Menopause

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www.otago.ac.nz/whrc
Useful info

• www.menopause.org.au
• www.menopausetoday.com
• E-book Dr Beverley Lawton “Menopause: A Guide for Every Woman”
• www.wellingtonmenopauseclinic.co.nz
• AMS conference September 2014 Auckland
Menopause is the gateway to healthy aging
Opportunity

- Wellness
- Successful aging
- Healthy Aging
- Maintenance or enhancement of QoL with increased years
- Chronic disease prevention
Overview

• What is it?
• Treatment?
• Prescription medications
• HRT
• Prescribing
The Menopause – What Is IT!

Simply means stopping of periods
Menopause

- It represents a significant endocrine (hormone) change in a woman.
- Average age is 51.
- The ovaries make several hormones including estrogen, progesterone and testosterone.
- Hormonal soup - stories
At the Menopause

- The follicle production becomes erratic.
- Symptoms can occur 2-5 years before the last period.
- Eventually no more follicles are produced.
- Estrogen levels fall.
- FSH and LH levels rise and can be tested.
Some History

• 1700’s treated by leeches

• 1800’s treated by surgical removal of the uterus and ovaries – strongly advised against sexual activity during and after the menopause

• 1900’s depression related to loss of fertility
Perspectives can differ

In 1818, Elizabeth Wirt, a Virginia-born woman then living in Washington, D.C., had her last child and entered menopause.

Her husband, U.S. Attorney General William Wirt wrote an oblique letter to a physician asking about her health.

Elizabeth wrote a letter to her mother expressing her joy
Vasomotor Symptoms

- Hot flushes
- Night sweats
- Palpitations

- Menopause is associated with an increased risk of osteoporosis
Symptoms?

- Joint and muscle pains
- Mood
- Memory
- Self Esteem
- Skin
- Hair
- Headaches
- Libido
- Sleep
Who gets symptoms?
Sleep Disturbance

- Increases the risk of accidents
- May decrease workplace performance
- Affects family life

- Associated with increased risk of illness such as obesity, diabetes, hypertension and diabetes

Help With Hot Flushes

- Open Windows
- Reduce coffee
- Avoid hot spicy foods
- Avoid alcohol
- Plan clothes - layering
- Fan
The Dilemma...why treat at all?!

• Common reason for seeking medical advice ¹

• **Significantly** affect QoL for 25% of women

• For 10-20% of women these symptoms persist for more than 10 years ²

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Complementary and Alternative Medications (CAMS)
“Natural is good marketing”
All therapeutic agents have:

- Risks
- Benefits
- Side-effects
- Interactions

Dilemma in not treating:
- Opportunity Costs
- Placebo effect
Prescription Medicines

Antidepressants Venlafaxine, Paroxetine, Fluoxetine

- Shown to have variable affect on vasomotor symptoms. Generally fast acting
- May be useful in breast cancer and/or presence of depression
- Nine month RCT - citaloprim and fluoxetine showed no effect on flushes compared to Placebo

Antidepressants

• Caution as regards side-effects
• Small numbers and short duration of trials to date
• Venlafaxine has been associated with hepatitis

Paroxetine

- Paroxetine (Brisdelle) SSRI paroxetine mesylate Low dose (7.5mg)
- Only non-hormonal treatment for hot flashes approved FDA (2013)
- 2 studies (12 week, 24 week)
- Side effects headache, fatigue and nausea vomiting
- Not to be used with Tamoxifen

http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm359030.htm
After breast cancer

- Tamoxifen - Venlafaxine, citaloprim, clonidine and gabapentin. (avoid fluoxetine and paroxetine)

- Do not use CAMS such as St Johns wart, phytoestrogens and black cohosh
Clonidine

- May be helpful
- Side-effects limit use
  - Drowsiness
  - Tiredness
  - Constipation
  - Dry mouth
  - Headache
  - Dizziness
Gabapentin

