to delivery- no data
 - * Blood levels of antidepressants drop across pregnancy- no data on prophylactic management
- * Only 3 small well-controlled studies on the prevention or treatment of postpartum depression with meds
- * More studies on psychosocial interventions and psychotherapy but these approaches have barriers
- * Until now research is complicated by the fact that not every woman who is pregnant is at high risk

Epigenetics Defined

- * Heritable changes in gene activity which are not caused by changes in DNA sequence
- * DNA methylation and histone modification alter how genes are expressed
- * Why differentiated cells in a multicellular organism only express the genes they need
- * Environmental exposures (like hormone levels during pregnancy) can induce epigenetic changes and change gene expression

Epigenetic Mechanisms



First... the Mouse

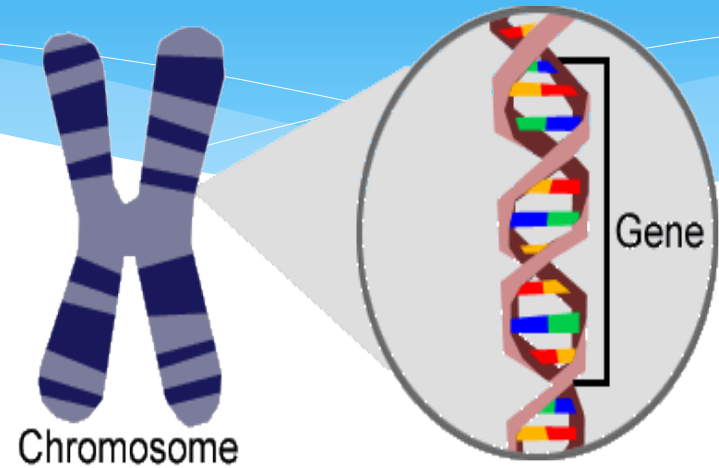
- * Screened for genetic loci responsive to high doses of estrogen (to model pregnancy) in the mouse brain
- * Identified loci were cross-referenced with DNA methylation differences identified in blood from women who did and did not develop PPD

The Prospective Study

- * 93 subjects
 - * 30 women with Bipolar Disorder
 - * 63 women with Major Depression
- * Psychiatric medication use was common and ranged from 49.4%-65.5% during pregnancy
- * 75.4% met DSM-IV criteria for a MDE either during pregnancy, postpartum or both
- * 38 women were clinically well during the 3rd trimester prior to delivery
- * 15 developed PPD (39.5%), 23 remained well
- * 80% of those with PPD had been on meds during the 3rd trimester

Epigenetic Biomarkers of Postpartum Depression

- * We identified two biomarker loci at the **HP1BP3** and the **TTC9B** genes that predict PPD in pregnant women with ~80% accuracy
- * Exact functions are unknown
- * HP1BP3 has been shown to associate with the β estrogen receptor
- * TTC9B has been shown to be responsive to gonadal hormones
- * We have replicated these findings in 3 other small samples



The Future: Prevention Trials of Women at High Risk based on Biomarkers

Conclusions

- * We need to educate both the general public and physicians that psychiatric medications do not have to be stopped for pregnancy as well as the adverse consequences of untreated psychiatric illness during pregnancy.
- * There has been a lack of research on the proper management of psychiatric illness during and after pregnancy.
- * Interpretation of the literature has been complicated by poorly controlled studies and media hype.
- * Identification and use of biomarkers of PPD will allow more sophisticated and efficient studies on ways to prevent PPD.
- * Stigma continues to complicate psychiatric treatment decisions for women, particularly during and after pregnancy.

Goal: Healthy Mom, Healthy Baby!