

Women, Hormones, Mood and Sex

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How the king of beasts handles PMS:



Outline

- The Female Brain
- Puberty, the Menstrual Cycle and PMDD
- Pregnancy, Mood and Postpartum
- Perimenopause, Mood and Sex
- Menopause, Mood and Sex

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Female and Male Brain

Male: XY

- Until 8 wks old, every fetal brain looks female. Female is nature's default gender setting
- At 8 weeks of fetal age: Y chromosome (SRY gene) produces the fetal testicle, which produces a testosterone surge
- Testosterone kills off cells in the communication centers and grows more cells in the sex and aggression centers
- This permanently changes structure and function into the male brain program

Female: XX (the archetypal brain)

- If the testosterone surge doesn't happen, the female brain continues to grow
- The female brain sprouts more connections in the communication areas and areas that process emotion
- Women are more talkative than men

Female and Male Brain

- Under fMRI scan, we can see differences in female vs male brains.....

WOMEN:

- Language and hearing brain centers: women have 11% more neurons than men
- The hippocampus (hub of emotion and memory formation) is larger in women
- Circuitry for language and observing emotion in others is larger in women
- Women (on ave) are better at expressing emotion and remembering details of emotional events

Female and Male Brain

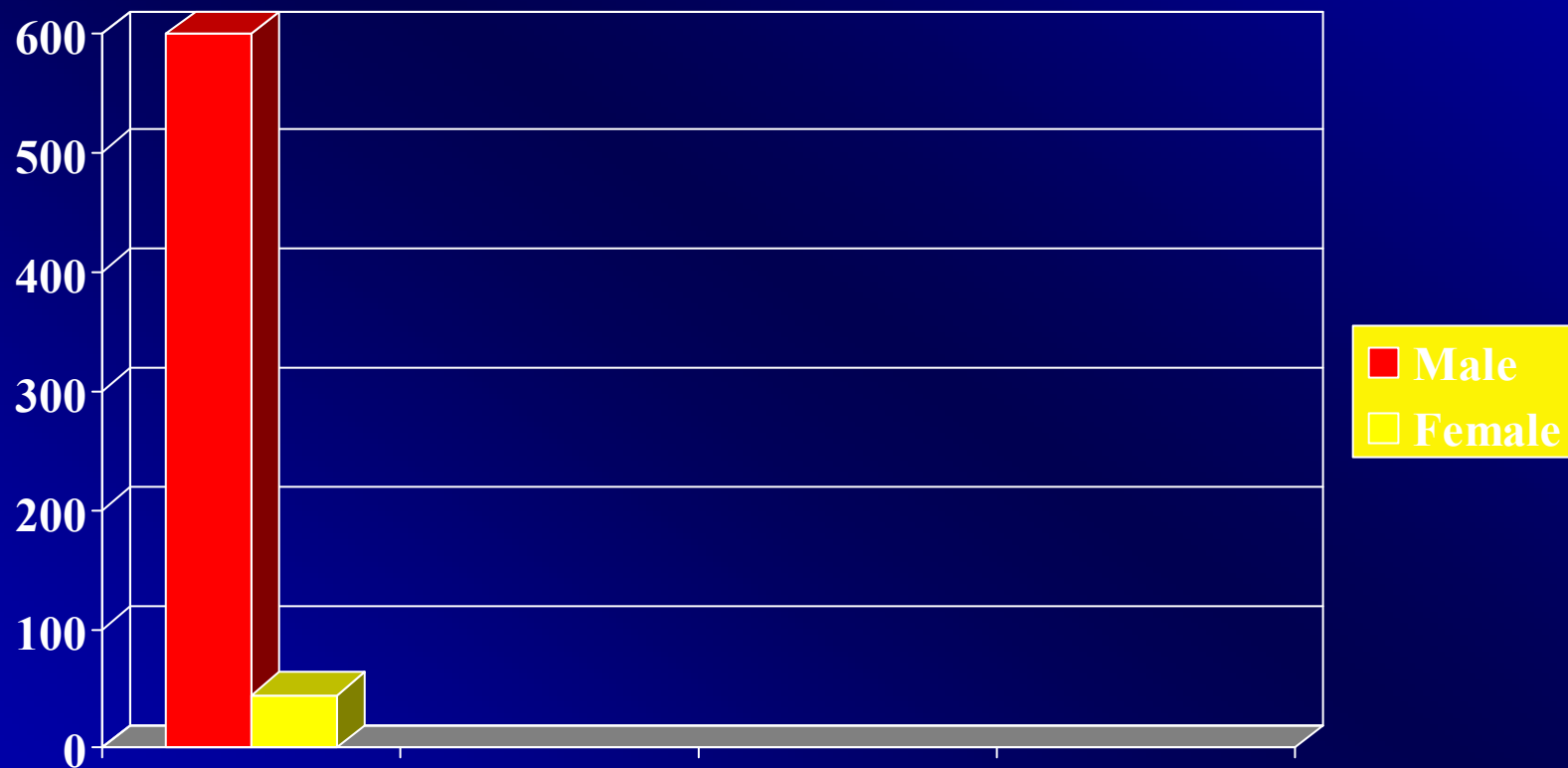
MEN:

- Men have 2 ½ times the brain space devoted to sexual drive
- Larger brain centers for action and aggression

Female and Male Brain

- Sexual thoughts float through a man's brain every 52 sec on average
- Through a woman's mind.....?
- About 1x/ day. 3-4x on her hottest day

Male/Female Testosterone Levels



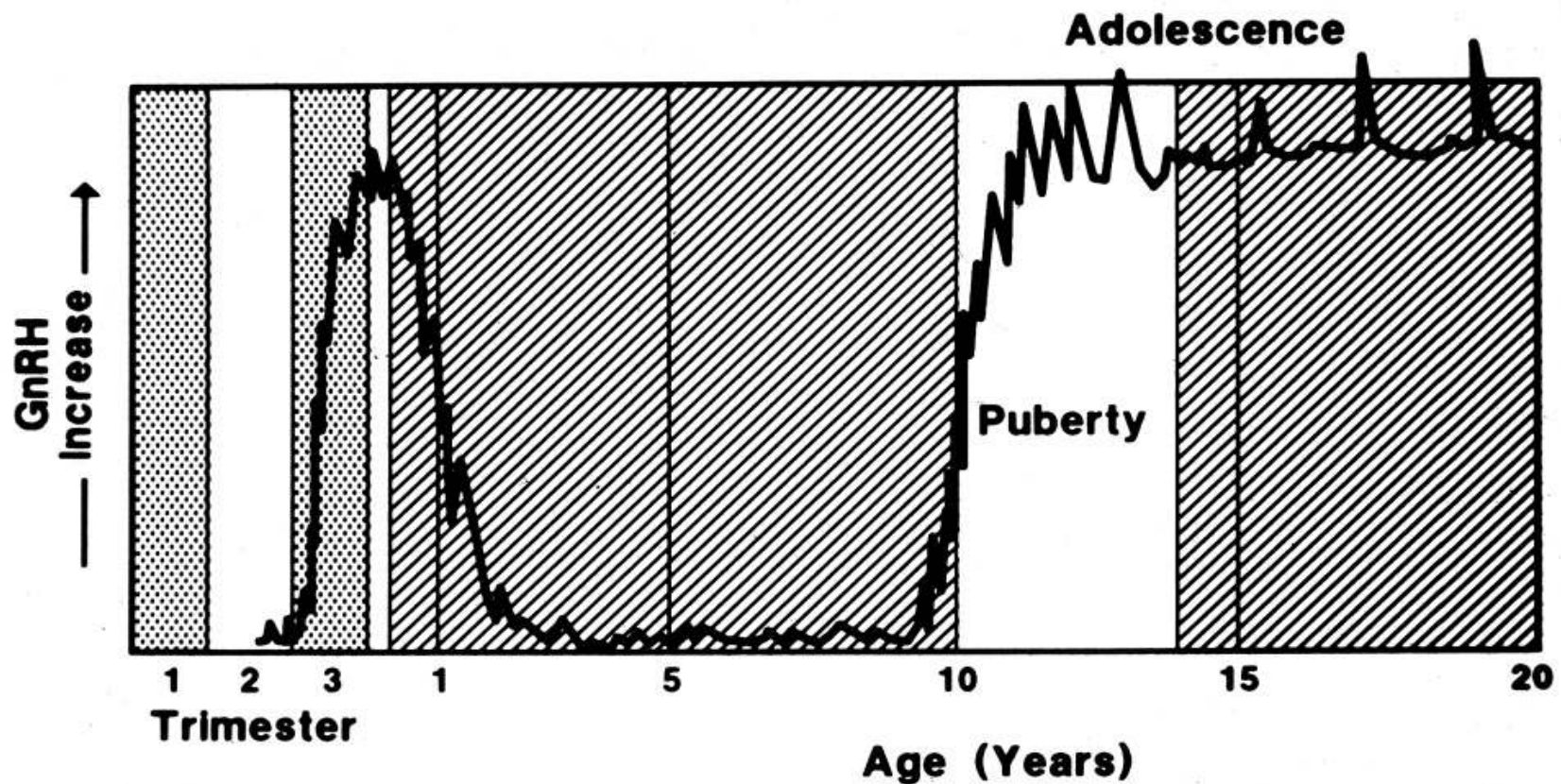
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Female Puberty

- Starts age 8-9 years old
- Gradual awakening of the ovaries
- Ovaries secrete more and more estrogen every year finally triggering puberty
- Estrogen takes control of the hypothalamus and initiates the menstrual cycle, age 12.4

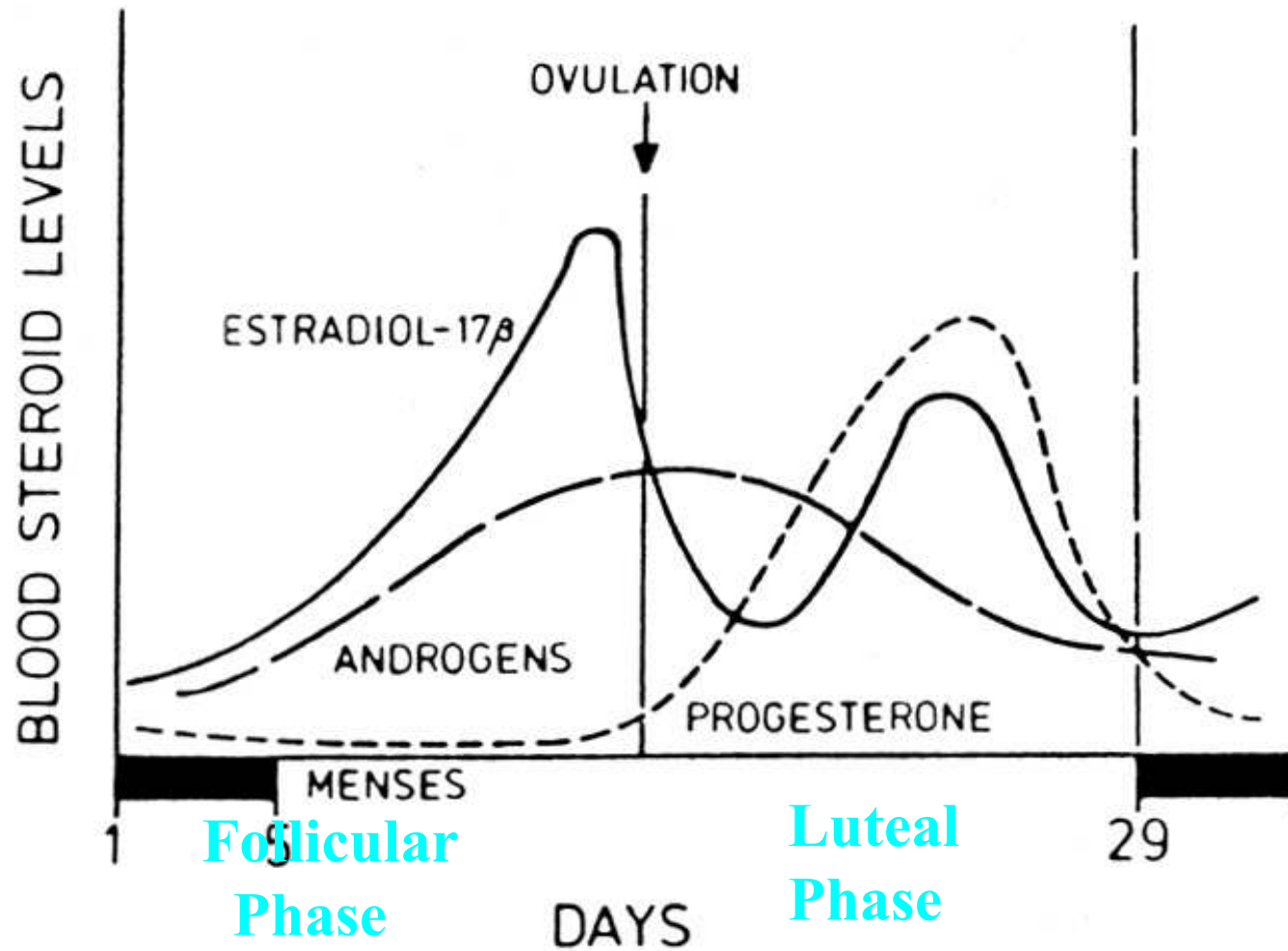
Hormone Pulses from the Hypothalamus: Fetal Life to Puberty



