# Perinatal Depression: Current Concepts

Identifying risks and guiding treatment

Nelda Scott, MD

1. Depression during pregnancy
   - symptoms
   - effects on OB course
2. Postpartum mood changes
   - “blues” vs. depression
   - risk factors and diagnosis
   - effect on the newborn
   - psychosis
3. Treatment
   - medications/ECT
   - psychotherapeutic

# Myths about pregnancy and mood

- Pregnancy is protective against depression
- Pregnancy is a time of more depression

# Rates of depression in pregnancy

The rate of depression is generally no higher during pregnancy than at other times, but the risk of untreated depression

is significant!

Prevalence of depression in pregnancy:

7 to 26%

may be higher in lower SES (variable data)

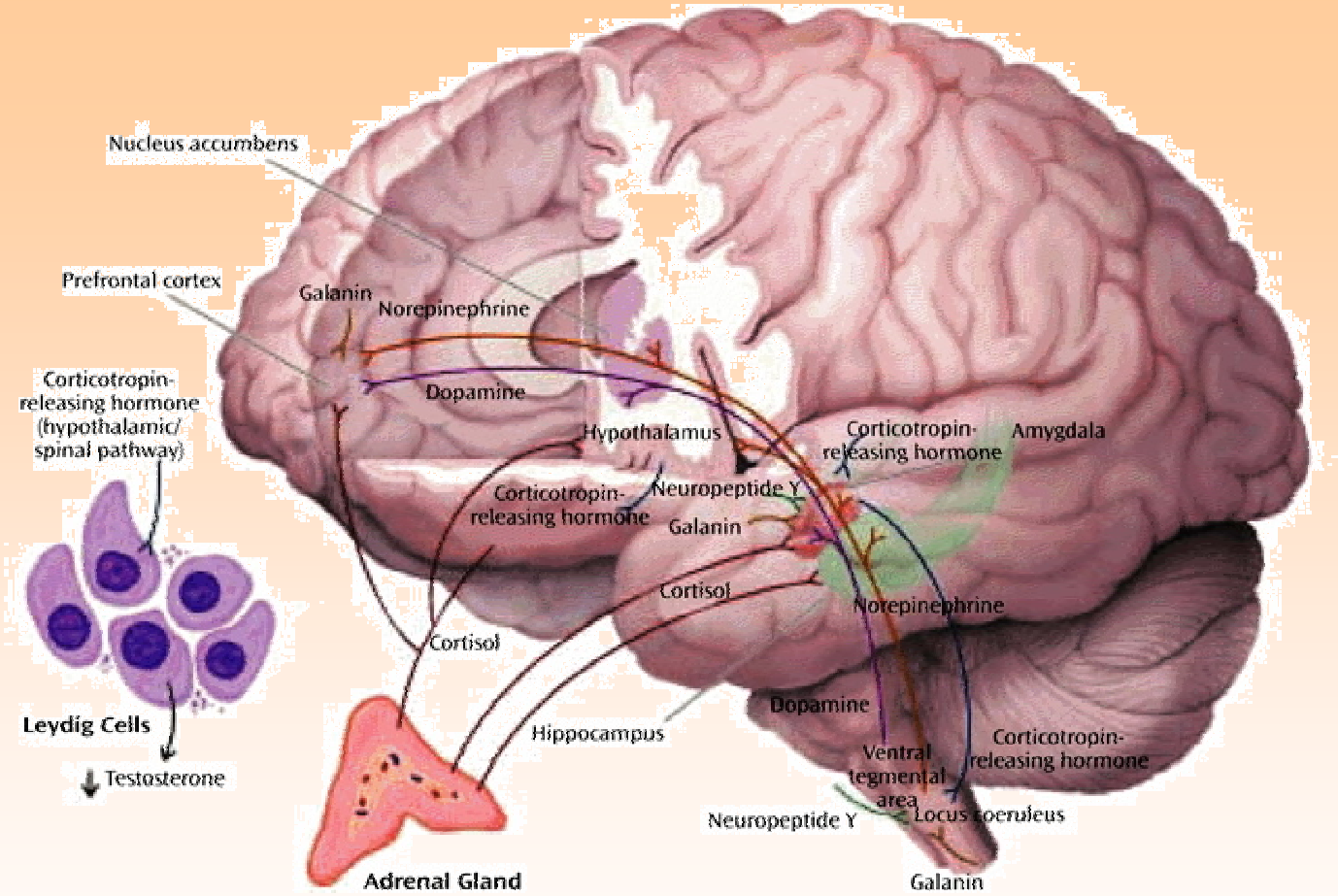
# Symptoms of Depression that are similar to normal pregnancy

