- Proinflammatory cytokines rise in last trimester
- Women's highest risk of depression in the last trimester
- Cytokines remain elevated postpartum

- Depression and anxiety increase the risk for preterm birth

- French prospective study of rate of prematurity
  - 9.7% for depressed women
  - 4% for non-depressed women

- Increased IL-6, TNF-α in stressed and depressed moms
- IL-6, IL-8, TNF-α ripens cervix
- Levels increase in pre-eclampsia and infection
- CRH triggers parturition

- Randomized trial with DHA-enriched vs. regular eggs
  - 291 low-income moms in last trimester of pregnancy
  - Increased gestation length by 6 days (+2.3)

Dayan et al., Psychosom Med 2006, 68: 938-946
Smuts et al., Obstet Gyn 2003, 101: 469-479
• 2,586 women in U.S. in neonatal period
• Women with severe breastfeeding pain Day 1, Week 1, and Week 2 significantly more likely to be depressed at 2 months postpartum
• Breastfeeding help was protective of mental health for women with moderate or severe pain


• 50% had nipple pain at 5 weeks postpartum
• 52% reported sore or cracked nipples at 2 months postpartum


• Severity of post-birth pain, but not mode of delivery, predicted postpartum depression
• Prospective, longitudinal study of 1,288 women
• Acute pain increased the risk of depression by three times
• And the risk of persistent pain by 2.5 times


• Pain increases inflammation
• Inflammation increases pain
• Inflammation also increases prostaglandin synthesis


• Both depression and trauma compromise sleep quality

Kendall-Tackett, Trauma, Violence & Abuse: 8, 117-126
Sleep abnormalities in depressed new mothers
- Decreased sleep time and reduced REM latency


Chronically disturbed sleep increases inflammation (IL-6, TNF-α) and increases risk of cardiovascular disease and metabolic syndrome


Survey of Mothers’ Sleep and Fatigue Full Sample (N=6,410)
- Hit or slapped hard enough to leave a mark 34%
- Raped as teen or adult 13%
- CSA—rape 2%
- All types contact CSA 25%
- Parent depressed 36%
- Parent hit, bitten or kicked 16%
- Parental substance abuse 32%

Rates of birth-related PTSD up to 9% in U.S. surveys
- 18% had PTSD symptoms
- 46% described their births as "traumatic"


Dunedin Multidisciplinary Health and Development (N=1,037)
- At 32 years, those who experienced adverse childhood experiences (low SES, maltreatment or social isolation) had higher rates of:
  - Major depression
  - Systemic inflammation
  - Having at least 3 metabolic risk markers

Danese et al. *Arch Ped Adolesc Med* 2009; 163: 1135-1143

Rates of birth-related PTSD up to 9% in U.S. surveys
- 18% had PTSD symptoms
- 46% described their births as "traumatic"

Prior depression or trauma primes the stress response
More rapid inflammatory response to current stressors

Reduce maternal stress
Reduce inflammation

Goals of Prevention & Treatment

Breastfeeding protects maternal mood by downregulating the inflammatory response system
Breastfeeding difficulties can cause depression

Breastfeeding decreased ACTH & cortisol
Lower stress response to induced stressor
Suckling provided short-term lessening of stress response

Oxytocin Response
- Well-being
- Affiliation
- Bonding

Stress Response
- Depression & anxiety
- Alienation
- Hostility & interpersonal strife

Heinrichs et al., J Clin Endo Metabol 2001, 86: 4798-4804

Reduce Maternal Stress
Breastfeeding improves mother-infant interaction and stops intergenerational transmission of abuse and trauma.

