50 is the new 30:
Demystifying Menopause

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Demystifying Menopause

- Menopause – a definition
- Peri and post menopause – an experience
- Hormone therapy – a history lesson
- Treatment options
  - Hormones?
  - No hormones?
- Genitourinary symptoms of menopause – what happened to my vagina???
- Resources – what next?

Menopause – a definition

- Menopause is the time of the last period
  - Average age 51-52
  - Normal 45-58
  - Early (but still normal) 40-45
- Defined as one year without menses – diagnosis of retrospect
- Perimenopause can be several years prior to the last period
  - Not the same as premenopause

Women spend approximately 1/3 of their lives in post menopause!

Menopause

- Is it natural?
- Is it normal?
- Is it a problem?
- Does it need a solution?

Menopause – a physiology lesson

- Ovaries produce estrogen and progesterone after puberty
  - Estrogen is produced when the ovary is getting ready to release an egg, and thickens the lining of the uterus in preparation for a possible pregnancy
  - Progesterone is produced after the egg is 'dropped', to support the thickened lining if there is a pregnancy
  - Not pregnant? Progesterone levels drop, the thickened lining sloughs off and that is a period
- In menopause, the ovaries stop producing eggs, and estrogen levels drop
- Drop in estrogen levels causes menopausal symptoms
- In perimenopause the ovaries will produce follicles on and off
  - Estrogen levels fluctuate, so do symptoms
- Small amounts of estrogen still produced after menopause

Menopause

- Is there a test?
  - Not reliable, results fluctuate almost daily until menopause fully established
- How long do symptoms last?
  - Varies greatly from person to person
  - 50% may have hot flashes for more than 5 years
- Does everyone get symptoms?
  - 15% have almost no symptoms
  - 15% have severe symptoms
  - 70% have variable severity of symptoms

Perimenopause – an experience

- The years leading up to the final period, menopause
- 0 to 10 years, and anything in between
- Ovaries stop responding as reliably as they did when we are younger
  - Estrogen and progesterone levels not as consistent
- Periods can change
  - shorter/longer; heavier/lighter, more frequent/less; more painful/less
- PMS more intense, mood issues, breast tenderness, ‘brain fog’
- Menopausal symptoms…

Menopause - what we see and feel

- Vasomotor symptoms
  - Hot flashes/flushes
  - Night sweats
- Sleep disturbance
  - Waking up frequently
- Genitourinary symptoms
  - Vaginal dryness
  - Painful sex
  - Bladder irritability, infections
- Joint aches
- Palpitations - rapid heart beat
- Memory loss
- Anxiety
- Mood changes
- Irritability
- Fatigue
- Poor concentration – 'brain fog'
- Decreased sex drive
- Weight gain, change in weight distribution

Menopause - what we don't see and feel

- Bone health
  - Increased rate of bone loss at time of menopause, 'bone thinning'
  - Rate of loss levels off over time
  - Higher rates of osteopenia, osteoporosis
  - Higher risk of fractures
- Heart health
  - Loss of protective effect of estrogen
  - Influenced by other simultaneous changes
    - Increased weight at time of menopause
- Heart disease is the leading cause of death in North American women
  - More than all cancers combined

So…what do we do about it? Lifestyle!

- Smoking, alcohol, drugs
  - 2 drinks/day increases breast cancer risk 60% (1-2% per year)
- Healthy eating, healthy weight
  - Obesity linked to breast cancer, endometrial cancer, heart disease
- Exercise
  - Weight bearing activity for bones – walking, running, (light) weight-lifting
  - Aerobic activity for heart – get your heartbeat racing
- Adequate calcium and vitamin D for bones

Lifestyle modifications

- Vasomotor triggers
  - Caffeine
  - Alcohol (red wine)
  - Spicy food
  - Hot beverages, soup
- Dress in layers
- Bedsheet cooling fabrics
- Fans

Hormone Therapy (HT) – what is it?

