

September 25, 2014

Perimenopause

Dr. Uma Ananth

Dr. Anita Somani



MANEUVERING THROUGH MENOPAUSE AND BEYOND

Midlife

Time of change

- *Body*
- *Mind*
- *Life*
- *Aging*

Question

- *Is it normal aging, disease, or menopause?*

The Change – What happens?

Perimenopause

- Not an event but a continuum
- Decrease in the number of follicles in the ovaries
- Decline in production of Estrogen, Progesterone, Testosterone, & DHEA
- Effects felt by entire body via receptors

Other Changes

Other changes in women's life

- *Aging process – decreased physical ability*
- *Growing children – “Empty Nest”*
- *Aging parents – care-giving*
- *Work place stresses*
- *Changing relationships*
- *Sandwich generation*
- *Returning adult children*

Why so much attention to a natural process?

- Multitude of symptoms
- Short term changes
- Long term consequences
- Time of change to evaluate health

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Symptoms

- Hot Flashes
- Night Sweats
- Irregular bleeding
- Fatigue
- Aches and pains

Comprehensive
Women's Care
Leaders in Minimally Invasive Surgery

Symptoms

Insomnia

- Difficulty falling asleep
- Waking up wired
- Ruminating

Decreased sex drive

- No desire
- No orgasm
- Painful sex

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**"Frankly I wouldn't mind the insomnia at all
if I hadn't lost my libido at the same time!"**

More Symptoms

- Headaches and migraines
- Heart Palpitations
- Urinary leakage with coughing, sneezing and laughing

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Short-term Problems

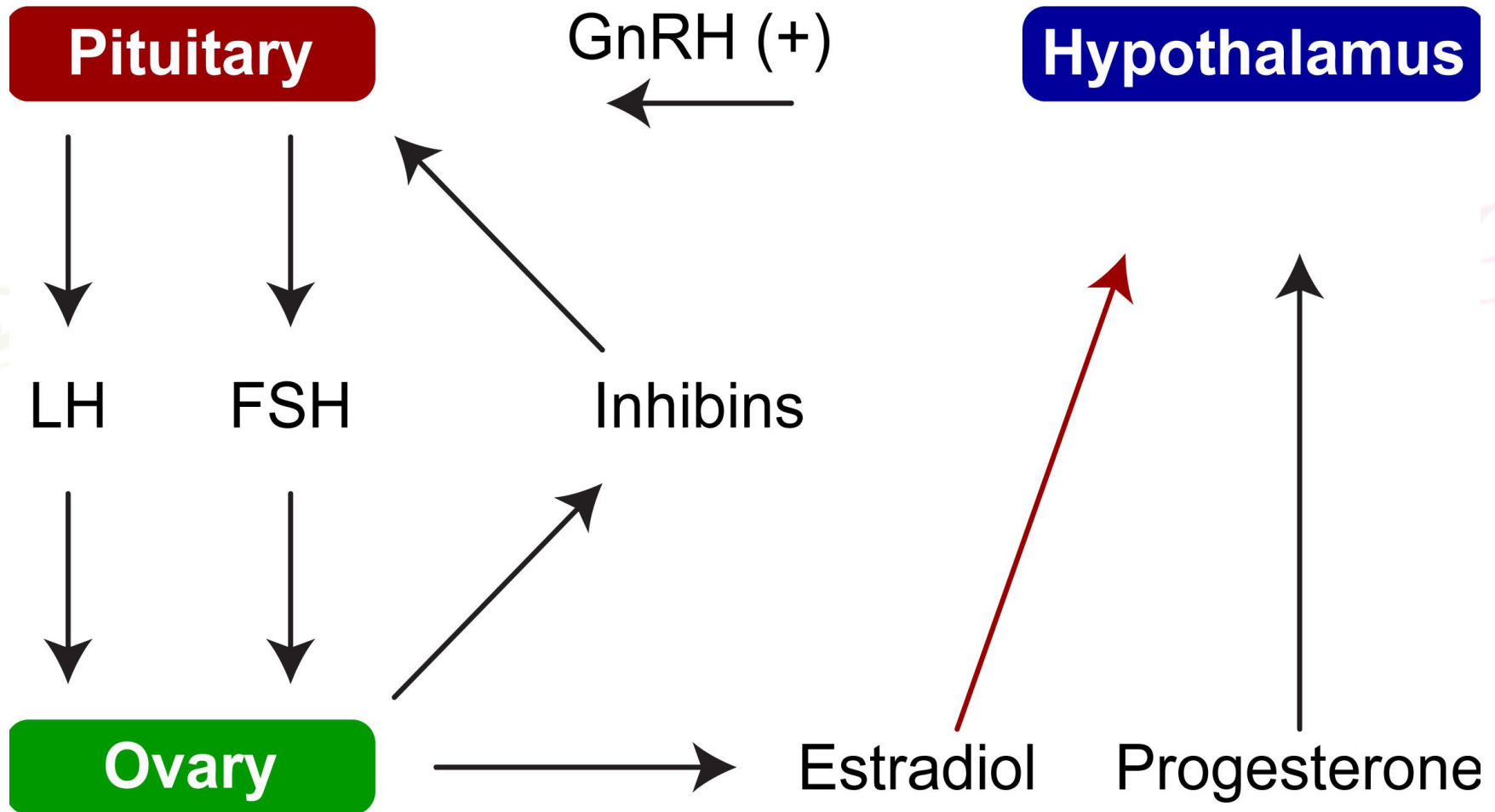
- Vaginal dryness and discomfort
- Frequent bladder infections
- Skin changes – dryness, irritation
- Hair loss & thinning
- Weight gain