- Sleep disturbance
- Increased appetite
- Decreased energy
- Mild change in concentration

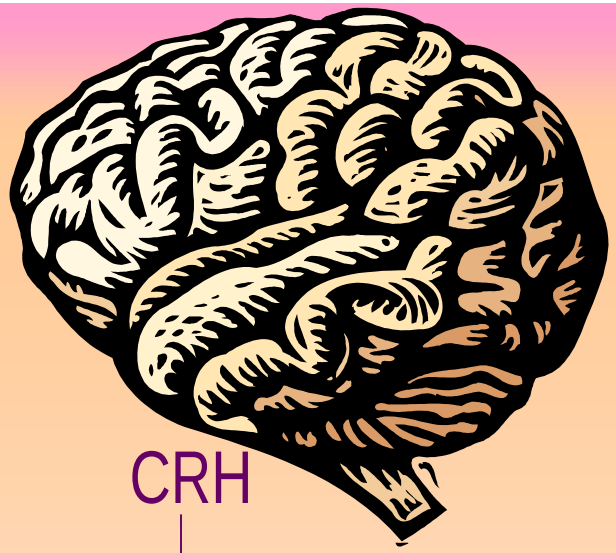
# Risks of untreated depression During Pregnancy

- Worse obstetrical outcome
  - Preterm labor
  - Growth retardation
  - Placental abruption
- Decreased prenatal care
  - later recognition
  - amotivation
- Poor weight gain
- Increased substance use

# Depression and the HPA axis/CRH

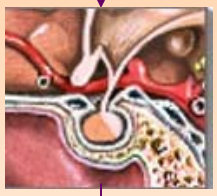


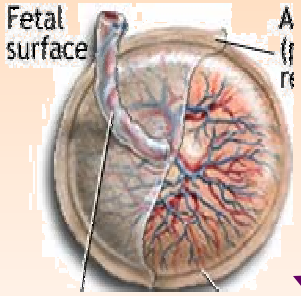

- From Charne, Dennis Psychobiological Mechanisms of Resilience and Vulnerability in Am Jnl Of Psychiatry 161



CRH

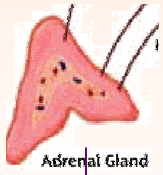
placental CRH






ACTH

placental CRH




cortisol

catecholamines

## Effects of cortisol ("stress")

early labor initiation

impaired growth

cortisol transfer through placenta

may effect fetal brain dev.

# Effects of cortisol ("stress")

- Early labor initiation
- Impaired growth
- Prolonged heart rate reactivity (Monk et al)
  - possible marker for emotional regulation
- Direct placental transfer
  - may effect fetal brain development

# Preterm labor

- Major cause of preterm delivery
- Possible relation to anxiety and/or depression
  - conflicting data
  - varying factors studied
    - “distress” vs. depression vs. depressive symptoms
    - preterm labor vs. preterm birth

# Studies Supporting Role of Depression in Preterm Labor

- Dayen et al 2002
- Outcome: women with depression had twice the risk of preterm labor (OR 2.1)
- Depression + low BMI (<19) further increased risk

# Depression and Preterm Birth

- Orr et al: Psychosocial Factors and Preterm Birth study
- African American women in Baltimore
- n=1399
- depression measure: CES-D
  - measured depressive symptoms
- 12.7% high (top 10%) CES-D group had preterm birth vs. 8.4% in the low (less depressed) group

TABLE 2. Association of spontaneous preterm birth with clinical and behavioral factors among African-American women in the Psychosocial Factors and Preterm Birth Study, Baltimore, Maryland, 1991–1993

| Variable | Adjusted odds ratio* | 95% confidence interval |
|---|---|---|
| High CES-D score | 1.96 | 1.04, 3.72 |
| Low body mass index | 2.58 | 1.52, 4.35 |
| Previous poor outcome | 1.59 | 1.01, 2.52 |
| Alcohol consumption | 0.63 | 0.24, 1.69 |
| Bleeding | 1.87 | 0.70, 5.02 |
| Drug use | 1.13 | 0.50, 2.55 |
| Smoking | 1.35 | 0.80, 2.27 |

* Estimated by conditional logistic regression with all variables listed in the model.

