Menopause & PMS
Endocrinology and Management

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Hormonal Soup

- Your patient population?
- PMS/ Premenstrual Dysphoric Disorder
- Depression is more common at the menopause
- Menopause can be debilitating
- History is crucial
Should Psychiatrists be prescribing oestrogen therapy to their female patients?

BJPsych 2013
Hypothalamic-pituitary ovarian axis

- GnRH
- Inhibin
- Steroids
- Hypothalamus
- Pituitary
- Gonadotropins: LH, FSH
- Ovary

Feedback hormones
Hormone levels over a normal menstrual cycle
Testosterone levels over the menstrual cycle
Estrogens and the CNS

Within CNS, estrogen acts as a neuroprotective agent
- Genomic (delayed)
  - mediated by the activation of estrogen receptors and gene transcription
- Non-genomic (rapid)
Estrogen, progesterone and neurotransmitters

- Estrogen regulates activity and synthesis of serotonin and acetylcholine
- Interacts with noradrenaline and dopamine
- Estrogen generally lifts mood
- Progesterone, via a metabolite, alters the GABA system and enhances MAO activity which decreases noradrenaline, dopamine and serotonin
- Progestogens may lower mood and enhance sedation
Mood and the menstrual cycle

- Individual reactions to hormone cycle changes lead to:
  - PMS/PMDD
  - Post-natal depression
  - Menopause related mood changes, anxiety and psychosis

- The change in hormone levels rather than the absolute level is the problem

- Recurrent at different stages of their reproductive lives.
Hormone levels over a normal menstrual cycle

- **Estrogen**
- **Progesterone**

- **LH**
- **FSH**
Androgens and mood

- Excess androgen has been associated with:
  - low mood
  - anxiety
  - increased risks of PMS and eating disorders, particularly bulimia

- Mental health issues not tightly linked to the presence of sx
Androgen excess

Not all women with androgen excess have obvious signs.
Polycystic ovary syndrome

- Affects 5-10% of women regardless of ethnicity
- Genetically determined metabolic disorder
- Insulin resistance triggers weight gain and excess androgen production
- Irregular periods, acne, hirsutism, alopecia and/or weight gain.
- They may have no sx at all
- Effects on fertility and CV health
Menstrual Mood disorders
Sally (45 years of age)

- PMS symptoms are getting worse - become crippling
- Gets very angry for the second half of the cycle
- Negative self talk, memory shot, affecting work, Dark places
- Has 2 young children - not safe for 2 days of the month
- Period comes - “lights get switched back on”
- Feels better when she is pregnant, felt awful on the depo provera
Menstrual mood disorders

- PMS/PMDD increase with age, particularly after 35yrs of age
- Hormone swings mid-cycle and pre-period
- A cascade of changes in neurotransmitters and other hormones (androgens, mineralocorticoids) occurs leading to physical and psychological sx.
- If PMS before 30yrs there is often an underlying hormone disorder, particularly polycystic ovary syndrome
PMS symptoms

- Mood swings,
- Irritability, depression, anxiety,
- Bloating, fluid retention, breast tenderness,
- Sugar cravings,
- Headaches and poor sleep

Tell them they are not going mad and we can alleviate symptoms although it may take time
Premenstrual Syndrome

- 40% of reproductive age women report sx of PMS
- 3-8% meet the criteria for PMDD.
- **PMDD**: 50-75% lifetime incidence of psychiatric disorders
- Mutations in the estrogen receptor have been detected in women with PMDD
- Sx begin after ovulation and resolve early in the cycle
- There is always a clear window without sx during the later follicular phase of the cycle
- The pattern is consistent over 2-3 cycles

Huo et al., Biol Psychiatry. 2007;62(8):925-33
Reducing hormone swings reduces sx

Treatment options include:

- Diet/lifestyle/ exercise
- Calcium/magnesium- Low ionized calcium in women with PMDD
- Yaz- Anti-androgen and anti-mineralocorticoid
- Spironolactone- Anti-androgen and anti-mineralocorticoid
- Cyproterone- Anti-androgen and anti-gonadotrophic (FSH,LH)
- SSRIs
  - Rapid onset of action
- Create a medically-induced menopause + estrogen/progestogen (GnRH agonists-zoladex)
Use of oestrogens

- Patch in luteal phase
- HRT (half a Trisequens)
- Add back progesterone if uterus present
- Take a good Hx and follow up
Menopause
The Menopause – What Is IT!

Simply means stopping of periods

- It represents a significant endocrine (hormone) change in a woman.

- Average age is 51.
Definitions

- Menopause
  - The final menstrual period

- Perimenopause
  - The transition when periods begin to change in length and sx may begin to occur

- Postmenopausal
  - 12 months after the final menstrual period
Definitions

- *Early menopause*
  - Last period between 40 and 45 yrs

- *Premature menopause*
  - Last period before 40 yrs
  - May be spontaneous or induced by surgery or cancer treatment
Diagnosis of menopause

- Information is power- women need reassurance this is normal
- Need to take a good history – timing and symptoms
- 80 % of women have symptoms
- Blood tests are not helpful
The menopausal transition

- Takes about a decade
- Early signs
  - menstrual cycle shortens by 2–3 days, detectable at about age 38–40\textsuperscript{1,2}
  - infertility — oocyte aging, increased incidence of anovulation\textsuperscript{3} basal temperature up in 30–50% of cycles after 40 years age\textsuperscript{4,5}
- Exhaustion of the ovarian supply of oocytes\textsuperscript{6,7}, numbers declining steeply from age 37–38