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Menstrual Cycle

- The normal menstrual cycle is controlled via a complex interplay of the hypothalamic-pituitary-ovarian axis
- Loss of ovarian follicles with aging leads to the menopause transition and ultimately, cessation of menses

Hypothalamic-pituitary-ovarian Axis



Antimüllerian Hormone

- Given the long-term correlation of antimüllerian hormone (AMH) with ovarian reserve, and its relative stability across the menstrual cycle, AMH may eventually be clinically useful in predicting age of menopause
- According to STRAW+10, lack of standardized assays for key biomarkers such as AMH remains an important limitation in efforts to stage reproductive aging and to translate research findings to cost-effective clinical tools

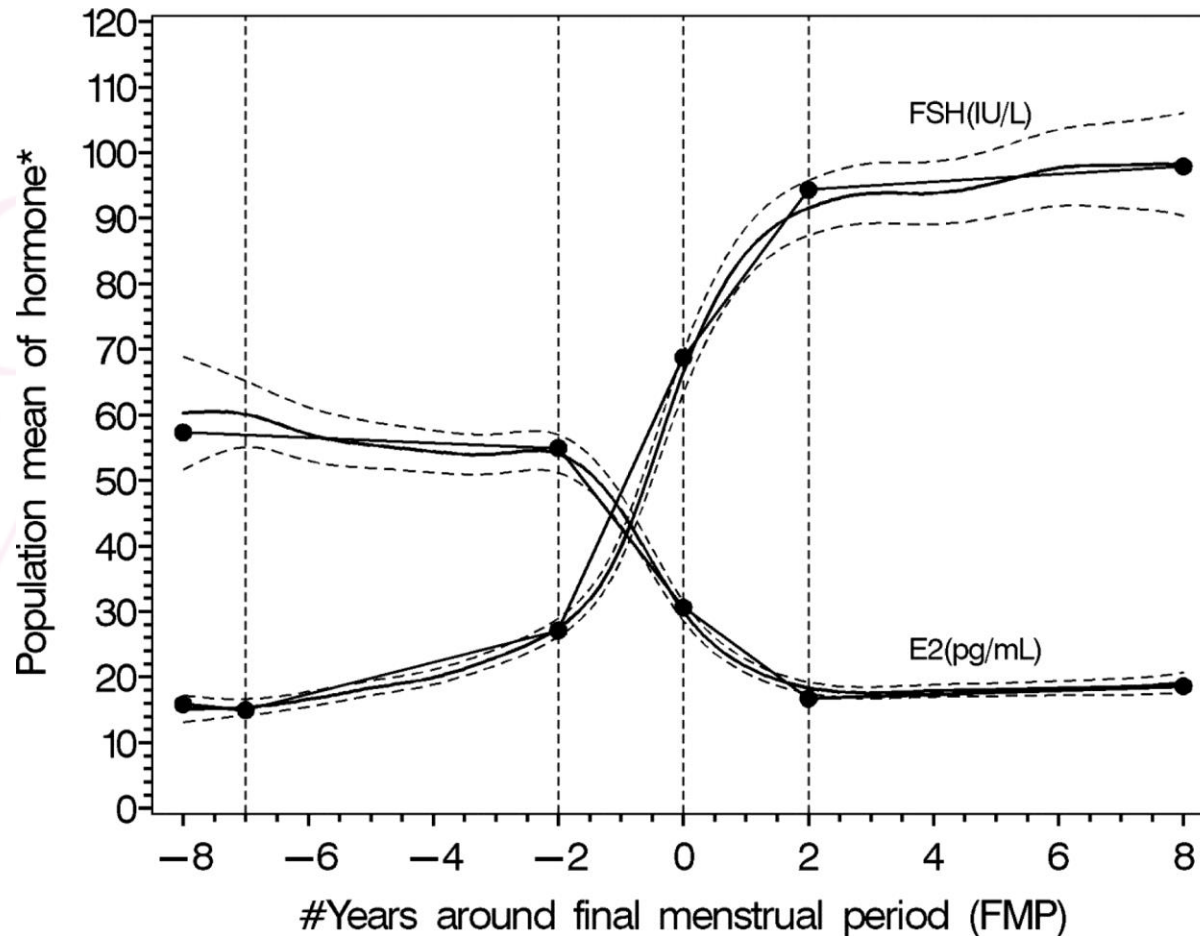
Estrogen Receptor Activity

- Two estrogen receptors (ERs): ER- α and ER- β
- Both are present in the ovary and the central nervous system, as well as in many other tissues
- Estrogen has many complex beneficial and deleterious effects on the body

What is ovarian aging?