Ovaries Take Over the Brain

- Fluctuating levels of estrogen from the ovaries now control the hypothalamus and pituitary
- Estrogen activates the brain (more alert effect) and progesterone deactivates the brain (more calming effect) during the normal menstrual cycle

Menstrual Cycle



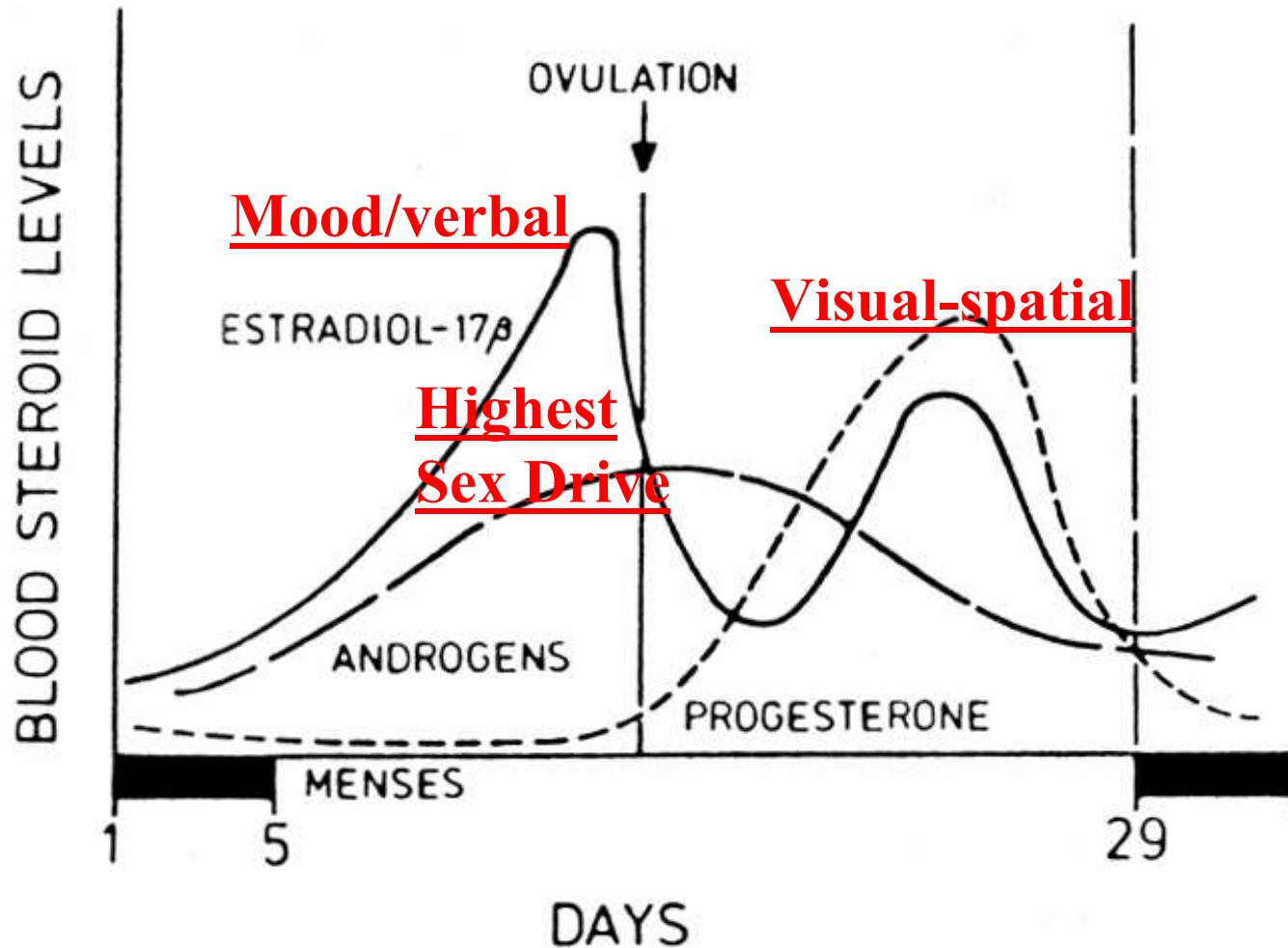
Sex steroid changes in human menstrual cycle.

Brain Variability Controlled by Ovarian Hormones

Depending on where a woman is in her cycle, there is variability in the following:

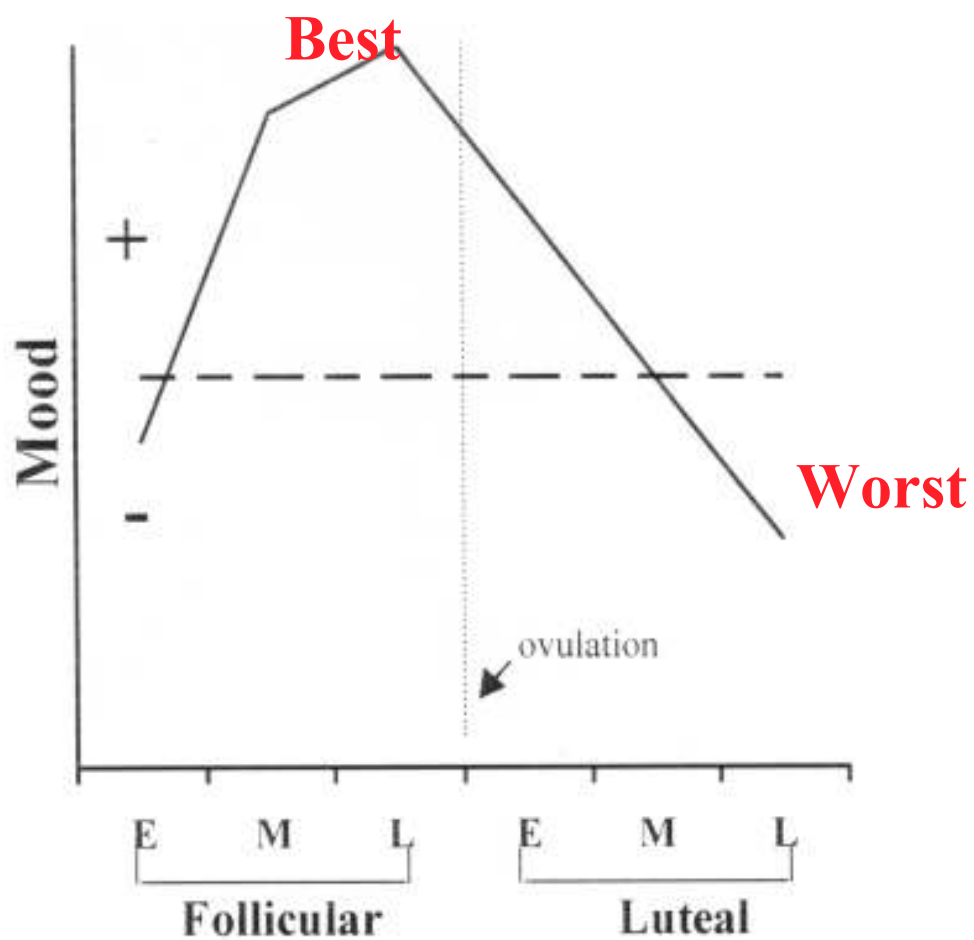
- Mood: 20% variability in normal women
- Verbal performance: 25% variability in normal women
- Sexual interest: 30% variability in normal women
- Visual-spatial performance: 20% variability in normal women

Menstrual Cycle



Sex steroid changes in human menstrual cycle.

Mood Changes Across the Menstrual Cycle



week 1 2 3 4

Mood

- **80%** of women acknowledge some increased emotional sensitivity before their period starts
- **8-10%** have severe 'hell-on-earth' mood changes the 2 weeks before their period

What is going on here?

- The female brain experiences hormonally determined emotional fluctuations
- Not a big deal for 80%
- A **VERY** big deal for 8-10%

PMDD vs Normal PMS

Normal PMS (Premenstrual Syndrome):

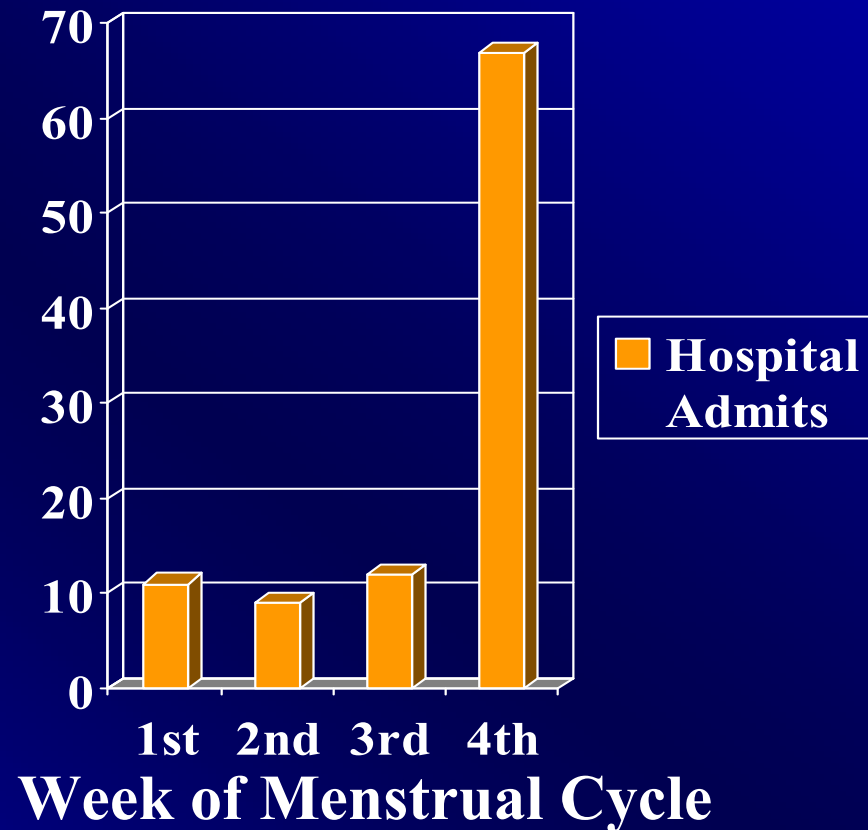
- 80% of women
- Mild to moderate emotional fluctuations

PMDD (Premenstrual Dysphoric Disorder):

- 8-10% of women
- Severe moods swings, depressed mood, irritability, anxiety and physical symptoms (occurring exclusively during the luteal phase (weeks 3-4) and remitting within 3 days of the onset of menses)