- Many, many hormones in our body
- Estrogen and progesterone are at play in menopause
- Estrogen treats symptoms, but overstimulates the uterus
- Progesterone protects the uterus
- If you've had a hysterectomy, you don't need progesterone
- Can be given by mouth, through the skin, through the vagina

Hormone Therapy – a history lesson

- HT (estrogen) known for a long time to be the best at managing symptoms of menopause
  - This is not up for debate. Full agreement.
- 1970-80-early 90's
  - Lots of studies suggesting women lived longer if they took HT
  - Specifically seemed to keep women more 'heart healthy' and 'bone healthy'
  - Questions remained about the relationship of HT to breast cancer, stroke
- 1990's – 2004
  - Women's Health Initiative, the 'WHI Study'
  - Hoping to show that HT helped symptoms AND helped women live longer and healthier

FINANCIAL REVIEW

Menopause drug scare hits women

600,000 women warned to stop combined HRT medication

Hormone alert for cance

True degree of therapy risk lost in the clamour of commentato

Expert panel backs HRT cancer warning

Latest guidelines

- Limit HRT therapy to no more than three years
- Review its use in the treatment of osteoporosis
- Remains an appropriate short-term treatment for symptoms of menopause

'There can be risks with stopping medication suddenly without supervision'

More needed to settle HRT scare

The hormone replacement therapy scare inspired last month by US researchers is having predictable results. Australia's biggest supplier of the oestrogen-progestin combination has reported a 30 per cent decline in sales since American doctors cut short a long-term study of 16,000 HRT users to warn the world that the therapy increased the risks of breast cancer, heart disease, stroke and blood clots, particularly among women who took the therapy for five years or more. A Melbourne specialist went further, claiming two-thirds of his patients had quit HRT. These outcomes will suit, if not fully satisfy, doctors who embraced the US warnings. What has not been answered is whether doctors too quickly ruled out HRT for women trying to prevent or minimise the debilitating symptoms of menopause, including sweats, sleeplessness, hot flushes and deterioration in bone density.

For the defenders of HRT, the American report prompted understandable panic among its users. This might have been avoided, or at least lessened, had the researchers not highlighted their findings with a simplistic, misleading and, arguably, mischievous set of statistics. The ensuing furore left little room, for instance, to counter arguments such as women being twice as likely to develop breast cancer if they took two alcoholic drinks a day, instead of HRT. The American report said an HRT user's breast cancer risk, for example, jumped 26 per cent (with similarly alarming rises in the risks of other side effects). To women who know little about statistical interpretation, this might (and probably did) suggest their odds of developing breast cancer would increase by 26 chances in 100. In fact, the odds grew by 0.08 per cent. In Australia, where 600,000 women used HRT pre-scare, this would mean 1200 extra cases a year of life-threatening heart attacks, strokes, breast cancer and pulmonary embolism. Conversely, abandoning HRT would lead to 6660 extra cases a year of bowel cancer and hip fractures because the therapy limits those risks. No one suggests these numbers are insignificant. But the preliminary reports about the drop-out rate from HRT provide no assurance that women are making informed choices about this important decision. Indeed, they are accompanied by anecdotal evidence of scared women quitting HRT on little more than their own poor understanding of poorly presented statistical results. They deserve better than that. They deserve a clear lead from those best placed in the medical and scientific world to warn, advise and reassure.

HRT linked to cancer and stroke: doctors demand drug restrictions

Deborah Smith
Science Writer

The NSW Cancer Council has called for a common form of hormone replacement therapy to be restricted to short-term use after a new study linked it to breast cancer.

United States doctors have abruptly halted a major clinical trial of combined oestrogen and progestin use by healthy post-menopausal women because the harm from the drugs was found to be significantly greater than the benefits.

Along with a 26 per cent increase in breast cancer, the study showed the hormone combination also led to an increase in heart disease, stroke and blood clots.

The Cancer Council's chief executive, Andrew Penman, said the increased risk of breast cancer would occur after three years of combined HRT use. "This is much earlier than previously thought and of concern to the women who have been using the treatment for over 10 years."