- Ovaries begin decreasing in size
- Number of follicles decreases substantially
- Production of inhibin and AMH by ovaries decreases
- Remaining follicles respond poorly to elevated FSH and LH
- Erratic ovulation with occasional double ovulation results in menstrual cycle irregularity and potentially high estradiol levels

Changes in Estradiol and FSH during Menopause Transition (SWAN)



*The y axis is unit-less. The units of hormone are marked in the corresponding curves
Harlow SD *Menopause* 2012;19:387-95 (reproduced with permission from Randolph
JF *JCEM* 2011;96:746-54)

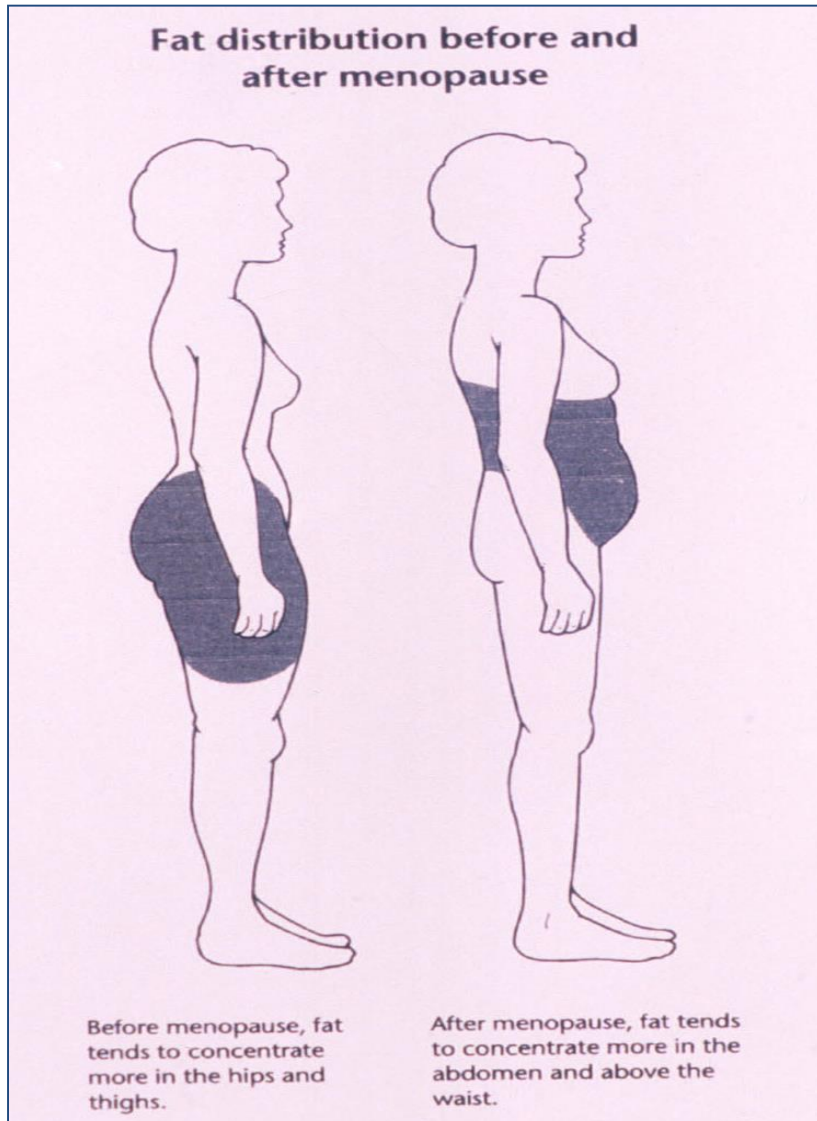
Serum Hormone Levels at Menopause

- ↓ Circulating estrogens
- ↓ Ratio of estrogen to androgen
- ↓ Sex hormone-binding globulin secretion
- ↑ Peripheral aromatization of DHEA to estrone
- ↔ Reversal of estradiol (E_2) to estrone (E_1) ratio
- ↔ No significant change in testosterone levels



BODY CHANGES

Changes in Fat Distribution



- From pears to apples
- Mid fat increases risk of heart disease
- Increases risk of insulin resistance
- Changes start as early as age 35
- Processed carbohydrates are main culprits
- Is this preventable?

Weight Gain

- Many women gain an average of 5 lb (2.27 kg) at midlife related mostly to aging and lifestyle, not menopause or hormone therapy (HT)
- However, menopause may be related to changes in body composition and fat distribution

Body Mass Index for Women

Underweight	$<18.5 \text{ kg/m}^2$
Normal weight	$18.5\text{-}24.9 \text{ kg/m}^2$
Overweight	$25.0\text{-}29.9 \text{ kg/m}^2$
Obese	$30.0\text{-}39.9 \text{ kg/m}^2$
Morbidly obese	$\geq 40.0 \text{ kg/m}^2$