Menstrual Cycle Week and All Psychiatric Admissions

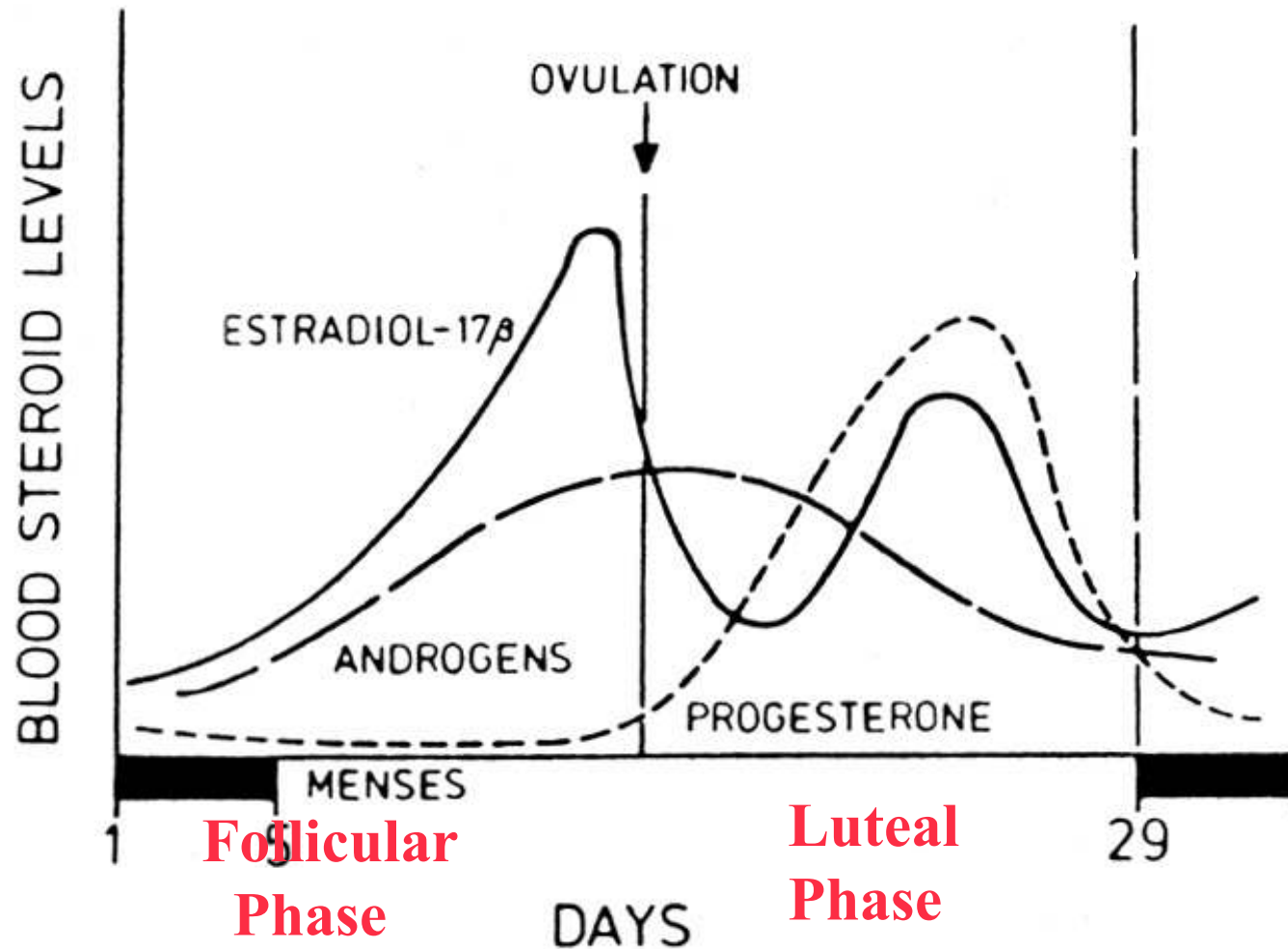
- If random, admissions of women to psychiatric hospitals for all psychiatric diagnoses would be 25% on each week of the menstrual cycle



How does estrogen and progesterone effect the brain?

- Estrogen acts to increase neuronal excitability thus producing a brain stimulant-like effect.
- The progesterone metabolite, allopregnanolone (ALLO), produces a sedating/calming Valium-like effect.

Menstrual Cycle



**Follicular
Phase**

**Luteal
Phase**

Sex steroid changes in human menstrual cycle.

PMDD

Progesterone → Allopregnanolone (ALLO)

soothing, like Valium

- ALLO= a neuroactive metabolite of progesterone and works on GABA (gamma-aminobutyric acid) receptors in the brain
- Hence, ALLO is a powerful anxiolytic, anticonvulsant, and anesthetic agent which decreases anxiety and depression.
- Barbituates, benzodiazepines and alcohol also work at this receptor.

PMDD

Progesterone → Allopregnanolone (ALLO)

soothing, like Valium

- Prozac, Paxil and Zoloft were found not only to increase Serotonin, but also to increase ALLO production by activating 2 enzymes that convert progesterone to ALLO
- Imipramine (Tofranil) had no effect on ALLO production.

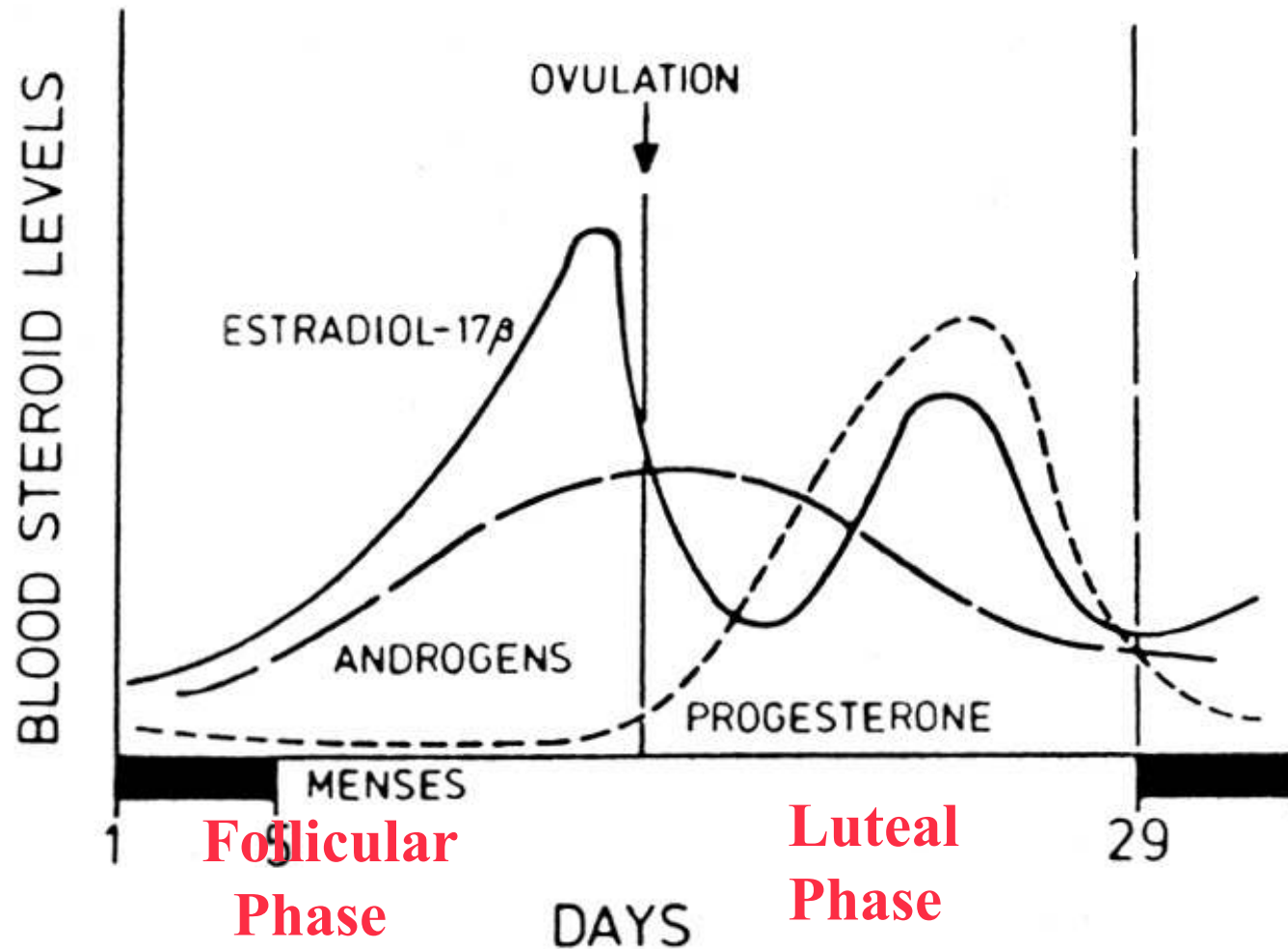
Journal:

-Lisa Griffin, MD, PhD and Synthia Mellon, PhD.

Selective serotonin reuptake inhibitors directly alter activity of neurosteroidogenic enzymes.

Proc Natl Acad Sci U S A. 1999 Nov 9;96(23):13512-7.

Menstrual Cycle



**Follicular
Phase**

**Luteal
Phase**

Sex steroid changes in human menstrual cycle.

PMDD

Possible Treatments

- **Hormones:**
 - Start an OCP, or change to one with a progesterone good for mood
 - Take OCP continuously
 - Women are sensitive to hormones in different ways – some to the hormone fluctuation, some to the amount, and some to the progestin type
- **SSRI's:**
 - Either 7-10 days before menses to help boost ALLO, or daily if also depressed

All Possible PMDD Treatments

Antidepressants

- SSRI*
- SNRI*
- Clomipramine**

Ovulation Suppression

- OCP's*
- GnRH Agonists (Lupron)**
- Danazol (inhibits LH/FSH)
- Oophorectomy

Anxiolytics

- BZD**
- Buspar**

Other

- Exercise
- Calcium**
- CBT*
- Chasteberry
(may reduce FSH or Prolactin)
- Vit B6
- NSAIDS
- Diet

*Efficacy in double-blind studies of PMDD

**Efficacy in double-blind studies of PMS

-Teri Pearlstein, M.D. Warren Alpert Medical School of Brown University, APA Conference 2008

Which birth control pill is good for mood?

- Lower progestin potency:

Ortho Evra patch

Ovcon 35

Ortho-TriCyclen

Othro-Cyclen

Brevicon

Modicon

Necon 1/35

Alesse

Levlite

Tri-Levlen

Triphasil

Trivora

Which birth control pill is good for mood?

- Women are sensitive to hormones in different ways – some to the progestin, some to the amount and some to the hormonal fluctuation.
- Seasonale, or any monophasic oral contraceptive pill (OCP) taken continuously (having only 1 period every 3 months) can also help stabilize mood.
- Of note, YAZ® is the only OCP given an indication for PMDD. However, it has a high progestin potency and may not be ideal for every woman.
- YAZ shortens the placebo week from the regular 7 days to 4 days – to minimize the time of hormonal fluctuation.
- Women who are sensitive to hormonal fluctuation should avoid triphasic OCP's.

Which birth control pill is good for mood?

- Bottom line: Treatment needs to be individualized for each patient and trial and error may be necessary. It takes about 2 cycles to see if a certain OCP will work for a woman or not. Evidence based studies comparing one OCP to another are lacking.