Dr Penman said the council would recommend to the Pharmaceutical Benefits Advisory Committee that combined HRT be restricted to symptomatic relief of menopausal symptoms, and not be taken for more than two years.

However, the president-elect of the Australasian Menopause Society, Susan Davis, cautioned against a "knee-jerk reaction" by doctors and women. "I don't think this changes anything for women who are peri-menopausal and aged around 50, or who have used any form of HRT for less than five years."

The American trial, part of the Women's Health Initiative run by the US National Institutes of Health, was due to be completed in 2005 but was stopped after the women were followed for an average of 5.2 years. It involved 16,600 women aged 50 to 79.

The results were published yesterday by the *Journal of the American Medical Association*. Although the risks overall outweighed the benefits, only a small number of individual women – about 2.5 per cent – had problems.

Compared with women taking a placebo, for every 10,000 women taking combined HRT eight more would get breast cancer, seven more would have heart attacks, eight more would have strokes, and 18 more would have blood clots, in a year.

But six fewer would get colorectal cancer and five fewer would have hip fractures, the researchers said. They stressed, however, that the new study did not apply to women without a uterus taking oestrogen-only preparations.

The Cancer Council says an estimated 600,000 Australian women aged 45 to 64 use some form of HRT. Concerned women should see their doctors or call the Cancer Helpline on 131 120.

HORMONE THERAPY

THE RISKS
41% increase in strokes; 29% increase in heart attacks; doubling of venous blood clots; 26% increase in breast cancer.

THE BENEFITS
37% cut in colorectal cancer; one-third reduction in hip fractures; 24% reduction in all fractures.
Source: Journal of the American Medical Association.

Study

...study at ...demiology ...l, Oxford, ...a "rough

Some ... hormones to menop... suffering from incontinence... thinking the treatment would ... But the new study, published ... of the American ...

...lowest dose for ... possible.

HT – a history lesson

- What was the WHI?
  - A VERY large VERY well-designed study of 27, 000 women comparing HT to placebo
  - Stopped early due to an increased risk of breast cancer (not unexpected), stroke and blood clots (not entirely unexpected) and increased risk of heart disease ***(totally unexpected),***
- What wasn't the WHI?
  - A study of newly menopausal women
  - Average age of women in the study was 63
  - <39% within 10 years of the onset of menopause

WHI - what happened?

- Age matters
- HT composition and route matters (probably)
  - What specific type of estrogen and progesterone hormone, how it gets into your body
- Overall mortality matters (to some)
  - Are you going to get breast cancer OR are you going to live longer, even if you get breast cancer?

Age matters

- Cardiac benefits clear for women starting within 10 years of menopause
  - Fewer heart attacks!
  - Fewer deaths related to the heart
  - No difference in strokes

HT composition and route matters

- HT used in WHI is quite different than what is usually prescribed now
- Premarin and Provera
  - conjugated equine estrogen and medroxy-progesterone acetate
- Current formulations
  - estradiol and micronized progestin
  - Different impact on breast tissue
  - Different metabolic effects, less clotting risk, less heart risk
- Giving estrogen through the skin instead of by mouth can decrease clotting risk

Overall mortality matters

- Focus on individual outcomes vs. overall outcomes
  - Breast cancer, blood clot risk vs. overall risk of death
- Several meta-analysis and systematic reviews
  - Women within 10 years of onset of menopause, and/or < age 60
    - Overall mortality benefit from HT
    - Women taking HT live longer

WHI bottom line – what do we know?
HT if started <10 years from menopause

Benefits

- Vasomotor symptoms
- Bone health
- Heart health
- Colorectal cancer
- Diabetes
- Sleep
- Depression?
- Cognition?

Risks

- Breast cancer
  - +3-4/1000 after 5yrs of use or longer
    - <1% per year
  - Maybe less with newer HT's
- Blood clot or pulmonary embolus
  - Maybe less with newer HT's
- ~~Stroke~~

HT – for how long?