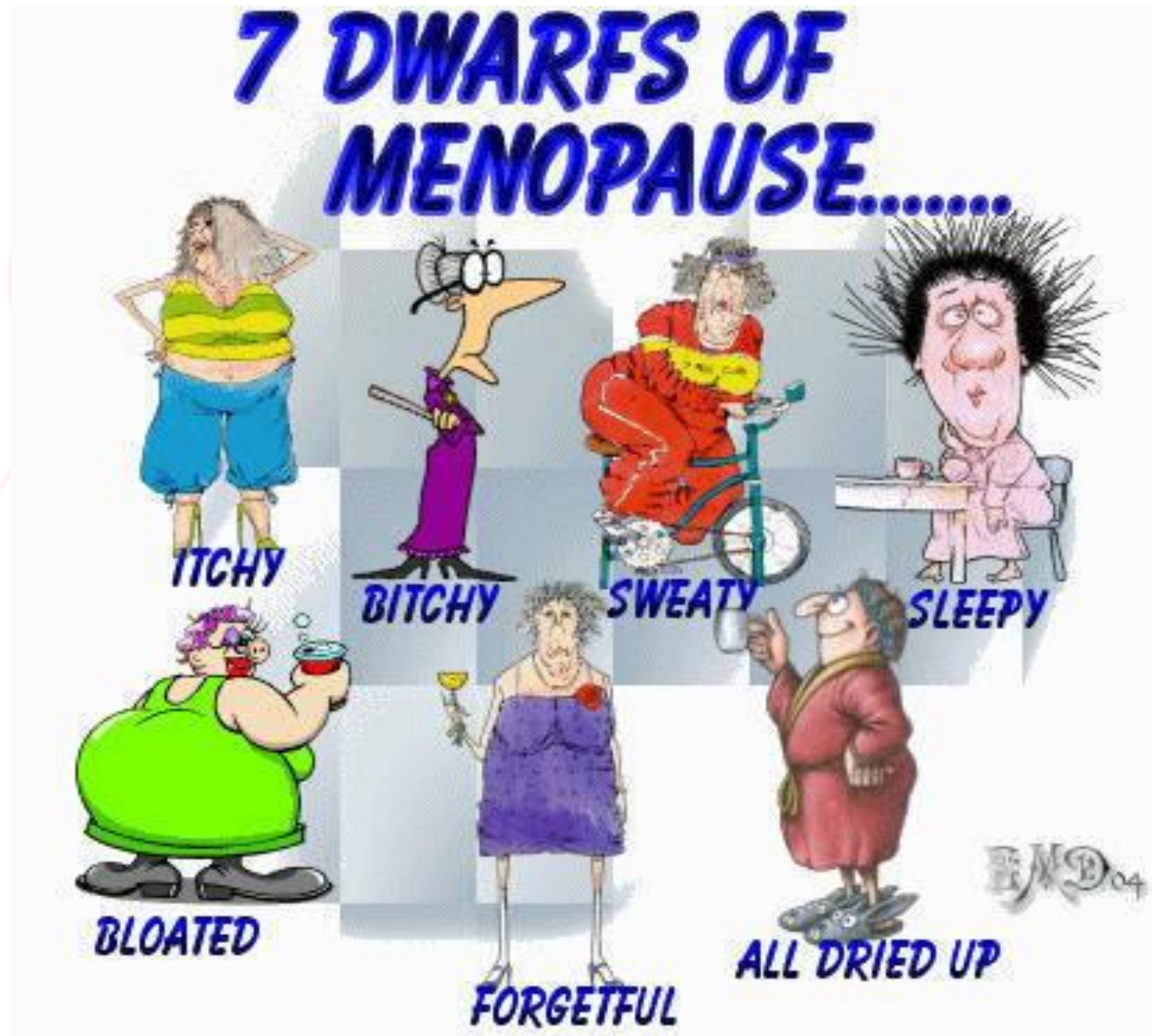
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Percent of Population Overweight in US

- 70% of women ages 55-75 and 65% of women ages 45-55 are overweight
- Approximately 40% are obese

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Know how you Feel, Sister!



Dental Changes

- Tooth loss after menopause has been associated with osteoporosis, although periodontal disease and tooth decay are the leading causes
- For each 1% per year decrease in whole-body bone mineral density (BMD), the risk for tooth loss more than quadruples
- Regular dental examinations are recommended

Skin Changes

- 30% decline in skin collagen in the first 5 years after menopause, ~2% per year decline over next 20 years
- Greater correlation between skin thickness and skin collagen content with years since menopause than with chronologic age
- Estrogen receptors are present in significant numbers in skin

Hair Changes

- Increase in the ratio of androgen to estrogen during the menopause transition may influence hair changes in some women
- Female pattern hair loss (thinning on crown) most common diagnosis
- Large “rogue hairs” can appear on the chin around menopause

Ocular Changes

- Include dry eye syndrome, blurred vision, increased lacrimation, tired eyes, and swollen and reddened eyelids
- Visual performance may be altered by increased corneal, lid, and conjunctival edema during certain phases of the menstrual cycle and perimenopause
- Prevalence of cataract higher in women than in men of the same age; the reason is unclear

Hearing Changes

- The menopause transition acts as a trigger of a relatively rapid age-related hearing decline in healthy women
- More men than women suffer from hearing loss; the third leading health problem after age 50

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Clinical Issues at Midlife

Perimenopause Overview

- Changes may be acute or gradual
- Not all midlife symptoms are attributable to menopause as many changes primarily associated with aging are happening at the same time

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Decline in Fertility

- Fertility wanes in mid-30s, before perimenopause signs occur
- By age 45, risk of spontaneous miscarriage increases to 50%
- Risk of having a child with congenital anomaly increases dramatically
- Spontaneous pregnancy still possible until 1 year after FMP

Menstrual Bleeding Changes

Changes in both menstrual flow and frequency are common and usually normal:

- *Lighter bleeding*
- *Heavier bleeding*
- *Duration of bleeding*
- *Cycle length*
- *Skipped menstrual periods*

Mental & Emotional

Cognitive changes

- *Short-term memory loss*
- *Difficulty in concentration*

Mood changes

- *Irritability*
- *Depression*
- *Anxiety*
- *Mood swings*

Long term Consequences

- Heart Disease
 - *increased risk after menopause*
- Osteoporosis
 - *most bone loss happens within 2 years of menopause*
- Alzheimer's Disease
- Cancers

Osteoporosis



"IT'S NOT MY OSTEOPOROSIS... I RECENTLY DISCOVERED SLOT MACHINES!"

