Use of Hormones in Mental Health Care

How Our Practices are Similar

- Odd symptoms that don't fit familiar pattern
- Narrow thinking inside specialty box
- Must have Psy issue or hormone problem

Why Rx Fail

- Look for patterns not single value
- Normal range is not normal
- Lack of knowledge about drug biology and BCP design
- Lack of understanding about reproductive biology

SHBG is Altered by

- Oral T_4 Rx
- Oral E_2 Rx
- Insulin resistance
  - ↑ androgen
  - ↓ SHBG

Hormone Issues During Life Cycle

- Teen
- Young (20-30 yo)
- Reproductive (<40 yo)
- Perimenopause
- Post menopause (natural or surgical)
- Senior

Teen

- Average age puberty 11.5 yo
- ↓ last 100 yrs
- Frish nomogram – 48 kg
- After menarche 50% cycles anovulatory for 2 yrs

Issues

- Breast development
- Pelvic pain -1° vs 2°
- Weight (high or low)
- Sports (5'4" ~ 114 to 135 lbs)
- Eating disorders
- Insulin resistance - Hb A1c 5.7↑
- Adolescent adjustment reaction
- Bone development (mature at 25-30)

Chronic hypothalamic anovulation is most common form

CHA

- ↓ WT
- ↑ Stress
- ↑ Exercise

= Slowing Arcuate Nucleus Pulse Frequency

AN

Chronic Pelvic Pain Syndrome

- Teen who believes she is ill
- Been given incorrect Dx or Rx
- Parent issues
  - A. No father present
  - B. Over bearing mother
  - C. May look like Munchausen by Proxy

A. Patient
  - B. Young
  - C. Thin
  - D. White
  - E. Little education
  - F. Limited future

- Multiple drugs
- May be addicted

- Usually depressed
- Low estrogen levels
- Cyclic hormones useful

Young 20-30 yo

- Menstrual dysfunction
- PCOS
  - A. Wt
  - B. Acne
  - C. Hirsutism
- Endometriosis
- Libido ↓ by BCP
- Infertility
- Bones still an issue

Menstrual Function

What is Normal Function?

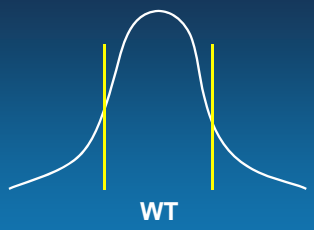
- 26 to 32 day cycle
- 2 to 8 days flow
- Ovulation between day 12 to 16
- Follicular phase has set length
  - Evidence?

Concept of Dysfolliculogenesis

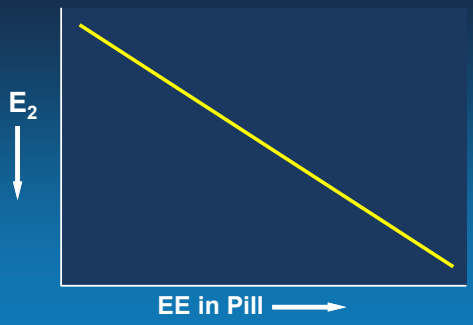
- Recruitment and cohort size
- Selection (FSH)
  1. ↑ # granulosa cells, i.e. # FSH receptors
  2. Induce LH receptor
  3. Induce aromatase
- Dominant follicle
- Exponential growth
- E/P trigger LH surge
- Ovarian micro environment
- Luteinization

Pill Design

1.



2. ↓ E_2 (Market advantage)



Facts About BCP

- Progestin dominant
- ↓ libido & ↑ depression
- Pill only approved for contraception
  - A. Regular cycle
  - B. Normal wt
- We use off label
  - A. AUB
  - B. Pain
  - C. Acne
  - D. PMS & PMDD
  - E. PCOS
  - F. Endometriosis

Reproductive Age <40

- Fertility Issues
  - A. 35 yo AMA
  - B. IVF best done under age 40 yo
  - C. Cancers
  - D. PMS & PMDD
  - E. Hirsutism & alopecia
  - F. ↑ Wt

- Cohort size ↓
- Egg quality ↓
- Genetic damage

Perimenopause

- 2 to 15 years before menopause
- Symptoms vary
- Cluster in 3 phases (Straw Study)
- FSH of ≥40 is menopause
  but
  5-10 is reproductive level
- Cycles ↓ 23 -26 days

Look in the Right Place
E_2/P_4 Alters of These Things!