# Postpartum mood reactivity ("postpartum blues")

- Very common (50 to 80% of women)
- Mood is generally not "blue"
  - happy
  - emotional lability (cry easily, irritable)
- Peaks by 3-5 days post partum
- Lasts days to weeks
- Self resolves

# Postpartum mood reactivity ("postpartum blues")

- Risk for development
  - no relationship to psychiatric history
  - no relationship to stressors
- Etiology (theories)
  - hormonal withdrawal (estrogen/progesterone)
    - lower allopregnanolone levels
  - activation of mother-infant attachment system
    - oxytocin/limbic system (higher activation)
      - leads to emotional reactivity/intensity
- relationship to postpartum depression
  - none in most women
  - some may develop postpartum depression

| Characteristic | Blues | Postpartum Depression |
|---|---|---|
| Incidence | 50-80% | 10-15% |
| Onset | 3-5 days after delivery | within 3-6 months |
| Duration | Days to weeks | Months to years (if untreated) |
| Associated stressors | No | Yes (especially lack of support) |
| Sociocultural Influence | No (seen in all cultures and socioeconomic levels) | Yes (much less common in supportive cultures) |
| History of Mood Disorder | No association | Strong association |
| Tearfulness | Yes | Yes |
| Sleep disturbance | Sometimes | Almost always |
| Suicidal thoughts | NO | Almost always |
| Thoughts of harming the baby | Rarely | OFTEN |

# Postpartum Depression

- Non psychotic Major Depression in first 6 months after delivery
  - depressed mood or loss of interest plus
    - insomnia or hypersomnia
    - loss of interest/pleasure
    - excessive guilt or worthlessness
    - decreased energy
    - poor concentration or indecisiveness
    - change in appetite and weight
    - psychomotor agitation or retardation
    - suicidality or thoughts of death

# Clues to postpartum depression

- Persistent sleep disturbance
- Loss of appetite (vs. weight loss that is normal to postpartum)
- Poor concentration
  - simple tasks are overwhelming
- Significant feelings of inadequacy
- ego-dystonic thoughts of harming the baby
    - thoughts are like obsessions
    - mothers rarely act
      - severely suicidal women may act

# Postpartum Depression

- 10-15% of new mothers in the United States
- May be first lifetime depressive episode
- Onset: within a month post partum
  - often not diagnosed until 3-6 months
- Duration: months to years

# Risk factors for postpartum depression

Previous major depression

- non postpartum  may have 30% risk
- PPD recurrence rate may be up to 70%

Premenstrual dysphoric disorder (PMDD)

Life stress (incarceration is a life stress)

Poor social support

Bereavement

Prior stillbirth

# Adolescents

- Often have more stressors than adult parents
- Life stress predicts distress in teens
- In depression: more likely to have hostility and irritability
- Girls at higher risk than boys
- Similar life factors predict pregnancy and psychological problems
  - poverty, abuse, school problems
  - High risk/depressed even prior to pregnancy

# Postpartum depression in Adolescents

- No higher depression than matched non-pregnant controls (Moore 2001, Troutman 1990)
- Higher depression than the general teen population
- Higher depression vs. adults postpartum
  - 2x higher ( in 15-17 age group) (Deal 1998)
  - largely due to poverty and marital status
- High depression predictors
  - More than one child
  - Poor support
  - Poor early relationships with caregivers (abuse)
    - affects attachments
    - affects their concept of parenthood
    - affects transition to parenthood