- Difficult to diagnose
- No symptoms
- Increased risk of fracture
- Ask your mother
- Get a bone density scan

Goals of Management

- Short-term Goal
 - *Improve symptoms*
- Long-term Goal
 - *Prevention – CVD, Osteoporosis, Alzheimer's Disease*
- Improve quality of life
 - *Enjoy healthy emotional physical sex life*
- 5-7 years are CRITICAL!



Maneuvering Through Menopause

Uma Ananth, MD CMP

What do you do?

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“Night sweats and hot flashes are nature’s way of lowering your heating bill so you can save more money for your retirement.”

What is the big deal?

- 25 million U.S. women are reaching menopause
- The drug industry is using this captured audience as a great market
 - *Pharmaceuticals*
 - *Herbal & Other Supplements*
 - *Who do you trust?*

What is the big deal?

- Women are living longer.
 - *Decreased mortality from major killers*
 - *50% of the female population was > 50 years old by 2010*
- Almost 1/3rd of their lives is spent in the postmenopausal period

What can you do?

Life style modifications

- *Exercise*
- *Nutrition*
- *Relaxation, meditation, yoga*
- *Adequate sleep*
- *Smoking cessation*

Vitamins & Supplements

- *Beware of false advertising*

Celebrity Solutions



Rule out Illness

- Thyroid disease is a great imitator
- Symptoms like hot flashes are caused by other disorders
- Bleeding may mean fibroid, cancer, etc.
- Check other medications you are on.
- Rule out side effects of medications.
- Have regular check-ups!!!!

A Healthy Lifestyle Can Help

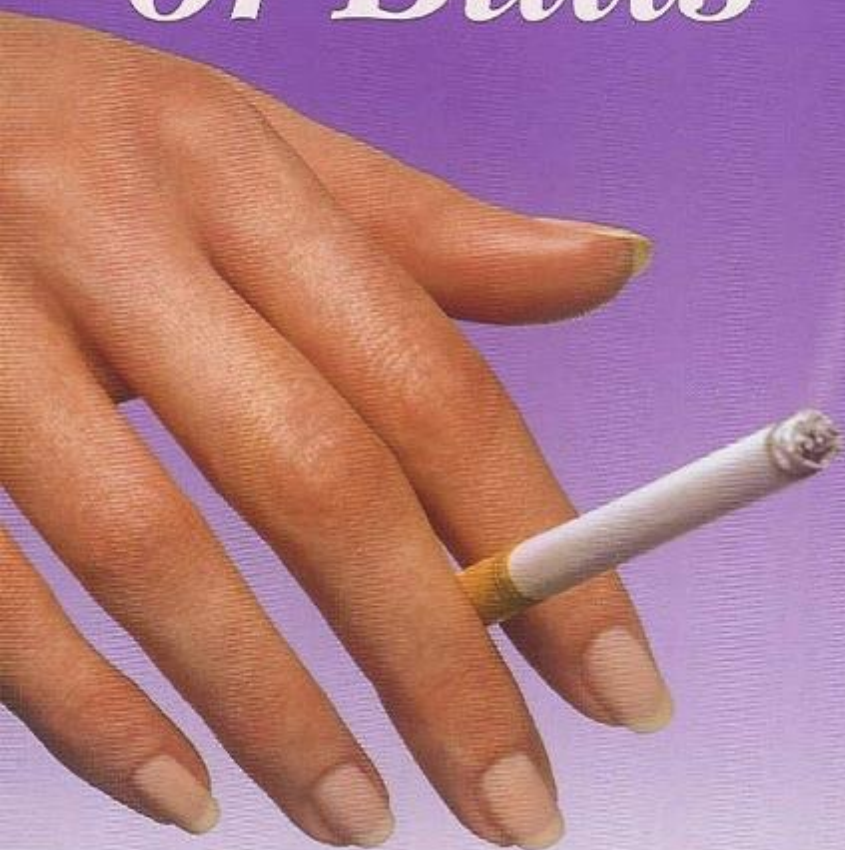


Exercise-Mix it up

- **Aerobic**
- **Strength**
- **Prevent injuries**
- **Have fun**



*No Ifs,
Ands,
or Butts*



Smoking hazard

- Causes Cancer! - Lung, breast, uterus, cervix, and ovaries
- Premature menopause
- Worsens PMS symptoms
- Stroke Heart attacks
- Migraines
- & MORE!