Blood flow
Balance
Memory
Mood
Depression
Energy
Psychomotor stability
Cardioregulation
Libido
Skin
Weight
Sleep
Repro organs

Breast function
Vaginal health
Bone strength
Muscle strength
Aggression
Nutrition
Vascular tone
Liver function
Clotting
Lipid met
Biliary function
Vision
Brain health

Basic science data cannot be contested!

Sleep is Major Issue

- No lymphatics in brain
- In sleep glial cells develop pores
- This lets brain detox
- Sleep deprivation produces mini organic brain syndrome

Work Up of Perimenopause

- LH, FSH
- PRL
- T_4, TSH
- E_2 (remember E_2 surges)
- Testosterone profile
- Ultrasound endometrium

Treatment Perimenopause

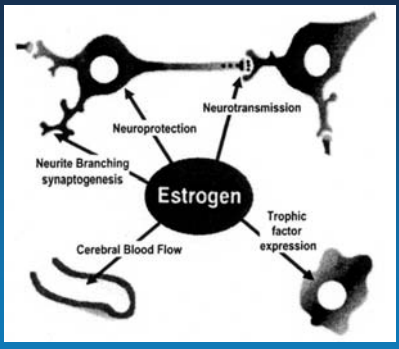
- Cyclic estradiol/progesterone best
- E_2 Ṫ mg days 1-25
- P_4 100 mg days 16-25
- 5 days rest
- BCP usually don't work

Post menopause

- Surgical removes 95% estradiol & 50% testosterone
- Symptoms start in < 1 wk
- Many patients get pushed into surgery
- No benefit in removing ovaries < 63 yo unless diseased
- Natural ↓ estradiol, testosterone the same but declines over time

What about Estrogen and the Brain?

Effects of Estrogen on Neural Function



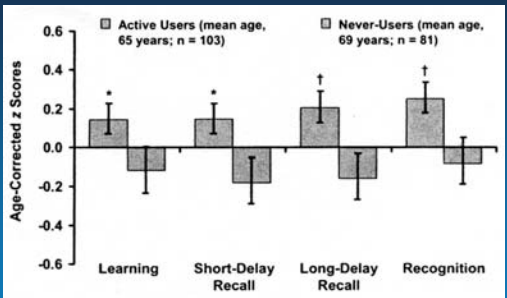
Adapted from Birge SJ. Menopause Management 2000;July/August:13-21

Perimenopausal Women Notice Cognitive Changes With Aging

- 230 women enrolled in the Seattle Midlife Women's Health Study were interviewed (mean age = 46.7 yrs)
- 62% reported an undesirable change in memory
- Changes included:
  - Difficulty recalling words or numbers
  - Forgetting events and actions
  - Difficulty concentrating
- Women attributed these changes to stress, health, and age rather than hormonal changes

Mitchell ES, Woods NF. J Womens Health Gend Based Med. 2001;10:351-62

ET/HT is Associated With Better Performance on a Test of Verbal Memory in Postmenopausal Women



*P<.05;†P<.01 compared with never-users.

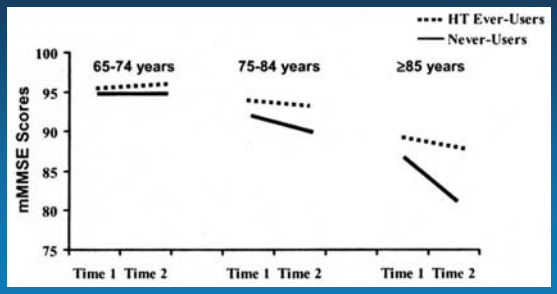
Adapted from Maki PM. et al. Am J Psychiatry. 2001;158:227-33.

Cache

Short term HRT in younger women decreases incidence of dementia

Effect of HT Use in Reducing Cognitive Decline in Older Women: Cache County Study

Mean Age ≥72 Years at Baseline, 3-Year Follow-Up



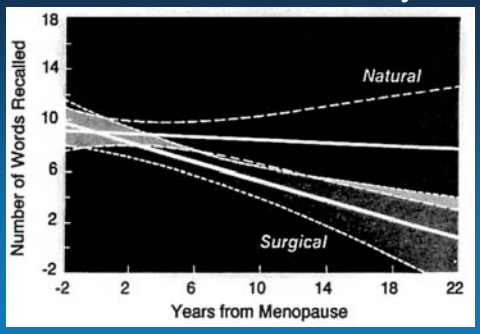
Carlson MC et al. Neurology. 2001;57:2210-6.