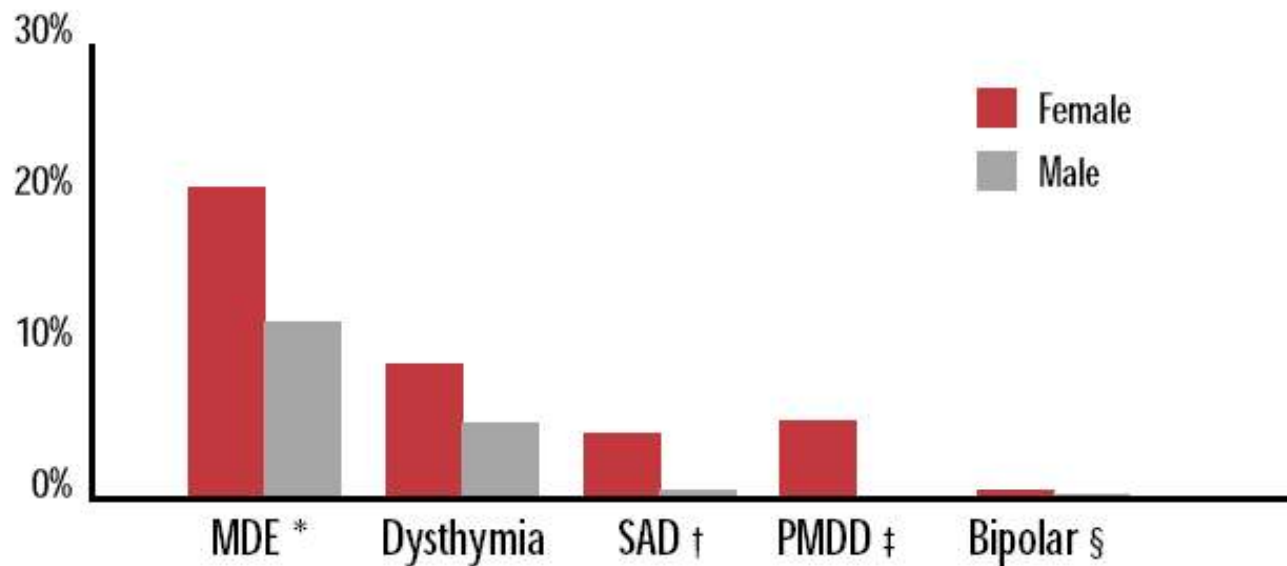
Disorders with Premenstrual Exacerbation (PME)

- Affective disorders
- Anxiety disorders
- Psychotic disorders
- Eating disorders
- Personality disorders
- Substance abuse
- Migraine
- Allergies
- Asthma
- Seizures

Male/Female Differences in Mood Disorders

- 2:1 ratio worldwide female greater than male
- 165 cultures, ratio varies from 1.7:1 up to 2.2:1
- Remarkably stable throughout cultures
- Ratio in childhood is 1:1
- Ratio starts to move toward 2:1 during puberty
- Near menopause, ratio returns towards 1:1

Prevalence of Mood Disorders by Gender

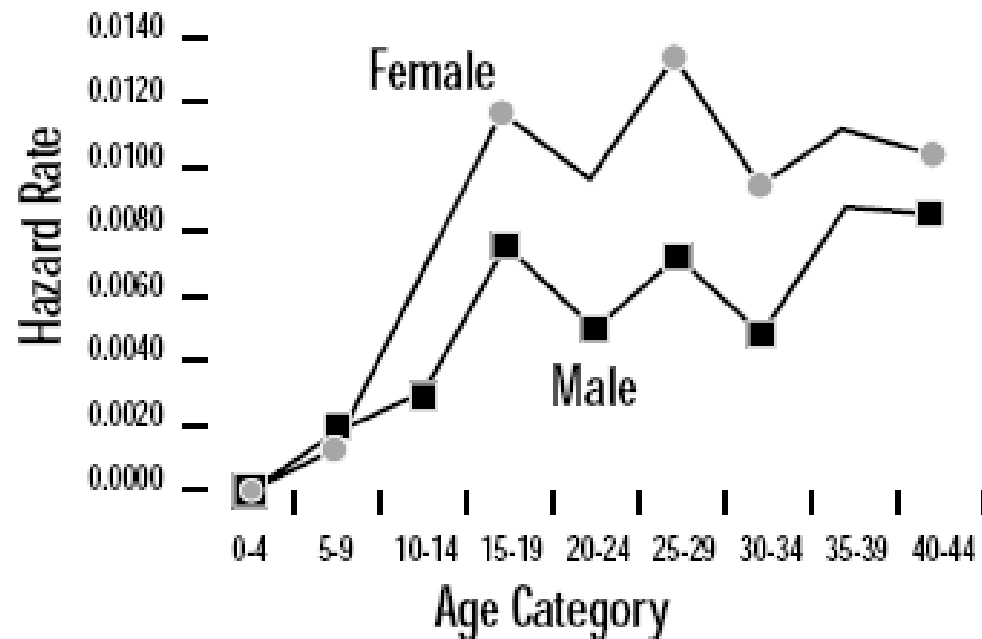


* Kessler RC, et al. *Arch Gen Psychiatry*. 1994;51:8-19. † Parry BL. In: *Psychopharmacology: The Fourth Generation of Progress*. 1995:1029-1042. ‡ Rivera-Tovar AD, Frank E. *Am J Psychiatry*. 1990;147:1634-1636. § Weissman M, et al. *J Affect Disord*. 1993;29:77-84.

Risk for Depression by Age & Sex

Depression Over the Lifespan

MDE Hazard Rates by Age and Sex



Kessler RC et al. *J Affect Disord.* 1993;29:85-96.

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The Mommy Brain: Hormones, Pregnancy and Mood

- The smell of a newborn baby stimulates the woman to produce oxytocin – a love potion creating baby lust.
 - Oxytocin is also released when talking to friends, or creating a connection
 - “A feel good” hormone – released in bonding and during orgasm
- Throughout pregnancy, a woman is marinated in neurohormones manufactured by the fetus and placenta.

The Mommy Brain: Hormones, Pregnancy and Mood

- Progesterone: Spikes from 10-100x normal!
 - This has a calming, Valium-like effect
 - Get sleepy, eat more
- Thirst and hunger centers on full blast
- Women become sensitive to smells, especially of foods, to avoid eating something that could harm the fragile fetus.
 - But, it could make her nauseated most of the time.

The Mommy Brain:

Hormones, Pregnancy and Mood

- Estrogen and progesterone help protect against stress hormones (like cortisol) during pregnancy.
- By late pregnancy, the stress hormones in a woman's brain are as high as they'd be with strenuous exercise!
 - However, their impact isn't stress, but to make a pregnant woman more vigilant about her safety, nutrition, surroundings – and less concerned with other tasks: like conference calls and organizing her schedule.
 - That's why pregnant woman (especially in the last month of pregnancy) complain of feeling disorganized, distracted, forgetful.

The Mommy Brain: Hormones, Pregnancy and Mood

- At the same time, the size and structure of a woman's brain are changing, too!
- Between 6 months to the end of pregnancy, fMRI scans show that her brain is shrinking!
- This state gradually returns to normal 6 months after giving birth.
 - This may be parts getting larger as others get smaller.
 - Some studies show that the cortex (the thinking part) enlarges during pregnancy.
 - We still don't know what this means.
 - Major restructuring and metabolic changes going on.
 - It's not that the woman is losing brain cells. Scientists think the woman is about to start restructuring so the shrinkage is a result of changes in cellular metabolism required for restructuring brain circuits.
 - In the final few weeks before birth, the brain begins to increase again, as it constructs large networks of maternal circuits.

Depression and Pregnancy

- Out of every 10 women who are pregnant, one or two have symptoms of major depression.
- Women who have been depressed before are at higher risk.
- Depression is a serious medical condition. It poses risks for the woman and her baby. But a range of treatments are available:
 - counseling, psychotherapy, support groups, therapy with light, and medications
 - Individual therapy is highly recommended

Depression and Pregnancy

- Often a pregnant woman wonders whether antidepressant drugs, such as Zoloft and Prozac, will harm her baby or herself.
- There are no simple answers. Each woman and her health care providers must work together to make the best decision for her and her baby.
- The drugs used to treat depression have both risks and benefits.

Depression and Pregnancy

- Depression carries serious risks for the pregnant woman and her baby. These risks include:
 - Poor weight gain
 - Use of drugs or alcohol to self-medicate
 - Suicidal thoughts and/or suicide
 - Poor nutrition
- The above symptoms can lead to premature birth, low birth weight and developmental problems.
- In addition, depressed mothers are often less able to care for themselves or their children, or to bond with their children.

What are the symptoms of depression?

- A woman who is depressed feels sad or “blue” and has 4 other symptoms that last for two weeks or longer:
 - Trouble sleeping
 - Sleeping too much
 - Lack of interest
 - Feelings of guilt
 - Loss of energy
 - Difficulty concentrating
 - Changes in appetite
 - Restlessness, agitation or slowed movement
 - Thoughts or ideas about suicide
- Things other than depression can cause some of these symptoms. For instance, changes in appetite and trouble sleeping are common in pregnancy. Some medical conditions, such as anemia and hypothyroidism, can cause a pregnant woman to lack energy.

Depression and Pregnancy

- During pregnancy, two patients—the mother and the fetus—are exposed to the drug.
- Medications that are safe for a woman are sometimes risky for a fetus.
- Because of this, researchers have not studied many drugs during pregnancy.
- Several drugs have been used for many years without any obvious signs of serious risk to the baby. But some researchers have reported that some antidepressants may have increased risks.
- Research has clearly shown that women who are not pregnant and are depressed are very likely to become ill again if they stop taking their medications.
- A recent study in 2006 suggests that the risk of depression relapse is high in pregnant women who discontinue their antidepressant during pregnancy.

Depression and Pregnancy

- What I tell women: the risks....
 - During pregnancy
 - During delivery
 - After delivery

During Pregnancy

- One study in 2006 found that pregnant women with major depression are very likely to become ill again during their pregnancy if they stop taking their medication.
- Many studies have found no link between antidepressants and serious malformations in newborns. But in 2005, the FDA issued a warning about Paxil based on several studies: taking the drug during the first three months of pregnancy may increase the risk of birth defects, particularly heart defects.
- Other studies have found small increased risks of: heart defects, hydronephrosis (kidney defects), cleft palate (5% vs the usual 2-4%).

During Pregnancy (cont)

"Clinicians and patients need to balance the small risks associated with SSRIs against those associated with undertreatment or no treatment."

-September 2009, *The British Medical Journal (BMJ)*

During Delivery

- ***Neonatal Abstinence Syndrome (NAS):***
 - Some babies born to mothers who are taking SSRI antidepressants show signs of “withdrawal:” breathing or feeding problems, jerky movements, seizures, irritability, abnormal crying and tremor.
 - Symptoms usually subside from 48 hours to a few days.
- ***Persistent Pulmonary Hypertension of the Newborn (PPHN):***
 - In February 2006, Christina Chambers and her team came out with this study.
 - Babies exposed to SSRIs in late pregnancy (after 20 weeks) may be more likely to have PPHN.
 - Only 6 to 12 women per 1,000 who use SSRIs late in pregnancy will have babies with pulmonary hypertension (vs. 1-2 per 1,000 in the general population).
 - 99% of women on SSRIs late in pregnancy won't get PPHN.
 - One explanation is that Serotonin has vasoconstrictive properties and can increase pulmonary vascular resistance.

During Delivery (cont)

- Multiple studies have found that both untreated depression and SSRI exposure have been correlated with early or preterm birth.
- One study published in March 2009 in the *American Journal of Psychiatry* found that SSRI use in late pregnancy correlated with an elevated risk of gestational hypertension and preeclampsia in the mother.

After Delivery

- Some researchers have studied children whose mothers took antidepressants. They have found no link to serious problems with language, behavior or intelligence.
- There has been no data reported on long term effects of antidepressants on the baby's well being. So far, there is no evidence of long term effects.

Choosing an Antidepressant

- We don't know all the answers. No drug is entirely safe. A woman and her health care team must look at her case and carefully weigh:
 - The risks and benefits of various drugs
 - The risks and benefits of other types of treatment
 - The risk of untreated depression for the woman and her baby
- If a woman has been or is currently stable on a certain SSRI, that medication is sometimes continued, unless it is Paxil, which is generally contraindicated.
- Choosing an antidepressant needs to be done on a case by case basis. Of note, the literature changes frequently in this area.

