MATERNAL DEPRESSION

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Objectives
• Describe the effects of maternal depression on fetal and neonatal health
• Describe normal changes in mood and anxiety symptoms during pregnancy and postpartum
• List and describe different types of mood and anxiety disorders in the postpartum

Depression: Age of Onset Distributions for Men and Women (NCS)

Treating women of reproductive age
• 49% of pregnancies are unintended
• 82% of women have children
• Many clinicians do not discuss contraception/ family planning with their patients when prescribing medication


Depression: most common major complication of maternity

The mother’s emotional state in pregnancy and in the early postnatal period can have long lasting effect on her child

Hines et al. JAMA Q 1992;268:136-144 [Evidence Level B]
Fetal Programming

The environment in the womb during different sensitive periods for specific outcomes can alter development of the fetus with long lasting effects on the child into adulthood.

National Institute of Child Health

The programming hypothesis brings a new perspective to public health. Diseases that were once thought to arise near the time of their manifestation are now known to have their roots in pre and early postnatal life.

Prenatal Stress in Humans

- Reduced birth weight
- SGA
- Asthma
- Altered immune functioning
- Decreased telomere length
- Mixed handedness
Prenatal stress

- Increased anxiety and depression
- Behavioral problems, ADHD, conduct disorder
- Impaired cognitive development
- Sleep problems in infants
- Neonatal behavior/more difficult temperament
- Victimization in childhood
- Schizophrenia
- Autism

ALSPAC Study: does antenatal stress affect child behavior

- Determine affects of antenatal stress and depression on behavioral development of the child while allowing for WIDE range of confounders
- Large prospective birth cohort N=14,000 pregnant women recruited in Bristol, UK 1990-1992
- Follow longitudinally children ages 4,7,11, 13yo

ALSPAC Study

- Maternal anxiety at 18 and 32 wks of pregnancy
- Compared most anxious/depressed (15%)
- Child behavior: Report from 4-13yo Strengths and Difficulties Questionnaire (SDQ): ADHD, Anxiety, Depression, Conduct disorder

Multivariate Analysis

N=7,363

- Maternal and Postnatal anxiety and depression
- Paternal pre and postnatal anxiety and depression
- Parenting
- Maternal age
- Birth weight
- Gestational Age
- Smoking
- Alcohol
- SES
- Maternal education

The combined effects of raised anxiety both antenatally (32 weeks) and postnatally (33months) on child outcome up to 13 years

Similar results with depression
Summary of ALSPAC

- For 15% most anxious/depressed pregnant women the rate of mental illness in children doubled from 6 to 12% at age 13 after controlling for wide range of confounders.

- Attributable load of prenatal anxiety and depression in association with a mental disorder is 10-15%.

- Links are similar with prenatal anxiety at 18 wks gestation.
- Similar with depression.
- Not just first trimester.
Does pregnancy protect against mood disorders?

- Higher in utero exposure to cortisol is associated with lower cognitive function

- Sensitive early mothering can reverse the effects of high in utero exposure to cortisol
Time to Relapse in Patients Who Maintained VS Discontinued Antidepressant


Psychotropic medications in men vs women

Women: Psychotropic Medications
- Analysis from prescription claims data from 2.5 million Americans from 2001 to 2010
- 1 out of 4 women are dispensed medication for a mental health condition, compared to just 15 percent of men
- Antidepressant use among women is up 29 percent since 2001

Suicide leading cause of maternal death
- Suicide and homicide are leading causes of maternal death

EDITORIAL
Suicide: the leading cause of maternal death
Margaret Tofield
The British Journal of Psychiatry Sep 2003. 183 (3) 279-281. DOI: 10.1192/bjp.183.3.279

Perinatal Depression /Anxiety Care
(from Gauwin, Meltzer-Brody, Glover, and Goyanes in press)

Summary of current knowledge about SSRI during pregnancy
- NO increase risk
- Birth defects
- IQ reduction or behavioral problems
- Autism
- Increased risk
- Neonatal side effects, esp tremor
- Premature labor (as does untreated depression)
- Neonatal persistent pulmonary hypertension (very, very rare)
- Might increase risk
- Miscarriage (highest quality studies do not show increased risk)
- Low birth weight (not clinically significant)
7th Annual ECMH Conference 2016
Alison Reminick, MD

Long term sequelae OF AD EXPOSURE

- Fluoxetine (prozac) (n=135) vs TCA non-exposed
- No significant differences up to age 7: IQ, language, temperament, behavior, mood, distractibility, or activity level
- Delayed language maturation associated with maternal depressive symptoms, not with SSRIs
- Autism: initial study found small increased risk. Subsequent studies have ruled out after controlling for confounders
- Same level of risk for non-exposed sibling

Depression Risks

Risk to mother:
- Worsened depression
- Pre-eclampsia (2.3-3.2 RR)
- Increased risk of postpartum depression and somatic symptoms PP (HA, fatigue)
- Possible increased risk SAB

Depression Risks in Pregnancy

Risk to baby:
- Poor maternal self-care during pregnancy
- Pre-term birth (RR 2.0-2.5)
- Lower birth weight (180-200gms)
- Poor bonding postpartum
- Increased infant reactivity (esp >30wks)
- Infant sleep disturbance
- Child anxiety, language delay, ADHD, conduct disorder
- Increased adolescent depressive sx's

Depression Risks Postpartum

Maternal depression and anxiety linked to:
- Withdrawn mother: fussy baby
- Anxious, intrusive mother: detached baby
- Lower IQ
- Delayed language development
- Poor infant growth and incr diarrheal episodes
- Higher rates of anxiety and depressive sx's, and behavioral problems in toddlers, preadolescents and adults

Depression Risks Postpartum

Remission of maternal depression benefits children:
- 151 mother-child pairs in STAR*D study
- Remission of maternal depression after 3 mos of treatment associated with significant reductions in children's depressive, anxiety, and disruptive behavior disorders and symptoms
Major Depression

- Women in reproductive age group are at same age as typical onset of MDD
- 10-15% of women have depressive symptoms during pregnancy and postpartum
- Many women with depressive symptoms have some negative impact on function as a result

 Behavioral Effects?