- Most women spontaneously stop within 5 years
- 50% continue to have symptoms, often less intense
- Breast cancer risks apparent at 5-10 years or longer
  - Risk diminishes after stopping
- Bone loss after stopping
- Bottom line – consider trial of lowering the dose every 3-5 years
  - If still symptomatic, and comfortable with risk/benefit discussion, there is no need to discontinue HT
  - Reassess yearly, review risks and benefits

What about 'bioidenticals'?

- Natural?
  - Estrone is bioidentical, produced by the body – can only be made in a lab from a chemical called estradiol
- Plant based?
  - Conjugated estrogen is plant based, but it is not estradiol
- Compounded products have inconsistent dosing
- Progesterone cream is not adequate to protect uterus
- Absolutely no role for measuring/monitoring serum hormones
  - Treat to manage symptoms, not lab values

Other hormones

- Tibella
  - Estrogen, progesterone and androgens (‘male’ hormones)
- DHEA
  - Studies show no consistent benefit
  - No commercial DHEA approved for use in Canada
  - Vaginal DHEA – Prasterone (Intrarosa), USA
- Testosterone or Androgens (‘male’ hormones)
  - Benefit shown for treatment of post menopausal women with hypoactive sexual disorder/dysfunction or female sexual arousal disorder
  - No benefit for general well-being
  - Side effects potentially significant
  - Virilization (lowered voice, hair growth), bad for cholesterol
  - No preparation approved for women in Canada

Non-hormonal options - prescription

- SSRI family of antidepressants (Cipralex, Lexipro, Effexor, Paxil)
  - 40-60% effective compared with placebo
- Gabapentin/pregabalin (Neurontin)
  - almost as good as estrogen
  - consider nighttime dosing only
- Clonidine (Dixarit)
  - 40% effective
  - Dry eyes, mouth

Alternative/complementary options

Placebo - 30%+ efficacy for vasomotor symptoms

- Black cohosh, soy, St. John's wort
  - No better than placebo
  - BC and SJW combination shows benefit
    - Beware drug interactions with SJW
- No benefit
  - dong quai, ginseng, evening primrose oil, wild yam, ginkgo
- Acupuncture
  - No better than placebo
- Cognitive Behavior Therapy (CBT) - helpful in study of women with breast cancer
- Hypnosis – some benefit
- Exercise – no benefit
  - Yoga is the exception

Botanical Therapies
Depression

- St. John's Wort
  - Improvement in mild to moderate depression
  - Photosensitizing – skin reactions in the sun
  - Interacts with some antidepressants
  - Interaction with anesthetic agents reported – inform if having surgery
- Valerian Root
  - May be useful for sleep disorders

Botanical Therapies
sex drive, vaginal dryness, painful sex

- Soy/Isoflavones
- Chasteberry/Vitex
  - Limited evidence
  - May have profound hormonal effects
- Ginseng
  - No documented evidence
  - Product content varies substantially
  - Often with added caffeine
  - Potential for bleeding problems

Alternative Therapies

- Remifemin
  - Black Cohosh
- Promensil
  - Red clover
    - poor data, initial studies showed small benefit
- Femarelle
  - Isoflavone (soy) and flax seed

Genitourinary Symptoms of Menopause – what happened to my vagina???

- GSM – previously referred to as urogenital atrophy, or vulvovaginal atrophy
- After (and sometimes prior to) menopause the vaginal and vulvar skin changes
  - Thinner
  - Less elastic, loss of ruggae (the rolls in the vaginal skin)
  - Less discharge and natural lubircation
- Symptoms include pain with intercourse, burning/itching, cracked/bleeding skin
- Bladder symptoms may include urgency, frequent UTI's
- Women frequently do NOT report these symptoms, suffer in silence

GSM – can it be better?