Olmsted County

Removed ovaries prior to 65 yo – no HRT

Shows increased risk of cognitive impairment

Effect of Surgical Menopause on Short-term Verbal Memory



Nappi, Gynecol Obstet Invest 47:29, 1999

KEEPS

The Kronos Early Estrogen Prevention Study

Summary of Study

Double-blinded, placebo-controlled of low dose oral or transdermal (patch) estrogen and cyclic monthly progesterone. Age 42-58 (mean 52) 3 yrs post menopause. 727 women, randomized to 3 arms for 4 yrs

- Control
- Premarin 0.45 mg qd
- Climara patch 50 µg/day

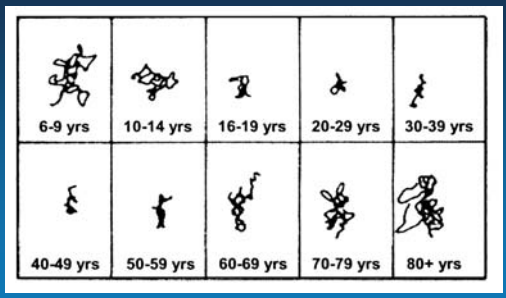
Findings

- No ↑ in BP
- Oral CEE ↑ HDL and ↓ LDL, ↑ triglyc.
- Transdermal ↓ insulin resistance
- No effect on CV disease
- ↓ CNS symptoms
- ↑ mood, sexual function and bone density
- No effect on breast or endometrial cancer, MI, TIA, stroke, VTE

662 patients enrolled in the NIH Cognitive and Effective Ancillary Study

- ↓ depression
- Better recall
- Improved memory

Effect of Age on Sway

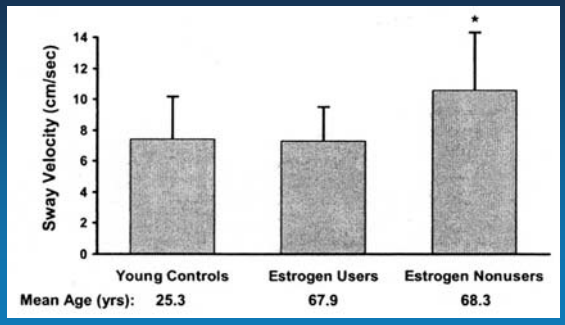


Sheldon JH. Gerontol Clin (Basel). 1963;5:129-38.

Mechanism for Maintenance of Balance

Afferent Sensory Input	→	Central Integrative Processing	→	Efferent Musculoskeletal Effectors
Visual, vestibular proprioceptive systems		Central nervous system		Motor neurons, muscles, skeleton

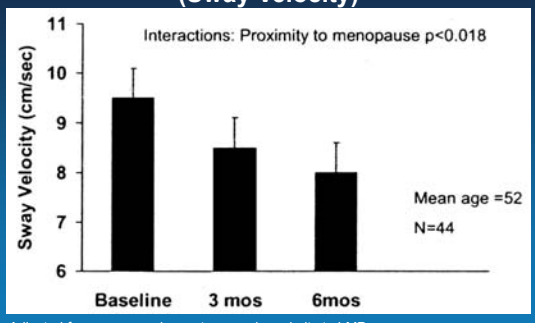
Effect of Estrogen Deprivation on Postural Balance (Sway Velocity)



*P =.007

Naessen T. et al. Am J Obstet Gynecol. 1997;177:412-6.

Effect of Estrogen on Postural Balance (Sway Velocity)

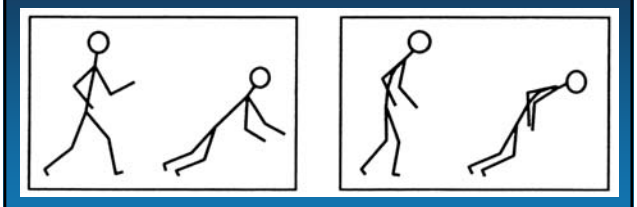


Adjusted for menopausal symptoms and proximity to LMP

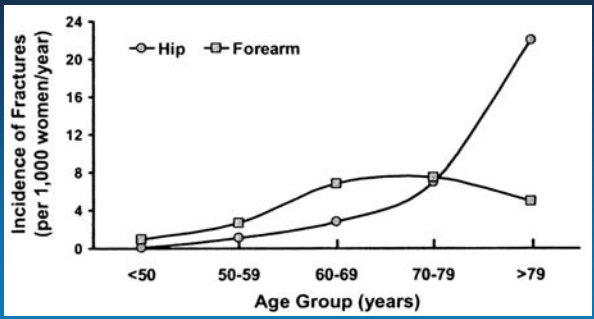
Naessen T et al. Menopause, 2006

Age-Associated Effects on Falls

Young Faller Old Faller



Age-Specific Incidence of Hip Fracture



Cummings SR, et al. Epidemiol Rev. 1985;7:178-204.