Vitamins & Supplements

- B-Complex – B6, Niacin, Folic Acid,
- Antioxidants – Vitamin E, C,
- Minerals – Calcium, Zinc, Boron, Selenium
- Herbals – Evening Primrose Oil, Flax Seed,
- Soy, Black Cohosh, Red Clover
- St John's Wort
- Supplements – Glucosamine, chondroitin sulfate
- Vitamin D

Black Cohosh

- Contains glycosides
- Has estrogen-like actions
- Decreases hot flashes & other menopausal symptoms
- Sold as Remifemin
- Dose- 40mg twice/day
- Approved by German Commission E



Red Clover

- Sold as Promensil
- Contains Isoflavones
- Decreases hot flashes
- Decreases breast tenderness
- Available in 40mg tab

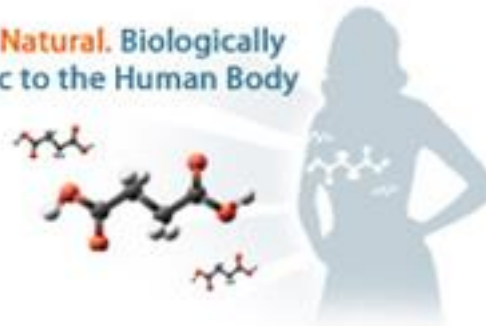


Supplement Facts

Serving Size: 2 Capsules
Serving per container: 30



100% Natural. Biologically
Organic to the Human Body



	Amount per serving	%DV
Proprietary Compound	400 mg	
Ammonium Succinate		*
Calcium Disuccinate		*
Monosodium L-Glutamate		*
Glycine		*
Magnesium Disuccinate Hydrate		*
Zinc Difumarate Hydrate		*
Tocopherol Acetate		*

* Daily Value not established

Other Ingredients: Gelatin, Rice Flour, Magnesium Stearate, Silicon Dioxide, Titanium Dioxide, Riboflavin, Carmin, Water.

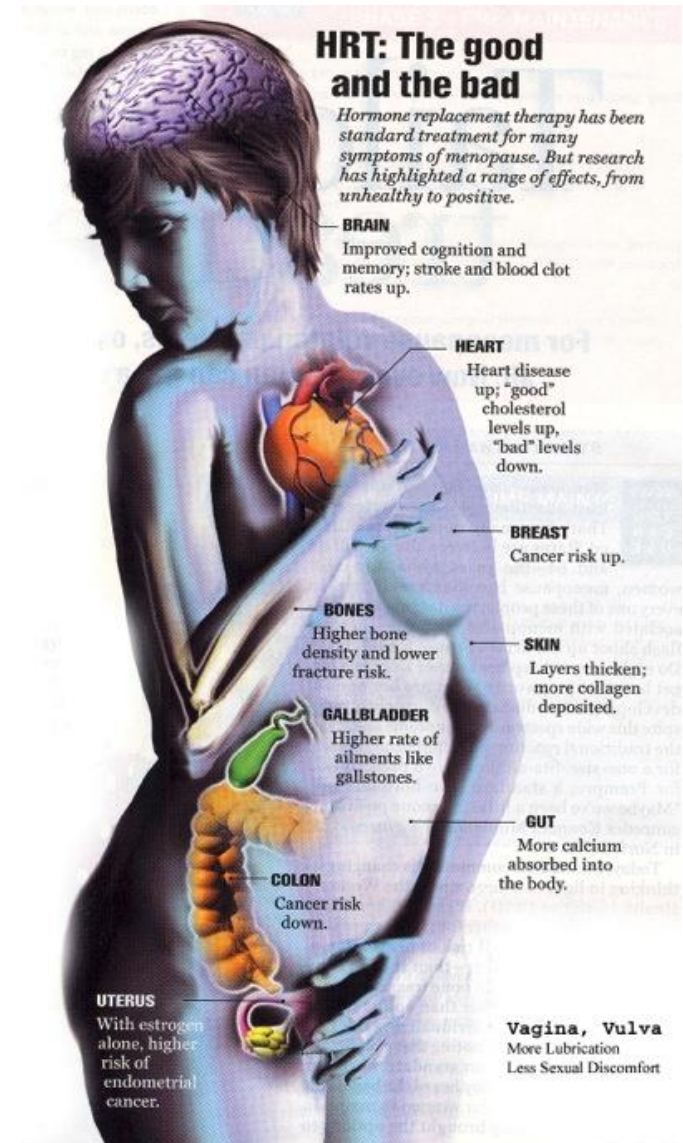


Other Alternatives

- SSRIs like Effexor
- Clonapen
- Clonidine
- Neurontin
- Birth control pills
- Evening Primrose Oil
- Melatonin

Hormone Therapy

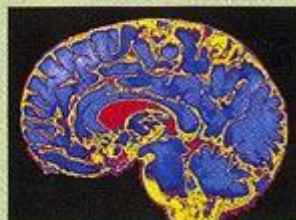
- Receptors in all parts of the body
- Alfa and beta
- Different effects



FROM ELIXIRS TO SITCOMS

In the 60 years that hormone replacement therapy has been available, it has drawn both yeas and naysayers, each with some claim to scientific proof.

1942 Premarin, the nation's first hormone replacement therapy, hits the market.



1952 An early study of estrogen's effect on the mind shows hormone treatment may help enhance verbal memory in elderly women.