# Postpartum depression in Adolescents

- Rate of depressive symptoms (CES-D)
  - National Maternal and Infant Health (1988) (Deal et al 1998)
    - 27-48% (primiparous only)
    - Didn't include stillbirth/non-custodial
  - up to 26% (Troutman 1990): Iowa sample
    - study didn't include adoption planners
    - higher rates of prior depression treatment and suicide attempts than controls
- Up to 59% have depressive symptoms 1-3 years postpartum (Collette 1983)

# Incarcerated Women

- Most have children (80%)
  - up to 25% are pregnant/recently delivered (Safyer 1995)
- Higher rates of depression
  - vs. incarcerated men/general population
  - 62% (Staton 2003)
- Poor access to care
  - only 24% may get “services” (Teplin 1997)
- High rates of prior trauma, substance abuse and prior mental illness
- High risk of suicide
- Limited data about postpartum depression

Nature Morte (Picasso)

# Post Partum Psychosis

- Most severe and least common
  - 1-2 out of 1,000 women
  - higher risk in women with bipolar disorder
    - risk may increase to 1 in 5
- Abrupt onset (days to 3 weeks postpartum)
- Most are bipolar (some have major depression with psychotic features)
- Symptoms include:
  - confusion (“perplexity”)/disorientation
  - delusions
  - hallucinations
  - rapid mood swings
  - insomnia
  - abnormal/obsessive thoughts

# Post Partum Psychosis

- Difference from non-postpartum psychoses
  - more disorientation and lability
    - may look well temporarily
  - more likely to act on thoughts of harming baby than post-partum depression
    - no increased risk to baby after treatment
    - harm to baby is a higher risk with poor social support
- High likelihood of recurrence (including outside postpartum period) without treatment
- Differential diagnosis
  - other psychiatric disorders
  - medical conditions (thyroid, low B12, etc.)
  - substances

# Risks of untreated depression after delivery

- Abnormal neonatal behavior (fussiness)
- Poor bonding with baby
- Marital tension
- Cognitive, Psychiatric, Neurobehavioral problems in the child
- Recurrence of depression
- Suicide
- Homicide (infanticide)

# Maternal Infanticide

- Oberman (5 categories)
  - Neonaticide (within first 24 hours)
    - can include teenagers/pregnancy denial
  - killing in conjunction with domestic violence
  - death due to neglect
  - excessive discipline (accidental)
  - purposeful infanticide
    - can include poorly controlled mental illness
    - if PPD (unlikely), killing is usually “altruistic”

# Effect on Parenting

- Interactions with infant/child
  - less positive (both mother and baby)
    - babies have reduced eye contact
    - reduced playfulness
  - less sensitive and engaged
    - less cognitive stimulation
    - less modeling of emotional regulation
    - less modeling of effective problem solving
  - less harmonious interactions
    - more punitive (Reis 2001)
  - more impairment with other risk factors
    - poor support, financial/family problems

**(NICHD Early Child Care Research Network. 1999 )**

# Parenting effects (continued)

- "Fake" depression (Crohn and Tronick '89)
  - 3 minute depression simulation
  - Babies became distressed
    - looked away, wary, disengaged
    - effect continued after return to normal maternal behavior
- Variable actual behavior
  - withdrawn vs. intrusive vs. normal
- "Normal" behaving depressed mothers
  - babies may have normal behavior
- Effect is worse for chronic depression

# Adolescents

- (Non-depressed) Compared to adults
  - Less parenting skills
  - Less responsive to infant
  - Less knowledge about child development
    - unrealistic expectations
  - higher risk of child behavior problems
  - higher risk of educational problems
- Teen mothers: more likely to be depressed as adults

