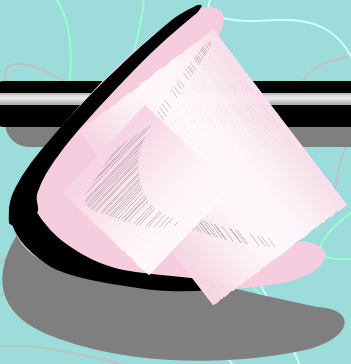


# Alternatives to Menopausal Hormone Therapy for Treatment of Hot Flashes

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# Why All The Concern?

- Evidence-based data regarding long-term menopausal hormone therapy suggest revisions to the use of this intervention in postmenopausal women
- If we stop using menopausal hormone therapy (MHT), we will have to deal with the consequences





# What Do We Know About MHT?

## Benefits

- Relieves symptoms of menopause
- Increases bone mineral density and decreases fracture risk
- Likely decreases colorectal cancer rates

## Risks

- Cardiovascular events
- Breast cancer
- Thromboembolic disease
- Gallbladder disease




# Extrapolating the Numbers

- The absolute risk for any individual woman is small
- WHI numbers predict that for every year a group of 10,000 women on MHT there will be:
  - 8 *more* cases of breast cancer
  - 8 *more* strokes
  - 8 *more* pulmonary emboli
  - 7 *more* heart attacks
  - 6 *fewer* cases of colorectal cancer
  - 5 *fewer* hip fractures



# Public Health Perspective

- ~6 million women in the US on MHT
- 11,000 excess events per year
- 1 in 100 women expected to have an adverse event or outcome



# Basic Recommendations for Clinical Practice

- Treatment of menopausal symptoms is the primary indication for use of MHT
- Do NOT use MHT for cardiovascular protection
- Use for the shortest duration of time possible consistent with treatment goals
- Use the lowest dose possible
- Consider the risks versus the benefits before using MHT
- Consider alternative treatments



*Pictures of the year by NBC*



Jim Lavrakas / Anchorage Daily News

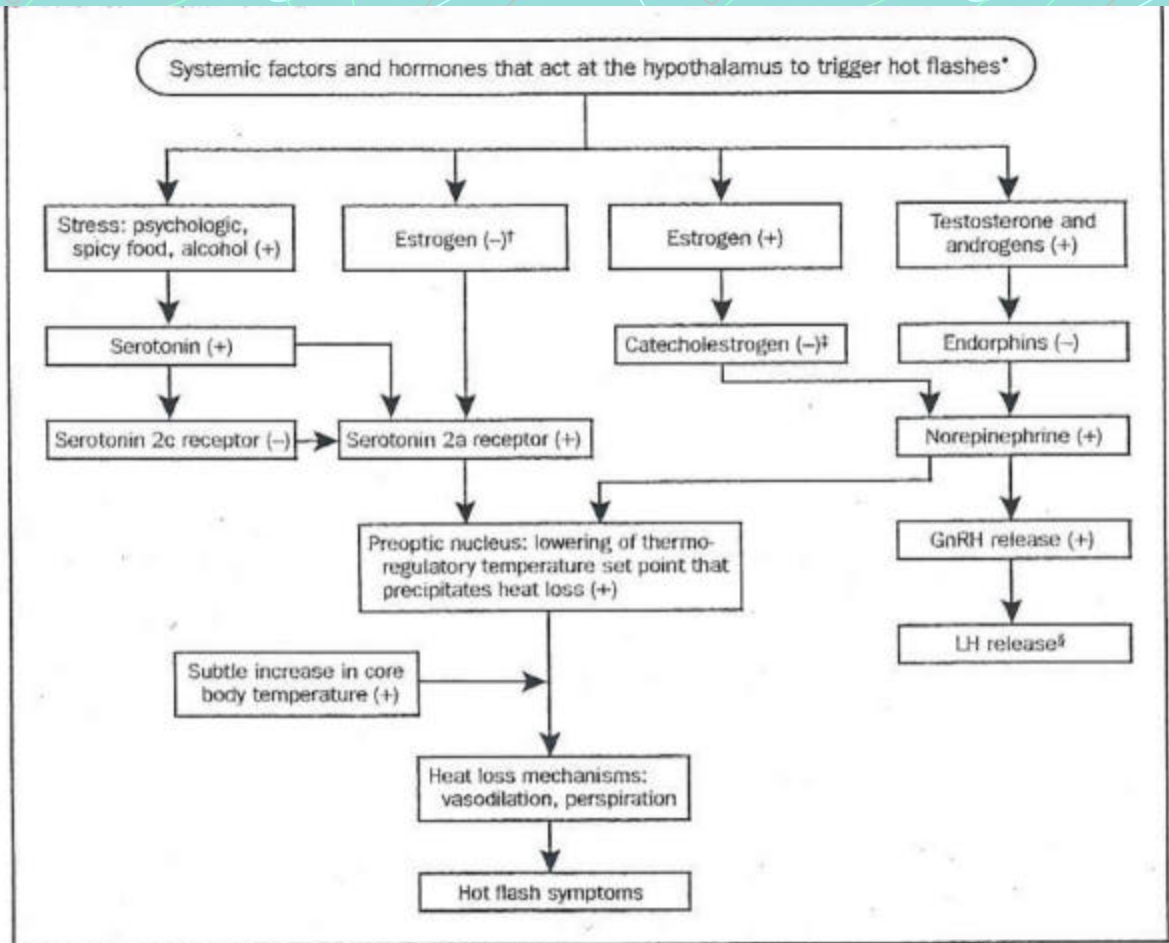


Figure 1. Proposed model of pathways involved in hot flash symptoms. GnRH = gonadotropin-releasing hormone.