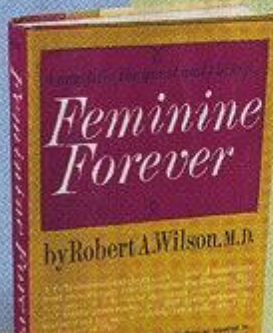
1959 *JAMA* article touts benefits of prolonged estrogen therapy. A 25-year study of 113 women shows estrogen protects bones and relieves menopausal symptoms. The authors add: "Fear that breast and cervical cancer may result from this therapy appears to be unfounded."

1962

Robert Wilson reports in *JAMA* that taking estrogen during menopause reduces breast and genital cancers.

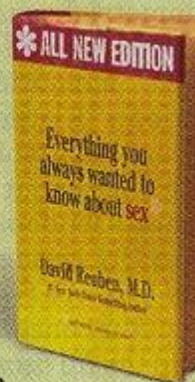
1966

In the bestselling *Feminine Forever*, Wilson recommends estrogen as the "cure" for "the tragedy of menopause." Women who use the drugs, he argues, "will be much more pleasant to live with and will not become dull and unattractive." Later, the FDA says that Wilson's recommendations go beyond approved use and that it will no longer accept his data. Wilson's studies are allegedly sponsored by several drug manufacturers.



1969

A new runaway bestseller, *Everything You Always Wanted to Know About Sex** by David Reuben, promotes estrogen as a menopausal cure-all. Without estrogen, he writes, "a woman comes as close as she can to being a man. Increased facial hair, deepened voice, obesity, and the decline of breasts and female genitalia all contribute to a masculine appearance."





1995 Prempro, the first estrogen-plus-progestin HRT pill, is approved by the FDA.

1998 The first major placebo-controlled trial of HRT shows that the hormones do not help women who have already had a heart attack and, in fact, caused more heart attacks, strokes, and other cardiovascular events.

2000 The Women's Health Initiative tells study participants that some women are experiencing heart attacks and strokes and offers them the chance to drop out.

Model and Wyeth posterwoman Lauren Hutton is featured in a *Parade* magazine cover story saying that if she could keep only one piece of her health and beauty regimen, it would be estrogen.

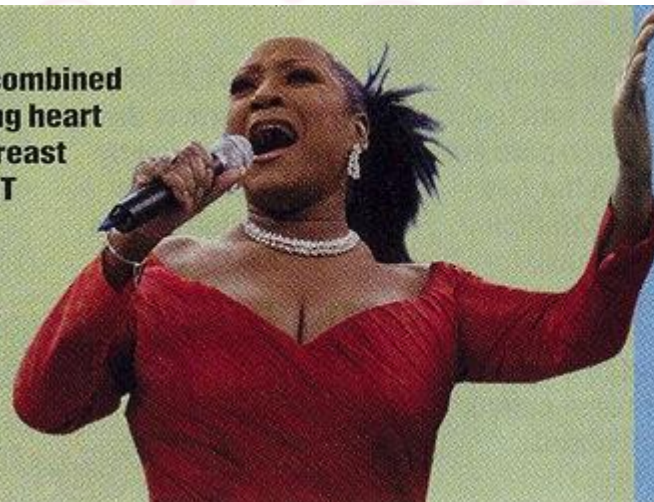


2001 More than 11 million women use a Premarin product.

2002 The Women's Health Initiative combined HRT study is stopped because of continuing heart events and an increased risk of invasive breast cancer. Doctors are urged to prescribe HRT only for short-term relief.

A study of nearly 1,900 women suggests that HRT may help forestall Alzheimer's.

Soul diva Patti LaBelle (paid by Wyeth) sings the praises of HRT.



2020 Some 60 million American women will be in or through menopause.

WHI

	10,000 women/year taking placebo	10,000 women/year taking combination HRT	Difference per year
Breast cancer	30	38	8 more women with breast cancer
Heart attacks	30	37	7 more women with heart attacks
Strokes	21	29	8 more women with strokes
Blood clots	16	34	18 more women with blood clots
Colorectal cancer*	16	10	6 fewer women with colorectal cancer
Hip fractures*	15	10	5 fewer women with hip fractures

*HRT is not indicated for the prevention or treatment of colorectal cancer or hip fractures.

The Pendulum Keeps Swinging Where is it now?



Hormones
Save Lives

Hormones
Kill You

Hormone Therapy

- Estrogen is the key hormone
- Must add Progesterone if uterus present
- Many forms available
- Oral and non oral

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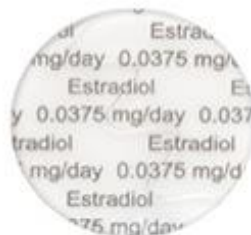
Bio-identical HT

- Means identical to what your body makes – 17 β estradiol, Progesterone, Estriol, Estrone
- Comes from plant source mostly soya and yam
- The powder is compounded into gels or capsules by compounding pharmacist
- Not usually covered by insurance
- Now available from pharmaceutical companies