# Incarcerated mothers

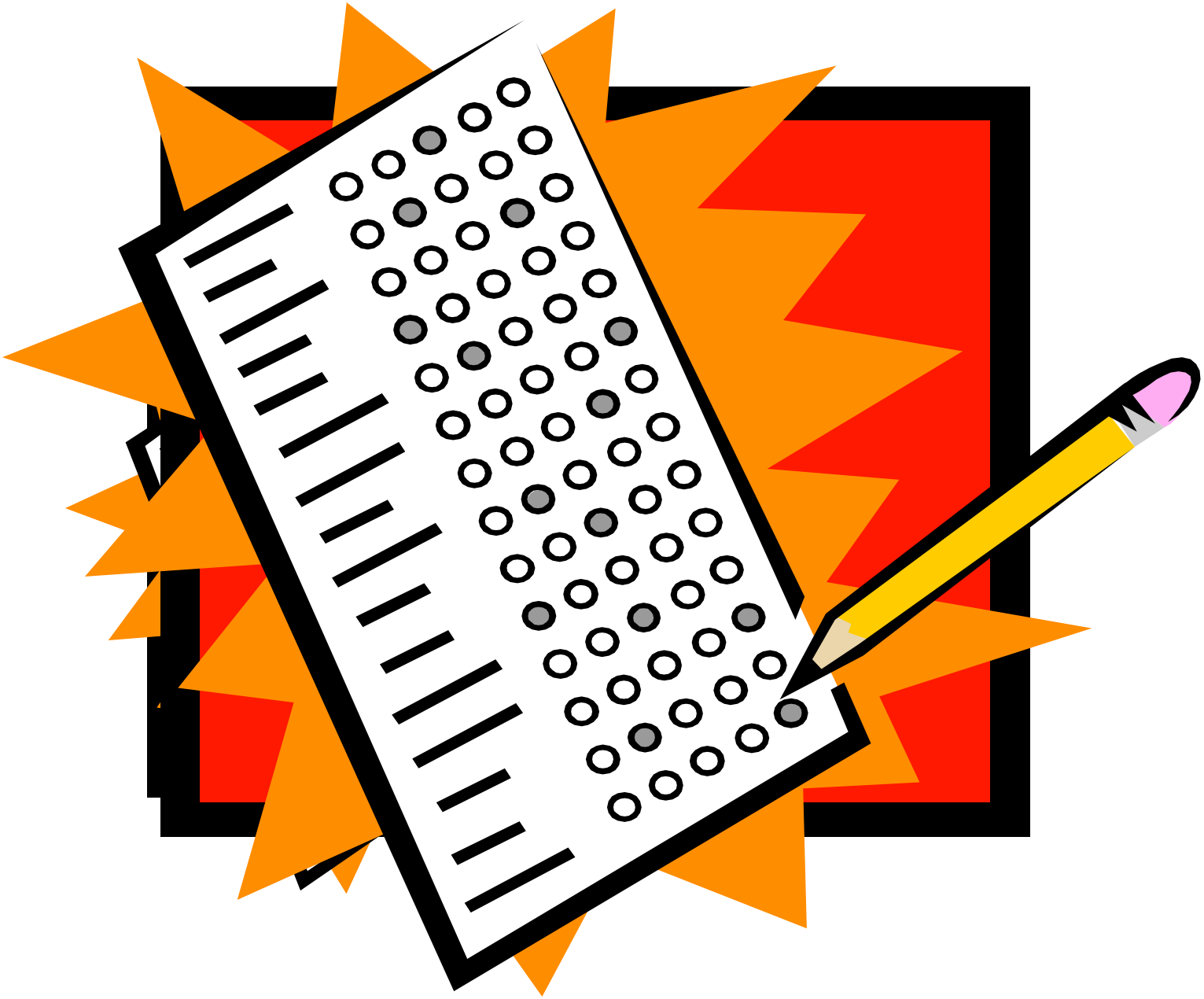
- Anticipation of separation
  - changes bonding with the baby during pregnancy
- May be grieving loss of other children
- Separation from the child (Hufft 1992)
  - affects attachment
  - affects the role transition to motherhood

# Neurobehavioral effects of maternal depression (neonates and infants)

- Abnormal Brazelton (neonatal behavior)
- Decreased responsivity to facial expressions
- Decreased infant expressivity
- Increased fussiness
- Sleep changes
- Change in cortisol levels

# Effects on children

- Impaired cognitive development
  - delayed object permanence
- insecure attachment
  - can lead to future psychopathology
  - risk for incarcerated women (limited contact)
- Behavior problems
  - aggression
- Depression
- Gender effects vulnerability
  - boys may be more vulnerable
- Vary based on quality of interaction