What estrogen does not do

- Make you gain weight
- Cause cancer

Cancer

- No evidence that any hormone causes cancer at cell or molecular level
- WHI showed minor association with Prempro (1.26 RR)
- Multiple other trials no change
- Even WHI show no difference in longevity
- Pill vs topical – no difference

What Drug to Use

- Estradiol best
- Progesterone vs NE
- Use as continuous combined or cyclic overlapping
- Beverly Hills Protocol

What About Testosterone

Abuse of Anabolic Steroids

- 1 – 3 X 10^6 abusers
- Average age 25
- Middle class men
- 78.4% not body builders
- 74% college educated
- 56% did not tell doctors of use

Effect on Sexes

Men
- ↑ penis size in children
- ↑ vocal chord size
- ↑ libido
- ↓ natural sex hormones
- ↓ sperm production
- Develop breast
- ↓ size testicles

Women
- More masculine
- Voice deepens
- Hirsutism
- ↓ Breast size
- ↑ clitoral size

More effect on upper body

Adverse Effects

- Neuro psychiatric
  1. Aggression
  2. Violence
  3. Mania
  4. Psychosis
  5. Suicide

Personality Profiles

1. Borderline
2. Antisocial
3. Paranoid
4. Schizotypal
5. Histrionic
6. Passive-aggressive
7. Narcissistic
8. Bipolar
9. Substance depending
10. Conduct disorder

Physiological

1. Immune depression
2. Alters FBS
3. ↑ CV disease
4. Acne
5. Baldness
6. Thickening left ventricle
7. ↑ Bp
8. Arrhythmias
9. CHF
10. MI
11. Sudden cardiac death
12. ↑ LDL and ↓ HDL
13. Gynecomastia ♂
14. Testicular atrophy
15. Masculination in ♀
16. Focal segmental glomerolosclerosis
17. Peliosis hepatis

Mood

1. Hypomania
2. Irritability
3. Elation
4. Recklessness
5. Racing thoughts
6. Invincibility

DSM IV

Anabolic steroids do not produce physical but psychological dependence

"Roid Rage"

Anabolic Steroids

- Induce addictive behavior
- Withdrawal occurs – mood swings, fatigue, restlessness, ↓ appetite, insomnia, ↓ sex drive, steroid craving. Depression can lead to suicide

Testosterone Use

- Men should have level <250 and have hypothalamic disease
- CV risk and polycythemia
- Women – no society recommends wholesale use but can be used to alter estrogen bioavailability

Seniors ≥ 65 yo

- Widow/divorced
- Financial issues
- Aging
- Retirement
- Health
- Appearance (hair loss)
- Kids
- Prevents aging

Retirement = ½ the income & 2 x the spouse

Should Older Women Take Hormones?

- Endocrine Society, ASRM, NAMS, ACOG, "Hormones are safe and should be used for symptomatic women"
- Medicare cite Beer's criteria of American Society of Geriatric Medicine – too risky
- Individualize Rx – healthy women for better quality of life

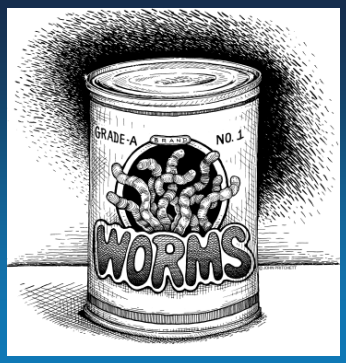
Should the Mental Health Professional Prescribe Hormones?

Issues to Consider

- FH disease
- Contraception
- Uterus +/-
- Bleeding
- Medical history
  1. Clots
  2. Breast disease
  3. TIA
  4. MVP
  5. Insulin resistance

Issues to Consider (cont'd)

- Drug interactions
- ↑ BP
- Lipids
- Pregnancy



Where You Won't Get Help

- Internist will tell patient not to take ERT/HRT
- REI wants to do IVF
- Gyn does not want to deal with mental health
- Gyn may not believe in ERT/HRT
- Holistic Dr and compounding pharm will tell patient only their agents are natural and safe

Where You Won't Get Help (cont'd)

- Medicare & insurance don't cover meds after 65 yo
- Coverage will vary with drugs and carrier
- Lots of paper work and phone calls

Should hormones be part of your therapy

Yes