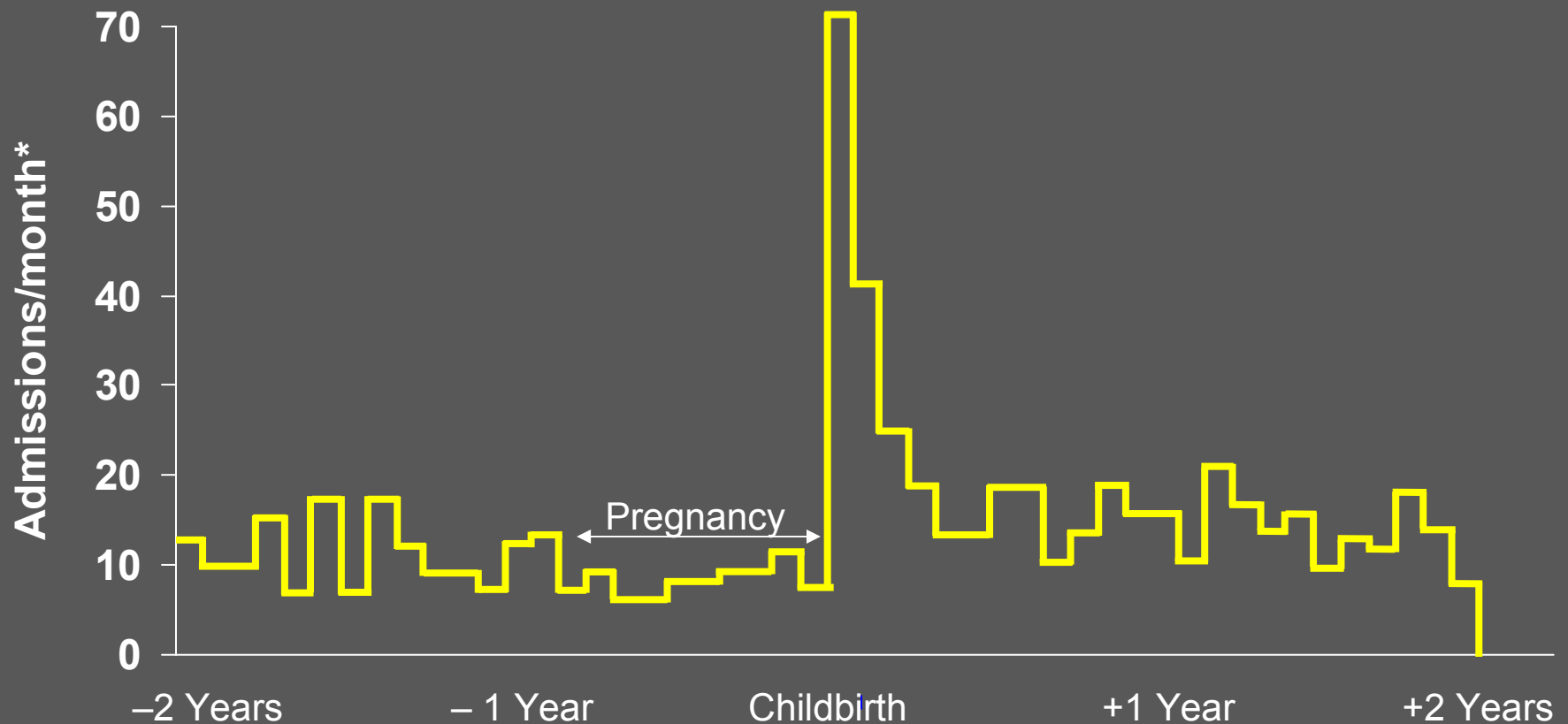
Important Points

- Make sure that the pt is followed closely by a therapist and/or psychiatrist and an Ob/Gyn
- Recommend prenatal vitamins and folic acid
- Check thyroid, blood count and other lab work to rule out medical reasons for low mood or energy
- It is a good idea to deliver the baby in a hospital versus at home by a midwife, as they can adequately monitor and assess any possible delivery complications
- Stress reduction techniques and individual therapy (at least weekly) are both encouraged
- It is always a good idea to be on the lowest number of medications possible, and on the lowest dose necessary
- With any medication during pregnancy, start low and go slow

Within the first 12 months after giving birth: 10% of women will have had 'Postpartum Depression'

- Huge 'crash' in hormones after pregnancy
- Postpartum: the brain and ovaries experience the re-establishment of menstrual cycle hormone-pulses just as during the onset of puberty

Psychiatric Admissions in 2 Years Before and After Delivery



*Rate of psychiatric admissions in the 2 years before and after delivery in a population of 470,000 people with 54,087 births in a 12-year period
Kendell RE, et al. *Br J Psychiatry*. 1987;150:662.

Postpartum Depression

- Postpartum Depression:
 - Technically, onset is within 4 weeks after childbirth, but can be seen up to 1 yr later
 - 10-15% of women will experience postpartum depression within the 1st 12 mo after giving birth
- 'Baby blues':
 - Affect up to 80% of women during the 10 days postpartum (usually lasts 2 weeks)
 - These are transient, do not impair function, and don't meet MDD criteria

Postpartum Mood Conditions

Disorder	Incidence (%)	Onset/tx	Presentation	Sequellae
Postpartum blues	80%	1-2 wks, support-reassurance	80% resolve by week 2; 20% evolve into PPD; Mood lability, irritability, tearfulness	None
Postpartum depression	10 to 15%	sx begin within 1 month; antidepressants	Major depression often with obsessions re: baby's health	Increases risk of future postpartum and non-postpartum mood disorders
Postpartum psychosis	0.2%	95% begin within days-antipsychotics, mood stabilizers, benzodiazepines, consider ECT	Symptoms like BPAD/mixed/rapid cycling risk of infanticide	Increases risk of future postpartum and non-postpartum mood disorders

Bright. *Am Fam Physician*. 1994;50:595. Suri R and Burt VK: *Jrnl Prac Psych Behav Hlth* 3:67-77, 1997. Cogill et al *BMJ*: 1986;292:1165-7, Sharp et al *J Child Psychiatry* 1995;36:1315-36, Stein et al *Brit J Psychiatry* 1991;158:46-52

Bipolar Disorder and Pregnancy

- Prescribing meds requires balancing the potential for neonatal malformations against the high risk of relapse when patients discontinue their medications.
- **Most psychotropics are category "C" or "D,"** which imply a chance of harm to the exposed fetus. Category "B" drugs would appear safer, but this rating could simply indicate a lack of adequate human data or that no data have shown harm in animals.
- **No psychotropics are classified as "A,"** meaning either some risks are associated with every psychotropic or the risk of some agents has not been adequately explored. Furthermore, no psychotropics are FDA-approved for use during pregnancy.

Bipolar Disorder and Pregnancy

- **Risks without medication:**
 - Teratogenicity notwithstanding, psychotropic intervention is the most effective treatment for women with bipolar disorder.
 - Patients who discontinue mood-stabilizing medication after conception increase their risk of relapse into depression or mania, either of which could lead to complications and untoward effects on the fetus.
 - **Depression during pregnancy** has been linked to low birth weight and preterm delivery. Other risks are decreased appetite, substance use and abuse and lower use of prenatal care.
 - **Untreated mania during pregnancy** may lead to impulsive, high-risk behaviors that endanger her and the fetus.

Bipolar Disorder and Pregnancy

- Risks to review with each medication....
 - During pregnancy (teratogenicity)
 - During delivery (obstetric and perinatal complications)
 - After delivery (long-term abnormalities)

Bipolar Disorder and Pregnancy

- Treatments:
 - Mood Stabilizers (lithium, valproate, lamictal and carbamazepine)
 - Antipsychotics
 - Benzodiazepine
 - Antidepressants
 - ECT
 - Therapy

Bipolar Disorder and Pregnancy

- Lithium:
 - Cardiovascular malformation, such as Ebstein's anomaly (risk is 20x higher than unexposed baby, but still low: 1/ 1,000 births)
 - Thyroid and kidney problems in mom or bay (must monitor this)
 - “Floppy baby” syndrome
 - Stop Lithium 24-48 hrs before delivery and check levels in mom and baby
 - No long-term sequelae
 - If breastfeeding, monitor levels in baby and watch for side effects

Bipolar Disorder and Pregnancy

- Anticonvulsants:
 - Neural tube defects such as spina bifida and encephaly in 2 to 5% of those exposed
 - Taking folic acid helps prevent this (4 mg/ day before conception and at least 3 months after)
 - Craniofacial anomalies, microcephaly, growth retardation, and heart defects
 - More minor malformations: rotated ears, depressed nasal bridge, short nose, elongated upper lip, and fingernail hypoplasia
 - Vitamin K should be taken to promote mid-facial growth and the formation of proper blood clotting factors in fetuses
 - Teratogenicity increases with the use of multiple anticonvulsants and possibly with higher maternal plasma levels and toxic metabolites

Bipolar Disorder and Pregnancy

- Lamotrigine (Lamictal):
 - In 2006, the North American AED Pregnancy Registry, located at Massachusetts General Hospital in Boston, Massachusetts, found that infants who are exposed to lamotrigine as monotherapy in the first 3 months of pregnancy (lamotrigine was used as the only AED by the mother) have a much higher risk of having an oral cleft problem (cleft lip or palate), than infants born to women in a comparison group and who were not exposed to lamotrigine during pregnancy
 - In this study, of 564 women who received lamotrigine alone, 5 instances of isolated cleft lip or palate were seen
 - This data gives a prevalence rate of 8.9/1000 of cleft problems on lamotrigine (0.008% risk)
 - The rate for oral cleft problems without lamotrigine in the general population is 0.50-2.16/1,000 (0.0005-0.002%)

Bipolar Disorder and Pregnancy

- Take Home Points:
 - The three most commonly used mood stabilizers are all teratogenic
 - The least risk may occur with lithium (0.1%) versus valproate (2 to 5%) or carbamazepine (1 to 3%)
 - The data for lamotrigine is new, but there is a 0.008% risk of oral cleft problems seen so far
 - These risks must be weighed against the up to 50% chance of relapse with medication discontinuation

Bipolar Disorder and Pregnancy

- First-Generation Antipsychotic Medications:
 - Since they have a longer history of use than many mood stabilizers, their effect on pregnant women is better documented
 - Can be used instead of a mood stabilizer in either the 1st trimester or the entire pregnancy – especially in women who have responded well to these meds for mood stabilization in the past
 - Though studies are small, no adverse effects have been noted in the majority of cases where women take first-generation antipsychotic medications during pregnancy or breastfeeding

Bipolar Disorder and Pregnancy

- Second-Generation Antipsychotic Medications:
 - Few studies reported
 - Not associated with birth defects
 - However, they are associated with weight gain, gestational diabetes, and high blood pressure
 - Weight gain, blood sugar levels, and blood pressure should be monitored carefully in all pregnant women taking second generation antipsychotic medications

Bipolar Disorder and Pregnancy

- Benzodiazepines:
 - Rarely a primary treatment for mania or depression
 - Difficulty sleeping and anxiety are powerful triggers for the recurrence of episodes in bipolar disorder
 - Medications that stay in the body the least amount of time are preferred
 - Some early reports of possible cleft lip/ palate when taken in the 1st trimester (<1/1000 cases)
 - Excreted in breast milk, but few reports of complications
 - Watch baby for sleepiness/ lethargy

Bipolar Disorder and Pregnancy

- ECT:
 - Proven effective for acute mania and depression
 - ECT has few side effects and may be safer than drug therapy in this population
 - Two reviews support the efficacy and relative safety of ECT treatment during pregnancy, although more evidence is needed:
 - Miller LJ. Use of electroconvulsive therapy during pregnancy. *Hosp Community Psychiatry* 1994;45:444-50.
 - Ferrill MJ, Kehoe WA, Jacisin JJ. ECT during pregnancy: physiologic and pharmacologic considerations. *Convuls Ther* 1992;8:186-200.