# Edinburgh Postnatal Depression Scale (EPDS)

## JL Cox, JM Holden, R. Sagovksy[1]

- 10 item scale
- Self report
- Widely tested
  - cross cultural validity
  - available in many languages
- Good sensitivity (86%) and specificity (78%)
- Can be used during pregnancy

1 Br J Psychiatry. 1987 Jun;150:782-6

# Edinburgh Postnatal Depression Scale

1. I have been able to laugh and see the funny side of things.
2. I have looked forward with enjoyment to things
* 3. I have blamed myself unnecessarily when things went wrong
4. I have been anxious or worried for no good reason.
* 5. I have felt scared or panicky for not very good reason.
* 6. Things have been getting on top of me.
* 7. I have been so unhappy that I have had difficulty sleeping.
* 8. I have felt sad or miserable.
* 9. I have been so unhappy that I have been crying.
* 10. The thought of harming myself has occurred to me.

* Severity of symptom increases from 0 to 3

| | |
|---|---|
| most of the time | 3 |
| often/sometimes | 2 |
| not often | 1 |
| never/not at all | 0 |

<u>Unstarred items</u>:

severity of symptom increase from 3 to 0

| | |
|---|---|
| most of the time | 0 |
| often/sometimes | 1 |
| not often | 2 |
| never/not at all | 3 |

# Interpretation of the EPDS

- Maximum score: 30
- Possible depression: 10 or greater
- Always look at item 10 (suicidal thoughts)

# Screening guidelines

- Offer screen to everyone
- Consider 3 screening times
  - During pregnancy
  - Peripartum or 6 weeks postpartum
  - At a pediatrics visit
- Use an assessment tool for high scores

# Peripartum Mental Health Consultation Service

- Assist providers in recognizing and managing perinatal depression
- On site clinic visits
  - Provider education and training
  - Formulating assessment questions
  - Arranging screening system
  - Reviewing the efficacy of the system
- Available by phone, fax, or e-mail

# Treatment

- Comprehensive
- Biologic
  - antidepressants
  - ECT
  - estrogen
- Psychotherapeutic
  - individual or couples therapy
  - parenting coaching
  - support groups

# Antidepressants

- SSRIs: citalopram, fluoxetine, fluvoxamine, paroxetine, sertraline
- Tricyclics: amitriptyline, desipramine, nortriptyline
- Others: bupropion, duloxetine, mirtazapine, nefazodone, trazodone, venlafaxine, MAOIs

# FDA pregnancy categories

- A: No risk (human controlled studies)
- B: No risk in animals and no adequate human controlled studies; OR risk in animals not shown in human controlled studies
- C: Risk in animals; no human controlled studies; benefits may outweigh risks; OR no studies available
- D: Risk to fetus; Need for drug justifies known risk
- X: Contraindicated in pregnancy

# Limitations of FDA pregnancy categories for psychiatry

- No psychotropics are category "A" (no risk)
- Teratogenicity varies across species
- FDA categories may not adequately state human safety data
- Drugs can get demoted to higher risk category the more they are studied
  - Category "B" medications (eg. bupropion) may be (falsely) seen as safer than a category "C"

# SSRIs in pregnancy, safety: Morphologic teratogenicity

- No increase in major anomalies
  - Many studies of SSRIs
    - citalopram, fluoxetine, fluvoxamine, paroxetine, sertraline
  - Includes fluoxetine meta-analysis (Addis and Koren 2000)
- Increased multiple MINOR anomalies in 1 study of fluoxetine (Chambers 1996)
    - fluoxetine mothers were significantly older
    - fluoxetine group had benzodiazepine use
    - concurrent trazodone and tricyclic use
    - fluoxetine group had more alcohol use
    - confounders corrected for
  - results not found in other studies

# Antidepressants in pregnancy, safety: Major Morphologic teratogenicity

No major malformations

- Tricyclics: many studies
- Venlafaxine
  - Einarson (2001)
- Limited data (possibly insufficient)
  - nefazodone and trazodone
    - Einarson 2003 n=147
- Insufficient data
  - bupropion
  - mirtazapine
  - duloxetine