Non oral Estrogens



Vivelle-Dot®
0.0375 mg/day



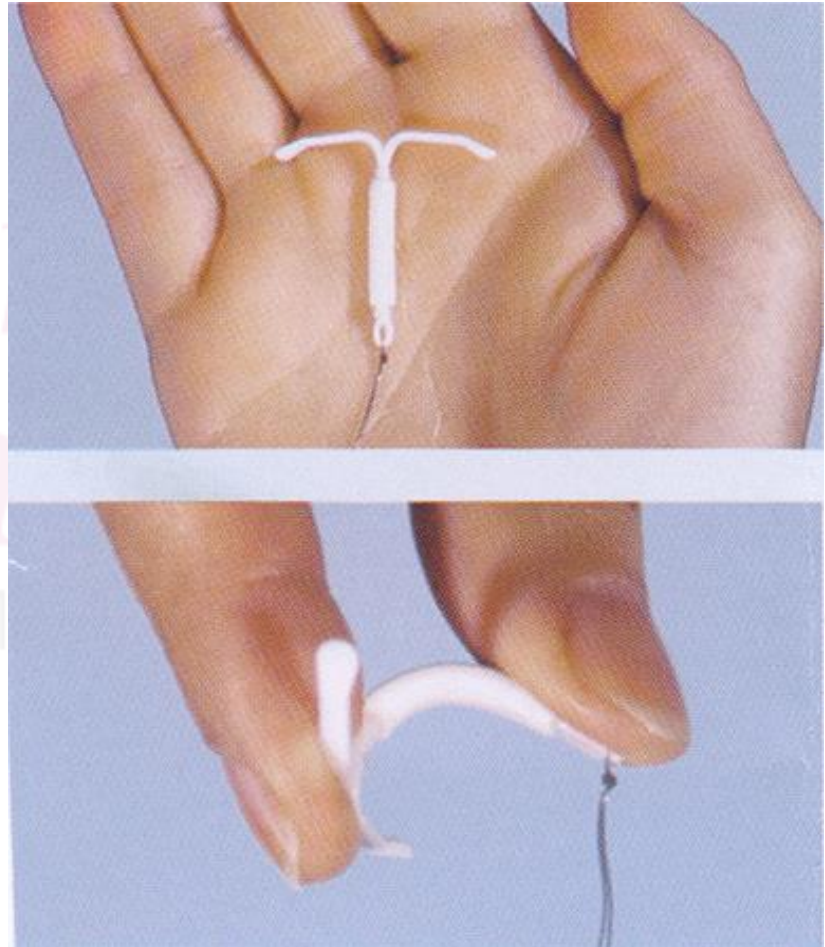
Minivelle®
0.0375 mg/day



Patches and dime are proportional but not shown at actual size.



Progesterone



Vaginal Estrogens

- Vagifem Tablets
 - Estring
 - Premarin Cream
 - Estrace Cream
-
- Minimal absorption in blood stream. Provide a good alternative to manage vaginal dryness and pain



Role of Testosterone Therapy

- May increase sexual desire, arousal, and orgasm
- May increase bone mineral density
- May increase sense of well-being
- No testosterone therapy is approved for these purposes in North America

DHEA

- Was called “Hormone of Desire”
- Research in Canada shows promise
 - *Intravaginal helps improve libido and decrease pain*
 - *Has to be compounded*
- Supplements from health food stores - Beware of hype
 - *25-50 mg orally in the morning*
 - *7 Keto DHEA may also help and help with weight loss*



Osphena

- Oral tablet for painful intercourse due to vaginal atrophy
- Taken daily, improves the
- Not Estrogen
- Unknown risk of breast cancer and blood clots
- No long term studies

SEX
AFTER MENOPAUSE
shouldn't have to hurt.

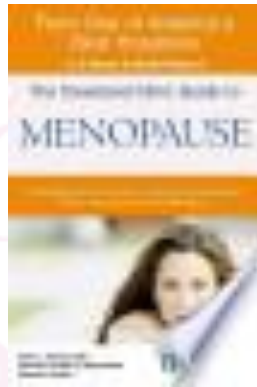
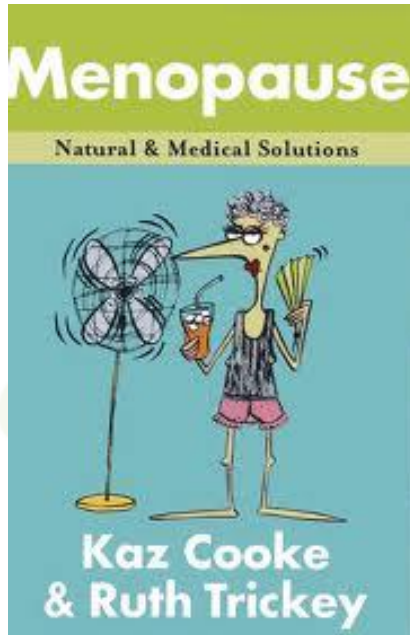
HT Summary

- HT formulation, route of administration, and timing of initiation produce different effects
- Individual benefit-risk profiles are essential
- Absolute risks in healthy women ages 50-59 are low
- Long-term use or HT initiation in older women, however, has greater risks
- Breast cancer risk increases with EPT beyond 3-5 years
- ET can be considered for longer duration of use due to its more favorable safety profile

The Decision

- Make an informed decision
- Assess your risk- breast cancer, heart disease, stroke, osteoporosis
- Ensure you have ruled out medical problem
- Be aware of what you are treating
- You have choices
- Weigh your risks against the benefits

Resources



www.menopause.org

www.cwc4women.com



QUESTIONS?

Please contact us at (614) 583-5552

On the web at www.cwc4women.com



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Thank You

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