\textsuperscript{1}Lenton 1984; \textsuperscript{2}Klein 1996; \textsuperscript{3}Treloar 1970; \textsuperscript{4}Döring 1963; \textsuperscript{5}Vollmann 1977; \textsuperscript{6}Baker 1963; \textsuperscript{7}Richardson 1987
Hormone Roller Coaster
Determinants of the age of menopause

Earlier age of menopause:

- oophorectomy, e.g. for endometriosis, cancer
- chemotherapy, e.g. cyclophosphamide
- ovarian irradiation
- hysterectomy (up to 4 years earlier)
- familial and genetic factors (e.g. ER-α polymorphism, twinning)
- cigarette smoking – by about 2 years
Symptoms clearly related to estrogen deficiency

- Vasomotor symptoms
- Vaginal or genital dryness
- Recurrent UTIs
- Joint pain or stiffness
- Generalized aches and pains
- Sexual dysfunction
- Mood disturbance

Barnabei et al., 2005 Obstet Gynecol, Welton et al., 2008 BMJ KEEPS Study, NAMS 2012
Menopause Symptoms

- Who gets symptoms?
- 5-10 yrs before periods stop and reflect the swings in hormone levels
- 20% of women will have long-term sx
- Different ethnic groups may have different experiences of menopause
- May be last straw- Grief reactions, co-morbidities (including mental health), other life stresses
- A surgical or chemo-induced menopause have worse symptoms for longer.
I DON'T HAVE HOT FLASHES...

I HAVE SHORT, PRIVATE VACATIONS IN TROPICAL-LIKE CONDITIONS!
- These symptoms can be debilitating
- Unable to function
- Sleep or flushes?
- Impacts on partners and children
- Unable to have sex due to vaginal dryness/atrophy
Body temperatures during hot flushes

Adapted from Molnar. *J Appl Physiol* 1975;38:499–503
Menopause and mood

- Associated with depression
- The rates of women experiencing their first episode of depression during the peri-menopausal years are 2 to 14 times higher than in the premenopausal years.
- Debate continues as to the role of estrogen deficiency vs sleep deprivation in altering mood and cognitive function.
- It is probably a mixture of both.

Worsley et al., Maturitas 2014 77(2):111-7
Gibbs et al., Women Health Issues 2013 23(5):301
Management of menopause
WALL STREET: LOSING SAVINGS—AND TRUST

IS THIS OUR FIRST ANCESTOR?

THE TRUTH ABOUT HORMONES

Susan Pierres, 60, of Miami, has been on hormones for 10 years. She is angry and confused but not yet ready to stop taking them.

Hormone-replacement therapy is riskier than advertised. What's a woman to do?
Menopausal Hormone Therapy

- Estrogen alone (oral or transdermal)
- Estrogen + progestogen (oral or IUS)

Benefits:
- Reduces sx
- Reduces risk of colon cancer
- Reduces fracture risk
- Reduces risk of CAD
- Reduces all cause mortality
- Estrogen alone reduces breast cancer risk

Risks:
- Age related – CVA/VTE, gallbladder
- Progestogen related – breast cancer
Menopause transition

Flushes
Night sweats
Joint and muscle aches
Sleep disturbance
Mood and cognitive change
Vaginal dryness
Sexual dysfunction

Genito-urinary problems
Osteoporosis
Increased CAD risk
• The most effective treatment for symptom control- 7-21 days

• There is no consistent formula that works for every woman.

• Adjustment of doses is critical

• Mood improves in 68-80% of women
Surgical Menopause

• Women with a surgical menopause may require higher doses of estrogen to settle sx

• The risks of menopause before age 45yrs are substantial. Hormone therapy should be used unless there are contraindications.

• HRT should be continued until the normal age of menopause
Alternatives to HRT

- Exercise
- CAMS: Remifemin, St John’s wort, acupuncture, hypnosis, CBT, mindfulness
- SSRI: escitalopram, paroxetine*, venlafaxine
- Gabapentin
- Cetirizine
- Clonidine
- Stellate ganglion blockade
Hypnosis

FIG. 2. Change in weekly composite hot flash scores.

Elkins et al., Menopause 2013
Escitalopram

Change from baseline in quality of life, comparing hormone therapy with escitalopram.

Soares et al., Menopause 2006
FIG. 2. A: Mean Insomnia Severity Index from baseline to week 8 by treatment assignment. B: Mean Pittsburgh Sleep Quality Index from baseline to week 8 by treatment assignment. Vertical bars represent SE.
Stellate ganglion blockade
Oestrogen and Psychiatric disorders

Menopause associated with a worsening of Bipolar illness (Marsh 2012)

Oestrogen (adjunct) versus placebo for women with schizophrenia:

Cochrane protocol June 2016
Estrogen

Scott O'Grady, Part 2: The Big Spin

Every Woman's Dilemma
Take home messages

• Hormones have significant effects on neurotransmitters and mood
• Individual women may have increased vulnerability to normal hormone changes over their reproductive lives
• A rocky menopause superimposed over an existing psychiatric illness may increase morbidity
Should Psychiatrists be prescribing oestrogen therapy to their female patients?

BJPsych 2013
Your practice

- Be aware and proactive
- Take a good history
- ? Prescribe
- 7-21 days the magic oestrogen window
- Buddy up with someone who has an interest
- USE Australasian Menopause Society Info
Quality of Life
Kia Ora

www.otago.ac.nz/whrc

Women’s Health Research Centre

Research making a difference to women