# Neonatal antidepressant side effects

- Fluoxetine: higher special care nursery admissions (Cohen et al 2000)
  - difference is greater for late pregnancy exposure
  - no difference in Apgars, premature delivery, or birth weight
- Swedish Medical Birth Registry, N=987 mothers on various antidepressants during pregnancy (Kallen 2004) (SSRIs and tricyclics)
  - significant increase in:
    - respiratory distress
    - hypoglycemia (tricyclics)
    - (some had lower Apgar scores and a few had convulsions)

# Possible Neonatal side effects

- Hypotonicity
- Transient, mild respiratory distress
- Jitteriness
- Hypothermia
- Weak cry or increased crying
- Tachypnea
- Irritability
- Poor feeding

# Course of Neonatal antidepressant side effects

- Symptoms began within minutes to hours after birth
- Most fully resolved within 24 hours
- All had fully resolved by 48 hours
- No difference in length of hospital stay in exposed infants and controls
- No differences in development at age 2 months & 8 months
- Higher rates with multiple medications

(Oberlander et al 2004)

# Other effects studied

- Birth weight
  - conflicting data (increase vs. normal vs. decreased)
- Pregnancy loss
  - no significant increase

# MAOIs

- Risk for hypertensive crisis
- contraindicated with tocolytics (agents to prevent preterm labor)

# Behavioral Teratogenicity

Prospective studies: (no deficits)

- Nulman (1997) (followed up to age 7)
  - 55 fluoxetine, 80 tricyclics, 84 controls
  - nl IQ, language, mood, temperament, behavior
- Hendrick (2001) (up to 18months)
  - citalopram, fluoxetine, paroxetine, sertraline
  - normal Bayley Scales of infant development

# Guidelines for antidepressant choice during pregnancy

- Consider better-studied agents with human data
  - SSRIs
    - Expert consensus guideline
      - top choice if not breastfeeding :fluoxetine
      - #2 choice if not breastfeeding: paroxetine
      - top choice if planning to breastfeed: sertraline
  - tricyclics (desipramine, Nortriptyline)
  - (venlafaxine): may elevate blood pressure

# Guidelines for antidepressant choice during pregnancy

- Avoid during tocolysis
  - monoamine oxidase inhibitors
    - increased risk of seizure and hypertensive crisis
- Agents to avoid during preeclampsia:
  - bupropion
  - (maprotiline)

# Antidepressants in pregnancy

- SSRIs: considered first line
  - none cause major malformations
    - no systematic data for escitalopram
  - no behavioral teratogenicity
- Tricyclic antidepressants (nortriptyline, desipramine)
  - many studies and registry reports
  - used for decades
  - no behavioral teratogenicity
  - sedating
  - watch for anticholinergic effects
- venlafaxine, nefazodone (2003)
  - one systematic study each
    - no physical birth defects
    - behavioral teratogenicity unknown

# Antidepressants in pregnancy

- Bupropion, mirtazapine, duloxetine
  - no systematic human data
  - few case reports
  - not first line treatment
  - bupropion can lower seizure threshold
- MAOIs: avoid if possible

# Antidepressants in pregnancy

- Customize treatment to patient symptoms and historical response
- Start with medications with HUMAN data
- Dosing
  - start lower
  - consider dose reduction at 36 weeks if stable
    - lowest effective dose
    - may minimize neonatal “withdrawal”
- can do blood levels with tricyclics
- If a woman wants to stop medications, gradually taper

# Electroconvulsive Therapy

- No controlled trials (>300case reports)
- Permissible in pregnancy since the 1940s
- No increase in miscarriage
- Not linked to stillbirth/neonatal death or behavioral teratogenicity
- Rare contractions/bleeding (no adverse outcomes)
- Make modifications (position, hydrate, raise gastric pH, fetal monitoring, avoid excessive hyperventilation)

Miller, Laura: Use of Electroconvulsive Therapy in Pregnancy. 1994

# Estrogen (Postpartum treatment)

- Rapid decrease may play a role in etiology
- Gregoire et al (1996): transdermal
  - RCT, double blind
  - n=61
  - many in active and control groups also on concurrent antidepressants
  - estrogen group improved significantly (4wks)
- Ahokas et al (2001): sublingual
  - open label n=23
  - most recovered from depression