Bipolar Disorder and Pregnancy

- Therapy:
 - Therapy can help improve functioning in social and occupational settings, minimize loss of sleep (which often precipitates mania), and help prevent relapses
 - Structured daily activities, which help minimize sleep deprivation and reduce rapid shifts in moods, are very important during pregnancy

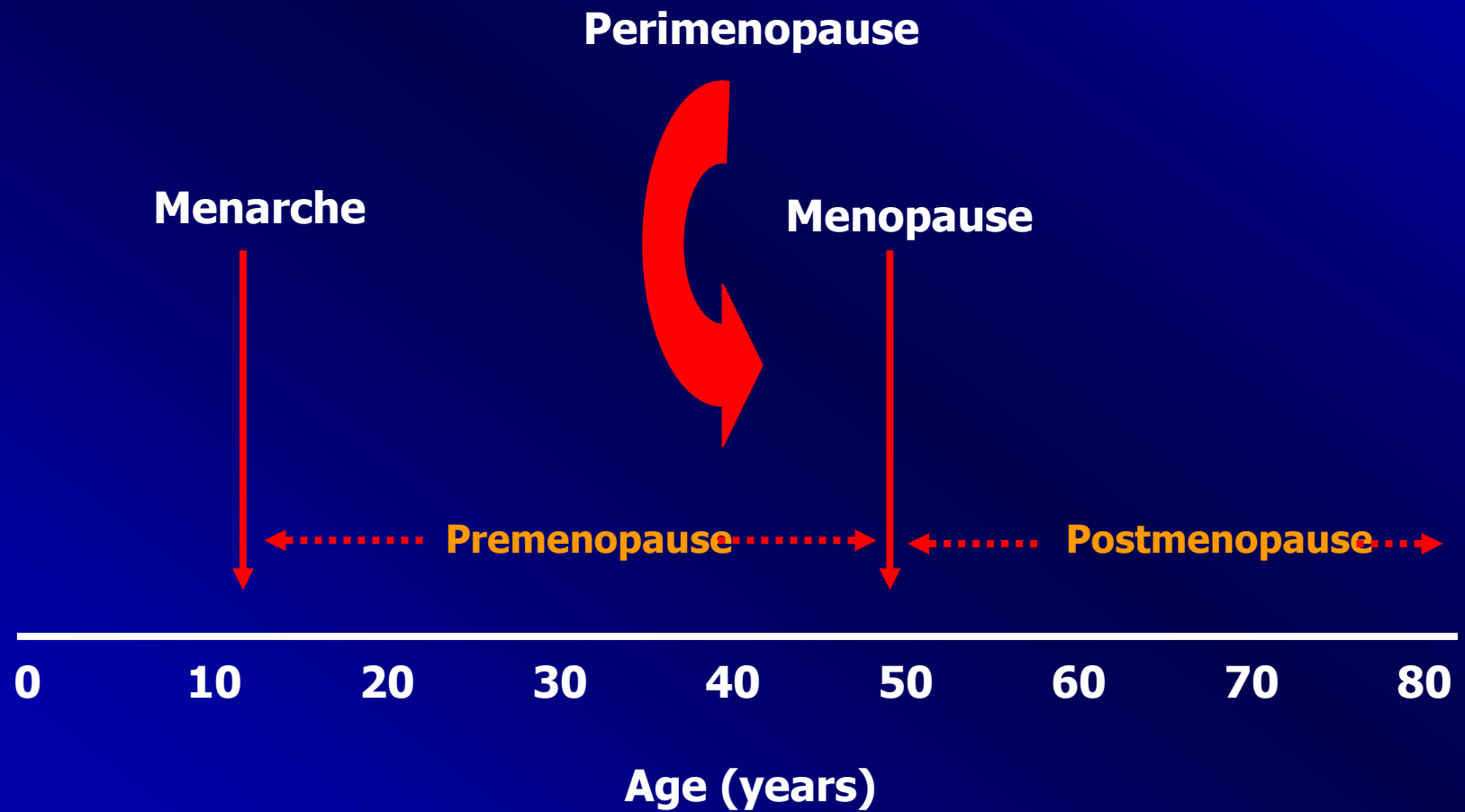
Return of Sexual Interest after Delivery

- If breastfeeding, after 6-12 months
 - Testosterone levels and menstrual cycle remain suppressed longer
- Without breastfeeding: 3-4 months

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Reproductive Life Cycle



Perimenopause: 2-9 years

- 40-60% complain to M.D. about
 - Irritability and insomnia
 - Mood swings and crying easily*
 - Fatigue and weight gain
 - Sexual complaints
- 52% get a first time diagnosis of depression or anxiety, even without a prior history of depression!!

Depression and the Menopausal Transition

- Symptoms may appear up to 7 yrs prior to last menses
- Mild mood symptoms are common
- A hx of Major Depression increases the risk of Major Depression during menopause
- Estrogen replacement therapy often relieves minor symptoms, but not MDD

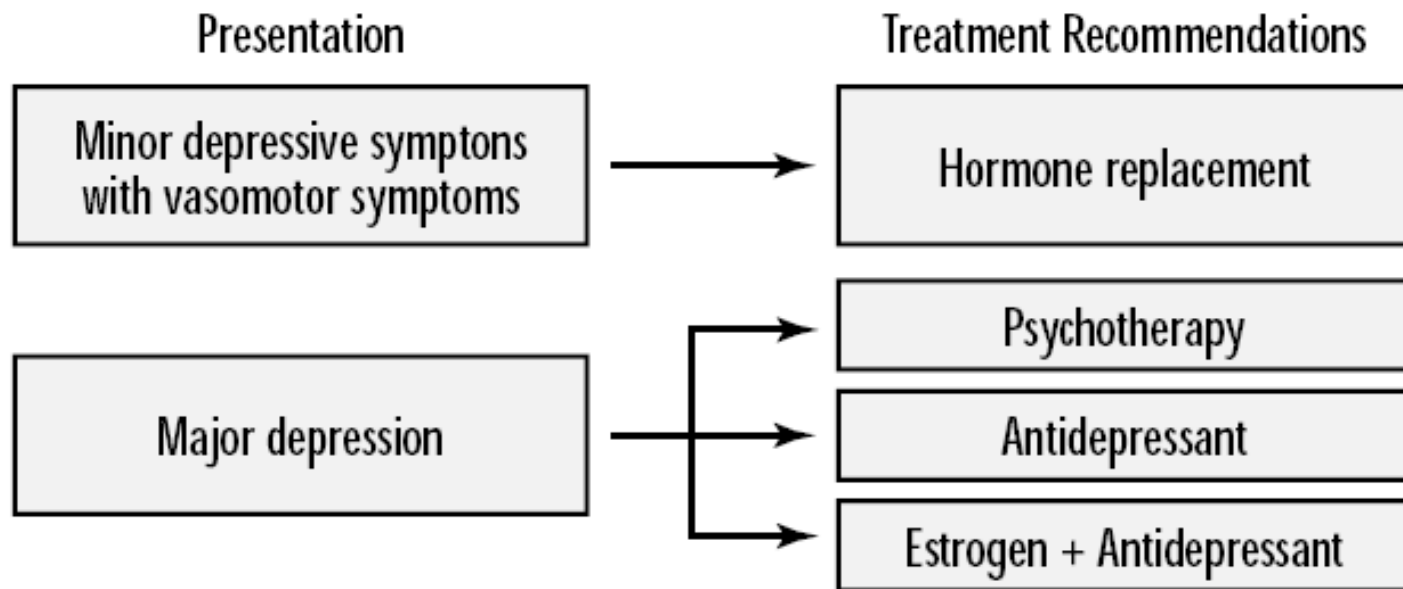
Signs and Symptoms of Ovarian Decline in Peri and Postmenopausal Women

- Menstrual cycle changes
- Insomnia
- Vasomotor symptoms
 - hot flushes, night sweats
- New or increased depression
- Generalized anxiety
- Increasing FSH with hormonal variability
- Vaginal dryness
- Cognitive symptoms: brain fog
- New onset migraines
- Low libido

Risk Factors for Perimenopausal Depressive Symptoms

- Hot flushes
 - Depressive symptoms 4.6 times more likely
 - Association specific to perimenopause
- Prior depression
 - Depressive symptoms 4–9 times more likely

Perimenopausal Depression: Treatment



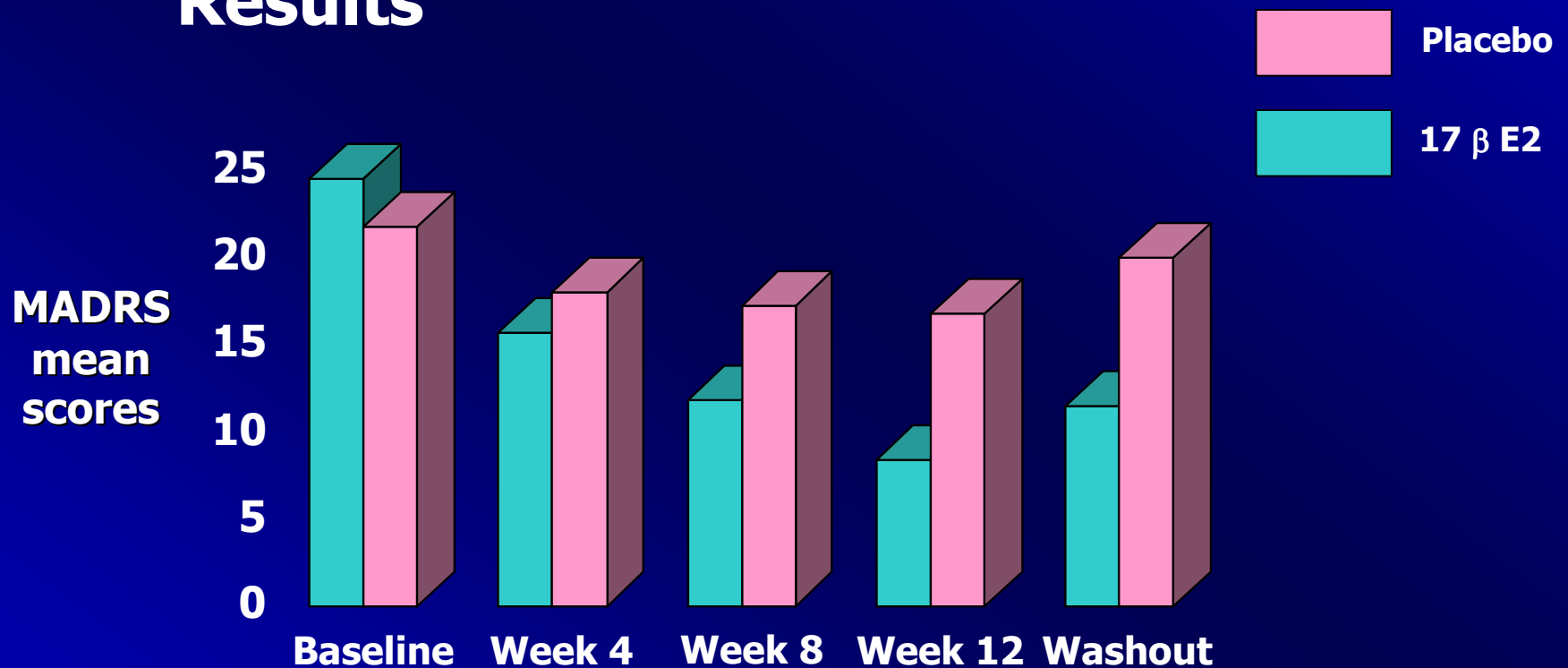
* If no contraindications exist. Brady. Available at:

http://www.medscape.com/Medscape?CNO/2000/APA/Story.cfm?story_id+1188. Accessed: 5/31/00.

Hunter. Brit Med J. 1996;313:1217. Burt et al Harv Rev Psychiatr 6:121-132, 1998.

Efficacy of 17 β -estradiol (n=25) vs placebo (n=25) for the treatment of perimenopausal depressive symptoms

Results



C Soares, et al., 2001.