- An RCT of 59 women showed reduction of hot flushes by 45% compared to 29% placebo \(^1\) another as effective as oestrogen \(^3\)
- Adverse effects - somnolence, headache, dizziness, ataxia, fatigue, disorientation and nystagmus (1 in 4)
- Safe and effective for short term use \(^2\)
- Not approved by FDA for flushes due to side-effects

1. Guttuso T, Obstet, Gynecol 2003;101:337-345
3. Siresha Y, Obstet, Gynecol 2006;108, NO1
Stellate ganglion blocks

- Used for 60 yrs for pain syndromes and vascular insufficiency;
- 0.5% bupivacaine is injected on the right side of the anterolateral aspect of the C6 vertebra under fluoroscopy
- An effective block confirmed by the presence of Horner’s syndrome.
- Initial trials reduces flushes
Bio-identicals, NHRT

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• Compounded therapies
• Often contain mixtures of powerful hormones
• Efficacy, safety and pharmaco-kinetics unknown\(^1\)
• Must be considered experimental therapies

Progesterone Cream

- Conflicting efficacy data
- Variable uptake
- No bone protection
- Limited safety data for the uterus
- Long term safety data needed

Davis SR et al, J Endocrinol (2005) 185, 207-222
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Don’t forget what we sit on!

• Vaginal dryness is common
• Intercourse can be painful if not impossible
• Vaginal lubricants can help
• In most cases topical or oral oestrogen will be needed
• Libido
Vaginal mucosa during the fertile period and postmenopause

Fertile period

Postmenopause
Vaginal treatments

- Ovestin - oestriol
- Vagifem - oestradiol vaginal tablet
- 80-90% achieve improvement in symptoms\(^1\)
- Caution when using with Aromatase inhibitors\(^2\)

NAMS, *Menopause* 2007 14:3
Kendall 2006 *Ann Onc* 17:584-587
Dilators
WALL STREET: LOSING SAVINGS—AND TRUST

IS THIS OUR FIRST ANCESTOR?

THE TRUTH ABOUT HORMONES

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

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

1949-oral estrogens
1966 *Feminine Forever*
1975 endometrial ca
1995 PEPI
1998 HERS no benefit secondary prevention
2002 WHI EPT
2007 WHI – age ?
HRT for menopausal symptoms

- Oestrogen-containing HRT is the most effective treatment for menopausal symptoms (Maclennan et al 2002)
  - Reduces hot flushes by 70%
  - Also improves vaginal dryness
Hysterectomy

YES
N= 10,739

Conjugated equine estrogen (CEE) 0.625 mg/d

Placebo

NO
N= 16,608

CEE 0.625 mg/d + medroxyprogesterone acetate (MDA) 2.5 mg/d

Placebo
WHI Chronic Disease Prevention -

• Average age 63
• Largely asymptomatic
• Majority well past menopause

Results

• Increased risk of cardiac events
• Increased stroke risk
• Increased risk breast cancer – E+P non-statistical
• Possible increased Alzheimer’s disease.
Selected Risks and Benefits after 5 Years of combined estrogen and progestogen HRT for all women aged 50-79 (WHI Study, 2002)

OESTROGEN WITH PROGESTOGEN

Breast Cancer: Increase 8
CVD: Decrease 7
Pulmonary Embolism: Increase 8
Stroke: Increase 8

Bowel and Uterine Cancers: Decrease 8
Fractures Hip and Spine: Increase 10

10,000 Women Years

* Not statistically significant
Selected Risks and Benefits after 7 Years of estrogen only HRT for all women aged 50-79

(WHI Study, 2004)

OESTROGEN ONLY

- Breast Cancers
- CVD
- Bowel Cancer
- Pulmonary embolism
- Stroke
- Fractures Hip and Spine

10,000 Women Years

- Increase
- Decrease

* Not statistically significant

Breast Cancers: 8
CVD: 5
Bowel Cancer: 3
Stroke: 12
Fractures: 12

* Not statistically significant
Window of Opportunity for HRT

- Risk modified by years since menopause.\(^1\)
- Supported by animal studies and observational studies.
- <10 years from menopause may have a reduction in CHD events and a reduction in mortality (50-59ys of age).
- Lower risk of stroke in women aged 50-59 years of age.