# Breastfeeding and antidepressants

- All are excreted in breast milk
  - varying levels
  - no clear relationship of timing of feedings
- SSRIs and tricyclics have the most data
- Monitor baby for adverse effects
  - consider doing blood levels on baby if indicated

# Antidepressants & lactation: relative doses to nursling

| Medication | % Maternal Dose |
|---|---|
| Sertraline | 0.4% - 1.0% |
| Fluvoxamine | 0.5% - 1.6% |
| Paroxetine | 0.1% - 4.3% |
| Desipramine | 1% |
| Venlafaxine | 5.2% - 7.4% |
| Citalopram | 0.7% - 9.0% |
| Fluoxetine | 1.2% - 12.0% |
| Nortriptyline* | not known |
| Bupropion | not known |
| Mirtazapine | not known |

(Miller & Wiegartz 2003)

# Antidepressant Transmission

| Medication | Possible breast feeding side effects (nursling) |
|---|---|
| Sertraline | none |
| | |
| Paroxetine | none |
| Desipramine | none |
| Venlafaxine | none |
| Citalopram | Uneasy sleep |
| Fluoxetine | Vomiting, watery stools, excessive crying, difficulty sleeping, tremor, somnolence, hypotonia, decreased weight gain |
| Nortriptyline | none |
| Bupropion | 1 case of infant seizure primarily unknown |
| Mirtazapine | not known |

*From Illinois prescribing guide in perinatal depression 2004;* Table based on Wisner et al *Postpartum Depression* Article in *N Eng J Med*, Vol. 347, No. 3, July 18, 2002, pg. 196.

# Psychotherapy

- Interpersonal psychotherapy
  - time limited
  - focus on interpersonal problems/role transition
    - interpersonal inventory
      - symptoms in an interpersonal context
      - assess expectations (of birth, family, etc.)
    - integrating new and old roles
    - problem solving/clear expectations
- may also deal with grief
- effective in depression reduction

# Psychotherapy (continued)

- Cognitive Behavioral Therapy
  - various studies
    - many with small samples and no control group
  - individual and group
  - sometimes as effective as medications
    - Appleby 1997

# Other therapies

- Couples
  - Marital discord can be a risk factor for PPD
  - Part of comprehensive treatment
    - depression and childbirth effect entire family
- Parenting Coaching
  - Data on “normal” functioning depressed women
  - Teach sensitive parenting
  - Increase face to face contact

# Tools for adolescents and mothers abused as children

- Counteridentification (Bretherton1985)
  - identification with prior hurts
  - may increase motivation to nurturance and protectiveness
- Reframing ( from Brophy-Herb 1999)
  - crying infant (intrusive vs. communicating needs)
  - making a mess vs. exploring
  - attention to child development
- Both are part of “reflectivity”
  - difficult to learn due to hard wiring of abuse

# Support groups

- Support Groups
  - Some studies combine depressed and non-depressed mothers
    - heterogeneity didn't result in depression improvement
  - Telephone support: decreased depression (sig) Dennis 2003 n=42

# Self Help

- Definition (Honikman 1999)
  - Mutual help provided/given
  - peers sharing a common problem
  - voluntary (free/low cost)
  - group controls the process
- Some groups have professional members
- Provide education and support

# Summary

- Peripartum mood changes occur frequently
  - Severity varies (blues to psychosis)
  - Risks vary by mood disorder
- Significant effects on OB outcome and parenting
- Screening:
  - Offer to every woman
- Treatment
  - Comprehensive and individualized
  - Safety data on medication use in pregnancy and breastfeeding

# Web sites

Postpartum support international

http://www. postpartum.net

(Illinois chapter: www.PPDIL.org)

PPD IL HELPLINE 847-205-4455

Depression after delivery

http://www.depressionafterdelivery.com

Melanie Blocker Stokes

http://www.melaniesbattle.org

# Peripartum Mental Health Consultation Service for Providers

1-800-573-6121

# Video: Descent into Desperation

Courtesy of Digital Realm
Oak Brook, Illinois