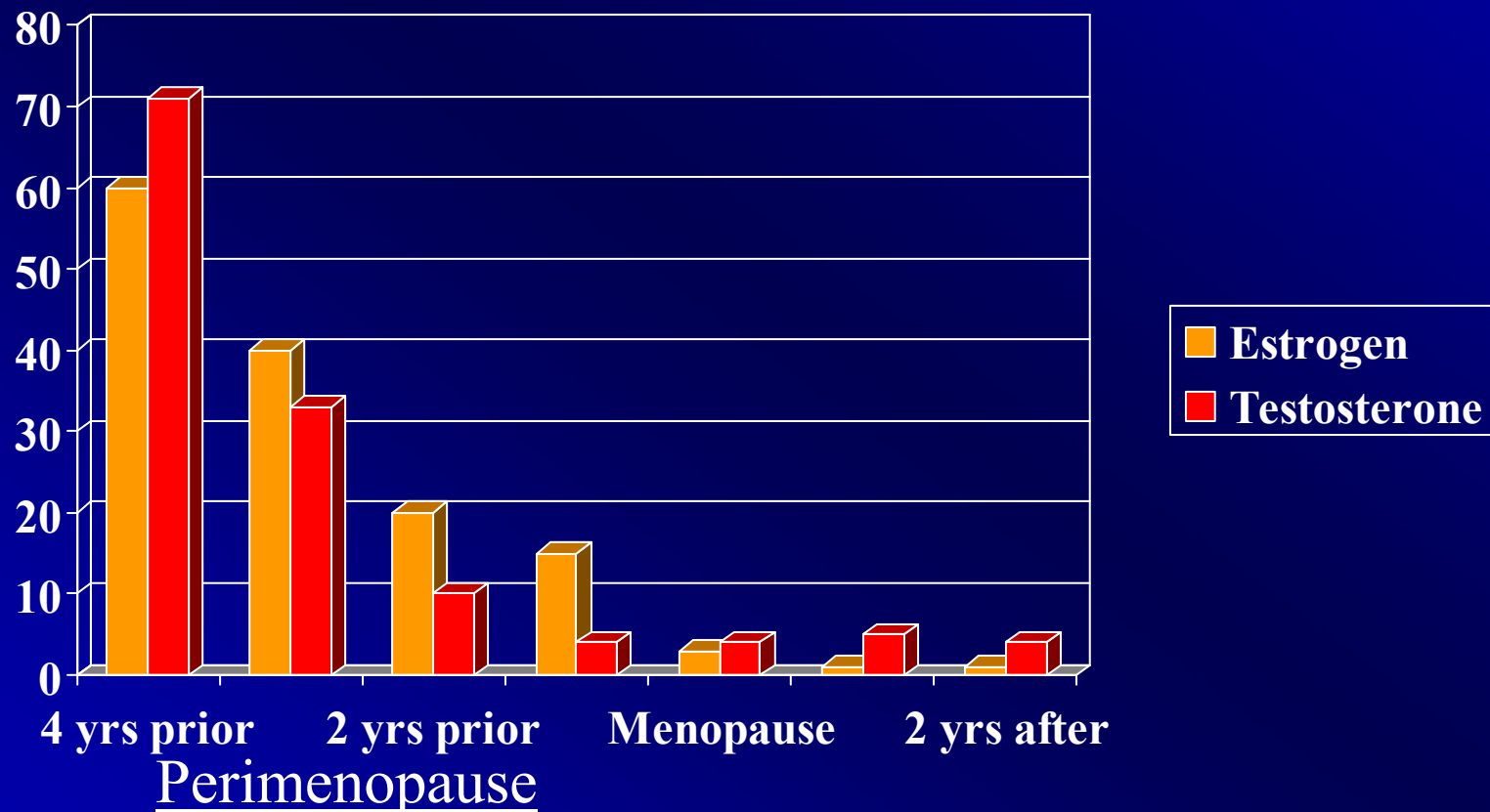
Sexual Desire in Women

Norms:

“I think about sex less than 1x per month or NEVER”

- age 20-30: 32% Premenopause
- age 40-60: 56% Perimenopause
- age 60-80: 77% Postmenopause

Transition to Menopause



Lack of Sexual Desire

- Prevalence - married, well-adjusted couples
 - Women 35%
 - Men 16%

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JUST BEFORE SEX
WHAT'S ON HIS MIND...

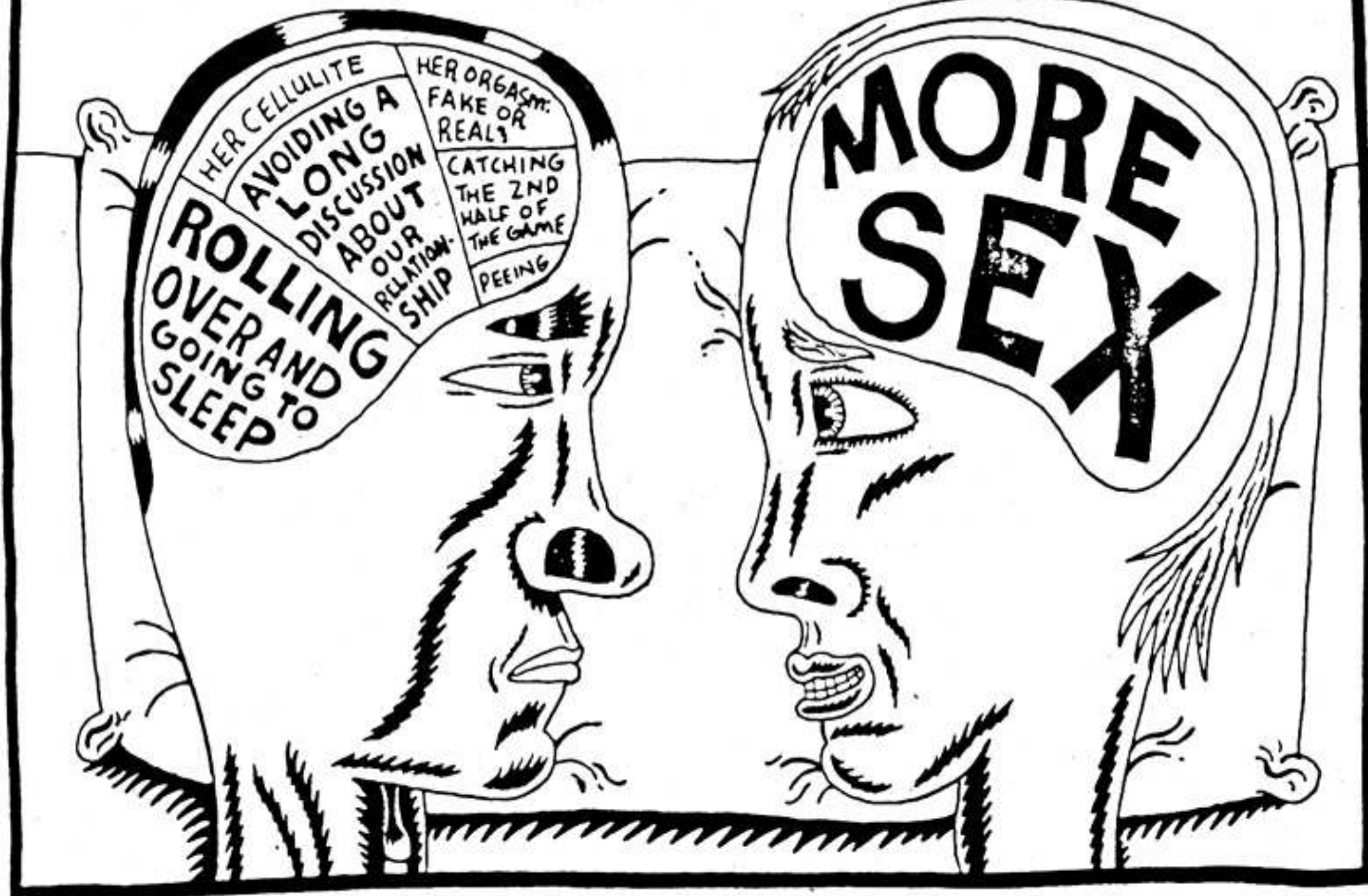


WHAT'S ON HER MIND...



JUST AFTER SEX
WHAT'S ON HIS MIND...

WHAT'S ON HER MIND...



Sexual Desire in Men

Norms:

“I think about sex more than twice per day”:

- Age 20-30 85%
- Age 40-60 68%
- Age 60-80 38%

-Bancroft J *Int J Impotence Res* 1998;10:S40-S43.

Female Sexual Interest

- Which hormone is primarily responsible?
 - TESTOSTERONE
- When is the testosterone level highest during the menstrual cycle?
 - DAY 10 – 14, just before ovulation (Mother Nature's sexual boost)
- What decreases a woman's testosterone?
 - Birth control pills, nursing, oral estrogen, perimenopause and menopause decrease it
 - Exercise increases body's production of testosterone

Lack of Desire

- Causes of new onset Lack of Desire:
 - Low free testosterone
 - Ovarian and adrenal production decreases in perimenopause, menopause and aging
 - Increased binding protein: estrogen, birth control pills, overactive thyroid
 - Medical
 - Vaginal atrophy, hyper- or hypothyroidism
 - Medication side-effects
 - Antidepressants: all except Serzone, Remeron and Wellbutrin
 - Antihypertensives: especially B-blockers
 - Estrogen and birth control pills
 - Psychosocial
 - Stress, fatigue, relationship conflict
 - Psychological Problem
 - Depression, anxiety, substance abuse