\* (+) = Stimulates downstream signal; (-) = inhibits downstream signal.

† Estrogen acts to down-regulate serotonin 2a receptor concentration.

‡ Catecholesterogen inhibits tyrosine hydroxylase metabolism of tyrosine to norepinephrine.

§ Luteinizing hormone (LH) release occurs in the pituitary gland.



# Nonhormonal Treatment Options

- Selective Serotonin Reuptake Inhibitors (SSRI's and SNaRI's)
- Gabapentin
- Clonidine
- Bellergal (belladonna + phenobarbital)
- Vitamin E
- Soy products
- Herbal remedies
- Behavioral therapies
- Acupuncture



# Placebo Effect

- Multiple studies have shown about a 25% reduction in hot flashes with 4 weeks of placebo treatment
- 1 in 5 women will have a 50% reduction in hot flashes
- 1 in 10 women will have a 75% reduction in hot flashes
- Important to scrutinize trials on medications used to treat hot flashes



# SSRI's and SNaRI's

- 1990's: anecdotal reports of decreased hot flashes in depressed women on SSRI's
- 1998: Mayo study found in a nonrandomized trial that venlafaxine use in 28 breast cancer survivors had a 50% reduction in hot flashes
- 1999: Similar response in 16 men undergoing androgen ablation for prostate cancer
- 2000: Randomized double-blind placebo-controlled trial of 191 breast cancer survivors showed a significant reduction in hot flashes and improved quality of life



## continued

- Randomized, double-blind placebo-controlled trial of fluoxetine in women with breast cancer had a 50% reduction in hot flashes compared to a 36% decrease with placebo
- Non-randomized trial of paroxetine in 30 breast cancer survivors showed a 67% reduction in of flashes. Currently, there is an ongoing double-blind placebo-controlled trial of paroxetine
- Side effects: GI upset, dizziness, somnolence, sexual dysfunction, sweating, dry mouth, nervousness, abnormal dreams



# Gabapentin

- Mechanism of action unclear
- 6 case reports showed a 75% reduction in hot flashes after they were started on gabapentin for neurologic disorders
- 2 nonrandomized trials show a 50% reduction in hot flashes
- Ongoing randomized trials have been initiated
- Side Effects: dizziness, fatigue, somnolence, tremor, nausea, ataxia, nystagmus, back pain, and edema



# Clonidine

- Centrally acting alpha adrenergic antagonist
- Double-blind placebo-controlled trial of 194 breast cancer survivors found a 37% reduction in hot flashes compared to a 24% in the placebo group
- Other studies have had similar results
- Side Effects: insomnia, dry mouth, dizziness, orthostatic hypotension, constipation, drowsiness, pruritis



# Bellergal

(belladonna + phenobarbital)

- Clinical trials of this combination, widely used in the 1970's, showed modest benefit over placebo but had methodological flaws
- Belladonna is a mixture of atropine, hyoscyamine and scopolamine
- Side effects: risk of dependence



# Other Options

- Vitamin E
- Isoflavones
- Red Clover
- Black Cohash
- Dong Quai
- Evening Primrose Oil
- Wild Yam
- St. John's Wort



# Non-Pharmacological Options

- Relaxation training and paced respirations
- Exercise
- Acupuncture





# General Recommendations

- Take a thorough history regarding the frequency and severity of the hot flashes and how they affect the individual's ability to function (work, sleep, recreational activities, etc...)
- Match the aggressiveness of treatment interventions to the severity of the symptoms
- Discuss the risks vs. the benefits of the various options



# Case 1

- 72 year-old caucasian female in for a routine health maintenance exam. She has a family history of postmenopausal breast cancer in her mother and a sister. She has been on MHT for greater than 20 years. She heard about the WHI last summer and stopped her hormones cold turkey. Since then she complains of 10-12 severe hot flashes per day.



## Case 2

- 51 year-old obese female with a past medical history of hypertension, hyperlipidemia and non-insulin requiring diabetes mellitus comes in with complains of hot flashes, night sweats, irritability, anxiety and decreased concentration.



## Case 3a

- 49 year-old female with no significant past medical or family medical history complains of menopausal symptoms so severe that she is at risk of losing her job.



## Case 3b

- 49 year-old female who was successfully treated for premenopausal breast cancer 5 years ago, now complains of menopausal symptoms so severe that she is at risk of losing her job.



## Case 3c

- 49 year-old female being treated with tamoxifen for breast cancer complains of menopausal symptoms so severe that she is at risk of losing her job.



## Case 3d

- 49 year-old female with no significant past medical or family medical history now complains of hot flashes occurring about 1-2 times per day, lasting for approximately 1 minute each.



*Pictures of the year by NBC*

Jason Plotkin / The York Dispatch



# General Recommendations

- Take a thorough history regarding the frequency and severity of the hot flashes and how they affect the individual's ability to function (work, sleep recreational activities, etc...)
- Match the aggressiveness of treatment interventions to the severity of the symptoms
- Discuss the risks vs. the benefits of the various options

# Questions?