• Study of 139,681 postmenopausal women (Mean age=63)
- Lifetime history of lactation of more than 12 months related to lower
  - Hypertension
  - Diabetes
  - Hyperlipidemia
  - Cardiovascular disease

Babies of depressed-breastfeeding mothers had normal EEG patterns
- Depressed-BF moms touched, stroked and looked at babies more than depressed-non/BF moms

Jones et al., Biol Psychology 2004; 67: 103-124

A 14-year longitudinal study in W. Australia of 2900 pregnant women. Children assessed at 2, 6, 8, 10 and 14 years. Longer duration of breastfeeding associated with better child mental health at every assessment. Dose-response effect.

Child Behavior Checklist Scores
- Total morbidity
<table>
<thead>
<tr>
<th>Never BF</th>
<th>BF 12+ Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 2</td>
<td>16.1</td>
</tr>
<tr>
<td>Age 5</td>
<td>26.3</td>
</tr>
<tr>
<td>Age 8</td>
<td>19.4</td>
</tr>
<tr>
<td>Age 10</td>
<td>15.2</td>
</tr>
<tr>
<td>Age 14</td>
<td>16.7</td>
</tr>
</tbody>
</table>

Risk of neglect decreased with breastfeeding duration
- OR=1.0 >4month
- OR=2.3 for <4 months
- OR=3.8 for non-breastfed

15-year cohort study of 7,223 Australian mother-infant pairs. 512 substantiated maltreatment reports (4.3% of cohort). Breastfeeding decreased risk of maternal-perpetrated child maltreatment
- OR=2.6 for non-breastfed
- OR=1.1 for breastfed

Risk factors for violence

Percentage who are breastfeeding

Hours Mothers Sleep

Sexual assault: F(1,5837) = 14.07, p = .000
Feeding method: F(1,5837) = 26.79, p = .000

• All treatments for depression lower inflammation

• Breastfeeding was related to lower C-reactive protein
  – CRP is an inflammatory marker for cardiovascular and other chronic diseases
  – Study of 26-year-old women who participated in the Dunedin Multidisciplinary Health Study

Kendall-Tackett et al. Breastfeed Med 2013: 8(1); 16-22

Williams et al., J Epidemiol Comm Health 2006; 60: 146-148
Exercise

- Exercise is an effective treatment for even major depression
- High-fitness leads to lower inflammatory response to stress


- 32-longitudinal study of 163 people
  - Followed since birth
  - Attachment measured (Strange Situation) at 12-18 months
- At age 32, those with insecure attachments at 12-18 months significantly more likely to have inflammation-based illness


EPA & DHA

- Populations with high fish consumption have lower rates
  - Postpartum depression
  - Major depression
  - Bipolar disorder
  - Suicide risk


Many pregnant and postpartum women in the U.S., Canada, Europe, Australia, and New Zealand are deficient in EPA/DHA

Pregnancy further depletes maternal stores of both


Polyunsaturated Fatty Acids (PUFAs)

Omega-6s

- Linoleic Acid (LA)
- Gamma-Linolenic Acid (GLA)
- Arachidonic Acid (AA)

Omega-3s

- Alpha-Linolenic Acid (ALA)
- Eicosapentaenoic Acid (EPA)
- Docosahexaenoic Acid (DHA)

Wang et al. Agency for Healthcare Research & Quality, 2004
Population study found high Omega-3s related to low IL-1α, IL-1β, IL-6, TNF-α
Opposite true of people low in Omega-3s
Fernuchi et al., J Clin Endo Metabol 2006, 91: 439-446

Students with higher EPA/DHA had a lower inflammatory response to a lab-induced stressor
Mann et al., Biol Psychi 2000, 47: 910-920

St. John’s wort
- Antidepressant constituent is hyperforin
- Hyperforin is anti-inflammatory and reduces proinflammatory cytokines
Balch, Prescription for herbal healing, 2002

SSRIs are specifically anti-inflammatory and decrease production of pro-inflammatory cytokines

Inflammation is an important contributor to the onset and severity of depression

Summary & Implications
Wellness ↑ Stress
Breastfeeding attenuates stress and protects maternal mood.
But breastfeeding problems increase risk of depression.

All effective treatments for depression are anti-inflammatory.