\(^1\)Roussow *JAMA* 2007 pgs 1455-1477
Combined Estrogen + Progestogen HRT outcomes when initiated under age 60.
(Data from 5,522 women in WHI Study)

- Breast Cancer: 2 increase, 7 decrease
- CVD: 7 increase
- Pulmonary Embolism: 1 decrease
- Stroke: 4 increase
- Diabetes: 13 deaths
- Fractures: 59 increase
- All Deaths: 7
Estrogen only HRT outcomes when initiated under age 60
(Data from 3,310 women in WHI Study)

10,000 Women Years

Increase

Decrease

Breast Cancer

CVD

Pulmonary Embolism

Stroke

Total Deaths

All Fracture

Diabetes

11

8

1

2

59

22

3

15

0

15
Benefits Hrt < 10yrs post menopause

Prevention and treatment osteoporosis
Decreases vasomotor/vaginal
Improves QoL
Improves sleep, aches and pains
Improves sexual function
? Heart
? Alzheimers

¹WISDOM study Welton, BMJ 2008;337:a1190
HRT Risks <10 years from menopause

**Definite risks**
- Venous Thrombosis
- Endometrial cancer
- Breast cancer (after 5 years cHRT)
- Cholecystitis

**Possible - Stroke**

**Hysterectomy**
- ? Safer

Other HT

Progestogens are also effective

• Megestrol Acetate 20mg/day produced 85% reduction in flushes (Cancer 1998; 82: 1784-8)

• Are progestogens safe??????
HRT prescribing

There are three main types of HRT for women

• **Estrogen-only HRT** - prescribed for women who have had a hysterectomy (uterus and ovaries removed).

• **Cyclical (sequential) HRT** - prescribed for women who have menopausal-like symptoms but are still menstruating. Cycles monthly, with an estrogen + progestogen dose at the end of the menstrual cycle for 10-14 days.

• **Continuous HRT** - prescribed for post-menopausal women. Continuous estrogen plus progestogen is administered.
Estrogen-only HRT

- Estradiol 1mg (Estrofem or progynova)
- Climara patch 25-50 mcg/24 hrs
- Estradot (twice weekly)
- Possibly premarin
- Titrate to symptoms

- Precautions with endometriosis
Cyclical (sequential) HRT

• Continuous oestrogen and add a progestagon for 2 weeks of the month
• Progestagons- provera, utrogestan(200mg daily), norethisterone
• My favorite is trisequens- usually starting with a half trisequens daily
• Titrate to symptoms
Continuous HRT

- Kliovance
- Kliogest
- Oral contraceptive pill
- Mirena and transdermal
- Utrogestan (100mg daily) and transdermal

- Advice re spotting, headache, bloating
- Check for progestagon intolerance
Best pick?

- Transdermal oestrogen
- Limit progestogens
- Oral micronised progesterone - Utrogestan
  e.g. Climara 50ug weekly with utrogeston 100mg daily
- Cost barrier
- Review all treatments annually
Natural menopause—the urban myth

• Science based information
• Everyone's experience is different
• Empathy and support
• Access to treatment if needed
• Opportunity cost
Challenge for the Future

• Further designer drugs on the horizon
• Identify safe – effective CAMS
• Identify safe – effective pharmaceuticals
• Identifying safer women for safer estrogen
• Ovarian transplant
• Ovarian rejuvenation
Summary

• Menopause has a significant affect on the quality of life of many women
• Treatment options are available
• For most women the benefits of HRT will outweigh the risks
• The Menopause is an opportunity to address quality of life and chronic disease prevention
We want to be fit!