SSRIS AND AUTISTIC SPECTRUM DISORDERS:

Is there evidence of risk?

Caveat: Read each study very carefully before coming to conclusions...

Kaiser Permanente Medical Care Program: Croen Article 2011

- Population based case-control study
- Based on pharmacy and medical records
- 298 case children and mothers, arbitrary exclusion criteria based on date of study
- 1507 control children and mothers
- 20 case (6.7%) children and 50 control (3.3%) children exposed to SSRIs
- 2 fold increase risk of ASD with SSRI exposure
- Particularly with 1st trimester exposure

Croen La et al; Arch Gen Psychiatry. 2011 Nov;68(11):1104-12.

SSRIs and Autism:

Case study in how the media can mislead

- Problems with Croen study:
  - based on only 20 exposures (actually only 15 after exclusions)
  - Family genetic risk not reported
  - Did not report underlying medical illness, smoking, EtOH use, substance abuse, other prescription or OTC medications
  - Psychiatric illness in mother not accounted for as risk factor for autism
- Result: many women stopped medication, and became ill

SSRIs and Autism

- Compared sibling pairs (exposed and unexposed)
- Conclusion: No evidence that SSRIs are neurotoxic
- Maternal depression CAN be neurotoxic
  (Nulman et al. J Clin Psychiatry. 2015 Jul;76(7))
- Data were drawn from three large Boston-based health systems and state birth certificates.
- For both ASD and ADHD, no significant increase in risk associated with prenatal antidepressant exposure (Castro VM, Translational Psychiatry (2016) 6, e708)

Summary of VPA Findings Across Pregnancy Registries

- Valproic acid (VPA) is associated with highest risk for all major malformations >20%
- Spina bifida risk 1-5% (15-30 days postfertilization)
- Craniofacial defects (incl. oral clefts), heart defects, polycystic, hypospadias, LBW
- Cognitive developmental delay

Morrow J et al. J Neurolog Neurosurg Psychiatr 2006;77:103-6
Valproate

- "Fetal valproate syndrome"
- Organ dysgenesis: NTD 5-9%
  - Risk dose dependent
  - related to use 17-30 days postconception
- Intrauterine growth: part of "fetal valproate syndrome"
- Neurobehavioral: data not definitive, MR?
- Neonatal toxicity: HR decelerations, irritability, feeding difficulties, abnormal tone
- Use during pregnancy:
  - switch to another mood stabilizer before conception

Valproate (VPA) teratogenicity

- Increased risk of neural tube defects
- Risk increased by obesity and low folate
- Increased risk of other anomalies
- Increased risk of developmental delay, lower IQ
- Possible increased risk of autism
- Higher teratogenicity risks than other mood stabilizing medications
- Risks may be dose dependent, significantly greater with doses of >1000mg

Long-term Effects of Li

- Observational retrospective study of 15 children investigated at 3-15 years of age
- 1 child had signs of minor neurological dysfunction but without further clinical implications
- Cognitive, behavioral and general development not affected


Etiology of PPD

Genetic susceptibility
Inflammation
Sleep and Circadian
Hormones
Postpartum depression
Neurotransmitter changes
Social role transitions
Pain

Hormones Changes at Delivery

Risk of Psychiatric Illness During Pregnancy and Postpartum Period

Pregnancy
Risks for First-Time Psychiatric Admission Postpartum

Diagnosis-Specific Risks for First-Time Psychiatric Admission Postpartum

POSTPARTUM MOOD DISTURBANCE SEVERITY

BLUES DEPRESSION PSYCHOSIS

Impact of PPD on infant
- Poor maternal child bonding / attachment disorders
- Less likely to breastfeed
- Failure to thrive
- Lower global IQ / poor language/ cognitive and social delay
- Developmental delay on Bayley Scale at 1 year
- Behavioral problems / emotional dysregulation
- Early onset of ADHD, mood, anxiety conduct disorders, autism
- Suicide/infanticide

Postpartum Mood Disorders

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Incidence (%)</th>
</tr>
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<tbody>
<tr>
<td>Postpartum blues</td>
<td>80%</td>
</tr>
<tr>
<td>Postpartum depression</td>
<td>10-22%</td>
</tr>
<tr>
<td>Postpartum psychosis</td>
<td>0.1%</td>
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Suri and Burt, 1997

UCSD Maternal Mental Health IOP

Postpartum Health Alliance: postpartumhealthalliance.org
Postpartum Support International
Apps: PPD Gone (Shoshanna Bennett, PhD)

Resources for Medications in Pregnancy and Breastfeeding

- Reprotex: www.reprotox.org
- Motherisk.org www.motherisk.org 1-877-439-2744
- Infantrisk.com (806)-352-2519 also phone app available
- MothertoBaby: www.mothertobaby.org Good Handouts
- MGH women's mental health program: www.womensmentalhealth.org
- E-Lactania: http://www.e-lactancia.org/ingles/inicio.asp
- toxnet.nlm.nih.gov

Healthy mom = healthy baby