Determinants of Free Testosterone

- **Production**

- Ovarian - 25%
- Adrenal - 75%

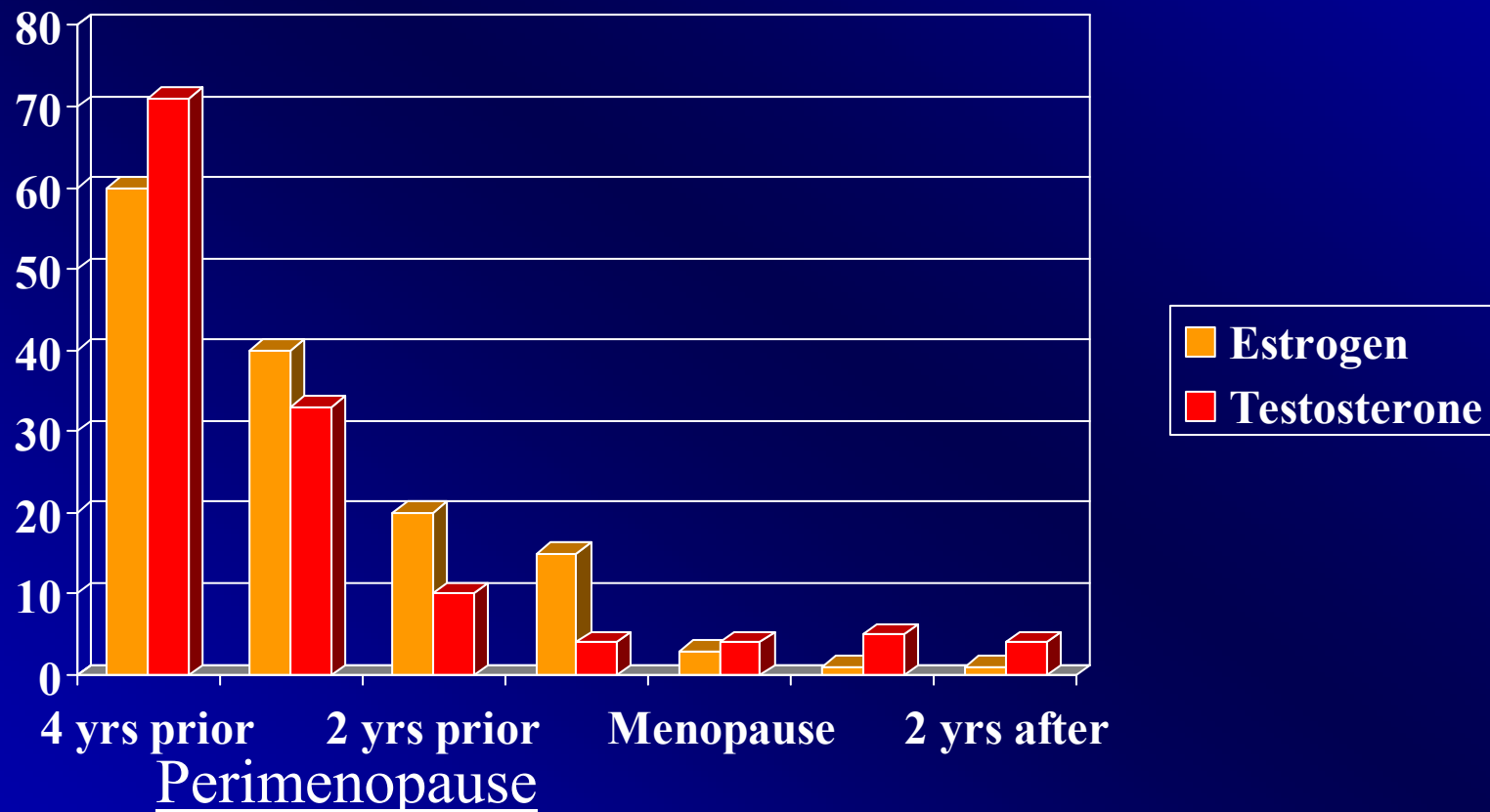
- **Binding hormone**

- SHBG=sex hormone binding globulin
- Increased SHBG → lower free testosterone
- Oral estrogen and thyroid increase SHBG
 - Oral estrogen passes through the liver (vs the patch or endogenous estrogen) and binds up SHBG, increasing production of SHBG
 - SHBG also binds free T3 and T4
 - So when you start a woman on oral estrogen you should re-check her TSH after 3 months

Sex and Estrogen

- Estrogen is a mood elevator. It works in the brain to maintain interest in sex, but it also works at the level of the genitals, helping to increase sensation and just making sex more pleasurable
- Without it, not only can desire take a dive but vaginal tissue begins to dry and shrink
- As a result, intercourse can become uncomfortable, or even painful
- Moreover, avoiding sex because of pain only leads to more pain
- The old "use or lose it" theory *really* does apply

Transition to Menopause



Female Sexual Response

- Sexual Desire
 - Sexual fantasy
 - Testosterone dependent
 - Masturbation
 - Testosterone dependent
 - Tactile stimulation
 - Testosterone dependent (nipples/clitoris)

Symptoms of Androgen Deficiency in Women

- Decreased libido
- Decreased interest in being intimate
- Decreased motivation
- Flat mood
- Decreased well being

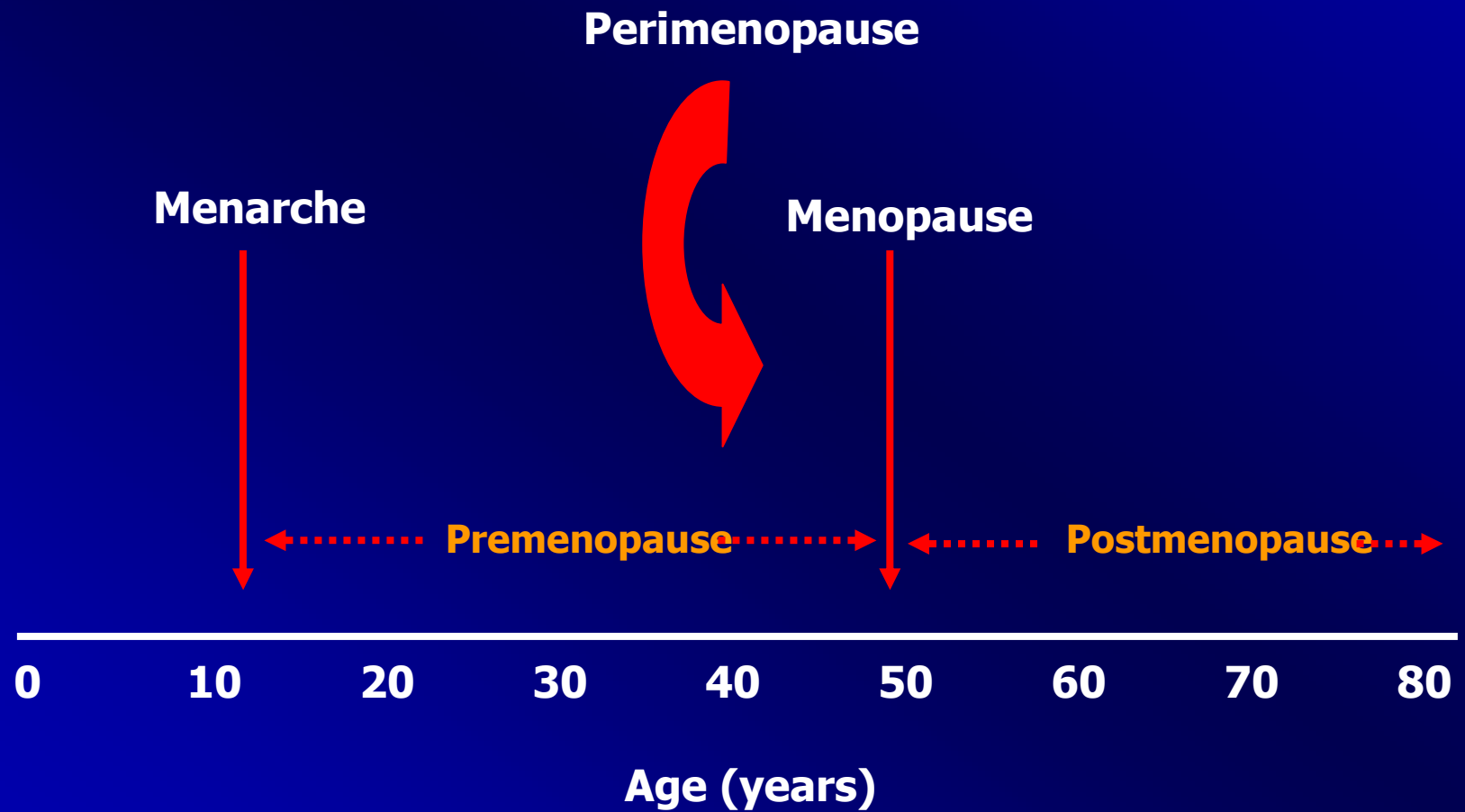
Outline

- The Female Brain
- Puberty, the Menstrual Cycle and PMDD
- Pregnancy, Mood and Postpartum
- Perimenopause, Mood and Sex
- Menopause, Mood and Sex

Menopause

- Many people think of menopause as encompassing a several-year time span.
- In actuality, menopause lasts for one single day – the day 12 months after a woman has had her last period.
- After this, we use the term “postmenopausal.”
 - Perimenopause, which is also termed “the menopausal transition,” refers to the several-year period leading up to menopause and usually begins in the mid 40s.
 - Most of the troubling physical and psychological symptoms occur during perimenopause.

Reproductive Life Cycle



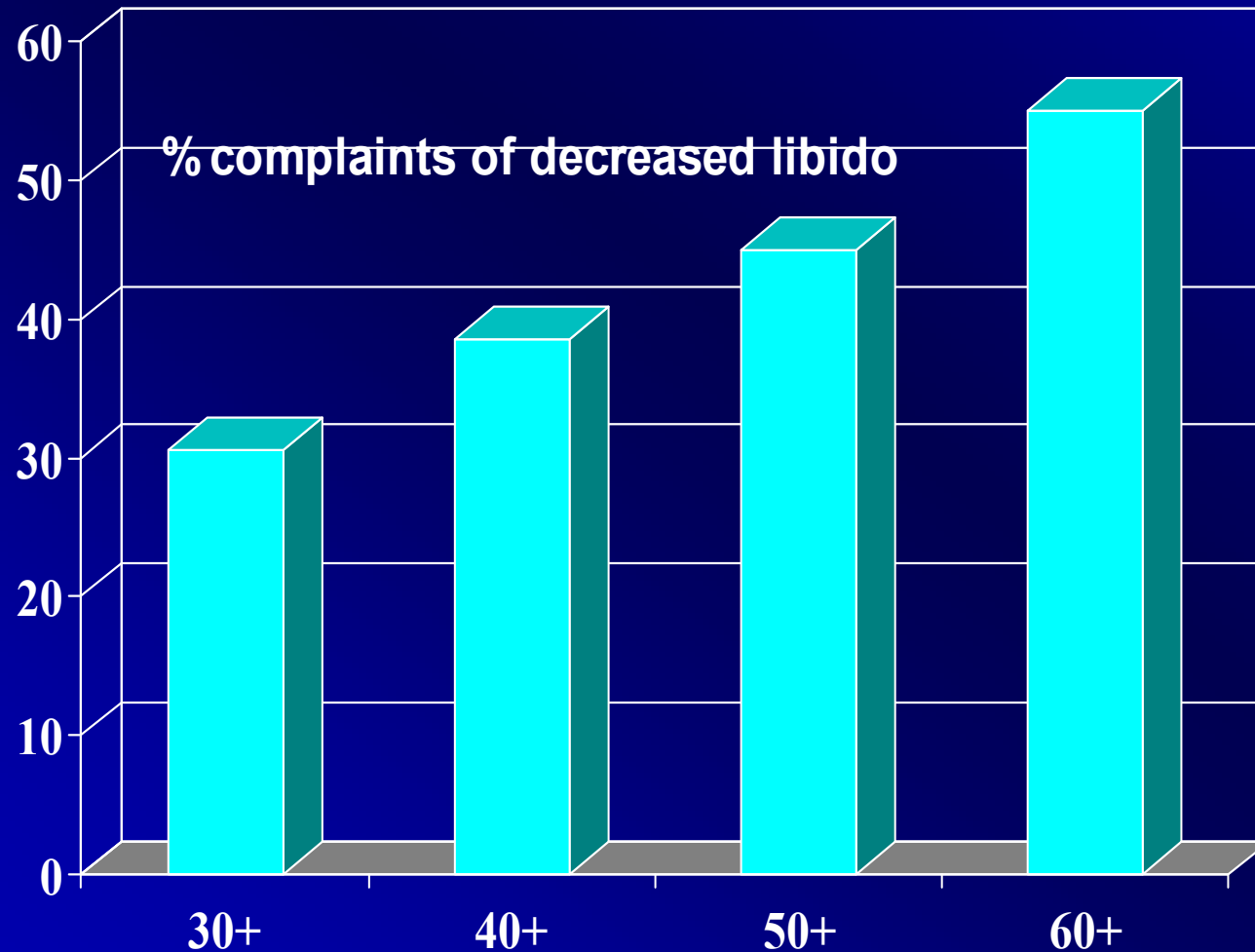
Menopause

- Average age: 51.2
- Surgical menopause: 15-20% in USA today
- Complete cessation of menses for 12 months
- Symptoms have usually been present for at least several years prior
- 20% have few or no symptoms

Clinical Features of Menopause

- Vasomotor symptoms
 - HOT FLASHES, night sweats
- Sleep disruption
- Psychological complaints
 - Forgetfulness
 - Mood changes
- Reduced skin collagen and skin thickness
- Urogenital changes
 - Vaginal dryness, atrophy
 - Frequent urogenital tract infections
- Sexual dysfunction

% of Women Complaining of Decline in Libido by Age



Solutions to Sexual Interest Decline

- Exercise more
- Stop oral estrogen (HRT, Birth control pills)
- Can try estrogen patch
- MORE FOREPLAY, better sex
- New partner (works for 6 months)
- Add TESTOSTERONE

Summary

- The Female Brain
- Puberty, the Menstrual Cycle and PMDD
- Pregnancy, Mood and Postpartum
- Perimenopause, Mood and Sex
- Menopause, Mood and Sex

The End

Thank You!

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