- Topical or local estrogen is highly effective, more effective than systemic estrogen for GSM
  - Local means estrogen for the vagina only, without getting into the entire body
- Minimal systemic (whole body) impact
  - Blood levels are the same as women not taking local estrogen
  - Does not mean you won't notice things – breast tenderness, nausea at the onset
  - Local estrogen akin to topical steroids – NOT the same as steroid pills
  - Beware the product insert

GSM – hormonal prescription options

- Vaginal tablets, ring, cream
- Estragyn/Premarin
  - Messy
  - Useful if symptomatic on the outside
- Vagifem
  - Daily for 2 weeks
  - Twice weekly, sometimes once
  - Symptoms at onset of treatment – nausea, breast tenderness
- Estring
  - Convenient, insert and leave in for 3 months. DIY.
  - Sense of bladder support
  - Intercourse with or without it

GSM – hormonal options in the US

- Osphema (pill)
  - ospemifene – SERM
  - Health Canada application submitted 2019
- Intrarosa (in the vagina)
  - prasterone – DHEA
  - Approved in Canada 2019
  - Availability?

GSM – non-hormonal options

- Vaginal moisturizers (M=maintenance)
  - Products with hyaluronic acid or glycerin
  - Available without a prescription
  - Many options (repagyn, gynatrof, zestica, replens….)
- Daily for 2-4 weeks, then twice weekly for maintenance
- Lubricants for penetrative activities (L=lovemaking)
  - Water based can be irritating – KY-Jelly, Astroglide
  - Silicone based products
  - Coconut oil
- Laser
  - Expensive, may require repeat treatments

Special populations

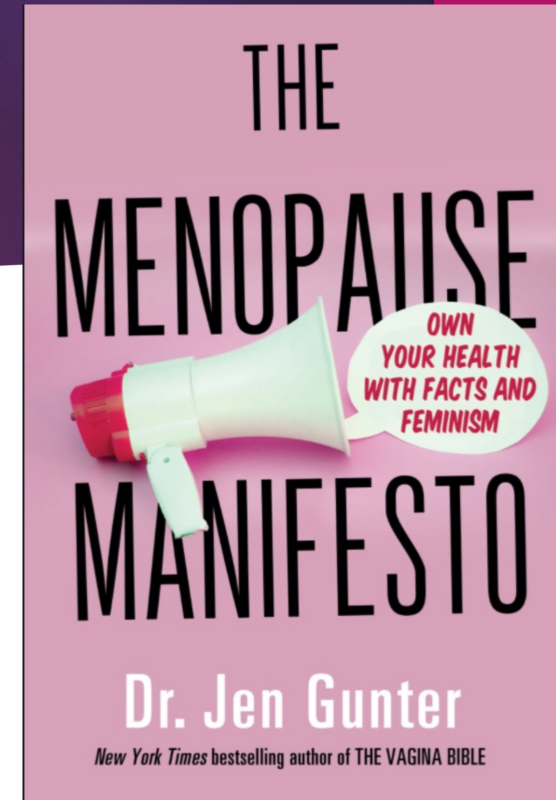
- Personal history of breast cancer
  - Local estrogen acceptable to many cancer doctors
  - Laser highly effective (anecdotal)
  - HT use occasionally considered
    - Very symptomatic, unresponsive to other treatment options
    - Depends on kind of breast cancer
  - Consider non-hormonal options
    - Consider other symptoms such as mood, sleep, pain when choosing between Neurontin or antidepressants

Special populations

- Surgical menopause in younger women – removing the ovaries
  - Do NOT compare data on HT in older women to younger women
    - Ovaries naturally produce much higher doses of estrogen and progestin than given with HT
    - Earlier menopause associated with death at a younger age
    - Strong evidence to support the use of HT for young surgically menopausal women for ongoing health, mortality benefits until an average age of menopause (51-52)
- Family history of breast cancer or women with a BRCA gene
  - No increased risk of breast cancer seen when HT used after ovarian surgery
  - HT-associated increased risk of breast cancer negligible compared to genetic/family risk

Resources

- North American Menopause Society
  - Menopause.org/for-women
- American College of Obstetrics and Gynecology
  - https://www.acog.org/womens-health/healthy-aging
- Society of Obstetrics and Gynecology of Canada
  - Menopauseandu.ca
- British Menopause Society
  - https://www.womens-health-concern.org/help-and-advice/factsheets/hrt-the-history/
- The Menopause Manifesto (2021) – Dr. Jen Gunter



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QUESTIONS?